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Kaleidoscope

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In 2013 the OCTET study on the effectiveness of community treatment orders (CTOs) created considerable controversy, showing that the new legal powers had not improved outcomes. One criticism was that the 12-month follow-up failed to capture a true clinical picture, and that more time was necessary to demonstrate their worth. The team that carried out this original work have now published 3-year data on 330 individuals detained under section of the Mental Health Act,[1] randomised on discharge to CTO or voluntary status via Section 17 leave. No improvements in readmission rates, time to first readmission, or duration of readmissions were found for those placed on CTOs. The findings are even more powerful than the original results; CTOs now exist in various forms in over 75 jurisdictions, but no solid scientific evidence has yet been produced to support them. If there are subpopulations for whom (or specific circumstances in which) they work, such characteristics have yet to be delineated. A 'least restrictive' principle underpins the Mental Health Act, and a strong rebuttal is needed to justify ongoing CTO use – so-called 'revolving-door patients' should not be replaced by revolving-door policy.

What's in a name? There is confusion when antipsychotics are used to treat depression, and antidepressants to treat anxiety disorders. A somewhat random medication nomenclature has arisen wherein some drug classes are named after their pharmacological action (e.g. selective serotonin reuptake inhibitors), some by their own biochemistry (e.g. tricyclic antidepressants), and some by marketing (e.g. second-generation antipsychotics). The current system had not been reviewed for 60 years; now, a consensus statement[2] from all major international colleges of neuropsychopharmacology has proposed a new model – Neuroscience-based Nomenclature (NbN) – with the aim of better informing rational prescribing and providing more useful information to clinicians and patients. This recognises that drugs can have actions on more than one system (hence why it is appropriate for some to be prescribed antipsychotics for depression), and specifies these in a hierarchical order; it further includes information on approved indications, efficacy and side-effects, practical notes, and neurobiology. For all its failings, we have become accustomed to the current system; there will be considerable challenges implementing a new one, even if it is superior. A free NbN app is available to 'translate' current medications to NbN for those who wish to test the new model.

Something from the heart: in psychiatry our interest in all things cardiac has largely been limited to pre-antipsychotic electrocardiograms and cardiometabolic monitoring, but perhaps we should be listening more carefully. A low resting heart rate (RHR) is the best replicated correlate with antisocial and aggressive behaviour in children, but this had not been rigorously tested in adult cohorts. Latvala *et al*[3] evaluated physiological measures and long-term criminal behaviour on national registers of over 700 000 Swedish men. After adjusting for general and cardiovascular health, cardiorespiratory fitness, psychiatric, cognitive, and socioeconomic variables, those in the lowest quintile (heart rate $\leqslant$60 beats/min) showed a 39% higher hazard of being convicted for violent crime, and a 25% higher hazard for non-violent crime than those in the highest quintile ($\geqslant$83 beats/min). What is underlying this? Interoception is the perception of one's bodily signals, such as RHR. The 19th-century James–Lange theory[4] first linked this with emotional processing, though this has been heavily critiqued and refined in the years since. A 'fearlessness theory' argues that chronically low levels of physiological arousal may be a manifestation of generally reduced responses to stressful stimuli, promoting more risky behaviour; a 'low arousal' model posits that low baseline physiological arousal levels lead individuals to pursue more 'stimulating' antisocial experiences. The current study was not designed to differentiate these theoretical models; further work is needed to unpick these and to determine whether such factors can be prospectively identified and used at the individual level to support violence prevention work.

Disturbed interoception might contribute to other difficulties with emotional processing. Borderline personality disorder (BPD) is, perhaps, the exemplar of emotional dysregulation, but any link with interoceptive accuracy has not been well defined. A case–control study[5] compared heartbeat evoked potentials (HEPs) – the cortical representation of the cardiovascular system – of individuals with BPD and of healthy controls. Those with BPD showed deficits in the processing of bodily signals that were state dependent, with individuals in remission showing a normalisation of processing towards that of the control group. The results support a role for bodily signals in the perception and regulation of emotions, as well as suggesting this might be a fruitful target for psychotherapeutic intervention.

In 1943, McCullough and Pitts proposed a simple model of how neurons perform basic computations. Later, Donald Hebb mathematically modelled synapse adaptation (Hebbian learning), demonstrating associative learning between groups of neurons. Widrow and Hoff's 'delta rule' advanced this with supervised learning, where the model could adapt its behaviour when a 'teacher' reports the error between a learned stimulus–response association and the desired response for that stimulus. And then came Harry Klopf, who in 1972 noted that organisms do not usually have a supervising 'teacher' but instead learn from trial and error. This resulted in the modern formulation of reinforcement learning and, later, temporal difference learning. The key term is *prediction error*: the arithmetic difference between the predicted reward for an action and the actual reward delivered. When Schultz *et al*[6] noted that these models could describe the dopaminergic neuron's response and prediction in relation to reward, theorising about the cognitive processes underlying psychotic disorders changed forever. While these models *describe* the behaviour of neurons and synapses, they do not tell us how the biological substrate *implements* the computations. As Eshel *et al*[7] note, little is known how the error between predicted and actual reward signals is computed: how do neurons implement subtraction *in vivo*?

In the ventral tegmental area (VTA), dopaminergic (DA) neurons synapse with GABAergic neurons. DA neurons show a robust and predictable response proportional to reward intensity, and further, the magnitude of this DA response is also dependent on close temporal delivery of the reward after the execution of action. GABAergic neurons have been previously shown to respond proportionately to expected reward; these GABAergic signals could work by either subtraction or division to reduce the magnitude of the DA phasic firing. Computational models predict subtraction, but this arithmetic operation is rarely found in neural mechanisms (where multiplicative and divisive computations are often more plausible). Using laser stimulation to reliably control the pattern of GABAergic firing onto DA neurons, Eshel *et al* showed that the phasic DA firing pattern was reliably reduced (during reward presentation) in a way best fitted by a subtractive, rather than divisive, model. GABAergic interneurons in the prefrontal cortex express 5-HT_{1a} receptors

– one of the primary affinities for the atypical antipsychotics. Perhaps this GABAergic/serotonergic interface may explain some of the antipsychotic effect of the atypicals in reducing psychotic symptoms dependent on aberrant reward evaluation.

Santayana cautioned 'that life is worth living is the most necessary of assumptions and, were it not assumed, the most impossible of conclusions'. Wishing to end one's life is a complex concept, embracing, for many, philosophical, ethical, and religious constructs; it interfaces psychiatry with sociology and politics, and in the UK the Assisted Dying Bill was recently rejected.[8] An online sample of 500 American adults were read five pairs of vignettes about individuals experiencing suicidal thinking after a major life event; each pair contained one significant but non-terminal disability and one non-disability condition, and participants were asked about the relative acceptability of suicide in each case. The results[9] showed that participants found suicide significantly more acceptable in the disability condition, even if they, or family or friends, had disabilities. The authors ask the disquieting and unanswered question of how an apparent greater acceptability of ending their lives will be perceived by those with disabilities, particularly if they are feeling suicidal.

Figures estimate one in six children and adolescents will engage in non-suicidal self-injury (NSSI), but perhaps only one in five of these will receive professional help. There has been a growing awareness that peer victimisation can be a critical provoking factor, and self-harm in this context can have complex combinations of further self-punishment, providing tension relief, and/or be calls for help. It can be difficult to get accurate data on bullying because of variations in definitions and reporting, but typical figures show it occurs in up to a fifth of adolescents. A meta-analysis by van Geel *et al*[10] of over 20 000 children and adolescents found a significant positive relationship between peer victimisation and NSSI; of especial concern, younger children reported significantly more such behaviour when bullied, which the authors hypothesise might be due to their having fewer coping strategies. A call for active interventions to prevent childhood bullying is not new, but must clearly remain an ever-stated priority, not least as NSSI is a predictor of later suicide.

The positive cognitive effects of caffeine are well-known, and it is an essential part of the Kaleidoscope team's routine, especially as our copy deadline approaches. However, effects during pregnancy have been understudied – despite it being the most commonly consumed psychotropic during this period. A French population-based cohort of over 1000 mother–child pairs has been followed up,[11] measuring maternal caffeine intake during pregnancy and the child's IQ to the age of 5.5 years. Mothers who consumed $\geqslant$200 mg/day of caffeine were also more likely to drink alcohol and smoke during this period, but multivariable modelling correcting for this (and socioeconomic variables) still showed a significant negative relationship between caffeine intake and the children's IQ at age 5.5, by a unit of IQ per 100 mg daily caffeine intake. Consumption $\geqslant$200 mg/day was associated with a two-fold increase in the risk of borderline or low intellectual functioning. The study was observational, so causality cannot be confirmed: women *reducing* caffeine intake might have been an alternative factor for healthier pregnancies, and a high consumption against guidelines could be a proxy marker for other risk behaviour. Nevertheless, these findings and animal toxicity data would currently support NHS guidelines that recommend a maximum of 200 mg/day during pregnancy: two double-espressos, in Kaleidoscope terms.

Finally, Henry Rollins remarked 'If you think about it, every single species is endangered. *Homo sapiens* at the front of the line, mosquitos and lawyers at the back'. Fisman *et al*[12] are interested in the back of this queue (lawyers, not mosquitos), and wonder how their decision-making preferences might affect everyone else at the front. They took 208 Yale Law School (YLS) students as an 'elite' group as it is the most selective law school in the USA and tends to draw from high socioeconomic strata (apparently, in the past century, over half of US presidents attended Harvard, Yale or Princeton). They used a control group of American Life Panel members, a non-selective group of people who volunteered to take part in online surveys and experiments. Both groups played the modified version of the *dictator game* that in economics has been used to study so-called distributional preferences. A participant is asked to divide a fixed amount of monetary tokens into 'hold' and 'pass' amounts – they keep the former, and give the latter to another anonymous person; the pattern of hold and pass divisions demonstrates individuals' preference for altruism versus self-interest. The game can be modified such that on each trial the ratio of hold-to-pass amounts is varied – for example, every token kept resulting in two tokens being given away – allowing economists to also explore efficiency versus equality (when the ratio becomes more unfavourable, an economically efficient person chooses to award themselves more). Overall, 79% of the YLS group showed distributional preferences consistent with economic efficiency over equality, whereas this figure was just 49% in the ALP group. Interestingly, the YLS group were (at a ratio of 10:1) self-identifying as Democrats rather than Republicans in their political alignment. The authors followed up the YLS participants' eventual career choices and found that those who were efficiency-focused tended to opt for private rather than public sector employment upon graduating. Just to balance any perceived deficit in professional courtesy: a lawyer and a physician had a dispute over precedence. They referred it to Diogenes, who gave it in favour of the lawyer as follows: 'Let the thief go first, and the executioner follow'.

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