

Kaleidoscope

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Among the criticisms of diagnostic systems is ‘diagnostic inflation’: with time criteria relax, the number of conditions expands and everything is pathologised. It is a common refrain, with the release of DSM-5 attracting particular notoriety. But, is it actually true? Fabiano & Haslam reviewed 123 studies in which a research sample was concurrently diagnosed using two consecutive DSM editions.¹ Meta-analysis determined the average of 476 risk ratios was 1.0: namely, neither diagnostic inflation nor deflation from DSM-III to DSM-5. The overall stringency has been stable over time. This infers that, in general, any reported changes in population prevalences of illnesses are not because diagnostic systems altered ‘capture’ but are either the result of genuine change in numbers or their better detection. However, that is not to say all conditions were the same, with the altered criteria resulting in increases and decreases in prevalence of certain disorders across editions. It might not surprise you that attention-deficit hyperactivity disorder, autism spectrum disorder, eating disorders and substance use disorders showed inflation with time. One imagines that for these, there will be considerable debate as to whether this is just better recognition and detection. Nevertheless, the authors conclude that the notion of ‘concept creep’ across diagnostic systems has been overstated, and is not supported by the evidence.

There is renewed interest in what you eat and its impact on the brain: is diet helpful in depression? Thomas-Odenthal et al systematically reviewed 19 narrative reviews, 10 systematic reviews and 12 meta-analyses on the effects of diet on depression.² They were particularly interested as to whether the strength of authors’ opinions were associated with the type of review they wrote, noting that this nascent field has some high-profile expert proponents. 42% of narrative and 20% of systematic reviews came to strong conclusions supporting the role of diet in depression; none of the meta-analyses did. Of note, the narrative papers typically included far fewer studies (which is not too surprising given their methodology), were more likely to be written by authors with greater conflicts of interest and 7–90 times more likely to come to particularly strong findings and recommendations. An interesting emerging phenomenon, which parallels the pharmaceutical industry, is that food companies are beginning to fund studies – with increased positive findings – and there are related concerns about authors fully disclosing any such relationships. No one is suggesting you ditch your quinoa salad for a full English, but more circumspection is required in this topical area of nutritional psychiatry.

To the other end of the food chain, and gastrointestinal microbes: faecal transplant is evidenced for certain gastrointestinal complaints, but given the brain–gut link, is this relevant to psychiatry? Bajaj et al report on a fascinating double-blinded, randomised control phase I trial for the treatment of alcohol use disorder (AUD).³ The principle is that AUD is associated with microbial changes, which have been noted to be exacerbated by cirrhosis. Faecal transplant has previously been explored to test the impact on liver functioning, but some early work suggested it might also have an impact on cognitive and behavioural functioning, putatively through this gut–brain axis. Twenty individuals with AUD-induced cirrhosis, but currently abstinent of alcohol, were randomised to receive a 90 mL enema of either a placebo or faecal microbial transplant (FMT) enriched in *Lachnospiraceae* and *Ruminococcaceae*

bacteria. FMT was associated with greater microbial diversity and reduced inflammatory serum interleukin-6 levels. Those receiving the active intervention also showed a significant reduction in alcohol craving and improved cognitive performance and quality of life, compared with placebo, at day 15. Across the 6-month follow-up the FMT group had fewer AUD-related events, and no increase in adverse events. Fascinating preliminary research, with many unanswered questions on precise mechanisms of action and potential therapeutic implications.

Two more novel therapeutic interventions: a proposed hormonal treatment for anorexia nervosa and one for paedophile sex offenders. Adipose tissue is far more physiologically active than once thought; a loss of fat mass leads to a drop in the hormone leptin, signalling homeostatic adaptations to starvation. Hypoleptinaemia has also been linked with a range of anorexia nervosa pathologies including low mood, cognitive inflexibility and repetitive thoughts and hyperactivity. This raises the question as to whether leptin replacement might be helpful. Milos et al report on the off-label administration of metreleptin – a recombinant analogue – for up to a fortnight in three seriously ill women with life-threatening anorexia nervosa.⁴ Depressive symptoms rapidly improved in all, with a reduction in inner restlessness and hyperactivity, weight phobia and a drive for activity in two of them. Clearly this carries heavy caveats in an uncontrolled small case-series, but the morbidity associated with anorexia nervosa supports moving to a methodologically robust trial.

There is a lack of evidenced interventions for those with paedophilic disorder. Psychological therapies form the mainstay of therapy, but lack rigorous randomised controlled trials, and the so-called ‘chemical castration’ – typically via testosterone-lowering drugs such as cyproterone – has limited use because of ethical concerns. Landgren et al randomised 52 men who had sought help with a paedophilic disorder to receive either two subcutaneous injections of degarelix acetate – a gonadotropin-releasing hormone antagonist that lowers testosterone – or matched placebo.⁵ After 2 weeks, the active intervention showed a significantly reduced composite score across five domains of child sexual abuse, including in the categories of paedophilic disorder and sexual preoccupation. It did not have an impact on self-rated risk or impaired self-regulation. A total of 77% of those given degarelix reported positive effects including improved attitude or behaviour on sexuality, although this group also had an increased rate of physical adverse effects, limiting acceptability. The treatment’s effects appear to occur quite quickly, raising questions of how long they might last, and how effective they might be in real-world settings. The authors note that child sexual abuse affects approximately one in five girls, and one in ten boys, with less than an estimated 1% of offenders being prosecuted. Given that studies have shown offenders typically report struggling with their sexual urges for about a decade before committing a crime: this may offer a treatment opportunity.

Finally, ‘#JustSaysInMice’ is the common eye-roll to translational models, but they are a spine upon which our significant understanding of human behaviour and health has been forged. This is particularly relevant in the study of environmental influences on neurodevelopmental disorders. Epidemiological studies consistently point toward proximity to roads during the third trimester of pregnancy as a risk factor for the development of autism spectrum disorder. Animal models have supported this, but the designs to date have failed to capture real-world circumstances. The Silverman lab address this⁶ by using a housing facility where air from the entrance of a near traffic tunnel was shunted into an insulated and stabilised space, mimicking residential levels of noise and vibration, as well as the natural variation in traffic concentrations and traffic-related air pollution (TRAP) exposure throughout the day. Three groups of pregnant rats were assayed: one stayed with

the university team as a control; one got the unfiltered TRAP; and one was in the motorway facility, exposed to the same noise, vibration and general road proximity, but filtered air. Animals were exposed in utero during the equivalent of trimester 3, as well as during early life. Two males and females from each litter were tested in their early gestation and in adolescence. No differences were noted in litter size or gender breakdown between the groups, but there was an impact on pups with real-world exposure during the development of their nervous systems. Of note, both groups in the roadside facility failed to meet their developmental milestones (height, weight, reflexes and ultrasonic vocalisations). As juveniles, they displayed altered social interaction in the form of anogenital sniffing as well as in following and chasing play, in the absence of other motor deficits. Elevated self-grooming, a classic repetitive behaviour in rats, was also seen but only in males. So, while the filtered group was exposed to significantly less particulate matter in the air, both traffic-proximal groups support a causal relationship for what has been seen in so many large-scale human correlational studies. Although the contribution of TRAP, noise and vibration will have to be further teased apart, the data support taking action to minimise this exposure during critical periods in development in order to reduce the incidence of neurodevelopmental disorders.

References

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