

Kaleidoscope

Derek K. Tracy, Dan W. Joyce,
Dawn N. Albertson, Sukhwinder S. Shergill

Individuals with dementia seek intimacy and companionship just like everyone else, but in the face of cognitive decline there are inevitably concerns about their vulnerability. It is an issue often perceived through the prism of safeguarding against abuse, rather than primacy of a basic human need, not least in settings such as residential homes. Sorinmade and colleagues give a thoughtful account of this often ignored but important issue, including for individuals who lack capacity to consent to intimacy or sexual contact.¹ They highlight how sexuality in older people is at best ignored, and often seen as ‘the inappropriate’, but a majority of both men and women with dementia report being sexually active, including over two-fifths of those over the age of 80. There have been some high-profile civil and criminal cases related to this, often with quite complex aspects, such as what should happen when one partner in a long-term relationship loses capacity to consent to have sex. The law in the UK requires that those without the capacity to consent should be prevented from sexual relations, even if there is no abuse, harm or exploitation. The authors propose an instrument – the Advance Decision on Intimacy – to empower individuals to make decisions on how they would wish to express their sexuality when they do lose capacity to make decisions; taking this decision away from the legal authorities or family who might intervene with their preference. This brings the issue back in line with the United Nations convention on the rights of persons with disabilities.

There are strong links between early adversity and later psychosis, but the precise mediators remain unclear. If we can identify *how* these traumas modify biological and psychological processes, then we can open up therapeutic opportunities. Alameda et al systematically reviewed 48 studies that covered approximately 85 000 individuals.² They determined a solid evidence for negative cognitive schemas about the self, the world and others mediating this link; dissociation and post-traumatic stress disorder symptoms also play a role, particularly with hallucinations as an outcome. There was a lack of good data for any biological mediators, although this may well be a research bias rather than evidence of absence. Interesting data emerged suggesting that loneliness was a factor for some, although this factor was less explored in the literature. The authors note that their proposed pathways are overlapping and not competing, and offer the possibility of some non-traditional interventions in psychosis. They argue that as well as exploring a history of adversity in those with psychoses, one should explore for such mediators, although the impact of any psychological intervention is yet to be tested.

The profound personal impact of psychosis on individuals with the condition scarcely needs stating. However, the literature has often focused on symptom burden and social outcomes, with less exploration of how individuals’ self-perceptions can be altered. Maev Conneely and colleagues synthesise the literature, determining five major ways individuals perceived changes in their identity: the characteristics of psychosis; the consequences of altered cognitive functioning; the consequences of internalised stigma; the consequences of lost roles and relationships; and reflections on personal growth.³ These important factors can be profoundly meaningful for individuals: delivering thoughtful, compassionate care requires that these should be kept in mind for our discussions with those we try help, and, indeed, again potentially new therapeutic avenues are opened. The last observation, upon reflections of personal growth,

particularly offers us the reminder of how from difficulties, we may also develop too as people.

Cannabis and mental health have a difficult relationship. Paul et al explored the impact of prenatal cannabis exposure on childhood outcomes, taking data from the cross-sectional adolescent brain and cognitive development study of over 11 000 children aged 9–11 and their caregivers.⁴ The issue is highly relevant given that US data show a greater than 100% rise in past-month cannabis use in women between 2002 and 2017, and there is evidence that Δ -9-tetrahydrocannabinol (THC) crosses the placenta, interfacing with the fetal endocannabinoid system that is involved in brain development. In the era of cannabis-derived medicinal products, there have also been debates on using cannabis for nausea in pregnancy. In this sample, 5.7% of children had been exposed to cannabis prenatally, and compared with those with no exposure, it was associated with significant harm. There were greater rates of subsequent psychotic-like experiences, both internalising and externalising problems, social difficulties, sleep problems, and lower cognition and grey matter volumes. Importantly, of the 5.7%, 3.6% were exposed before maternal knowledge of pregnancy: when controlled for various confounding covariates, it was exposure to cannabis *after* maternal knowledge of pregnancy that remained associated with harms. This affords a public messaging information opportunity that while cannabis is associated with harm, this can be militated against once one becomes aware of the pregnancy.

Cannabis dependency is estimated to occur in about 10% of heavy cannabis consumers. There is interest in pharmacological treatments for this, and putatively one might approach that in one of two ways. The first is controlled replacement and reduction via THC – akin to opioid replacement therapy in heroin users. The second is through the use of cannabidiol (CBD), the other major component of cannabis, and one with some evidence for ‘opposing’ actions of THC. Tom Freeman and colleagues took the latter approach, with the first double-blind randomised clinical trial of CBD for cannabis use disorder.⁵ It was an adaptive Bayesian trial, meaning that in the first stage optimal CBD dosing could be tested as 48 participants with cannabis use disorder were randomised 1:1:1:1 to receive either placebo or oral cannabidiol at doses of 200, 400 or 800 mg, with 12 people in each who were trying to abstain from cannabis. (To contextualise this, the increasingly widely available – and poorly regulated – over-the-counter CBD is typically in the range of 25 mg/day). In the second phase, 34 new participants were randomised to receive either placebo or the ‘optimal’ CBD (now determined to be 400 or 800 mg: randomisation was 1:1:1), with primary outcomes of urinary metabolites of THC. The results were both positive – both of the higher doses of CBD showing significant superiority to placebo in reducing use – and safe, showing good tolerability. Whatever one’s politics on cannabis, consumption numbers and THC strength are rising, and more people have been seeking help for dependency; effective pharmacotherapy will be very welcomed.

‘Traditional scientific method has always been, at the very best, 20–20 hindsight. It’s good for seeing where you have been. It’s good for testing the truth of what you think you know, but it cannot tell you where you ought to go’ noted Robert M. Pirsig.⁶ It has been a decade since the Research Domain Criteria (RDoC) ambitiously tried to overhaul the scientific study of psychopathology and mental illness. The RDoC framework articulates a matrix of cognitive and behavioural system domains, alongside a high-to-low level decomposition from experimental paradigms and behaviours, down to physiology, circuits and cells, and finally, units of molecular biology and genetics. On its tenth birthday, Sanislow gives an update on fruitful transdiagnostic

approaches to trials, experimental and translational studies.⁷ The global message is that RDoC has ‘unharnessed’ research from classical diagnostic constructs in an attempt to rediscover phenotypes that might be clinically useful both for identifying disorder (case-ness) as well as providing treatment. Sanislow attaches weight to computational psychiatry and cognitive science, in mapping experimental paradigms to the RDoC matrix. However, RDoC has also attracted criticism, for example, RDoC has been discussed in the context of being a wholesale replacement of the ICD and DSM categorical diagnostic systems, something it was never intended to be. Carpenter noted ‘RDoC and endophenotypes are experimental approaches that can cut across current clinical diagnostic boundaries and reduce heterogeneity within syndromes. They are not diagnostic systems and do not compete or replace DSM and ICD systems.’⁸ Weinberger et al has argued that RDoC was seductive by framing psychiatry as the clinical discipline of ‘neural circuit disorders’, but was unable – despite its promise – to articulate a plausible continuum from normality through to impairment and disorder.⁹ The pointed example was ‘Height is a continuous metric, but do we assume that all short individuals just happen to have gotten a bad spin at normal DNA roulette’.⁹ If, for example, the RDoC system revealed common patterns for symptoms of anxiety, then this would imply that one ‘could successfully treat in a singular fashion all individuals who score high on a negative valence scale or amygdala reactivity’ but that this ‘is non-scientific and clinically irresponsible’.

The problems inherent in the continuum and dimensional model have been taken up by Ross & Margolis who appraised RDoC as being too focused on deviation from normative neuropsychological and behavioural processes.¹⁰ This variation ‘does not imply that clinical syndromes are simply extremes on dimensions anchored in normality’ and ‘even though a clinical phenomenon is quantifiable, it does not follow that such a phenomenon can best be understood as an extreme of dimensional variation along a normal axis’. For example, schizophrenia and bipolar affective disorder result from something more than being located at the extremes on a number of continuous domains like ‘negative valence’ and ‘social processes’ or subdomains of ‘sustained threat’ and ‘perception and understanding of self’ respectively. Qualitative or categorical differences emerge on putatively continuous dimensions using the example of IQ: the accepted symmetric-normal distribution actually has a left-sided ‘bump’ representing a threshold where qualitatively different genetic syndromes (Rett’s and Angelman syndrome) appear. Ross & Margolis have lamented the emphasis on ‘top-down’ speculative domains (like valence systems) and the progressive refinement or mapping to circuits, molecules and genes – arguing instead that nosology, diagnostic differences and targeted treatment in oncology have proceeded (successfully) in the other direction. So, as RDoC enters its second decade, it is perhaps less clear that RDoC can tell us where to go next and the cynical might even opine it did not really give us 20–20 hindsight either.

Finally, it is a truism of coronavirus disease 2019 that technological gains that might have taken 10 years were achieved in 10 weeks. Muting and unmuting ourselves, removing ‘old hands’ after asking a question, waving at the camera before turning off – we are all pros now. As we move towards a new normal hybrid future, a good moment to evaluate digital interventions in mental health, particularly for low- and middle-income countries (LMICs). Fu et al systematically reviewed 22 relevant high-quality studies.¹¹ Digital psychological interventions, primarily studied in individuals with depression and substance misuse, were superior and effective relative to control conditions with a number needed to treat of three. This included a wide range of intervention

types – including specifically for perinatal and HIV-related mental illness – and digital formats, but most had content similar to traditional face-to-face equivalents. The obvious attractions of such tools include the potential to spread out rapidly and at scale, and – at least potentially – at lower cost once the necessary digital infrastructure is in place. The authors remind us that 80% of the population of LMICs have mobile phones, and half have access to the internet.

Which takes us nicely, but perhaps uncomfortably, to a follow-on: the rise of venture capital investment in mental health. Globally, need is rising, but traditional services will not match this; we are seeing the growth in technological options, and, well, ‘big finance’ (the even-evil twin of ‘big pharma’) has taken note. Shah & Berry provide a viewpoint, showing how venture capital investment grew by a factor of 22 from 2013, to reach \$637 million last year, and noting that the smartphone app ‘calm’ (that guides individuals through meditation) was the first mental health start-up to reach a valuation of more than \$1 billion.¹² Interestingly, although the focus is often on self-guided smartphone apps, the editorial shows that the market is actually dominated by face-to-face clinical services. There is always an argument that without external investment and innovation, centrally funded services will not develop optimally. It is not a topic we are particularly familiar with in the UK, and one that we suspect will raise lots of anxieties: indeed, the authors caution we *should* be worried, contrasting healthcare’s *primum non nocere* with Silicon Valley’s motto of ‘move fast and break things’. We lack good frameworks to guide this process, and privacy concerns and payment models remain a concern. However, it seems here to stay – and grow – even if an anathema to the National Health Service and academia.

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