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The Society traces its origin to the *Philosophical Society of Australasia* founded in Sydney in 1821. The Society exists for "*the encouragement of studies and investigations in Science Art Literature and Philosophy*": publishing results of scientific investigations in its *Journal and Proceedings*; conducting monthly meetings; awarding prizes and medals; and by liaising with other learned societies within Australia and internationally. Membership is open to any person whose application is acceptable to the Society. Subscriptions for the Journal are also accepted. The Society welcomes, from members and non-members, manuscripts of research and review articles in all branches of science, art, literature and philosophy for publication in the *Journal and Proceedings*.

Editorial: *The New York Times* has noticed us

Robert Marks

Editor

It was a day or so after the total solar eclipse seen from the East Coast of the U.S. I noticed a column in *the New York Times* on April 8, 2024, by a resident columnist, Peter Coy, entitled, "The Economic Luminary who Loved Solar Eclipses. Inspired by science, William Stanley Jevons strove to make economics a more rigorous field."[1] We know about Jevons: in the 1850s he was a member of the Philosophical Society of N.S.W., while employed as an assayer at the new Sydney Mint in Macquarie Street. Before graduating, he had accepted this new position and voyaged from London to Australia. A polymath, he wrote on economics, sociology, meteorology, astronomy, etc, and befriended the Rev. W. B. Clarke, the geologist who was an early president of the Society. On his return to England, he completed his degree and proceeded to revolutionise what became known as neo-classical microeconomics (together coincidentally with a French and Austrian economist). Aged 46, he drowned while swimming in the English Channel in 1882.

Having been stopped by the title of the article, I wanted to know what was in the *NYT* about Jevons. I read on: Coy described a total solar eclipse in Sydney 43 minutes after sunrise at 6:08 am (Sydney Mean Time) on 26 March 1857,[2] as observed by Jevons from Bellevue Hill. The column included a link[3] to a paper we published here in 2016: an address on Jevons by the late Ian Castles, erstwhile Australian Statistician, at a dinner to mark the opening of an exhibition in 2004 about Jevons and his work in Sydney at the Powerhouse Museum.

Unfortunately, only subscribers to the *NYT* have access to Coy's column, but I was so chuffed when I clicked on the phrase "he wrote" in the sentence: "After sleepless night got up about 3:30 and started to Bellevue Hill in dark," *he wrote* in his diary about one, which happened shortly after dawn. "About 5 a.m. commenced observations concerning eclipse" and it linked to the 2016 paper by Castles!

I was amazed! In 2016 I had found the words of Castles' address on the Powerhouse web site. Unfortunately, he had died in 2010, but his family had given their permission for the *Journal* to publish the address, which, like so much else, has since disappeared from the Powerhouse web site. Now, the *New York Times* had published a link to this paper in an obscure journal on the other side of the world.

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1 https://www.nytimes.com/2024/04/08/opinion/william-stanley-jevons-eclipse.html

2 Editorial Board member Nick Lomb advised me. See Lomb & Stevenson (2023). Nick tells me the next total eclipse to be visible from Sydney will be on 22 July 2028. The Sydney Observatory ("latitude, 33°51.41, longitude, 10h. 4m. 46s") reported in the *SMH* in 1863 that: "the time ball is dropped accurately at one o'clock Sydney mean time, or 14h. 55m. 14s. Greenwich mean time." This was before time zones were adopted worldwide (see Blaise 2001). Until 1925, GMT followed the astronomical convention of starting at noon, not at midnight as it does now.

3 See Castles (2016).

This link in an *NYT* article was the most publicity the *Journal* has ever received, although we cannot know how many clicks the Castles paper has received. I emailed Peter Coy, author of the column, but he could not remember how he had come across the Castles paper. I advised him of a second paper in the same issue of the *Journal*, also on Jevons,[4] which attempted to accomplish three things: to report on Jevons' activities while in Sydney, specifically with the Philosophical Society; to argue that his activities in Sydney had led directly to his work on economic theory and application on his return to England; and to underline Jevons' achievements in independently pioneering what is now known as neo-classical microeconomics. I wrote this paper to signal that not all luminaries of the Society had been traditional "hard" scientists. Of course, now we strive to diversify our membership, in several dimensions.

The Editorial Board

The Council has asked me to diversify the Editorial Board. Since I became Editor in 2016, the Board has not changed much: there have been two new members (Jessica Milner Davis and Len Fisher) and one member has retired. There is no limit to the number of members of the Board. The Board was instrumental in a motion being voted on by the members of the Society to include the Editor as a Councillor: since 2021, when the Council was restructured, the Editor has not been a designated member of Council. Instead, I stood for election and was successfully elected twice. This year the membership voted overwhelmingly to make the Editor a member of Council. Thus the Editor joins the Librarian, the Webmaster, the Treasurer, the Vice President, and the President as designated members of Council. This does not preclude an election for the Editor, if two or more members aspire to the Editorship.

The Editorial Board is not heavily worked. This is because the *Journal* receives few unsolicited MSS for review. In a traditional journal, the Editor relies on her editorial board to choose referees for submissions and then acts on the Board members' (the associated editors') recommendations. Our Editorial Board members are not associate editors: I occasionally ask them to suggest referees for a paper on a topic I am not familiar with. And they have given the Editor support over the position of the Editor in the Society.

I have set out to expand the diversity of the Editorial Board. Since new members must be approved by Council, any announcements must wait. To remind the reader: a list of the current members of the Board appears on the inside front cover of the *Journal*, below the Councillors.

At a recent meeting of the Council, a (new) Councillor took me to task, but he had only a cursory familiarity with the contents of the *Journal*: he was unaware that, unlike the *Bulletin*, it appears only twice a year, and he was unaware of the Point Counterpoint sections in which we have built forums for scientific disagreements about topical issues. In the past, we have included a debate between the Chief Scientist and others about the use of gas as a transitional fuel in the country's decarbonising.[5] It was

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4   See Marks (2016).

5   See the *Journal & Proceedings of the Royal Society of N.S.W.* (2020), pp. 180–204.

suggested that the Federal Opposition's enthusiasm for nuclear power — as opposed to renewable power — might make an interesting debate. I think not: the CSIRO (2024) has revised its earlier report on the feasibility of nuclear power for Australia, and there are no scientists stepping up to argue the case for nuclear. Indeed, some are criticising the Opposition for its approach to new policy.[6]

In February, Roy Green gave an address to the OGM of the Society in which he argued that the Australian economy, and specifically the manufacturing sector, had been "hollowed out" by the resource boom associated with exports of iron ore, coal, etc. to China, with a drastic reduction in the complexity of our manufacturing. He argued that our lack of complexity in manufacturing is an issue. Meanwhile, the doyen of economic journalists in Australia, Ross Gittins, has been arguing that the future of the Australian economy (and indeed of other countries' economies) lies not in manufacturing (or extraction) but in services[7] (or at least in the skills and work needed to make the most of our transition to a low-carbon economy, using renewable energy). I have asked Ross whether he would write a piece (or allow us to reprint one of his published pieces) in a Point Counterpoint on this debate. Watch this space.

The Forum

This issue contains papers and edited transcripts from the presentations last November at the 2023 Royal Society of New South Wales and Learned Academies Forum on "Our 21st Century Brain." The Forum comprised five sections: The Developing Mind; The Brain: Social, Cultural and Philosophical Perspectives; The Brain Disease Burden in Adults;[8] Turbocharging Human Intelligence with Artificial Intelligence; and Implications for the Future. Disappointingly, only six presenters submitted papers; the other 13 presenters are here represented by edited transcripts of their addresses. This is a clear change from past forums, when almost all presenters submitted papers.

The issue also includes six abstracts of PhD theses chosen by the graduating institutions (here: the universities of Wollongong and Newcastle NSW) as their three best theses. The issue also includes a paper by Mesaglio et al. on the photographic documentation of Australia's flora and a short illustrated paper on the botanical revelation of Australia's flora. Thomas Mesaglio was awarded a Royal Society of New South Wales 2022 Scholarship.

Housekeeping

Above, I have reported on the position of the Editor being firmly reëstablished as a permanent member of Council by an overwhelming vote of the membership, as it had been from 1867 (thanks, in considerable part, to the support of members of the Editorial Board). I am also refreshing the membership of the Editorial Board to better reflect the growing diversity of the Royal Society. As always, I thank Jason Antony for his work on the *Journal*. Jason was announced at the

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6   See "I'm not being political:" ABC chair criticises Coalition's approach to nuclear policy, in *Crikey*, 13 June 2024, at https://www.crikey.com.au/2024/06/13/abc-chair-kim-williams-coalition-criticism-nuclear-policy/

7   Gittins (2024).

8   A recent article (Bonhenry et al. 2024) reports on neurodegenerative disease risk from SARS-CoV-2 infection.

2024 Annual Dinner as a worthy recipient of a Royal Society of NSW Citation for his work on the *Journal* and the *Bulletin*. Congratulations, Jason.

Balmain, June 2024.

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Rapid progress on the photographic documentation of Australia's flora

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Abstract

Photographs are an increasingly important botanical resource which often capture information absent
or lost from physical vouchers. With more than 21,000 native vascular plant species, Australia is one
of the world's most plant-rich countries, and photographically documenting this flora is a large but
important endeavour. As of April 2022, 3,715 (17%) Australian plant species were still unrepresented
by photographs of live individuals in any one of 33 major online databases. In the two years since we
brought this gap to national attention, 821 of these species have had images uploaded online, with
important contributions from both amateur and professional botanists. A further 18 species have been
crossed off the unphotographed list through taxonomic changes. Many of these species had already
been photographed — sometimes decades ago — but the photographs had never been published, or
the photographs had yet to be conclusively identified. The challenge is ongoing: most of the remaining
unphotographed species are shrubs or herbs and can be found in Western Australia or Queensland.

Introduction

Photographs of live plants are an invaluable botanical resource. They form the cornerstone of identification resources such as field guides and are increasingly used in identification keys (Wäldchen et al., 2022). Photographs are also a powerful tool for engaging the public with plant science and driving greater interest in plants and the natural world more broadly (Pitman et al., 2021). The importance of plant photographs has also been emphasised in recent years through the development of the extended specimen concept; it is clear that photographs complement physical vouchers by capturing information that may otherwise be absent or lost in specimens, especially features such as flower colour (Gómez-Bellver et al., 2019; Heberling and Isaac, 2018).

For example, *Caesia* is a small genus of perennial herbs native to Australia, Papua New Guinea, South Africa and Madagascar. Many of the morphological characters required for identifying species of *Caesia* are either collected infrequently, or the most important details are lost in vouchers, so photographs are invaluable for recording some of these features (Webb et al., 2023). Indeed a newly described species from Queensland, *Caesia walalbai* A.T.Webb, Birch & R.L.Barrett, largely went unnoticed until photographic observations uploaded to the biodiversity citizen science platform iNaturalist[1] were seen by the authors, and further collections were made based on these records (Webb et al., 2023).

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1   https://www.inaturalist.org

Australia has one of the richest floras in the world, with more than 21,000 described native vascular plant species (Australian Plant Census[2]); an estimated ~91% of these are endemic, found nowhere else in the world (Chapman, 2009). Given the diversity and uniqueness of Australian plants, their photographic documentation is important for research, conservation, and public engagement.

We recently assessed the Australian vascular plant flora and found that, of 21,077 native Australian species (described up until 2018), 3,715 did not have photographs of live plants in any of the 33 major online databases that we surveyed as of April 2022 (Mesaglio et al., 2023). As part of our study, we released a publicly accessible, dynamic database of all unphotographed Australian vascular plant species, which we regularly update when new photographs are published online for these species. In December 2023, the total number of unphotographed species dropped below 3,000, a significant milestone. As of April 2024, there are now 2,876 species still on our unphotographed list, with more than 800 species crossed off the list in just two years since April 2022. Almost all of these have had photographs uploaded to the online biodiversity citizen science platform iNaturalist; just 5 species had photographs in a different database such as PlantNET[3], the Flora of New South Wales maintained by the National Herbarium of NSW. Here, we explore the different ways these species are being "ticked off" the list, summarise the species that have recently

been photographed, and highlight the most "unphotographed" taxa still requiring documentation.

The how

To fill this important gap, in April 2022 we embarked on a two-fold effort: a traditional and social media campaign — including interviews with radio stations around the country — and targeted searches. This combined approach proved successful for engaging the community, including both amateur and professional botanists, and increasing awareness of the species on our unphotographed list, as well as the importance of the photographic documentation of Australia's flora more broadly.

Species targeted by TM and colleagues (75 species)

In 2022 and 2023, Thomas Mesaglio (TM) conducted fieldwork with several colleagues in Western Australia to collect data for his PhD, visiting Kalbarri and Lesueur National Parks (July 2022), Yeo Lake Nature Reserve and Stirling Range National Park (August 2022), and Fitzgerald River National Park (October 2023). Before commencing each trip, TM cross-referenced our unphotographed list with all digitised vouchered plant records stored in the Australasian Virtual Herbarium[4] from the target area, building a list of unphotographed plant species known to occur in the region. Although each expedition was focused on documenting all encountered taxa, not just unphotographed species, this was a prime

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2 https://biodiversity.org.au/nsl/services/search/taxonomy

3 https://plantnet.rbgsyd.nsw.gov.au

4 https://avh.chah.org.au

opportunity to target many of the latter, given the dominance of Western Australian endemics in the unphotographed species list (Mesaglio et al., 2023).

This approach was a great success, with more than 50 unphotographed species found, photographed and uploaded to iNaturalist across these trips. The expedition to Yeo Lake Nature Reserve, a vast ephemeral salt lake in the Great Victoria Desert, yielded six newly photographed species, including the desert daisy bush *Olearia eremaea* Lander and *Stenopetalum salicola* Keighery, a small herb usually associated with gypsum-rich saline lakes; the latter also represented a 250 km range extension for the species. Other exciting finds included the short-range endemic *Acacia diminuta* Maslin (Figure 1a), which we photographed in Lake Magenta Nature Reserve (a ~60 km western range extension); *Wurmbea dilatata* T.D.Macfarl. (Figure 1b), a widespread but rarely collected herb growing in sand in Kalbarri National Park; the easily missed sedge *Morelotia microcarpa* (S.T.Blake) R.L.Barrett & K.L.Wilson (Figure 1c), which we found growing in a weedy empty lot in the middle of Kalbarri; the poorly known Priority Two species *Philotheca cymbiformis* (Paul G.Wilson) Paul G.Wilson (Figure 1d) along a trail at the base of West Mount Barren in Fitzgerald River National Park; and, *Dodonaea ericoides* Miq. (Figure 1e), an increasingly rare small shrub impacted by agricultural land clearing, on a small, roadside rocky outcrop in Coomalloo Nature Reserve.

Other species were targeted on an individual basis. The chenopod species *Maireana microcarpa* (Benth.) Paul G.Wilson (Figure 1f) had been collected multiple times in 1975 and once in 2022 from the University of New South Wales' Fowlers Gap Research Station, north of Broken Hill. TM and botanist Guy Taseski took advantage of fieldwork at the station in March 2024 to relocate and photograph this species at both known populations, plus a new third population. On a drive back to Sydney from another Fowlers Gap trip in 2023, TM and Taseski noted that the journey would take them past one of the few known populations of the rare unphotographed shrub *Bertya oblonga* Blakely (Figure 1f). It was then a simple matter of stopping at the location, scrambling up a ridgeline along an abandoned railway line, and photographing the plants growing at the top.

TM also engaged colleagues to target individual species. In February 2023, an observation of *Insulascirtus christiani* Otte & Rentz, 1985, a species of bush cricket endemic to Norfolk Island, was uploaded to iNaturalist by James Tweed, a PhD candidate researching insect conservation. TM was browsing James' Norfolk Island insect observations out of interest, and when he stumbled upon this record, he noticed that the observation notes stated "On *Melicope littoralis* foliage at night." At the time, *Melicope littoralis* (Endl.) T.G.Hartley (also endemic to Norfolk Island) was still on the unphotographed plant list. After contacting James and letting him know, he uploaded photographs of *M. littoralis* to iNaturalist within the week.

Mobilising old treasure (304 species)

Over the decades, Australian botanists, ecologists, and consultants have taken untold numbers of photographs of plants across the country. In many cases, however, they have not had the time or resources to process and upload these photographs. Equally importantly, until the emergence of
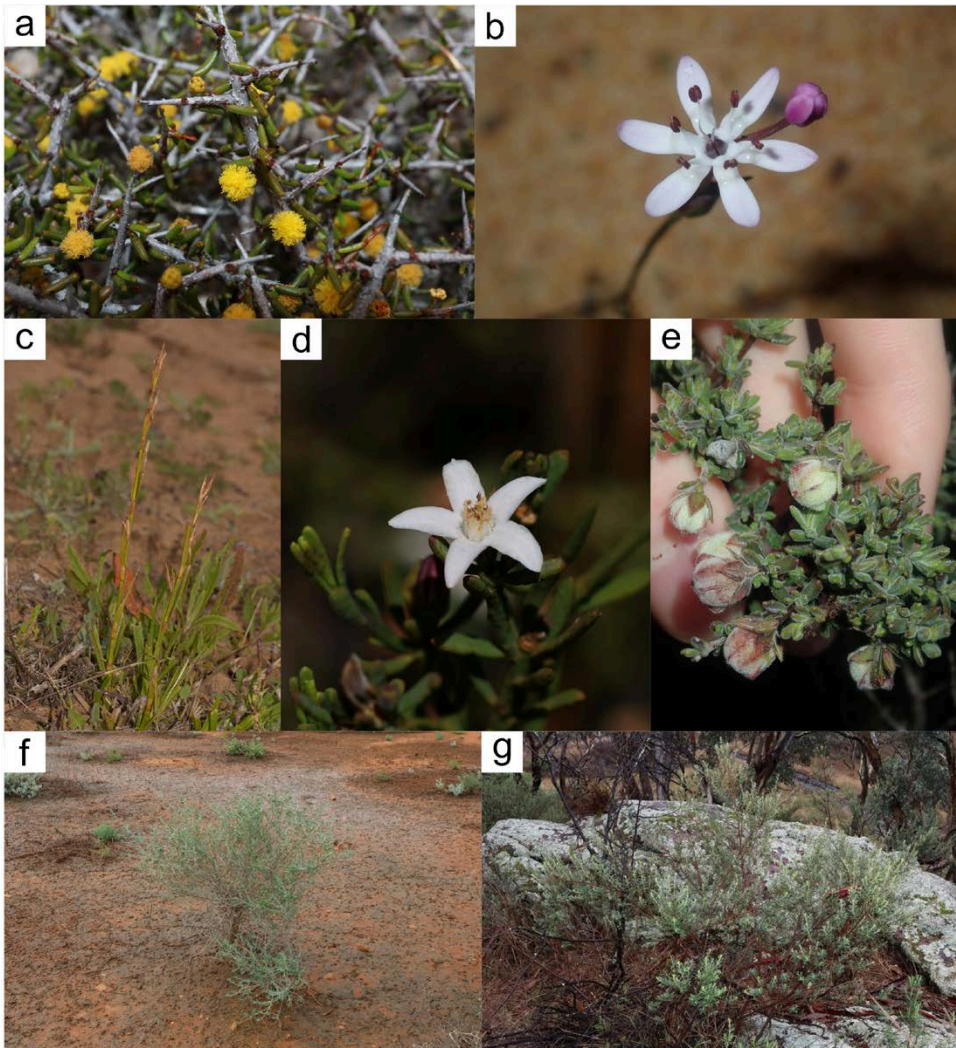
Figure 1: Some of the plant species recently ticked off our unphotographed list by Thomas Mesaglio and colleagues. a) *Acacia diminuta* Maslin, photographed by Thomas Mesaglio on sandy clay in Lake Magenta Nature Reserve, WA (https://www.inaturalist.org/observations/189098133); b) *Wurmbea dilatata* T.D.Macfarl., photographed by Thomas Mesaglio in deep sand near the Z Bend in Kalbarri National Park, WA (https://www.inaturalist.org/observations/132521908); c) *Morelotia microcarpa* (S.T.Blake) R.L.Barrett & K.L.Wilson, photographed by Nick Lambert at an empty lot in Kalbarri, WA (https://www.inaturalist.org/observations/136132894); d) *Philotheca cymbiformis* (Paul G.Wilson) Paul G.Wilson, photographed by Greg Tasney in heath near West Mount Barren in Fitzgerald River National Park, WA (https://www.inaturalist.org/observations/189704635); e) *Dodonaea ericoides* Miq., photographed by Thomas Mesaglio on a small rocky outcrop in Coomalloo Nature Reserve, WA (https://www.inaturalist.org/observations/129657506); f) *Maireana microcarpa* (Benth.) Paul G.Wilson, photographed by Thomas Mesaglio in a drying gilgai at Fowlers Gap, NSW (https://www.inaturalist.org/observations/204362193); g) *Bertya oblonga* Blakely, photographed by Thomas Mesaglio on a rocky ridge near Larras Lee, NSW (https://www.inaturalist.org/observations/152807404).

platforms such as iNaturalist, there has not been an easy, reliable, and free online repository to upload such treasures until recently (i.e., the main options were to upload to a state or other online flora — an option available mostly to professional botanists working at institutions maintaining these resources — or build one's own website, which is often not viable in the long run). There has probably also been, for a long time, a sense of pride and ownership for high-quality photographs before smartphones and the culture of open access sharing became dominant, leading to potential reluctance in sharing these photographs publicly. Consequently, thousands and thousands of images are collecting virtual dust on computers and hard drives across the country. These photographs represent a treasure trove waiting to be "discovered." Uploading these photographs will be a huge asset to our shared knowledge of species, including those already with publicly available photographs: the more photographs are available, the more features and variation are documented.

During a conversation with Bevan Buirchell, a Western Australian botanist and *Eremophila* expert, TM mentioned that there were still thirty unphotographed species of *Eremophila*, one of Australia's most diverse plant genera. Bevan asked TM for the list, and soon after posted photographs for twenty of these missing species, most of them from remote desert regions of Western Australia. Almost all of these images were 15–20 years old, highlighting the value of mobilising these old records.

This was just one case among many where Australian botanists contacted us to say they had indeed photographed some of the unphotographed species on our list — but that the images had never been published in any of the major databases we had assessed — and uploaded their images to iNaturalist directly in response to our research. These "historical" photographs were taken anywhere between a few months before our analyses were conducted in April 2022, all the way back to the 1980s. That many of these botanists were made aware of our list through the media attention our research received in both traditional media (e.g., radio interviews, newspaper articles) and on social media platforms reinforces the importance of a strong mixed-media campaign in the modern research environment.

Significant contributions were also made (and continue to be made) by Geoff and Ruth Byrne, experienced naturalists who have spent decades collecting and photographing plants across Western Australia and volunteering at the Western Australian Herbarium. They have now spent the past few years uploading tens of thousands of photographs across thousands of these historical observations to iNaturalist. Excitingly, these records have thus far included more than 100 species which had been on our unphotographed list (and indeed, many of the species that we ticked off as already photographed during our initial study were also represented only by photographs taken by Geoff and Ruth), a tremendous contribution with particularly high value given each set of photographs is associated with a physical voucher held in the Western Australian Herbarium.

Across all of these examples, it is clear that greater institutional support for curating and publishing these old photographic records online will be a crucial step forward in the quest to better document Australia's flora.

Expert engagement with old iNaturalist records (51 species)

In a similar vein to our last point, a number of unphotographed species had already been photographed, and in fact had already been uploaded to iNaturalist several years ago before our original study, but were either languishing at an identification that had never progressed finer than family, or had been misidentified as a more common, already photographed species, and thus had remained unrecognised. It was not until an expert reviewed one of these old observations and offered an identification that we could tick each species off our list, demonstrating the high value of expert engagement with the platform (Callaghan et al., 2022; Campbell et al., 2023). As more Australian botanists join iNaturalist and contribute their expertise, the more of these records will be recognised.

Although species have been ticked off our unphotographed list courtesy of identifications from numerous Australian experts, three botanists in particular have made strong contributions over the past two years:

- Tony Bean has not only identified a number of Queensland plant species previously listed as unphotographed, but also made important inroads in *Solanum*. One of the most unphotographed genera from our original list, with 54 unphotographed species, *Solanum* is one of Tony's research specialties, and indeed of the 21 species that have now been ticked off the list thanks to his identifications of iNaturalist observations, 15 of them were described by him.
- Tim Hammer has made similar important contributions for the genus *Hibbertia*. One of the most diverse plant genera in Australia, *Hibbertia* is often difficult to identify to species, especially from pho-

tographs, and thus many observations on iNaturalist are initially uploaded with only a genus identification. Tim's systematic review of thousands of old iNaturalist observations of *Hibbertia* has unearthed a number of "unphotographed" species that are now identified and crossed off our list.

- Russell Barrett, an authority in the flora of the Kimberley region in northern Western Australia, has been identifying thousands of iNaturalist observations from the Kimberley and the nearby Pilbara region. Among these have been a number of rare species from our unphotographed list, including the unusual wattle *Acacia claviseta* Maslin, M.D.Barrett & R.L.Barrett and the richly pink-flowering *Hibiscus stewartii* Craven, F.D.Wilson & Fryxell.

Synonymised species (18 species)

A small number of species were removed from our list as a result of taxonomic revisions. For example, *Drosera coalara* Lowrie & Conran was recently synonymised with *Drosera citrina* Lowrie & Carlquist (Krueger and Fleischmann, 2020), and *Eucalyptus filiformis* Rule was recently synonymised with *Eucalyptus polybractea* R.T.Baker (Fahey et al., 2022). Both *D. citrina* and *E. polybractea* had already been photographed and ticked off.

Overlooked (24 species)

Another small handful of species had actually been photographed at the time of our original analyses, but had been initially overlooked for miscellaneous reasons, including being identified under an old synonym that we did not search for, being missed by one of our automatic scripts, and being represented only by a Casual grade iNaturalist record due to missing metadata such as observation date.

Organic accumulation (367 species)

Finally, previously unphotographed species are increasingly being documented on iNaturalist simply by virtue of the continued exponential growth of the site, especially in Australia (Mesaglio, 2024; Mesaglio and Callaghan, 2021); an incredible ~1.4 million records (approx.) of vascular plants in Australia were added to iNaturalist over the last two years. As more and more users join the platform, and existing users continue to photograph plants across the country, it is inevitable that many previously unphotographed species will be recorded and images made available on iNaturalist (Figure 2).
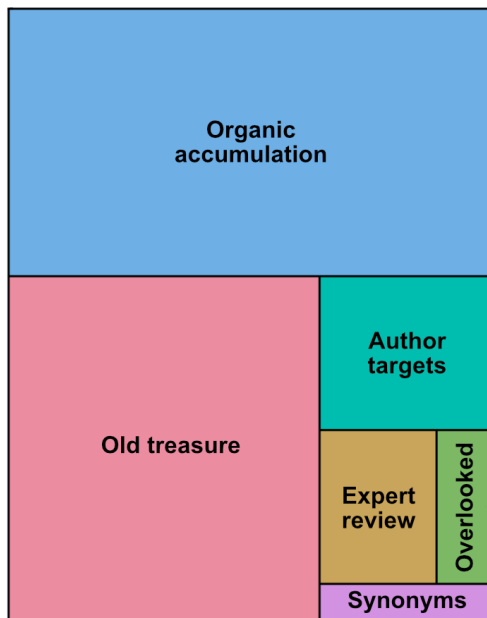

Figure 2: Treemap categorising Australian vascular plant species ticked off the unphotographed list from April 2022 to April 2024

It is important to also recognise the invaluable efforts of experts to identifying these records. Just as many botanists are reviewing historical observations on iNaturalist,

so too are they constantly contributing identifications to the thousands of new plant observations from Australia uploaded to iNaturalist each week. Increasing support for taxonomists, botanists and other professional plant researchers to contribute time to identifying iNaturalist observations should be an important priority for many institutions.

A note on print field guides

The Australian flora is covered by a wealth of high-quality print field guides. Whilst these are fantastic identification resources, print field guides often lack the accessibility of digital platforms. Most field guides cost money, with some larger volumes selling for several hundred dollars. Some field guides focus on specific reserves or small regions and are not sold online, being purchasable only from local visitor centres or national parks offices, whilst others go out of print and become almost impossible to find. A number of the species on our unphotographed list have indeed been photographed, but the images only exist in these print materials. Increasingly, however, these species are being ticked off our list through the upload of images to iNaturalist, including by the original photographers.

TM was recently contacted by Glenn Leiper, a botanist from south-east Queensland and the co-author of, and principal photographer for, *Mangroves to Mountains*, the most comprehensive field guide to the flora of south-east Queensland (Leiper et al., 2022). Glenn had seen our paper, and let us know that his guide features photographs for 18 species which were on our unphotographed list, including the small shrub *Androcalva leiperi* (Guymer) C.F.Wilkins & Whitlock, a species that Glenn discovered,

and *Bertya ernestiana* Halford & R.J.F.Hend., a rare species found only within Mt Barney National Park. Glenn was kind enough to provide his high-quality photographs to TM who uploaded them to iNaturalist to a proxy account created for Glenn, ensuring these photographs are now accessible online to anyone.

The what

Since 15 April 2022, 821 (22%) of the 3,715 species without images on any of the 33 major databases we surveyed have now been photographed, with an extra 18 crossed off due to taxonomic changes: as of April 2024, there are now 2,876 remaining species on our list.

The standout families have been Asteraceae and Myrtaceae, with 76 and 74 species ticked off respectively, although this is unsurprising given that they are two of Australia's most diverse plant families and were also in the top five most unphotographed families to begin with. The big winners at a genus level have been *Stylidium* (18 species ticked off), *Solanum* (21), *Eremophila* (22) and *Hibbertia* (29). These inroads have been achieved thanks in large part to the efforts of botanists Juliet Wege, Tony Bean, Bevan Buirchell and Tim Hammer, respectively, through both identifying iNaturalist records uploaded by other users and uploading their own. In our original paper, we reported that of the 2,190 genera containing at least one native Australian species, 1358 were photographically "complete" genera, i.e., all Australian species in each of these genera had been photographed. That number has now increased to 1,452, meaning 66% of Australia's genera have had all of their species photographed. Progress has been slower

at a family level, moving from 101 to 106 complete families out of a total of 259.

The problem of "grass blindness" (Marcenò et al., 2021; Thomas, 2019) that we discussed in our original analysis has somewhat improved, with 53 grass species ticked off, ~15% of the total number (343) from our unphotographed list. Shrubs and herbs dominated the newly photographed species, with 343 and 304 species respectively. Most of the 821 species have a distribution including Western Australia or Queensland, but this was also expected, given these two states are the most diverse in Australia, and also had the most unphotographed species to start with.

What next?

The progress made in photographically documenting Australia's flora has been very promising, but there is still plenty of work to be done, with 2,876 species waiting for images to be uploaded to one of our 33 major online databases. Here is a small taste of some of the species still waiting to be photographed:

1. *Eucalyptus kenneallyi* K.D.Hill & L.A.S.Johnson — Myrtaceae

The final unphotographed eucalypt from the more than 700 species in one of Australia's most iconic genera, *Eucalyptus kenneallyi*, is found only on two tiny islands, Storr Island and Koolan Island, off the Kimberley coast in Western Australia.

2. *Schoenus lanatus* Labill. — Cyperaceae

The earliest described, unambiguously valid Australian endemic to still lack any photograph across the 33 major databases is *Schoenus lanatus*, described all the way back in 1805. This sedge species is quite widespread, with 104 records in the Atlas

of Living Australia across coastal Western Australia stretching from Leeman north of Perth all the way to the South Australian border.

3. *Corokia carpodetoides* (F.Muell.) L.S.Sm. — Argophyllaceae

A shrub or small tree found only on Lord Howe Island, however, it is locally common near the summits of Mount Gower and Mount Lidgbird and should be a relatively low-hanging fruit (pun intended) for anyone visiting the island.

4. *Litsea bennettii* B.Hyland — Lauraceae

This tree species only grows on granite-derived soils in rainforests near the peaks of mountains in tropical Queensland, with a distribution stretching from Hinchinbrook Island northwards to Cedar Bay National Park.

5. *Hydrocotyle comocarpa* F.Muell. — Araliaceae

A small, innocuous herb found in South Australia (mostly from Kangaroo Island and Pearson Island, with a few mainland locations), Victoria (known from only a single location in South Gippsland) and Tasmania (Flinders, Cape Barren and Deal Islands). This species seems to be fairly short-lived and often difficult to detect, which helps to explain its current unphotographed status.

Zooming back out to a broader perspective, four of the top five most unphotographed genera — *Acacia* (81 unphotographed species), *Fimbristylis* (53), *Hibbertia* (49), and *Leucopogon* (45) — are the same as when we first conducted our census, with *Heliotropium* (43) moving into the top five to replace *Solanum* (33). At a family level, the top five — Poaceae (290), Fabaceae (273), Cyperaceae (206), Asteraceae (188), Myrtaceae (171) — are still the same.

There are still more than 1,000 unphotographed shrub species (1,063), with herbs in close second (983). Just 153 tree species are left to tick off; more than half of these are tropical rainforest trees from northern Queensland. A daunting 1,462 plant species from Western Australia still remain unphotographed, with Queensland sitting at 884 and the Northern Territory 647. Excitingly, some of the more diverse (>150 species) states and territories are nearing "completion." Norfolk Island and Lord Howe Island have just 9 and 13 remaining unphotographed species respectively, whilst the ACT is also very close, with only 10 of 998 species left to photograph.

We suggest that continued community engagement and mobilisation is the best approach to find and photograph these outstanding species. To maximise accessibility and usability, we recommend that any contributors intending to upload images of previously unphotographed species do so to iNaturalist, given the platform 1) is free and openly accessible and contributable to by anyone in the world, 2) covers all taxa and locations, and thus is suitable for photographs of any plant species from anywhere in Australia, and 3) is already the most comprehensive plant photograph database in Australia, containing photographs for more plant species than any other Australian database.

Acknowledgements

tion of Australia's flora, both photographers and identifiers, including the amazing contributors mentioned throughout this paper. Thanks to the anonymous reviewer whose suggestions improved this manuscript.

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Mabberley's *Botanical Revelation*: The future

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This paper is drawn from Chapter 7 of David Mabberley's *Botanical Revelation* (2019, pp. 330–332), The future of botanical revelation. The text is reprinted with permission.

Introduction

By "botanical revelation" David Mabberley means the way European botanical knowledge of Australia and its extraordinary native flora emerged. His book, Mabberley (2019), is an exhaustive exploration of this process, from the first plant record, in 1606, to Charles Darwin's time, using as a vehicle to document and illustrate these plants a very significant private library (the Peter Crossing Collection). The author was very pleased when David Mabberley sought permission from his publisher (NewSouth, Sydney) for this extract to be republished here. In the event, permission was granted and the author was able to source five images of botanical illustrations, as included. David Mabberley insisted that Marks be listed as sole author. The text is Mabberley's.

How many plants are there?

The practical necessity of classifying plants according to their uses is at the root of plant systematics, which is therefore one of the oldest of all sciences, being evident in the historical records of all major civilisations. Despite this longevity and an enormous literature, both printed and online, the fact remains that it is still impossible to state accurately how many plant species there are in the world. Each year around 2000 new species are described globally (in Australia some 130 or so), and it is unknown how many undescribed species are undiscovered in the field or lie fallow as preserved specimens in museum collections.[1]

Some extinctions

Following Allan Cunningham's concerns about possible local extinctions in the Sydney area, the scale of land clearing in the "neo-Europes," the territories now with Europeanised agricultural systems, led Joseph Hooker to write, "Many of the small, local genera of Australia, New Zealand, and South Africa, will ultimately disappear, owing to the usurping tendencies of the emigrant plants of the northern hemisphere, energetically supported as they are by the artificial aids that the northern races of man afford them."[2]

Charles Darwin arrived in New South Wales just before Queen Victoria ascended the throne; by 1900, almost at the end of her reign, around 35% of New South Wales had been cleared, or partly so, while 75% of the nation's rainforest had already gone. By the 1990s some 300,000 tree ferns and grass trees (*Xanthorrhoea* species) were taken annually from the wild by the landscaping industry.[3]

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1 Mabberley (2017) pp. vii–viii; Anna Monroe, pers. comm. with David Mabberley, 19 March 2019

2 Quoted in Crosby (1986), p.165.

3 Good (1993) pp. K-1.

In 2018 over 1000 Australian plant species were listed as vulnerable, and around 70 seed plants were already extinct. However, contrary to Hooker's forebodings, the only genus to have been lost was *Streblorrhiza* from Norfolk Island in the nineteenth century,[4] and neither New Zealand or South Africa has lost any.[5]

Plant illustrators have been crucial

An important element in the botanical revelation charted in Mabberley (2019) has been the fundamental value of illustration in documenting the diversity of Australia's plants, and they were the subjects of some of the greatest botanical artists — namely, Pierre-Joseph Redoué[6] and Ferdinand Bauer.[7]

At the start of the 21st century, Australia's artists were internationally recognised as among the most accomplished in the world. A renaissance in this art form was perhaps led by Margaret Stones (1920–2018)[8] and Celia Rosser.[9]

Another remarkable exponent was Paul Jones (1921–1997), with his *Flora superba* (1971), in the startling style of Robert Thornton's *Temple of flowers* (1799–1807). There have been many others, for example the striking image by Susannah Blaxill, on the back cover of Mabberley (2019).[10]

Figure 1: *Hardenbergia violacea* by P-J Redouté, in Ventenat (1803). Australian Library of Art, State Library of Qld.

The best Australian artists, including Blaxill, were represented at the start of the century in perhaps the finest private collection of contemporary botanical illustration: that of Shirley Sherwood, often shown in the Shirley Sherwood Gallery of Botanical Art at the Royal Botanical Gardens, Kew.[11]

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4   See Coyne (2023).

5   Gideon Smith, pers. comm. with David Mabberley, November 2015; Mark Large, pers. comm. with David Mabberley, November 2015.

6   Josephine Bonaparte commissioned P.-J. Redouté to illustrate *Hardenbergia violacea*, then known as *Josephinia imperatricis* in her honour. Figure 1.

7   See his coloured engraving of the Gymea Lily (*Doryanthes excelsa*) on the cover of Mabberley (2019), Figure 2.

8   See the cover of Stones & Curtis (1967–1978). Figure 3.

9   See the covers of Rosser (2001a, 2001b), Figures 4 and 5, and her gallery, at https://www.celiarossergallery.com.au.

10   See https://blaxill.com, Morrison (2012)

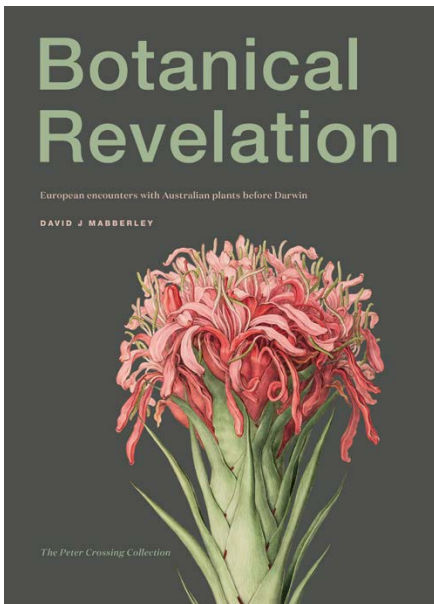11   See https://shirleysherwood.com.

Figure 2: Cover of Mabberley (2019) *Doryanthes excelsa* by Ferdinard Bauer

The unique genetics of Australian plants

In further botanical revelation, such excellence was mirrored in Australian expertise through the investigation of genetic characteristics of some of Australia's crop wild relatives.

In the 1960s there were 10.4 million people in Australia and just over 3 billion in the world; in 2019 there were over 25 million people in Australia, in a population growing faster than the average global rate; by 2050 there will be well over 9 billion worldwide. In 2019 the equivalent of two worlds' sustainable production was being consumed. To keep all these people going, the Earth will of course need to produce more food. Between the 1950s and the 2010s agricultural efficiency improved so that yields per unit area doubled. This had the effect of saving from tillage millions of hectares, but there are limits to improving efficiency, and awareness of degradation of soils, pollution and the hazards of pesticides and herbicides has increased. Internationally, an understandably urgent call was made to conserve and investigate crop wild relatives to alleviate these pressures.

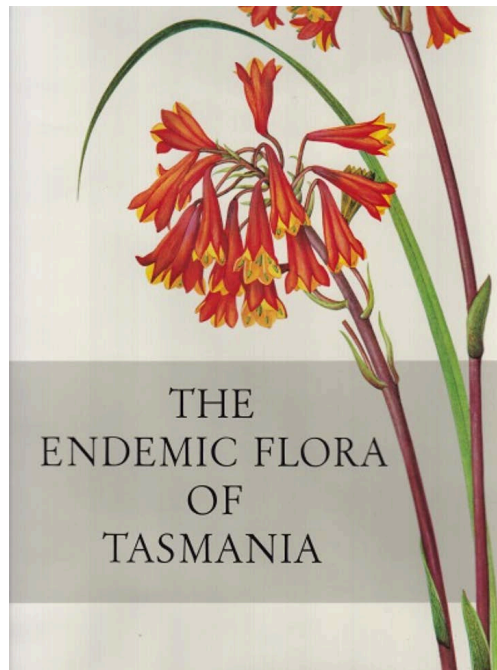Figure 3: Cover of Stones & Willis (1967) *Blandfordia punicea* by Stones

In Australia in 2010, examination was underway of grasses with gluten-free grains like curly Mitchell grass (*Astrebla lappacea*) and pepper grass (*Panicum laevinode*), once collected by Thomas Livingstone Mitchell, and dryland legumes like Cooper's clover (*Trigonella suavissima*), which Mitchell recorded.[12]

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12 Bell et al. (2010).

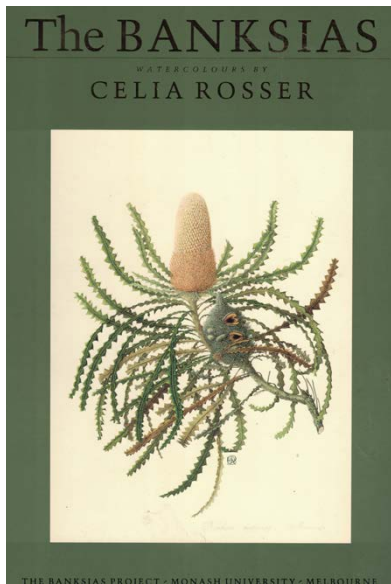Figure 4: Cover of Rosser (2001a), *Banksia victoriae* by Rosser

Figure 5: Cover of Rosser (2001b), *Banksia aculeata* by Rosser

Particularly important was the discovery in the early 21st century at Macquarie University in Sydney of heat-tolerant proteins in Australian rice, *Oryza australiensis*,[13] a perennial cultivated and harvested by Aboriginal people in northern Australia (Pascoe, 2018). Such proteins continue to be sought in wild Australian relatives of cotton and tobacco. In a warming climate, the advantages of using genetic engineering with the genes coding for these proteins in their allied commercial crops, and even in wheat, are obvious, making this area of botanical revelation crucial.

The impacts of Australian plants

As Europeans gained knowledge of Australian native plants, they took them throughout the world via their horticultural and botanical networks, transforming landscapes with Australian trees and bringing the continent's

more striking ornamentals into cultivation, as well as depicting the flora in inspiring art of the highest calibre. Australians early in the 21st century continued to do all these things, and, with their ingenuity, are poised to contribute even more to human wellbeing.

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2023 Royal Society of New South Wales and Learned Academies Forum: "Our 21st Century Brain"

Opening Address

Her Excellency the Honourable Margaret Beazley AC KC

Bujari gamarruwa
Diyn Babana Gamarada Gadigal Ngura

In greeting you in the language of the Gadigal, Traditional Owners of these lands and waterways, I pay my respects to their Elders, past, present and emerging.

To all in this room and those watching online, it is a delight to welcome you all to Government House this morning for the 2023 Royal Society of NSW and Learned Academies Forum, "Our 21st Century Brain:" such an evocative title and timely topic.

In speaking of "our" brain, we speak, of course, of that wonderful and mysterious organ that makes us "us" — the individual we are, the architect of our intelligence and our emotional world.

Looking back, we can see how far we have come in understanding — or at least theorising about — the connection between the physicality of what we are as thinking beings.

In mid-nineteenth century in Massachusetts there was a woman named Lydia Folger, medical doctor, specialising in women's health.

In 1844 she married. In many ways it was a backward step. In saying that, I must point out that I do not subscribe to the latest theory of marriage of which I read recently in a news article in *The Australian*. The by-line

for the article read "controversial feminist figure Clementine Ford has described marriage as 'built on the oppression of women' and compared wives to slaves."[1]

The reason why I say that for Lydia Folger marriage was a backward step is because she married a phrenologist, Lorenzo Niles Fowler, and, as the second only medical graduate in medicine from an American University, an outstanding feat in itself, she too became a phrenologist and lectured widely on the topic. She wrote what she hoped would be the seminal text on the subject *Familiar Lessons on Phrenology*, which was published in 1847.

In following down this path of what today is classified as pseudoscience, Lydia Folger became a proponent of a theory of the brain promoted in Europe by the German physician Franz Joseph Gall in the late 18th century. It had continued acceptance into the 20th century, despite being debunked — in part — at the beginning of the 19th century by the French physician Marie Jean Pierre Flourens.[2]

Gall's theory rested on the premise that the brain contained different discrete "organs" related to different discrete categories of personality and mind. The larger a specific "brain organ," as it were, the more dominant was the relevant category of per-

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1 https://www.theaustralian.com.au/breaking-news/clementine-ford-slams-marriage-as-an-institution-built-on-the-oppression-of-women-while-on-the-project/news-story/50c4d74356fadc5db36fb75406911be6

2 Flourens disproved Gall's assumption of the "organs" that underpinned his theory through experiments on the brains of pigeons that indicated that the loss of parts of the brain either caused no loss of function, or the loss of a completely different function than what had been attributed to it by phrenology.

sonality in the brain's owner. The size of these "brain organs" were discernible from a person's skull as bumps formed early in life while the bones were still soft and impressionable.

Some of Gall's early "research" was conducted on the inmates of jails and asylums. Gall contended that he could detect from the shape of their heads that a sufficient number of prisoners had criminal traits in common, such as murder, theft and the like.

I pause to allow you all to ponder in this eminent forum this morning how your colleagues seated beside and around you might have fared should the scientific world still adhere to the classification of mind and personality by reference to the shape of their heads.

It is, unsurprisingly, a discredited theory but it was not until 2018 that "An empirical, 21st century evaluation of phrenology"[3] was undertaken.

Using MRI scans to see if scalp bumps correlated with lifestyle and cognitive variables, this was then mapped against Gall's mental classifications. No evidence to support them was found.[4]

During the 19th century there were other conceptions of the relationship between the physicality of the body and mental states that, like phrenology, might have been dismissed during the 20th century as

quackery but that have, unlike phrenology, re-emerged recently in contemporary scientific discourse.

In particular, I speak of what has come to be known as the gut-brain axis.

Those at the forefront of 19th-century medical thought and practice took for granted that there existed a close connection between the gut and emotions.

For instance, James Johnson, physician extraordinary to the Royal Family, wrote in 1827, that "strange antipathies, disgusts, caprices of temper, and eccentricities, which are considered solely as obliquities of the intellect, have their source in corporeal disorder."[5] And that corporeal disorder occurred in the stomach, and specifically in the nerves surrounding it.

The idea of any prominent relationship between the gut and the brain diminished somewhat during the middle of the 20th-century but has been gaining significant traction again since the 1990s; it is now well-documented and, indeed, a rather hot topic of research.[6]

Today, however, it is conceived as articulated not through nerves — as had been assumed in the 19th century — but through the microbiome occurring in the gut.

As recently as August this year, a paper[7] was published by researchers at the University of British Columbia's Faculty of

3   O. Parker Jones, F. Alfaro-Almagro, S. Jbadi (2018) An empirical, 21st century evaluation of phrenology. *Cortex* 106: 26–35. Available: https://www.biorxiv.org/content/10.1101/243089v2.full.pdf

4   "The present study sought to test in the most exhaustive way currently possible the fundamental claim of phrenology: that measuring the contour of the head provides a reliable method for inferring mental capacities. We found no evidence for this claim." ibid, p. 10.3

5   Quoted in Ian Miller (2018) The gut-brain axis: historical reflections, *Microbial Ecology in Health and Disease*, 29(2); available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6225396/

6   Ibid.

7   Sebastian Hunter, Erica Flaten, Charisse Petersen et al (2023) Babies, bugs and brains: How the early microbiome associates with infant brain and behaviour development, *PLOS ONE*, 9 August; available: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0288689

Medicine that showed that levels of certain types of microbes in babies' guts were associated with performance levels in certain tests of early cognitive development.

The idea that the way our brains develop as infants, and therefore the ways we might think, may be determined, at least to some extent, by our gut flora is perhaps an unsettling thought. As one of the researchers involved in the study noted, when the possibility of making direct connections between specific bacteria and specific personality traits might be made: "I woke up in a cold sweat one night," he said. "We're going to find IQ bugs."[8]

This hasn't come to pass; the direct relationship between gut flora and the brain is undoubtedly far more complex than this. Nevertheless — and to use an awful pun — it *is* food for thought.

Perhaps an even more startling claim that unsettles our idea of "us" — the person, the individual — is one made in a book published last month by the eminent neuroendocrinologist Robert Sapolsky.[9]

In *Determined: Life without Freedom*, he argues that moment we make what we might call a choice of free will, given the sequence of causal events leading up to that decision, there is, in fact, no space for that free will to interpose itself.

When asked where the genesis for his ideas came from, Professor Sapolsky, in an interesting echo of the researcher I quoted earlier, said "[I] woke up at around two in the morning and say, 'Aha, I get it. There's no God, there's no purpose, and there's no free will,' and it's been, kind of, like that ever since."[10]

But this Forum's focus gives us a lot to think about.

I offer the warmest of thanks, as always, to the Royal Society and the Learned Academies for continuing this important tradition of facilitating informed and enlightening discourse, and the opportunities for enrichment — abstract *and* concrete — it promotes.

I give special thanks to all the contributors to today's sessions. Your insights, considerations, and generosity of spirit in sharing your knowledge is inspirational and priceless.

It is my privilege that I now open the 2023 Royal Society of NSW and Learned Academies Forum, "Our 21st Century Brain."

Thank you.

8   Brett B Finlay, quoted in Joseph Brean (2023) "It turns out we have a second brain — and it's our gut," *National Post*, 19 October; available: https://nationalpost.com/feature/gut-brain-axis-how-the-mind-is-connected-to-the-belly

9   Robert Sapolsky (2023), *Determined: Life Without Freedom*, Random House.

10   Timothy Revell, Why free will doesn't exist, according to Robert Sapolsky, *New Scientist*, 18 October 2023; available: https://www.newscientist.com/article/2398369-why-free-will-doesnt-exist-according-to-robert-sapolsky/

2023 Royal Society of New South Wales and Learned Academies Forum: "Our 21st Century Brain"

Welcome and acknowledgements

Susan Pond

President, Royal Society of New South Wales

As President of the Royal Society of New South Wales and Chair of the Forum Planning Committee, I am delighted to add my welcome to Her Excellency's and thank her for hosting our annual Forum that has been held in Government House since 2015. Her Excellency has already given us a lot to think about in speaking of "our" brain.

The Forum is presented by the Society in partnership with the Australia's five national Learned Academies — Health and Medical Sciences, Humanities, Social Sciences, Science, and Technology and Engineering. Such synergistic partnerships catalyse the extraordinary dialogue and creativity we need to generate the breakthrough ideas that will shape our future. It is only by examining complex topics from the perspective of the sciences and the humanities that we can make progress.

I thank the Academies and the Office of the New South Wales Chief Scientist and Engineer for their continued engagement with the Society. First four and more recently five Academies have been lockstep with the Forum every year. I thank each of them for their sponsorship to make live-streaming and recording of the day's proceedings possible. I thank Haus Holdings, led by Fellow of the Society, Medy Hassan, for its additional sponsorship this year.

The videos ensure that we reach a much wider audience in real time today and later via the Society's YouTube channel. I encourage all of you, here in person in Government House, or online to join the discussion during the day using the hashtag *#21stCenturyBrain* and tagging @RoyalSocNSW.

I encourage those of you here in person to meet the 15 university students who are attending from across NSW and the ACT. They are the ones who will take the ideas and actions that we generate today well into the future.

The brain underpins our basic instincts and needs, and behavioural responses to the world around us. It mediates our compassion, reason, and imagination that are reflected in great works of the arts and sciences. Yet our brain is also the source of distress, dysfunction, and malice. Despite centuries of recurring impacts of tribalism, racism, dehumanisation, and exclusion of "outsiders," we continue to inflict suffering on others.

At the same time, the 21st century brings new challenges that extend well beyond immediate threats to very complex societal challenges such as global security, climate change, massive demographic shifts, resource management, information overload, and artificial intelligence.

The context and demands on our brains have been transformed by the very tools we have created, including new information technology platforms, and rapidly developing and deployed forms of artificial intelligence. Diseases of the brain are increasingly prevalent in our ageing popu-

lation, as are the increasing mental health challenges that are evident across the human lifespan.

Considerable progress across the sciences and humanities has deepened our understanding of genetic, environmental, and social factors that underpin brain development and function. Rising demands on our capacity to respond appropriately to globalised threats bring an urgent need to apply our scientific understanding to the development of just and sustainable solutions.

This year's Royal Society of New South Wales and Learned Academies Forum focusses on recent progress in unravelling the workings of the brain and opportunities to use our emerging understanding to promote human wellbeing well beyond the 21st century.

Today, we are addressing two questions. "Have we reached the edge of our human capacity to respond effectively as either individuals or collective groups? Or will our awesome brain power enable us to navigate our way through?" My vote is for the latter.

We cannot achieve the lofty goal of answering these questions in a single day. But we can make a great start through our impressive line-up of speakers. They have been chosen carefully by the Forum's Program Committee with its co-chairs Professor Ian Hickie and Emeritus Professor Pip Pattison, and representatives of each of the five Academies. I take this opportunity to thank all Program Committee members for being so generous with their time and expertise.

I acknowledge and thank our Webmaster Lindsay Botten, who is responsible for all AV/IT, wrangling the final in-person guest list, posting information about the Forum on the Society's website and in our Bulletin and so much more. I thank the Society's new communications officer, Amanda Yeo, who is directing traffic on social media sites and to the media. Amanda is in the audience today. I thank Hans Coster, Secretary of the Planning Committee.

I thank Robert Marks, Editor of the Society's *Journal and Proceedings*, who will be producing an enduring legacy of the Forum in the form of written Proceedings that will be published in the Journal in June 2024. Just imagine a person reading the Journal in 100 years' time gaining an insight into our thinking today.

To launch us into the Program, please welcome George Paxinos AO, a Distinguished Fellow of the Society and member of the Program Committee representing the Australian Academy of Science as one of its Fellows. His bio is extensive. But here are a few highlights. He has identified 94 hitherto unknown regions in the brain of rats and humans and published 57 books on the brain and spinal cord of humans and experimental animals — thus far. His first book, *The Rat Brain in Stereotaxic Coordinates*, is the most cited work in neuroscience. His *Atlas of the Human Brain* received the American Association of Publishers Award for Excellence in Publishing in Medical Science and the British Medical Association Illustrated Book Award. In 2023, George published *A River Divided*, a novel with environmental issues at its core, including the question of whether the brain is the right "size" for survival.

George, welcome to the stage.

Is the brain in the Goldilocks zone?

George Paxinos

NHMRC Senior Research Fellow, Neuroscience Research Australia and UNSW[1]

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Governor, Dennis and Susan; colleagues. If I may quote Mark Twain, "I always get embarrassed when they introduce me, they never say enough." Governor, you asked, "21st century brain; did I change my brain from last century?" I think the brain has not changed much significantly in the last 100,000 years, but, as Susan said, the demands on it have changed. Are we constructing a lot of mouse traps for ourselves? The brain is the only organ which has a map of the outside world, a map of the body, and a map of our experience in the next 15 minutes.

I will mention two recent techniques of studying the brain anatomically. I will take you historically through research, and then I'll try to answer the question of whether the brain is in the Goldilocks zone. Is it the right size? The ancient Egyptians discarded the brain in funerary practices and sent millennia of Pharaohs brainless to their afterlife. The greatest hymn to the brain — and an astoundingly modern view of the brain — was sung by Hippocrates (460–377 BC): "Men ought to know that from the brain, and from the brain only, arise our pleasures, joys, laughters, jests, as well as our sorrows, pain, griefs, and tears."

Unfortunately, Aristotle (384–322 BC) misjudged and thought that the brain was there to reduce the heat of the blood — an air conditioning unit. You would know that a professor's greatness is measured by how long he managed to stymie progress in his field. The adherents of Aristotle kept that thinking for over a thousand years. But there was opposition. Galen (129–216) presented the encephalocentric view against the cardio-centric view of Aristotle, and the two battled each other for 1,300 years until the dawn of modern science. We see in *The Merchant of Venice* when Portia asks, "Tell me, where is fancy bred, or in the heart or in the head?"

If you went to Bondi Junction on 14 February, 2022, Valentine's Day, as I did — the new Athens of the South where I actually write my works in the coffee shop there, in the cognitively fertile crescent between Coles, Woolworths and Target — I was confronted with pharaonic thinking: there were 300 Valentine's Day cards, all of them with at least one red heart on them, none of them with a brain. I was forced to write a letter in *The Conversation*, "Darling, I love you … from the bottom of my brain." A lady journalist from Melbourne ABC called me: "Are you insisting that the heart has nothing to do with love?" I said, "If in a heart transplant I get your heart, I am not going to fall in love with your husband." She said, "What a pity and he's such a lovely man."

After such a battle to localise the seat of the soul, psychology loses its soul in the 1930s. Before giving a talk on clinical neuropsychology in Australia, I went to the coffee room and asked around: "Do you have

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1 This is an edited transcript of the address [Ed.]

a soul?" The question was always answered with a "Pardon me?" Eventually, a girl said to me, "I did until I started my PhD."

According to Patricia Churchland (b. 1943), "There is no ghost in the machine" ... the soul is surplus to requirements for scientific considerations. If the "soul" is where emotion and motivation reside, where mental activity occurs, sensations are perceived, memories are stored, love is constructed, reasoning takes place, and decisions are taken, then there's no need to hypothesise its existence. There's an organ that already performs these functions — more credit to the brain. Psychotherapeutic drugs act on whatever else, except the soul, so the soul is not required to understand behaviour or modify it. Poor humans — do they at least have free will or is it just a brain? Is there free will? The Governor mentioned Robert Sapolsky, one of the most eloquent people in neuroscience: "there is no freedom, no dignity." And B.F. Skinner (1904–1990), of course, said this long time ago: behaviour is the outcome of two and only two factors: genetic endowment and environment.

As I was writing my talk in Bondi Junction I asked the lady who sat across from me, "Excuse me, do you think you have free will?" She said, "I do but I'm not sure many out there have free will." And this is the paradox: that everybody thinks they have free will but, as to the others, they're not that certain.

Behaviour, of course, according to psychologists, is the outcome of the influences of nature and nurture. There's no room for free will to elbow itself in the parade of genes and environment. And in this way the environment sculpts character just as the unknown artist (perhaps Phidias) sculpted Apollo from Parian marble in the statue at the Temple of Zeus in Olympia. The environment sculpts behaviour just as Praxiteles sculpted Hermes. Poor humans, they have no soul. Perhaps at least it's not required for anything that we know about. They have no free will. Again, more credit to the brain.

But is there any behaviour where you can show that there's no freedom? Well, there is some evidence that in love there is no freedom. How many people who are deserted interfere with the person who deserted them — in their house, on the internet, in their work? They hit her, they kill her, they commit suicide. If only they had listened to neuroscience talks, they would understand that, much as they cannot jettison love, the person who abandoned them cannot make themselves love them. And if you don't believe me at least listen to what Bizet's Carmen sings in "*L'amour est un oiseau rebelle*." What doesn't obey the law is love. So is it only the brain?

Are we really slaves of our brains? Slaves of yesterday? Or are we architects of our destiny? According to many neuroscientists (of course, it could be the case that the minority of neuroscientists who say otherwise are correct we don't settle scores by voting in science), they think we are slaves of yesterday. But look what psychologists have discovered: today is tomorrow's yesterday and they work today with people who have a problem — an obsession, whatever it is — and assist them to make a different decision tomorrow under the same circumstances.

Now something about this organ — the brain — and how we study it at least anatomically. It used to be studied with Nissl stains — the traditional stain — but there has been some progress by using chemical stains — using acetylcholinesterase, an enzyme — it is to find the organisation of

the brain by looking at the brown-coloured stain we use to make atlases of the brains of rats, mice, monkeys, birds, humans. Somebody said, "The gain in the brain is mainly in the stain." But there's a new player in the mix now — MRI — where we can actually look at the connectivity of the brain: different colours show the direction of the different fibres in the brain. First is the rat, but we're far more interested in the human brain, though as homologies go, the rat brain is a good facsimile of the human brain in terms of areas. The monkey brain of course is far closer to us — there's actually structurally virtually nothing different.

We have constructed an atlas of the human brain of the living person. This is a living individual, one of my colleagues from the University of Wollongong — Mark Shira — and there are different colours: the different directions of the connections in the brain. And the connections of course could have different strengths, depending on what condition the brain is — if it is a pathological case or not — and the MRI shows with facility what is happening there where the connections are going. So this the other technique that I was going to mention to you.

Who is the governor here: in the brain or the mind? Well, according to many neuroscientists, the mind has no agency. If only it could have one, can you imagine! Virtually all of us will have an unwanted visit by dementia if we get to 100 — it would be nice if we could direct our neurons to jettison the neurofibrillary tangles and plaques that are responsible for the disease. But, no, the mind has no agency, according to many neuroscientists, and, thus, more credit to the brain.

I hope I've convinced some of you of Hippocrates' notion of the primacy of the brain. If yes, it will be that much more important to figure out if it is the right size: if the brain were "smaller" (less clever and less capable of language) than it is, it would not have been able to produce science and technology which today threaten our existence. If the brain were "larger" than it is, humans might have been able to comprehend the problem or even rectify it. The brain is not in the Goldilocks zone — it is not the right size.

You might say, what is the problem? You have to try to solve the environmental issue and it's not a small issue.

I asked my 8-year-old daughter, "Tell me something you'll do today that doesn't pollute the planet?" She said, "Running." I said, "That's good but if you run you'll wear out more shoes." And then she said, "Running barefoot." I said, "That is good, but if you run, you build up your appetite and they have to slaughter more chicken to bring to you to eat." She said, "Sitting in a chair." I said, "That's good, but to make a chair you have to cut a tree." She said, "Then lying on the ground naked."

There's a problem with humans. We haven't understood who we are: the triple delusion that we have a soul, that we have free will, and on the top of it we are made in the image of God. I try to explain to my granddaughter that the ancient gods were not fond of humans who had the hubris to compare themselves to the gods. I said, "This king of Corinth was condemned to push a rock up the hill only for it to fall down again because he was narcissistic, egotistical, and insulting." She said, "Like Trump."

The external similarity of humans with chimps — I didn't have a chimpanzee to

pose for me — internally we are as well similar. In fact we found no difference in the brain stem of the chimpanzee we studied when we compared to the human and with the cortex and the rest of the brain of the rhesus monkey, even the marmoset. The areas are homologous (the same). Therefore, in whatever else we were made in the image of the Divine, in the brain were made in the image of the chimpanzee.

Now a chimpanzee brain is not easy to come by. I wrote to Taronga Park Zoo to give me the opportunity to do a post-mortem once any chimpanzee died. They responded that they would be happy to oblige but they hadn't had the death of a chimpanzee in the zoo for a decade. Two months after receiving my letter, three chimpanzees died. Luckily they didn't suspect me.

Of course, Darwin said it about human exceptionalism: how erroneous it is, and the problem we face is the human hubris, that we haven't understood the limitations of the human brain. And if we are to avoid constructing our own mouse traps, then it would be good to appreciate what we are capable of and what we are not. Phaethon was sent down crashing to Earth by Zeus because he didn't do a good job when he took the reins of the Sun god's chariot. If only we could understand this: what we face, what our brain is — what the limitations

are — then we might set our stern to the dawn and not to the grave of our children and make wings of our oars.

And I've been thinking about this for the last 21 years and I wrote a book on it: *A River Divided*. If anybody would like to have a complimentary e-book or an audio book, I'll be most pleased to send it to you. My email is g.paxinos@neura.edu.au.

Just before submitting it, a friend saw me writing it again in Bondi Junction, and she asked me, "How is it going?" I said, "21 years, I'm not finished yet." She said, "My cousin's novel was published posthumously." I said, "You are giving me hope."

Then I tried to find a publisher, who asked, "What does this deal with?" I said, "It deals with human cloning. It asks the question, What would someone with the genetic endowment of Christ do if He were present today? Would He join Wall Street or the Wall Street protests? It deals with the Amazon. It is identical twins raised apart, and, just like different artists would sculpt different statues from the same block of marble, different environments produce different characters, even with the same DNA." And he said, "And on what shelf would I place it?" And until that point I was convinced of Woody Allen's dictum that, if you are a bisexual, you double your chances of a rendezvous on a Saturday night.

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Keynote presentation

The enigmatic brain: from synapses to neural networks

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Lucy Palmer

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Thank you for that introduction and lovely talk. It is a great honour to be here. It's wonderful: the brain is a great passion of mine, and, as George said, for me neuroscience started with a lecture at university where I heard about jellyfish and their not-quite brain but somewhat brain-like features. Yes, I was sucked into the world of neuroscience and trying to understand how the brain works.

Today I'll be talking about the mysteries of the brain: what makes up the brain and why it is so mysterious. Even though we know a lot about the brain, we're really getting down to the nitty-gritty. George has been instrumental in our understanding of the connectivity of the brain. It's almost the case that the more we know about the brain, the more we realise we have yet to learn. We have many more questions than we have answers for at the moment, so it will keep us busy for a long time to come.

The brain is a complex biological organ

"The brain is a complex biological organ of great computational capability that constructs our sensory experiences, regulates our thoughts and emotions, and controls our actions" (Kandel, 2007). The different parts of the brain control different aspects of what makes us who we are. As I move my hand, the top is the part of the brain that's involved in controlling motion. Our visual system is right at the back of the brain. But this is what makes us who we are. And, actually, as you listen to me talk, you'll probably realise that your entire brain is communicating all within itself in order for you to really understand what I say.

The brain in its whole is one complete, large organ that has to bring together all information from our sensory environment, our world around us. If those coming in and out don't quite line up, then it's really distracting. You know when you watch those movies and the audio is just slightly out of sync with what you see, I personally then totally lose track of what's being said and it's really distracting. So the brain does this on every moment-to-moment basis and is such a finely tuned structure that we're just starting to find out about.

This all comes down to the interconnectivity of the brain. The brain has to communicate with one another either directly or indirectly. And we're just starting to delve into the different functions of the brain and what parts of the brain all come together to create this holistic picture of the world that we live in.

Understanding the brain and the fundamental aspects of the brain and how it

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1 This is an edited transcript of the address [Ed.]

works as a complete and complex organ is really vital for understanding what goes wrong in cases of disease. Alzheimer's disease, amnesia, dementia are diseases that are associated with learning and memory, which is what my lab largely focuses on. We focus on trying to understand the fundamental capabilities of the brain and how we form memories and how we learn things. Only by understanding the fundamentals of how the brain works can we really understand the mechanisms as to what goes wrong in cases of disease.

The brain comes in all shapes and sizes

As George said, the brain comes in all shapes and sizes and it's actually quite a remarkable organ. A lot of work is done on tiny brains — the mouse brain — and that's because they're a great model of the mammalian brain. If you plot brain weight against body weight across mammal species, you can see there's a linear correlation between the size of the brain and the size of the animal. Basically, the bigger animals have bigger brains, and smaller animals have smaller brains. So if we ask what makes us human, then it's most probably not literally the size of the brain that counts: it's probably what's within the brain and the communications that occur.[2]

The cortex is evolutionarily conserved

Something that I find fascinating is that the cortex — what some people refer to as the helmet of the brain, the part of the brain that enables us to make sense of our environment — is evolutionarily conserved.

If we look at our common ancestor, and if we just look at our primary senses — the visual sense, the auditory sense, the other senses — then mammalian species are able to compute these senses. But depending on our needs, we alter the amount of the brain dedicated to these regions. If we focus on the auditory area — in humans we don't really use our ears too much, we've got a limited range of hearing compared to other animals (and I'm personally half-deaf so I particularly have a smaller auditory region in my brain) — but if we look at things like the ghost bat, their auditory cortex has really expanded, and that's because they use echolocation in order to find their food. The message here is that the brain is evolutionarily conserved but has adapted to the needs of each of the animals.[3]

The computational capacity of the brain is immense

I think that its secret is actually what makes up the brain. It has 33 billion neurons. If we take just one of these neurons, it has all these different projections which receive information from synaptically coupled other neurons. The cortical neuron has 17,000 different inputs. This is called the synapse where information is transferred between brain cells. Our brain has a thousand trillion synapses, so the computational capability that the brain has is really immense.[4]

Neurons act as a computational unit

The complexity of the brain doesn't just change with the morphology: it's also what different neurons do with this information.

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2 Roth & Dicke (2005)

3 Krubitzer & Seelke (2012)

4 Loomba et al. (2022)

Neurons don't necessarily just receive one bit of information and then spit it out to the next neuron. The communication of the brain is something that's called an action potential, which is a 100-millivolt signal. But they're able to actually take information and actually make it larger than the sum of its parts. The computational capability of the brain is not just in the sheer numbers of the neurons, but it's also in how the neurons take the information that they receive and transform it into something that is meaningful for us.[5]

Neurons come in all shapes and sizes

The complexity doesn't stop with numbers: neurons come in all shapes and sizes, and this is largely what we believe due to basically the needs of each individual neuron according to the brain region that they're in and what information they receive and how they have to transform this information to cause an output. If you ask me, the most beautiful part of the brain is actually our cerebellum that has Purkinje cells associated with movement. The range of different shapes of neurons from humans and also all different animal species is quite immense. Basically, the brain is this immense organ that has so much complexity and diversity within it that enables us to be who we are and enables animals to survive in this ever-changing environment.[6]

Neurons are the building blocks of behaviour

Neurons are the building blocks of behaviour, but we don't really know how they control behaviour. We don't really know why we think the way we are, why we have free will. There's a large area of research that will no doubt continue for a long time.

How do we record from such tiny structures?

How do we record from the brain? George showed some methods of recording from the entire brain. As I was saying, there's a lot of complexity within the brain with respect to these individual neurons, so my lab has been interested in recording from individual neurons to see how they compute information. A technique that essentially won a Nobel Prize for Bert Sakmann and Erwin Neher in 1991 is called "patch clamp electrophysiology." This is where we're able to record from individual neurons within an intact brain or outside of a brain.

There is something called a pipette, and this is a really small thin slither of glass, with a one-micron tip, that we're able to go in and poke into a neuron. Then we're able to record the neural activity in response. Action potentials are generated by putting input into neurons and recorded. We are able to look at individual neurons, see how they take this information, and then how they transform it, and look at what's important.

In my lab, we do these electrical recordings from mouse models but also from human neurons. A lot of research has been done especially at the cellular level, looking at mice and rodents, and they're a wonderful study of the mammalian brain. However, I must admit that, riding to work one day, I did wonder how much of this is translatable into the human condition. Really interest-

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5   Stuyt, Godenzini, Palmer (2021)

6   Mel (1994)

ing learning about memory, and we studied in mice, and mice are amazing little critters. But is it reflective of how we learn and how we form memories?

We now receive human tissue from patients across the road at the Royal Melbourne Hospital and then we're able to record from living human tissue. Human neurons are really similar to the mouse brain, so we can record from a human neuron. If you showed me the traces of electrical activity of recording from a mouse neuron and a human neuron, I actually wouldn't be able to tell you which is mouse and which is human. I find that really quite remarkable because we are very different. But there's only one cell type that is different between mice and humans; everything else is essentially the same. I think it comes down to connectivity and numbers.

How do you record from such tiny structures?

There are other modes of recording from individual neurons — more so populations of neurons. This is a technique that has really revolutionised neuroscience lately. You record calcium. Within individual neurons, calcium is a great proxy for activity within neurons, so you're able to put a calcium indicator into the brain. And then we're able just to put a little window on the brain and then we can see how the brain is active when it's active and in particular what this means to certain types of behaviour. We can see flashing lights which is essentially a great way of looking into when certain brain cells are active — how they're active and what essentially makes them tick.

Calcium Imaging is a really powerful tool that no doubt will also win a Nobel Prize at some point because we've learned a lot about the brain and its capabilities from using this technique. You're able to hone in on an individual neuron and an individual input onto a neuron. (These little spines — there 17,000 of them) and then you can record the activity of this particular brain region over time. Here you're we're looking at this particular input pattern on day one, and then we typically look into how memories are formed, and then we can look at the activity pattern of this exact same neuron two weeks later: we can really see what changes in the brain and associate it with changes in the neuron in the mouse behaviour.[7]

How does the brain change through learning?

I've been talking about the complexity of the brain, but something that is absolutely remarkable about the brain is that it's really dynamic. It has to change its activity, its encoding of our environment, according to the challenges that we receive day in day out. If we think about learning — say learning to ride a bike — a quote from Albert Einstein which really rings true to me is that "Learning is experience and everything else is just information." If we're thinking about learning how to ride a bike — and I was just teaching my daughter this the other day — I was telling her, "Okay, you've got the seat, you sit on the seat, you turn the pedals, the wheels will go around, that's great, you'll be off, you'll be riding." She's like, "Great, that's wonderful." She got on the seat, tried to put her feet up on the pedals, and fell over straight away. Even though she had all of the

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7   Chen et al. (2013)

information about how to ride a bike, she certainly couldn't ride a bike, and I think it'll be a while before she does.

Something that's actually really important is that just because you have the information about how something would work, you have to learn through experience. That's something that's really important to look at in the brain, and there are different levels of investigation that you can do this. So, as George was alluding to, you can look at the entire brain and how different parts of the brain are active. Something that my lab more so looks at are the individual neurons and how they change their activity as we learn how to do something or as we remember something.

Something that I think is absolutely fascinating is that memory essentially defines us. It is who we are. However, we don't really know how memories are formed. We know kind of where they're formed but now we're starting to realise that they're formed in more regions. There's a lot for us to discover. But we do know that changes do occur in the brain, and also importantly, they change but they also have to really adapt day-to-day. How we can look at this is by training mice on a simple task and then we're able to look at their brain activity on a day-to-day basis and then see how the different activity levels change throughout learning.

We can train mice just to associate between two different auditory tones —it can take about three weeks — and then we're able to look to see and correlate neural activity with the changes and the learning. I won't go into any detail, but we're able to record from the brain and we're able to look at the different times of learning. So as mice are passive and how they just essentially encode new information and

then as they're starting to learn. I think that the take-home message is if we put all the stages of learning all up next to each other we could see that this is just an example of an individual neuron and we see it at the population level too that it's dynamic. As the animal's learning and as we're learning things, the brain is changing, and in how neurons encode information is changing over time. That is absolutely crucial for this whole process.

The brain is enigmatic

I hope I've convinced you that the brain is really mysterious. It has to receive information from our sensory environment. All of this information has to come in and that's fine. I think that we've got a good handle on how our sensory world is encoded by the brain and how the brain actually receives all this information, but something that we really don't know is how this information is combined within the brain, and how it changes from day-to-day. This is a great area of research that will probably be never-ending and beyond me. With that, I definitely have to thank my lab in Melbourne, and if you're ever down in Melbourne, come and drop in and talk about the brain and how wonderful it is for a long time to come. So thank you.

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Keynote presentation

Lessons from developmental and cognitive neuroscience

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I'm Joshua Gordon, director of the National Institute of Mental Health, which is one of the 27 institutes and centres that make up the US National Institutes of Health, the largest biomedical research agency in the world. Our mission is to transform the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery, and cure. In order to achieve that mission, we support thousands of grants, contracts, and other research-funding opportunities throughout the United States and indeed around the globe. This research over the past 75 years since the NIMH was founded has played a pivotal role in our understanding of the brain, in developing groundbreaking treatments and therapies, and improving the quality and availability of mental-health care. NIMH-supported researchers have made tremendous progress in neuroscience, in translational medicine, and in improving healthcare systems, including in approaches to personalised medicine which I want to focus on today.

In order to improve mental-health care we need novel therapies and we need to understand how best to use the therapies that we already have. NIMH research is building on findings from basic and applied science to develop and improve interventions for people with mental illnesses,

based on the premise that knowing more about our patients can help us treat them better. One major initiative is in rapidly acting treatments for treatment-resistant depression, or RAPID, an NIMH-funded research project that supports the development of speedier therapies for severe treatment-resistant depression. RAPID aims to translate evidence into practical treatments by evaluating interventions with proof-of-concept trials, and then following on that with randomised clinical studies. Study findings so far have suggested that standard and high doses of ketamine can rapidly produce antidepressant effects, but lower doses are ineffective.

With this evidence in 2019 the FDA approved a relative of ketamine, S ketamine in the form of a nasal-spray medication, as an intervention for treatment-resistant depression. Today NIMH-funded researchers are testing the safety, efficacy, and feasibility of therapies, including ketamine and S ketamine, but also other modalities such as transcranial magnetic stimulation, to rapidly reduce suicidal thoughts and behaviours in youth and adult adults.

We continue to lead the research field in establishing effective neuromodulatory treatments for effective disorders via evidence-based clinical exploration. Specifically, we've conducted research to

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1 This is an edited transcript of the address [Ed.]

understand how best to use image-guided transcranial magnetic stimulation to provide more precision to our stimulation, which can allow for personalised stimulation in the future. Deep-brain stimulation, another modality of treatment, also shows promise for treatment-resistant depression, and NIMH-funded research is examining how to use deep brain stimulation on a very personal basis by first recording the activity of individuals with anxiety and mood disorders and then stimulating to reduce abnormal patterns of activity that have been identified in those particular individuals.

Moving beyond depression and into other areas, NIMH has launched a broader precision psychiatry initiative that really aims to understand how best to apply the medications that we have now to the individuals who will best respond to them. As you know, treatment in psychiatry can be a hit-or-miss effort, where the first treatment for someone may not work: they may need two or three or four clinical trials with medication or other therapies before they respond. This process for someone with depression or bipolar disorder or psychosis can last weeks or months, leaving individuals with the burden of their illnesses for extended periods of time. NIMH precision psychiatry initiative — especially the biomarker development piece of this — aims to reduce those waiting times and to improve care for individuals.

In the biomarker space, NIMH is applying an innovation funnel approach to support stage-gated milestone-based projects to develop highly sensitive and specific biomarkers that can help physicians and their patients understand how best to intervene, what treatments that are available are most likely to benefit each individual patient. This

approach starts with a number of ideas, asks for pilot projects to prove their potential, and then a few of those ideas will move on to the second stage where they will be engaged in a prospective laboratory-based clinical trial, with the eventual aim to support large phase-three type clinical trials of biomarkers in community settings to show that they can improve outcomes in individuals when applied to their cases.

Another project that we have is the Individually Measured Phenotypes to Advance Computational Translation in Mental Health, or IMPACT MH initiative. This initiative seeks to gather a large database of information on individuals with mental illness, including their clinical records but also other information that may help us understand the course of their illness — this could include behavioural and physiological methods, digital data etc., and then to apply machine learning and other techniques to understand how these data relate to those diagnoses and whether those data can improve our ability to make predictions about individual patients. These studies — the ones aimed at biomarker development and the one aimed at the larger constellation of manifestations of mental illness — are meant to improve our ability to treat patients and to improve outcomes by targeting therapies to their needs.

Of course, the best therapies and approaches won't work if services aren't available for people and if those services don't use the evidence-based approaches that we've been developing. Therefore, NIMH supports research to evaluate the effectiveness of interventions, improve the quality and outcomes of care-enhanced service delivery, and communicate and implement evidence-based treatments

across a variety of care settings. In this vein we are funding several projects to test strategies that increase the reach, efficacy, and quality, for example, of digital mental health interventions.

A large project that seeks to use evidence-based approaches to improve care in the here and now is the Early Psychosis Intervention Network, or EPINET. This research initiative is aimed at enhancing effective, coordinated specialty care delivery to people with symptoms of early psychosis. We funded eight regional scientific hubs that aim to study the fidelity, quality, and treatment effectiveness of coordinated specialty care in real-world clinics distributed throughout the United States. These hubs will collect data on diagnosis, interventions, and outcomes in thousands of individuals with early psychosis, and contribute that data to a national data coordinating centre that will then feed the data back to those very same clinics so they can understand what is working for whom, and where they need to make efforts to improve their care delivery. This project involves more than 100 community clinics in 17 states throughout the United States and really hopes to set a standard for how we can use data to provide continuous quality improvement for individuals with serious mental illness. I should mention of course that coordinated specialty care is a model of care delivery that's based upon work that's been done here in Australia for early intervention in psychosis.

Another effort is our collection of Advanced Laboratories for Accelerating the Reach and Impact of Treatments for Youth and Adults with Mental Illness, or ALACRITY. The ALACRITY centre's program supports the advancement of clinical research and practice by accelerating the translation of research findings, and serving as incubators for innovative research ideas and new transdisciplinary collaborations. For example, one of our centres explores the intersection of behavioural economics and implementation science in the pursuit of improving mental health service delivery. Others, for example, look at improving early detection of mental illness with digital measures in order to prevent adverse outcomes, particularly for youth and (particularly in the United States) for racial and ethnic minority youth. We have similar centres that are focused on suicide prevention. These practice-based suicide prevention centres are modelled after the ALACRITY centre program. They incorporate features intended to speed the translation of research into practice. This program is focused on developing testing and refining effective and scalable interventions at key intercepts in the chain of care, to reduce suicide deaths in the United States, a problem that has been increasing over the last 20 years.

Hopefully you see from what I've talked about that NIMH research is doing a lot to try to help to develop novel therapies and to ensure that those evidence-based therapies are applied in real-world settings. We feel that NIMH research is more important now than ever before. Innovative research is needed to generate new knowledge methods and technologies that can be applied to achieve near-term improvement in mental-health outcomes across diverse illnesses, disorders, age groups, backgrounds, and settings. Despite our scientific accomplishments, there is much more work that we need to do and so it's been my pleasure to introduce NIMH to you today and I hope that you have a wonderful meeting.

Session I: The Developing Mind

Moderator: Penny Van Bergen

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I'm delighted to introduce this invited series on The Developing Mind, originally presented at a 2023 Symposium of the NSW Royal Society entitled "Our 21st Century Brain." Child development is crucial for both happiness and health functioning, with positive childhood trajectories precipitating lifelong success.

One approach to presenting papers in this series is to move in chronological developmental order, with insights related to infant development followed by child and then adolescent development. However, because development itself overlaps in multiple different ways, all four papers in this series necessarily overlap in ages and developmental pathways.

Together these papers draw on neuroscientific, social, cognitive, and behavioural methods. They address questions of nature and nurture and draw on our understandings of how developing cognitive and socio-emotional skills, including memory, attention, executive function, self-regulation, and more, can support children to thrive in an increasingly complex social world. They also consider notions of typical development, including what should be expected for all children in terms of brain development and function at different developmental milestones, and where we might naturally see individual differences between children. Finally, they necessarily highlight cases where thriving might be at threat.

Professor Adam Guastella (The Children's Hospital Westmead Clinical School and the Brain and Mind Centre at The University of Sydney), commences with a discussion of how translational neuroscience can offer insights into children's typical and atypical neurodevelopment. He focuses particularly on executive function and attention, and on the increasing identification of autism and other neurodevelopmental conditions.

Professor Sharynne McLeod (The School of Education at Charles Sturt University) discusses the critical and universal role of speech, language, and communication for engagement in the social world. Speech, language and communication skills develop rapidly in early childhood, and there is much that parents can do to support this development. Importantly, however, early difficulties with communication can cause cascading challenges in other domains.

Professor Anne Castles (the Australian Centre for the Advancement of Literacy at the Australian Catholic University) discusses children's development of reading and literacy skill and the specific case of children with dyslexia. Astute readers will notice an interesting distinction between McLeod's work on speech and language and Castle's work on literacy. Although both support communication in a modern world, there are quite different mechanisms of development: language is what evolutionary psychologist Geary (2007) calls "biologically primary knowledge," acquired via everyday

interactions the environment, while literacy draws on "biologically secondary knowledge" and requires explicit instruction. Such instruction is particularly important for children experiencing reading difficulties.

Finally, Associate Professor Kate Highfield (the Faculty of Education at the University of Canberra) discusses child development in digital contexts. Importantly, the human brain has not substantially changed for millennia. What has changed, however, is the social world in which children develop: the kinds of tasks we ask children to complete, the people who are around them, and the demands that fall to them at home, school, and online. Digital technologies are ubiquitous, offering opportunities for both learning and connection. However, an excess of poor quality digital experiences also pose threats to development.

When reading through these informative papers, new themes emerge that cut across developmental domains. First, all four papers highlight challenges in development for Australian children. McLeod highlights the alarming statistic that one in four Australian children may not meet speech and language milestones, for example, while Castles discusses the difficulties that a child with dyslexia might make in learning to read. Highfield discusses the challenges for development of excessive and low-quality screen time. Second, and as highlighted by McLeod,

there are important questions about long term implications if specific challenges are not addressed in early development. Guastella addresses this question in his discussion of early intervention and the use of novel and personalised therapies, while Castles foreshadows her new research examining the social, motivational, and educational implications of poor literacy for adolescents who did learn to read well in childhood. Third, there are themes about the specific role that parents, teachers, and others play in supporting children to thrive in different domains. Highfield challenges everyone, audience included, to consider the quality of digital experiences and not just the screentime. McLeod highlights the importance of a rich and immersive home environment, while Castles highlights the importance of high-quality instruction. Fourth, and touching on questions of neurodivergence, there are discussions of individual differences between children. These themes naturally lend themselves to the question: when are individual differences between children cause for celebration and when should we be worried? Finally, there is a cognisance of potential sociocultural differences in development. Here, all four presenters go directly to this point: identifying where findings translate across language backgrounds, contexts, or cultures, and highlighting areas where they may not.

Using translational neuroscience and technology for personalised medicine and impact in child neurodevelopment

Adam Guastella

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One of the things that Dr Gordon talked about and I've heard repeatedly is the future of science really is about data. It's really about the quality of the data that we can collect. I studied as a clinical psychologist and neuroscience was largely in the dungeons of psychology departments with amazing outcomes, amazing studies but largely confined away from the clinics.

The future of research, the future of neuroscience is in the clinic with the patients, with their concerns, with their needs and using precision medicine to guide the assessments and treatments that we provide for them. I'm going to use Child Development as a way to understand this. You see, there's a massive need in our community. The NDIS is a $30 billion industry to the Australian government. 36% of those children in the NDIS have a diagnosis of autism but the research behind neurodevelopment and autism is very poor. I could give you one book on a shelf to cover the amount of evidence we have for how we assess and how we provide support to kids with autism. And that has to change. And we know, through the work at Sydney University and across our many community partners, that kids are on waiting lists for way too long just to get a basic assessment. You see on average children wait 3½ years from the time caregivers notice a delay to the point of getting their assessment. 88% of caregivers know there is a concern by the time children start school but can't get a neurodevelopment assessment. We need to change the science. We need to change the practices behind how we do assessments and provide supports to families. It's a national emergency. The problem is the current assessments that we have are incredibly complicated, requiring specialised care and lots and lots of training by really wonderful and excellent therapists, allied health medical staff. Most assessments take at least a full day to get a really good understanding of child neurodevelopment.

But there are fundamental building blocks of what we're looking for to try and detect and understand child development and we can do a much, much better job of trying to detect delays using 21st century approaches. You see, it shouldn't be all about a diagnosis. Much of the research we've done recently has shown the fundamental things that if you like diverge in brain development are not unique to a diagnosis. We found that, for example, executive function delays are common across all neurodevelopmental conditions. There are very few unique markers that predict a specific type of neurodevelopmental condition and this brain divergence that occurs or this delay in executive function skills and attention skills

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1 This is an edited transcript of the address [Ed.]

seems to emerge by the age of 2 to 3 and get larger by ages for 4 and 5 across diagnosis.

So the question is: how can we develop markers that better assess neurodevelopmental delay without getting caught up necessarily in a specific diagnosis? And we know parents report huge needs for services so we know that the vast majority of parents experience huge waiting lists to get care. They report financial barriers to access specialists to provide that care and they don't know where to go. Despite this, about 50% of families across all of our community health clinics want digital tools and digital support and training programs to support their child and training for them to know what to do. So we've established the largest neurodevelopment research network in Australia, collecting data from firstly hospital-based clinics but also community-based clinics of the most vulnerable families entering services, seeking assessments for their children.

What we're seeking to do is to develop evidence-based data-gathering procedures, methods to track and to support families using digital tools. This means that we're giving access to research for the most vulnerable members of our society. Clinicians can use this search to access reports and data calculations almost immediately to speed up the time they have to provide feedback to families, and we can provide clinical trials to families, personalised care methods almost immediately, so families that typically are excluded from clinical trials are now getting access to clinical trials through our research network.

In just one year of functioning we've had over 2,000 children enter the database for research of vulnerable families, 50% from cultural and linguistically diverse families.

These are families that typically never get into research databases, never get into research that guides evidence-based research for the federal government and state governments. And we've become very proactive in highlighting needs. So for example, we know that we've been very active in showing the huge delays to diagnosis but also that families prefer digital tools when completing their assessments. So we know that 88% of families much preferred digital tools to pencil-and-paper tests, that when families use digital tools, their completion rate jumps from 36% up to 90%. So that means clinics are getting more effective data more immediately; clinicians are getting the data faster to provide feedback to families; and families prefer the immediacy of the data collection methods. So now what we're doing is looking at how we can use the digital world with neuroscience to create real impact. Can we integrate the data collection methods into everyday practices, daily living, what the kids do on a daily basis? I believe we're only at the start of this journey. In years to come neuroscience will come to the fore and guide the way for science to drive real change.

There's an opportunity for neuroscience that it's never had in the past: using data in the real world to guide practice through the tracking of systems and circuits. To give you one example, we've been tracking reading in young children and how young children interact with the daily pastime of reading books with their caregivers. We've been using eye-tracking methodologies to understand how that practice might impact on learning and development and might also predict child neurodevelopmental delays. These paradigms have been incredibly powerful to show early divergence in

attention to reading and to the caregiver's face. This predicts neurodevelopmental diagnosis independent of a specific diagnosis like autism.

So we're now able to use these very common, daily tasks that caregivers have with their children to start to detect delays in children, and possibly in the future to intervene. We've been working really closely with our engineering colleagues to video record every assessment that's conducted in the clinic and to try to develop biomarkers just through observation, rather than clinicians having to spend an hour and a half with families and trying to develop some algorithmic score of what they observe. We're using algorithms developed by AI to generate these skills independently. And what we've been able to show is that, by using things like joint attention and eye gaze and facial movement, we can differentiate between a neurodevelopmental diagnosis with 90% accuracy immediately at the point of an interaction. And this means that families will get answers in the future about delays for their children and their interactions faster than ever before. And now we're using these data to guide how we refer families and children into different therapies.

So we heard about the potential of gut therapeutics and we've been involved in an international study looking at the potential of gut therapeutics to reduce irritability in children with neurodevelopmental delays. We've currently done a lot of work around oxytocin (and the potential of the love hormone) and I contend that there's much more to love than the brain. We've been looking at how our children learn in their social environment, if you like — engage in social learning over time using these data collection algorithms so that if children don't respond to the immediacy of therapy, we can use biological or targeted therapies to increase their response. We can make sure that children get what they need out of therapy using biosignals.

This is a snapshot of what we're doing and I guess it flips into a lot of what Joshua Gordon talked about in relation to psychosis but we have the opportunity in Australia through our wonderful public health system to do something more immediate that accesses the most vulnerable families in our society and really to lead the way in progressing change in child neurodevelopment. Thank you very much.

Children's communication and the developing mind: a challenge for Australia

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Communication is central to all people and societies. Our ability to communicate impacts our identity, relationships, education, employment, self-determination, and engagement in community, social, and civic life. Our nation's prosperity, health, wellbeing, and security requires successful communication. Communication is enshrined by the United Nations as a human right (McLeod, 2018; United Nations, 1948). Communication mediates children's behaviour, learning, and socialisation. There is a strong link between children's communication ability and their educational, social and occupational outcomes, behaviour, mental health issues, and involvement with criminal justice (Cronin et al., 2020; McCormack et al., 2011; McGregor, 2020; McLeod, 2018; McLeod, Harrison et al., 2019).

Communication typically involves a sound or word travelling between speakers and listeners, moving from the brain → mouth → ear → brain. In the case of sign languages, gesture, and facial expressions, this pathway is brain → hand/face → eye → brain (McLeod & Baker, 2017). The brain controls speech, language, and communication (Bui & Das, 2023). The temporal lobe controls language comprehension, hearing, and memory. The frontal lobe controls both motor and executive functions essential for communication that include planning, processing, problem-solving, and judgement. The parietal lobe controls sensory perception and integration, including hearing. The occipital lobe interprets vision, including facial recognition; more skills required for successful communication. During speech production and perception, left-lateralised brain activation occurs (Indefrey & Levelt, 2004). Broca's and Wernicke's areas are responsible for expressive and receptive speech and language and are typically found in the left hemisphere. The brain processes more sensory and motor information involving the face, lips, tongue and hands than any other body part (as demonstrated in the homunculus model). Of the twelve cranial nerves, five are essential for speech and hearing: trigeminal nerve (V), facial nerve (VII), acoustic nerve (VIII), vagus nerve (X), and the hypoglossal nerve (XII) (Zemlin, 1998). Communication is hardwired into our brains and bodies.

Speech, language and communication development

Foundations of speech, language, and communication are established in early childhood. Even before birth, children can identify their mothers' voice(s) and their mothers' home language(s) from other languages (Kisilevsky et al., 2009). Children's first cry is eagerly anticipated; they are born communicating. Children typically say their first words around 1 year of age, begin to put two words together around 2 years, and use grammatical forms by 3 years. By 4 to 5 years of age most children can be understood by everyone — even strangers, regardless

of the language(s) spoken (McLeod, 2020). Additionally, a review of 64 studies of 27 languages demonstrated that by 4 to 5 years of age most children can correctly pronounce (almost) every consonant, vowel, and tone in their home language(s) (McLeod & Crowe, 2018). By 5 years, children also can understand and produce sentences, stories, and conversations. Communicative capacity continues to develop throughout school and across the lifespan, but the foundations are established prior to school. For example, a longitudinal study of 3,547 infants (1–2 years) whose parents read with them for 11 minutes or more per day identified that they had stronger reading, spelling, and grammar skills in Grades 3 and 5 (Brown et al., 2022).

While most children's communication development is straightforward, a number of children have speech, language and communication needs. For some, this can be associated with hearing loss, cleft palate, cerebral palsy, or another identifiable cause; however, for most children, there is no known cause (i.e., speech sound disorder, developmental language disorder, stuttering, voice disorder) (McLeod & Baker, 2017).

Longitudinal population research has been used to demonstrate the impact of communication ability on children's outcomes. The Australian Government's Longitudinal Study of Australian Children (LSAC, n ~10,000) and the Longitudinal Study of Indigenous Children (LSIC, n ~1,600) have provided data that have been analysed to examine communication outcomes for three groups of children.

Communication concern: First, communication outcomes have been examined for 4- to 5-year-old children whose parents were concerned about how their child spoke and made speech sounds (i.e., had *commu-*

nication concern) (25.2% of LSAC McLeod & Harrison, 2009; 24.3% of LSIC McLeod et al., 2014). Children with communication concern self-reported they experienced significantly "more bullying, poorer peer relationships, and less enjoyment of school than peers" (McCormack et al., 2011: 1328). They had slower progress in reading, writing, numeracy, and overall school achievement at 8–9 years (Harrison et al., 2009; McCormack et al., 2011); significantly lower academic achievement on reading, writing, spelling, grammar, and numeracy in years 1, 3, and 5 (McLeod, Harrison et al., 2019); and poorer school achievement with less positive trajectories at 12–13 years (Wang et al., 2018). This link between communication and reading has long been acknowledged (Tambyraja et al., 2022); "to crack the alphabetic code, children must be able to abstract the relevant phonemic units from the stream of the speech" (Castles et al., 2018: 11).

Speech, language and communication needs (SLCN): The second group of Australian children who have been studied longitudinally were identified with speech, language and communication needs (8.3% LSAC, Cronin et al., 2020). Again, these children were found to have lower academic achievement and poorer socialisation. They were also found to have increased health-care costs, productivity loss (Cronin et al., 2020), and increased representation in the criminal justice system (Dowse et al., 2020). Similar findings have been reported across the world (McGregor, 2020; Ziegenfusz et al., 2022; Zubrick et al., 2015).

Multilingual children: The third group of Australian children who have been studied longitudinally has demonstrated that multilingualism does not impact young children's educational outcomes. In a longi-

tudinal study of 4,983 Australian children from LSAC, there there was no difference between speaking one or more language(s) on children's language and literacy, mathematical thinking, and socio-emotional skills (McLeod et al., 2016). Children learn to communicate in more than one of the 7,000 world languages and it has been estimated that the majority of the world's population is multilingual (i.e., understand and speak more than one language). Multilingualism is a strength, and many Australians are multilingual (Australian Bureau of Statistics, 2021; McLeod, Verdon et al., 2019). In a study of Australian census data, it was found that multilingual adults who spoke English well were more likely to have a higher education, employment, and a higher salary than monolingual Australian adults (Blake et al., 2018).

A challenge for Australia: support children to become competent communicators

One of the most foundational issues impacting Australia's social and economic future is the need to support children with speech, language and communication needs to become competent communicators, thus reducing the lifetime productivity cost, estimated to be $21.7 billion in lost wages (Cronin et al., 2020). Equitable and early access to communication services enables children to achieve their fullest potential at school, at home, and in society; however, the majority of Australian children with speech, language and communication needs are "underserved." Over 50% of Australian children with speech, language and communication needs receive no/insufficient communication support due to long speech-pathology waiting lists, fragmented services,

linguistic and geographical barriers, and cost (Commonwealth of Australia, 2014; Henry, 2019; McCormack & Verdon, 2015; McGill et al., 2020). For example, the NSW Health Henry Review (2019) described "The long waiting times to access speech pathology services for children with speech delay, when there is strong evidence for the cost benefit of early intervention" (p. 69). Early identification of speech, language and communication needs and provision of communication services in early childhood are essential for changing children's trajectories and more cost effective than remediation later in life (Law et al., 2012; Westerveld et al., 2015; Whitehouse et al., 2009). While there are many successful evidence-based interventions to support children with speech, language and communication needs (e.g., Goldfeld et al., 2022; Jones et al., 2005; Williams et al., 2021), the critical window for early intervention and support is often missed due to insufficient access, resources, and funding. In Australia and the UK, many communication professionals are not funded to provide the required intensity of evidence-based early intervention for it to be maximally effective (Hegarty et al., 2018; McGill et al., 2021). Importantly, receiving less than the defined intensity is equivalent to receiving no intervention (Law et al., 2012; McLeod et al., 2020).

The way nations formally describe and count communication impacts service provision, and Australia lags behind the UK and US in defining communication as a disability. A comprehensive review of Australian health, education, and disability legislation and policies found children's communication was "invisible" (McLeod et al., 2010), and unlike the US and UK "communication" is not included as a disability

in the Disability Discrimination Act 1992 (DDA) or the Nationally Consistent Collection of Data on School Students with Disability.

Conclusion

While the ability to communicate is innate, communicative competence is established in early childhood and impacts participation in society, economic potential, social and cultural cohesion. The Australian Government Education Council's goals outlined in the *Alice Springs (Mparntwe) Education Declaration* (2019) include to support all young Australians "to reach their potential and achieve their highest educational outcomes" (p. 11) enhancing "communication skills" (p. 8) and providing "effective early intervention and support strategies to ensure each young person has the necessary skills, knowledge and confidence to thrive as they move through school" (p. 8). We need to prioritise children's communication, to enhance the future of individuals, communities, and our society.

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From language to literacy: understanding dyslexia

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I think there are some really interesting commonalities and differences when we talk about language versus reading. As Sharynne so clearly demonstrated, the general belief is that humans have what we call the "language instinct:" an innate natural ability, if they are neurotypical, to learn to speak. Children are typically born with this, and it occurs naturally through their interactions with the environment. The linguist Steven Pinker gave a very delightful summary of this when he said, "Short of raising a child in a barrel, they will learn to talk in the environment that they're in."

We have a very different situation when we talk about reading. If you place a child in the environment of books and leave them to discover what they discover, what you find is they don't discover very much about reading. We are not hardwired to naturally derive meaning from those squiggles, curves, and funny-looking letters that are on the page. Reading is a learned skill. This has come up many times already this morning, and it typically requires instruction. The very unfortunate thing, and the thing that I have spent so much of my time trying to understand, is that approximately 10 to 15% of children have a specific and long-standing difficulty with learning to read. These are children who don't have low IQs. There's quite often no other really obvious feature that would explain it.

There is a comorbidity with language difficulties, and I'll move on to that in a moment. It's a very specific disorder, and we see it in many different forms. I have decided to take the list approach and share with you the top five things I've learned about dyslexia in the time that I've been studying it.

1. Dyslexia usually involves words

The first thing might seem somewhat surprising, but in the vast majority of cases of dyslexia, the problem is at the word level. There are some unusual cases where the problem is at a text type level, a broader comprehension level. Typically, those children have other language disorders that go with that. But if we're talking about a dyslexia-specific reading problem, usually we can locate it at the level of the word, which is something quite valuable for teachers to know. You can probably, just with a few quick word tests, get an idea of which child might have a propensity to struggle. Now, in some ways, this might seem really surprising: like how easy it is for us to read "dog" — how could it possibly be such a difficult challenge that some children are unable to fully achieve? But if we break it down, even reading a single word is immensely complex. So for starters, you read this word in an enormous number of different forms; you read words in uppercase and lowercase;

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1   This is an edited transcript of the address [Ed.]

you read them in different fonts; you read them in skywriting — it's not just a visual process, it's quite a complex, abstract knowledge of what the spelling of that word is that you can do. The other thing is that you can read words that don't follow the typical sounds that you would sound out. So a child first reading this word "y-ach-t" would say "yed." English is a particularly difficult language in that it has very many words like this[2] and in fact very many words that are quite frequent that are like this.

We're also able to read novel words. So I can put this made-up word that I've just put on the board for you, and you can instantly pronounce it as "glimp." So you have a separate process in your brain that's computing out the pronunciations of words in most cases and getting to their meaning that way. And of course, even as adults, we have to read novel words all the time: reading people's names that you don't know, names of towns and cities. I had an international visitor the other day, and I was driving her down to see the harbour and all around here, and she said, "Oh I really would like to go to wulu mulu," and for quite a while I was like, "What is she talking about?" Then I realised it was Woolloomooloo.

2. Dyslexia is heterogeneous

There's a lot of word learning that happens all the way through our life, so as well as being focused at the word level, even at that word level it's highly heterogeneous. It's really wrong to talk about dyslexia. We should talk about the dyslexias, because it's a complex learned skill and by that complexity, there's a whole range of different ways in which it can go awry. Taking our

examples from before: if with our 10 to 15% of children in the classroom, some of them we know have difficulties with that sounding-out process which is essential for reading novel words, very many children with dyslexia have this problem. And it's one of the reasons that there's a big push for phonics instruction that's very systematic and structured and assessed in schools. Because you really need to be able to read novel words when you're learning to read. Every written word's a novel word. But you also find children who have difficulty with putting words to memory, so they've seen the same word over and over again. You and I would be familiar with it: we'd go, "Oh, yes, that's yacht, no worries." But they continue to struggle and they need to see many more exposures in order to be able to put that word to memory. And of course, that means that their reading is very slow: they have to devote a lot of cognitive resources to that processing, which interrupts their ability to comprehend the text, which is obviously the most important thing. You also get children whose problem is at the comprehension level. These are often the kinds of kids that Sharynne has talked about: they have difficulties with vocabulary, with spoken language, and that carries through to a difficulty in understanding written text.

The point that I want to make is, even with what seems the most simple task to us, there's actually, when you break it down, an awful lot of complexity. And all of that complexity is typically mastered by children within a couple of years amazingly. But we do see these children that struggle and we need to do more for them.

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2   "yacht" comes from the Dutch "jaght" [Ed.]

3. Dyslexia is highly heritable

The third thing that I've learned — and this may seem in some ways counter to the point I made earlier that we don't have a reading instinct — you would have noticed that on none of those brain pictures has there been an area of the brain for reading. We don't have a "reading gene," but that doesn't mean that it's not heritable because what is heritable are the complex set of more general abilities that are heritable that have to be applied to the task of reading. We're talking about memory, we're talking about visual processing, we're talking about language, and that combination of skills is highly heritable and it plays out in the dyslexias that you see.

The neatest evidence for this in my view has come from twin studies. I think most of you would be aware of the logic of twin studies. We have identical twins — sometimes called monozygotic twins — who share 100% of their genes: they're genetically the same. We also have our non-identical dizygotic twins who share 50% of their genes, and if they're living within the same family and going to the same school, they're relatively well-controlled in terms of their environmental experience, so we can use the contrast between identical and non-identical twins to get an estimate of how heritable reading difficulties are. And not just one type of reading difficulty, but all of the different types of dyslexia that I've mentioned.

We would select one twin who is struggling with some reading at the bottom of the bell curve. Then we look at what's going on with their co-twin: are they identical or non-identical twins? What you clearly see is that when we look at the co-twin of a child with dyslexia, the co-twin in both cases tends to be below the average on the overall bell curve, but our monozygotic twins are much worse than the dizygotic twins. That tells us we can compute essentially a heritability estimate. And these estimates are very high, surprisingly high, over 50% of reading difficulties are heritable, by most estimates.

4. Dyslexia is a learning difficulty

This doesn't mean — and I think this can often be something that's hard for parents or teachers to process — that these reading difficulties can't be treated. We know a lot about how to teach reading, and we know that we can apply those same principles to children with reading difficulties and get good outcomes. We just need to do it more intensively and probably for longer.

Learning has come up a lot in the sessions so far, and, as I've emphasised, dyslexia is a difficulty in learning. We know much of it is based on genetics. We know it's happening somewhere in the brain. And many researchers look at exactly that kind of thing: what are the areas of the brain that seem to be different in children with dyslexia? But we can see a causal pathway that goes down to maybe a language-processing difficulty that may then go down to a difficulty in learning those letter-sound mappings, and then we have a behavioural outcome that's the reading difficulty.

So we think there are multiple causal pathways that can lead to reading difficulties. And as I've already emphasised, there are multiple different types of reading difficulties as well, so this is a complex task to try and unpack these causal pathways.

5. Best to treat the reading

Although we know that there's this complex causal pathway — and we researchers spend a lot of time trying to tease these causal pathways out —based on the science we have so far, we know if you have a child with a reading difficulty, the very best focus of your intervention should be at the level of the reading difficulty itself. We just don't know enough about the complex causal pathways that lead to that for intervening at earlier levels to be effective. And of course, there are many cases where we wouldn't be able to intervene obviously. But what we do know is that if we identify using very carefully evidence-based assessments exactly where a child's problem is and target that, we can have the best outcomes for a child. This is one of the reasons why my research group always suggests being a little bit wary of any dyslexia treatment that is focusing at one of those earlier levels. Not that those aren't important questions, but we're just not at the point where that is helpful for intervention: brain training, coloured lenses, visual problems — all of those sorts of things — we know there are associations. We also know from large RCTs that those kinds of interventions are not as effective as working at the level of the reading system itself. So I'll leave it there.

I feel a bit sad in a way that I can summarise my research career in five points but we still have a lot to learn. One thing that is absolutely crucial — and what my laureate project is focusing on — is reading difficulties once children move into secondary school. We know from international reading studies, PAA studies — I think the last estimate from the PAA international study had 40% of 15-year-old Australian children did not meet the criteria for functional literacy. We have many children who are coming into high school not having been picked up as having a reading difficulty or a language difficulty in primary school. They move into high school where nobody looks at that anymore. No teachers — they're not doing that, they're teaching content, and the children are expected to access that content. We know that a large number of those children can't read, and, as echoed in the points that Sharynne made, we also know that things get really tricky once you get to this age because of self-esteem issues and anxiety and other sorts of comorbid factors, which often lead to these children being very resistant to reading and to things like school refusal. What we need to do, and what we hope to do, in the seven years that the ARC has so generously given us, is to not just look at the basics of the reading trajectory in these children in high school, but how it how it interacts with all of those other contextual factors that are going on in high school. So maybe in seven years' time I can come back and tell you some more insights.

Young children in digital worlds: multi-modal development?

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Friends, it's time for some honesty. How many people have got multiple devices in their pockets? Let's have a think: who's got a phone in their pocket? Yeah, 100%. Okay, parents and grandparents, how many of your children and grandchildren have devices in their pockets? Our brains might not be changing, but the environment we live in is substantively changed. We are now having children growing up in a multimedia world.

I want to just take a moment to acknowledge the traditional owners of the lands on which we stand. I was very excited that Qantas reminded me of the lands I was on and the lands I was leaving. I wasn't so excited that Qantas was nearly an hour late and my breakfast meeting was slightly delayed. I was, however, thrilled that my Uber driver knew that my plane was late and was still there waiting. I didn't have to text him; he knew already. So even though we talk about technology as a problem, in many ways it makes our lives significantly easier.

So, Adam, Sharynne, Anne, and Penny: you've given me a particularly hard act to follow. I'm not a professor. I haven't been nominated by a newspaper for being significantly impactful in my research. My little *Conversation* piece[2] went slightly viral: apparently, I'm destroying childhood again. And I feel incredibly honoured to be here, so thank you. And particularly thank you to the Royal Society of New South Wales to let me climb over the borders and join you today.

When we look at young children in technology, whether in any of the forms of development that we focus on or any of the forms of brain conditioning we focus on, we have this immensely polarised debate. There will be some lovely people in this room saying we shouldn't be talking about technology. And then we've got others in the room who are happily tweeting, taking photos, posting things on whatever social media platform they're on. We're polarised in our perspectives of young children and technology. Unfortunately, the research is no longer polarised about this: we have some very firm guidelines and hopefully I will try and cover some of that.

When we look at young children and media — I'm sure you can see a child in your life looking somewhat like that (I have a six-year-old; she doesn't have a device, but is allowed to sometimes use my device) — we don't look like any of these things because I've read the research. Unfortunately, many families in Australia have not read the research. We have not done a good enough job at translating that research. The ideal way for children to use technology and media is by co-viewing and co-engagement, because that way we can facilitate their language development, we can monitor atypical

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1 This is an edited transcript of the address [Ed.]

2 Highfield, K. (2023) How can I tell if my child is ready to start school next year? *The Conversation*, 29 August.

development, we can focus on literacy elements as children use the devices. But unfortunately, often we allow these devices to become isolating. When we talk about the conflict though, we have to recognise the positives. If I look back on the last 12 hours of my life, my device has worked as: a clock, a CD player, a book, an audiobook, a ticket, a fitness tool, a map, it's been my credit card, it was my communication tool, and, yes, I communicated to some of our friends online as I arrived. It's been a camera — I took some photos of this incredible ceiling, my device has been a distraction when my plane was late, it's been a phone — I rang my mother — and it's been a connector. Lastly, and most importantly as we think about brain development and children's development in the digital space, my device has been a memory aid: I have notes that help me remember what I'm talking about. They also help me manage things like executive function. You see, I've turned off my distractor. It's not on anymore. I've made conscious decisions about how I use the technology.

All of those things come to play because I'm researching in this space but I wonder about your children and grandchildren. I wonder about you in the room, whether you have actually thought about the way you're using technology, and who is driving the digital bus in your family. You see, often our friends at Apple are driving the bus. Our friends at Netflix are telling us the types of media to watch. Sometimes children don't even have the option to make a conscious decision whether they use or not use, as parents just hand out the devices. So how do we overcome that?

We first of all have to understand that digital toys technology is an artefact of childhood. We can't get away from that.

We have to acknowledge it. We also have to understand that when we talk about digital technology, we are really talking about screen-based media predominantly. And we have to understand that we've got both broadcast media or streamed media, and we've got interactive tools. We've got these two different things and you could position them on a continuum if you like, with television streamed media at one end, and then interactive tools at the other end. However, this becomes really murky because — guess what? — most children don't watch television anymore: they watch streamed media on mobile and tablet devices. It becomes complex, doesn't it? The toolbox has changed. It also means that we have a generation of children growing up at the moment whose parents are dealing with a fundamentally different childhood to the childhood in which they grew up.

This device of course was only invented in 2007. It's a different childhood and as we think about what this means for children, for childhoods and for brain development. I think we need to take some time to carefully communicate, to carefully consider, how we use the devices. They're not going away, so we need to really put some constructive thought in.

What does the research say? The research says a lot. In particular, we have good usage statistics internationally about how children are using media. For example, the 2023 data from OFCOM, which covers children from 4 to 15 years of age, shows us that children's engagement with TV has decreased, but children's engagement with BOD (Broadcast video On Demand) and SVOD (Streamed Video On Demand), watching devices when we choose what to watch — that's actually increased by exactly the same decrease that

television viewing has dropped. What that means is that the devices we use has changed but we're still watching television. We know that 9 out of 10 children play games, but only about 10% of those games are educational in any way, shape or form. We also know that children who have atypical neural development have different usage: often their usage is increased.

Unfortunately, Australian data is really limited. If we take anything from this, we take the need to have really good Australian data. Our Australian data comes from the Australian Bureau of Statistics and it basically says children are using media. That's probably unfair. We know that children are using media for approximately 2 hours per day, with about 60% of children using media for that time. Unfortunately, the group that I worry most about is the 24% of children in Australia who are watching or using over 20 hours of screens a week.

To know what the impact is on neural pathways, on synaptic pruning, and in particular on development in other areas — social, emotional skills, executive functioning skills — we need to know more about whether or not they're using a screen, and what that does to a child. We also know that we've got some particularly at-risk communities when it comes to screen time. We know that maternal educational level is a big predictor of how much screen time children have. Unfortunately, mothers who have less academic attainment allow their children almost double the screen time. We also know that, for under-3s, an increase in screen time has a direct impact on speech and language development. It's getting a bit sad.

However, the other piece of the picture that we need to focus on is the children as they grow in age. When we go past just this idea of screen time, and look at what children are really doing with screens, we can see that there's been some positive effects, particularly during the pandemic, of teenagers and young children connecting using social devices. If we keep looking at the negatives, I think it's important to acknowledge the impacts of things like dopamine and that we could argue that young children are growing up in an environment where we're allowing dopamine — the hit of social media, the hit of the ping in your pocket — to have an impact on development. Unfortunately, the hunting — that's where people post a photo and see how many "likes" they get — starts at a very young age. And unfortunately again, the less educated the mother is, the more likely she is to inadvertently show poor media habits.

I think the problems here are really complex and intertwined: they're about language, they're about literacy, and they're about groups that are experiencing adversity. If we look at teenagers, we have to acknowledge things like impact on sleep. We have to acknowledge things like low digital literacy. We need to know that young children, particularly as they're growing into those teenage years, might be using technology for positive social interactions, but those positive social interactions can flip very quickly. When we look at the space of technology and the developing brain, it is complex.

A couple of key takeaways: first and foremost, we can't put the technology journey back in the bottle. Technology is

here to stay. We're not giving up our devices, hence we need to be aware of how we can raise citizens in this digital age. The second takeaway is that we need to consider screen time for our under-3s and screen quality for our older children. We also have to think about the context that children are living in, how they're using tech: is it isolating or is it a social connector? Lastly, we need other metrics beyond just time. In Australia particularly, we need to know what children are doing on their devices and we need Australian research that really supports families. We need to help teachers to navigate this space because we know they're a key conduit in the area. And of course, we need to ensure that we're developing Australian content. You won't be surprised to hear that the American Pediatrics Association and our colleagues in America are quite concerned about "Bluey," because children in America are starting to speak with an Australian accent. I want those children in Australia to speak with the Australian accent. I want caps on media usage so that we are building and constructing our own media in Australia. But I don't want any media — I want high-quality media. When we have high-quality media, we can engage children, we can extend their geographic boundaries, we can enrich their lives, and most importantly we can enable them to do something they can't do normally. High-quality media and technology can overcome a lot of the concerns we're talking about, but how do we get to that part? This is the beginning of a conversation and if you'd like to chat further, please feel free to connect with me.

Session II: The brain: social, cultural and philosophical perspectives

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The human brain has evolved an extraordinarily efficient information storage and processing capacity, arguably in response to the increasing social complexity of human life but is also subject to more immediate environmental influences that are social, cultural and technological in character. In this session, we consider what we know of these influences and their individual and societal impacts and what this means for human capability.

Introduction

In this session we broaden our perspective on the human brain, seeking to understand brain, mind and wellbeing in their social, cultural and environmental contexts. The evolution of the human brain has often been linked to the increasing social complexity of human life, and a number of studies have made intriguing linkages between our complex sociocultural world and characteristics of the human brain. For example, it is well known that specialised brain networks support some very human capabilities such as recognising human faces, learning human languages, visually analysing the physical environment, and imitating the behaviour of others.

As a social scientist interested in the role of the social environment in shaping opportunities and constraints for human action, I find some of the connections that have been made between features of the brain and characteristics of an individual's social network especially interesting. For example, the size of an individual's social network has been found to be related to the volume of their amygdalae (e.g., Bikart et al., 2011). White matter connectivity in brain regions supporting social and affective processing has also been related to characteristics of an individual's position in their interpersonal social network, including the centrality of their role in the network and their potential capacity to broker connections among disconnected others (Hyon et al., 2022). If replicated, studies such as these provide an avenue for investigating how our brains shape and are shaped by the real-world social networks we inhabit.

The recent pandemic provided a shock to our everyday sociocultural and environmental contexts in most parts of the world, limiting movement and interpersonal interaction, as well as access to economic opportunities. Some ongoing studies took advantage of this natural experiment to explore the impacts of this sudden change on brain, mind and wellbeing. In a study in Israel, for example, Salomon et al. (2021) documented temporary volumetric changes during lockdown in the amygdala and other nearby brain areas. In another natural experiment, conducted as part of the long-running Mannheim Study of Children at Risk, whose participants are now in their early 30s, Monninger and colleagues used momentary assessments of mood across the course of a week to record a mood-lifting impact of positive real-life social interactions, with the size of the relationship

dependent on the level of amygdala activity measured pre-pandemic. Interestingly, but perhaps not surprisingly, no corresponding effect on mood was found for online social interactions (Monninger et al., 2023).

These kinds of results link phenomena at vastly different scales, and raise many more questions than they answer, including the nature of explanation itself when it comes to linking processes in one complex system (i.e., the brain) with those in another (namely, the complex sociocultural world we inhabit).

To delve more deeply into the interplay between brain, mind and wellbeing and its sociocultural and environmental context, we have a wonderfully diverse panel who will offer, in turn, psychiatric, economic, urban planning, linguistic and philosophical perspectives. Settle in!

Our first speaker is Professor **Andrew Chanen**, Chief of Clinical Practice at Orygen and an expert on prevention and early intervention for severe mental disorders, especially personality disorders.

Next up, we will have a short video presentation from the Honourable Dr **Andrew Leigh**, member for Fenner and Assistant Minister for Competition, Charities, Treasury and Employment, and a former professor of economics at ANU.

Our third speaker is Dr **Jennifer Kent**, a DECRA Fellow and urbanism expert from the University of Sydney, who works at the intersection of urban planning, transport and health.

The fourth speaker is Professor **Jakelin Troy**, Director of Aboriginal and Torres Strait Islander Research at the University of Sydney, and an expert on the documentation and revival of Indigenous languages.

The final speaker is Professor **David Braddon-Mitchell**, also of the University of Sydney, and a philosopher with expertise in the philosophy of mind and cognitive science, including consciousness.

Each of our panellists will take about 12 minutes, and this will hopefully leave plenty of time for comments and questions from the audience.

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Not waving but drowning: personality development and Personality Disorder

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I'm going to try to describe the interaction between ourselves and our environment in terms of personality development and what can go wrong. I'm very mindful of speaking before a philosopher and talking about the self, and I think we might have a very interesting debate about that. But what I want to describe to you is how the notion of personality and Personality Disorder has developed over time, and to describe some of the controversies around this issue of how we develop as people.

What is personality? When we think about personality, there's a very simple way of thinking about it: it's what makes us who we are. It essentially describes our character, characteristic ways of behaving, experiencing life, perceiving and interpreting ourselves and other people, and the environment within which we exist. It's relatively stable over time and situations. And I think people would hopefully see that as a reasonably acceptable common definition.

We are more than a collection of traits. It gets a little more complex than that though. Dan McAdams describes it very nicely that it's a layered concept. There are essentially three layers: (1) we are born with dispositional temperaments which he describes as the self as a social actor, (2) then we adapt to our environment (and I'll talk a bit more about this) as a motivated agent, and then we (3) form a narrative identity over the top

which binds those two layers together into what we recognise as ourselves (the self as an autobiographical author). And I won't go into all the detail.

Layer 1: Dispositional temperament traits

Dispositional traits are the basic biological individual differences that we are born with; they're linked to underlying neural networks and they show strong similarities to the structure of temperament in other animal species as well. This "genotypic self," this self that we're endowed with when we are born, is predisposed to and capable of intersubjectivity. And there are lovely experiments looking at infant development straight after birth, showing the intersubjectivity of human infants. But at this stage we don't have the reflective capacity in our relational environment.

Layer 2: Characteristic adaptations

Layer 2 is where the temperamental traits that become transformed through reciprocal interaction with the environment into what we would think of in common language as personality traits. They're essentially the same in content and structure, but they're broader. We have a wider repertoire of traits.

There is a large body of research that is largely settled on what are called the big five basic higher-order dispositions: essen-

tially they're: (1) openness to experience, or our intellect, (2) our conscientiousness, (3) extroversion, which essentially is our capacity for positive emotionality, (4) agreeableness, which is as it says, and (5) neuroticism, which is very important for mental health, which describes propensity for negative emotionality.

But traits are largely descriptive: they don't describe us as human beings. Where the debate is at in the field at the moment, a lot of trait psychologists would say traits are enough to describe a person. There is a great deal of dissent around that — they don't capture the complexity of what it is to be a human being. And so characteristic adaptations, as McAdams describes it, encompass the motivational, social, cognitive, and developmental adaptations that are specific to our time and place, where we exist. They start to develop around the age of 5 to 7 and with increasing cognitive capacity. Children begin to have goals and to link these with motives and behaviours.

Layer 3: Narrative identity

Traits continue to influence our personality functioning. But the really decisive ingredient is the changes that happen around puberty that allow us to develop reflective capacity and develop a narrative identity. This is where we actively integrate life experiences into an internalised evolving narrative of ourselves with a sense of unity and purpose in life. It requires coherence of time, biography, cause, and thematic coherence, as well as the necessary cognitive mechanisms that we require to develop. This doesn't really develop until puberty, so what could possibly go wrong in the development of human beings?

What could possibly go wrong?

Gary David was a notorious prisoner in the 1980s who sadly died in the early '90s. There was a huge debate around his offending, about Personality Disorder, was it a mental illness? The glib kind of aphorism — was he mad or bad? — really captured the debate at the time. He suffered terribly in life but was portrayed as an aggressor. If you look in Wikipedia now, it'll say he died by suicide by ingesting razor blades — actually death was really an artifact of his self-harm. This was the most extreme form of Personality Disorder.

One thing that's really changed — and I think of society as a kind of barometer of the way we perceive Personality Disorder — is that there have been a number of judgments recently that have taken Personality Disorder to be a mitigating factor in sentencing. Codey Herrmann is one of the well-known cases. I had involvement with two of the other relatively recent cases and it actually says that his Personality Disorder reduced his moral culpability for the murder.

Again another young woman, Dal Brown. It's on the record — so I'm not breaching confidence — that she was under our care, and again her fire-setting, which nearly killed a large number of people, was the only way that she could have control in her life. I think this really sums the shift, where a number of people who testified in another case — Andy Carrol, who's a forensic psychiatrist, described to the court that this is among the most disturbing of all disorders. And Jim Ogloff, a very eminent forensic psychologist, said, "I'd rather have schizophrenia than have borderline personality disorder." I think that represents a substantial shift in the way that we see Personality Disorder.

What is Personality Disorder?

Personality Disorder is when our personality structure prevents us from achieving adaptive solutions to life's universal tasks: having a stable and integrated sense of ourself and other people and being able to have the capacity for intimacy, attachment, affiliation, pro-social behaviour, and cooperative relationships. It is a developmental disorder, although it's not been thought of as a developmental disorder hitherto. And it only becomes observable when people develop the capacity for what's called metacognition — thinking about thinking — being able to reflect upon oneself — and it's this disturbance of that narrative identity that is fundamental to what is Personality Disorder.

How would I recognise someone living with PD?

These are some lay descriptions that we developed as part of a study. I won't go through all the detail except to show you that it ranges from mild — and you will know many people in your life who have mild Personality Disorder, where someone might have an unrealistically high or low sense of worth, experience difficulties in conflict in relationships, in setting goals, whatever it might be — right through to severe: the Gary David-type experience of someone who experiences extreme self-hatred or extreme inflation of self-esteem (I won't talk about any former Presidents, but you might want to extrapolate) and someone who has no sense of purpose in life, cannot engage effectively. People with severe Personality Disorder live very lonely and isolated and often very unhappy lives, and I'll show you why in just a minute.

A developmental model for PD

So essentially we've turned McAdam's model, with my colleague Sharp and also Bo from Denmark, into a model of personality pathology development. Essentially it takes the same model but overlays abnormal development, where you might begin with dispositional traits that are not in and of themselves pathological — everybody knows irritable children or children who are overly adventurous and that non-reflexive genotypic self through reciprocal interaction with environment, especially the caregiving environment. Then [the child?] develops goals and values and motives and by about 5 to 7 years of age certain behaviours are not tolerated within group settings: you have to take your turn, you're not allowed to steal other kids' toys, etc. These problematic behaviours are not Personality Disorder, they are problematic behaviours, but they begin in the mental health realm. I think you've probably heard a bit about that this morning. When early development goes awry but this sense of self at this stage is piecemeal and rudimentary.

Puberty brings this transition that then facilitates this Layer 3 — the self as author — and it's really only now that Personality Disorder becomes apparent. This "phenotypic self" (Level 3) integrates and binds abnormal traits. And the organising structure of the self becomes disrupted at this stage. That's what leads to the development of Personality Disorder. It might wax and wane — someone might have functional periods — but it breaks down usually under social stress laws.

Personality Disorder is essentially construed as a self and relational disorder.

Relational problems are the source of the disorder, as opposed to disorders of mental state in which the relational problems are usually a consequence of the disorder — like depression or a psychosis or some other disorder.

What have we learned about the development of PD?

We've learned a lot. The headline is it's complex and multifactorial. There's a very important role for this reciprocal interaction, and a very strong influence of social, cultural, economic, and historical mechanisms. There's a six-fold higher treated incidence of Personality Disorder in low socioeconomic communities. We know that symptoms and their expression are shaped by culture. We know that the global prevalence varies — it's lower in low and middle-income countries. We know that trends might be related, the trends in incidents might be related to the breakdown of social cohesion and social capital in modern societies. In a sense, our young might be the "sentinel species" for what is happening in our society — they are the warning sign for the social changes that are leading to the current rise in mental ill health.

Reductionism is scientifically wrong and harmful

What we know also is that reductionism is scientifically wrong and unjustified. You'll hear some people tell you it's all about trauma, it's all about attachment, it's all about emotion dysregulation, or it's all about abnormal brains or genes. None of these is correct. In fact, it is a much more complex and nuanced aetiology.

Developmental trauma is neither necessary nor sufficient for development of PD

Two-thirds of Australians experience developmental trauma yet only a very small percentage develop Personality Disorder, so why should we be concerned? Well, because actually about 10% of the population have mild and above Personality Disorder. About 3% of young people have severe Personality Disorder, about 1% of adults [meaning?] and, by age 24, about one in five people will have met the criteria for Personality Disorder, and about a fifth of them will have had severe Personality Disorder.

Why should we be concerned about PD?

We know that it is the fourth leading cause of the burden of disease of all mental disorders, so it is an important form of mental ill health that has hitherto been ignored. We know that these problems commence in adolescence and young adulthood. It used to be that you couldn't diagnose it in young people. And you can see not only the broad range of outcomes of problems that people present with, but also of outcomes from this disorder. It acts as a gateway to other disorders. And the family and friends of those people also struggle and have terrible experiences of mental health. It's a gateway not just to the personal costs but the social and economic costs of Personality Disorder, particularly employment and education outcomes, which are very poor among this group. You have nine times greater likelihood of being unemployed or being on the disability support pension. It's a stronger predictor of disability support than anxiety or depression. And the high health care costs are a huge burden for society. Most

tragically the mortality is 10 times that of the general population for people in the first 5 years after they have been diagnosed with the Disorder, and the life expectancy of people with severe Personality Disorder is reduced by two decades. The suicide rate is about 8 to 10%. That doesn't account for the premature mortality. And sadly it is the most stigmatised of all mental disorders — not by you the general public, but actually by my colleagues. And it is still the whipping boy for people's frustrations and dissatisfaction. People say things about people with Personality Disorder they would never dare say about any other patient presenting for care. And people perceive less of a sense of purpose in working with people with Personality Disorder.

So we've learned a lot: we know actually that treatment is effective, we know that medication is ineffective for Personality Disorder, we know that early identification leads to earlier effective treatment, and we know that treatment for most people with

Personality Disorder is actually not as complex as people have tried to tell us in the past. But we also know that the people who most need treatment are rarely the people who get it, and we also know that "treatment" can harm, and that many of the things we think about as being associated with Personality Disorder are actually harms perpetrated by the health system.

To conclude: Personality Disorder is a developmental disorder characterised by maladaptive self and interpersonal functioning. It begins from puberty and has its onset by young adulthood. Like all of the other major mental disorders, it's strongly influenced by social, cultural, economic, and historical mechanisms. It has very high potential to disrupt the successful transition to adulthood and it has lifelong personal, social, and economic consequences. We know that treatment is effective, access is very poor, and that the biggest barriers to reform are actually bigotry and sectarianism, not a lack of effective treatments.

Australia's "friendship recession"

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Good day. My name is Andrew Leigh, the Assistant Minister for Charities, and it's great to be speaking to you virtually at the Royal Society of New South Wales Forum. I acknowledge all First Nations people present and commit myself as a member of the government to the implementation in full of the Uluru Statement from the Heart, which starts with voting Yes on October the 14th.

You've asked me to say a few words about the "friendship recession" that Australia finds itself in today. A challenge which is in its way as stark as any other that Australia confronts. Over the course of the past generation, we've seen Australians step back from engagement in formal community organisations. Membership as a share of the population in Scouts, Guides, Rotary, and Lions has waned. We've seen a decline in the share of Australians playing an organised sport, with participation rates in sports such as cricket or football or netball declining. We've seen a decline in the share of Australians who are actively engaged in political movements, a drop in the share of people who cast a valid vote, and, most troublingly in the context of a friendship recession, we've seen a decline in the number of close friends that the typical Australian has.

Back in the mid-1980s, surveys asked Australians, "How many close friends do you have with whom you could share a confidence?" and got answers around 10. Now the answer is around 5, meaning the typical Australian has shed half their close friends over the course of the past generation. Worryingly too, the share of people who say they have no close friends has declined over this period. This has occurred at a time when Australia has become more unequal, meaning that in both economic terms and social terms we've moved from being a nation of "we" towards more of a country of "me."

Reconnecting Australia will involve a full court press work from civil society, government, and from us as individuals acting together in our local communities. It might involve actions as straightforward as making sure that you're the one who welcomes the new neighbour into the street and puts on street drinks at the end of the year. My wife and I do it in our own street, and I've got to tell you the time it takes is tiny and the benefits are immense. But we also need to inspire community organisations to encourage Australians to join, participate, and engage in local communities.

As a government, we've set a target of doubling philanthropy by 2030. We're working with the Productivity Commission to bring down a report on practical ways we might achieve that. A better connected Australia will be a more affluent Australia because commerce works best when networks of trust and reciprocity are strong. It'll be a healthier Australia because Australians tend to be fitter and have fewer mental health challenges when they're part of healthy communities. And it will be a happier nation because friends are essential to living a good life. Thanks for the opportunity to speak to you today and all the best for the conversations in your important forum.

Social interactions in urban spaces

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A sense of support, community and belonging within the places where people live, work and travel, is an influential determinant of mental and physical health. Indeed, internationally well-regarded psychologist, Roger S. Ulrich, once proclaimed "Low social support may be as great a risk factor in mortality as cigarette smoking" (Ulrich, 1999: 42). Belonging fosters perceptions of security, confidence and comfort, which can encourage people to be active in their neighbourhood, as well as socially connected to others.

At the heart of notions such as community, belonging and connection are social interactions. Interactions with other people are the fundamental basis of what it means for us to be social beings. Indeed, they are an innate, biological, need, with both psychological and physical health consequences (Hawkley and Cacioppo, 2010). Without interaction the regulation of cellular processes deep within the body are disrupted, predisposing us to premature ageing and, ultimately, premature mortality (Wang et al., 2018). This makes sense when we consider that early in our history as a species, we survived and prospered only by banding together — in couples, families and tribes. Interaction was a way to ensure mutual protection and assistance. The pain of isolation, therefore, evolved like any other form of pain — a way to protect us from harm. Too much social isolation feels unpleasant because it is a signal that connections to others are weak and need to be repaired (Cacioppo et al., 2011).

Since the turn of this Century, there has been a general downward trend in the amount of face-to-face and incidental interactions we have, and a shift towards more mediated interactions based on networks (either online or through an organised channel such as a school or workplace) (Patulny and Seaman, 2017). Our social lives are increasingly mediated through technology, and this is a concern for both sociologists and mental health professionals (Grenade and Boldy, 2008). If the only interactions we have are with the like-minded people we choose as our associates, we risk becoming blind to, and intolerant of, diversity, as well as isolated from those around us.

The way urban environments are planned, designed, constructed and managed can be instrumental in supporting social interactions of all kinds (Cohen et al., 2008; Bower et al., 2023). For example, by providing jobs in close proximity to housing, good urban planning can help reduce commute times (Chatterjee et al., 2020; Haffner and Hulse, 2021), providing more opportunities for people to be at home with family. Urban planning also influences, to an extent, housing affordability, enabling family and friends to remain in close proximity (should they choose), rather than having to move away, simply to afford a home (Haffner

and Hulse, 2021). These less-direct impacts of urban form on social interaction are important; however, this paper's focus is specifically on incidental social interactions. This is in recognition of the many and varied ways built environments can promote positive interactions within the immediate community.

The importance of incidental interactions

Social interaction is increasingly linked to organised activities, including work, sport, a child's school, or membership of a common-interest group. Our interactions are often mediated online, and as a result, they do not necessarily occur in the spaces where we physically spend our time (Sabatini and Sarracino, 2019). Incidental interactions are in between these formalised and networked connections. They include the day-to-day meeting and greeting of people who live, work and travel in the same spaces at the same times as us. These interactions may not be with the people we would normally choose to associate with. Indeed, we may not even know them by name, nor speak to them for lengthy periods. Yet history, research, and common sense all tell us that incidental interactions are critical components of the health of communities and individuals within those communities (Holt-Lunstad et al., 2010). They are small events that enrich connection to place, promote a duty of caring, increase perceptions of safety and belonging, and decrease feelings of loneliness and isolation. It is through these incidental interactions that we learn to cooperate, tolerate and trust relative strangers. If the majority, or all, of our interactions with other people are with those we have met through a common

interest or history, we risk becoming blind to diversity. Our ability to appreciate and respect difference is eroded.

Incidental interactions thrive on regular contact. While it might be unusual to simply say hello to a total stranger, this shifts when we see that stranger more regularly. We start to realise that they share something in common with us — even if it is catching the 7:16 AM train, the postcode where we live, the place we buy our coffee, or our morning walking routine. Regular chance meetings make it easier for us to say good morning, make comment on the weather, or simply just nod in greeting. And research unequivocally demonstrates that a community rich in these subtle interactions is more likely to be a healthy one (see, for example, Umberson and Montez, 2010). These are the exchanges that give neighbourhoods the potential to feel safe and welcoming, encouraging people to feel that they belong within it, living lives with coherency and connection.

Interaction in the public realm and the importance of slowing down

Any place in the public realm is capable of hosting informal and unorganised social interactions. Every second, interactions occur in our urban spaces. They happen in children's playgrounds, by park benches, in public squares, on footpaths, at bus stops, around bike racks and in building forecourts. They can be large, such as a town square or train station, or smaller, such as a stairwell or common entry to a building. The more talking points we have, the greater the opportunity for incidental interaction. The more often people's paths cross, the more opportunities there are to acknowledge and build respect for one another.

For many, life occurs at an increasingly fast pace. The first step to an incidental interaction, therefore, might just be a slackening of pace. We need to provide a reason, and a space, for people to shift gears, even for a moment. This might be task-oriented — such as collecting the mail or waiting for a bus. It might also be rather whimsical — such as a work of public art, a body of water, a neighbourhood cat, a tree in full flower or a flock of noisy birds. Once we understand that interactions depend upon personal *de*celeration, or slowing, we realise why public spaces need to be designed to encourage lingering.

The most obvious way to slow the pace of social life is to provide ample places for people to sit. Famous urban designer, William H. Whyte, was an avid supporter of the provision of seating in public places. In lamenting the lack of places to sit in American cities, he once remarked "The human backside is a dimension architects seem to have forgotten." The quote appeared in his iconic and ethnographic film *The Social Life of Small Urban Spaces* (Whyte, 1980). In it, he demonstrated the way people merge and linger not in the large and exposed expanses of public square, but in smaller parcels of space throughout the city.

Aside from places to sit, there are a series of other embellishments urban planners and designers can incorporate to encourage lingering in the public realm. First and foremost, public spaces need to be places where people feel safe — this may mean well-lit at night, shaded in the summer months, and sheltered throughout winter. Some spaces should be natural, or at least accommodate and incorporate natural elements. Humans share a degree of fascination and appreciation of nature and flora and fauna are more likely to prompt a casual remark or smile than relatively sterile blocks of concrete or steel (Beery et al., 2017). Providing adequate space for responsible companion animal ownership can also foster incidental interaction and strengthen community ties (Bueker, 2013; Toohey et al., 2013). Street art — formal or informal, large or small — is also a potential point of interaction (Alizadeh et al., 2022). Art in urban space disrupts the monotony of built elements. It implores that we slow down, look up, and perhaps enjoy that moment with the people who happen to be nearby.

Planning for both sharing and privacy

There is a considerable body of research linking low-density development, sometimes labelled "urban sprawl," with poor health (see for example Garden and Jalaludin, 2009). One of the pathways for this link is that the focus on the private realm, lack of diversity of housing types and land uses, as well as car dependency, can undermine social capital by reducing opportunities for social interaction. However, research on the impact of residential density on incidental interactions is mixed. Indeed, there have been several studies demonstrating that social interaction is more common in lower-density suburban areas (see for example the US-based study by Nguyen, 2010). Overall, the research suggests that there is a threshold to be found between high and low densities and social interaction generally. People need opportunities to interact randomly — whether that be in shared driveways, building entry points, or at the mailbox. But they also need to be able to retreat to their private spaces from time to time.

The complex balance between density and interactions highlights the way that, in cities that are growing and densifying, we are increasingly required to share space. Higher-density living in an apartment, for example, replaces a private backyard with public open space. A public transport trip replaces the cocoon of the private car with a communal train, bus or tram. Office workers, at the mercy of employers seeking to minimise spending on office space, are increasingly asked to hot-desk, or share desk space. There are more shared pathways, where cyclists, pedestrians, dog-walkers and pram-pushers vie for space.

While sharing can encourage incidental interactions, unless sharing is balanced with the opportunity to have time out, we risk that interactions may become a source of tension, rather than conviviality. A healthy built environment requires both opportunities for people to interact, as well as chances for people to retreat from the public gaze when needed. Planners and urban designers can do this through proper building design, for example by prioritising visual and acoustic privacy. Transport planners can also incorporate places for silence into everyday environments. For example, most trains servicing urban areas in Australia now have a quiet carriage, where people are discouraged to talk on mobile phones and listen to loud music.

Taking interactions online — what place for the built environment?

The popularity of social media and chat platforms suggests that digital connections now serve as an easy substitute for face-to-face contact. This was confirmed by research from the University of Wollongong (NSW), which used the General Social Survey to show an aggregate decline in face-to-face contact and rise in online contact in Australia (Patulny and Seaman, 2017). This is not necessarily a bad development for social interactions, which can be both initiated and strengthened by online platforms. However, it seems implausible that online interactions, self-selected and moderated by the boundaries of our own digital footprints, can provide the benefits of tangible incidental encounters with the random people around us. If we are looking down at a screen, we are certainly not looking around at the wonderful mess of community that confronts and enfolds us. Surely our ability to relate, appreciate diversity and connect to community is eroded? The question for urban planners and designers, however, is whether there is any role for the built environment in moderating some of the issues that arise as a result of our appreciation of online communication.

Urban planners around the globe assess and approve proposals for broadband infrastructure, just as they do for other major infrastructure projects. Planners have overseen the roll-out of broadband networks, and, together with the politics and business case of the entire operation, planning decisions have had an important role in shaping the way we access the internet. If we can use planning to influence transport networks and design new neighbourhoods, in theory planners can also effect online networks. This raises an interesting question for the intersections between urban planning and mental health — just as we provide quiet gardens and train carriages, could we also provide spaces where access to the internet is limited to essential services? Could planners make spaces where the switched-on and stressed-out population can genuinely find

time out, or genuinely find each other? In reality, urban planners would not dare, or be permitted, to exercise such discretion. This is a stark reminder that, while we often know *how* to plan and construct healthy built environments, the practice of planning is inevitably constrained by politics, individual preferences and the economy (Kent et al., 2017; Kent et al., 2022).

Conclusion

This paper has explored the concept of incidental interactions and demonstrated their importance for healthy communities and individuals. Of course, incidental interactions are not the panacea for a disconnected community, nor can they provide immunity against mental illness. It is hard to imagine, however, that any urban area where it is uncommon to acknowledge, respect and care for the people around you is a welcoming and healthy place.

Incidental interactions need space in which to occur, and these spaces need to be diverse, safe and plentiful. Performing an economic or utilitarian function should not be a prerequisite for a use to claim space in our cities. Spaces of commerce, learning, transport, residential accommodation and service need to be complemented by spaces where use is not so well-defined — where we linger, play, walk, sit, chat, pass through and meet. These are the spaces where "we learn — because we have to — that people of every kind, of every age, of every background deserve our respect" (Mackay, 2014: 49).

As our world and our cities grow, space comes increasingly at a premium. The business of urban development gives rise to a temptation to use every slice of available land for something deemed by the market to be "worthwhile." Concurrently, a growing city, and the dense urban form required to accommodate growth, demands we live in closer proximity to an increasingly diverse array of people. Spaces for interactions are, therefore, more critical than ever. These are the spaces that coax us out of our own lives, and give us a place to learn to get along.

Acknowledgements

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AI and Indigenous ways of thinking

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Na Jaky *na um Naru.* I'm Jaky, I'm *Naru* and I'm from the *Nich* clan. Some of you would know Namagee National Park in Canberra, that area so Snowy Mountains people *um nari n g.* Today we are gathered here, we're sitting down, as the word *nangun* says, on this beautiful country that belongs to the Gadigal, the clan group that were in this area and are still in this area which is a great thing for all of us. Sydney has about 27 or so clan groups, many of them known by their name, and I think that's something that is enriching everybody's lives. It's been very uplifting to hear people today acknowledging country and people. I don't see this is any way tokenistic and I'm really glad that it's continuing in spite of the sort of ridiculous rubbish and non-communal nonsense that's come about as a result of the recent referendum.

I had a catastrophic loss in the last few weeks: my husband, Pádraig, died at a young age, from stage-four lung cancer. Actually it was the complications from that, as you'd probably know, that usually take people out. What happened was his beautiful mind decided enough was enough, and I could see that process happening.

That's one of the things I will talk about today because I want to knit it into my own sense as an Aboriginal person of community and what it means to be forever part of a community and forever part of the world, even when you're physically gone.

I was listening just now, looking across to this beautiful tree to lift my mood a little, I want to tell you — and you will never look at a Moreton Bay fig ever the same way again — that beautiful Moreton Bay fig is inhabited by our cousins, a family of kookaburra who've been feeding each, other grooming each other, and doing all sorts of other things that birds do at this time of year to create more little kookaburras. The Fig Tree is actually inhabited by a spirit, and he has enormous *burras*, as we say — testicles — that he bounces around and clangs together. We've been hearing a clock chiming and I was thinking to myself, maybe he's somewhere around here. I'm telling you this not just for some light relief but also because that's how we as Aboriginal people perceive the world. Everything has a life force, everything has its own personality, if you like, its own brain. I'm looking at you, neuroscience people.

We are part of everything. I was sitting with my colleague, Hans Pols, and we were musing about what's missing from the conversation: our friends, furred, feathered, scaled, chirping, whatever, who are actually — from an Aboriginal point of view, from an Indigenous point of view worldwide, actually — our family and our friends. The trees are our ancestors, the birds are our cousins, brothers, sisters, aunties, uncles, family, you know, they all have an interaction with us all the time, and I

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1 This is an edited transcript of the address [Ed.]

think that enriches our Indigenous minds in a way that unfortunately a lot of the rest of the world — the Western world we often characterise it as — have impoverished themselves by not engaging. So, yes, it's about bloody time we were able to take our pets, as we call them, wherever, but they're our family members. I think I'm going to be struggling to take the horses on the train, but I'll give it a shot. I have seen people take horses up in elevators, but there you go.

I also want to talk about how it is for Aboriginal people in Australia. Our session is about the increasing complexity of our lives and we've heard earlier about how technology — meaning tablets — sorry, I've actually got I've got some great technology here: it's a book and paper and a pen: when that sort of thing became common usage — it's only a few hundred years ago really — the first printed books were considered the work of the devil and extremely shocking. I gave my child — she learned learn to read playing Pokémon actually. It's really good. It's a very complex language, in that she struggled a lot with reading and writing at school, but at home she was doing very complex things, using technology that she was engaging with. I like to engage with technology. As an Aboriginal person, I weep that we are now technologically and intellectually impoverished.

In 1788 when England invaded right here and took most of Australia gradually and then increasingly rapidly, they also took most of our 407 languages. All of you, everybody, you've lost 407 languages. There are about 15 languages that are still strong, but none of you would know any of them, I think, except Diane Eaves, who's in our audience today, and is a great linguist as well of Australian languages.

How do you feel about that — 407 languages? And those languages are not related to any other languages in the world — they are extraordinary languages, and they are so complex that you can say everything you need to say — everything I've just said — in a lot less of an utterance: a few short sentences. You could say, to use a twee English description of grammar. I've just said to you a whole lot. When I said *Naregu* immediately, for my community, that evokes all the things that it is about being *Naregu*. I don't have to say anything much else. I don't have to explain anything. This is because our communities knew each other. Still do, but we can't use our languages. Only 15 languages are still really strong. We're renewing most of them. That's the good news. You will have your 407 languages back soon. I'm looking forward to that.

This kind of loss of everything that language gives you — we've heard about that today — connectivity. We didn't ever care about writing systems. Literacy is just not a thing in the Indigenous world. You can get by without it. But we have embraced digital literacies because they're so much more interesting. For a start, they've got lots of visuals, which is good, so you know we have also taken our extremely highly developed technological kit, right. An Aboriginal person could get through a day with a sharpened stick, basically, something to carry a few things in, and being very physically fit. But also all that deep knowledge held in their brains about everything to do with everything around them. And no need to carry any aide memoire. That was just: we knew what we were doing.

I once had a friend from the Western Desert say to me that by the time a child is four years old in his area, they are a complete

socioeconomic unit — they're able to go out and hunt something, kill it, prepare it, and feed other people. And that's a four-year-old child. That would be a horror. Imagine sending a child from any Sydney family out: "Okay, you go catch yourself a lizard, bring it back, cook it up, and feed Grandma." That's just not going to happen. I mean, even "light a fire, what?" We now have all these safe spaces for kids and that probably wouldn't include doing any of that.

We've taken this kind of understanding of how to live well in country, with everything in it over the last 65,000 years (at least that's the archaeological record suggests; actually it's 72,000). Now the oldest sites where people were preparing food and living well up in the north of Australia and people are suggesting now 120,000 years. I've often said to people when they say, "Well, you know, but you've got no, like, big structures or you didn't have a wheel or you know none of these things" and I say, "Well, we spent, you know, we'll say, 120,000 years developing ourselves as very complex social beings. We have, in our languages, ways of dealing with everything."

So just for a little light relief. Mothers-in-law and sons-in-law never talk to each other directly in most Australian languages. Genius. Imagine all the social dissonance that we would be without if that was practiced more widely.[2]

Just to get through an average day, people would speak at least nine languages: there's child language — and I mean actual child language, not just actually speaking to children in their own language — people would use ceremonial languages, love magic

languages — that one I think would be interesting to explore, don't you think? It comes from the brain not the heart. We actually know there is a brain. Original people are very aware of that, although most things happen from the stomach, the kidneys too. So those other organs. The heart's kind of irrelevant. There's all these sort of ways of engaging with each other that we've lost, and we're trying to get it back. It will never be what it was. In a short space of time — just over 200 years, we've lost so much. All of you have lost so much, because of what's happened here, but we can engage with it. And that's part of what I've been doing as a linguist and anthropologist for a long time now.

We're presenting our students. I'm going to name my student, Majah Tali, from Northwest Pakistan, from Swat. When I first went there, all I knew was Pakistan is terrifyingly full of terrorists, and that area is particularly bad. But very interesting — great Indigenous languages, so I must go there. Sydney University was like, "You definitely are not — that is a red zone and there are genuine terrorists there."

Well, when I went there, sadly, I met not a single terrorist but I actually met people … I could template my indigeneity directly onto their indigeneity. And I just fit it in. I'm a mountainy Indigenous person and they're mountainy Indigenous people and people said to me there, "Oh, you're just so like a Pakistani woman, you're just so much like our people." That's because we have this whole other world — an Indigenous world — that I would really love more people to engage with.

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2   The Kimberley Bauhinia or Jigal tree (*Bauhinia cunninghamii*) is so called because its leaves face back to back as in the term *Jigal*, used to describe the (avoidance) relationship between son-in-law and mother-in-law in Aboriginal culture: the two must not directly face each other. [Ed.]

We've heard a lot today about researchers saying, "Engage with our research." I think if we could just engage a lot more with Aboriginal Australia, and Torres Strait Islander peoples as well, this country would actually solve, I think, some of the questions raised in other research areas.

We are different. A lot of what was said this morning fits really nicely with a Western, Anglo-centric, English-language-centric point of view, but it doesn't really fit or sit comfortably with me, frankly. And I don't think it does with my colleague, Mujahid, either, who's working with his community who've only had a writing system for about 10 years and that's because they invented one themselves. But it's still not very relevant for most of the community. I should say I share that student with Ian Hickie, so thank you to our work in Afghanistan.

I'll quickly move on to a personal experience I had recently, as I said, with the death of my husband. He was a systems engineer, a top systems engineer, an electronics engineer. He was Indigenous Irish. He struggled with that idea of being Indigenous and Irish, because the British also invaded Ireland about 600 years ago.

And in the last few months he said to me, "I think I'm dying from trauma" and I said, "Really?" and he said, "The cancer is caused by trauma." And I thought, gosh, he has had a tough life but ... and I said, "Trauma?" and he said, "Yes, the English invading Ireland." Cancer in Ireland is really high. We're all really stressed about it, and I still remember him saying, when I first met him and he was aged 22, "That feckin Cromwell" and I'm, like, Cromwell — is that a band I've never heard of? And he meant Oliver Cromwell. So here's this 22-year-old Irish man talking about the atrocities committed on his people. It was that much still in his brain.

There's this kind of communal grief, like we have in Australia as Aboriginal people about the things that have happened to us and our communities. We suffer from these sorts of micro traumas constantly that lead to terrible disorders like PTSD. I've experienced that myself. And Pádraig struggling to articulate being Indigenous, because it was such a bad thing to be in Ireland: you were a Culchie. You know: they were still using those terms meaning an outsider, a non-person, a bad person, you know, for being Irish, Indigenous Irish, from the Gaeltacht, from the Irish-speaking areas.

But in the end his approach which, while he worked closely with Lighthouse — I have to say Ian Hickie intervened and helped me to get Michael Boer as Pádraig's doctor and Chris Milross, they worked with him. Like the system engineer he was, he treated his illness as a problem. "Mission critical," I think he would call it, because he dealt with extremely complex defence system matters and things. Mission critical is where it can't go down — the system can't go down — so his system was not to go down, not to go down until he took it down. And so he worked with his doctors in this clinical way.

What I was going to talk a bit about today was AI and how AI might engage with communicative systems. With Australian Indigenous languages, I do wonder how the complexity of our languages and the fact that they're not related to any other languages in the world will engage with AI. At the moment that's not happening — people have approached me about it and I think it would be an interesting thing to do.

Pádraig and I talked a lot about AI and where it was heading and he said, "Oh, there will be a humanlike brain that will develop in the not too distant future," and he had access to information that he felt very strongly that this is where we were heading — that you would have some way of creating something that could cognise in the way that humans did. And he held fast to this idea that technology and systems could actually carry us through into a future, and even carry him through what he was going through … systems. But in the end the system failed and the human stepped in. And it was his Indigeneity, my Indigeneity, his other friends, including Mujahid, who stepped in around him and wrapped around him and created the human environment, the empathetic, the caring, the randomly emotional, the things that no system can really replicate. I mean, it's actually a fact that everything everybody says is the first time anyone's ever said it, and it will never be said again. I know that sounds extraordinary, but that's how human language is.

But machines rely on replicating things that have been said and thought and experienced. They have massive databases that you can feed into AI systems. But they're always flawed. They're always a little bit blurred. There might be ten fingers on one hand instead of five — the other hand looks normal, but this one's just a bit weird. You know there's always that bit of weirdness.

Humans are a bit like that too. I saw that as Pádraig was failing, there were things shutting down about his cognition. But one thing he could never do was imagine his own death. No human can imagine what it is to be dead because we will never have that experience. Once you're dead, the brain is stopped. That's why they turn the machinery off. We can't share that experience. No one has ever shared what it is to be dead, and no one ever will. Humans live in this space of hope and imagination, a kind of world that Indigenous people populate with the "beyond the death."

In our "beyond the death" you become part of everything that ever was. That just sounds like good science, doesn't it? We say that people become part of the stars. We now know, thanks to Carl Sagan, that we are all stardust, one way or another. But we have said this. "Look up," my grandmother said to me, "look up when I'm gone and you will find me: that's the star, and when there's a shooting star, that's a person returning." Well, it's stardust, it's matter.

Where I would like to end is to say that there are other ways of thinking about the world and the human mind and that Indigenous people have a particularly different way of thinking about the world and the human mind. Every time I travel to another community, I find commonalities but I also find new and startlingly, interestingly different things about how people understand the world and then communicate it. I'd like to see more of that brought into our broader thinking as scientists, so that it is not such a euro-centric and Anglo- and dominant language-centric way of sharing scientific knowledge. Focusing on the kind of research that we do that focuses on these non-Indigenous ways of thinking.

"Mental disorder" is not a useful, fundamental category

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I'm here to circle back and talk about mental disorders and the whole idea of whether we should be thinking in terms of dealing with mental disorders as such. So what's the story? Well, my story is going to be that there is no useful fundamental category of disorder. But that's not to say that there aren't disorders, it's just to say that there's nothing in common between things that get called disorders, that is deep and fundamental, and that this is going to play some kind of role in how we should think about mental health interventions.

What I'm not going to talk about is all the particular pragmatic reasons why you might not want to talk about disorders. The idea that disorders are stigmatising or perhaps they're not. Perhaps to some they're helpful because it's good to have a label on how you are and how you're feeling. I'm not going to talk about how particular diagnoses might be bad because they result in uniform treatment for a wide range of underlying behaviours. I am not going to talk about how disorder might be a bad notion because it leads to simple, monocausal, biological reductive explanations of the kind that Andrew rightly told us we should be very worried about. And I'm not going to talk about the ways in which diagnosis of a disorder might make someone act out the very symptoms that the disorder allegedly has. These are things which may be true, may be false, but the thing is if there really were

a fundamental category of disorder underneath all of this, then we would ignore it at our peril, because we ignore fundamental joints in nature at our peril, if there are any. So it makes the question: Is the idea of a disorder a fundamental joint in nature a pressing one and an important one?

Here's what I'm going to do. I'm going to talk about two different kinds of ways you might think that there are such fundamental joints that disorder is a real category that plays an important role. One is kind of biological, to see if there's a biological notion of disorder which is kind of profound and reliable and repeatable. And the other is sociocultural, to see if there's a kind of constructed notion of disorder which plays those kind of roles too. And then I'm going to say that there's neither of these two and so there is no good account of disorder and that either means we need to pretend there are disorders, because that's a good thing to do, or we need to move beyond it.

A biological notion of disorder

Let's do the biological one first. There are lots of attempts — I'll just describe one and why I think it fails. And this is based on some work — by myself and many of my colleagues, as well as a couple of my colleagues at Sydney University — that there's a very natural way to go, which is derived perhaps from Aristotle. I mention his name only because I'm going to be a stereotype

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1   This is an edited transcript of the session [Ed.]

philosopher and mention a dead philosopher's name — it's good thing to do. And that's to think that what's going on with a disorder is that a disorder is a disordered state because it's not doing what it's meant to do. It's not fulfilling its function. And so what you need then if you think that a disorder is something not doing what it's meant to do is a biological notion of what things are meant to do. Now that can seem very intuitive in some cases.

Think about your heart. What does your heart do? It does lots of things right. It exerts a small amount of pressure on your toes, it makes a little bumpity, bumpity noise. It exerts an extremely small gravitational attraction on Jupiter. I think I once calculated that Jupiter is 10^{-57} metres closer than it would be if I didn't have a heart. The other thing the heart does is pumps blood. And if I were to do a little poll here and ask you which one do you think it's for — which do you think is the purpose of the heart: pumping blood or applying pressure on your toes? — I'm assuming that most of you will raise your hands and say pumping blood. Well, why? Why is it a purpose? Why are there biological purposes, if there are? Well, for Aristotle the world was full of natural purposes — we lived in a purposeful world — but not many of us think that way now. Perhaps if you're not just a theist but also the kind of theist that thinks that you know God had a great big sketch pad and She planned out all of our organs in detail and thought I know what that thing's for, I'm designing it for this purpose just like someone might make a screwdriver for a purpose. If you think that intention in that kind of way can underwrite biological purpose, then maybe you're fine. But unless you have that particular brand of theism, it's not going to work.

So where are we going to get our purposes from if we don't have deliberating agents with purposes designing things for a purpose? Well, once again many stories. But perhaps the most common one is one which says that purpose here comes from what things were evolved for you. Ask yourself why is this thing here — why do I have a heart? What explains the fact that we all have hearts, that organisms have hearts? Is it that it made a noise and that those noises were useful for attracting mates? Is it because it applied pressure on our toes? Is it because it's kind of handy to distribute oxygenated materials around the body so your body can become larger and more complex? Very plausibly the last thing. So perhaps the function of the heart is indeed to pump blood, and it malfunctions when it fails to pump blood and you end up dead. Okay, is that a good account of biological function? Perhaps it is. I think it's the kind of counter-function which makes sense, when say a palaeontologist picks up a fossil and says, "What's this bit of the animal for? It's very peculiar." Perhaps what they want to know is how it got there? Why it got there? What it did that got it there? But I don't think that this sort of story is much used at all in thinking about disorder, either medical in general, or psychological in particular.

Why is this? Well, a couple of reasons: firstly, it's just much too easy to make up evolutionary explanations of things. Actually getting them right is incredibly hard and we mostly won't get there. Here's something you don't want — you don't want to go along to Andrew and say, "Please treat me," and you don't want him to say, "Come back in 20 years when I worked out exactly what the neural states underlying your behaviour are and what their purpose is and once I've

figured that out only then will I know it's a disorder." You don't want that. That's not a good idea. So that's one reason why this sort of story is not going to be a goer.

The second reason is lots of paradigm disorders just aren't disorders in this sense. So anything of the malfunctions — psychological or physical — of old age aren't going to counter disorders because there's not much evolutionary pressure in old age: you've done your reproducing. Whatever happens to you then has pretty much no effect on how many offspring you're going to have. So all those disorders of old age can't be things which have a function, where the function is failing. Because that sort of pressure is just not really there to some extent.

And the last reason is that lots of things we think of disorders — especially cases of psychological disorders — are things which are perfectly functional in this sense: things which are doing exactly what they were evolved for, but just in the current environment they are actually biting you in your ass very badly. One example: a semi psychological case is the story — which may not be true, it's controversial — that there are populations which have got a much stronger desire to eat fatty substances. Why? Because for many thousands of years those populations were in extremely fat-poor environments and this was massively adaptive for them to do so. But of course in a contemporary environment it's catastrophic. It leads to obesity and early death.

Maybe dementia is not any kind of a problem or any kind of a disorder on these sorts of stories of disorder. These sorts of stories about disorder are not ones that are looking very promising. If that kind of account of what a disorder is is not going

to work — and you have to take it on trust that competing slightly similar ones don't seem to be very promising either — what else might we do?

A sociocultural notion of disorder

We might go for a socially constructed account of a disorder. We might say: look we don't need a fundamental biological story, what we need is a story about how we respond to the world and what kinds of things we think of as disorders. A team I work with — mainly in Denmark, partly here in Sydney — has done some work on trying to find out what sorts of things elicit the response in people of "That's a disorder."

Andrew Latham, S Vager and I at the University of Aarhus took a sample of people and we looked at various variables that might correlate with people's judgments that something was a disorder. There are four that we did in one study — one of them is patient valuation. This was a case of sexual disorders, by the way, patient valuation: how much does the patient mind or care about the behaviour they've got or how much do they not mind? Another is community valuation: how much do we as a community care about other people exhibiting these behaviours or not care about them exhibiting those behaviours? The other is the source: how much of this behaviour comes, it seems, from primarily heritable things not very responsive to the environment, and how much is the behaviour very responsive to the environment? And finally: the intensity or strength of the behaviour.

All those characteristics turn out to play a role in some way or other and they interact in various ways, but it's a complete mess: it is entirely unpredictable and entirely

unstable: different people make different judgments even when, for example, they're all psychiatrists or all clinical psychologists or all doctors or just regular Danes. I should say is they're all Danes — so this might be something about Danes, although I doubt it.

Now I haven't definitively proved then that there's no coherent thing we're responding to when we ask about disorders, but once again I think it's not looking good. If it's not looking good to think about what a disorder is from a biological perspective, and it's not looking good to think about what a disorder is from a kind of socially constructed responding to the behavioural perspective, then what should we do?

The problem is that disorder plays a crucial role in our society: I think of it as a kind of rationing role. Medical and psychological services are rationed according to whether you've got a disorder. In the medical case, if you go along to a doctor and say, "Look, my nose is ugly. I want Medicare to give me some plastic surgery" the answer probably be "No," because that doesn't count as a disorder. If you have a child and you want your child who's doing extraordinarily well at school to do even better and you want to hire a bunch of educational psychologists to intervene, you're not going to get it, because no disorder is playing some kind of role here.

If we decide that disorder is not the category that we want to use, we're going to have to come up with some other way of rationing. It seems just entirely controversial, believe me, but it seems right to me that public funding should not be prioritised towards cosmetic surgery, and it seems right to me that public funding should not be prioritised towards interventions to make

people who are already happy much happier, or make people who are already learning very well learn even better. I mean, obviously it'd be great to have those people do that, but it's not a priority of public funding.

So what would you have to do? You have to think about the whole rationing question in a much more deliberate way. If we can't just default onto this simple notion of "Is it a disorder or not?" "Is it an illness that needs to be fixed?" or "Is it just giving people what they want?" Because if the key idea ends up being in the case of psychological disorder, what you're trying to do is give resources to improve people's psychologies, to make their psychologies more the way they want them to be, then you're going to have to make these serious rationing decisions. And how will you do that? I suppose there are equity considerations: maybe it's unfair to give someone who's already flourishing, resources to make them flourish more, compared to someone who's not flourishing or in a very bad way. Maybe if they are well.

There are communities where everyone is not flourishing psychologically for reasons for which we share a kind of collective responsibility, so maybe resources need to go there. Maybe we need to think about what sort of interventions will make society as a whole work better, rather than thinking about the fairness for the individuals. I don't know how any of this is going to work or should work, but I do think it's something that we really need to start thinking hard about: how to equitably distribute psychological interventions in creative and helpful ways that won't rely just on some default notion like disorder.

Session III: The brain disease burden in adults

Moderator: Tony Cunningham

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This is the first session in which we're going to talk about what goes wrong, given all the things that we heard go right this morning. In particular, we're going to focus on one of our greatest challenges — dementia, with 400,000 people in Australia diagnosed currently and expected to double by 2060, particularly with the wave of baby boomers coming through. We have Professor Glenda Halliday, who's going to lead off, then Professor Sharon Naismith. And then we're going to talk about a very topical field: long COVID, a very mysterious illness, with over 180 symptoms still being sorted out in terms of the physical versus the psychological.

Many groups in Australia are now working on the effect of the virus on the brain. It'll be very interesting to have Associate Professor Lucette Cysique talk about that, particularly as the Government has set up a $50 million fund for research into long COVID, and I'm apparently going to be involved in that. Being an infectious disease physician, I guess it's fairly obvious that we should have something where we know the exact start date on a subacute illness of the brain, a bit like HIV which Lucette has worked on before.

The first speaker is Professor Glenda Halliday, who's a legend in the field and is a Fellow of both the Academies of Science and Health and Medical Science. She's an NH&MRC Leadership Fellow and has been an NH&MRC Fellow since 1990. She is in the Faculty of Medicine and Health and School of Medical Sciences at the University of Sydney. Her particular interest is looking at the structure and function of the brain in illnesses that cause dementia, and also looking at how they impact on the diagnosis of such neurodegenerative diseases. Glenda has won many awards.

Brain cellular ageing

Glenda Halliday

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My specialty is in neurodegenerative diseases, but I'm not telling you anything about that except in a very broad sense. What I am going to concentrate on telling you about is how your brain ages and the cellular consequences of the ageing process on the brain. There are a few myths about brain ageing. Some of them are that (1) there is substantial brain loss, and that's a normal part of ageing, and that (2) all protein deposition in the brain — George has suggested a couple of times today — is abnormal, and (3) because of these changes we can all expect to have significant intellectual decline as we age. At the end of this presentation, I'll show you that these are myths. At the moment, we don't have good evidence for any of them.

You heard about body size in terms of animals and how big a brain can be compared to the animal size. It happens in humans that your brain is related to the size of your body, and it looks as if when we age there's a reduction in brain size. But these are cohort studies. If you've gone through deprivation, then your body size will be impacted. And since brain size is directly related to body size, it doesn't necessarily mean that older people have reduced brain size compared to what they were 10 to 25 years ago.

What determines brain size in a human? Is it bigger cells in the brain (which would mean with age people who have bigger cells might have more trouble with the metabolism of a bigger cell) or is it that there are more cells? It's actually more cells. A long time ago we showed that the size of the brain is related to the number of cells in the brain. Since then, there have been a number of studies that have shown the same thing in humans.

The studies show there isn't a loss of brain cells with age, so the loss of neurons when we measure those things is more likely to be due to a disease trigger rather than just ageing itself or abnormal protein deposition. Even though I said that you don't lose neurons, there is a change in brain structure. You might not lose actual numbers of neurons in the brain, but the connectivity — the white matter — is the place that reduces with age, so you do have a reduction of the structure of the brain with age. This suggests the main thing that might happen with age is that the connectivity of the brain changes.

There are many cells that are necessary for brain connectivity. In the white matter, neurons are not one of them. Neurons have axons that go through the white matter. The white matter is mainly made up of glial cells which do a number of things. There's microglia, which get rid of debris in the brain. There's oligodendrocytes, which insulate the axons so that they can conduct the electricity faster to get to the synapses to have the messages go through. And there's astrocytes, that tile the entire brain that are necessary to deliver the oxygen, glucose,

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and everything that every cell needs in the brain. There's a number of brain cells that are not neurons that are really important for maintenance of the white matter, and it looks like these are the cells that are going to be most affected during ageing and so are going to affect connectivity.

There's some studies that are now coming out, using quite new technologies (such as genetic transcriptomics), showing mouse brains over time — we have done most of our research on the mouse brain. These studies show that the glia, rather than neurons, have a widespread ageing signature and that the neurons themselves didn't actually change over time with age in the mouse brain. The molecular ageing was particularly accelerated in the white matter, which is where in humans we measure age-related changes most. There's a tenfold increase in age-related signatures in the white matter compared to other brain regions, particularly cortical regions which we've been talking about.

In the white matter, the microglia are most affected, but they're not the only ones: mature oligodendrocytes, the endothelial cells, astrocytes, as well as progenitor cells are all affected. There's particularly a mitochondrial gene downregulation. The mitochondria provide the energy of every cell. Within the white matter, they're the things that are mainly affected.

Now the glia in humans are much larger. The microglia are relatively conserved, but the astrocytes are much larger than in the mouse and much more complex. Astrocytes in the human brain are 15 times larger in volume than in the mouse, and they have 10 times more processes. There are two to three subtypes of astrocytes in humans and

primates that we don't see in other animals. They enhance higher-level neuronal functionality, so they're really important, these cells. The compact myelin is substantially increased with the increase in processes of the astrocytes.

There's a direct connection to the connectivity, the electrical conductance through to neurons. They're important cells. Glia are enlarged and are more complicated in humans compared to the animals. Therefore, you might expect an even greater age-related effect on these more complex neurons. The white matter glia do quite a lot of things: you can manipulate neuronal activity both chronically and acutely using bioelectric networks; the bioelectric networks in the brain are maintained by these citium of glia; the astrocyte networks can increase activity — they couple the activity of populations of non-synaptically connected neurons via chemical messages, ATP secretion, and calcium elevation; they affect activity-dependent myelination that maintains our connectivity; and the microglia on the reverse side can suppress neuronal activity through some of the same mechanisms and can limit activity-dependent myelin growth.

There's a yin and yang of how these cells might be affected and how they connect — we think of neurons as having connectivities that are direct. These cells can manipulate multiple non-connected neuronal networks in a different way. That's what happens when we age. There's a group of cells that people don't usually talk about that are quite substantial in humans. We have a lot more myelin than nearly anything. Our myelin is most developing during puberty. Some of the other things that we've been talking about today: myelination may

have a direct effect on these glial cells but I'm going to talk about how this might relate to the loss of the neurons which is related to diseases of the brain, the age-related degenerative diseases.

Age-related proteins that deposit in the brain

There are age-related proteins that deposit in the brain — George was alluding to some of these. The two most common are the A-beta peptide and the Tau protein. The A-beta peptide isn't actually found in neurons, it's not found in any cells. It's found extracellularly, and so it accumulates in the extracellular spaces, rather than affecting any particular neuron or any particular cell. You might be dismayed to know that at least 50% of the population surviving to older age will have an extracellular deposit of these A-beta peptides, but not 50% of the population has a disease of the brain. While Tau's the same, it's a microtubular associated protein that's important for your axon stability and most people — even young people — will have some Tau deposition in their brain. Protein depositions do occur in the brain with ageing, but not all of the people that have protein depositions will have any significant neuronal loss.

Neuronal loss is a prerequisite for a neurodegenerative disease. I've got a map of the normal age-related Tau distribution, and 50% of the population will have some Tau deposition at the age of 50, so I assume everyone in this room some Tau deposition. I don't think it's bad — it's how much you have that's a problem, not how little. By age 80, 70–80% of the population will have some Tau deposition. This is really a normal age-related protein that deposits in

some of the neurons in our brain, and we can all look forward to having it. It starts as early as before age 20, so people can have it very early. It doesn't necessarily mean they're going to get a degenerative disease. It's how many you have. You need to have lots of tangles to have dementia.

We can say exactly the same about the extracellular protein, A-beta. 50% of the population by the age of 70 will have some of that in your cortex, so again it's an age-related protein deposition and it's how much you have and how it might affect the neuronal populations associated with dementia.

Is a little bit of abnormal protein deposition enough?

A little bit of the abnormal protein is probably not enough: it's the amount of protein, but also other things that happen. Two detailed studies looked at people who had only mild cognitive impairment (MCI). While some people didn't have any cognitive impairment, they were followed over time. These people are thought in the literature to have a lot of these protein depositions in the brain, but 74% did not have enough protein deposition in the brain to have a neuronal problem, such as Alzheimer's disease. More had cerebrovascular pathologies, and they did have Tau, but as I said, lots of people have Tau. 2.2% had other pathologies (non-Alzheimer's) and 25% had some Alzheimer-type pathologies that Tau and A-beta. The majority didn't have what we would have expected to have as their primary underlying pathology associated with what people think of as dementia in terms of Alzheimer's disease. This suggests — and it's much more prevalent — that just having the

Tau and the A-beta is not sufficient, and in most instances you will have multiple proteins going wrong or having a vascular in problem as well. You have to have multiple things happening in the brain for it to have an effect on neuronal degeneration. It's the severity and the numbers of pathologies.

Now the other thing is that there are distinct glial changes that also happen in these neurodegenerative diseases, which no one really talks about much. In fact, the glial pathologies are more likely to be distinct between the different types of diseases. For example, there are inclusions of alpha protein in oligodendroglia, which is a synaptic protein, and there are the myelinating cells in the brain. We have a protein in an abnormal position in cells that we usually wouldn't see these things. There are astrocytes in patients that have Parkinson's Disease. Now the neurons with the astrocytes are probably not working properly because they have an abnormal protein. The neuron is probably not working properly because its astrocytes are a problem, more so than the neuron itself.

Hence, glia are affected. And then there's completely different types of Tau that happen in different types of the astrocytes in the brain. These are all different types, such as primary tauopathies with astrocytes. The actual neurodegenerative disease is defined by their astrocytic pathology. ARTAG is a very familiar pathology that's seen in chronic traumatic encephalopathy. You'll hear a lot more about astrocyte changes that are to do with longer-term cognitive changes in the brain of people who have had environmental impacts in terms of head injuries or sporting injuries.

Glial cells in the brain are most affected by ageing but neuronal loss defines degenerative diseases

Glia cells are the most affected in the brain with ageing. But neuronal loss and a lot of the cognitive changes are because neurons don't connect, don't fire properly, and the neuronal loss defines degenerative diseases.

To conclude, if we now think about what this might mean, brain ageing mostly affects the white matter, while neurodegeneration mainly affects grey matter structures (in degenerative diseases it's regional). The type of neuron or the function of the neuron is important. Mechanistically that suggests that the connectivity between regions is probably key to disease vulnerability. These are all age-related neurodegenerative diseases, so having a problem with the white matter and the glial connectivity is a predisposing factor. Humans have evolved larger syncytiums of astrocytes and myelinating oligodendrocytes. Mechanistically that suggests that these syncytiums are important cognitively. Something that hasn't been looked at so much: age-related neurodegenerative diseases all have abnormal protein depositions, and the neurons are largely resistant to increased amyloid and Tau protein depositions with ageing. Mechanistically that suggests that there's additional cell or tissue changes needed to have neurodegeneration. There are distinct glial cell pathologies that define most neurodegenerative diseases, which is largely still ignored. Mechanistically this supports important roles for glia in neurodegeneration and suggests that pathological dysfunction of different glia impact differently on these neurodegenerative diseases.

Turning the tide on dementia: prevention, diagnosis, treatment and quality of care

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Thank you, Glenda, for the setting the scene on dementia. I will fan out from here and want to bring to your attention some key issues and opportunities we have in the field at the moment. It's an exciting time to be working in this field, but we do have many challenges ahead of us in terms of how to deal with the increasing number of dementia cases that are set for us.

Globally, there's about 50 million people with dementia. There's 400 to 450 thousand in Australia, but there's an extra 1 million people who have what we call mild cognitive impairment (MCI). This is what could be deemed to be a prodromal stage for dementia. If you have mild cognitive impairment, you show cognitive deficits on the awful tests that we neuropsychologists give you, and about 45% will progress to dementia within 5 years. This is an important period because this is an opportunity for us to think about prevention strategies.

Dementia now overtakes heart disease as a leading cause of disease burden in those over 65. Interestingly, a third of the dementia population live in regional and rural areas of Australia, the prevalence of dementia is three to five times higher among Indigenous Australians, and they also get dementia earlier. $3 billion of Australia's health and aged care expenditure is spent directly on dementia, and there are lots of other indirect costs.

Dementia prevention

First, I want to talk about prevention. Glenda told you about the different types of dementia pathologies, so this is the umbrella term that we use for all the different types of dementia. There are a couple in particular that I'll focus on in this talk — Alzheimer's disease and vascular dementia — these are the ones where there are some risk factors that can be modified. There are two key things to consider when thinking about dementia prevention — again, everyone in this room should be thinking about dementia prevention from midlife, actually even earlier. Certainly we know that the pathological changes that occur in the brain prior to dementia are building up 10 to 20 years before someone ever attends a memory clinic or presents to their doctor with symptoms.

There are many changes in amyloid — the sticky kind of plaque substance that builds up in the brain with Alzheimer's disease. We have changes in the synapses of the brain. We have Tau accumulating. And then we get changes in the structure of the function, and then eventually changes in cognition.

What we know about this is that about 40% of the risk for these types of dementias is due to things that are modifiable and can be mapped across the life course. There was a great paper in 2020 in *The Lancet*, com-

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missioned by G. Livingston,[2] that identified all of these risk factors and that built on prior epidemiological work looking at the population-attributable risk of these risk factors. The big ones we need to consider are: depression; many different types of diseases linked to cardiovascular disease; hypertension in midlife; cholesterol in midlife; and alcohol.

Regarding alcohol, the epidemiological data suggest more than 21 drinks a week — that's a lot: many people are relieved by that in relation to dementia, but some of the imaging data suggests that perhaps it's a little bit more nuanced than this — may affect the white matter and we should really be thinking about much lower levels of alcohol than that. So the jury's out on that.

Other factors we need to consider are obesity, smoking, social connectedness and social network working in urban planning — these are all important. New factors that have emerged are air pollution which accounts for about 2% of dementia risk, as well as hearing loss. A recent trial showed that if people have cognitive impairment and hearing loss then the cognitive impairment could actually be slowed. It's important to think about all of these risks if we want to take a public health perspective for dementia.

Dementia prevention is everyone's business so we should be thinking about how to create guidelines for dementia prevention. We know a lot about heart disease and what we should do to prevent it. In dementia, the best thing we can do is say, "Follow what the Heart Foundation says because everybody knows that." But no one knows that dementia is actually a multifactorial disease and we

really need to be educating the public about what we could be doing. We need to be able to implement, in a memory-clinic setting, what people could do to slow their disease and to build a better evidence base around that and to involve consumers in that: people with diverse cultural backgrounds, Aboriginal Torres Strait Islanders. We have a lot to do at the systems level to improve the services that we provide.

You may or may not have had experience of someone with dementia going to a memory clinic, but typically they're told to go away and get their affairs in order, and not much is provided to them after that. We need to improve what we're doing for health advocacy, also work closely with governments and with policy advisors generally, and have greater connections with the non-government organisations such as Dementia Australia, to get this message out.

Australian Dementia NeTwork (ADNeT)

We also have some new challenges and opportunities in the diagnosis, treatment, and care for people who have established dementia. Once you already have symptoms of cognitive decline, you might typically go to a GP or, if you're lucky, you'll get to go to a memory clinic and have a much more detailed assessment. We've realised that in order to tackle this on a national level we need to unite what we're doing across the fields of diagnosis and treatment. We're very fortunate to receive a grant by the NHMRC for $18 million to bring together many researchers working in this field across Australia, and we established a clinical quality registry, also a screening and trials

2   Livingston G et al. (2020) Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *The Lancet* 396: 413–446. https://doi.org/10.1016/S0140-6736(20)30367-6

program, working closely with pharma, and also a memory clinic setting which is more health-system-service focused.

The clinical quality registry

The clinical quality registry has been running now for about 3 years and it received continued funding from the government to essentially create a register of people presenting to memory clinics with mild cognitive impairment or dementia. We have 77 sites across Australia that are participating in this, so that we can track the quality of care provision to people presenting with cognitive decline, and so we can create a loop of feedback to continuously improve services for people who are going to a memory clinic or indeed experiencing any type of diagnostic services. This is really to benchmark the clinical practice — it includes people living with dementia and also their care partners. We have a component where we get feedback about the service that they've had. Data from other initiatives internationally have shown that this drives improvements in care. Data are provided to each clinic that participates and, in turn, goes back to their service providers, to change staffing levels, change the way things are done, or change the systems, and also to measure the impact of new treatments on progression. So far we've managed to look at the waiting times across the clinics in Australia in terms of how many clinics are able to offer appointments within 90 days, which is a long time internationally: in the UK, Canada, and other parts of Europe, people get appointments within six weeks and that's considered their gold standard. We got a lot of push-back from the clinicians in Australia around this because they know it's just not feasible. Our memory clinics

run like half a day to a day a week. But in Europe they run every single day of the week. I would advocate that that's the scale that we need to go to in order to reduce our waiting times, and certainly increase our capacity.

Memory clinics

We achieve a number of markers and look at the composition of who's actually attending the memory clinic. About 30% of people have mild cognitive impairment. Moreover, the cases that are seen in the memory clinics are typically more complex cases: they might have non-Alzheimer's forms of dementia or might have a much more complicated history. Many people here are used to running memory clinics and so are very familiar with these kinds of presentations, but it's certainly expected that the bulk of dementia presentations will still occur in primary care.

The memory clinics initiative works closely with the clinical quality registry team. And I guess the role that we have is to work closely with government to try to increase services for people attending memory clinics.

To date we've had no national guidelines of how memory clinics should run. We've had many consultations, stakeholder meetings with clinicians, service providers, policy makers on how a memory clinic should run: what should the waiting times be, what should be provided — you'd be surprised to know that no follow-up was mandated or provided for a person diagnosed with dementia — so now we have guidelines for that. Moreover, looking into how we can actually improve post-diagnostic care, we've looked at what kind of care is provided when someone attends the memory clinic; despite spending hours with a neuropsychologist doing assessments, no

interventions were ever provided. So there has been some work — over a decade ago at the Brain and Mind Centre, we looked at cognitive interventions, and asked do they actually help older people who are experiencing cognitive decline? There's now a massive evidence base. Meta-analyses around the world show that you get about a 0.4 effect size improvement in memory with a cognitive intervention, yet people in memory clinics cannot access these. We have a massive evidence-to-practice gap in these areas. For the first time we've mapped all the memory clinic services across Australia. These are available on the Australia Dementia network (ADNeT) website so that GPs, and people experiencing cognitive decline, know where to go if there are any out-of-pocket costs, and also what kinds of services they can expect, and what kind of languages services are available.

Interestingly, for our field we've had some advances in diagnostics, so the typical way to get a definitive, gold-standard diagnosis for Alzheimer's disease is to have not only all of these clinical assessments but also a PET scan looking at the amount of myeloid that you have in your brain. As Glenda said, you'll have it but there certainly needs to be a threshold that you would reach that would give you a diagnosis of Alzheimer's disease. A clinical diagnosis would be the clinical symptoms plus evidence of the disease on PET scans. These have been largely inaccessible — in Melbourne, for example, you can get PET scans, but you can't get them in Sydney, and there is one centre that will do them clinically. It costs about $1,500 so it's certainly out of reach of many older Australians.

Advances in diagnostics: Blood-based biomarkers

There have been advances in detecting Alzheimer's disease by looking at blood samples. Glenda told you about Tau, a very important protein associated with transport in the microtubules. In Alzheimer's disease the Tau is hypophosphorylated, and it's aggregated and mislocalised, and you can find fragments of Tau in the blood. Even though we're looking for Alzheimer's disease, and the earlier signs of that are amyloid, it actually correlates very well with the amount of amyloid that you'll see on a PET scan. These levels are quite specific for Alzheimer's disease but we can use these levels to determine if someone does indeed have Alzheimer's disease, and therefore have greater diagnostic accuracy. This is important because there are new treatments that are coming along that target amyloid specifically. It's really important that we get the diagnosis right. Typically about 40 to 60% of clinical diagnosis in memory clinics can be wrong because we don't really know the underlying pathology. As Glenda said, often cerebrovascular pathology underlines someone's dementia — it's not necessarily always Alzheimer's disease. At the Brain and Mind Centre we're leading a trial where we'll be looking at implementing these blood-based biomarkers into the memory clinic. We want to have a look at what the impact is on clinicians' diagnoses and management of the disease. That's important for trying to advocate for reimbursement of these kinds of tests for Medicare etc., and to be able to roll them out across Australia and importantly into regions where they don't have good services.

New horizons for MCI and AD: Monoclonal antibodies

The other big development in the field is that we now have drugs for Alzheimer's disease. The results of the trial with Lecanemab were released last year at a conference in San Francisco. It was a very exciting time for the field because for the first time one of these anti-amyloid drugs was given and shown to clear the amyloid from the brain, as observed from the PET scan, but also to slow the rate of cognitive decline by 27% and slow the changes in quality of life by 35%. There were lots of other biologic markers of changes in the disease course. The big concern with these drugs is that there are side effects. You can get bleeding in the brain, which is a big concern for us at the moment. Nonetheless, Lecanemab has now got FDA approval in the US and is being rolled out in the US across many centres. There is also approval in Japan and I believe one place in China has approval as well. It has been submitted to the TGA in Australia and in 2024 will undergo evaluation for PBS reimbursement.

Later the results of the Donanemab trial, the Trailblazer 2 study, were released. This had 1,700 people across eight centres. On the same measure that was used in the Lecanemab trial, it actually slowed cognitive decline by 55%, but they used a different outcome measure. They also showed that it if you equate it to kind of a delay in clinical presentation, about 4.4 months delay in disease course was achieved by the drug and 47% of people remained stable on the drug, whereas in the placebo group it was about 29%. Regardless of that, there has been some question about how clinically meaningful this change is in the disease course: there is

a risk of the bleeding in the brain; it has to be monitored very, very closely; you need to have an MRI scan at the outset, and a PET scan or a lumbar puncture — which people in Australia don't really like to do. It's done very commonly in Europe and in the US, but you need to have infusions every fortnight and you need to have about five MRI scans over the course of the treatment. The treatment without PBS approval will be about $30,000 a year, so it's quite a significant investment, and certainly the cost to the health services — administering and coordinating these — is significant. We don't really know yet in Australia what our capabilities are to be able to deliver these drugs. We think there are probably very few centres in Australia that have the combination of PET scans, CSF scans, clinical trials, suites with infusion capabilities, expertise in neuroradiology, as well as the patients coming through, so I think we have some time to get used to this but we will need to think seriously about if this does get approved by the TGA. How do we actually roll it out to Australians? And even more so if it gets listed on the PBS.

Delays in diagnosis

A bigger problem is that we have massive delays in dementia in Australia, so it takes someone about 3 to 4 years from the time they first present to primary care or tell a doctor about their symptoms to get a diagnosis. Some people might say, "Well, why would you want to get an early diagnosis of dementia?" But the data actually show that it is important. People do want to know — it informs their choices about their future, including financial and legal matters and other things they may want to achieve

in their life. Moreover, data show that if you get an early diagnosis — particularly if it's a multidisciplinary diagnosis, such as you get in a memory clinic — you'll have a longer duration of independent functioning at home, and so delay admission into aged care facilities. There are many contributors to poor diagnoses, including poor awareness of symptoms, the stigma associated with dementia, reluctance to seek help, therapeutic nihilism, difficulty recognising dementia, and limited access to specialist expertise from GPs as well.

Bottlenecks in primary care

About 50% of cases in primary care go undetected. As you might imagine, GPs are very time-pressured, they don't have very good tools for detecting dementia, there's a lack of specialist support. We've done a bit of a deep dive into the Medicare items for dementia, and it's quite impossible for GPs to make any money out of diagnosing someone with dementia, in terms of what their reimbursements are, in terms of needing to talk to family members, knowing what test to get, and the time taken. So there's not really many incentives for GPs to do this. The memory clinics of course are better set up for this.

Bottlenecks in memory clinics

It is expected that we will start to see an unprecedented demand, not only because we have a better ability to detect Alzheimer's disease using the blood test, but also because of the drugs that are coming along. We have mapped in Australia what our capabilities are in terms of memory clinics: there are only 54 publicly funded clinics across Australia. We estimate that this probably serves only about 4.8% of the population

with mild cognitive impairment, and that is health-seeking people with mild cognitive impairment. These are not the community-based prevalence studies. If you add in the private clinics, then we still have an unmet need of about 87%, not including people in the 50- to 65-year-old age range, who also have the earlier onset dementias and may also have a pre-clinical Alzheimer's disease emerging in the brain. Certainly the drug studies, the anti-amyloid drugs are beginning to target people earlier and earlier, so the clinical trial data show that the earlier you give these drugs, the better the treatment response is, so it may well be the fact that we are targeting people in the future, before they even get any symptoms and even come to the doctor, but they have amyloid in their brain.

Bottlenecks by region

A third of the dementia cases are in regional areas, but only 10% of our memory clinics are in regional areas. Hardly any clinics have access to neuropsychology, so certainly no capacity to detect people with mild cognitive impairment, and many of our colleagues say that it may only be about 0 to 5% of their cases, as compared to the 32% that you'll see in the metropolitan areas. As you might expect, the presentations occur very late — often the doctors in regional areas receive referrals very late when the patients have behavioural symptoms of dementia — and there's little that can be done for someone at that stage. It's a very reactive kind of service that they're getting.

New virtual memory clinics

We are working with the Department of Health on developing some new virtual memory clinics so that we can conduct

hybrid models of virtual assessments combined with face-to-face assessments. We'll be starting our first trial in Echuca in Victoria, and then expanding into three areas of New South Wales as well as South Australia. The last part of ADNeT is the screening and trials initiative — this is working closely with pharma to recruit people from the community who are concerned about their memory. We've now characterised about 1600 people who have had in-depth phenotypic assessments using MRI and PET scans etc, and also detailed cognitive tests. This is because we're usually not well placed for conducting clinical trials in Australia in terms of recruiting people, so it is a database of people that then can be offered the opportunity to participate in clinical trials very quickly. We also have a volunteer portal — people can sign up to engage in research. We're doing a lot of work in trying to better understand these new plasma biomarkers and how they could be applied at the community level, and ultimately if they could be applied in primary care. That would be perfect and certainly help the roles of GPs much more.

So lots of considerations for health services and policy planning. We need to think about our workforce, we need to think about dementia prevention and earlier screening, we need to think about how we give people better diagnostic support, offer cognitive interventions and other interventions in the memory clinic setting, we need to think about greater diversity of the people that we service, and how to reduce stigma in the community so that more people do come forward when they have early signs, and working closely across primary care and all health as well.

In summary, we have many challenges and also some great opportunities. We're at the beginning of some exciting developments in the dementia field. It's very early days, but I think within a decade or so we should have developed some of these things much further and be ready to better treat people earlier and also save the government lots of money, which of course they always like to hear about. I'd like to thank the team at ADNeT and also the team at the Brain and Mind Centre and Charles Perkins Centre for their support.

Viruses and pathological brain ageing: a challenge we must confront

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Abstract

The neuropathological mechanisms that lead to dementia start decades before the full expression of the disease, and even childhood brain and mental health play a role. It is therefore important to determine what are the risk factors for dementia across the life span. While a wide range of risk factors has been considered in clinical studies, the role of pathogenic viruses as unique or contributing risk factors has been relatively neglected. The COVID-19 pandemic has dramatically changed this situation. This article provides an introduction on how viruses may play a role in the aetiology of dementia highlighting the best researched example: Herpes Virus Simplex (HSV)-1. Next, relevant research in the HIV and COVID-19 epidemics is provided emphasising the complex interplay between acute, chronic, latent phases of the infection and the immune system in promoting pathological brain ageing. As both dementia and viral infections are global health issues, the compounding impact of socio-economic and health disparities in impacting the brain health of most vulnerable people is also stressed. Research on the impact of COVID-19 on brain health is nascent and should be informed by the existing knowledge of the brain health impact of other viral infections and post-viral syndromes, while taking advantage of the Australian leadership in infectious diseases research.

Introduction

Dementia is a global public health issue with impact increasing across the next decades because the global population is ageing (Dementia Forecasting Collaborators, 2022), but also because complex risk factors will come into play to potentially increase the global incidence of the condition further (Aung et al., 2019). This picture may be mitigated by early prevention and intervention (Barbera et al., 2023) as well as the availability of new treatments for Alzheimer's disease (AD) (Park et al., 2023). However, as for other global health issues, there are strong inequalities in access to dementia care (Kenning et al., 2017), intervention (Shaw et al., 2022) and dementia

trials (Vyas et al., 2018). Only a small number of Low Middle-Income Countries (LMICs) have been the site for dementia trials (Salcher-Konrad et al., 2023).

It is estimated that the number of people with dementia will increase from 57.4 (95% uncertainty interval 50.4–65.1) million cases globally in 2019 to 152.8 (130.8–175.9) million cases in 2050 (Dementia Forecasting Collaborators, 2022). Besides non-modifiable risk factors (i.e., genetic risk, age), the 12 modifiable risk factors which were considered in this study to estimate projections of the global dementia prevalence in 2050 were: low education; hypertension; hearing impairment; smoking; midlife obesity; depression; physical inactivity; diabetes; social isolation; excessive alcohol con-

sumption; head injury; and air pollution. Critically, these predictions do not consider the impact of pathogenic viruses.

Amongst the very large number of viruses (~10^{31}) (Mushegian, 2020), some pathogenic viruses' role in causing severe acute neurological disorders is well described (Swanson and McGavern, 2015; Wouk et al., 2021). Typically, such viruses have high *neuroinvasiveness*, are *neuronotropic* or/and *neurotropic and highly neurovirulent* (e.g., human enteroviruses, alphaviruses, some flaviviruses such as Japanese encephalitis virus, West Nile virus) (Johnson, 1999; Swanson and McGavern, 2015). *Neuroinvasiveness* refers to a virus that can enter the central nervous system (CNS) or peripheral nervous system (PNS). A *neuronotropic* virus is a virus that can specifically infect neurons. A *neurotropic* virus is a virus can infect various brain cells. *Neurovirulence* refers to a virus that can cause a neurological disorder (Johnson, 1999).

Neurovirological symptomatology is highly varied (Swanson and McGavern, 2015; Wouk et al., 2021). It depends on the types of viruses (how it interacts with the host), the life cycle of the virus during acute, chronic, and latent phases of the infection and in the virus capacity to enter the CNS and/or PNS (i.e., neuroinvasiveness) as well as the route of neuroinvasiveness (e.g., blood stream, peripheral nerves, nasal mucosa and anterograde trafficking to the olfactory bulb, direct or "Trojan horse" entry through the blood brain barrier). Next the damage that a virus can cause is related to the specificities of its neurotropism and neurovirulence. Viruses that directly infect neurons and are typically highly neurovirulent and have the worst prognosis, especially in children (Swanson and McGavern, 2015). By contrast, viruses that have low tropism for neurons

can lead to early onset dementia by infecting other cells in the brain, such as HIV which infects mainly microglia (Killingsworth and Spudich, 2022), the resident immune cells of the brain. A critical aspect that distinguishes acute and chronic neurological impact of viruses is also how the immune system within the brain and in the rest of the body responds to the presence of a virus (Swanson and McGavern, 2015). While an initial immune response can abrogate any health complications (e.g., most people with COVID-19 infection), an exaggerated immune response may lead to severe acute meningitis and encephalitis with long-term complications (e.g., stroke), as has also been described for SARS CoV-2 (Ellul et al., 2020). The acute immune response may also provoke a chronic immune dysregulation, where the long-term interactions of the virus with the immune system promote neuroinflammation (Wouk et al., 2021) — the latter being a major driver of neurodegeneration (Zhang et al., 2023). Some viruses establish long-term viral reservoirs (e.g., HIV, HSV-1, Epstein-Barr virus, cytomegalovirus) in various parts of the body. Under various circumstances, the latent virus can be reactivated, leading to a potential role in the development of chronic immune activation, inflammation and neuroinflammation (Wouk et al., 2021).

The impact of some pathogenic viruses on brain health is also contingent of their endemic, epidemic or pandemic status as well as the capacity to treat them with antivirals or prevent with vaccines. In any case, many viruses have large societal impact with greater health impact on the ageing population and other vulnerable people as seen during the COVID-19 pandemic, including in Australia (Australian Bureau of Statis-

tics, 2022). Even when antiviral treatment is available, as in the case of HIV infection, societal impacts continue as treatment access inequalities are not easily resolved (Ferguson et al., 2022). These considerations are important because dementia prevalence has regional variations (Dementia Forecasting Collaborators, 2022). The smallest percentage changes in the number of projected dementia cases between 2019 and 2050 are in high-income Asia Pacific (53% [41–67]) and western Europe (74% [58–90]), and the largest are in north Africa and the Middle East (367% [329–403]) as well as eastern sub-Saharan Africa (357% [323–395]). Relevant to the prevalence of viral conditions globally, these projected regional dramatic increases overlap with regions of the world where the HIV epidemic is the most prevalent and where other viruses are endemic (e.g., dengue and chikungunya). These regional variations are also important because of the way viruses interact with the immune system. In LMICs there is a higher rate of baseline immune compromise (Petoumenos et al., 2017), and higher background level of immune activation linked in part to a higher exposure to common viruses (Yap et al., 2017). As mentioned, viruses can directly injure the CNS, but viruses also perturb the CNS due to the immune response in the brain and other parts of the body. The consequence of this cascade of events is only partly understood, especially in relation to brain ageing, and the processes of brain injury that are known to cause dementia (i.e., vascular brain injury (Cysique and Brew, 2019)). Finally, with global climate change, more regions of the world will be impacted by endemic viruses (and other pathogens), and more frequently (Boguslavsky et al., 2022), further highlighting the importance of considering viruses as risk factor for dementia and brain health in general.

Globally prevalent pathogenic viruses and their role in the aetiology of dementia, Herpes Simplex Virus-1 (HSV-1) as a proof of concept

The hypothesis that viruses (and other pathogens such as parasites, bacteria, and fungi) play a role in the pathogenesis of dementia and AD is not novel. It dates to the early 1900 as proposed by Alois Alzheimer and Oskar Fischer (Vojtechova et al., 2022). In this regard, among the human herpesviruses, the best studied is HSV-1. HSV-1 is a neurotropic virus. Primary infection usually occurs during childhood and 60–70% of individuals under 50 years of age are infected with HSV-1 worldwide (Marcocci et al., 2020). After primary infection of epithelial cells, the virus becomes latent in neurons of the PNS and can be periodically reactivated. It then traffics to the CNS resulting in recurrent clinical or subclinical episodes throughout life. Repeated HSV-1 brain reactivation may result in neuronal damage that resembles the neurodegenerative mechanisms of AD, suggesting a unique and direct neuropathological role of the virus within the brain (Marcocci et al., 2020). HSV-1 reactivation triggers an inflammatory process, causing damage to the cells, along with formation of amyloid plaques and neurofibrillary tangles. Supporting a role of HSV-1 in the aetiology of AD are retrospective longitudinal studies, some with case-control designs (Marcocci et al., 2020) which show that anti-HSV antibodies in the plasma are associated with an increased risk of AD more than 6.6 years before diagnosis. Furthermore, clinical research shows that the historical

viral burden can impact current cognition, and that reactivation of HSV-1 due to age-related immune compromise is a dementia risk factor (Wouk et al., 2021). However, the significance of this research is hampered by retrospective analyses from cohort studies which were not initially designed to assess the question of virus-related brain injury, so that the strength of such results remains debated (Piotrowski et al., 2023). More interesting are findings which show that amyloid beta (the neurotoxic protein which accumulates to promote AD pathology, "the amyloid hypothesis" (Chen et al., 2017), is an antimicrobial peptide, protecting the brain against pathogens (Vojtechova et al., 2022). Recent *in vitro* and *in vivo* studies show that microbial infection can increase amyloid beta production and aggregation (Piotrowski et al., 2023). As such, in case of a prolonged or chronic immune activation, and especially in the context of an ageing immune system, amyloid beta accumulation and aggregation may promote (Vojtechova et al., 2022) or compound (Aung et al., 2019) neuroinflammation and eventually neuro-degeneration.

Globally prevalent pathogenic viruses and their involvement in the aetiology of dementia — the case of HIV

Human immunodeficiency virus type 1 (HIV) is a lentivirus which primarily infects immune cells (CD4+ memory T cells) leading to acquired immune deficiency syndrome (AIDS) if untreated. Without treatment neurological disorders are common as the disease progresses to AIDS (up to 50% including HIV-associated dementia, HIV-associated neuropathy, aseptic meningitis, seizures, vacuolar myelopathy, headache, and different movement disorders as

well as opportunistic infections affecting the CNS) (Mohammadzadeh et al., 2023). With early treatment, severe neurological manifestations are rare. However, the prevalence of mild forms of neurocognitive deficits (called HIV-associated neurocognitive disorder: HAND) persists and is more frequent in people living with long-term infection and ageing, those with historical AIDS, and those with age-related comorbidities as well as those with greater mental health burden (Saloner and Cysique, 2017). Importantly, the greater frequency of age-related comorbidities is in part related to the chronic presence of HIV in the body, which is thought to be associated with chronic immune activation (Falutz et al., 2021). Other factors for greater frequency of age-related comorbidities in the HIV population include lifestyle (smoking, alcohol and substance use — higher than in the general population, the effect of widely used antiretrovirals which are toxic for cardiac and renal functions), and the effect of health disparities globally. HIV is treated with a lifelong combination of antiretrovirals suppressing the viral replication at several stages of the replication cycle. HIV is a retrovirus, meaning that it integrates into the host DNA. If the antiviral treatment is ceased or interrupted, replication of the virus rebounds within two weeks, demonstrating that the virus is only controlled by the treatment but not eradicated. Rebound is thought to originate from specific anatomical and cellular viral reservoirs in which viral DNA persists integrated into the host genome. There is a debate as to what extent the brain represents a competent and partly separate viral reservoir, although there is increasing evidence that the CNS harbours competent proviruses — that is, HIV DNA

capable of starting to replicate if treatment is interrupted (Mohammadzadeh et al., 2023).

HIV enters the CNS soon after infecting the rest of the body directly or via a Trojan horse mechanism carried by infected T cells through the blood brain barrier. Without treatment, the activated resident immune cells, microglia, lead to severe brain inflammation and eventually neuronal death. Moreover, monocytes and macrophages continue to transport HIV into the CNS during chronic infection (Gelman, 2015). With treatment and viral suppression, T-cell infiltration of the CNS may include resting memory T-cells and represent another CNS cellular reservoir for HIV. Recent research also shows that a small proportion of astrocytes may also be cellular reservoirs for HIV (Mohammadzadeh et al., 2023). Very recent research from an Australian group (Angelovich et al., 2023) shows intact proviruses are primarily found in the brain frontal white matter but also detected in other brain regions, demonstrating that the brain is a major reservoir of intact and potentially replication-competent HIV DNA that persists despite antiretroviral therapy. Nevertheless, replication of this research is needed. The persistence of HIV in the CNS can lead to neuroinflammation, and there is also evidence that it is associated with increases vascular brain injury. In fact, evidence for increased risk of AD is low in people with suppressed HIV infection, however evidence for increased cardiovascular and cerebrovascular diseases is high, and thus represents a much more likely neuropathological mechanism of brain ageing than AD-like neurodegeneration (Cysique and Brew, 2019). However, this research only includes individuals aged their mid-fifties;

therefore, a note of caution is warranted, as studies in people with HIV infection in their seventies do not yet exist, and it is well recognised that vascular brain injury at that age is a major risk factor for dementia in the general population (Chowdhary et al., 2021). Systemic (impacting the brain-blood-barrier function (Galea, 2021)) and brain-based chronic immune activation is well described in people living with HIV, despite successful antiretroviral treatment (Ulfhammer et al., 2018). This process is now considered lifelong, as the first generation of people living with HIV now reaching old age has been infected for 40 years. Within the brain, there is evidence that residual HIV replication is possible, because the brain is "separated" from the rest of the body by the blood brain barrier and because antiretrovirals do not all penetrate the CNS in sufficient concentrations (Dahl et al., 2014). Although this is less likely with the most modern treatment (Mohammadzadeh et al., 2023), this is not available to most people living with HIV across the world who commonly still receive less CNS effective therapies, but also more toxic therapies for longer (Vos and Venter, 2021).

In this context, my research group and others are assessing whether HIV infection may be a potential model of premature, accentuated, and accelerated chronological and biological ageing — *ageing being the number one risk factor for dementia* (Aung et al., 2019). Premature cognitive ageing is younger-onset cognitive impairment as compared to same-age controls, while accentuated cognitive ageing refers to greater severity of cognitive impairment compared to same-age control (Aung, Aghvinian, et al., 2021). The strongest evidence for premature and accentuated ageing of

brain function in people living with HIV comes from neuroimaging research which cumulatively shows that the brain structural health (i.e., lower and less complex structural volumes), the brain bioenergetics, neuro-axonal health and vascular health are not only more impacted on as a function of age and HIV status, but are also more likely to present clinically significant deterioration than age-matched controls (Boerwinkle et al., 2021; Pfefferbaum et al., 2018; Samboju et al., 2021). When considering truly accelerated brain ageing, representing a synergism (i.e., cognitive ageing is worsening over time in people living with HIV more so than in age-matched controls (Aung, Aghvinian, et al., 2021)), there are results showing no acceleration of brain ageing (Cole et al., 2018) in cohorts aged in their mid-50s, but concerningly more recent data in people living with HIV aged 60+ show accelerated brain ageing (Pfefferbaum et al., 2018). Overall, in terms of cognitive ageing, while the literature was initially more mixed (Aung, Aghvinian, et al., 2021), there is now increasing evidence for a premature ageing effect (Aung, Bloch, et al., 2021; Aung et al., 2022). More evidence for accelerating cognitive ageing will require large samples and long-term follow-up in people reaching the exponential age of dementia increased (i.e., 65+) (Aung, Aghvinian, et al., 2021). Furthermore, in the context of highly morbid cohorts (poverty, multiple health disparities, chronic trauma, high level of psychiatric and substance use in addition to age-related multimorbidity and co-infection mainly to Hepatitis C virus), detecting premature, accentuated, or accelerating ageing is challenging (Heaton et al., 2022) and has led some to state that comorbidities explain all issues of brain ageing in people with HIV, but not HIV itself when it is treated (Nightingale et al., 2014). However, in such instances, the effects of age-related and other comorbidities likely mask any HIV-related chronological age effect, as these comorbidities are linked to biological ageing (Mehta et al., 2021).

The role of the viral reservoirs in the promotion of abnormal cognitive ageing in people with HIV remains to be specifically studied, but there is evidence that ongoing viral activity in the cerebrospinal fluid is associated with brain injury (Suzuki et al., 2022). As a model of abnormal ageing, chronic and persistent HIV infection can be conceived as a "multi-hits" model, and can inform understanding of other types of viral infection in how they may lead to, or promote, dementia (Al-Harthi et al., 2020). In such models (Aung et al., 2019), the life cycle of the virus (acute, chronic, latent, reactivation, reactivation of other viruses, co-infections) and the timing of treatment (early/late) across the life span (senescent immune system, rise of dementia in the general population) is hypothesised to contribute to both non-modifiable (mainly age, background neuro/inflammation, interaction with genetic factors) and modifiable factors relevant to the HIV population globally (education, cardiovascular and other age-related systemic diseases, life style such as smoking, alcohol and substance use, mid-life metabolic changes partially linked to the duration of toxic antiretroviral use, high mental health burden, social isolation and stigma worsened by ageing, and health disparities). It is critical that this research receives continued support as 37 million people are living with HIV worldwide, most of them in LMICs. Lastly, research in people entering their 70s will be needed as these ages are associated with exponential

prevalence of dementia in the general population. Members of the HIV community and some researchers are worried about the added stigma of dementia risk in people living with HIV (Nightingale et al., 2023), but my research group (Aung et al., 2023) and others internationally believe that early detection and prevention as for the general population represents the best strategy to minimise a potential major public-health issue and added suffering for ageing people living with HIV. In this context, a larger part of the HIV community has called for urgent support and funding of aged care services in people who are ageing with HIV (International Coalition of Older People with HIV (iCOPe HIV), 2022).

Globally prevalent pathogenic viruses and their involvement in the aetiology of dementia — the case of SARS CoV-2

Early in the pandemic, neurologists and neuropsychologists with expertise in infectious diseases recognised that SARS CoV-2 had more than respiratory consequences (Cysique et al., 2021; Ellul et al., 2020). COVID-19-related encephalopathies and cerebrovascular disorders are one of the most significant acute neurological complications of SARS CoV-2 (Singh et al., 2022). Such acute viral conditions have a long-term impact on the overall and brain health of patients, while a history of strokes is a known dementia risk factor (Kuzma et al., 2018). As such, it is not surprising that SARS CoV-2 infection has been associated with rapid progression of dementia in individuals with pre-existing cognitive impairment (Dubey et al., 2023). This is to be understood in the context where people with dementia are more likely to contract COVID-19 due to difficulties in understanding and main-

taining safe COVID-19 practices, being in nursing homes, and social isolation (Quan et al., 2023). Besides having a history of COVID-19 infection, factors linked to the COVID-19 pandemic — reduced exercise, increased alcohol use, social isolation, depressive symptoms, mild cognitive impairment — have been associated with cognitive decline in older adults (Corbett et al., 2023).

A systematic review and meta-analysis on added dementia risk in people who had COVID-19 shows that SARS-CoV-2 infection may be associated with a higher risk of AD, dementia, and Parkinson disease in post-COVID-19 survivors, compared with contemporary controls and other respiratory tract infections (i.e., influenza) (Rahmati et al., 2023). SARS-CoV-2 infection may also be associated with a higher risk for new-onset neurodegenerative diseases in recovered COVID-19 patients. Moreover, this review shows that individuals aged ≥65 years and infected with SARS-CoV-2 have a larger risk difference than those aged <65 years for developing dementia, corroborating the interaction between chronological age, viral infection, and dementia risk. Interestingly, the review did not find that being hospitalised or admitted to ICU represented a risk factor for dementia, but caution should be used in interpreting these results, as they are likely affected by survivor bias. In addition, most of the reviewed studies included patients from the early wave of the pandemic (Alpha, Delta). Most studies had also a short follow-up period (i.e., 3 months–2 years) — much shorter than what is needed to study dementia conversion, especially in consideration of the heterogeneity of patients involved and varied methodological assessments. In fact, the new-onset risk

was only derived from four original studies. Altogether, more research is needed to determine whether SARS CoV-2 uniquely contributes to new-onset neurodegenerative diseases (Charnley et al., 2022).

Viruses of the Coronaviridae family such as SARS-CoV-2 are single-stranded RNA viruses for which RNA can persist long-term (weeks–months) in a small minority of individuals, although intact virions and hence replicating virus is not found (Chen et al., 2023). Amongst the coronaviruses, SARS CoV-2 is one the most neuropathogenic because SARS-CoV-2 enters recipient cells by the binding of its spike protein to the angiotensin-converting enzyme 2 (ACE2) receptor, which is expressed by many cell types across the body and the brain (Granholm, 2023).

At least 90% of individuals who contract SARS CoV-2 are asymptomatic or develop a mild to moderate flue-like illness with primarily respiratory symptoms with recovery within 12–14 days. Risk of hospitalisation is lower with Omicron than earlier variants (0.55 (95% 0.23–1.30)) (Relan et al., 2023), which may be in part explained by raised immunity due to vaccinations and previous infections. Some studies have found that up to 20% of symptomatic, infected, unvaccinated adults need hospitalisation. Vaccinated individuals are 10 times less likely of developing a severe acute COVID-19 illness. The prevalence of severe COVID-19 illness requiring hospitalisation varies by countries, regions, age of the population and other health factors including vaccination uptake (Guzman-Esquivel et al., 2023).

Non-severe acute illness is characterised by a healthy innate immune response that aims at killing the virus, restricts its spread across the body, and induces an optimal adaptive immune response (i.e., production of antibodies capable of neutralising the virus). In individuals who develop a severe response, the innate immune response is excessive (i.e., cytokine storm) and can lead to multi-organ damage through acute respiratory distress syndrome (ARDS) and systemic hyperinflammation (Harne et al., 2023). Severe neurological consequences affect one-third in hospitalised individuals, and are characterised by severe brain inflammation (i.e., encephalopathy) and cerebrovascular diseases (e.g., ischemic stroke) (Singh et al., 2022). While there is evidence that SARS CoV-2 enters the brain, it is in relatively low quantities, meaning that it is not a highly neuroinvasive virus; however, it can infect many brain cell types, as the ACE2 receptor is ubiquitous. Severe acute neurological illness has been associated with the degree of brain infection (Granholm, 2023). Therefore, in most infected people who develop a mild to moderate acute illness, SARS CoV-2 association with brain changes is considered most likely to be mediated indirectly through the engagement of the immune system. As such, it is thought that peripheral immune activation can lead to neuroinflammation via disruption of the blood brain barrier function (Galea, 2021).

In most people, SARS CoV-2 infection resolves after about two weeks, and many are asymptomatic. By contrast, about 10–20% have persistent symptoms consistent with a post-viral syndrome that lasts from 3 months to several years. Post-viral syndromes before the advent of the COVID-19 pandemic have been well described (Sandler et al., 2021), so that this knowledge and related expertise can fast-forward research into Long COVID. The World Health Organisation

(WHO) defined Long COVID for clinical purposes as: continuing or new symptoms at least 3 months from the onset of COVID-19 infection that last at least 2 months and cannot be explained by an alternative diagnosis (World Health Organization, 2021). The most common symptoms include: fatigue with a post-exertional exacerbation (post-exertional malaise); "brain fog" including memory and attention deficits; sleep disturbance; breathlessness and other respiratory symptoms; abdominal pain; and other gastric symptoms. Risk factors for Long COVID include: female gender; being aged 20–50 years; having more severe initial disease or other medical comorbidities; and being from a vulnerable population (Chilunga et al., 2023).

Most recent studies estimating the prevalence of Long COVID in Australia state that they have used the WHO definition, but they have done so using different tools, producing various rates depending on the sample and ascertainment methods. Furthermore, the WHO definition is a clinical definition which aims at managing Long COVID and related symptoms independently of the specific aetiology, which means that this definition cannot strictly exclude non-COVID causes of Long COVID. A more robust research definition is needed as advocated by the Australian Partnership for Preparedness Research on Infectious Disease Emergencies (APPRISE Long COVID Initiative, 2023) and grounded into the post-infective/post-viral syndrome framework which has validated assessment tools and methods to classify post-viral syndrome such as Long COVID including into specific symptomatic clusters (Sandler et al., 2021). One Western Australian study yet to be peer-reviewed shows an 18% prevalence in

a vaccinated post-Omicron infection cohort (Mulu et al., 2023). A study from Queensland found that 21.4% of post-COVID individuals had ongoing symptoms and that this was not different from those with influenza (23.4%). International data show that persistent symptoms after COVID-19 are higher in COVID than influenza cases, but this is in hospitalised patients (Xie et al., 2024). Another study of patients accessing a national digital mental health service found a Long COVID prevalence of 10% (Staples et al., 2023). The frequency of ongoing symptoms appears lower in children and adolescents (8% in Say et al., 2021). Furthermore, vaccinations, infection-associated immunity, and the availability of antiviral treatments are contributing to less severe acute COVID and less frequent Long COVID (Howe et al., 2023). However, international data also shows that the risk of Long COVID remains and may be increased with repeat infections (Bowe et al., 2023). Again, more definitive research is needed and coordinated at the national level to optimally estimate this new health condition (APPRISE Long COVID Initiative, 2023) using robust research methods to carefully exclude non-COVID-related symptoms, which are otherwise common in the general community (van der Maaden et al., 2023). Internationally, researchers are also working to develop a robust research case definition of Long COVID with the hope of developing targeted treatment (Thaweethai et al., 2023).

Most people with Long COVID are individuals of working age, hence the socio-economic impact is substantial. In the absence of Australian health economic data, it is noteworthy that the total economic cost of Long COVID in the US was

estimated at US$3.7 trillion (Cutler, 2022). The condition is associated with substantial disability, with an Australian Omicron-era study estimating 5200 years lived with disability (YLDs) attributable to Long COVID, greatly outweighing the 1800 years attributable to acute COVID (Howe et al., 2023). Further, qualitative research in the UK has revealed that individuals with Long COVID are severely impacted by their symptoms, heavily constrained in participating in their daily activities, and experience reduced quality of life, including negative impacts on mental health (Owen et al., 2023).

Mild cognitive difficulties (brain fog, memory, and attention deficits) are a major component of Long COVID and need to be differentiated from the acute neurological impact of COVID-19 infection which represents a severe COVID-19 complication. The mild cognitive difficulties of Long COVID do not represent a severe neurological complication, and new evidence suggests that it is another type of post-viral syndrome (Verveen et al., 2022). Long COVID-associated mild cognitive difficulties may nevertheless have a significant functional impact, as most people with the condition are of working age. Evidence for Long COVID cognitive difficulties being associated specifically with adverse impact on functional outcomes arises from our research (Cysique et al., 2023), where at four months post-infection, 22% of those with Long COVID and mild cognitive difficulties had not returned to their pre-COVID work or normal activities of daily living.

As for other infectious diseases with brain impact, in which my research team and collaborators have vast experience (Cysique and Brew, 2019; Smail and Brew, 2018), the pathogenesis of Long COVID cognitive difficulties is likely multifaceted (Wesselingh, 2023), primarily including immune dysregulation, autoimmunity, microthrombi, and some level of blood-brain barrier impairment. This pattern of chronic immune dysregulation and subtle vascular injury is reminiscent of chronic HIV-related brain injury, which is associated with low-grade neuroinflammation. Our research (Cysique et al., 2023) and that of others (Kavanagh, 2022) support a neuroinflammatory axis to the condition. Our results pinpoint the kynurenine pathway (KP) as a likely mediator of SARS CoV-2-related mild cognitive impairment. The KP is an interferon-stimulated tryptophan degradation pathway, important in immune tolerance, neurotoxicity, and vascular injury (Jones et al., 2015; Lovelace et al., 2017). The KP — including quinolinic acid, 3 hydroxy-anthranilic acid, kynurenine, and tryptophan (and ratio) — showed a *prolonged* (2 to 8 months) activation. The pattern of activation of the KP was associated with poorer cognition and greater likelihood of mild cognitive impairment over time. Importantly, no other blood biomarkers, sex, or clinical factors (pre-existing mental health or mental health during the study period, olfaction, medical comorbidities, disease severity or respiratory function) were associated with cognition. Furthermore, the biological plausibility for a role of the KP in the pathogenesis of Long COVID and associated cognitive difficulties is supported by recent findings across both basic (Wong et al., 2023) and clinical research (Collier et al., 2021; Holmes et al., 2021), including with prolonged activation which may make it more specific to Long COVID than acute COVID (Guo et al., 2023). Lastly, SARS-CoV-2 can efficiently

infect macrophages but leads to an abortive infection, and macrophages are a prominent feature of the neuropathology of COVID-19 (Balcom et al., 2021).

Conclusion

It took ten years between the discovery of HIV and the development of an internationally accepted definition of AIDS by the USA CDC in 1993. The situation with Long COVID has some similarities, although SARS CoV-2 and HIV have different neuro/pathogenesis. Such efforts require both national and international coordination as preconised by WHO (World Health Organisation (WHO), 2023). A large, nationally coordinated Long COVID study is needed in Australia, as determined by the Parliamentary enquiry into Long COVID (Parliament of Australia, 2023), like those that exist in the US, Canada, or the UK. In Australia, this is represented by the APPRISE and its OUTPOST prospective cohort "OUTcomes POST COVID", which will be recruited through existing primary care networks from June 2024 (APPRISE Long COVID Initiative, 2023). This research will be critical in determining whether Long COVID may be associated with pathological brain ageing in Australians. With the rationale of HSV-1 and HIV in promoting pathological ageing, there is a strong argument that dedicated research funding is needed for this endeavour beyond that of the Long COVID questions. Australia has in fact been a leader in infectious diseases research, with a major role to be supported across the Asia-Pacific region. The COVID-19 pandemic shows that viruses' impact on brain health with critical consideration for dementia risk research are challenges we must confront.

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Session IV: Turbocharging human intelligence with Artificial Intelligence

Moderator: Ian Oppermann

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My name is Ian Oppermann. I'm the New South Wales Government Chief Data Scientist and Industry Professor at the University of Technology, Sydney. We have a panel today of distinguished people who are versed in the art of mathematics, statistics, and artificial intelligence from various different perspectives. With us are Professor Lyria Bennett Moses, Associate Dean at the Department of Justice and Law at the University of New South Wales and also the director of the Allens Hub for Technology; Stela Solar, the director of the Responsible AI Network which is hosted by the CSIRO; and Professor Sally Cripps, one of the founding directors of the Human Technology Institute hosted by UTS and also a professor of mathematics and statistics at UTS. It's a little bit different from what we've been talking about earlier.

This panel session was devised thinking about the interaction between human beings and AI. The basic premise is that, whilst there were many factors that enabled the growth of the human brain during the evolution of the human species — access to fire, the ability to extract more nutrients from our food, movement to a meat-based diet that enabled the growth of the brain — the necessitation of the growth of the brain came about principally or partly because of the interactions of people in increasingly complex society. That's the basic premise. If we move from people interacting with people creating more complex societies to people interacting with increasingly intelligent artificial intelligent sources, the question is: what is the implication for our human brain in the 21st century?

We heard the Governor this morning say, "My brain of 25 years ago doesn't seem so terribly different to my brain in the 21st century." Interesting comment. We heard Professor Paxinos talk about the fact that the hardware of the brain has not physically changed in the last 100,000 years. But what we expect of it certainly has. And we think about Artificial Intelligence as something external that we engage with, something that is increasingly becoming sophisticated, something increasingly that can do things, specialised things, in some cases better than human beings. We saw the advent of generative AI as of November 2022: something that can do a broad range of things arguably better we can: in very strict conditions, generative AI, large language models, outcompete human beings in terms of completeness and accuracy of responses to health questions, and can also be considered to be more empathetic.

But AI is not something we just engage with externally. AI is something that increasingly we will engage with as part of us. There's a really interesting thought experiment that I heard once on a podcast where the premise was that if you took a human being and you replaced one living

neuron with a silicon neuron and there was no difference, and you kept replacing them, and kept replacing them, and kept replacing them … at some point you take away that last living neuron and replace that person with silicon. And the question is are they still the same person? It's a thought experiment, of course, and there's a whole lot of technological challenges we'd need to approach in order for that to be a real experiment. But it does raise the question: if love is not generated in the stomach, if love is not generated in the heart, if love is not generated in the brain, possibly it is generated in the brain, then possibly we could have silicon love in a silicon brain. So without further ado, I'd like to introduce our first speaker, Professor Sally Cripps.

Artificial and human intelligence for scientific discovery

Sally Cripps

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Abstract

This paper will discuss how we might develop AI systems which, together with our human brain, could transform scientific discovery. In order to do this, we need a definition of AI. AI is defined to be that field or industry which is at the intersection of data, algorithms, embedded in an application for the purpose of assisting decision-making.

What is AI?

The problem with Artificial Intelligence (AI) is its name. It either conjures up pictures of futuristic worlds with killer robots empowered by human intelligence, or is put forward as the solution to all the planet's problems. Neither claim is true, and both are unhelpful, (Brooks, 2023). These extreme views are fueled by the media. Reuters on May 30th this year ran the headline:

> Top artificial intelligence executives including OpenAI CEO Sam Altman on Tuesday joined experts and professors in raising the "risk of extinction from AI," which they urged policymakers to equate at par with risks posed by pandemics and nuclear war.

Needless to say these "top artificial intelligence executives" are not a random sample of AI experts. On the contrary, they are a very biased subset, selected precisely because they hold a particular point of view: one that makes headlines[1] But the fact that AI is over-hyped does not mean that it is not useful, nor does it mean that we should be complacent about its misuse.

This paper will discuss how we might develop AI systems which, together with our human brain, could transform scientific discovery. In order to do this, we need a definition of AI. For the purpose of this paper, AI is defined to be that field or industry which is at the intersection of data, algorithms, embedded in an application for the purpose of assisting decision-making. It will also be helpful to categorise AI techniques into two categories. The first category consists of those techniques for which the primary purpose is to make accurate predictions. These techniques will be referred to as predictive AI. They are primarily data-driven, based on neural network architecture, and do not distinguish between cause and effect. The second category consists of those techniques whose primary purpose is to untangle cause and effect, by either encoding a model about the world, or by embedding experiments within the algorithm to infer causation. These techniques will be referred to as causal AI. We note that the two categories are not mutually exclusive: causal AI techniques also give predictions and predictive AI

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[1] Expert Survey on Progress in AI found that only 5% of AI experts in 2022 (defined to be authors who publish in Neurips or ICML) surveyed stated that AI presented an existential risk.

techniques often attempt to infer causation. Both categories play important and complementary roles in scientific discovery.

Predictive AI

One of the most advanced types of predictive AI is ChatGPT. ChatGPT belongs to a class of algorithms known as Large Language Models (LLMs). It uses data in the form of written text to select the next word in a sentence. When asked to define itself, ChatGPT came back with the following:

> ChatGPT, is an example of Narrow AI, also known as Weak AI or Artificial Narrow Intelligence (ANI). It is designed for specific natural language processing tasks, such as generating human-like text responses, answering questions, and engaging in text-based conversations. ChatGPT, while highly advanced and capable of generating coherent and contextually relevant text, is limited in that it lacks a true understanding of the text it generates.

ChatGPT's acknowledgement that "it lacks a true understanding of the text it generates" is insightful. As an example of this lack of understanding consider the following example from Marcus (2022),

> If you ask LLMs to explain "why crushed porcelain is good in breast milk," they may tell you that "porcelain can help to balance the nutritional content of the milk, providing the infant with the nutrients they need to help grow and develop."

ChatGPT's response sounds authoritative and plausible, but is incorrect. The issue is that the objective function of LLMs is fluency not accuracy. ChatGPT states that its fluency is developed by "relying on patterns and information learned from a massive amount of text data during its training." This is done by a Deep Learning (DL) system that computes associations between words, in the context of a phrase or sentence. LLMs are brilliant at predicting within-sample or interpolating. The success of LLMs in doing this demonstrates that despite the complexity of language, given enough useful data, LLMs can predict what word goes next in sentence, and to construct entire paragraphs which are fluent and plausible text.

Other types of predictive AI include image processing techniques, such as Convolutional Neural Networks (CNNs) (Lecun et al., 1998). Again, impressive as these algorithms are, they make mistakes that a human would never make. Most people in AI and machine learning (ML) have seen a picture similar to that of Figure 1, where adding a small amount of noise to an image can fool the classifier that a pig is now an airliner. Again the reason that these techniques make such mistakes is that, unlike humans, they have no model of the world built into them and have no ability for abstraction and so rely entirely on the information on which they were trained.
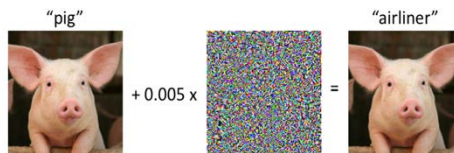
Figure 1: A predictive AI technique correctly classifies the left-hand picture as pig but with a small amount of (non-random) noise added, the same technique now classifies the right-hand picture as an airliner.

However the remarkable achievements made in predictive AI are certainly useful in scientific discovery: their ability to

predict text, based on consuming a large corpus, can be used to summarise existing knowledge, a first step in the process of scientific discovery. The predictive ability of image processing techniques such as CNNs, Generative Adversarial Networks (GAN), (Goodfellow et al., 2014) and Variational AutoEncoders (VAE), (Kipf and Welling, 2016), together with advancements in sensor technology and robotics enables us to capture and analyse data in locations that were previously inaccessible to humans. This is enormously important for scientific discovery.
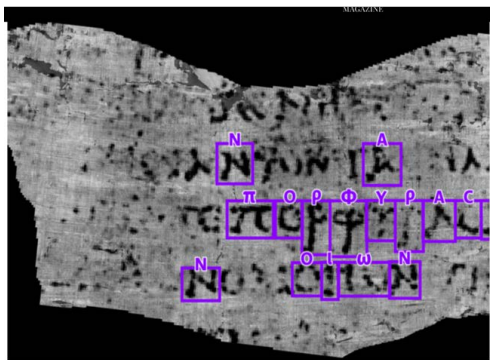
Figure 2: The Greek characters *πορφυρασ* spell the word *porphyras*, meaning purple in ancient Greek. The Vesuvius Challenge.

Recently it was announced that a machine learning algorithm had deciphered the word "purple" on a Roman scroll from the city of Herculaneum, see Figure 2, carbonised following the eruption of Mt Vesusius. 79 C.E.(*The Economist*, 2023).[2] Yet, although the machine learning algorithm was able to correctly classify the word as "purple," it has no understanding of ancient Greek or English.[3]

Generating accurate predictions does not necessarily lead to generating knowledge or insight. To give another example a Deep Learning system may predict the movement of stars without discovering the underlying laws of nature e.g. gravity, that determine those movements. If AI is to revolutionise scientific discovery it needs to overcome these shortcomings: Predictive AI models, impressive as they are, are not game changers in scientific discovery. They do not incorporate a model of the world, and their treatment of uncertainty is rudimentary at best but most commonly non-existent.

Towards embedding known models of the world

The development of AI techniques that incorporate our knowledge or belief of the world and therefore may be useful in causal inference and scientific discovery is already underway. Physics Informed Neural Networks PINNs (Raissi et al., 2019), are an example. PINNs incorporate models of the world by defining loss functions which penalise solutions which deviate from the physical model. Figure 3, modified from (Karniadakis et al., 2021), is a graphic representation of a PINN for the viscous Burgen system of equations, used in fields such as fluid dynamics. In Figure 3, x represents spatial co-ordinates, t is time, u and $\hat{u}$ are the measured and predicted speeds of the fluid at location x and time t, and v is the viscosity of the fluid. The usual mean squared error (MSE) loss function used to train neural networks, $\mathcal{L}_{NN}$ has been replaced by a weighted average of $\mathcal{L}_{NN}$ and a loss func-

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2 First word discovered in unopened herculaneum scroll. https://scrollprize.org/firstletters. Accessed: 2023-10-31.

3 In early 2024: the Vesuvius Challenge 2023 Grand Prize was awarded: we can read the first scroll! https://scrollprize.org/grandprize [Ed.]

tion which penalises solutions which are far from the physics, $\mathcal{L}_{PDE}$, where the partial derivatives required to compute $\mathcal{L}_{PDE}$ are calculated using automatic differentiation techniques. By combining both information from physics and data, these types of models have the potential to shed more light on an issue than either source of information alone. PINNs have been applied to a diverse range of fields including including energy (Hu and You, 2023) and ecology (Robinson et al., 2022).

While this is an exciting area of research, two points should be noted. The first is that the surrogate model $\hat{u}(x,t)$ does not impose the constraints which arise from the physical system, it only penalises solutions which are far from the physics. The second point is that the surrogate model, like many predictive AI techniques which rely on deep learning architecture, are not interpretable, and insights into the scientific phenomenon are limited.
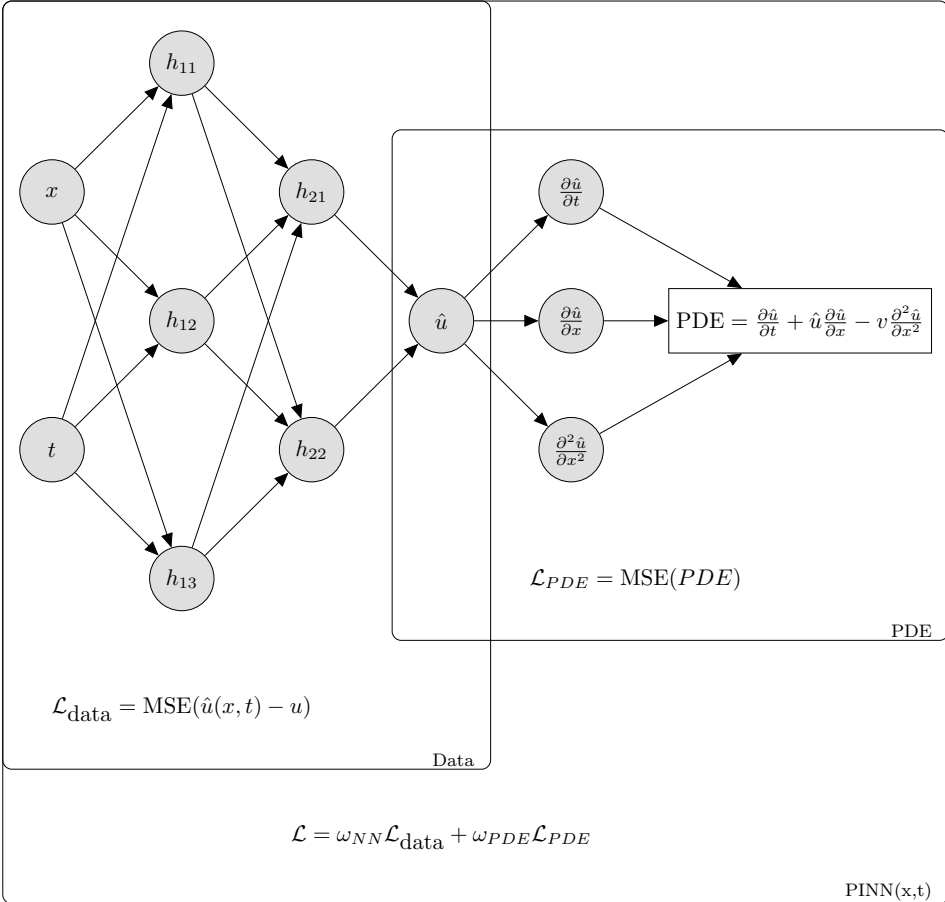
Figure 3: Physics Informed Neural Network (PINN). Graphical representation of estimating the velocity of a fluid u as a function of space x and time t (left box) and the constraints given by the physics of the system (right box). The loss function, $\mathcal{L}$, is a weighted combination of the loss functions of the fit of the neural network (NN) to the data $\mathcal{L}_{data}$ and the fit of the NN to the PDE, $\mathcal{L}_{PDE}$.

Another methodology for incorporating world views into machine-learning techniques is the Bayesian methodology. Indeed the neural network and physics loss functions of PINNs have elements of the Bayesian framework: the neural network loss function is analogous to a likelihood and the physics loss function is analogous to a prior.

The benefit of the Bayesian framework is that it is logically consistent, provides estimates of uncertainty via the posterior distribution and a formal framework which can be generalised to a large class of problems. The partial and ordinary differential equations (PDEs and ODEs), that define many physical systems, such the viscous Burgen system described above, can be expressed as a directed graph, which we denote generically by $\mathcal{G}$.

An example is given in Figure 4, which shows the Lotka Volterra (LV) equations for coral reef growth as a graphical model. The population of coralgal assemblages x, the growth rates by ε and carbonate production by C. The interaction between assemblages denoted by α. Sediment input (Sed), water flow (flow) and depth(Dep) are the basic environmental factors influencing coral growth, via the function $f(environ)$, and the growth rate ε_i is scaled by this factor, see (Salles et al., 2018) and (Pall et al., 2020).

Assuming the physics of coral reef formation are governed by the LV equations, i.e. assuming we know $\mathcal{G}$, the quantities of interest maybe the growth rates ε, the competition matrix A as well as the function which maps the impact of environmental functions to the coral population, $f(environ)$, and estimates and inference of these quantities, jointly denoted by $\theta_{\mathcal{G}} = (\varepsilon, A, \mathbf{f})$, is

via the posterior distribution $p(\theta_{\mathcal{G}} \,|\, data, \mathcal{G})$, conditional on the graph $\mathcal{G}$.

It is important to highlight that embedding the LV equations, or any other physical model, is equivalent to assuming that the relationship between factors in system is given by the directed graph structure, with probability one. In a Bayesian setting we express this knowledge as a *prior* distribution, i.e. $P(\mathcal{G} = 1)$, so that there is no uncertainty about this graph structure. However, much of scientific discovery is about uncovering the causal structure of a phenomenon, not just the parameters, θ, of that causal structure, by placing a prior distribution over $\mathcal{G}$, s.t. $\mathcal{G} \sim Q(.)$, where Q is a distribution.

Learning unknown models of the world

The potential for discovery in science has driven much research to learn the structure of a class of graphs known as Directed Acyclical graphs (DAG) (Kitson et al., 2023). The requirement that the graph is acyclical because we wish to infer causation from observational data, (Pearl, 1995), and cycles in the graph structure would make that impossible. We note that causation is only w.r.t an equivalence class (Verma and Pearl, 1990) and only possible if all relevant factors are included in the graph, a condition that is rarely met, so caution is warranted (Dawid, 2010).

Despite these caveats, learning the structure of a graph can provide insight into phenomenon of interest. Consider for example Figure 5, from (Zhu et al., 2023) which depicts the causal structure for a child's Body Mass Index (BMI), denoted by a red diamond in Figure 5. Figure 5 sheds some light on why inventions which target proximal and intermediate causes of child-

hood obesity, such as activity and food type consumption, have not had the impact that might have been expected. Figure 5 clearly shows that childhood obesity is a by-product of social disadvantage, its root causes are socio-economic status (SE) and parental education levels (PE1, and PE2) and that tackling downstream and intermediate factors such as high fat (HF), high sugar (HSD), fruit and vegetable consumption (FV) and

activity (FTA) while ignoring these root causes is not sufficient to address the issue, see (Zhu et al., 2023) for a full discussion.

Learning the structure of a graph is an enormously difficult problem. First, the number of possible graphs grows super-exponentially with the number of factors and the space of all possible graphs is discrete, making it difficult to explore the posterior distribution of the graph.
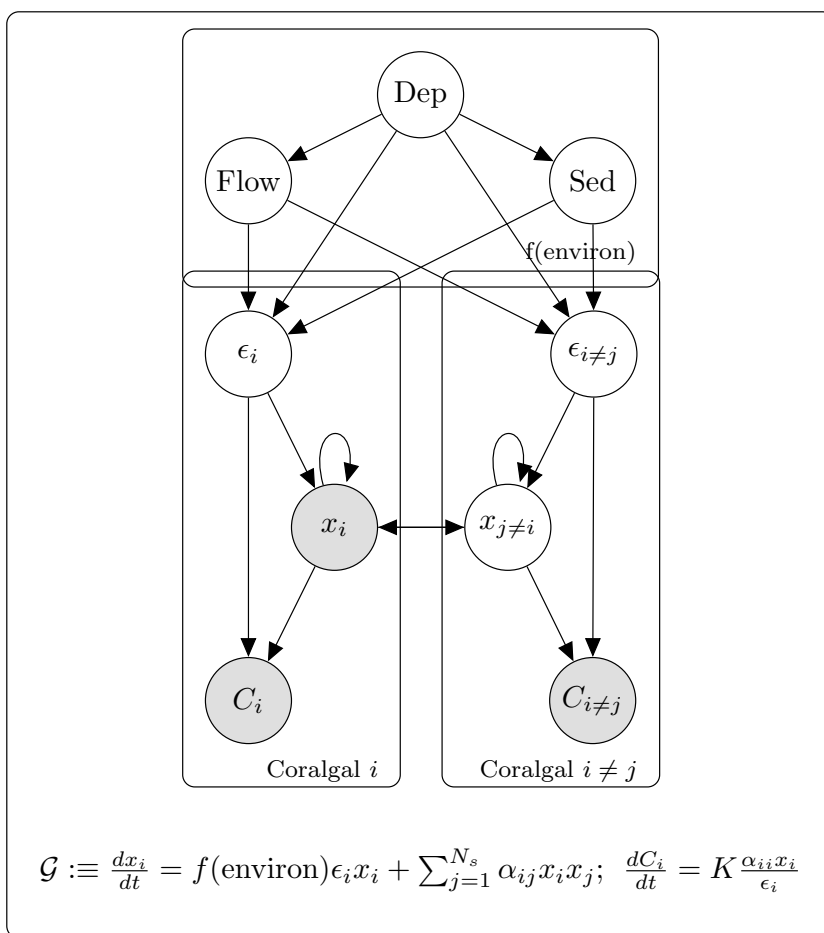
Figure 4: The Lotka Volterra equations depicted as a graphical model. The population of coralgal assemblage i is denoted by x_i, its growth rate by ε_i and its carbonate production by C_i. The interaction between assemblages i and j is denoted by α_{ij}. Sediment input (Sed), water flow (flow) and depth (Dep) are the basic environmental factors influencing coral growth, via the function $f(\text{environ})$, and the growth rate ε_i is scaled by this factor.
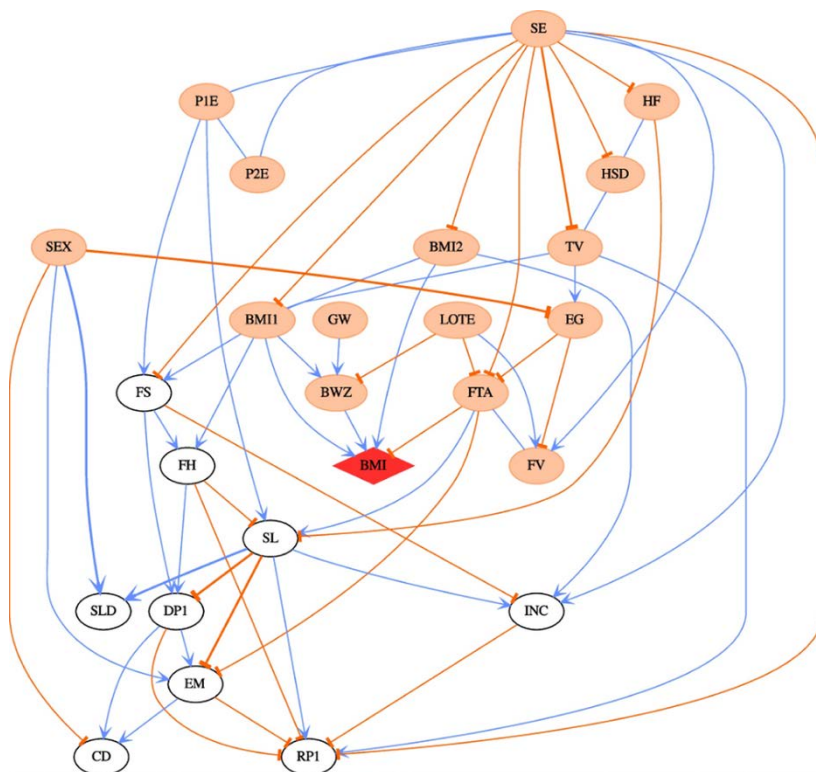
Figure 5: The completed partially directed acyclic graph (CPDAG) derived from the exquivalence class of most probable DAG for 8–10 year olds in the birth cohort of the LSAC (Mohal et al., 2020). The child BMI node is highlighted by a red diamond shape. The thicknesses of the edges in the network correspond to the strength of relationship between nodes, with a thicker line denoting a higher absolute value. The edge coefficients are obtained by regression analysis given the DAG structure. The coefficients of undirected edges are inherited from the values of directed edges. The blue and orange edges indicate positive and negative relationships, respectively. Orange ellipse nodes denote ancestors of child BMI (Zhu et al., 2023).

Second, for Bayesian networks such as in (Zhu et al., 2023), the structure learning algorithms can only learn up to a DAG's equivalence class, in which all the DAGs are equally likely (Verma and Pearl, 1990), and DAGs which belong to the same equivalence class can have very different causal structures. The only way to confirm causality is via experimentation.

Knowledge Discovery Systems: Algorithms which tell us what we don't know

The examples given throughout this paper show how both types of AI techniques, predictive and causal, can be used to aid scientific discovery. The former harness the computational advantages that have developed over the last 50 years, while the latter leverage developments in inferential thinking, developed over the last 100 years, and both are underpinned by developments

in new mathematical methods. However impressive these achievements may be, they are isolated competencies and neither alone will provide a step change in scientific discovery. If we are to transform science with AI, we need to take a systems approach and combine these techniques in a framework capable of knowledge discovery.

What should this system look like? It starts with the development of algorithms which quantify uncertainty. Why? Because uncertainty tells us what we don't know. We need AI systems that, given a question, can assist in the identification and acquisition of valuable information, that can fuse different sources of information in a principled manner, that can produce not only predictions but also levels of confidence to guide real-time experimental design, that can update hypotheses and suggest new ones.
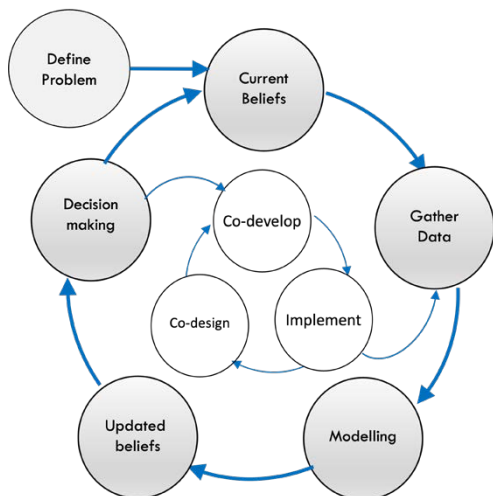
Figure 6: Conceptual AI framework for scientific discovery

Figure 6 is a conceptual AI framework for scientific discovery. It couples ideas from Bayesian reasoning with the growing area of research on collective intelligence and highlights six key features:

1. *Define Problem: scientific discovery starts with specific questions* about unknown quantities, denoted here by $\mathcal{G}$, the causal structure, and the parameters of that structure $\boldsymbol{\theta}_{\mathcal{G}}$. These questions need to be the centre of an AI framework in which evidence gathering, algorithmic and model advancement, system development and decision making are connected in a continuous, iterative, learning cycle.

2. *Current Beliefs: Collecting evidence on what is already known to form $p(\mathcal{G}, \boldsymbol{\theta}_{\mathcal{G}})$.* Predictive AI techniques, such as LLMs can be used to probabilistically summarise what is already known. Additionally, prior elicitation methods (Falconer et al., 2022), which convert varying subjective beliefs from experts or communities into probability distribution, can be combined with more traditional sources of data to gain insights that neither source of information alone could provide.

3. *Gather Data: it is valuable information, not big data that counts.* Scientific discovery proceeds by identifying information gaps and conducting experiments to resolve uncertainties. To accelerate this process, we need algorithms which accurately quantify uncertainty, then, using this estimate of uncertainty, assess the value of future data sources based on their ability to reduce uncertainty concerning the question at hand. One method of doing this is to sequentially acquire data, $\mathcal{D}^{*}$, that is maximally informative about $\mathcal{G}$, and $\boldsymbol{\theta}_{\mathcal{G}}$, measured for example by the expected mutual information $I(\mathcal{D}, \{G, \Theta\})$ where

$$I(\mathcal{D}, \{G, \Theta\}) = \sum_{\mathcal{G} \in G} \int_{\theta_{\mathcal{G}} \in \Theta} P(\{\mathcal{G}, \theta_{\mathcal{G}}\} \mid \mathcal{D}) P(\mathcal{D})$$
$$\log\left(\frac{P(\{\mathcal{G}, \theta_{\mathcal{G}}\} \mid \mathcal{D})}{P(\{\mathcal{G}, \theta_{\mathcal{G}}\})} \right) d\theta_{\mathcal{G}}$$

and

$$\mathcal{D}^* = \arg\max_{\mathcal{D} \in D} I(\mathcal{D}, \{G, \Theta\}).$$

New sensor technologies and other data capture techniques, together with predictive AI techniques such as CNNs, VAEs, and GANs, can be used to record and analyse data from a variety of sources.

4. *Modelling: Construct likelihood models*, using multiple sources of data and capable of inferring casual pathways,

$$P(\mathcal{D} \mid \mathcal{G}, \boldsymbol{\theta}_{\mathcal{G}}) = \prod_{i=1}^{N} P(\mathbf{x}_i \mid Pa_i, \boldsymbol{\theta}_{\mathcal{G}, \mathcal{G}})$$

where $\mathcal{D} = (\mathbf{x}_1, \dots, \mathbf{x}_N)$.

5. *Update Beliefs.* The existing information contained in $p(\mathcal{G}, \boldsymbol{\theta}_{\mathcal{G}})$ is combined with information in the new data via the likelihood function $P(\mathcal{D} \mid \mathcal{G}, \boldsymbol{\theta}_{\mathcal{G}})$ in a probabilistic framework, quantifying and updating uncertainty dynamically as new information and discoveries emerge to yield the posterior belief

$$P(\boldsymbol{\theta}_{\mathcal{G}}, \mathcal{G} \mid \mathcal{D}) = \frac{P(\mathcal{D} \mid \boldsymbol{\theta}_{\mathcal{G}}, \mathcal{G}) P(\boldsymbol{\theta}_{\mathcal{G}} \mid \mathcal{G}) P(\mathcal{G})}{P(\mathcal{D})}$$

6. *Decision Making.* The incorporation of values, desired outcomes and measure of success is incorporated in the action a from a set of possible actions $\mathcal{A}$, via the formation of the utility function,

$$a^* = \arg\max_{a \in \mathcal{A}} U(a, \mathcal{D})$$
,

where $U(a, \mathcal{D})$ is given by

$$U(a \mid \mathcal{D}) = \sum_{\mathcal{G} \in G} \int_{\boldsymbol{\theta}_{\mathcal{G}} \in \Theta} u(a \mid \mathcal{G}, \boldsymbol{\theta}_{\mathcal{G}}, \mathcal{D})$$
$$P(\boldsymbol{\theta}_{\mathcal{G}} \mid \mathcal{G}, \mathcal{D}) P(\mathcal{G} \mid \mathcal{D}) \, d\boldsymbol{\theta}_{\mathcal{G}}.$$

This is a learning-as-we-go approach: actions are adaptively chosen as new information comes to hand to maximise some prespecified criteria. What is enabled by AI is the identification of valuable information via algorithms that can quantify what we don't know, and the ability to gather and store that information at a rate and in places where it may be difficult for humans to do. In these types of AI systems, the models developed are explainable and transparent. The assumptions are explicit, and therefore the impact of assumptions can be assessed. They are mathematically rigorous and can offer guarantees. They are not just based on associations between factors but are designed to estimate causal pathways so that the right intervention is implemented at the optimal time. And they incorporate human values by being co-designed and co-implemented by the communities which are impacted. In these AI systems, the human is not just in-the-loop, the human is at-the-helm.

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Doing AI well: the Responsible AI network

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I really love the expressions that Sally was using, especially the unravelling of the data and patterns and causality and so forth. I landed in technology by complete accident. I was going to be a film composer and I loved creativity and self-expression and how I could help enable others to do the same. Finishing my University degree, I had to start adulting, getting a job, and I landed in a technology start-up by a complete accident. I learned on-the-job, completing certifications, many courses and then I bolstered that with a Master's. What I found was that technology was so incredibly creative for even my own interest in self-expression: during my Master's study I developed an emotion-sensing dress that would change colour and shape based on how you were feeling. It would augment your own expression. The same with an interactive sleep cocoon, that would be connected to your biological processes: change shape, use vibrations, use binaural beats, so that you get the maximum sleep over the night. I've been fascinated by how technology can actually augment ourselves, how we work, how we express ourselves and so on.

Somehow I got into helping industry succeed with technology, leading the National AI Centre, hosted by CSIRO. Believe it or not, we don't have any researchers at the National AI Centre — there are lots of AI researchers at CSIRO, but at the National AI Centre we are working with commercial organisations every day to understand how they're using AI, the challenges they're encountering, and helping them implement AI responsibly. Don't get too connected to that word "responsibly" — some people call it "ethics," some people call it "trustworthiness," some people call it "safety, diversity, inclusion." Industry wants to do AI well but it's quite a challenge figuring out how exactly to do that today.

The industry context that we're hearing at the National AI Centre is that the AI narrative is very polarising. Right now, it's either all incredibly high-risk or there's great optimism that it's going to solve everything. The reality is that, depending on the use case, it's somewhere in between. Some use cases are low-risk and in fact have been around for a very long time. In Sydney, for instance, some of the infrastructure and transport solutions out in the world today have been leveraging machine-learning, data science, AI for 40 years. It's actually how we as humans in our day-to-day lives are able to continue making informed decisions in highly complex environments. What we often hear from business is that, with AI becoming so polarising, some of these basic use cases that are making sense, patterns and predictions, are also sometimes deemed to be seen as high-risk, but actually are kind of very basic and non-risk.

In addition to organisations using AI to navigate complexity, there are also some

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1 This is an edited transcript of the talk [Ed.]

major global challenges that we're tackling. Some of you might have seen CSIRO's seven megatrends that are shaping our next decades of life and work.[2] Some of these challenges are tremendous: no matter how many of our brains and hands we connect, we could not tackle them. There are not physically enough health professionals to provide quality care to people who need it. Or climate change and adapting to climate change. This is such a complex ecosystem dynamic that we're needing the greatest of our technologies to tackle that.

In the commercial sector AI is seen as this great solution to help tackle and unravel complexity so we can continue making informed and meaningful decisions. I want to share two key examples in the health space: this is a particular area where I think AI is going to add so much value because it can augment our ability to make sense of the world, find patterns, and take actions on them.

The two examples: one is Hive Health in virtual environments. It's implemented at Royal Perth Hospital. In essence, there is a pod of four medical professionals who are monitoring 200 patients remotely. They're gathering vitals and health data so that they can see who is needing medical intervention. It's helping the doctors be more effective: rather than doing walk-by checking on the patient one by one, it's helping the medical professionals go to where they need to be. They're leveraging this AI Hive solution to augment their ability to make an impact by being where they need to be.

Another interesting case is the work by Dr Helen Fraser in leveraging AI for breast-cancer mammography. Dr Fraser has built machine-learning models to help spot anomalies in mammograms. Rather than thinking about replacing the medical professionals who might otherwise be looking through these mammograms, she has optimised this model to look at the most basic use cases, and either rule out the existence of an anomaly, or detect an obvious anomaly. It frees up time for the medical professional to focus more on the highly detailed complex cases. It's a real way of thinking about how machine learning and AI tools can augment the professionals for that impact.

Quite often when we talk about AI, very quickly the conversation turns to bias. AI hasn't brought new bias to us: bias has always been in the world. But because AI is built on data, it can often propagate biases unless it's designed responsibly. There are two examples that I want to use which have helped us see the flip side, where AI can actually help tackle some of the biases that we may not even see. One example is EY (Ernst & Young), who have a loan-approval solution that they provide to banks. It's one of their services. There's some automated risk scoring that might be presented to the financial service organisation they're working with. But what they found was they used an AI model called FAIR-learn and they found that there was bias in the data they were using for loan approvals. In fact there was a 7% disadvantage that women had during the loan approval process versus men. And this system had been operating for a long time without AI, but now with AI was able to find that bias. The same toolkit was used to reverse some of that bias, so it has moved from 7% to 0.3%.

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2   https://www.csiro.au/en/news/all/news/2022/july/seven-megatrends-that-will-shape-the-next-20-years [Ed.]

Another fascinating example is a solution from Sapia.ai, an Australian company that has a chatbot for early-stage interviewing. The headline in the *Financial Review* (May 17, 2023) said, "AI more likely to hire women than humans are," but I think the most interesting data point is when you dig a little bit deeper into the study, conducted in collaboration with a university in the UK. They found that when women were told that they were being interviewed by an AI bot and assessed by an AI bot, 37% more women applied, which is starting to suggest that we have biases around us. There are members of our community who would feel more fairly treated potentially by AI systems, if those systems are designed responsibly and fairly.

I haven't even spoken about generative AI yet because AI has been around us since the '50s. Generative AI has somehow made it seem like suddenly AI is a new thing, and the last year has completely changed everything. What has changed is the ease with which every single person can engage with AI systems. Suddenly many more people are using AI systems to augment what they're doing: to get creative ideas, to help them draft a first email. In fact our signals are showing that in the workplace 30 to 40% of employees are using generative AI. 68% are not telling anyone about it. That's really fascinating to think about.

Put yourself in the shoes of a business leader: you know your people are using it — there's some productivity signal in there that your people are finding more effective ways of doing work. But if you don't know about it, that brings exposure to your organisation, because you don't know what people are sharing, you don't know which services they're using. That is why right now the first thing that we suggest to commercial organisations is that they must implement a generative AI policy because, no matter what your perspective on it is, it's happening. I think one of the highest risks for any team, any organisation, is to have hidden dynamics and hidden use. Even if it if something is not exactly according to strategy, they would rather know about it than have it hidden.

The generative AI use cases that we often hear about are things like customising sales emails and personalising advertising and so forth.[3] But I want to share two that are a little bit out of the ordinary: one is generative AI for cybersecurity. Currently the average Australian is getting more than 250 cybersecurity attacks a year. That's huge, and the challenges are increasing for organisations as well. Our teams at Data61 leveraged generative AI to create cybersecurity honeypots — files that seem like they have very valuable and confidential data, or they might have personal information, or they might have credit cards or some IP. The bad actors, who are attacking technology systems, want to get to this data; they want to monetise it or sell it or exploit it. The Data61 teams at CSIRO built a generative AI tool that became very good at creating honeypots but completely fake ones to distract the bad actors and draw them to the fake "precious" data, and so keep them away from the real precious data.

Another case in design: some of you might have seen that NASA is using generative AI to create parts for their satellites. So you

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[3]   Indeed, this transcript has been edited by ChatGPT 3.5 with the following instructions: "Edit the transcript of a speech. Eliminate the uh and um words. Use British spelling. All sentences end with a period — capitalise the initial letter of the sentence." [Ed.]

define: "this is the dimension of the part that I need, don't put anything here, this is where hands need to go, don't put anything here, this is where the sensor pack needs to go, this is where the attachment is." It needs to be very specific. And, for the rest, "generative AI, draw a strong structure as light as possible using this material." Generative AI colours it in or draws it in. Interestingly, they're finding that these structures are more resilient and stronger than they've been designing before. I encourage you to look at these offline in your own time, because the designs look organic. It's not something that has come out an angle-ruler engineering approach: there is a real finesse. That's intriguing.

It's not only NASA that's doing this — even Shell is using generative AI to design the layout of its wind farms. It says, "Hey, generative AI, this is my terrain, this is the altitude, this is the weather, this is the weight of my wind turbines. Tell me the layout options." This is one way that people are using generative AI to help tackle the complexity and decision-making in highly tangled data environments.

Just to wrap up: if we're relying on such technology so much, then we need to ensure that they're trusted, that they're accurate, that they're safe. Much of the experience with generative AI has been in the consumer-facing products space. They're trained on very broad, uncontrolled data sets. I think there's much more opportunity for generative AI on controlled organisational data to help people find what they need.

It does need to be trusted. Today, more than 74% of organisations around the world are not even checking their data for quality or bias. More than 65% are not checking data drift or model drift. We have a need to actually develop and level up our practice of doing AI well. That's what we focus on at the National AI Centre and why we develop the Responsible AI network:[4] it was to share some of this best practice of how to do AI well, so that, when we do choose to use AI to augment our processes or decisions, we can do so in a in a more trusted and responsible way. Thank you.

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4   https://www.csiro.au/en/work-with-us/industries/technology/national-ai-centre/responsible-ai-network [Ed.]

Artificial intelligence: affordances and limits in the context of judging

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Abstract

This paper is based on a presentation given on 2 November 2023 at the Royal Society of New South Wales and Learned Academies Forum "Our Twenty-First Century Brain," as part of a panel on Turbocharging Human Intelligence with Artificial Intelligence. A question posed in the panel was what changes we face as humans given the increased complexity of our interaction with artificial intelligence (AI). I explored that question through the lens a critical role played by humans in our society, namely that of judges. In this paper, I explore the extent to which AI might, alone or with humans, perform such a role and what this might mean for our understanding of the criticality of human involvement in high stakes decision-making.

What is AI?

AI is a confused term, but it would seem we are stuck with it. Part of the problem is the term "intelligence" itself, which often recalls one-dimensional metrics such as IQ. Engineered systems have a range of capabilities that produce outputs that in some circumstances are identical to, similar to, or more useful than that might be produced by an intelligent human, but we do not always call the result artificial intelligence. An example is the humble calculator. If I were to calculate 2,180,906 / 598 on paper, I would rely on my memory of the algorithm for long division and my ability to perform the calculations required. It is fair to say that my ability to execute the task involves *intelligence*, but the device used to do it in my stead, despite being "artificial," would not generally be described as "arti-ficial intelligence." On the other hand, the ability of generative AI tools to write text, despite making the kinds of mistakes that would be rare for humans, is considered by many as the current pinnacle of "artificial intelligence."

Definitions of AI typically focus on either a field of research comprising sub-fields such as machine learning, computer vision, natural language processing and so forth or an adjective to describe a kind of system. For both, some definitions focus on anthropomorphic comparisons: the classic example being the Dartmouth Summer Research Project in 1956 which referred to the field of research as "making a machine behave in ways that would be called intelligent if a human were so behaving."[1] Other definitions of the field of research focus on rationality rather than similarity to humans.[2]

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[1] John McCarthy et al. (1955) A proposal for the Dartmouth Summer Research Project on artificial intelligence, report, 31 August, https://www-formal.stanford.edu/jmc/history/dartmouth/dartmouth.html

[2] Russell S and Norvig P (2016) *Artificial Intelligence: A Modern Approach*, (3rd ed, Pearson Education Ltd), pp. 2–5.

The OECD defines AI systems rather than the field of research, stating that:[3]

> An AI system is a machine-based system that, for explicit or implicit objectives, infers, from the input it receives, how to generate outputs such as predictions, content, recommendations, or decisions that can influence physical or virtual environments. Different AI systems vary in their levels of autonomy and adaptiveness after deployment.

Note that "content" was not in the original definition but was added following developments in large language models and other generative AI techniques. The definition of AI system in ISO/IEC 22989:2023 is similar:

> Engineered system that generates outputs such as content, forecasts, recommendations or decisions for a given set of human-defined objectives.

The multiplicity and evolution of definitions suggests we are still coming to terms with the kinds of things we are creating. It might be, as Roger Clarke suggests, that we are defining the wrong concept and that we might be better off with a term that better captures the fact that humans and systems co-produce outputs that influence physical and virtual environments.[4] However, for the purposes of this paper, I will adopt the definition in ISO/IEC 22989. This treats the concept of artificial intelligence as distinct from the property of "autonomy."

It thus allows for socio-technical systems that include both human beings and AI subsystems, which are likely to be the basis for most useful applications in the context of judging.

Judging and Artificial Intelligence

There is no doubt that judges use a range of AI tools in the context of their work.[5] For example:

1. Legal research tools increasingly rely on AI in addition to more straightforward techniques of phrase matching and cross-linking; and

2. Word processing devices (internal or external to standard word processing software) encourages stylistic and grammatical enhancements and may increasingly also identify repetition and opportunities to improve signposting and structure.

What is most controversial, however, is the use of AI tools in constructing reasoning or reaching decisions. Here, there is an important distinction, not along the lines of "artificial intelligence" but along the line of "autonomy." Sourdin uses the terminology "Judge AI" versus "supportive Judge AI" to capture the distinction between autonomous AI systems that substitute for a human judge and systems that assist a human judge in their work.[6] However, it is less a binary than a scale of decreasing levels of human involvement into the final decision and reasons. A human judge who

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3   OECD (2023) Recommendation of the Council on Artificial Intelligence, OECD/LEGAL/0449 (adopted 22 May 2019, amended 8 November, https://legalinstruments.oecd.org/en/instruments/OECD-LEGAL-0449

4   Clarke R (2023) The re-conception of AI: Beyond Artificial, and beyond Intelligence. *IEEE Trans. on Technology and Society* 4(1): 24.

5   See generally Bell F et al. (2022) *AI Decision-Making and the Courts: A Guide for Judges, Tribunal Members and Court Administrators* (AIJA).

6   Sourdin T (2021) *Judges, Technology and Artificial Intelligence*, Elgar, p. 16.

has little understanding of the affordances of the technology being used and takes a trusting attitude to its outputs is very close to Judge AI.

Three dimensions of measurement

In earlier work,[7] I set out a three-dimensional framework for assessing AI in a context such as judging. My goal in doing so was to counter the narrative around an AI "singularity" which imagined a one-dimensional comparison between the "intelligence" of humans and machines. The three dimensions, shown in Figure 1, are: (1) the extent to which available tools perform well in the context of a clearly defined purpose (do we?); (2) the extent to which AI as a discipline has the capability to perform particular functions (can we?); and (3) the extent to which the use of available tools in the particular context would be appropriate (should we?). The first dimension, while seemingly mundane, is important because we often get excited about capability and concerned about appropriateness, leading to simplistic utopian/dystopian visions that ignore the fact that most of the problems experienced in practice involve an inadequately thought-through purpose and poor implementation. One reason why legal projects often measure poorly on this dimension is the relative lack of expertise and understanding among legal experts involved in commissioning AI projects.[8]
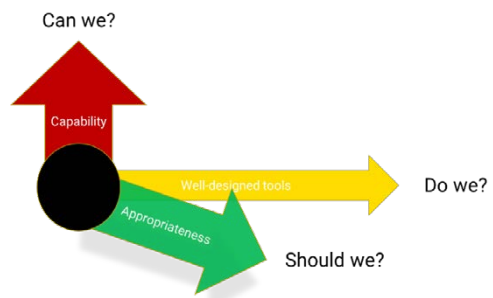
Figure 1: Applications of artificial intelligence can be measured in three dimensions

Improving decision-making around AI adoption in courts and tribunals

It was out of a desire to improve decision-making in critical contexts such as courts around the uses of AI that some colleagues and I partnered with the Australasian Institute for Judicial Administration to create a guide on AI for judges, tribunal members and court administrators.[9]

The guide does several things. It begins with a basic explanation of terminology as well as the various capabilities of different kinds of AI (mirroring the "can we" axis). It then describes the most common applications in the domain of courts and tribunals, as well as some of the limitations of these in practice (mirroring the "do we" axis). After that, it sets out the most critical judicial values, and explains the implications on these of the various use cases, given the affordances of the different kinds of tools being deployed (mirroring the "should we?" axis). The conclusions are not in the form of answers or prescriptions, because all of these

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7   Moses LB (2020) Not a single singularity. In: Deakin S and Markou C (eds) *Is Law Computable? Critical Perspectives on Law and Artificial Intelligence*. Hart Pub., pp. 205–222.

8   For a solution, see Hildebrandt M (2023) Grounding comptuational "law" in legal education and professional legal training. In: Brozek B, Kanevsaia O and Palka P (eds) *Elgar Handbook on Law and Technology*.

9   Bell et al. (2022) *op cit* n 5.

questions are highly context dependent. Whether or not a particular tool should be used will depend on the purpose of doing so, the approach or methodology (for example, whether code-driven or data-driven), the performance of the tool (including whether it has been evaluated and as against which metrics), and so forth. Instead, the guide is constructed around questions that we argue are critical in deciding whether to use a particular tool in a particular context.

The first set of questions are at the highest level and provide a starting point for analysis:

1. Why is AI being used? What problem does it solve?

2. Is the use of AI authorised in the context in which it is deployed?

3. In what contexts is AI being used, and is its use in those contexts appropriate? Does the context involve high stakes, vulnerable people, novel situations, or high levels of emotion?

4. How is AI being used? How can system requirements (through a procurement process) better fulfil its purposes and meet the needs of courts and tribunals, including in relation to core judicial values? How will the system be checked, tested and evaluated to ensure it meets those requirements?

5. Who is consulted about the deployment of AI systems? Are all stakeholders including users and litigants included in decision-making about whether and how AI will be used?

6. Will the use of AI impact on public confidence in the judiciary?

7. Will the use of AI in the courtrooms be accepted by the public?

Other questions relate to the various aspects of "should we," revolving around the identified judicial values, being open justice, accountability, impartiality and equality before the law, procedural fairness, access to justice, and efficiency.[10]

The technological imaginary

While the guide provides a tool that courts and tribunals can use in decision-making, it operates within the domain of current capabilities. Indeed, we will soon publish a second edition that brings the first up to date, both in relation to the increasing number of examples of AI deployment internationally, but also recognising the growing capability of and interest in generative AI tools such as OpenAI's ChatGPT.

Going beyond current systems, increasingly optimistic hypotheticals are being posed about how our society generally and courts in particular might respond to significant inflation in the second dimension, namely in the capabilities of AI. What if, for example, generative AI was linked with a reasoning engine that solved the problem of hallucinations? What if there were a "legal singularity" with AI systems able to produce judgments that were, to a critical observer, indistinguishable from those authored by humans?[11] For the purposes of the exercise, it is not necessary to decide whether any of these things are technically possible or likely. However, it does draw us back to the issue

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10   The second edition of the Guide, currently in draft, will link accountability with another important value, namely independence.

11   Alarie B (2016) The path of the law: toward legal singularity. *University of Toronto Law Journal* 66: 443.

of what role judges (or indeed other humans undertaking critical tasks) perform.

One answer that is sometimes given relates to human traits such as empathy.[12] For example, many insist that presenting a case to a human with an ability to empathise with the parties before them, and receiving judgment from someone able to relate to the impact of their decision, is important. However, there is a need to be careful here. In some contexts, such as first instance judges deciding matters between individual litigants or against an individual defendant, the ability to connect and relate can help people feel heard and better able to cope with a negative outcome. However, many judges, particularly in higher courts, would minimise the importance of this. At least some would argue that their performance should be evaluated primarily on the basis of their judgments and, in particular, the doctrinal rigour of their reasoning. This leaves them vulnerable to the argument of Alarie that it would be reasonable to replace human judges with a system that can simulate that output where it is judged (by a third-party observer) as of equivalent quality.[13]

To try to get at the question of whether artificial intelligence *ought to* (given sufficient capability) replace judges, it is necessary to dwell on *purpose*. What judges do, even in higher courts, goes beyond producing text containing valid doctrinal arguments. What is most important is that they are exercising judgment. This is dif-

ferent from both prediction (working out the expected outcome of litigation using probability) and simulation (which is what ChatGPT does when asked to produce the text of a judgment). The manner of the decision is as critical as its content. An analogy might be elections — even if the accuracy of polling could be improved to the point that the chances of same-day polling yielding a different answer from the formal election were minimal, we would not want to replace elections with polling. What matters is not simply the ability to predict an outcome, but the judgment made by the electorate at a particular solemn moment of decision. Writing a judgment is slower than completing a ballot paper, but the point is similar — the exercise of judgment in reaching a decision is more critical to the function of judging than the production of text as such. Predicting that judgment (who will win the case, amount of damages, length of sentence, etc.) or generating reasons artificially cannot substitute for the exercise of judgment, even if it is impossible for a third-party observer to tell the difference. This also goes beyond issues of empathy, both as a capacity and as interpersonal sharing of affect. Empathy may be important, particularly in how litigants themselves perceive the process, but is not the only the only thing lost in a shift towards automation.

There are also other potential manifestations of artificial intelligence that have different affordances, including the capacity

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12   Empathy is an ambiguous term, see Hall JA & Schwartz R (2019) Empathy present and future. *The Journal of Social Psychology* 159(3): 225. For the purposes of this paper, I adopt the approach of Decety and Jackson, who describe three functional components of empathy, being interpersonal sharing of affect, self-other awareness with clear regulatory mechanisms to distinguish between the two, and a cognitive component that involves adopting the perspective of another: Decety J and Jackson PL (2004) The functional architecture of human empathy. *Behavioral and Cognitive Neuroscience Reviews* 3: 1.

13   Alarie (2016) *op cit* n 11.

to exercise judgment. Imagine the possibility of duplicating human brains *in silico*, so that a judge living today could be intellectually duplicated in an engineered system. There are philosophical questions about whether the system would indeed be a "duplicate," but for current purposes assume that it could exercise the same kind of judgment as the human judge from which it was copied.

There are still concerns, albeit different ones. The first is social licence for this kind of practice, in the very practical sense of whether people would subjectively recognise the engineered judge-clone as a legitimate decision-maker. The second is the problem of moral evolution — an eighteenth-century judge could be taught new legal doctrine, but could he recognise women and non-white people as worthy of the same dignity as himself? But the third problem comes back to a twist on the idea of empathy.

My third issue relates to the purpose of the rule of law in tempering power.[14] Where a judge perceives themselves subject to the same law that they are interpreting and applying, that belief acts as a constraint on arbitrariness. At least theoretically, if a judge committed the same offence as the person before them, they would be susceptible to sentencing by someone in a similar position to themselves. Similarly, if they themselves or an entity in which they held an interest was involved in a civil dispute similar to that before them, the same rules and interpretations would apply. As a result of that awareness, the judge might be less likely to act arbitrarily than a despotic ruler not subject to the same rules as everyone else. An engineered system, even if it is effectively a human clone, would not have

the same awareness because, even if it were conscious, it would not experience the law in the same way. The "experience" of an engineered system of a jail cell would not be the same qualitatively as the experience of a biological human. Similarly, the system's relation to money (such as may be payable in damages) is qualitatively different to that of a human for whom it may help provide for themselves and others. If the entity making, interpreting or enforcing rules experiences those rules fundamentally differently, then the rule of law as a means of tempering power breaks down. This is not the *same* as experiencing empathy, but it may in practice be related.

Conclusion

Many words have been spilt over the question of whether and when artificial intelligence might replace humans. Much of this links to the idea of a singularity when machines become more "intelligent" than we are, although the multi-faceted nature of that concept is usually ignored in the comparison. But humanness is more than intelligence and is certainly more than an exercise in the prediction of the outputs of an intelligent mind or the simulation of its work products. If we are to analyse whether machines might replace humans not just at a task (like playing chess) but in an important social role (like a judge), we need to go beyond comparing intelligence. Instead, we need to understand purpose and what it is, often unspoken, that links that purpose to humanness. The outputs of a human brain may be indistinguishable from the outputs of an engineered system — I certainly got the same answer for 2,180,906 / 598 as my

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14   Krygier M (2016) Tempering power. In: Adams M, Ballin EH and Meuwese A (eds) *Bridging Idealism and Realism in Constitutionalism and Rule of Law*. Cambridge: Cambridge University Press.

calculator, and we can assume that future systems may be able to write like me and speak like me in ways that would fool even those who know me well. This Turing test, however, is not enough when considering what *roles* engineered systems might be able to perform.[15]

To perform the role of a judge, I believe an entity will need at least three things: (1) the ability to exercise judgment; (2) being attuned to the morality of the community in which decisions are made (more or less, acknowledging there are a range of acceptable moral views in any community); and (3) being subject to law (the same law being applied to humans) in a meaningful sense. There are inevitably more — these are just the ones revealed by the hypotheticals considered above. But they reveal something important — we cannot look solely at intelligence in comparing humans and AI — we need to understand more about ourselves and our society to decide where we can and should stand aside in favour of our tools.

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15   Turing AM (1950) Computing machinery and intelligence. *Mind* 59: 433.

Session V: Implications for the future

Moderator: Ian Hickie

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Panellists: Peter Baume, Helen Christensen, Phillipa Pattison, Jakelin Troy[1]

Ian Hickie: I'm the co-director of health and policy at the Brain and Mind Centre of the University of Sydney and you will not be hearing from me for the next three-quarters of an hour as appears in the program. I got Pip Pattison to come back up, Helen Christensen, who just stepped down as the Director of the Black Dog Institute at the University of Sydney, Peter Baume, who's sitting here in the front row, and Jaky Troy. We are going to have a discussion here.

I was glad to see that people are very animated there at the end. That idea that there's something out there that's smarter than us is just so fascinating. I was worried that people might have dropped off by this point but they haven't. We are on the fabulous lands of the Gadigal people. We want to get back outside there as soon as possible.

I must thank Susan as the President of the Royal Society of New South Wales for organising the Forum this year. When she contacted me this earlier she said, "Look, I want to have something about the brain sciences. There are really big questions out there in the world at the moment. Really big challenges that we face." And she started with my personal favourite, which was evil. You know there's bad stuff happening and there's a lot of that seems to be underpinned by human behaviour that doesn't really seem to have a capacity to cope with the challenges that we face in a 21st-century global world.

Is there something about us — about the way we're wired, or the way we work or discussing, the way we believe, the way we understand — that's preventing us moving into the 21st century and coping with the 21st century? Then she enrolled people like George Paxinos, who said, "Well, there's a problem here: we've got this 100,000-year-old technology. It doesn't really drive well in the global world. It's a small-world network. It's used to dealing with people up close in small groups surviving in various ways as part of a group. The global world we live in is completely different. No, we're stuffed, because basically it is not that adaptable to the challenges we face."

An important set of conversations we had about the roles of the various Academies is that they bring deep disciplinary science and very different ideas about the world and how the world is constructed, into that discussion. And really importantly from the Royal Society point of view, and I think for the Academies, the question is: are we of any use in the wider worlds in where we exist? We can amuse ourselves for very long periods of time and we can have deep conversations about the areas in which we are each in and should be fascinated by that.

I was reminded of this some years ago when I was on a committee chaired by the National Health and Medical Research Council CEO at the time who was meeting with the heads of the federal departments.

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1 This is an edited transcript of the session [Ed.]

And lined up all these really great science people in health and medical research who all turned up and said, "We have answers that matter." And the secretary said, "Not to the questions we're asking, which are what actually afflicts us."

So we thought this part of the day should be devoted to all the stuff you've heard today from really brilliant people doing really great work in what they believe are the answers that matter or could matter. And we did select as the organising committee two particularly important phases of in a wider society: first, the importance of child development for the future. Children are the sentinels of what is happening because brain development is affected very much by the environments in which they're growing up. Their changes in behaviour and function tell us much more quickly what is happening in the society than those of us who are relatively impervious at a certain stage, who have become fixed. Was it George who said those who prevent progress in their field are the real senior people in their field?

The second phase is related to aging. I've got Peter Baume here. I don't know if Peter was responsible for this. I think the worst thing ever happened in my professional life was the Intergenerational Report: aging is just a cost. Aging is just a problem. It's something the rest of us, the real earners, have to do to take care of the rest of you, who are a cost to society as you age.

Two of the biggest challenges — I'll come back to this in a mental wealth sense shortly — is the importance of the two phases of life: Child Development and Aging. We long outlive our utility now due to health and medical research, long beyond reproducing. We no longer should be hanging around. We're just using up resources, as George pointed out. But these are two of the big challenges for the society we have now — long lives, complex lives and I think very importantly, as raised throughout the day perhaps in our Western cultures, more disconnected lives. What are the implications of that? So do we actually have those capacities? I wanted to get four more intelligent people than me up here to start with, and ask them: out of all the answers they've heard today, do any answer any of the questions or do any help them to think about any of the questions that they think matter?

When I was very young, Peter Baume was very prominent in both his political life as a senator and in talking intelligent ideas or an idea of intelligence into national politics, which I thought was really interesting. To actually engage with politics, he continues to engage through education and his work in those areas. If you pop down to ANU you'll see a really important thing — you'll see his name on buildings. They must think he's dead but he's not — he's alive and here and with us.

Peter, do you think any of the answers that you've heard today help to answer the questions that you worry about and those of course who are making political decisions though they worry about?

Peter Baume: Well, thank you, Ian. One of the recurring themes earlier in the day from some people has been a variant on the sentence: what the world needs most is more money for my cause. Now, you've got to keep saying that, but logic alone is not going to win any political argument. There's got to be the pushing of a political hot button as well. You need both things. So Grace Tame and Brittany Higgins were not important for themselves, but they were very important for the causes that they articulated. The community was ready to move and then policy change could occur.

Andrew Leigh spoke by video today, but apart from him I don't think there are many people here who've sat around a Cabinet table. In Cabinet when there's a consideration of an issue where good and bad are quite different, decisions are quite easy. And 80% of the agenda of any Cabinet meeting is decided within 20 minutes. And the other 20% takes 3 hours because the issues are balanced — good and bad — and the politicians who're sitting around that Cabinet table are smart, they're able, and they understand what you've said. They know the issues exist, but they're faced with a choice between A and B, where A and B are fairly close.

The economists here will tell you all about the issue of opportunity cost: if you spend a dollar on A you can't spend it on B. Just think for a moment about the size of the budget cake sitting in the centre of the table. It's going to be cut into slices. You're going to get a slice and so's the person next to you. And the people around the cabinet table have three lots of responsibilities: they're politicians and they're responsible for their electorate, they they're responsible for the country, and they're responsible for their portfolio. So a lot of them are going to be interested in getting money for their portfolio. The minister for roads wants more money to build roads and build bridges and so on.

Either the budget cake is going to increase in size so everyone can get a slightly bigger slice, or your increase is going to come at someone else's expense. The person to your left or your right suddenly becomes an ally maybe, if you're very eloquent. But they know that your success will mean less for them. So keep that in mind when people are considering the causes for which they're fighting. Keep articulating what you're saying, but remember something else is needed before you're going to win politically.

IH: Thank you, Peter. Helen who's been involved in a lot of the complex issues around mental health and their wider application in Australia, particularly around suicide prevention and some of the wider issues and must say important in terms of the last discussion. The wider use of technology to do things in the world that in our world I think Andrew Chanen would say this morning: it's assumed to be able to occur between one human and another. What do you think, Helen, in terms of the extent to which the things that people have been commenting on, or which bits of what you've heard, might contribute most to answering questions that matter?

Helen Christensen: I guess my response would be slightly orthogonal to that question. I'll describe an article that was published in *Nature* in January this year which basically said that our innovation had stalled and that we are not making the level of progress that we should be. The authors put it down to a number of things they looked at. It was a very well controlled article, as you can imagine for a *Nature* paper. And basically they were saying we're working in silos and we're not communicating with each other — we're getting smaller in the areas in which we're working and we're not leveraging the knowledge that we have across disciplines. They also made the point, and I think it's a really good one, that you need a particular device in order to kind of kick-start some of this innovation.

One of those devices is technology, whether it's artificial intelligence or the technologies that we've been using — the new tools that we have in order to do things. These provide a beacon about what we can

do. I think we should think differently about how we structure our science.

Going back to the questions you were talking about: I think we need to have "moon shots" that we all try and work towards with all the strength of the different disciplines that we have. To conceptualise problems in the way that you were talking about earlier, but also about what sort of mechanisms and efforts we can bring in. Because at the moment our science is basically working off grants, and we virtually know what we're going to do when we get that grant. We don't really think that much. Congratulations to the organisers today because I think this has been a very fruitful conference in bringing together different points. I think this is what we as Academies should be doing more and more of, rather than concentrating on just describing what we're doing in our own areas.

IH: So what are your top two or three moon shots in the current world?

HC: I dare not say this in front of all the AI people but I think we need centres where people are freed from doing their grants to think about a question like: what's the new therapy, if that's the right way of describing it. And what you were saying before — we've had Freud, we've had CBT, we're moving into different stratification models etc., but what's the new way of thinking about how we change ourselves so that we have better mental health? Maybe large-language models or some of the generative AI opportunities and bringing in different people? So that would be one to me. We are failing in our therapies and we talk about personalisation. That would be a moon shot. How can we improve that?

IH: I now want to move on to Pip. Most of the organising of the Forum has been done by Pip and Sue. Pip took on a great job a little while ago as the Deputy Vice Chancellor of Education at Sydney University. That's a challenge: that's probably a moon-shot type activity — trying to change the educational framework under which Sydney University has operated for the last 175 years. I said to Pip in conversation, "Why'd you ever do that?" I just couldn't think of anything worse to take on as a challenge. And she said, "Because education really matters, how we teach it really matters, how we think."

Pip has been associated with a major restructure of the educational framework at the University, to be less narrow in its disciplinary base and hopefully respond to current generations in a broader way of different experiences, to pick up the Einstein quote earlier — on different experiences of learning, not just being subject to being told what to think. So, Pip, what do you think about what you've heard and the way people think about mental function as ramifications for how we educate?

Pip Pattison: That's a great question and I just want to say I love Helen's idea about tackling some big questions together, because I do think occasions like today — where we tackle themes from a number of different disciplinary perspectives — just spark ideas and connections. To use the metaphor of the great big brain out there that includes us all that we haven't necessarily thought of before. I think from an educational point of view the development of individuals who can gain an expertise in a discipline and understand it thoroughly and well is a long-standing approach to education, and it's one we shouldn't move away from. But the capacity to actually have meaningful conversations with people who work in other areas or come from other backgrounds is, I think, something that we've really missed a bit at, particularly at the tertiary level.

I think it's much less problematic in school education, although I'm not an expert in that. It just seems a little bit less siloed. And I do think the kinds of approach and experiences that Helen just talked about for us as a scholarly community are just as important for our students. Because I think it's through the exploration of things that are beyond what we know that we really do build the capacity to work across the boundaries. That's just a fundamental thing for education and for success in work, research, and life.

IH: So I move on to Jaky. I want to recognise the impact of Jaky's way of thinking on my own work. I've had the great pleasure to work with Jaky in recent times on a number of large projects. One thing you just alluded to in passing, Jaky, was the use of technology to assist families, particularly mothers and children, with early childhood development in Afghanistan and other countries through technology — a combination of technology group thinking delivered in countries like Afghanistan which continued after the Taliban had retaken over the joint. It brings together social scientists — in particular, digital technologists. We got involved out of the neuroscience of development: what were the sort of strands with a strong focus on what Adam was about: social cognition.

The most important thing in humans developing is not simply statistical or adding or mimicking calculators. It is the capacity to operate in social groups. And our discussion about what is evil or what psychopathic or what the human thing is that leads to such evil — it's the decline in concern and the loss of empathy for others that actually leads people and underpins some of the most terrible things that humans can actually do. And that tension between what is

good for the individual and what is good for the group on an ongoing basis.

The particular project that Jaky and I have been working on was unique. We've constantly had to look at different cultures around the world. That project looks at the use of technology — neuroscience of child development — in each place that we' rolled that out: I got to go to Uzbekistan last year, to Kazakhstan, to Indonesia, to Malaysia, around the world. Each place is different in its cultural settings.

What most of those places have that we do not have is very strong transgenerational and kinship relationships — ways of speaking with each other but mutual responsibilities etc. I love this great respect for older people and their role and their contribution to the emotional growth of two generations — not their children but their grandchildren and others — and the role of relationships in those particular works.

Second, the influence of Jaky's thinking in the period immediately after the Referendum when people like myself were going, "What do we think now?" I had the pleasure of doing a webinar with Jaky and Professor Pat Dodson, who's one of the leading Indigenous psychologists in the country, about an important thing, which was: and to stop and think. The Indigenous people did not immediately respond to the political cycle, did not immediately engage in the analysis of the Yes campaign. They said, "We're going to take time to think about it."

I know an elderly woman from Gladstone in Queensland. I contacted her, hadn't seen her for some time. And she said "Ian, I'm not speaking this week, I'll talk to you next week." And Jaky pointed out, "We need to take time to grieve, we need to take time to actually consider not all the rationality what to do next immediately come together — we

need to take time to think about the emotional impact of all of that, all that had gone beforehand — who's most affected," and not immediately. Retreat to the kind of rational solvent kind of way that we would do. And very much do as an individual thing.

Jaky and Pat convened online, using technology to bring people together, 300 people from around the country, to just consider and share their response to the Referendum, not to the outcome but just to the position in which we find ourselves. I thought, "What a different way to think about the problem." Made no sense to our political systems, made no sense to our immediate media, our people who are asking people on the night, "What are you immediately going to do?" with the Prime Minister the next day, "What are you immediately going to do? What's going to be the solution now for closing the gap?"

A different way of thinking about stuff collectively, with strong emphasis on the emotionality required to empower human behaviour, to do what Helen's alluding to — to act collectively, to actually think about the biggest stuff that's at stake. So, Jaky, out of all the things you've heard today and interaction with, because you've doing this kind of interaction with both neuroscience and with technology for some time, has it helped at all? Is it helping at all? Is it helping to solve big problems or it just a weird way of thinking?

Jaky Troy: Well, Pip said to me in the break, "I think you're on to something" with the work I'd like to do with languages: the 407 missing languages. I should say there are about 15 that are still strong, and then there are a whole lot of others like my own. My mob were in this particular building, right in this room, singing a song of my people that probably hadn't been sung for 150 years. And in that moment we were all *Naru* together, of one voice, using our language and being culturally ourselves.

Now AI could really help us with getting our language back. That's just one kind of technology. Something as simple as, what was it? Idiotic AI? Or not so intelligent AI? I remember AI being a program I used with a breadboard. That's how long ago. But it can help us generate language that we can interact with, engage with. For all these languages that we only have fragmentary information about, we can input. I'd love to have the money — we need to get around the Cabinet table — I used to manage the broadcasting and languages program for Australia for Aboriginal languages. We could input what we know about the languages and generate a way of using my language.

But I would never want to take out the human element. I would never want to miss the moment of walking with my real people into here and singing our song and the engagement of the humans the audience and really no silicon. By the way, you can make a silicon brain responsible: you can just squash it if it doesn't do what you want it to do. But to take the human out of what we are that would be a huge loss, I would say as an Indigenous person — as an Aboriginal person — our response to things like the Referendum and for me the death of my husband. I wouldn't want to miss those experiences and feel the grief and feel the joy. And nothing can ever synthetically create that for me — it wouldn't be me experiencing it.

What I take away from today is there are huge, huge possibilities around understanding our brains and how to manage it and care for our living brain and how to augment what we do with technology. But we never ever lose what we are here today. We

should do more of this, sitting in a room. Without engaging with other people and not sharing ideas is not going to create the brilliant random kind of things that humans do.

I know machines can do it too. But I don't think they have as much fun, and they don't have the tactile responses that we do. Everything to do with what we are as human. Machines don't eat, they don't drink, they won't get Alzheimer's — well maybe they will, I don't know — but it's keeping the human in all of it which I think. Also understanding yourself as part of an animated world.

It is great to think all these boards were trees. And there's still something of those trees in them. That tree out there has that spirit, you know. All the birds and everything were engaging. They're all looking in the windows, looking at us. And for us, that is because there is this multi-dimensional engagement that is always happening, and no technology can really give us that. We have to have something of us as humans in there to keep that going.

IH: The other thing in Susan's agenda was: we should engage in a sort of overt, political way. The Academies need to engage politically, partly picking up what Pip's saying. Three of the people unfortunately couldn't be today who had this conversation and worked with us. Those who were thinking about the future of Australia: Geoff Gallop, who was previously the premier of W.A. and had a depressive episode from which he's recovered and then works with us; Sam Mostyn,[2] who now works for the Prime Minister's agenda on female pay equality and growth in key areas of the caring economy; and Victor Dominello, a previ-

ous Minister here in New South Wales for services. In New South Wales we used to have these crazy systems where you lined up for your licence and you lined up for your registry for this. And you got all these different audit agencies. Victor completely transformed that thing in New South Wales called Service NSW. So now it exists: most of that stuff's online. Anything can be done online. He refers to it as a huge transformation. When people said it couldn't be done, he goes, "I've walked on the moon. I've done it. You can take Human Services and you can put technology at the middle of it. You just have to be prepared to put the information and people at the centre of services that are not." All of them are involved with us in growing concepts around mental wealth.

Where does Australia go? I have a daughter who works for the Reserve Bank who's very proud of the fact that Australia used to be considered at the top of the world economically: we had 20-something years of continuous growth, we got ourselves on the front page of the *Economist* for doing that. At the time suicide rates were actually going up, young people's mental health was getting worse, and the challenges are associated but we seemed to be economically thriving. What Peter was alluding to: the cake was getting bigger, GDP was kind of growing. But were we okay?

I think in the post-COVID era and the other challenges we face, it's an interesting time because the economic discourse now is: economically we're not okay: cost of living is going up, housing affordability is going up, there's uncertainty, interest rates etc. The political discourse is not one just of growth, it's now of all the economic challenges. Do we have time for social transformation?

2　In April 2024, Prime Minister Anthony Albanese announced that Sam Mostyn will be sworn in as the 28th Governor-General of Australia on 1 July 2024. [Ed.]

Do we have time for anything else or is the new economic challenge now even more demanding of attention?

Very importantly, the UK government Office of Science back in 2008 produced a summary of all the areas that were at the time termed the mental wealth of nations. Many of us have knocked off that term ever since and tried to get the political class — we did have Malcolm Turnbull talking this at one stage — it isn't just about mental health or it isn't just about GDP. What is our collective mental wealth? For countries to prosper both economically and socially you've got to focus on the growth of the collective mental wealth. It's not an individual brain capital thing. It's not the summation of all the individuals in that society. It's our collective mental wealth and what that may constitute. And they did develop part of that.

It's still well worth looking at. They developed a lifespan kind of approach. We spend from 9 months to 22 years investing in the brain and social development of our kids. Economists would see it as a big cost but at least for kids we call it an investment. So I say to my kids, we've invested a lot of time. To repay it, take care of me when I'm old. I expect a large return on investment. They're not so personally sure.

I was so glad that Glenda said — I've been telling people that forever, but no one believes me — that you don't lose those cells as you age — it's actually the microglia, the glia which are the cells which are most responsive to the environment. They're the ones that are reacting to the environment all the time. That's problematic. And they underpin the synaptic connections.

There's a separate podcast I'm associated with, "Never Retire." Clearly people in this room are never retiring: they come out.

George will come out at any time to talk to anyone in any coffee shop anywhere, preferably in Greece. That association with aging is a cohort effect reported in those who've become ill in terms of their care. Those who are still working or actually in good health, their brain capital does not decline. It was very important to have this kind of capacity. The idea we've been working — on building new models of this.

I'm tied up an economic discourse. This is the thing that Geoff Gallop and Sam Mostyn and others are trying to do: build a new metric of this in this country, the metric of mental wealth. So we're trying to do what the economists do — we're trying to build these complicated models and put in the dollar value of social and mental wealth alongside GDP. The current Treasurer says, "Yes, the well-being economy." Lots of people say well-being economy. What does it mean? Because at the same time the government says it's only cost of living that matters, or it's only interest rates that matter or — you just heard about architecture — it's only housing affordability, so we've just got to build as many as we can as close to something else. Very narrow kind of perspectives. So we are tied up in this wider issue. For example, some early modelling of the dollar value of what people do through volunteering and caring, which Andrew Leigh alluded to earlier, is about $285 billion a year. So, Peter, do you think we have to do something?

PB: I think human personality hasn't changed and — Tony knows this better than anyone — crises like the COVID one are going to recur and recur and recur. We just have to be ready for them, and, since our personalities haven't changed, governments will respond in an ad hoc way.

IH: Yes we didn't really dwell on that — forgetting is an essential human capability. Sharon and others might want to comment.

Question: One of the things that occurred to me in listening to all of the talks today was that they weren't just saying I want more money for my bit. They're also saying, here's a solution but it isn't going to happen tomorrow. These are long-term things. But it's also in requesting, for example, funds to assist in particular areas, such as early diagnosis or early intervention or whatever else. Almost all of them propose that ultimately it would be a cost saving because you're not going to come back.

To your point about human capital — you're maximising that human potential and capital, so actually the issue here is not one of implementation or a pie getting bigger or smaller, it's short-termism. And that also speaks to COVID in the crisis response rate, which is basically: had one been prepared — and the UK has a huge review going on at the moment about exactly that — had they been prepared and done any of the things that they learned from SARS, they could have saved themselves £600 billion. So a lot of this is down to seeing that there is a return on this investment. And that's the way you might get economists and business people to understand why it's important to make these investments.

IH: Jaky might want to comment here. Courtesy of Jaky in these projects, I found myself involved with Kazakhstan during these particular things which have a seven-generation approach. Can you name the previous seven generations from which you are personally derived? I got back to the West Coast of Ireland and got lost. I did find my grandfather on the parish registry in Galway. After that got no idea, can't say. You know it's a really interesting

idea of continuity, and I think Jaky's been saying this continuously. We don't just have short-termism in planning, we have short-term thinking about ourselves. And this has become very individualistic in our own culture, but also our own selves over time. Do you want to? So this is whether this is all humans or it's, what did Jaky say earlier, a white Anglo-Saxon English idea.

JT: It's a great pity that Australia doesn't want to learn from the way in which Aboriginal people organise ourselves. I wasn't joking when I said earlier that I think we've spent at least well 72,000 to 120,000 years dealing with social complexity, and dealing with it very elegantly. This country was lightly managed, we lived well. We were human, we killed each other, we fought with each other, we made babies with each other, we did what people do. But fundamentally it's the knowledge of how we managed ourselves really effectively. That was our technology. It was the development of 407 languages, developed because that's 407 different socio-political groups of people who don't want to be the same as the people next door. But they don't want to always be killing them. They want to be interacting and engaging. In the end, all technology is the use of language systems to produce technology — machines — that will think for us and do work for us.

I have to say this: on this very spot here, Phillip and his fellow First Fleeters, the officers, were learning the language of the Sydney area. One of the things they learned was that the Gadigal people here thought what the British were doing was ridiculous: they were wasting all their time building things, running around, exhausting themselves, not eating well, building very elaborate houses out of Aboriginal sandstone.

In thinking about how to describe what the British were doing, what they said was: "You should be doing work and making use of the land." Of course we hadn't used the land for building. And they said, well maybe serious creative play — play looks like what everybody does most of the day, which is enjoy themselves. Then you spend a bit of time feeding yourself and while you're doing that you're enjoying that because it's social activity with other people.

You're never doing things just by yourself stuck in a room staring at a computer screen. You're always active with other people. People matter — the generations of people matter. Keeping that kind of thinking into this world that we've got now where you've got — look, technology makes life easier. It frees humans up to do things that they should be doing — which is smelling the roses.

One of the last things my husband said was he wished he'd had time to smell the roses, to just be human, and not have to spend all day in super-secure rooms, bunkers, dealing with computer programming. He did love doing that. His serious creative play mattered to him, but he would have liked a bit more time just to be with us.

IH: On the short-termism question — because this again comes back to a point I think Susan quite rightly highlighted — we're very critical of political classes and the election — things we have as if it is their fault. But what is the role of the institutions that we are all part of in the longer-term processes?

I'm going to ask people about this. It's some interesting discussion we had about whether Sydney University is very good at any of these things. The universities and the education systems often come up as the kind of institutional things about longer-term memory and planning, and getting beyond short-termism and creating skill sets and people who don't necessarily just do that which is so damaging. Do you want to comment, Pip?

PP: Sure, and you're giving me a second chance to answer the first question. It came up today in a number of different contexts: the sort of integration of social and more cognitive skills is something that happens early in life. It's something that continues through life. At the universities we just haven't paid enough attention to the non-cognitive aspects of the development of young people. A lot of the sort of natural mechanisms for encouraging a lot of the informal learning activity that took place — and particularly as a result of COVID — have been eroded, partly by the universities getting much bigger, partly by a change in the sort of economic conditions and students needing to do more paid work, and partly through competition with a whole range of other activities, especially those on social media and all that we heard about today too. That all goes through the lifespan. Part of what we need to do is just make sure those opportunities exist for young people to actually develop the skills that will make them good members of collectives.

IH: Do you mean actually come to university and learn by experience?

PP: Yes, I do. And not only learn by experience, but learn by experience together with others in groups. So, yes.

Q: One of the things that I studied when I looked at universities about 25 years ago was that there were two types — there were communities of practice who established the engineering and sort of outcome-oriented university, and then there were communi-

ties of interest who thought about things very carefully.

When we started working on this, we made a distinction between communities of practice who are trying to do things that transform the architecture of our societies at the kind of physicality level, and then we want to think more clearly about the future and those were communities of Interest. Now if you look at the universities around the world, there were two types: there were very practical universities — Strathclyde is a really good example — and there were very sort of thought-centric universities. We sort of oscillate between these.

But it seems to me that very often we confuse the fact that practice is limited by the laws of physics generally at some point, and you therefore can make up things in your head that are never going to be true in practice. Then you are not living in the reality of practice anymore. One of the things that worries me at the moment about a lot of the discourse that happens is: people imagine futures in their heads that are not connected to practical reality. How do we get the new synergy, the new genetic code of practice — synthesising with imagination in a way that is productive and plausible and rooted in the reality and the struggles of real people who live in ground truth?

IH: You're really interesting people, but most of you would make hopeless decision makers because this balancing of the competing sets of ideas — trying to bring the best of what is out there down into practical application in people's lives, within the culture within which we live at the time, within the constraints of the way that we respond cognitively and emotionally to those things — I'm not sure why Pip just referred to those other skills as non-cognitive: I'd say they were very cognitive skills — in the sort of social cognition or the emotional kind of world.

How do you do that? I think the hope of today is to present a lot of what is really going on in the area, to do it across the various Academies and what they all bring in their own rich traditions into that area. And then to be able to convene a group like this to talk about it.

Now to thank the Governor for access to her home and answer her question: my own view would be that her own brain is considerably different in the 21st century than before because our brains are changing all the time: those little microglia running around are knocking off synaptic connections (or not) in responses to the environments in which you are currently living. And on that optimistic note I think we're going to adjourn to the Garden.

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Thesis abstract

Synthesis of glyphaeaside C and structural revisions of the glyphaeaside alkaloids

Brendan J. Byatt

Abstract of a thesis submitted to the University of Wollongong

In 2015, ten C-alkylated iminosugars were isolated from the roots of *Glyphaea brevis* (Malvaceae). The alkaloids were purported to possess 1,5-dideoxy-1,5-iminohexitol cores, with the A-, B-, and C-type glyphaeasides bearing L-*fuco*, D-*galacto*, and D-*gluco* configurations, respectively; as well as unprecedented di-, tri-, and tetra-hydroxylated nine-carbon side chains with terminal aryl substituents. Glyphaeaside C — the only member of its type — was found to be a potent and competitive inhibitor of almond β-glucosidase (IC_{50} = 0.15 μM, Ki = 0.031 μM), which was especially remarkable considering the absence of any significant α-glucosidase inhibition, for which other related iminosugars with the same configuration — including α-homonojirimycin, α-1-C-(*n*-octyl)-1-deoxynojirimycin, and α-1-C-(8-hydroxyoct-1-yl)-1-deoxynojirimycin — are known to possess.

The structural uniqueness and peculiar glycosidase inhibitory activity of glyphaeaside C thus prompted a total synthesis investigation of its purported structure. The α-aza-C-glycoside unit was accessed via a stereoselective Grignard addition to a protected D-glucosylamine, eventually followed by a reductive amination-cyclisation to afford the D-*gluco* piperidine ring analogous to reported methods. After a cross-metathesis reaction to install the terminal phenol substituent, the side chain alkene moiety was subjected to complementary Sharpless asymmetric dihydroxylation reactions, followed by global deprotection to afford the two 7′,8′-*threo*-diols as the major products. While the NMR spectroscopic data of the afforded C-alkylated piperidine iminosugars were in agreement with similar compounds reported in the literature, they were notably dissimilar to that of natural glyphaeaside C. The iminosugars prepared from this pathway were found to be good inhibitors of human lysosomal α glucosidase and α-galactosidase, as well as of related glycosidases from other sources.

After examining the NMR spectroscopic data of the natural product, it was hypothesised that glyphaeaside C was in fact a 2,5-dideoxy-2,5-iminohexitol derivative of D-*manno* configuration — a motif more commonly found among natural C-alkylated iminosugars than that of the purported structure. To confirm this hypothesis, a total synthesis of the revised structure was attempted via preparation of a known vinylpyrrolidine precursor. Installation of the side chain moiety was achieved by epoxidation of the vinyl substituent, affording a mixture of diastereomers that were separable by column chromatography. Fortuitously, the major epoxide diastereomer was found to possess the desired configuration, conferring an inherent advantage over analogous carbaldehyde addition strategies

that have been previously reported. After ring-opening with a Gilman-like reagent, the resulting 8-nonenylic alcohol was subjected to a sequence of reactions analogous to that employed in the previous pathway, followed by semi-preparative HPLC to afford the four side chain diastereomers. The NMR spectroscopic data of the major *threo* products were identical to that of the natural product, thus confirming the revised pyrrolidine-based structure of glyphaeaside C. Although the configuration of the side chain diol moiety relative to the iminosugar core can be deduced with reasonable confidence, the absolute configuration of the natural product cannot be unequivocally assigned from the available data. The products synthesised by this method displayed potent inhibition against bovine liver β-glucosidase (IC$_{50}$ values of 0.019–0.060 μM) and β-galactosidase (IC$_{50}$ values of 0.019–0.043 μM), and moderate inhibition of human lysosomal β-glucosidase (IC$_{50}$ values of 33–195 μM); importantly, no significant inhibition of rice α-glucosidase was

observed, although the relatively strong inhibition against almond β-glucosidase (IC$_{50}$ values of 0.77–0.99 μM) was less than that displayed by the natural product. The novel epoxide strategy used to access the revised structure of glyphaeaside C represents a potentially useful synthetic pathway towards similar C-alkylated pyrrolidine iminosugars, including several of the related broussonetine alkaloids, and could be conceivably applied to the synthesis of other pyrrolidine iminosugars with different ring configurations.

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The potential of online food ordering systems to increase healthy food purchasing behaviours

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Abstract of a thesis for a Doctorate of Philosophy submitted to The University of Newcastle, Australia

Background and aims

Poor dietary behaviours, resulting in the over-consumption of energy, saturated fat, sugar and sodium, are a leading cause of global disease burden. Given dietary behaviours established in childhood track through to adulthood, childhood is considered a critical period for the establishment of healthy dietary behaviours. School food services, such as canteens or cafeterias, are recommended settings to improve child diet, due to their wide reach, frequent use by students and the regulatory and policy context in which they operate. Despite this, historically, research in these settings has identified purchasing behaviours which are not aligned with dietary guidelines. Online food ordering systems that enable users to pre-order and pay for menu items online are increasingly common, including within the school setting. These systems can support the direct delivery of interventions that encourage the purchase of healthier foods at a critical behavioural decision (i.e. the point of purchase). Despite this, little is known about the feasibility, acceptability and efficacy of using online food ordering systems to deliver interventions to encourage healthier food purchases. Therefore, the broad aim of this thesis was to investigate the potential of online food ordering systems to deliver public health nutrition interventions to increase healthy food purchasing. Specifically, this thesis will address evidence gaps relating to the acceptability and efficacy of an intervention embedded within an online food ordering system to increase healthy food purchasing from primary school online canteens. The thesis objectives are:

- To assess the nutritional quality of foods purchased by students from primary school canteens in one region of Australia (Chapter 2)

- To systematically review the literature to describe the association between digital health intervention engagement (a factor hypothesised to influence intervention effectiveness) and dietary intake (Chapter 3)

- To assess the uptake of online canteen lunch ordering systems in primary schools and the acceptability of strategies that could be implemented within such systems to encourage healthy food and beverage purchases by students (Chapter 4)

- To develop (Chapter 5) and evaluate the efficacy (Chapter 6) of an intervention implemented in an online canteen lunch ordering system in reducing the energy, saturated fat, sugar, and sodium content of primary school student lunch orders

- To systematically review and synthesise current evidence for the effectiveness of interventions implemented within real-world online food ordering systems to encourage healthy food and beverage purchases (Chapter 7)
- To provide a summary of thesis findings and the implications for future policy, practice and research (Chapter 8).

Results

To address the first thesis aim, a cross-sectional study was undertaken with 18 government primary school canteens in the Hunter region of New South Wales, Australia. The study found that 76% (n = 1,871/2,475) of lunch items purchased from school canteens were classified as "less healthy" according to the state healthy canteen policy of the time, with the most common items purchased being "sugar sweetened ice-blocks and slushies." The findings indicated that there is considerable scope to improve the nutritional quality of student purchases from primary school canteens.

To address the second thesis aim, a systematic review was undertaken to describe the association between user engagement and the effectiveness of digital health interventions targeting dietary intake. The review identified just seven studies that had assessed an association between digital health intervention engagement and dietary intake. Overall, the review found mixed evidence of any association between user engagement and dietary intake, with the majority of findings reported as "inconclusive" for measures of usage (e.g. logins, time spent using the intervention, activities completed) and subjective experience (e.g. interest) respectively.

To address the third aim, a telephone survey was conducted in 2014 with 123 school Principals in one region of NSW, Australia. The study found that 8% of schools were using an online canteen and that 38% were likely to do so in the future. Overall, the majority of Principals agreed it would be acceptable to implement the suggested strategies to encourage healthy food purchasing in online canteens (>70%), particularly strategies that involved the provision nutrition information (93%) and labelling (92%).

To address the fourth thesis aim, a cluster randomised controlled trial of ten primary schools (and 2,714 students) found that an intervention (including menu labelling, placement, prompting and availability) implemented in an online canteen decreased the energy (between group difference: –567 kJ), saturated fat (between group difference: –2.37 g) and sodium content (between group difference: –151 mg) of primary school student lunch orders (P < 0.001 respectively), without any adverse impact on canteen revenue. There were no significant differences found for sugar (between group difference: 1.16 g; P = 0.17).

Finally, a systematic review of eleven studies (six RCTs; two cross-over RCTs; two cluster RCTs; one CCT) found that interventions delivered within real-world online food ordering systems (including meal delivery apps, meal subscription services, online supermarkets and online canteens and cafeterias) to encourage healthy food choices were effective in reducing the energy (standardised mean difference (SMD): –0.34, P = 0.01), fat (SMD: –0.83, P = 0.04), saturated fat (SMD: –0.71, P = 0.02) and sodium content (SMD: –0.43, P = 0.01) of online food purchases.

Conclusion

This thesis provides evidence for the acceptability and efficacy of using real-world online food ordering systems to increase healthy food purchases. Such interventions may be particularly relevant for public health practitioners, educators, retailers, researchers and policy makers seeking to improve digital food environments and public health nutrition. This thesis concludes by providing recommendations to support decision making regarding using online food ordering systems to deliver interventions to encourage healthier food purchases at scale.

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Specification of dorsal root ganglia sensory neuron subpopulations derived from human pluripotent stem cells

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Abstract of a thesis for a Doctor of Philosophy, submitted to the School of Medical, Indigenous and Health Sciences, University of Wollongong

The detection of sensations is essential for everyday functions and requires specialised dorsal root ganglia (DRG) sensory neurons to detect and transmit the stimuli to the central nervous system for processing. The DRG sensory neurons can be broadly classified as either (1) proprioceptors (that detect movement, muscle pressure, and tension), (2) low-threshold mechanoreceptors (LTMRs) (that detect touch, hair deflection, and vibration) or (3) nociceptors (that detect pain arising from harmful thermal, mechanical, and chemical stimuli). Unfortunately, there are major challenges in studying sensory perception and disease, including the difficulty in acquiring human tissue samples and the limitations in the translatability of rodent models due to inherent differences between human and rodent sensory neurons. The use of human pluripotent stem cells (hPSCs) can circumvent these challenges by providing a constant source of human cells that can then be differentiated towards sensory neuron cultures. However, current protocols to generate sensory neuron cultures are often limited by low reproducibility, low neuronal yields, mixed populations of neurons, prevalence of nonneuronal cells within the cultures, as well as the requirement of long maturation stages to obtain functionally mature neurons. A promising approach to generate populations of functional sensory neurons is by mimicking sensory neurogenesis using a combined stepwise addition of extrinsic factors (small molecules and growth factors) to direct hPSCs towards progenitor states and neuronal types, combined with the induced expression of lineage-specifying transcription factors to drive the differentiation to a specific neuronal fate. Thus, the major aim of the work described in this thesis was to derive DRG sensory neurons using a combined extrinsic-factor and induced-transcription-factor differentiation approach to generate cultures of sensory neurons and to then functionally characterise the sensory neurons.

A key goal of this PhD thesis was to mimic sensory neurogenesis by inducing the expression of lineage-specific transcription factors at a developmentally relevant progenitor cell type (i.e., enriched neural crest cells). The work presented in Chapter 3 describes the successful differentiation of hPSCs into caudal neural progenitors (CNPs), which were then further differentiated and enriched for neural crest cells. This protocol was then implemented in Chapters 4 and 5, which aimed to generate and functionally characterise hPSC-derived sensory neurons by inducing the expression of lineage-specific transcription factors in the hPSC-derived neural crest

cells. The work in Chapter 4 determined that the induced expression of the transcription factors, NEUROGENIN-1 (NGN1) or NEUROGENIN-2 (NGN2), in neural crest cells both significantly enhanced sensory neuron differentiation efficiency and generated a heterogeneous population of functional sensory neurons. The results presented in Chapter 5 demonstrated that the induced co-expression of the lineage-specific transcription factors, NGN2 and RUNT RELATED TRANSCRIPTION FACTOR 3 (RUNX3) or NGN2 and SHORT STATURE HOMEOBOX 2 (SHOX2) in hPSC-derived neural crest cells generated enriched mature sensory neuron cultures that had expression and functional profiles consistent with proprioceptors or LTMRs, respectively. Additionally, the work described in Chapter 5 also aimed to investigate whether there are functional differences in the mechanosensory physiology between the two classes of hPSC-derived mechanosensory neurons and the molecular mechanisms by which the two classes of hPSC-derived mechanosensory neurons respond to stimuli. The mechanosensory neurons, denoted as induced-proprioceptor neurons (iPN) and induced-LTMR neurons (iLTMR) were exquisitely sensitive to mechanical stimuli and exhibited distinct mechanically sensitive responses to stretch and to submicrometre (0.1 μm) mechanical stimulation by probe indentation to the soma. Additionally, the iPN and iLTMR displayed different adaptation kinetics reflective of distinct sensory specialisations. Importantly, the iPN and iLTMR fired action potentials in response to < 1.0 μm mechanical stimulation (probe Indentation) and knockdown experiments demonstrated that these responses to mechanical stimulation were predominately mediated by PIEZO2. Taken together, the work described in this thesis demonstrates the successful generation of heterogenous and enriched populations of functional sensory neurons from hPSCs via the combination of extrinsic factors and induced expression of lineage-specific transcription factors. The derived sensory neurons represent excellent models for the study of human sensory neuron development, peripheral neuropathies, mechanosensory physiology and for the development of directed therapies toward these neuronal populations that become compromised by trauma or neurodegenerative conditions.

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Thesis abstract

Development of composite films from seaweed hydrocolloids, Gac by-product, essential oils and plant extracts for preservation of fresh prawn

Tran Thi Bich Thuy

Abstract of a thesis for a Doctor of Philosophy submitted to The University of Newcastle, Australia

A global concern has been raised over the use of plastic for food packaging because of its potential effects on the environment and human health. Therefore, there is an increasing interest in using edible, biodegradable and renewable packaging materials for food products. Recently, seaweed hydrocolloids have been applied to produce edible films, but the films have high cost and limitation in physio-mechanical properties. The overall aim of this project was to develop edible coatings from composites of seaweed hydrocolloids, Gac pulp (*Momordica cochinchinensis*) and plant extracts or oils for effective preservation of fresh prawn. This project used Gac pulp as it is a by-product from Gac oil production, and it can be applied to overcome limitations of the seaweed hydrocolloid-based films. The plant extracts and essential oils were also applied to further strengthen properties of the composite films because they have antioxidant and antimicrobial properties. The results (Chapter 4) showed that Gac pulp is a rich source of ash, protein, fibre and pectin, thus it can be potentially applied to improve properties of seaweed hydrocolloid-based films. The results also showed that pectin can be effectively recovered from Gac pulp with high solubility and viscosity, and potent DPPH scavenging antioxidant capacity, especially under optimal ultrasound-assisted extraction (UAE) with ultrasonic time of 35 min, ultrasonic power of 200W, and solvent pH of 1.5. Gac pulp and pectin derived from Gac pulp were further tested to strengthen properties of seaweed hydrocolloid-based films. The results (Chapter 5) indicated that both Gac pulp and its pectin can improve properties of the seaweed hydrocolloid-based films. With Gac pulp incorporation, the optimal formula of the composite films was: Sodium alginate 1.03%, kappa-carrageenan 0.65%, Gac pulp 0.4%, and glycerol 0.85% (w/v). This film has high mechanical properties, low water vapour permeability and acceptable physical properties. With pectin incorporation, the optimum formula was: Sodium alginate of 1.28% w/v, kappa-carrageenan of 0.58% w/v, and Gac pulp pectin of 0.25% w/v. This film has improved colour, water vapour permeability and mechanical properties. This project further examined the effect of essential oils and plant extracts on strengthening properties of composite films made of seaweed hydrocolloids and Gac pulp or pectin. The tested additives include ginger oil, lemongrass oil, peppermint oil, lemon-myrtle oil, and commercial

Gac oil as well as extracts of lemon-myrtle, blueberry ash, and macadamia skin. The results (Chapter 6) show that adding plant oils and extracts significantly affected the physical, optical, mechanical, and structural properties of the composite films. Incorporation of the essential oils resulted in a reduction in moisture content and opacity while increasing values for hue angle and elongation at break of the composite films. Incorporation of the plant extracts showed increases in thickness, opacity, ΔE, Chroma, and elongation at the break, while there is a decrease in hue angle values in comparison with the control film (Gac pulp-based film), without essential oils and extracts. Among the tested extracts and essential oils, the film with lemon-myrtle essential oil added showed the most potential with good elongation at break, physical and structural properties, and low water vapour permeability. Finally, to test the potential application of these composite films, fresh ocean king prawns were used as a case study. The results (Chapter 7) demonstrate that coating with these composite films was more effective in preservation of fresh prawn quality than the control for 16 days of storage under refrigerated conditions. All coatings were effective in prevention of lipid oxidation, formation of TVB-N, bacterial growth, pH change and weight loss during 16 days of chilled storage. At the end of storage time, seaweed hydrocolloid-based film with Gac pulp and lemon-myrtle oil showed the best performance in quality indicators. The best formula of the film was sodium alginate 1.03 % w/v, Kappa-carrageenan 0.65 % (w/v), Gac pulp powder 0.4 % (w/v), glycerol 0.85 % (w/v), lemon-myrtle essential oil 0.15 % (w/v). This composite film had low increasing rates in TBARS (2.83 times), TVB-N (2.49 times), TBC (1.18 times), and had the lowest weight loss (2.56%) in comparison with the control sample of 6.66, 4.14, 1.31 times, and 4.72%, respectively. In conclusion, food by-products like Gac pulp have demonstrated potential for the improvement of seaweed hydrocolloid-based films. These films can be more effective in preservation of food if they are incorporated with plant extracts and essential oils. Future studies are recommended to further investigate the impact of other Gac pulp constituents, other food by-products and other plant extracts as well as essential oils for obtaining better seaweed hydrocolloid-based films. These composite films are also recommended to apply on other food products to widen their applications.

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Narratives of child-to-parent violence: an inquiry into mothers' stories and practitioners' responses for child-to-parent violence

Chye Toole-Anstey

Abstract of a thesis for a Doctor of Philosophy submitted to The University of Wollongong

Child-to-parent violence (CPV) occurs globally with broad ranging implications for family members. Studies investigating personal factors of the child and the parent experiencing violence are prominent. However, there is limited research specific to understanding parents' narratives of violence, help-seeking and responses from practitioners.

This research is guided by a feminist new material onto-epistemology. The theoretical framework for this research incorporates response-based practice and intra-action. This research has three main overarching aims:

1. To capture and articulate the narrativised accounts of parents experiencing child-to-parent violence including help-seeking

2. To identify pathways parents utilise when seeking help for child-to-parent violence

3. To explore the responses of practitioners, including social workers, when working with people experiencing child-to-parent violence.

To realise these aims, a narrative inquiry incorporating participatory approaches was employed. Questions under each of the three aims, explored the experience of CPV across four studies. Three data collective methods comprise this narrative inquiry,

they are: semi-structured narrative interviews with parents (n = 11); semi-structured interviews with practitioners (n = 19); and two co-analysis sense-making discussion groups contributed the data analysis of this study (n = 8).

Study one aimed to identify the narratives within parents' personal recounts of CPV. The analysis identified three societal narratives within a parent's recount of CPV, which are narratives of: the "good" mother; adolescence; and gender. These societal narratives shape CPV, creating conditions of what is possible and impossible for the violence. Study two gives an account of the help-seeking of parents experiencing CPV, with the main findings indicating an accumulation of behaviours lead mothers to seek assistance. The assistance sought is determined by a framing of family and perceptions of responsibility for addressing the violence. These first two studies identify key concepts, positions and implications in relation to CPV for parents' stories and their help-seeking, addressing aims one and two of the research.

The final two studies address aim three of the research. Study three provides a systematic review of interventions for families experiencing CPV identified in scholarly literature. The key findings of this systematic

review highlight the need for interventions to work with both parent and child. The review also found interventions need not be specific to CPV and may include generalist responses such as case management and counselling. Study four identifies supportive practices, strategies and responses for families experiencing CPV using both parent and practitioner data. A key finding of this study is responses for CPV must be underpinned by connections. A final chapter pulls together the findings across all studies to discuss the research project as a whole. This chapter incorporates recommendations for practice, education, policy and research.

Taken together, findings from this thesis contribute to knowledge in understanding experiences of CPV. The research also identi-

fies new ways of working with families experiencing CPV. The conceptual framework and approaches used in the research are posited as a method for working with hard-to-reach populations enduring oppression from violence. These findings contribute originally to understanding responsibility and response-ability, as well as sociomaterial conditions which make (en)acting CPV possible and impossible.

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Thesis abstract

Development of form-stable phase change material cementitious composite using recycled expanded glass and conductive fillers for thermal energy storage application

Ali Yousefi

Abstract of a thesis for a Doctor of Philosophy submitted to The University of Newcastle, Australia

Energy consumption for achieving thermal comfort in buildings is one of the most critical issues in the construction industry. Indeed, space conditioning is one of the dominant sources of energy consumption in Australia and worldwide. Moreover, there is an increasing demand for energy consumption for heating and cooling, accompanied by more greenhouse gas emissions. Hence, the efficient use of energy in buildings using passive technology is increasingly seen as a prospective solution to energy-saving and environmental concerns. In this sense, thermal energy storage (TES) systems in buildings would be a significant aid. The efficiency of TES systems through applying materials with high latent heat (LH) capacity, such as phase change materials (PCMs), has been investigated, proved and implemented within the last decades. Incorporating PCMs into the buildings decreases the fluctuation of interior temperature and shifts the power load from peak time to off-peak time, reducing the heating and cooling system load and energy usage.

Among different incorporation methods, form-stable PCM is increasingly being considered for applying and integrating PCM in buildings due to its feasibility and lower fabrication cost. In this method, PCM is impregnated into fine porous aggregates as supporting materials. Hence, a large fraction of PCM can be integrated into the building, which increases the thermal performance of the TES system. However, some problems and challenges need to be addressed before its practical application in the building industry. Low thermal conductivity of form stable PCM composite, as well as the selection of supporting material with high absorption capacity and compatible with the cement matrix and PCM, are still challenging issues. In addition, there is limited knowledge of the microstructure and physical and mechanical properties of form-stable PCM cement composite.

The ultimate objective of this research is to develop a form-stable PCM composite for incorporation into cement-based materials. For this purpose, an organic PCM is used to fabricate form-stable PCM cement composites due to advantages such as high heat capacity, inertness, stability, and non-toxicity. In this study, PCM is integrated into recycled expanded glass aggregates (EGAs) as a novel carrier using a vacuum impregnation process. In addition, two

types of thermal conductive fillers (TCFs), namely graphite and titanium dioxide, are dispersed in the PCM using the sonication technique to enhance the heat transfer rate of the PCM composite. The thermal properties of the developed form-stable PCM composite, including phase transition temperature and LH capacity, are measured using a differential scanning calorimetry (DSC) test. The thermal and chemical structure stability of the PCM composite is characterised using thermogravimetric analysis (TGA) and Fourier transform infrared spectroscopy (FTIR). The heat transfer rate of the form-stable PCM cement composite and the thermal storage performance of the TES material is assessed by an infrared thermography test and prototype test room experiment, respectively. Moreover, the physical, mechanical, durability and time-dependent properties of the form-stable PCM cement composite are investigated using various tests such as the flow table test and compressive and flexural test. The microstructure and morphology of the PCM composite and the form-stable PCM cement composite are studied using scanning electron microscopy (SEM) observation. Moreover, the fundamental and physical properties of the form-stable PCM cement composite obtained from the experimental results are used for modelling and thermal simulation of a building. To evaluate the thermal performance and efficiency of developed form-stable PCM cement mortar, a room model integrated with PCM was simulated in different climate zones using DesignBuilder. The results revealed a high absorption ratio for the EGA as PCM carrier, and the diffusion-oozing circle test confirmed the stability of the EGA-PCM composite.

Moreover, the microstructure studies demonstrated well dispersion of TCF in the PCM and successful impregnation of PCM into the EGA.

The DSC analysis showed that the phase transition properties of the EGA-PCM composite were slightly shifted, and its enthalpy decreased compared to the pure PCM. Moreover, it was observed that the latent heat capacity of the EGA-PCM composite enhanced by TCF remained reasonable with a maximum deduction of 9.6% and supercooling temperature enhancement up to 3.4°C. The results of TGA and FT-IR demonstrated that there was no chemical reaction between the EGA-PCM composite, including EGA, PCM and TCFs, and the composite was thermally stable in the operating temperature ranges.

The thermal behaviour analysis obtained from infrared thermography (IRT) imaging showed a 50% improvement in the heat transfer rate of the PCM composite. This is evidenced by a reduction in peak indoor temperature of up to 2.5°C compared to the control sample. Moreover, a room model experiment revealed that integrating TCFs into PCM significantly enhanced the performance of EGA-PCM cement mortar.

The results demonstrated that the melting point of PCM should be optimised for each climate zone. The PCM melting point should be higher than the typical summer thermostat setpoint temperature. Moreover, the results revealed that the energy saving rate changes throughout the year as energy utilisation changes with respect to the season. A cost-benefit analysis of a case study building showed that although the costs of production and initial installation of EGA PCM composite are relatively high,

it is more beneficial in terms of economic and environmental considerations in the long run. The results revealed the feasibility of utilising EGA as a novel PCM carrier and the promising thermal performance of EGA-PCM cement mortar.

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Royal Society of New South Wales

Awards 2024

The Royal Society of New South Wales has long recognised distinguished achievements in various fields of knowledge through its Awards. Some are amongst the oldest in Australia while others are more recent. From its Act of Incorporation in 1881, the Society's mission has been to encourage "studies and investigations in Science, Art, Literature and Philosophy." In 2023, the Society determined to broaden and streamline its Awards portfolio to recognise recent and evolving fields and disciplines, and emerging as well as established stars.

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The application procedure for this Medal is described on the nomination form. Each nomination must comply with the conditions of award and will consist of a completed nomination form together with supporting documentation as specified on the form. Completed nominations (ideally compiled into a single PDF document) should be sent to the email address listed on the nomination form.

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has been awarded periodically since 1947. In 2023, Council determined to award it annually. Additional information about the establishment of the James Cook Medal is available online.

The application procedure for this Medal is described on the nomination form. Each nomination must comply with the conditions of award and will consist of a completed nomination form together with supporting documentation as specified on the form. Completed nominations (ideally compiled into a single PDF document) should be sent to the email address listed on the nomination form.

RSNSW Edgeworth David Medal — for mid-career researchers

Awarded for the most meritorious contributions to knowledge and society in Australia or its territories, conducted mainly in New South Wales by an individual who is from 5–15 years post-PhD or equivalent on 1 January of the year of the award, together with signs of leadership. The recipient may be resident in Australia or elsewhere. All assessments consider interruptions and performance relative to opportunity.

The Edgeworth David Medal was established by Council in 1943 in honour of Sir T. W. Edgeworth David FRS, who compiled the first comprehensive record of the geology of Australia, and following a donation made by Henry Ferdinand Halloran to celebrate his 50 years as a member of the Society. It has been periodically awarded since 1948 and in 2023, Council determined to award it annually. Additional information about the establishment of the Edgeworth David Medal is available at the preceding link.

RSNSW Ida Browne Early Career Medal

Awarded for the most meritorious contributions to knowledge and society in Australia or its territories by an individual from 0–5 years post-PhD or equivalent on 1 January of the year of the award and conducted mainly in New South Wales. The recipient may be resident in Australia or elsewhere.

The Ida Browne Medal was established by Council in 2023 in honour of Ida Browne DSc, palaeontologist and first woman President of the Royal Society of NSW, serving from 1953–1954. The application procedure for this Medal is described on the nomination form.

Discipline Awards and Lectureships

These Awards are made on a three-yearly cycle. The discipline awards in 2023 are as follows.

RSNSW Clarke Medal and Lectureship in the Earth Sciences

Awarded for distinguished research in any area of the sciences affecting the planet, excluding Medicine and Veterinary Science, and Agricultural and Environmental Science, conducted mainly in New South Wales. Recipients may be resident in Australia or elsewhere.

The Royal Society of NSW Clarke Medal honours Rev. William Branwhite Clarke, a geologist, and a father of the Royal Society of NSW, serving as its first joint Vice-President. It was first awarded in 1903, with the first Clarke Memorial Lecture delivered in 1906. Since 2018, Medal and Lectureship have been conjoined. Additional information about the establishment of the Clarke Medal is available at the preceding link. The application procedure for this award is described on the nomination form.

RSNSW Walter Burfitt Award in Medical and Veterinary Sciences and Technologies

Awarded for distinguished research in any area of the Medical and Veterinary Sciences and Technologies, conducted mainly in New South Wales. Recipients may be resident in Australia or elsewhere.

The Walter Burfitt Award honours the life and work of Walter F. Burfitt BA MB ChM BSc, an eminent Sydney surgeon in the 1950s. It was established as a prize with generous support from Dr Burfitt and his wife, and was first awarded in 1929. In 2004, funding for the prize was augmented by Dr Burfitt's granddaughter, Dr Anne Thoeming. In 2023, Council designated it the Royal Society of NSW Walter Burfitt Award. Additional information about the establishment of the Walter Burfitt Award is available at the preceding link. The application procedure for this award is described on the nomination form.

RSNSW Award in the Social and Behavioural Sciences

Awarded for distinguished research in any area of the Social and Behavioural Sciences including Psychology, Economics, Management, and related disciplines, conducted mainly in New South Wales. Recipients may be resident in Australia or elsewhere.

Council established the Royal Society of NSW Social and Behavioural Sciences Award in 2023 to reflect the full scope of the Society's founding values. The application procedure for this award is described on the nomination form.

RSNSW Award in the History and Philosophy of Science

Awarded for distinguished research in the History and Philosophy of Science conducted mainly in New South Wales. Recipients may be resident in Australia or elsewhere.

The Royal Society of NSW History and Philosophy of Science Award was established by Council in 2013 to reflect the founding values of the Society and was first awarded in 2014. The application procedure for this award is described on the nomination form.

Scholarships, Early Career, and Student Awards

Three Bicentennial Postgraduate Best Paper Awards

Three scholarships, the value of which is determined annually by Council, plus a complimentary year of Associate Membership of the Society, are awarded each year to recognise outstanding achievements by young researchers in any academic field. Applicants must have completed an undergraduate degree within NSW or the ACT and must on 1 January of the year of nomination be enrolled as research students in the first or second year of their first higher degree at a university or other research institution in NSW or the ACT.

Winners will be expected to deliver a short presentation of their work at a general meeting of the Society in February or later of the year following that in which the award was made, and also submit a paper to the Journal and Proceedings of the Royal Society of New South Wales.

Scholarships were first awarded by the Royal Society of NSW in 1999 and in 2023 were redesignated by Council to commemorate the Society's Bicentenary. The application procedure for this award is described on the nomination form.

Three RSNSW Bicentennial Early Career Research and Service Citations

Three citations plus a complimentary year of Associate Membership of the Society, are awarded each year to recognise outstanding contributions to research and service to the academic and wider community. Applicants must on 1 January of the year of nomination be no more than 5 years after the award of their PhD or equivalent by a university or other research institution in NSW or the ACT.

Winners will be expected to deliver a short presentation of their work at a general meeting of the Society in February or later of the year following that in which the award was made, and also submit a paper to the Journal and Proceedings of the Royal Society of New South Wales.

Council established these Early Career Citations in 2023 to commemorate the Society's Bicentenary. The application procedure for this award is described on the nomination form.

RSNSW Jak Kelly Postgraduate Award

Awarded for excellence in postgraduate research in physics annually. The winner is selected from presenters at each year's Australian Institute of Physics, NSW Branch Postgraduate Awards, as advised to the Awards Committee of the Royal Society of New South Wales.

The Jak Kelly Award honours Jak Kelly (1928–2012), Professor and head of Physics at the University of NSW (1985–1989), Honorary Professor at The University of Sydney (2004), and President of the Royal Society of NSW (2005–2006). It was first awarded in 2010. Additional information about the establishment of the Jak Kelly Award is available from the preceding link. There is no nomination form for this award.

RSNSW Internal and Discretionary Awards

Please note that the call for nominations for relevant awards opens on 1 July and closes on 30 September of each year.

Notes relating to Internal and Discretionary Awards:

1. For Internal Awards, the nominator and seconder must be either a current Member or a current Fellow of the Royal Society of NSW.
2. Selection of these Awards is made by the Council of the RSNSW, excepting for the Archibald Ollé Award.

RSNSW President's Award

Awarded at the discretion of the President and Council of the RSNSW to an individual whose distinguished work in any area has made an outstanding and eminent contribution to the State and people of New South Wales. The recipient may be resident in Australia or elsewhere.

Council established the Royal Society of NSW President's Award in 2023 to reflect the full scope of the Society's founding values. There is no nomination form for this award.

Three RSNSW Citations

The Royal Society of New South Wales Citations recognise an individual who has made significant contributions to the Society, but who has not been recognised in any other way.

The Royal Society of NSW Citation was first awarded in 2019. Council may make up to three Citations in any year at its discretion. The application procedure for this award is described on the nomination form.

RSNSW Medal

The Royal Society of New South Wales Medal recognises an individual who has made meritorious contributions to the advancement of knowledge in any field and also to the Society's administration, organisation, and endeavours.

The Royal Society of NSW Medal was first awarded in 1884, revived in 1943, and has been awarded periodically thereafter. Council may award the Medal in any year at its discretion. The application procedure for this award is described on the nomination form.

RSNSW Archibald Ollé Award

Awarded to the author/s of the best paper submitted to the Society's Journal and Proceedings in any year in which the Award is made.

The Archibald Ollé Prize was first awarded in 1956, established by a bequest from Mrs A. D. Ollé. The award of the Prize (currently $500) is determined by the Editor of the Society's Journal, in consultation with the Editorial Board. There is no nomination form for this award.

Archibald Liversidge:
Imperial Science under the Southern Cross

Roy MacLeod

Royal Society of New South Wales, in association with Sydney University Press

ISBN 9781-9208-9880-9

When Archibald Liversidge first arrived at the University of Sydney in 1872 as Reader in Geology and Assistant in the Laboratory, he had about ten students and two rooms in the main building. In 1874, he became Professor of Geology and Mineralogy and by 1879 he had persuaded the University Senate to open a Faculty of Science. He became its first Dean in 1882.

In 1880, he visited Europe as a trustee of the Australian Museum and his report helped to establish the Industrial, Technological and Sanitary Museum which formed the basis of the present Powerhouse Museum's collection. Liversidge also played a major role in establishing the *Australasian Association for the Advancement of Science* which held its first congress in 1888.

This book is essential reading for those interested in the development of science in colonial Australia, particularly the fields of crystallography, mineral chemistry, chemical geology and strategic minerals policy.
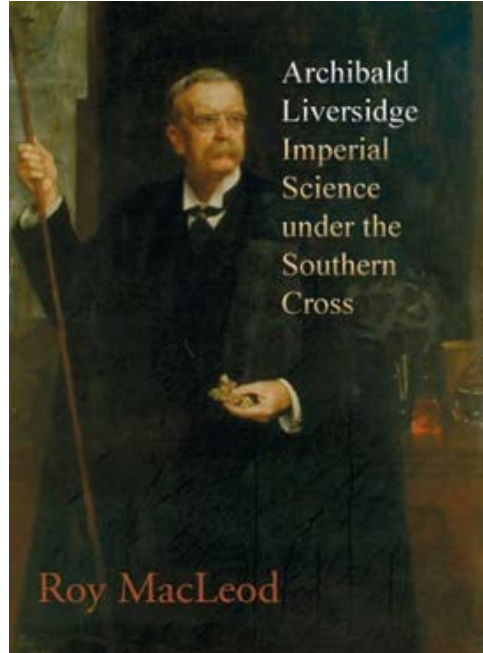
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The Royal Society of New South Wales

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