(Note: a preprint by Thibault and Raz replies to this comment on pages 6-9 of this document)

A framework for disentangling the hyperbolic truth of neurofeedback Comment on Thibault & Raz (2017)

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Abstract

In this comment, we propose a theoretical framework for disentangling the potentially multiple elements driving the effects of EEG-neurofeedback (EEG-nf) in order to clarify the roadmap for research in the field. Three questions are identified: (i) Do EEG-nf effects originate from a placebo effect related to the technological environment of a neurofeedback session? (ii) Do EEG-nf effects originate from a "*non-specific effect of cognitive brain training during neurofeedback*"? If so, a cognitive training would be underpinned by the brain activity regulation loop but this training would not be specifically related to the neurophysiological biomarker chosen. (iii) Do EEG-nf effects originate from a "*specific effect of cognitive brain training"*? If so, the effects of EEG-nf would be explained by the training of the specific neurophysiological biomarker chosen, depending on the pathophysiological mechanism(s) of the disorder. The proposed framework might thus allow to understand to what degree each of these level contribute to the effects of EEG-nf on the brain and behaviour in view of the psychosocial variables involved.

Key Words: Neurofeedback; EEG; Placebo; Learning; Training; Psychosocial influences

We read with great interest the article by Thibault and Raz recently published in *American Psychologist* (Thibault & Raz, 2017). Their paper emphasizes the fact that the field of EEG neurofeedback (EEG-nf) suffers from a "truthful hyperbole", a rhetorical tool using both an "oxymoron" and a "euphemism", praised by Donald Trump in *Art of the Deal* (1987) as "an innocent form of exaggeration and a very effective form of promotion". We totally agree that promoters of EEG-nf tend to unscientifically extend the use of this tool. Thus, the authors rightfully raise awareness on the risk of developing a "pseudoscientific" way of thinking in this area and we should encourage them to pursue their warning against non-evidence-based commercial devices (Thibault, Lifshitz, & Raz, 2017b). Nevertheless, in our opinion, asserting that "*EEG neurofeedback works, but it likely relies heavily on placebo phenomena*" is insufficiently scientifically fruitful for such a complex (i.e. characterized by several components interacting in multiple ways with various inter-dependencies) field. Moreover, the dichotomic position of Thibault and Raz, who claim that "*psychosocial factors (e.g., expectation and motivation) rather than neurophysiological parameters may mediate the reported clinical improvement*", greatly minimizes the potential interactions between psychosocial and neurophysiological factors (Thibault & Raz, 2016). To avoid these pitfalls and to clarify the roadmap for research in the area, we propose a theoretical framework for disentangling the potentially multiple elements driving the effects of EEG-nf according to three questions.

(i) Do EEG-nf effects originate from an "*electronic-machine-driven placebo effect*"? If so, the patient's perception of self-efficacy, his/her motivation and the social reinforcement linked with the technological environment of a neurofeedback session would then be the key point to explain the effects of EEG-nf ("*Neurofeedback demands high engagement and immerses patients in a seemingly cutting-edge technological environment over many recurring sessions, [which] may represent a powerful form of placebo intervention*"). We propose that this approach fall under the definition of a "*superplacebo*", defined by Thibault et al. as "*a placebo although neither the prescribing practitioner nor the receiving patient is aware of the absence of evidence to recommend it therapeutically*" (Thibault, Lifshitz, & Raz, 2017a).

(ii) Do EEG-nf effects originate from a "*non-specific effect of cognitive brain training during neurofeedback*"? If so, the changes induced by EEG-nf would be explained by both the "*superplacebo*" effect and the cognitive training underpinned by the brain activity regulation loop. However, this cognitive training would not be specifically related to the

neurophysiological biomarker chosen, falling under the definition of an "*ultimate placebo*" ("*a procedure that provides the patient with an effective means of preventing illness*") (Stroebel & Glueck, 1973). Such a placebo is not only an effective placebo, but also a placebo that would enhance the brain adaptation capacity of the subject. It is supposed that EEG-nf would not have a specific effect on a neurophysiological target, but would encompass unspecific neurophysiological compensatory mechanisms on brain dynamics (Gevensleben, Moll, Rothenberger, & Heinrich, 2014) and oscillation regulation between network flexibility and stability (Ros, B, Lanius, & Vuilleumier, 2014).

(iii) Do EEG-nf effects originate from a "*specific effect of cognitive brain training"*? If so, the effects of neurofeedback would be explained by the "*superplacebo*" and the "*ultimate placebo*" effects but also by the training of the specific neurophysiological biomarker chosen, depending on the pathophysiological mechanism(s) of the disorder (Gevensleben et al., 2014). In this way, the subject would specifically modify an EEG target presumed related to the cause of the disorder (i.e. correlational neurophysiological abnormalities, which however often do not complete the entire criteria for causation), with corresponding clinical improvement. Nevertheless, the evidence for such a relationship between neurophysiological variables and clinical outcomes is weak.

Consequently, we totally agree with Thibault and Raz when they state that EEG-nf needs well designed controlled studies, in line with some of the rigorous studies conducted with fMRI-nf (Thibault, MacPherson, Lifshitz, Roth, & Raz, 2018). We also think that refinement is needed when conceptualizing control groups, especially to understand the role of each of the levels described above. For further understanding of a potential "*superplacebo*" effect, the control group would be characterized by the use of an EEG-nf device with random feedback or feedback from a previous participant, with specific attention to the number of rewards. For the "*ultimate placebo*", it would be an EEG-nf device with feedback from a target different from the target of interest or inverted feedback from the target of interest.

To study a putative specific neurophysiological EEG-nf effect, a very important postulate is that during EEG-nf training, learning is essential to obtain a neuroplastic effect on the brain dynamic. Nevertheless, only a small number of studies investigated this relationship (Zuberer, Drandeis, & Drechsler, 2015). Moreover, as stated by Sitaram et al. (2016) "*much remains to be investigated, including the integration of the vast knowledge of training and learning*

psychology into neurofeedback protocols" (Sitaram et al., 2016). As a result, the neuroscientific challenge in the field of EEG-nf is not only to develop a specific "*EEGcopia*" linking neurophysiological biomarkers and cognitive processes / clinical dimensions with sufficient accuracy and evidence of a causal relationship (in line with the Research Domain Criteria -RDoC- project rather than the Diagnostic and Statistical Manual of Mental Disorders -DSM- classification) (Micoulaud Franchi et al., In Press), but also to better understand and control the learning processes underlying the EEG-nf procedure.

Firstly, it implies defining gold standard metrics to evaluate the training during an EEG-nf session, and the learning across EEG-nf sessions (Zuberer et al., 2015). The typical training metric is how often the neurophysiological target successfully crosses the threshold. Consequently, it depends on the method used to determine the threshold. Learning metrics are computed to quantify evolution throughout the sessions. Currently, however, there is no gold standard for these metrics. This issue is particularly important when attempting to identify specific indicators of neuroplasticity (Ros et al., 2014). Secondly, it implies identifying and evaluating the neurophysiological, cognitive and especially psychosocial variables that impact training and learning during EEG-nf in order to establish a clear framework of the effects of this technique. Interestingly, the growing Brain-Computer Interface field underlines the role of non-specific cognitive and psychosocial variables which are widely involved in placebo effects (e.g. expectation and motivation) but also in the training and learning processes (Jeunet, K'Naoua, & Lotte, 2017). In conclusion, our aim is not to launch a partisan dispute. Here, we propose a framework to better disentangle the effects of EEG-nf on the brain and behaviour and to allow the psychosocial variables involved to be considered, while going beyond a dichotomic vision. We believe that this is the only way to better "*apply this intervention in a manner that is both scientifically judicious and ethically acceptable*" as Thibault and Raz claim. Finally, we think that testing such a framework would offer a rigorous and fertile ground to develop optimized EEG-nf protocols for patients suffering from psychiatric disorders.

Conflicts of interest statement

The authors of the comments have no real or perceived conflicts of interest with any of the authors of the original paper.

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A Consensus Framework for Neurofeedback Research (and the perils of unfounded neuroreductionism) A reply to Micoulaud-Franchi and Fovet

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We were pleased to read the constructive commentary (Micoulaud-Franchi & Fovet, 2018) on our original piece (Thibault & Raz, 2017). In this response, we build on the theoretical framework for studying neurofeedback that the commentators sketch out while pointing out potential caveats to adopting a neuroreductionist approach.

Micoulaud-Franchi and Fovet suggest that researchers should interpret the effects of neurofeedback through three distinct mechanisms: (1) *psychosocial*—including the elements involved in the motivation for and expectation associated with participating in a clinical procedure, interacting with a practitioner, and interfacing with neurotechnology; (2) *cognitive*—including the process of actively engaging in a form of mental or behavioral training, regardless of the type or contingency of the feedback provided; and (3) *neurophysiological*—including the effects of regulating a specific brain signal. In our previous publications, we largely conflated psychosocial and cognitive descriptors into the terms placebo and nonspecific effects, interchangeably.

To increase the usefulness of this proposed framework, we recommend that researchers further discuss the effects of EEG-nf in two distinct categories and test whether these variables correlate: (i) changes to the brain signal trained, including related neurophysiology, and (ii) effects on behavior, mental state, or well-being (see Figure 1). In the EEG-nf literature, however, researchers often conflate these two outcome measures and assume that one implies the other. In other words, they speciously assume that the

"EEGCopia" that Micoulaud-Franchi and Fovet propose to develop, already exists.

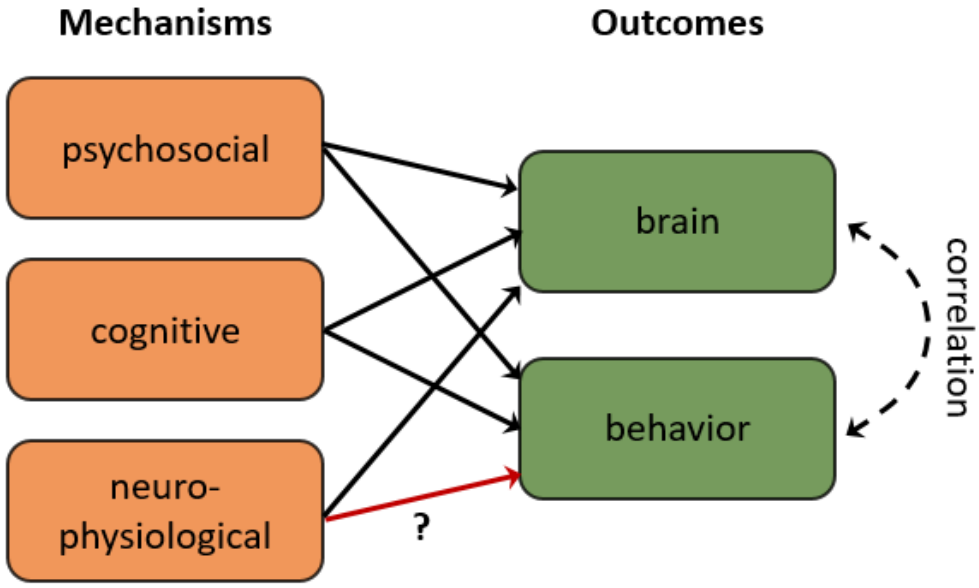

Figure 1. A framework for discussing neurofeedback. The red arrow depicts the fundamental interaction on which the practice of EEG-nf rests, but which remains tenuous (Thibault & Raz, 2017). In terms of altering brain waves, EEG-nf seems to function through psychosocial, cognitive (e.g., Ninaus et al., 2013), and specific neurophysiological mechanisms (e.g., Schabus et al., 2017).

Discussions of this type of EEGCopia harks back to the wishful idea that DNA sequences would eventually explain most medical conditions. Although scientists successfully reduced a few diseases to genes (e.g., sickle cell anemia and Huntington's disease), the etiology of most medical conditions remains largely polygenetic, multifaceted, and difficult to explain in genetic terms alone, let alone by single genes (Ahn, Tewari, Poon, & Phillips, 2006). Similarly, brain imaging is unlikely to single-handedly identify the causal mechanisms responsible for mental disorders (Borsboom, Cramer, & Kalis, 2018). Examining brain activity alone and neglecting to consider non-brain factors misses the critical insight that psychiatric conditions manifest through "significant distress or disability in social, occupational, or other important activities" (American Psychiatric Association, 2013).

Genes play a role in arguably all medical conditions just as brain activity plays a role in mental disorders. Neither of these statements, however, suggests that scientists best describe conditions in the "bottom-up" terms of genetics or neurobiology (Kirmayer & Gold, 2011). Because the neurofeedback literature

suggests that *psychosocial* and *cognitive* mechanisms, rather than specific *neurophysiological* targets, seem to drive *behavioral* change (italicized in reference to the framework proposed above), in our research we tend to discuss the mechanisms behind the *behavioral* benefits of neurofeedback as classifiable "top-down" psychological phenomena (e.g., motivation, expectation, implicit learning, effortful training, and time spent with practitioner). A mind-body dualist can speak of biology and psychology as independent processes; a cognitive neuroscientist cannot. Thus, we distinguish between bottom-up and top-down processes to discern quantifiable variables, facilitate discussion, and identify mechanisms of action in the hopes of fostering a better scientific understanding of neurofeedback and a more informed way of practicing it (Raz, 2011)—not to propose a dichotomy between the brain and psychological sciences.

One of us (RTT) recently met with Micoulaud-Franchi and Fovet and found a large overlap in terms of how we (RTT and AR) and they interpret the literature surrounding the application of EEG-nf as well as how researchers can best advance the field. Amidst this consensus, we mainly diverge on one non-empirical issue: whereas they maintain a steadfast optimism that an EEGCopia will soon emerge, we remain skeptical that science will soon find causal and engineerable EEG biomarkers for most mental disorders. Whether resolutely hopeful or principally proceeding by inquiry, the EEG-nf community would do well to hope for the best and prepare for the worst.

Footnote

We shared a draft of this reply with Micoulaud-Franchi and Fovet. They confirmed that the opinions ascribed to them herein accurately depict their viewpoints.

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