

Kaleidoscope

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Multiple sclerosis is an immune-mediated inflammatory demyelinating condition putatively triggered by a viral infection.

The Epstein–Barr virus (EBV) has been proposed as a causative agent in multiple sclerosis because of observations of an increased risk of multiple sclerosis in people who've had infective mononucleosis (glandular fever, usually caused by EBV) and evidence of EBV in multiple sclerosis lesions in some pathology specimen studies. However, for a stronger causal claim, the necessary natural experiment is to locate a large prospective cohort of people who are confirmed EBV negative at one time point and where some will be EBV positive at a later date. Bjornevik et al¹ exploited a 20 year prospective cohort of 10 million US military service personnel, where, at regular intervals, serum samples were collected and preserved in the Department of Defence Serum Repository. EBV is ubiquitous, with around 95% of adults having the infection, so the researchers located 801 people with multiple sclerosis and 1566 matched controls who had relevant samples available. They then located two serum samples: one baseline and another sample prior (median 1 year) to the multiple sclerosis diagnosis. In the later serum samples, only one of the 801 multiple sclerosis cases was EBV negative. At baseline, 35 of the multiple sclerosis cases and 107 of the controls were EBV negative, with all but one of the 35 multiple sclerosis cases developing EBV infection over time. This resulted in a hazard ratio of 32.4 (95% CI 4.3–245.3) for multiple sclerosis in the EBV-positive versus the persistent EBV-negative cases. Of note, infection with cytomegalovirus (CMV), which like EBV is transmitted in saliva, was used as a negative control and appeared to actually lower the risk of multiple sclerosis, suggesting that the immune response to CMV attenuates the risk conferred by EBV. Importantly, the authors provide a mechanism for this, showing how levels of sNfL (a marker of neuroaxonal degeneration that is sensitive to – but not specific for – multiple sclerosis) were elevated in the multiple sclerosis cases after EBV infection – but not before – helping strengthen their claim for forward causation. It's hard to exaggerate the scale of the achievements in this magnificent piece of work: it finally pins-down a cause for at least most cases of multiple sclerosis, explains mechanistically how this occurs, and opens a door to direct therapeutics and vaccinations.

Mindfulness: popular but overhyped? It's been propagated by business schools, promoted via innumerable smartphone apps, and given a fairly uncritical press in newspapers, magazines and television programmes. One challenge is pinning down what 'mindfulness' means: it has origins in Buddhist traditions and for some continues to reflect a spiritual path; for others, it's a way of living and an aspirational personality style often including meditation; and, of most interest to us here, it can mean a cognitive style trainable via mindfulness-based interventions (MBIs). One common definition of the latter is intentional self-regulation of attention to the present moment without judgement. The extant literature has been criticised for many methodological failings, including a reliance on self-report measures, small study sizes and a lack of active controls.

Redressing this, Goldberg et al² examine the actual underpinning empirical basis of MBIs, reporting on a systematic review of 44 meta-analyses of randomised controlled trials (RCTs). This pulled in 336 RCTs and over 30 000 participants, so quite a bit of data, and inclusion criteria ruled out lower-quality studies

that mixed passive and active controls. Overall, MBIs showed superiority to passive controls, but it shouldn't really be surprising that 'doing something' seems to be better than 'doing nothing', and is hardly a particularly high bar. When it came to active controls – doing something – MBIs typically did *not* achieve statistically significant superiority, and where they did, effect sizes were small. Has cold science placed a cruel hand of death upon mindfulness? It certainly raises the question as to whether resource-poor health-care systems should be providing mindfulness, not least as the authors note that the public risk being 'harmed, misled, and disappointed' by it. One can reframe the findings to state that there is some signal amongst the noise, and MBIs are perhaps showing early promise. Larger, better-designed trials might try unpick this, determining when and in whom they might be appropriate. There was certainly a wide variety of trials here, some looking at a particular problem (from anxiety through depression to psychosis) or population (from children to older adults), others a defined intervention type or delivery format. But with quite limited gains when applied to over 30 000 people in these trials, the onus is very much upon mindfulness advocates to overcome the null hypothesis.

Antipsychotics: unpopular but under-hyped? A paper in *Lancet Psychiatry* provides an update³ on the impact of antipsychotic medication and non-pharmacological treatment in first-episode psychosis and acute relapses within the first decade of diagnosis. In contrast to the mindfulness literature discussed above, there is a rather large body of literature on these medications of which much is of at least moderate quality RCTs. The literature on non-pharmacological interventions including cognitive-behavioural therapy, open dialogue, Soteria (a community approach providing space and typically non-medical staffing without the use of medication) and psychoanalytic psychotherapy is considerably smaller and typically of a lower quality. The authors renounce the myth that antipsychotics work via sedation and show that response is twice as likely compared with placebo, with recent studies demonstrating that about 70% should attain response in a first episode. In non-pharmacological trials, the evidence is more patchy, although the trials are fewer in number. Soteria and open dialogue studies have particular methodological problems, including the use of control groups from a decade or two earlier, quasi-experimental approaches, and concerns about their sample sizes and the reporting of findings. There were only two RCTs for psychosocial interventions, and they showed inferiority to medication at reducing hospital admissions. Studies of cognitive-behavioural therapy had the strongest non-medication results, although they generally had small sample sizes, and of the five RCTs on the topic, four were by the same group, had no placebo, no diagnostic interviews, no measure of medication adherence, and generally poorer responses to medication than those in the aforementioned medication studies. The work is also limited by a lack of placebo and treatment-as-usual groups, hindering any definitive statement on this being an 'alternative' to medication. There are dangers that this type of work becomes a binary of medication versus psychosocial interventions or, even worse, feeds a (particularly peculiar online) psychiatry versus psychology dynamic. It is not about claiming primacy but evaluating the evidence as we have it. The evidence supports antipsychotics, but clearly they don't work for all and can have side-effects; at this time, the evidence for psychosocial interventions is simply far more limited in terms of numbers of studies and their methodology.

Psychological studies are too WEIRD – with Western, Educated, Industrialised, Rich and Democratic participants. The lack of diverse representation has persisted, in part, because of an implicit

idea that the fundamentals of human behaviour were universal, making the cultivation of broader participant pools unnecessary. However, in reality, these ‘representative samples’ are true outliers on a host of psychological measures ranging from moral reasoning to visual perception. A call to action followed the coining of the WEIRD acronym a decade ago, and although this helped people to focus on the issue, a 2018 study of leading journals found little real progress. The vast majority of studies continued to focus on the same populations, with many not even bothering to report on demographics beyond gender, and over 80% failing to analyse or contextualise possible effects of race or culture.

A recent *Nature Reviews Psychology* article⁴ highlights the issues; by obscuring or ignoring the overwhelming Whiteness in research, it is maintained as an invisible default and there is a failure to challenge the inherent assumptions of power and privilege. It is hard to imagine a large study of global-majority participants not mentioning race, culture or location as observed in WEIRD samples. Rarely do we see a study with all White participants grounding their findings in theories of White identity and racial power, because there are decades of research that normalises equating the White experience with the human experience. Like our WEIRD problem, neuroscience must reckon with its Whiteness problem, not least being able to see the water in which we swim, and the commonly used White racial framework. Even our narrow samples of behavioural data tell us that outwitting our biases to see with true clarity is a near impossible task, but we should never allow such a repetitive and systemic threat to the quality of our science to stand. We lean on the scientific method to ward against our fallibility, but it has not always served us well. In a recent Kaleidoscope Live!^a, an extensive, almost Linnaean approach to cataloguing behavioural phenomena was suggested as an answer to the reproducibility crisis in psychology. The approach could be beneficial here as well, though it would need to be supported and augmented by racial and cultural grounding.

Finally, in the movie *When Harry Met Sally*, we’re told ‘No man can be friends with a woman that he finds attractive ... he always wants to have sex with them’. Is this true? A new paper by Szymkow and Frankowska⁵ examines the psychology behind this hypothesis, solely exploring heterosexual relationships. There are a number of evolutionary theories surrounding opposite sex friends (OSF) – for example, the ‘mating activation hypothesis’ that OSF are ‘back up’ mates (in the sense of keeping one’s reproductive options open). Previous studies have certainly shown that men emphasise physical attractiveness in OSF whereas women prioritise an ability to provide protection and economic resources, but

they have not determined which factors might moderate this. In this paper, the authors conducted experiments recruiting participants who were in committed cross-sex relationships who had at least one OSF who would also participate. So, in other words, the scientists could now evaluate both your other half, and your opposite-sex bestie.

The participant and the OSF were given sealed questionnaires to answer and return anonymously. The authors set out to test how men and women were influenced by the perceived sexual attractiveness and financial resources of an OSF to predict sexual interest. The twist is that they used the participant’s committed partner’s sexual attractiveness, financial resource and supportiveness as moderators. In regression analyses (conducted separately for males and females), the dependent variable was sexual interest in the OSF, with independent variables being perceived attractiveness, resources and committed partner’s supportiveness. For women, the model showed no association between sexual interest in the OSF and the predictors. For men, the model showed only that perceived attractiveness of the OSF was associated with sexual interest in them. In moderation analyses, only women who rated their committed partners as moderate or low on attractiveness and supportiveness showed sexual interest in the OSF. These moderating effects were absent in the male participants. So, to summarise, Billy Crystal’s movie character had a point, to a degree: men are more likely than women to be sexually interested in an OSF they consider attractive; having a supportive attractive partner reduces sexual interest, but only for women. The findings endorse the ‘mating activation hypothesis’, but we’ll just leave that take-home message hanging there for you to consider how much of an excuse you might find ‘it’s just my evolution’.

References

- 1 Bjornevik K, Cortese M, Healy BC, Kuhle J, Mina MJ, et al. Longitudinal analysis reveals high prevalence of Epstein-Barr virus associated with multiple sclerosis. *Science* 2022; **375**: 296–301.
- 2 Goldberg SB, Riordan KM, Sun S, Davidson RJ. The empirical status of mindfulness-based interventions: a systematic review of 44 meta-analyses of randomized controlled trials. *Perspect Psychol Sci* 2022; **17**: 108–30.
- 3 Jauhar S, Lawrie SM. What is the evidence for antipsychotic medication and alternative psychosocial interventions for people with acute, non-affective psychosis? *Lancet Psychiatry* 2022; **9**(3): 253–60.
- 4 Remedios JD. Psychology must grapple with Whiteness. *Nat Rev Psychol* [Epub ahead of print] 27 Jan 2022. Available from: <https://doi.org/10.1038/s44159-022-00024-4>.
- 5 Szymkow A, Frankowska N. Moderators of sexual interest in opposite-sex friends. *Evol Psychol* [Epub ahead of print] 24 Jan 2022. Available from: <https://doi.org/10.1177/14747049211068672>.

^a And if you haven’t been listening to our monthly webinars (live and records), what’s with you? They’re like your favourite podcast, but better. Sign up here: <https://maudslaylearning.com/webinars-podcasts/kaleidoscope-live/>.