Kaleidoscope

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A recent New York Times article – ‘Many people taking antidepressants discover they cannot quit’ – was just the latest in a populist series apparently designed to cause panic. Writing in the American Journal of Psychiatry, Perlis notes that despite Cipriani’s meta-analysis of over 100,000 individuals, showing these medications to be consistently superior to placebo, ‘media accounts still routinely treat antidepressant efficacy as an open question and toxicity as a near certainty’. He contrasts the newspaper’s uncritical marrying of solid scientific data with anecdotal reports and small descriptive studies of difficulties discontinuing treatment, and decries how it concludes with a conspiratorial inference that so many people on treatment must surely be a bad thing. He counters that the growing number of people who are given evidence-based interventions for depression heralds a public health victory. Discontinuation symptoms are problematic for many people and, like almost all drugs used across medicine, we know less than we would like about long-term effects. More work is clearly needed, but no more for antidepressants than antihypertensives. Why antidepressants evoke and provoke such feelings remains sociologically fascinating. Perlis cites Peter Kramer’s book Listening to Prozac to note the ‘general distrust of drugs used for non-therapeutic purposes and a conviction that if a drug makes you feel good it must be morally bad’. Poetry is when someone says something you have felt but never named, and we propose that was reached in the appellation ascribed to this phenomenon by Gerald Klerman: pharmacological Calvinism.

The nature–nurture controversy of the genetics of depression occupies significant public interest. Again, the debate moves around the fringes of the available data; to paraphrase Kramer, a seeming distrust that genes could be part of what makes individuals more or less prone to major depressive disorders (MDDS). There appears to be an anxiety, at least for some, that a genetic contribution somehow negates the psychosocial, although it is not clear why anyone would think that. Twin studies typically show MDD to be about 50% genetic, 50% environmental; but elucidating causal loci has been a challenge, and failure to find a simple Mendelian heritability is sometimes thrown as a strawman argument of wider field failure. The challenge is that many loci variants are likely involved, some common, some rare, producing multiple permutations that require very large samples to unpick – as is the case for very many common conditions across all branches of medicine. Against this backdrop, Naomi Wray heads up an impressive genome-wide association study meta-analysing data from almost half a million people, over 135,000 of whom had a history of MDD – the largest such work yet undertaken. A total of 44 independent risk alleles were identified as significantly associated with clinical features of MDD and relevant brain regions (notably the prefrontal and anterior cingulate cortices), and there was a smaller association signal for targets of antidepressants. Excitingly, 30 of these loci were new, while 14 have been significant in previous work. Lower educational attainment and higher body mass appeared to have a causal link with subsequent MDD. The authors note that their findings show a continuous measure of genetic risk underlies MDD; we have already named that at Kaleidoscope – the depressions. Their primary conclusion is the simplest and the most profound, but most likely to face opprobrium: ‘major depression is a brain disorder’.

The debate between ‘critical’ and ‘mainstream’ psychiatry often suggests they have very little common ground. The UK’s Critical Psychiatry Network argued that the diagnostic category of schizophrenia ‘obliterates meaning by transforming significant experiences into a narrow disease framework’ and further, ‘it is so important to attempt to understand psychotic experiences in the context of the person’s life story’. Meanwhile, mainstream (biological) psychiatry has, arguably, explained psychotic experiences in terms of cognitive neuroscience. For example, Powers et al’s previous empirical and computational work showed that overweighted perceptual priors lead to evidence from the senses being overpowered and the emergence of a hallucination.

However, Powers et al attempt a reconciliation of critical psychiatry with mainstream psychiatry using the theoretical framework of computational psychiatry. First, they situate hallucinatory phenomena on the spectrum of normal sensory experience in the way the Heaving Visions networks suggest. Then, they illustrate the (now familiar) Bayesian theory of perception in an elegant diagram that shows how in the presence of sensory ‘uncertainty’ there is an excessive influence of prior beliefs and juxtapose this with examples of how ‘uncertainty’ can be understood in terms of psychosocial factors. As an example, take a person who has migrated to a country, lives alone, and where almost all sensory input is novel and unfamiliar (notably, language). This person possesses well-established priors (expectations) for stimuli and perceptions as a function of their history and experiences in another country and culture. The bombardment of sensory novelty along with the experience of social isolation both serve to increase uncertainty, leading to increased dependence on learned priors that then skew the interpretation of novel stimuli leading to the generation of aberrant perceptions (for example hallucinations). By this explanation, Powers et al propose that all perception is ‘controlled hallucination’ and the failure of control leads to unusual experiences like auditory verbal hallucinations. Powers et al conclude that further reconciliation requires a common – and mutually acceptable – language and semantics for hallucinatory experiences and their explanations. This seems to be a dividing line in contemporary discourse on psychiatry: it will be interesting to see if computational–cognitive theories – with their language, implicit assumptions and resulting explanatory frameworks – are acceptable to those with lived experience of what psychiatry still calls psychotic experiences or symptoms.

The French polymath Jules Henri Poincaré said ‘In one word, to draw the rule from experience, one must generalize; this is a necessity that imposes itself on the most circumspect observer’, and cognition is no different. Taking the example of simple round fruit, we learn prototypes that enables us to both identify stimuli as well as discriminate between them. The categories of ‘apples’ and ‘oranges’ are similar along the geometrical stimulus dimension of being round and on average about 7 cm in diameter, but differ along the stimulus dimension of colour: ‘apples’ being typically bright green (having visible light wavelengths of around 495–570 nanometres) and ‘oranges’ (having colours around wavelengths of around 590–620 nanometres). So, assume you see a round, red-orange coloured object about 6 cm in diameter; measuring along the ‘geometry’ dimension we conclude it could be either an ‘orange’ or an ‘apple’ – the prototype for both is about 7 cm in diameter. But if we measure along the colour dimension, chances are red-ish colours are more likely to be ‘oranges’ than ‘apples’.


In cognitive science, this notion of ‘distance’ between stimuli and prototypes is embodied in Roger Shephard’s influential ‘universal law of generalisation’ where the similarity of two ‘things’ is an exponential function of their distance in dimensions of ‘psychological space’. One influential way to implement Shephard’s law is to assign a probability of being an ‘apple’ or ‘orange’ as a function of the distance from prototypes; in the example above, our novel red-ish 6 cm object would be given a probability of ‘apple’ = 0.5, and probability of ‘orange’ = 0.5 if we use the geometric dimension (both are equally likely), but the probabilities along the colour dimension would be something like 0.2 and 0.8 for apple and orange, respectively. Combining these probabilities (to arrive at a percept) is performed by the inference apparatus of our perceptual systems. However, now Sims proposes a new way of thinking about generalisation – rather than assuming that generalisation is a passive function of distance to/from prototypes, Sims proposes that first, our perceptual system is a capacity-limited transmission channel, like a telephone line where you can only squeeze so much data down it. Second, Sims proposes that the salient features transmitted in this capacity-limited channel are those relevant to – and having utility – for a desired purpose. So, the loss of information our perceptual system tolerates depends on the cost of confusing two different stimuli; as an extreme example, imagine you are allergic to oranges – your perceptual system will want to keep (transmit) the colour dimension, but can dispense with the geometric dimension as it has no discriminative ability. Sims shows how using this information-theoretic framework for transmission rate/distortion leads to Shephard’s law as a special case. Sims’ theory makes predictions that align with observed experimental results across a range of auditory, visual and tactile stimuli.

Predicting treatment response to antipsychotics could be game-changing. Striatal dopamine synthesis capacity (DSC) and neurotransmitter release have previously been shown to be raised in psychosis, including first-episode and affective variants, and indeed, increased striatal DSC has been seen in those at high risk of illness development and transition to schizophrenia. Jauhar et al assayed individuals’ striatal DSC with positron emission tomography prior to first-episode antipsychotic treatment and prospectively monitored clinical responses. Those with greater baseline DSC showed significantly greater response rates to medication, and these synthesis differences were evident before any medication commencement. The data suggest that response is not linked to duration of illness or medication prescription. Rather, the findings support the hypothesis of ‘dopaminergic’ and ‘non-dopaminergic’ subtypes of psychosis and, the authors argue, may provide a neurochemical mechanism to stratify individuals.

Finally, from ‘I want to believe it’ to ‘can I believe it’: we traverse from information on exercise to information from alcoholic drink producers. The existing literature on exercise and depression has been challenged for being unable to quantify the magnitude of any protection, and for being unable to tease out potential confounders such as gender and age. Schuch et al meta-analysed prospective cohort studies on the relationship between physical exercise and the development of depressive disorders. Over a quarter of a million people’s data were captured across just under 50 studies, and they showed that exercise was protective against the emergence of depression in all age groups and all studied geographical regions, and there were no differences between men and women. No more excuses, time to lace up those trainers.

Starting with cigarettes, and moving inexorably towards alcohol, gambling and unhealthy snacks, product manufacturers have been dragged – willingly or otherwise – into encouraging less unhealthy behaviour. We are all familiar with the ‘Do X responsibly’ warnings in micro-print on our favourite vices; but do these industry-led projects make a difference? Six years ago, a dozen international alcohol manufacturers jointly declared a wish to demonstrate their support of international efforts to improve health and social outcomes for individuals, families and communities. Mialon & McCambridge systematically reviewed the impact of corporate social responsibility initiatives from the alcohol industry, 21 relevant trials spanned five initiative types: information and education, drink driving prevention, research involvement, policy involvement and creating ‘social aspects organisations’. Company had different approaches to when the industry acted in unison, but the outcome was the same in both instances: there was no evidence of any reduction in harmful use of alcohol. Of note, what did emerge was that corporate social responsibility initiatives changed the framing of debates so that they often appeared more in line with the interests of the industry itself. The manufacturers’ body, the International Alliance for Responsible Drinking, has stated it wants to be ‘part of the solution’; these findings suggest that the solution is about 80% proof. Somehow, we find ourselves drawn ineluctably to the late great Bill Hicks and his diatribe on marketing and advertising, but we will let you google that for yourself.

References