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Neurofeedback or neuroplacebo?

This scientific commentary refers to 'Better than sham? A double-blind placebo-controlled neurofeedback study in primary insomnia', by Schabus *et al.* (doi:10.1093/brain/awx011).

Neurofeedback ranks high on the list of ostensibly 'scientific' tools available for moulding brain function and bolstering mental processes. And yet, as with other popular techniques such as computerized brain games, a dearth of robust evidence and well-controlled studies characterizes the research sphere of neurofeedback. In this issue of *Brain*, Schabus and co-workers report a carefully crafted experiment probing the treatment of insomnia; their findings suggest that the benefits of neurofeedback may derive largely from placebo-like effects (Schabus *et al.*, 2017).

In neurofeedback, participants attempt to self-regulate an ongoing feedback signal from their own brain activity (Sitaram *et al.*, 2017). Since the inception of this field in 1958, the dominant theory has contended that neurofeedback endows individuals with volitional control over brain function and, in turn, trains the capacity to self-regulate associated behaviours (e.g. deficits of attention or insomnia). To date, however, few studies have included the necessary control groups and experimental designs to directly test this hypothesis. Of the thousands of published reports on the topic of neurofeedback, the recent effort by Schabus *et al.* stands out as one of the few randomized, double-blind, sham-controlled trials. Their findings show that neurofeedback may work for reasons very different from what conventional wisdom might suggest.

Contrary to their hypotheses, Schabus *et al.* found little difference in insomnia outcomes when comparing genuine to sham neurofeedback (Fig. 1). For one phase of the experiment, the researchers provided sham (i.e. placebo) feedback from alternating frequency bands outside the range of interest. Such sham controls are crucial for teasing apart the effects of genuine feedback from other nonspecific influences involving motivation and expectation. In this study, however, genuine and sham neurofeedback propelled comparable improvements in subjective ratings of wellbeing and restfulness.

Crucially, whereas genuine neurofeedback helped participants amplify a subset of brain signals during training, this ability was independent of behavioural improvement. Neurofeedback, moreover, had no significant impact on either resting state brain activity or sleep activity as measured by polysomnogram. These findings hold special importance in a field that often relies on subjective measures of improvement and rarely probes whether participants actually master control over brain activity. The reported results also call into question the standard 20- to 40-session regimen that dominates the neurofeedback landscape; the capacity for neural self-regulation seems to plateau after only a few sessions. This well-conceived (and reasonably powered) study indicates that placebo factors play a central role in shaping the therapeutic outcomes associated with neurofeedback—more central perhaps than the role of brain feedback *per se.*

When prescribing neurofeedback, practitioners must consider what constitutes meaningful clinical improvement: brain changes, subjective reports, objective measures, or some combination thereof. The positive subjective outcomes Schabus *et al.* observed might appear sufficient to advocate for neurofeedback; after all, the sleep complaints, which led individuals to seek help, subsided. Objectively, however, poor sleep quality, which remained unaltered, often leads to deleterious health consequences. Thus, subjective improvements may satisfy patients in the short-term while carrying the potential to inflict future harm by impeding further treatment.

Proponents of neurofeedback may protest that this experiment reflects only one particular application of the technique. Perhaps a different frequency band, clinical condition, imaging modality, or number of sessions could lead to entirely different results. While this argument might hold true, the burden of proof continues to linger in the court of those who advocate for such claims (Thibault and Raz, 2016). To be sure, nascent forms of neurofeedback—e.g. leveraging functional MRI, large-scale connectivity analysis, or multivariate decoding algorithms (Cortese *et al.*, 2016; Sitaram *et al.*, 2017)—may eventually surpass the limitations of traditional EEG-based approaches. And yet, until we obtain independently replicable evidence supporting the benefits of neurofeedback over sham controls in double-blind randomized trials, the clinical efficacy of such interventions remains in question.

Neurofeedback may nonetheless offer a potent psychosocial intervention, even if genuine feedback rarely outperforms rigorous sham variations (Thibault and Raz, in press). Placebo

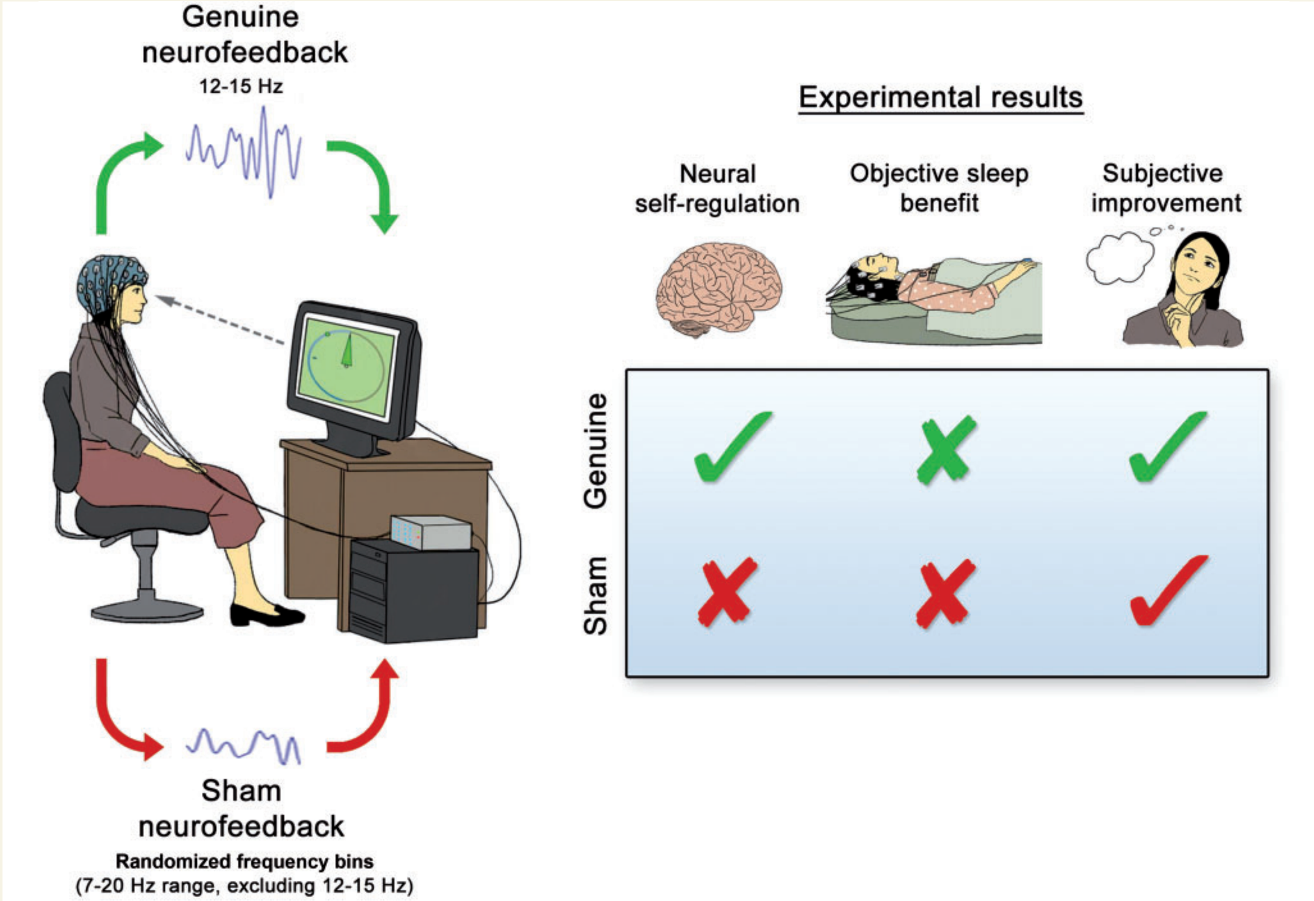

Figure 1 Comparing genuine and sham neurofeedback. In the study by Schabus *et al.*, participants received real-time feedback concerning their own brain activity: the more they successfully amplified the target neural signal, the farther the needle rotated on the monitor in front of them. Participants underwent 12 sessions of genuine neurofeedback followed by a washout period of 3 months, and then 12 sessions of sham neurofeedback (or vice versa). Whereas neural regulation improved in the genuine feedback group, neither genuine nor sham interventions improved objective measures of sleep quality. Moreover, in terms of subjective reports, genuine and sham feedback led to comparable improvements.

responses can be powerful, and they are not all equal. Coloured pills work better than white pills; large pills work better than small pills; and expensive pills work better than cheap ones. Moreover, two placebo pills relieve pain more effectively than one; placebo injections work better than placebo pills; and placebo surgeries trump all of the above (Raz and Harris, 2016). Whether real or sham, neurofeedback demands high engagement and immerses patients in a seemingly cutting-edge technological environment over many recurring sessions. Moreover, this form of neuroenchantment likely holds special sway over critical reasoning and can lead people to accept explanations they would normally dismiss (Ali *et al.*, 2014). In this regard, neurofeedback may represent an especially powerful form of placebo intervention—a kind of superplacebo. On the one hand, this line of thought implies that the sham-control benchmark may be stricter in neurofeedback than in other clinical domains, such as psychopharmacology. On the other hand, patients may well benefit more from neurofeedback placebo effects than from other available treatments.

Neurofeedback relies heavily on 'non-specific' mechanisms of healing (i.e. therapeutic influences peripheral to the supposed active ingredient of an intervention). Whereas clinical researchers often brush aside non-specific factors as nuisance variables, a subtler appreciation of these mechanisms could help practitioners offer better treatment. Contrary to what the name implies, non-specific factors can in fact lead to very specific psychological and physiological changes (Raz and Michels, 2007). Researchers can parse non-specific factors into discrete elements, such as the expectation to improve and the patient-practitioner interaction, each of which makes its own systematic contribution to outcomes (Kirsch *et al.*, 2016). A more scientific understanding of the so-called 'non-specific' elements that drive neurofeedback-mediated healing could help practitioners leverage and amplify these effects in

Glossary

Neurofeedback: A procedure wherein individuals learn to modulate real-time signals from their own brain activity; often leveraged to self-regulate neural processes for therapeutic ends. Schabus *et al.* investigated electroencephalography neurofeedback. This technique records electrical brain activity from sensors placed on the scalp and remains the most popular form of neurofeedback.

Sham neurofeedback: Feedback from an unrelated brain signal or from the brain of another participant; employed as a control condition to isolate the specific influence of genuine feedback.

Superplacebo: A treatment that is actually a placebo although neither the prescribing practitioner nor the receiving patient is aware of the absence of evidence to recommend it therapeutically.

neurofeedback as well as across other therapeutic domains.

The appeal of neurofeedback may profit from the big business and salient vogue of the self-help boom in Western society. Unlike some extreme and dangerous forms of self-help, neurofeedback seems reasonable and requires neither self-parboiling nor arcane systems that supposedly merge the law of attraction with quantum physics (e.g. James Arthur Ray). And yet, we have to remain duly sceptical while also sufficiently open-minded. Neurofeedback may offer self-regulation techniques that are less about bettering the self than about creating try-on realities in which our unimproved self remains primordially unaltered; or it may actually instigate some meaningful changes of therapeutic value. Whether or not these are the only two options to ponder, we must constantly ask what kind of experimental evidence and solid science supports a claim. When it comes to self-help in the form of neurofeedback, insights from the science of placebos—a strange and counterintuitive domain—would be necessary to unlock the nuances of therapeutic outcomes (Thibault *et al.*, 2015).

Scientists must conduct rigorous studies and report their results, even if those end up incongruent with private hopes, prior expectations, or plausible theories. It gives us special pleasure, therefore, to see the non-significant findings of Schabus *et al.* (2017) featured in a flagship journal such as *Brain*. We must follow data, not belief. This sentiment takes on particular importance in the context of psychological research—a realm replete with file-drawer effects, inflated claims, and non-replicable findings (Open Science Collaboration, 2015). Selective reporting and publication bias likely weigh heavily on the field of neurofeedback (Thibault and Raz, in press) while also extending across pharmaceutical domains, the neurosciences, and scientific research as a whole. To identify the prevalence of these questionable practices, researchers could consider applying a 'doping test for science'—a statistical trust-measure such as the R-index—to demonstrate replicability based on reported sample sizes and effects. We worry that such a test may reveal low replicability scores for the available neurofeedback studies.

Even more important than replicability, however, is sound methodology. The present study advances the field of neurofeedback by demonstrating that well-controlled experiments are not only feasible but rather indispensable to elucidate how this contentious intervention promotes adaptive brain activity and desired behaviour.

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