Impaired hippocampal neurogenesis has been implicated as forming an integral part in the pathology of several mental illnesses, including psychosis. Does this also offer a potential target for future therapy? Gobshits et al report on a transplantation study in rodents using a ketamine-induced model of psychosis. They transplanted bone marrow-derived mesenchymal stem cells; these are multipotent cells that can differentiate into several lineages including those promoting endogenous neurogenesis, and have been shown to have immunomodulatory properties. After being transplanted into the rodents’ ventricles on a single occasion they observed that they were successfully engrafted and able to survive for up to 3 months post-transplant. There were increases in hippocampal neurogenesis, reaching normal levels, at both 2-week and 3-month test points relative to non-treated animals. At the behavioural level, this was associated with improvements in social novelty preference and prepulse inhibition. The authors highlight the interesting finding that these behavioural improvements were initially correlated to FGF2 gene expression, a key proneurogenic gene that promotes cell proliferation and differentiation; but by the 3-month assay such levels had returned to those seen in the controls. At this latter point, behavioural changes were primarily correlated with the notch ligand DLL1, which has been linked to neural stem cell self-renewal. Another finding of note was that short-term treatment with clozapine was only effective during treatment, with results tapering off once it was discontinued; in contrast to the transplantation that seemed to offer a longer-lasting ‘fix’. Interestingly, the effects also seemed protective against age-related decline in neurogenesis seen in control rodents (and humans), and the authors speculate that bone marrow-derived mesenchymal stem cells might be protective against normal deterioration seen in cognitive functioning. Naturally, this raises the inevitable hashtag #justSayInMice, and interesting questions both around the translational potential to humans, but also speaks to the acceptability and secondary effects of such treatment.

From all-or-nothing to graded response; there is much still to learn about the functioning of even a single neuron. Writing in Science, Gidon et al explored the ex-vivo dendrites of layers 2 and 3 in human cortical pyramidal neurons – something previously done almost exclusively on rodent tissue. The human cortex, at about 3 mm, is unusually thick compared with other species, especially in the aforementioned layers, forming very big, complex dendritic trees. As it is the dendrites that determine axonal output, they can be considered the computational aspect of a neuron, managing multifaceted inputs. Cells were taken from surgically resected slices from individuals with epilepsy, and subjected to dual somatodendritic patch clamp recordings and two-photon imaging that allowed the team to directly investigate the cells’ properties. Astonishingly, they discovered an entirely new class of calcium-mediated dendritic action potentials (dCaAPs). These were very different to classical neocortical action potentials of N-methyl-d-aspartate spikes and dendritic calcium action potentials that increase with stimulus strength. Here, with dCaAPs they found that their impact on neuronal waveform output was graded, and not the all-or-nothing action potential typically described and understood. dCaAP amplitudes were greatest at threshold-level stimuli, and weaker for larger inputs. dCaAPs in dendrites thus allow individual neurons to decode linearly non-separable inputs, a computation the authors note that was previously considered to necessitate multilayered networks. What this means is that cells can compute an ‘anticoincident function for multiple input pathways’, which effectively limits the strength and number of inputs. A delicate balance of excitation and inhibition is required to generate a dCaAP, which the paper highlights means that counterintuitively, inhibition can actually increase the neuron’s excitability. This has never been seen before
in any neuron of any other species. To contextualise this, it had previously been thought that the dendritic input and axonal output can manage the logical operations of AND and OR. Here the authors demonstrated that a single dendritic compartment of a single neuron in your head can compute the XOR operation or logic gate; that is some seriously cool science.

**Callous–unemotional behaviour is a noted risk factor for the development of antisocial behaviour; but what causes the callous–unemotional nature in the first place?** Waller et al tested fear responses to social and non-social stimuli, and observed social affiliations in a sample of 620 pre-schoolers at age 3 years. Why examine children’s responses to fear? Decreased fearful arousal has been implicated in callous–unemotional behaviour because of a loss of inhibitory processes when faced with threatening cues. Similarly, lowered awareness of, or sensitivity to, fear displayed by peers infers problematic empathy. Social affiliation is the drive to have close relationships, manifesting through reduced physical distance, touch, eye contact, shared gestures and vocalisations. A lack of social affiliation risks loss of development of typical empathic learning. Following on from the initial assessment, the children’s callous–unemotional and oppositional and defiant behaviours were monitored over the subsequent 2 years. They found that fearlessness and low social affiliation predicted greater callous–unemotional behaviour, but not the oppositional or defiant types. The authors also tested the impact of parental input, measuring their harshness and warmth levels. Once again there was a divide on how it had an impact on the different behaviours in children: harsh parenting was associated with more callous–unemotional behaviour in fearful children, but more oppositional–defiant behaviour in fearful children. The findings are particularly interesting as they specify a longitudinal relationship between these early life factors, and delineate callous–unemotional as a subgroup distinct from oppositional–defiant disorder. Also, they open up potential intervention strategies for behaviours that can have profound and enduring subsequent emotional, societal and financial costs.

Finally, although we imagine ourselves as rational consumers of information, we all suffer from biases: discounting information that contradicts decisions we have made in the past, and favouring judgements delivered with confidence. Computational modelling and psychological theories suggest we actually lose sensitivity to information that contradicts our previous choices. Kappes and colleagues, assessed the impact of the deliverer’s confidence on our appraisals. Participants guessed the prices of houses for sale and placed a wager, which acted as a proxy for confidence. Then, during a function magnetic resonance imaging scan, they went over each decision again with the option to change their bet after hearing whether a supposed partner agreed and what their partner wagered, a proxy for their confidence. As expected, confirmation bias was found with participants making a change to their wager only when their partner agreed with them. From a neural perspective, this could be attributed to only one area: the posterior medial pre-frontal cortex, which appears to be involved in post-decision performance monitoring, signalling to adjust our behaviour accordingly. There was a relationship between the partner’s indicator of confidence and the signal strength here, but only when the partner agreed. So, this suggests that upon hearing something we disagree with we conceptualise it as invalid, discarding it and we are functionally deaf to the confidence of delivery. It seems intuitive, as evidenced by the public discourse around climate science and politics, but perhaps it is valuable to appreciate this vulnerability in cognition while practising in medicine and psychiatry, especially as it has an impact on both the clinician and patient perspectives. In science, we design and follow protocols to help mitigate our biases, but the tools we use are only as good as those using them.