

## Kaleidoscope

Derek K. Tracy, Dan W. Joyce,  
Sukhwinder S. Shergill

We always hope you enjoy the free journal that comes with your Kaleidoscope subscription. A paper in this month's issue (pp. 429–436) showed that most scales assessing risk performed no better than the clinician/patient predictions following self-harm; this provoked a lively discussion on the journal's Twitter feed. A new paper by Seena Fazel's team explores their utility in criminal justice settings and forensic psychiatry.<sup>1</sup> The authors note how such tools are used to inform critical aspects of patient management such as in-patient detention and discharge, custodial sentencing, parole, and post-release monitoring. This is despite a lack of reliable validation on predictive accuracy, especially in important groups such as women, ethnic minority populations, and those motivated by religious or political extremism. Furthermore, they find the literature is marred by significant publication and authorship bias, and suggest that better-quality data will allow better matching of relevant tools to clinical contexts. This is best exemplified by assessing the balance between optimising false positive *v.* false negative findings: highly sensitive tools (with low false negatives) may be optimal where 'protecting the public' is seen as key, whereas highly specific ones might best protect prisoner and patient rights and interests. Assessment tools have had accusations of implicit discrimination levelled against them, as they commonly capture sociodemographic data – age, gender, ethnicity, immigration status – that risk profiling and perpetuating stigma. But should this information be excluded, especially as some data may improve predictive accuracy? The analogy of racial profiling at airports is put forward: if this helps a limited, but highly contentious, screening resource prevent more atrocities, is it warranted? It's clearly a charged debate, and perhaps that is part of the problem, balancing emotion and fairness with science. In the absence of robust data, we walk the fine line between coarse variables that may perpetuate discrimination, and the risk of their politically driven removal.

What is the value of telephone follow-up after a suicide attempt?<sup>2</sup> In a controlled trial of 436 patients – limited to those seen either as one-off emergencies or admitted for up to 3 days – telephone calls were made at 8, 30 and 60 days after an attempted suicide. The study utilised a specially trained nurse, with the same individual completing all a given participant's calls; unanswered calls were managed by a protocol including voicemails, text messages, email or letter within 24 hours. Telephone contact reduced repeated attempts by about a third overall relative to the 387 patients with a suicide attempt seen the year before the intervention was instigated, with the first call having the greatest impact.

**Talking therapies and pharmacotherapies are two options for first-episode major depressive disorder (MDD), but which to choose?** There has been, debatably, little to delineate them from a general effectiveness viewpoint – though individual outcomes can vary considerably in this heterogeneous condition – with patient preference and resource availability often driving decisions. It would be helpful to know if preference 'mattered', and if we could better foresee outcome. The PReDICT project has just published two of its outcomes. In the first report,<sup>3</sup> 344 patients with treatment-naïve first-episode MDD indicated if they

had a preference of talking therapy or medication, and were thereafter randomised to receive either 12 weeks of escitalopram or duloxetine, or 16 sessions of cognitive-behavioural therapy (CBT). The study literature informed them that they would be randomised and that, on average, people benefitted about equally from the two intervention types. They were also told that any preference would not influence their randomisation, and that to enrol in the study they needed to be willing to partake in whichever was offered. There were no differences, in terms of reduction in depressive symptomatology, between the interventions; patient preference – which was roughly evenly divided between CBT, medication, and having no particular inclination – did *not* have an impact on remission rates, though those matched to their preferred treatment were more likely to complete it.

The second paper<sup>4</sup> reports on a subgroup of 122 from this PReDICT cohort who also underwent functional magnetic resonance imaging analysis, with the intention to determine if there were any biomarkers that might help predict outcomes in this treatment-naïve group. Although neuroimaging has been used in this way before, it has typically been in studies looking at one intervention type. Three brain regions with established roles in mood regulation were found to be differentially associated with remission and treatment failure: the left anterior ventrolateral prefrontal cortex/insula, the dorsal midbrain, and the left ventromedial prefrontal cortex. Positive resting-state functional connectivity for these regions was associated with remission in the CBT group but associated with treatment failure in the medication cohort, whereas negative functional connectivity had the opposite association. The authors question if psychotherapy-responsive depression thus represents a brain state with a specific resting-state connectivity.

**Justifying the output of their basic or applied science, researchers often face the Jerry Maguire shout of 'show me the money'.** Li *et al*<sup>5</sup> sought to find an answer to how publicly funded research results in patents (evidence – arguably – that research has led to a valuable return). They tracked 27 years of grants from the National Institutes of Health (NIH), which provides about one-third of the funding for 'applied' and almost all funding for 'basic' biomedical research in the USA. They linked published outputs with patent applications that derived from the same research: the result is a kind of 'family tree' of research funding, through results, to patents. They examined two sources of 'linkage' between funding and outputs. First, a direct result was one where a patent arises from an NIH grant-funded project – these are mandated to be reported to the US government. Second, an indirect linkage was one accounting for the incremental nature of science: NIH-funded projects result in publications, and these published results are cited later in patent applications. From 365 380 grants awarded between 1980 and 2007, they found that there was no difference between 'basic' and 'applied' research in generating patents overall (50% of these grants were disease-oriented and, therefore, applied research). However, they found that 30% of NIH grants led to research that was cited in patent applications – suggesting indirect intellectual lineage – whereas only 10% of NIH grants led directly to patents. The time from grant award to patent citation did not differ substantially between disease-focused or basic research, nor was there any difference between human or simpler-organism research. The authors conclude that the classic and hotly debated division between applied and basic research is not grounded in evidence for the impact of publicly funded biomedical research. To quote the great Jay Z (with kudos to Neil K. Aggarwal), 'The numbers don't lie. Check the scoreboard'.

**Has the 5-HTTLPR shibboleth shattered? Serotonin is reuptaken from the synapse into presynaptic neurons by an integral membrane protein.** A functional repeat length polymorphism (5-HTTLPR) in the promoter region of the gene that encodes this has attracted enormous attention. It has two alleles, short (S) and long (L), and those with either one or two copies of the S variant, which is associated with less transcription of the transporter, have been shown to be more likely to develop depression *in response to stress*. The original finding from 2003 was seminal, linking a key therapeutic target site (serotonin reuptake), genetic and, crucially, environmental inputs: a seeming Rosetta Stone for psychiatry. But following this landmark publication in *Science* – which has been cited over 4000 times – quarrels around this particular G×E interaction have plagued the literature. In a project of impressive magnitude, a consortium of almost all previously publishing groups reanalysed their data using an agreed analysis script and protocol.<sup>6</sup> this involved 31 data-sets and almost 40 000 individuals of European ancestry, and looked at narrow and broad stressors, and current and lifetime depression. No interaction was found, including secondary analyses of subgroups or variable definitions. The 5-HTTLPR S allele does *not* increase the risk of major depressive disorder in individuals exposed to stress.

**Playing Tetris to help one's mental health: you'd like that to be true, right? Especially if it could assuage the guilt of a Candy Crush binge.** A paper in *Molecular Psychiatry* presents a fascinating proof-of-concept study in trauma work.<sup>7</sup> Traumatic episodes can be marked by unbidden distressing memories, and these are associated with the subsequent development of post-traumatic stress disorder. Work on memory formation has shown an early plastic period of several hours when the consolidation of the trauma memory can be disrupted. From bench to bedside, Iyadurai and colleagues provided Tetris to randomised participants within 6 hours of a life-threatening motor vehicle accident (playing it for at least 10 min when they had trauma memory reminders) and compared this to a control task of a written activity log for the same duration. The choice of Tetris was based upon the high visuospatial demands it places upon players, which, it could rationally be argued, might compete with the visual components of intrusive memories. For those who played the game intrusive memories were fewer and they also decreased in intensity more rapidly over the 1-week assessment; further, as one might anticipate, participants found the active intervention fun and pleasingly distracting. The authors label it a 'therapeutic vaccine', a phrase we suspect you'll be hearing more of in the future.

Finally, many of us will have seen the recent widely reported egregious case of data theft by a peer reviewer, and restrained response of the duped research team to the plagiarisers.<sup>8</sup> A step-down from frank fraud, but a far more common phenomenon, is predatory publishing. At Kaleidoscope, we were recently bestowed the honour of being invited to submit a research article to a new journal promoting best practice in 'biotherapies'. Given the impressive pace of progress in this emerging discipline, the journal offered to turn around peer-review on our article in under a month, for a special reduced price of about £600. At last, an outlet for our work on mint tea for the treatment of post-grant-rejection transient stress-related profanity disorder (PGRTSRPD hereafter). In 2005, a group of graduate students at MIT – frustrated by the stream of poor-quality, for-profit, publishing opportunities – wrote software that automatically generated

'nonsense' papers. On their website (<https://pdos.csail.mit.edu/archive/scigen/>) you can see the list of successes they had with conferences and journals accepting the 'work'. They even managed to organise a conference symposium using only sessions generated by the same automated content generator.

Intrigued by this, Sorokowski *et al*<sup>9</sup> report on a new mission; to get a fake academic, with no verifiable credentials, named 'Dr Anna O. Szust' (*oszust* is Polish for 'a fraud') appointed editor in a variety of journals. They created a full CV, profile on social media (Google+, Twitter, academia.edu) and a fake university homepage, accessible only via a link on Dr Szust's CV. Of note, the CV contained no verifiable publications or evidence of academic citizenship in terms of reviewer or editorial positions. Sorokowski *et al* then applied for editor positions to 360 journals, of which 120 were respectable journals listed on JCR (Journal Citation Reports) with published impact factors; 120 were listed in the Directory of Open Access Journals (a 'whitelist' of reputable open-access journals); and 120 were on a widely used 'blacklist' of predatory journals. Among the predatory journals, 33% accepted the application and appointed the fictional academic to editorial positions, as did 7% of the supposedly whitelisted open-access directory journals. None of the JCR-listed journals accepted the application. Four journals immediately appointed Dr Szust to editor-in-chief. Further, a dozen journals offered Dr Szust a position if she paid a fee while others made offers of splitting profits with Dr Szust if she encouraged publication with them. After Sorokowski *et al*'s exposé, 39 of the 120 open-access directory journals have been de-listed, however, of the 8 that accepted Dr Szust as editor, 6 remain on the directory. The data suggest that academic publishing remains a lucrative business, with a particular attraction for the gullible, opportunistic and over-waged.

- 1 Douglas T, Pugh J, Singh I, Savulescu J, Fazel S. Risk assessment tools in criminal justice and forensic psychiatry: the need for better data. *Eur Psychiatry* 2017; **42**: 134–7.
- 2 Exbrayat S, Coudrot C, Gourdon X, Gay A, Sevos J, Pellet J, et al. Effect of telephone follow-up on repeated suicide attempt in patients discharged from an emergency psychiatry department: a controlled study. *BMC Psychiatry* 2017; **17**: 96.
- 3 Dunlop BW, Kelley ME, Aponte-Rivera V, Mletzko-Crowe T, Kinkead B, Ritchie JC, et al. Effects of patient preferences on outcomes in the Predictors of Remission in Depression to Individual and Combined Treatments (PREdict) study. *Am J Psychiatry* 24 Mar 2017 (<https://dx.doi.org/10.1176/appi.ajp.2016.16050517>).
- 4 Dunlop BW, Rajendra JK, Craighead WE, Kelley MR, McGrat CL, Choi KS, et al. Functional connectivity of the subcallosal cingulate cortex and differential outcomes to treatment with cognitive-behavioral therapy or antidepressant medication for major depressive disorder. *Am J Psychiatry* 24 Mar 2017 (<https://dx.doi.org/10.1176/appi.ajp.2016.16050518>).
- 5 Li D, Azoulay P, Sampat BN. The applied value of public investments in biomedical research. *Science* 2017; **356**: 78–81.
- 6 Culverhouse RC, Saccone NL, Horton AC, Ma Y, Anstey KJ, Banaschewski T, et al. Collaborative meta-analysis finds no evidence of a strong interaction between stress and 5-HTTLPR genotype contributing to the development of depression. *Mol Psychiatry* 4 Apr 2017 (<https://dx.doi.org/10.1038/mp.2017.44>).
- 7 Iyadurai L, Blackwell SE, Meiser-Stedman R, Watson PC, Bonsall MB, Geddes R, et al. Preventing intrusive memories after trauma via a brief intervention involving Tetris computer game play in the emergency department: a proof-of-concept randomized controlled trial. *Mol Psychiatry* 28 Mar 2017 (<https://dx.doi.org/10.1038/mp.2017.23>).
- 8 Dansinger M. Dear Plagiarist: a letter to a peer reviewer who stole and published our manuscript as his own. *Ann Intern Med* 17 Jan 2017 (<http://annals.org/aim/article/2592773/dear-plagiarist-letter-peer-reviewer-who-stole-published-our-manuscript>).
- 9 Sorokowski P, Kulczycki E, Sorokowska A, Pisansky K. Predatory journals recruit fake editor. *Nature* 2017; **543**: 481–3.