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Kaleidoscope

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We're all familiar with the mantra that while self-harm is common, suicide is 'rare' and prediction 'difficult'. Can we at least have confidence in suicide-prevention interventions? A meta-analysis examined subsequent suicide attempts following a brief, single-encounter, suicide-prevention intervention in 14 studies covering 4270 individuals.[1] The majority of interventions were multi-aspect, typically including care coordination, safety planning, short-term follow-up contacts and a brief therapeutic intervention. The specific therapeutic component varied between studies, but included techniques informed variously by motivational interviewing, problem-solving and increasing likelihood of engaging with mental health services. The interventions did reduce subsequent suicide attempts, with a pooled odds ratio of 0.69; this equates to about 78 fewer suicide attempts in 2241 patients. There was increased linkage to clinical engagement with a 22.5% increase in attending follow-up, but interestingly, no association with any reduction in depressive symptoms. The findings are heartening, and we are reminded how a very significant number of people who die by suicide have contact with services in the days and weeks prior to their death. These findings encourage wider roll-out of such specific interventions across clinical services, and a need for clarification of the aspects that work best and in whom.

Borderline personality disorder raises sometimes contentious debate around the relative contribution of environment and genes. Linehan's model remains influential, emphasising the impact of early-life adversity. This is echoed by reasoned calls to re-orientate clinical discussions to 'what happened to you' instead of 'what is wrong with you', and a diagnostic move towards complex post-traumatic stress disorder. However, others argue that there has been a limited impact of life events or upbringing in their own situation. It is clearly a challenge to disaggregate these intertwining factors. The concept of 'passive gene–environment correlation' may be helpful here: a parent's genetic make-up might lead them to create a potential 'toxic' environment, but it is actually their transmitted genes that are causally relevant. Given the prevalence of borderline personality disorder is 2–6% in the population, a greater understanding of the aetiological factors would be helpful.

In an attempt to do this, Fatimah et al extracted data from 409 adoptive and 208 biological families, and 580 twin families from across two separate longitudinal cohorts.[2] The inclusion of adoptive families – the first time this has been done – helps break any passive gene–environment correlation. The work captured parental characteristics and practices including borderline personality disorder traits, parenting behaviours and marital discord. A series of multilevel regression models found that parental conduct disorder, adult antisocial behaviour, nicotine, alcohol and illicit drug use, and borderline personality disorder traits all predicted children developing borderline personality disorder – but only in biological offspring. So, this suggests a prominent role for genetic transmission, with externalising psychopathology and behavioural disinhibition appearing to be key factors. However, maternal borderline personality disorder traits, parental conflict, lack of regard and involvement, also predicted child borderline personality disorder irrespective of adoptive status. So, both genes and environment matter, but they might influence risk through different mechanisms, which offers up potential for designing different interventional strategies.

Two fantastical sounding novel interventions: renal dialysis for schizophrenia and insulin for Alzheimer's disease. There actually is a logical rationale for each, and now some updated empirical data on treatments. Psychoses are associated with inflammatory states, although any causal roles for the various commonly detected raised cytokines, complement factors and auto-antibodies remain uncertain. Nevertheless, dialysis and plasmapheresis (the removal of plasma and large molecules such as immunoglobulins) offer a mechanistic way to remove them from the bloodstream. So, in theory at least, one can see how this might be therapeutic. Cox et al identified nine double-blinded randomised controlled trials on the topic;[3] all from the 1970s and 1980s when there was a vogue for dialysis, following the publication of an influential case series on individuals being 'cured' of schizophrenia via this intervention. Of the eight studies using dialysis, only one showed benefit (one showed harm, and six showed no impact); the one study on plasmapheresis demonstrated no advantage. Studies were generally of small size and considered at high risk of bias with poor descriptions of randomisation and statistical analyses. Therefore, one might argue that larger trials are needed to establish if there are psychosis subgroups who might benefit – however, for now, scepticism seems appropriate.

As for insulin, it has been shown to modulate some aspects of brain function that Alzheimer's disease has an impact on. Specifically, it directly alters neuronal glucose use in critical cognitive circuits, promotes glycogen uptake in astrocytes, enhances dendrite spine formation, modulates dopamine levels and alters the clearance of the amyloid-beta peptide. Furthermore, there are reported reductions in the level or activity of insulin, and greater insulin resistance in Alzheimer's disease. Craft et al randomised 289 participants with Alzheimer's disease or mild cognitive impairment to receive either 40 units of intranasal insulin or placebo daily across a 12-month blinded phase, followed by a 6-month open-label extension.[4] Intranasal insulin can bypass the blood–brain barrier while simultaneously not having an impact on peripheral insulin or blood glucose levels. No benefits were seen over placebo in cognitive or functional markers or in measured cerebrospinal fluid biomarkers. Another intriguing idea that did not deliver?

It takes guts as well as brains. Human intestines play host to hundreds of unique bacterial species, several of which have been shown to metabolise psychoactive drugs, although such microbiome-derived metabolism has been poorly characterised and is rarely taken into consideration when looking at pharmacokinetics during drug development. Javdan and colleagues cultured microbial communities from faecal samples and examined their metabolic effects on hundreds of common orally administered medications.[5] In total, the interaction between different species had an impact on 13% of the drugs, which spanned 28 distinct pharmacological classes. Previously identified metabolic outcomes were confirmed, but 80% of what was seen was novel: medication broken down into inactive compounds and the creation of toxic by-products, explaining some previously observed but poorly understood clinical effects. Interestingly, some of these metabolic changes were ubiquitous and evident across all samples, whereas others were found only in a subset of samples, highlighting interindividual differences and the potential importance of a personalised approach to drug effects. They were able to trace the influence of specific genes in a single species of bacteria within the sample, and extended the work to recreate the metabolic effect in a mouse model. This robust experimental framework established the translational

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potential for high throughput screening and a novel approach to drug discovery.

Finally, what was the deal with toilet roll hoarding during the onset of COVID–19? It's not difficult to speculate on why specific items such as hand sanitiser was in short supply (long shelf life, immediate need to clean one's hands) but toilet paper? (That and eggs and flour – how much sponge can a nation bake?) An early study of COVID-19-related hoarding behaviours used a personality taxonomy and concluded that hoarding was driven by a lack of solidarity in UK residents.[6] In an attempt to understand the drivers for this behaviour, Garbe et al considered two competing explanations: people selfishly stockpile anything that might run out; and presence of disease increases sensitivity to feelings of disgust (think of how you feel when you step in a pile of dog mess), with toilet paper symbolising the safety found in cleanliness.[7] (There's probably also a Freudian option on anal retentiveness, but neither the authors nor we wish to go there.) The authors employed a validated personality taxonomy (HEXACO) surveying 1029 adults from 35 countries, most from Europe, the USA and Canada ($n = 996$). Alongside the personality questions, respondents were asked about how frequently they shopped for toilet paper and how much they purchased per visit, and their behaviour for the week 23–29 March 2020. They also collected information on any lockdown/quarantine/shielding, political orientation and individuals' perceived threat from COVID-19.

Europeans shopped more frequently, but stockpiled fewer packages than Americans; of note US supplies are typically bumper-packs of 36 rolls, versus the more usual 8–16 rolls in Europe. Across both Europe and the USA, increasing age was a consistent predictor for more frequent and larger purchases. Perceived threat from COVID-19 was most strongly associated with shopping frequency and stockpiling. Along the personality dimensions, high 'conscientiousness' was positively associated with more frequent purchases, high numbers of rolls purchased and a larger stockpile. They also found an association with the 'emotionality' dimension: people self-rating as more emotional had higher perceived threat and this appeared to drive buying and hoarding of toilet paper. Analyses adjusting for personal lockdown/quarantine circumstances and sociodemographic factors (including political alignment) did not change these associations across Europe or the USA. They conclude by suggesting that low anxiety and less desire for future planning are likely the best predictors for people to not engage in stockpiling, but concede that the small amount of variance explained by the personality dimensions means other psychological factors are at play. Importantly, they suggest that how governments communicate the risk from the disease, as well as inform people about supply chains, might influence future pandemic responses.

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