It is a truth universally acknowledged that little gets mental health folk hotter under the collar than interpreting pharmacological trial data, so let’s do one on each of antidepressants and antipsychotics. The PANDA trial reports on the clinical effectiveness of sertraline in a pragmatic double-blind placebo-controlled randomised trial (RCT) in primary care. The intervention was a psychological therapy and the placebo was a ‘dummy’ treatment. The design included just over 11 000 students in ninth grade (14–15 years of age) and they were randomised evenly to either receive the psychological therapy or a ‘dummy’ treatment. Psychological therapy included: a self-reported fixed/growth mindset questionnaire (eliciting the student’s beliefs about ability and its flexibility). After randomisation, the first of the two-part intervention was delivered followed by a second session at around a median of 21 or 27 days. After the second session was delivered, all students took a repeat assessment of their beliefs about their mental ability and its flexibility. A post-test analysis was conducted to determine the effectiveness of the intervention. The results showed that the psychological therapy was more effective than the ‘dummy’ treatment, with a significant effect size. The authors conclude that the intervention was effective in improving mental health outcomes.

A Lancet commission concluded that improving education would be the single most useful intervention to improve health and well-being. The ‘growth mindset principle’ evolved out of the work of Carol Dweck and the central principle is that ability and intelligence can be developed, rather than being a fixed trait, by explicitly setting learning as a goal and in parallel with understanding that effort makes one ‘stronger’. It is appealing as a school intervention, but for a counterpoint, an interview with geneticist Richard Plomin was far less optimistic. An experiment was carried out, and in the National Study of Learning Mindsets an online growth mindset intervention was delivered to over 6000 students in 65 state-funded schools in the USA who were low achievers compared with their peers. Interestingly, the authors open their paper with a detailed discussion of heterogeneity of treatment effects and are explicit that they set out to analyse their data to find why the intervention does (or does not) work as a function of the school in which it was delivered. To guard against bias and false positive outcomes, the intervention and analysis were masked with pre-registered analyses and they pre-specified a priori effect size for significance. Further, they used an independent commercial research company to recruit schools so that the sample would be generalisable to the whole US state-funded school population.

The design included just over 11 000 students in ninth grade (14–15 years of age) and they were randomised evenly to either an online growth mindset intervention (challenging beliefs about intelligence) or no-intervention (a presentation on brain function but no emphasis on beliefs about intelligence). All students completed a self-reported fixed/growth mindset questionnaire (eliciting the students’ beliefs about ability and its flexibility). After randomisation, the first of the two-part intervention was delivered followed by a second session at around a median of 21 or 27 days. After the second session was delivered, all students took a repeat mindset questionnaire and took a maths test. On to the results: first of all, they measured change in mindset (away from ‘fixed’, toward ‘growth’) in 5650 students and found a non-zero effect size with those in the intervention being less ‘fixed’. By looking at the change in grade-point averages (GPAs) in core subjects – for posterior probability distribution; the relative weight assigned to the prior compared with the sensory data determines how much the latter updates beliefs or gets ignored. Pollak & Corlett give the analogy of speaking with people at a noisy party: it is far easier to talk to someone who is well known to you in such a setting, as you will have an already existing precise model of their speech against which to assimilate the received sensory input. Thus, the precision of your prior beliefs will be high, and one can more easily disregard prediction errors, and the likelihood of misunderstanding is lower. Taking this to psychosis, a Bayesian model has inappropriate weighting of irrelevant sensory stimuli, which erroneously update beliefs about the world. In the case of congenital blindness, they argue that this increases the precision and stability of higher-level ‘priors’ that protect against the computational deficits underpinning psychosis. In other words, such congenitally blind individuals are forced to rely on much more on their other senses such that their model of the world becomes far more resilient to false inferences from ‘noisy’ or ambiguous perceptual input in other modalities, as is seen in schizophrenia. The authors extend their argument to later-life visual impairment that is associated with hallucinations, such as Charles-Bonnet syndrome. Here the brain has ‘developed normally’ in early life, and thus higher-level predictions of reduced visually precise input will be explained confidently but falsely, resulting in visual hallucinations. They take this on to neurodegenerative conditions such as Parkinson’s disease and Alzheimer’s dementia, which are often associated with complex psychoses including visual abnormalities.
the intervention versus the control groups – they generalise their standardised mean difference effect size to conclude that the intervention would result in 5.3% (of 1.5 million students across the US school system) being prevented from having GPAs representing ‘off track’ target performance. Consistent with their analysis plan to explore heterogeneity across schools, they found that the fixed-mindset change was unaffected when the school was included as a covariate (consistent with the intervention being delivered by the same online platform), but that lower-performing students’ improvement in GPA performance did vary across schools. The authors suggest this represents ‘contextual mechanisms’ that either sustain or negate initial effects of the intervention. Indeed, the interaction of overall school performance with student’s change in GPA showed the highest effect in poorly performing rather than high-performing schools. The intervention costs 1 h of student time, appears most effective in lower-performing students in poorly performing schools and has the potential to change the educational trajectory of tens of thousands of students. The authors conclude by speculating on how their study demonstrates the importance of adolescents’ beliefs in the crucial maturational period post-puberty.

Post-traumatic stress disorder (PTSD), which has been argued to look more like a systemic illness than a mental disorder. This panel will need further testing with a series of diagnostic criteria and with Clinician-Administered PTSD Scale (CAPS) scores over 40 were considered PTSD positive; controls had current CAPS scores less than 20. In addition to basic physiological measures, blood samples were assayed for more than 1 million markers including DNA methylation, proteomics, metabolomics, miRNAs, endocrine markers, small molecules and routine clinical lab panels. Using a predictive model familiar to the financial sector called ‘wisdom of crowds’, they narrowed the panel to 343 unique potential marker candidates. To further refine this, after 3 years they invited 55 participants back and ran them through all testing again, settling upon 28 biomarkers representing alterations in DNA methylation, miRNAs, metabolites, physiological and clinical lab measures. To validate the panel, a new, independent, cohort was brought in consisting of 26 participants with PTSD and 26 controls.

Finally, links between creativity and psychopathology have long been recognised and continue to intrigue: so what about one creative group that might be close to your heart – successful academics? The broader description is of an inverted-U curve: low levels of psychopathology being associated with creativity, something that declines with greater symptoms. Parnas et al note that many studies looking at this use self-reported occupational role, which is prone to ‘status inflation’, also known as lying about your job responsibilities. They get around this by taking a group with assured track records of producing that which is novel, original, useful and valued – tenured academics. Taken from staff across three Danish universities, these were matched with randomly selected controls from the general population. Using the national civil register, first- and second-degree relatives of academics and controls were determined, and everyone’s mental health data were analysed from the Psychiatric Central Research Register. The total data-set incorporated over half a million individuals (almost 12 000 tenured academics), and analyses were adjusted for age, gender and educational level. The academics themselves had a considerably lower odds ratio than controls of having been diagnosed with any mental disorder, but their siblings, children and nephews and nieces had significantly increased risk for having schizophrenia; the risk was greater for maternal, but not paternal half-siblings. With regards to bipolar affective disorder, the odds ratio was significantly increased for their parents, grandparents and nephews and nieces. The risk of all other mental disorders was lower than those seen in controls. Schizophrenia and bipolar affective disorder are typically seen as the ‘creative’ mental illness-likes, and the findings hold here.

References