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Kaleidoscope

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Predicting future suicide attempts is a challenging area for psychiatrists. Even well-established individual risk factors tend to be quite weak predictors, and most assessment tools have been shown to add little or no value to a comprehensive clinical assessment. A lack of adequately sized data-sets and limited sample sizes are often blamed. Chen et al applied a machine learning approach to a national registry of over half a million psychiatric in- and out-patient attendances between 2011 and 2012.[1] Anxiety disorders (about 20%), major depressive disorders (17%) and substance use disorders (14%) were the most common presentations. An impressive 425 candidate predictors were extracted from electronic records covering clinical, demographic and socioeconomic factors. In total, 80% of the sample was used to train the algorithm – which looked for suicide attempts and deaths within 30 and 90 days – which was then tested on the remaining 20%.

The model performed significantly better than chance at both time points, and better than previous similar studies, with an area under the curve of 0.88 for the 90-day outcome. The authors note that at the 95th-percentile threshold, it would correctly identify about half of all suicide attempts and deaths that occurred within 90 days. Recent self-harm was the strongest predictor, although again the strength of the model is being able to hold a large range of potentially interacting factors for the individual rather than determining risk on any one factor alone. There is no suggestion this can or should replace clinical assessment, but the question remains as to how useful it might be in augmenting good real-world practice. False positives tend to be the bane of such systems, and it might best be integrated with clinician decision-making.

Assessing 'risk to others' can be even more contentious – although it remains a criterion by which individuals may be detained and treated against their wishes. A review of the current evidence on interpersonal violence reports that the relative risks of all violent outcomes are greater for all mental illnesses than in the general public;[2] increasing risk by 2–4 times even when important confounders such as familial influences were removed. This equates to an absolute rate of violent crime of about 5% over 5–10 years. Of course, the devil is in the detail: these rates increased to 6–10% in those with personality disorders and schizophrenia spectrum disorders, and over 10% in those with substance use disorders. Past criminal behaviour and drug use were strongest predictors of future violence. There is clear risk of stigma with such discussions: clearly a large majority do not commit violent acts, and most people who commit violence have no mental illness. The authors emphasise that between 2006 and 2016 there were 384 homicides in the UK by individuals with psychosis (6% of the total), and although tragic this also compares with 23 393 road fatalities during the same period. The paper concludes that a proportion of violence is potentially preventable, yet there is a current lack of useful standardised approaches to assessment and management, particularly outside of forensic settings.

Over the past half-century, medicine has largely shifted from a treatment to a preventative focus: what is the status of psychiatry? In a stimulating editorial, Hoare et al take the specific case of depression, the leading global cause of disability, and one where prevalence appears to be increasing.[3] They note the enormous challenge in a heterogeneous condition with a very diverse and complex range of interplaying individual, family and social factors. Most work to

date has been in high-risk individuals, such as school children with established adverse life events, but the wider applicability – and resource implications – of this as a primary preventative measure are challengeable. Nevertheless, schools and workplaces are highlighted as potentially appropriate targets for interventions, which should be implemented across multiple programmes and platforms rather than a one-size-fits-all approach. This could take the form of targeting individual cognitive strategies to wider well-being policies and social and cultural practices. A frustration is that we can identify the areas to target, yet each risk or protective factor might only contribute a small amount to outcomes, and we really lack good research on the topic. Further, this requires additional resource in already stretched systems, and there are well-articulated dangers of introducing well-intentioned but largely unevidenced based 'well-being interventions'. The counter is that surely mental health cannot forever remain a reactive field that only intervenes after problems emerge.

Treatment of depression remains important and Hare & Duman update us on the role of prefrontal cortical (PFC) circuits in therapy.[4] Reverse engineering of early antidepressants highlighted a role for monoaminergic neurotransmitter systems, notably serotonin and noradrenaline, in regulating specific brain functions. However, this albatross has, perhaps, hung heavy round psychiatry's neck in terms of keeping our gaze from elsewhere, and for ill-informed critics to bash a strawman 'chemical imbalance' theory no reasonable psychiatrist has espoused for decades. The advent of the glutamatergic antidepressant ketamine has shifted focus to circuit-level abnormalities across the brain, and the authors note the data showing structural PFC and hippocampal changes, and functional alterations to more distal regions in depression. Interestingly both ketamine and neuromodulation – such as repetitive transcranial magnetic stimulation and transcranial direct current stimulation – have been shown to reverse illness-associated changes. However, the exact mechanisms underlying their initial emergence and any therapeutic rectification remain unclear. (Incidentally, the authors note such actions might be the key to electroconvulsive therapy whose precise actions have long eluded us.) Hare & Duman describe emerging optogenetic and chemogenetic mechanisms to control neuronal activity – through light-sensitive channels to very precise, temporally specific levels or engineered receptors that allow longer-duration activation, respectively. These are beginning to show how PFC circuitry ordinarily functions, and how dysfunction might contribute to depression and anxiety. The novel tools allow identification of incredibly discrete PFC populations, and preclinical work is now exploring subregional involvement in illness-linked behaviours such as social avoidance and anxiety. Taken together, this neuroscience is sharpening our understanding of the pathophysiology of depression and targets for new interventions.

As the mental health benefits of spending time in green and blue spaces are increasingly acknowledged, interest in 'green prescriptions' has taken off. However, depression and anxiety can act as a barrier to the motivation needed to follow through on such guidance, and have been implicated in undermining the success of physical activity programmes. To date, studies supporting the recommendation of spending time with nature for those with common mental health issues has come from small, usually self-selected, samples. However, Michelle Tester-Jones and colleagues used data from over 18 000 people across 18 countries, gathered via the EU Horizons 2020 funded BlueHealth project, to ascertain levels of recreational contact with nature, the well-being associated with the visits and the impact of perceived social pressure to do so.[5] Using self-reported medication prescriptions as a proxy for

diagnosis, the sample contained 2698 individuals with anxiety and/or depression. Although all groups (depression, anxiety, both, or neither) displayed relatively high intrinsic motivation to spend time in nature, this was less so in those with common mental health issues. It was perhaps surprising to see all groups engaged with nature at similar rates, the majority of whom did so at least once a week, although those with anxiety did so the most. When thinking about their most recent visit, everyone reported high levels of happiness and low levels of anxiety as a benefit. However, with social pressure all groups became less motivated to engage with nature, particularly those with depression. Pressure did make a small positive impact on the frequency of getting out into natural spaces, an effect seen most in those with anxiety. Importantly, the perception of social pressure robbed everyone of the happiness, and increased the anxiety, they naturally felt in these excursions – an effect that was synergistic for those with common mental health disorders. The findings of an already high level of engagement with blue and green spaces in such a large sample of those with anxiety and/or depression was a welcome surprise, and hints toward its use for positive self-regulation. However, the results suggest caution, and the likely need for a nuanced approach, if green prescriptions are to move to the mainstream.

Finally, in the sitcom *Seinfeld*, Jerry explains 'When you're in your thirties it's very hard to make a new friend. Whatever the group is that you've got now that's who you're going with. You're not interviewing, you're not looking at any new people, you're not interested in seeing any applications'. As we get older, we prune our social network, favouring a smaller group of predictable and positive relationships and neglecting friendships that have proven to be shaky. This so-called *human social ageing phenotype* might be driven by socioemotional selectivity theory which posits that the driving principle is being conscious of the finite duration of life and the cost of investing limited remaining time on social activity. It is a kind of age-related exploration–exploitation dilemma: when young, the time–cost for widening one's social circles (exploration) is small because remaining lifespan is perceived as long – but as we age, we are more likely to focus our limited time on earth on valued, predictable social interactions (exploitation). A cognitive requirement of socioemotional selectivity theory is that we have a future time perspective that weights our decisions on the value of selective social interactions. However, if there is an adaptive value to narrowing one's social network, we might see the same age-related changes in social networks among animals without sophisticated future-oriented cognition. In a new paper, Rosati et al tested this by analysing 78 000 h of data over 11 years in 21 male chimpanzees in the Kibale National Park in Uganda.[6] Chimpanzees are an interesting comparator for humans because they have long lifespans and are known to display complex social behaviours. Of note, female chimpanzees are less social than their male counterparts, so Rosati et al focused on the latter.

Their first finding hinges on examining physical distance between pairs of chimpanzees: two males can: (a) mutually sit close to each other (mutual friends); (b) one can choose to move and sit close to another but this behaviour is not reciprocated (one-sided friends); or (c) a pair can avoid each other (non-friends). The authors found that the number of mutual friends increases as a function of age, whereas one-sided relationships declined. They examined grooming behaviours as a proxy for social investment and found that older mutual friends spent longer grooming each other than younger and one-sided friends. Subsequently, as the chimpanzees aged, both directed- and non-directed aggression decreased and grooming increased suggesting a parallel with human biases towards favouring valued and positive interactions as we get older. Rosati et al accounted for dominance and social status in their analyses, finding that this did not significantly change results as a function of age. So, the mechanism by which the social ageing phenotype emerges in primates' societies is perhaps not simply a property of sophisticated future-oriented cognition.

References

1 Chen Q, Zhang-James Y, Barnett EJ, Lichtenstein P, Jokinen J, D'Onofrio BM, et al. Predicting suicide attempt or suicide death following a visit to psychiatric specialty care: a machine learning study using Swedish national registry data. *PLoS Med* 2020; **17**: e1003416.

2 Whiting D, Lichtenstein P, Fazel S. Violence and mental disorders: a structured review of associations by individual diagnoses, risk factors, and risk assessment. *Lancet Psychiatry* [Epub ahead of print] 20 Oct 2020. Available from: https://doi.org/10.1016/S2215-0366(20)30262-5.

3 Hoare E, Callaly E, Berk M. Can depression be prevented? If so, how? *JAMA Psychiatry* 2020; **77**: 1095–6.

4 Hare BD, Duman RD, Prefrontal cortex circuits in depression and anxiety: contribution of discrete neuronal populations and target regions. *Mol Psychiatry* 2020; **25**: 2742–58.

5 Tester-Jones M, White MP, Elliott LR, Weinstein N, Grellier J, Economou T, et al. Results from an 18 country cross-sectional study examining experiences of nature for people with common mental health disorders. *Sci Rep* 2020; **10**: 19408.

6 Rosati AG, Otali E, Emery Thompson M, Muller MN, et al. Social selectivity in aging wild chimpanzees. *Science* 2020; **370**: 473–6.