Kaleidoscope

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I recall the awful news footage of emotionally abandoned children in Romanian orphanages following the fall of Ceaușescu's regime in the late 80s. I was a child myself at the time, and I remember in particular the feeling of sadness hearing about some babies who had learned to no longer cry, as it evoked no response. The Bucharest Early Intervention Project remains the only randomised controlled trial comparing foster care with institutional care and has been running for over two decades. As part of this work, King et al[1] report on the follow-up of 136 children who had been abandoned shortly after birth. They were randomly assigned to one of those upbringings between the ages of 6 and 31 months and were followed up as they grew. The authors provide links to papers addressing some of the ethical dimensions of this work, which are likely to initially sit uncomfortably with many of us. Of note, support of the foster care network ended by age 54 months, at which point it was transferred back to Romanian authorities. However, assessments continued at ages 8, 12, and 16–18 years. During this time, participants underwent repeated measurements of IQ, physical growth, brain activity via electroencephalographs, and evaluation for various types of psychopathology. More than 20 years and 7000 observations showed what you might expect, but with data and detail: placement in foster care hugely benefited the children, and gains were remarkably consistent across development through childhood to adolescence. The benefits were broad but most notable in terms of IQ and disorders of social relatedness. The communist East Europe of the 1980s might feel a lifetime away, but the paper notes how there are millions of children around the world in 2023 being raised in institutions. Of course, many such institutions provide good care, but neglect and even severe deprivation continue.

'That for which we find words is already dead in our hearts. There is always a kind of contempt in the act of speaking' taught Nietzsche; more prosaically, whence comes language? I've been interested in this from an evolutionary perspective, though as language only 'fossilises' through writing, we have to track back through similarities in sounds, semantics and syntax across language 'family trees' (think Spanish and Portuguese, etc.). Although behavioural modernism infers that it must have been present at least 50 000 years, historical linguistics has a 'ceiling' of 6000–10 000 years ago, before which we cannot see (though, fascinatingly, it's extrapolated that there were perhaps 20 000 languages at the start of the Neolithic, compared with about 7000 today).[2] A new paper in *Science*[3] explores the defining characteristic of how humans use words in a novel manner to express multiple meanings, something called language overextension. This happens both phylogenetically across time in our species and ontogenetically as children grow into adults. You know the stuff kids do – my son used to call the back of the mid-point of his bent arm his 'elbow-cap' – well, it's part of our cognitive creativeness as a species. We don't just 'have' language, we develop and grow it, and bidirectionally we expand how we think as we change how we talk (if you're bilingual, you'll also get some of the differences in creativity in phrasing across different languages). As well as changes seen across the lifespan, individual languages change over centuries (though when I speak to my now-teenage son and his friends, it appears to have morphed in the past decade to something I struggle to understand). The authors explored an impressive 1400 languages using computational models to build a parsimonious set of semantic knowledge types. This included four types based on our everyday experiences: visual perception, associative knowledge, affective knowledge and taxonomic knowledge. They show a unified foundation for our lexical creativity that aligns well with evolutionary data on both an individual's development and our change with time as a species. The patterns that children show in creating new words predicts the change of language itself and *vice versa*. The approach is novel and offers hope of helping to breach that 6000–10 000 year ceiling on language origins, and indeed of unpicking the origins of varying semantic knowledge type and acquisition.

Much newspaper ink is spilled on the 'growth' of mental illness; it's an important yet contentious topic, with research often really revealing better awareness and recognition of problems. However, it's important to get the best and most up-to-date data, and things can change with time, not least as societies and risk factors alter. Solmi et al[4] report on results on psychosis from the 2019 Global Burden of Disease (GBD). Over a 30 year period to the study end, the prevalence (total number with the condition), incidence (number developing it each year) and disability-adjusted life years all increased, by global averages of 65%, 37% and 65%, respectively. This occurred generally across all country types, though there was some variation. Those countries with a low socio-demographic index actually showed a drop in incidence, which the authors suggest may actually imply suboptimal detection. The male/female ratio remained unchanged over time. The thing that leaps out from this is the question of what that means: is schizophrenia 'on the rise', are we better at detecting it, or both? Another potential factor is that diagnostic manuals and criteria have changed over time; might that be affecting figures? The 2019 GBD data are certainly some of the best available globally right now. As a summary, the authors say that we have probably historically underestimated the burden of the condition and are really just catching up with the reality that psychosis poses for so many individuals and society as a whole.

With data showing a rise in maternal consumption of cannabis, there is a need to know more about any impact on prenatal brains. There are plenty of contemporary discussions on the decriminalisation and legalisation of cannabis, with reasoned social arguments on each side, even if many debates have more heat than light. Nevertheless, with a general move towards lighter-touch governmental control, it's always reasonable to ask about potential harms, even if a substance is 'allowed': we do this for alcohol and tobacco. Further, the endocannabinoid system appears to have critical early involvement in synapse formation and neural circuit refinement in the growing fetus. Sarikahya et al[5] provide an update with a rodent model of prenatal cannabis exposure (PCE). They found that both male and female offspring exposed to chronic Δ9-tetrahydrocannabinol showed long-term cognitive deficits from PCE, though, fascinatingly, these appeared to be mediated by different mechanisms in each sex. Both showed hyperactive prefrontal cortices (PFC), but in males the ventral hippocampus was hypoactive, whereas it was hyperactive in females. There was also divergence in terms of cortical oscillatory activity states and disturbances in dopaminergic and NMDA receptors (including topographically in terms of location) and other protein expression. The endocannabinoid system has well-established roles in regulating the PFC and hippocampal cognitive and memory functions via localised cannabinoid 1 receptors and availability of constituent long-chain polyunsaturated fatty acids, so induced changes there are not unexpected. What is fascinating is the breadth and long-term sequelae of PCE, and also how much they vary by sex. As ever, translating work to humans will be an essential, if very complex, next step.

Last month I wrote[6] on the methodological challenges of undertaking research on bipolar depression; as if by magic, a relevant paper in the *New England Journal of Medicine* has since appeared. Yatham et al[7] describe the largest double-blind randomised placebo-controlled trial in bipolar depression. Individuals with bipolar affective disorder (BPAD) who had recovered from depressive phases while being treated with either escitalopram or bupropion XL were randomised to either continue their treatment for a year ($N = 90$), or switch to placebo at 8 weeks ($N = 87$). This is interesting, as far fewer studies have looked at maintenance treatment, and most focus has been on attaining remission in the first place. Those study numbers look reasonable for a randomised controlled trial (though, again, read last month's thoughts on that), but the researchers had hoped for more, and slow recruitment led to trial termination. And for those who continued and completed the duration? Interestingly, those maintained on antidepressants did not have superior outcomes to those whose treatment was stopped shortly after recovery. My ramblings in September's *BJPsych* noted how it was difficult to confirm the canonical belief that antidepressants caused manic 'switching' (not that it can't occur, but causality is hard to prove) in patients with BPAD. These data perhaps add to our uncertainly in also suggesting that medications might not serve as effective prophylactic treatment either. Depression typically accounts for two-thirds of the illness burden in BPAD; its management remains a real challenge, with the art of practice often supplementing evidence from research.

Finally, German DJ Tomcraft imprinted my 20s with his track 'Loneliness': considering psychosis, how much is it affected by this social blight (isolation, not underground techno-trance anthems)? Chen et al[8] undertook a cross-sectional survey of 300 individuals with either schizophrenia or schizoaffective disorder. Perceived support from friends was associated with reduced magnitude of both loneliness and suicidal thinking and risk. Further, the more self-esteem people had, the less likely they were to suffer from depression. I'll tell you what most fascinated me about this work: that no one had tried to objectively capture this before, at least in this way. We have an established diathesis–stress model of suicidal behaviour that links to social isolation and feelings of alienation, but the moderating effects of friends and families have not been evaluated in schizophrenia. Our interventions in psychoses continue to emphasise medication approaches; we really need to better augment this by helping those we see to build and strengthen their social networks. In the UK, Integrated Care Systems would seem to offer one productive way forward. Loneliness is a chronic problem for so many in the world today, and it is so often compounded in those already more disadvantaged, including many individuals with psychosis. There are evidence-based programmes to help this, and, of course, you can reach out a metaphorical hand to people you see in your own life. The authors note how clinicians often don't routinely ask about loneliness in individuals with schizophrenia – indeed, how often do you ask this of any of your patients? If we don't know something is a problem, it's hard to offer any help or solutions. I'll conclude by passing back over to Tomcraft[9] and memories of München's *Das Heizkraftwerk (der reißt richtig ab!)*: 'Happiness seems to be loneliness, and loneliness chilled my world. How could you guess, when you're only thinking of yourself, and how you looked at other girls'.

References

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