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One in four people fail to perceive phosphenes during early visual cortex transcranial magnetic stimulation

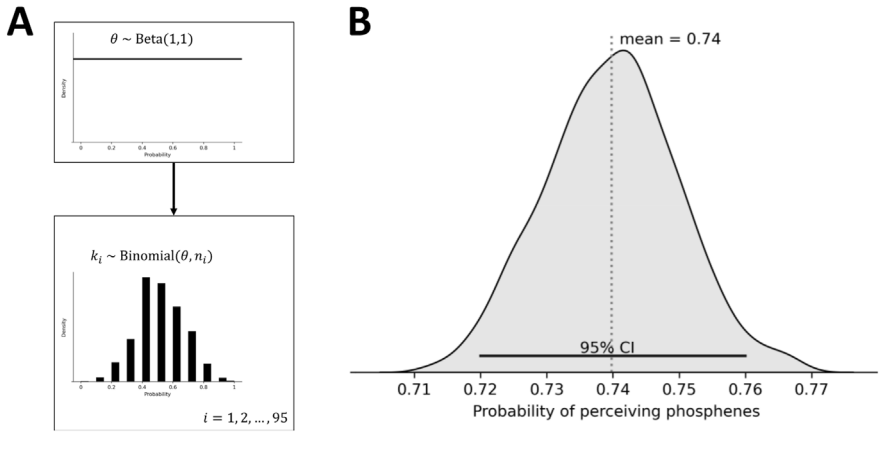
Dear Editor,

Transcranial magnetic stimulation (TMS) on early visual cortex (i.e., areas V1/V2, MT+/V5) can evoke visual percepts, known as phosphenes. Hence, TMS studies often rely on the induction of phosphenes as an early visual cortex localization method or as a brain excitability heuristic. Subsequently, researchers have depended on the induction of phosphenes for both applied and basic research. For example, studies have used phosphene induction to understand brain excitability differences in migraine patients [1], to test new technologies, such as transcranial focused ultrasound [2], and to investigate the neural substrates of visual perception [3] and visual working memory [4].

However, it is not always possible to evoke phosphenes in human subjects using early visual cortex TMS. This is reflected by the exclusion of participants in early visual cortex TMS studies, due to the failure of reporting the experience of any visual percepts. This failure has been attributed to various factors, such as the subjective nature of phosphene reporting, the lack of perceptual practice of participants, and differences in stimulation parameters [5]. Because of these factors leading to the exclusion of participants, TMS studies can often turn out to be underpowered and/or deviate from the initially planned sample size, thus limiting the conclusions reached by those studies.

Previous empirical studies, have provided numerous phosphene prevalence estimations, based on their experimental sample, with estimates of successfully inducing phosphenes ranging anywhere between 25% [6] and 100% [7]. Previous work has often reported that a common phosphene prevalence estimate is approximately 60% [8,9], however, this estimate was based on a single study with only four participants [5]. Yet, to the best of our knowledge there is no systematic estimate to date, that can inform TMS studies that aim to evoke phosphenes, as to the expected rates of successful and failed phosphene induction. Therefore, here, we systematically identified studies that used early visual cortex TMS to evoke phosphenes, with the aim of determining the expected prevalence of successful phosphene induction and, respectively, the anticipated attrition rate.

After systematically searching the literature, we identified 95 studies that have used early visual cortex TMS on healthy human participants, which also provided data regarding the success or failure of phosphene induction. Details regarding the search strategy and the identified studies are provided in the supplementary material. These 95 studies provided data from a total sample size of 1939



(A) The Bayesian model implemented to estimate the probability of perceiving phosphenes, and **(B)** the posterior probability that was computed by the model.

Fig. 1. Bayesian estimation model used to estimate phosphene prevalence from 95 transcranial magnetic stimulation studies.

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participants, out of which 1435 have reported the successful experience of perceiving phosphenes.

To calculate the prevalence of phosphenes (θ) we used Bayesian estimation (Fig. 1A). Specifically, we built a model that was informed by a Beta distribution with its parameters α and β set to 1, such that $\theta \sim \text{Beta}(\alpha = 1, \beta = 1)$. This prior distribution was chosen because it creates a uniform distribution, which means that equal probabilities are assigned to any possible prevalence percentage. Next, we calculated the binomial distribution for participants experiencing phosphenes (k), which was given by the probability θ for the total sample (n) in each study (i), which is expressed as $k_i \sim \text{Binomial}(\theta, n_i)$.

Following the model above, we were able to compute the posterior probability by implementing Markov chain Monte Carlo sampling. The posterior probability provided us with the estimated prevalence of phosphene induction (Fig. 1B). The posterior probability had a mean of 0.74 (95% *Credible Interval* = [0.72, 0.76]). This reveals that approximately 74% of participants can perceive phosphenes and, respectively, a 26% attrition rate should be expected for TMS studies relying on phosphene induction. Put simply, researchers and other stakeholders should expect that one in four participants will fail to report reliable phosphene experiences.

To date, and as far as we are conversant, this is the first systematic attempt to calculate phosphene prevalence. Our findings revealed that one in four (approximately 26%) healthy participants will most likely fail to perceive any phosphenes during early visual cortex TMS. This estimate is smaller compared to previous estimates (up to 40% failure in perceiving phosphenes), which were based on single studies with a small sample (e.g., 4 participants in [5]).

Conclusively, we provide an informative insight, which can guide future TMS research. Having an expected attrition rate is important for numerous reasons, such as allocating and saving resources, planning and organizing studies as well as study proposals, and having adequate statistical power and meaningful results [10]. Based on our findings, we can anticipate approximately one out of four participants to be unable to report phosphenes during early visual cortex TMS.

Declaration of competing interest

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brs.2022.12.012.

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