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Kaleidoscope

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Antidepressant effectiveness is a topic seldom out of the scientific or popular press, with claim and counter-claim about the disclosure, reporting, and interpretation of data. Hieronymus and colleagues[1] have thrown their hats into the ring: noting that about half of company-sponsored trials failed to show any superiority over placebo, they challenge that most studies evaluated changes in *total* scores on the 17-point Hamilton Rating Scale for Depression (HRSD-17), but that this might mask improvement in important subcomponents. Not all items equally correlate with illness burden, so they undertook patient-level *post hoc* analyses focusing on the four-point depressed mood subcomponent in 18 placebo-controlled industry trials of various selective serotonin reuptake inhibitors ($n = 6669$). The choice of this question was based on its diagnostic importance and the fact it had the highest baseline severity in the pooled sample. The result was that 91% of comparisons showed superiority of the active drug over placebo, compared with 46% where the summed scale was used ($P < 0.001$). The authors argue that the summed scale is insensitive, and clouds current views on medications. The end of the debate? We think not . . .

More on mean value masking: brain imaging studies typically compare between-group results, but might variation *within an individual* matter? Maybe some brains are 'noisier' than others, and perhaps this tells us something about illness or disease that is lost in the averaged group data. Dinstein *et al*[2] review evidence that within individual subjects, across different neuroimaging modalities, there is substantial trial-by-trial variation for the same stimulus. They present evidence that in people with autism and matched controls, the mean response in electroencephalogram and functional magnetic resonance imaging (fMRI) blood oxygen level-dependent imaging to simple visual and auditory stimuli showed no group differences. However, the people with autism displayed around 20% more within-subject variation in response to the same stimuli compared with controls. So, the standard deviation – not the mean – of the fMRI signal was statistically different in autism. In this instance, the authors explain these differences as a trade-off between reliability and flexibility; the brain needs to develop a reliable response to a given stimulus (which requires a reducing noise) but flexibility to adapt to novel stimuli requires noise to 'nudge' the neural network out of stable, fixed pattern of responding. They conclude by suggesting that this within- subject, regional neuroanatomical response variability across disorders and the life-span might be an as-yet untapped source of explanations for changes in cognition and behaviour.

There is growing support for links between immune dysfunction and mental ill health, but could infections reduce intelligence? We are all familiar with changes in cognition acutely with delirium and as part of enduring pathology, such as can occur with cerebral HIV and herpes, but what about systemic infections more generally, and might some changes persist? Benros *et al*[3] evaluated the medical records of over 160 000 male military conscripts (mean age 19.4 years), all of whom had undertaken cognitive testing on logical, verbal, numerical and spatial reasoning as part of their draft induction. Independent of a wide range of confounders – including gestational weight, age and substance misuse – there were significant associations between lifetime infections and reduced cognitive ability. Linear regression analysis showed that there was a dose–response relationship between the number of infections and the decrease in cognitive ability, affected by the severity of any infections: a prior significant infection was associated with a mean drop of 1.76 in standardised test score. It remains unclear what might be causing this, whether a direct result of the infection, a pathological by-product of an immune response, or epiphenomenal associations – for example, might individuals with lower IQ have additional risks for acquiring infections? One novel link between brain and immune system has recently been making news, following a paper by Louveau and colleagues[4] in *Nature* that described for the first time the existence of hitherto unknown functional lymphatic vessels lining the dura of the brain, which connected to the cervical lymph nodes.

A spectrum model of psychosis posits that there is a wide variance in presentation, and that psychotic symptoms may occur in a reasonably sized minority of the population, often in a transitory fashion. However, most work has just looked rather dichotomously at overall lifetime prevalence/absence, masking more nuanced data on symptom types and frequency. An 18-country general population community survey[5] of over 30 000 individuals, part of the World Health Organization's World Mental Health survey, has determined a mean lifetime prevalence of 5.8% having a psychotic experience (2% within the previous year), with hallucinations much more common than delusional experiences (5.2 *v*. 1.3%). Prominently, such experiences were typically infrequent – occurring only once in about a third, and from 2 to 5 times in another third – and over 70% only had a single symptom type. There was interesting variation between high-, middle- and low-income countries (with respective lifetime rates of 7.2, 6.8 and 3.2%), with greater rates in women (6.8%) than men (5.0%). These thought-provoking findings support the concept that psychotic experiences are not rare, but for most people they are short-lived and infrequent.

Continuing the theme, Satterthwaite *et al*[6] undertook fMRI work looking at brain connectivity in 188 young people (8–22 years old) with psychosis spectrum symptoms, but without an established psychotic illness. Compared with matched controls they showed hyper-connectivity of the default mode network (DMN) that was significantly related to cognitive impairment, and hypo-connectivity between the frontal cortex and the DMN. These changes are similar to those seen in psychotic illness; the findings reinforce the vulnerability and spectrum model, although whether such network change has the potential as a biomarker for identifying at-risk populations for transition to a psychotic illness remains unclear.

Collecting reliable data on the prevalence of alcohol misuse and its neurological harm can be difficult. DSM-5 has updated abuse and/or dependency criteria for an alcohol use disorder (AUD), including adding 'craving' to the symptom list and establishing a severity metric depending on the number of diagnostic criteria met. Utilising these, a nationally representative sample[7] of over 36 000 American adults determined 12-month and lifetime prevalences of AUD of 13.9 and 29.1%, higher in men (17.6 and 36.0% respectively). This astonishing figure that almost a third of adults will meet such criteria at some point in their life is underscored by the finding that fewer than one in five of these had ever received any treatment, although it was associated with considerable psychological, physical and social morbidity. This is reinforced by recent longitudinal neuroimaging work[8] that

followed up 134 adolescents over 8 years; 75 of these transitioned to heavy drinking and showed accelerated grey matter reduction in the frontal and temporal cortices, with reduced white matter growth of the corpus callosum. Alcohol use varies considerably between and within countries; it would seem prudent to call for greater public awareness and education, especially in young people.

Adult attention-deficit hyperactivity disorder (ADHD) can be a problem: professionals can feel therapeutically under-skilled, patients can feel clinically under-served. But might it be a *different* disorder to that seen in childhood? The general assumption has been that it is a continuation of a childhood-onset neurodevelopmental condition. However, a four-decade longitudinal cohort study by Moffitt *et al*[9] raises the possibility that many presenting with such symptoms as adults may have a fundamentally different disorder. Examining the New Zealand Dunedin birth cohort ($n = 1037$), childhood ADHD had a prevalence of 6% and fitted with the broader literature on the topic: most were male, and there were associations with comorbid difficulties (especially conduct and anxiety disorders), and neurocognitive deficits. Only about 15% of these still fulfilled diagnostic criteria in their 20s, although residual adult impairment persisted for many more. The prevalence of adult-diagnosed ADHD was 3%, with a near-equal gender balance, but rather unexpectedly 90% of this prospectively followed-up group had *not* had childhood ADHD symptoms. Further, they had neither the classical neuropsychological deficits nor the genetic risk factors seen in the childhood-diagnosed group, although they had high rates of comorbid depression, anxiety and substance misuse. Diagnostic classification and treatment guidelines are all predicated on a shared aetiology, so replication of the results are needed, perhaps without the *a priori* assumption that adult ADHD arose in childhood.

Finally, we know that as both scientists and bon viveurs many *BJPsych* readers will be familiar with the 'cocktail party effect'. First coined by Cherry[10] in 1953, it is the capacity to tune into a single conversation despite the hum of competing voices, and the ability to recognise important information, for example one's name being spoken, among many vying stimuli. Initial work was primarily interested in the safe operation of air-traffic controllers rather than the vagaries of party-goers. O'Sullivan *et al*[11] modelled the cocktail party effect, or the 'temporal coherence model of stream segregation' in more scientific terminology, utilising a stochastic auditory figure-ground stimulus: the 'figure' being a modifiable tone pattern that could be perceived to emerge from the background over time. Electroencephalography extracted the highly temporally resolved neural signature of brain coherence computations, identifying the underlying coincidence-measuring mechanism in both passive and active listening paradigms. An early neural computation of temporal coherence started at approximately 115 ms post-stimulus in the passive condition – and thus is likely to be preattentive – enhanced to persist significantly longer and peak with greater amplitude during active listening. The authors acutely note that 'the human brain has evolved to operate efficiently in highly complex acoustic environments' and can effortlessly separate multiple sources of auditory information into discrete objects that can be variously attended to and followed.

In visual science, meanwhile, the ability to construe three-dimensional structures out of two-dimensional cues, such as the illusion of two converging lines representing a surface receding in depth, have been thought to be learned through experience. A recent study by Gandhi and colleagues[12] has cast doubt on this theory by demonstrating that children who gained sight after extended early-onset blindness were susceptible to these illusions despite not having any prior visual experience upon which to base their percepts. Another facet to add to the rich nature–nurture argument in visual processing, and a couple of interesting studies with which to impress acquaintances at your next cocktail party.

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