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Kaleidoscope

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Mental Health First Aid (MHFA). It's one of those things like 'I Can't Believe It's Not Butter', where you want to have faith but wonder if it's as good as it promises. MHFA originated in Australia at the turn of the millennium. The principle was straightforward and had apparent face validity: improve the mental health literacy of the general population to enhance engagement with services and clinical outcomes. It fits with a wider destigmatisation and help-seeking approach. There have been variations of what MHFA encompasses, but the broad strategy involves teaching the symptoms of different forms of psychological distress, how to provide immediate input and support to those displaying this, and guidance on further signposting. The Cochrane Library updates us with a review of the evidence by Richardson et al.[1] They only included randomised controlled trials (RCTs) that had participants who were individuals from the communities in which the intervention was delivered; both active and no-intervention comparators were included. The authors included 21 relevant studies encompassing data from over 20 000 participants. And the answer? MHFA did not seem to do anything, with no clear advantage even when compared with no intervention. As with all research, one can challenge the findings, and one may pull a positive study or result here or there, or argue that with further and better research MHFA might be shown to have a role. This may be true, and the review noted a paucity of good-quality research and a high risk of bias in that which does exist. But, in an era of austerity and limitations on intervention roll-out, the onus now lies even more heavily on those who would propose a role for MHFA.

Artificial intelligence (AI) will soon cause the end of civilisation/the birth of a new age of prosperity (production team to delete as applicable when this goes to press); the 2023 Lasker award has been given for its application in protein folding.[2] A huge shift in understanding over the past few decades has emphasised that it is not just a protein's complex amino acid make-up that matters but how its geometric folding affects essential elements of its functioning. Almost a quarter of a million structures are described in the Protein Data Bank (www.pdb.org). A problem is that their intricacy has meant it can take months to years to elucidate the structure of a single complex protein. This matters. Missense variants – wherein genetic variations lead to altered amino acid sequencing and therefore aberrant protein construction – are common. These can be pathogenic, leading to various forms of loss of organism fitness through to disease and death, and they can be benign. However, an estimated 98% of the 4 million or so known missense variants have unknown effects. Some may offer opportunities to understand and target genetic illnesses with accurate treatments. However, with 4 million variants, each part of typically large and complex proteins with intricate structures… you can sense the challenge. Enter AI. Or the best minds (hence the Lasker award to Drs John Jumper and Demis Hassabis) applying AI to the problem. Writing in *Science*, the Albert Lasker winners and some colleagues from Google DeepMind[3] describe 'AlphaMissense', an accurate AI proteome-wide missense variant effect predictor. This tool can learn amino acid distributions conditioned on sequence context in an unsupervised manner without explicit training. It combines protein structural context and evolutionary conservation and, critically, fine-tunes these from population frequency data to avoid some of the biases typically seen in human-led examples. The authors found that almost a third of the previously undescribed variants could be classified as likely to be pathogenic. The findings offer a pathway for accelerated targeted molecular biological research, including experiments that probe saturating amino acid substitutions across our proteome. There's an old Irish ballad with the lines 'If the moonshine don't kill me, I'll live till I die': one has that sense with AI – if we can tame it and not let it kill us, it just might save us.

Anxiety causes tachycardia, and tachycardia can cause anxiety; what's the psychological impact of ablation treatment of atrial fibrillation? It's surprisingly understudied given the prevalence of both conditions, especially as perhaps a third with atrial fibrillation show signs of severe depression or anxiety. It was interesting then to see a study on this in *JAMA*,[4] the first to adopt a RCT methodology beyond the erstwhile observational and non-randomised data on the topic. One hundred participants with atrial fibrillation were randomised to have either catheter ablation or anti-arrhythmic medication to manage the fibrillation. Fitting with existing data on the topic, about a third of those enrolled had severe psychological distress (defined as a combined Hospital Anxiety and Depression Scale score of >15) at the time of the intervention, and this was positively correlated with atrial fibrillation severity. Those who received the surgical procedure showed significantly reduced anxiety and depression scores, and lower prevalence of severe psychological distress, at the 6 and 12 month follow-up time points compared with the medication group. The decision regarding treatment type in atrial fibrillation is complex and patient-specific. This study is helpful in both reinforcing how common mental health problems are in those with atrial fibrillation and potentially guiding care pathways. Although treatment of anxiety might not be a primary deciding factor for all, it might be of relevance in decision-making for some.

Sexual dysfunction is common but understudied in schizophrenia. Stigma and embarrassment – from clinicians as much as patients – and uncertainty as to what represents illness versus medication side-effects may limit this. Korchia et al[5] systematically reviewed the literature, synthesising data from observational studies and finally including 72 studies involving over 20 000 individuals with schizophrenia. Despite knowing that dysfunction is common, I was really surprised to learn that it had an overall prevalence of 56.4% (60% of women, 55.7% of men) – in other words, *most* people with schizophrenia endure this. In women, the most common specific problems were orgasm dysfunction (28%) and amenorrhoea (25%); in men, they were erectile dysfunction (44%), loss of libido (41%) and ejaculation dysfunction (39%). There was some heterogeneity across the studies of variable design, but frequency and severity were also affected by sociodemographic factors, alcohol use, illness severity and concomitant use of other medications. There was no clear improvement with time, and newer second-generation antipsychotics didn't seem any better than the older ones. Interestingly, the co-prescription of antidepressants and mood stabilisers was associated with reduced problems, which might be due to successful treatment of impacting affective components. A key missing factor is the general lack of data on metabolic factors and general physical health, which are both common and can clearly have physical and psychological roles in sexual functioning. Back to the issues of prevalence and clinician hesitancy: we need to do better at enquiring about this in those we treat.

Finally, in *A Streetcar Named Desire*, Blanche DuBois said 'I have always depended on the kindness of strangers'; what about the wisdom of crowds (WoC)? The misinformation on Twitter, 'X' or whatever it's called by the time you read this might turn one against mass wisdom or groupthink, but what does science have to say on the topic? There are data showing that crowds typically

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outperform any given member of a group, but, equally, groupthink can herd people towards unwise behaviour, as exemplified by rash copying actions that often precede financial market crashes. Broomell and David-Stober[6] explore *when* crowds might be wise and whether this requires better analysis of their constituent members and biases. Their fascinating piece proposes that if better understood, WoC might tap into helping to redress global problems such as climate change and pandemics. They present what they label a 'simple "toy" model' – though it certainly had significant mathematical complexity from this psychiatrist's perspective – that can be mapped to various societal issues. What is interesting about how they do this is that the model assumes that the judgements of a given individual are a 'random draw' from a heterogeneous population distribution. A weighted mean of these is then used to convey the crowd's overall opinions. Importantly, this produces internal subgroups of quite different opinions that can be tested to see how much they recalibrate the 'overall judgement'. The authors note that 'the study of collectives must rise to the level of a "crisis discipline" to meet the many societal challenges facing humanity', which, as the year ends, feels about most apposite statement of the 2020s so far. I'll finish, and sign off for now, with a line from Simon and Garfunkel that sometimes resonates when I feel wistful or heading towards despondency about population behaviours: 'I get all the news I need on the weather report'.

References

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