Journal of Psychiatric Research 137 (2021) 452–453

Contents lists available at ScienceDirect

Journal of Psychiatric Research

journal homepage: www.elsevier.com/locate/jpsychires

Letter to the editor: How some brain stimulation studies fail to evaluate blinding adequately

ARTICLE INFO

Keywords
Intervention
Brain stimulation
Blinding
Sham
tDCS
NIBS

Adequate blinding is a crucial aspect of study design that underlies the validity of experimental results across a wide range of scientific disciplines (e.g., medicine, psychiatry, psychology, education). This concept refers to the practice of withholding information that, by leading to the emergence of specific expectations regarding the effect of the applied intervention, could undesirably influence participants' responses (Day and Altman, 2000). Unblinding, on the contrary, arises when participants become aware of the experimental treatment they received. This, in turn, makes it more likely that expectations about the effect of the treatment and demand characteristics about the aim of the study might influence individuals' performance (Schulz and Grimes, 2002).

Unblinding is problematic for the following two reasons. Firstly, non-blinded studies may overestimate or underestimate experimental effects. Secondly, if not reported, blinding failure may undermine results' reproducibility. Thus, it is of pivotal importance for researchers to carefully examine blinding effectiveness by implementing appropriate methodological approaches and statistical analyses.

In this commentary, we highlight a mistake in the assessment of blinding that occurs in a recent publication (Schecklmann et al., 2021). In a sham-controlled randomised clinical trial, Schecklmann et al., 2021 investigated the effect of high-frequency transcranial random noise stimulation (hf-tRNS) on depression. The authors used hf-tRNS over the left and right dorsolateral prefrontal cortices, a protocol that yields cognitive benefits mostly in healthy volunteers (Frank et al., 2018; Snowball et al., 2013).

However, the results did not show a benefit of active vs sham hf-tRNS in patients with depression. Regarding blinding, the experimental findings report: "*in the group of patients, 39%* (2 sham*, 8 real treatment) subjects rated the treatment correctly*" (p. 119). Following, the discussion section highlights: "*blinding was conducted successfully*" (p. 120). Of note, this conclusion is not supported by inferential statistics. Moreover, the employed approach to assess blinding efficacy is inadequate. The latter issue is not uncommon in the non-invasive brain stimulation (NIBS) literature (e.g., Blumberger et al., 2016; Filmer et al., 2019). Hence, we here expand upon it more in detail.

The correct guess rate: a misinterpreted percentage

The first critical step in providing adequate blinding assessment involves identifying which data to analyse and compare. Schecklmann et al., 2021 focus on the *correct guess rate*, a procedure that indicates the percentage of participants that successfully guessed their experimental group and can lead to fallacious reasoning regarding blinding effectiveness (Fassi and Cohen Kadosh, 2020).

Consider the following scenario. In a NIBS experiment, the *correct guess rate* is 75% for both the sham and active condition. Does this imply that blinding was successful? Not necessarily. A 75% *correct guess rate* indicates that 25% of people in the sham condition thought they had received active stimulation and made an incorrect guess. This percentage is substantially lower than the number of people in the active stimulation condition that thought they had received active stimulation (75%). Hence, by correctly guessing their condition, the majority of the participants in the sham group realised they did not receive active NIBS. For this reason, the blinding of the sham condition may have been compromised.

Researchers are likely to reach justified conclusions regarding blinding effectiveness only when the *correct guess rate* is ~50%, indicating that all group equally thought to be receiving the active treatment. With an increase or a decrease from 50%, the similarity between the correct guess rates across the active and control condition does not necessarily indicate successful blinding.

Based on the above consideration, instead of the *correct guess rate*, we advise researchers to report the *active stimulation guess rate,* which indicates the percentage of participants who guessed they received the active treatment. If this percentage is similar across experimental groups, it is likely the participants in the active and control condition did not significantly differ in their experience of receiving the active intervention and, therefore, were unaware of their experimental group.

Returning to the study by Schecklmann et al., 2021, the authors reported that "*in the group of patients, 39%* (2 sham*, 8 real treatment) subjects rated the treatment correctly*" (p. 119). This sentence should be rephrased using the *active stimulation guess rate* to describe the number of subjects in the sham group and the real treatment group that rated the

https://doi.org/10.1016/j.jpsychires.2021.03.020
Received 11 February 2021; Received in revised form 5 March 2021; Accepted 8 March 2021
Available online 16 March 2021

treatment as active stimulation. Moreover, an inferential statistic should follow such a description.

In summary, we showed how the *correct guess rate* could lead to the wrong conclusions regarding blinding efficacy, and we argue that the *active stimulation guess rate* is a more suitable indicator of blinding success. Incomplete blinding reporting and/or assessment can undermine the validity, reliability, and interpretability of research findings. Without knowing if blinding was effective, it becomes impossible to assess whether beliefs and expectations inflated or masked the observed results. Consequently, experimental findings may lack internal validity, which, in turn, makes them unreliable. Altogether, we encourage present and future studies to properly examine and fully report blinding effectiveness.

Author statement

Roi Cohen Kadosh: Conceptualization; Methodology; Supervision; Writing - review & editing.

Luisa Fassi: Conceptualization; Methodology; Writing - original draft.

Declaration of competing interest

RCK serves on the scientific advisory boards of Neuroelectrics Inc. and Tech InnoSphere Engineering Ltd. RCK filed a UK Patent via the University of Oxford for “method for obtaining personalized parameters for transcranial stimulation, transcranial system, method of applying transcranial stimulation”. LF declare no conflict of interest.

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Luisa Fassi, Roi Cohen Kadosh*

Wellcome Centre for Integrative Neuroimaging, Department of Experimental Psychology, University of Oxford, UK

* Corresponding author.

E-mail addresses: luisafassi@live.com (L. Fassi), roi.cohenkadosh@psy.ox.ac.uk (R. Cohen Kadosh).