Multiverse Analysis of the Effect of a Non-Deceptive Placebo on a Neural Measure of Emotional Distress

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Abstract

The effect of a non-deceptive placebo on reducing a neural measure of emotional distress appears sensitive to alternative analytic decisions and has limited practical significance.

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D. A. Guevarra, J.S. Moser, T.D. Wager and E. Cross, *Placebos without deception reduce self-report and neural measures of emotional distress*, Nature Communications **11**, 3785 (2020), doi:10.1038/s41467-020-17654-y

1 Goal

Multiverse analysis was used to assess how a main effect observed by [1] – that a non-deceptive placebo (NDP) treatment reduced sustained late positive potential (LPP) amplitude, which is a neural marker of emotional distress – was influenced by alternative analytic decisions. In [1], this main effect was nested in a seven-way mixed ANOVA. Self-report and physiological effects of NDPs conflict [2, 3]. If effective, NDPs can resolve ethical issues regarding placebo use in clinical practice [4–6] and could provide efficient interventions for managing stress.

2 Methods

In this partially pre-registered (https://osf.io/6d3j9) multiverse, we varied the following to produce 16 unique outcomes:

- **Sample**: [1] pre-registered N = 100 but ultimately sampled N = 218 in two distinct stages. After exclusions, n = 102 (sample 1) and 96 (sample 2) were analysed. We randomly sampled $N = 100$, which achieved sufficient power based on [7]. We also ran the analyses on each sample separately.

- **Age**: [1] sampled participants aged 18-31. We sub-sampled participants between 18-21 years as [8-10] found differences in emotion processing and regulation between adolescence and adulthood.
- **Hemisphere**: We excluded left hemisphere electrodes as [11, 12] observed right hemisphere dominance during passive viewing tasks of emotional stimuli in a task like [1]'s and it is common practice to analyse electrode sites at which the component of interest is largest [13].

These outcomes were evaluated for statistical significance at three alpha levels levels (.05, .005, and .002). ERP (event related potential) studies often involve several multi-factor ANOVAs, with many effects that are not corrected for multiple comparisons [14]. In [1], the seven-way ANOVA gave rise to 127 possible effects, all evaluated for significance at $\alpha = .05$. As [1]'s effect is 'novel', we also used $\alpha = .005$, as recommended by [15]. Finally, based on [1]'s plan to focus on the effects of condition and its interactions, we used the Šidák-Bonferroni method to produce a corrected $\alpha = .002$.

These decisions were nested within a larger multiverse study [16] that also considered several Bayesian analytic alternatives.

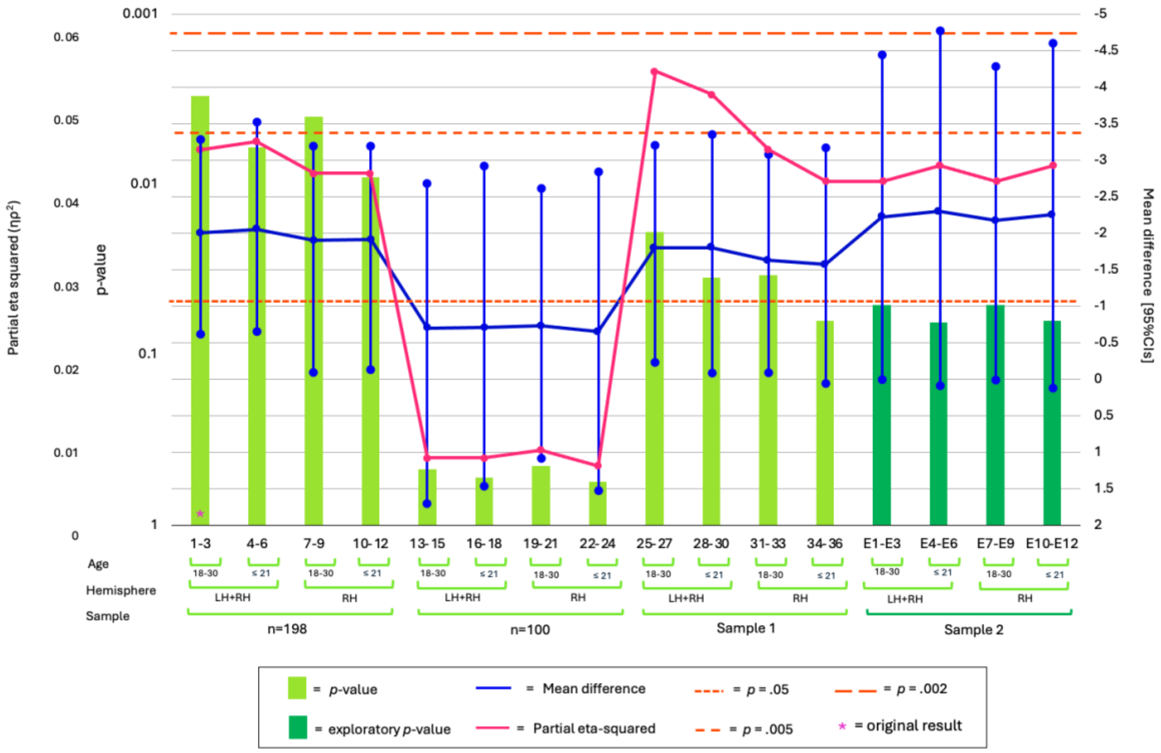

Figure 1. p-values and effect sizes for the main effect of condition (NDP vs. control) on sustained LPP amplitude in 12 pre-registered and 4 exploratory factorial ANOVAs in the multiverse analysis, evaluated for statistical significance at p < .05, .005, and .002. A reversed logarithmic scale is used for the p-values. Error bars represent 95% CIs for the mean differences between the NDP and control conditions. Mean differences < 1µV = low,

> 1.5μV = robust, and > 3μV = very robust, according to [7]. Sample sizes ranged from N = 87 to 198. LH = left hemisphere; RH = Right hemisphere.

3 Results

Of the 16 p-values in Figure 1, seven were statistically significant at $p < .05$, two were significant at $p < .005$ and none were significant at $p < .002$. P-values were smallest, and effect sizes were largest under the original sample. By contrast, p-values were largest, and effect sizes smallest under the randomly selected sample of $N = 100$. The effect appeared robust against the age sub-sample and alternative hemisphere selection alternatives.

Effect sizes (η_p^2) ranged from .004 to .054. The direction of the effects, which ranged from -0.65μV to -2.3μV, remained consistent across the multiverse. Wide CIs with lower-bounds often close to zero were routinely observed, indicating uncertainty regarding the true population effect size.

4 Conclusion

Although the NDP effect appears relatively robust to age sub-sampling and electrode selection, using alternative samples and multiple comparison corrections had a substantial impact on its statistical significance. Moreover, the practical significance of the effect is likely quite small. Although an NDP effect probably exists, its clinical utility appears limited.

Acknowledgments and Disclosures

Reproducibility The original effect was successfully reproduced using SPSS syntax accompanying [1]. It is located at https://osf.io/s3b8d/ (see Experiment 2 Data Files).

Code and Data Availability SPSS syntax for reproducing this multiverse analysis is available at https://osf.io/vxuhc/. The original data are available at https://osf.io/s3b8d/ (see Experiment 2 Data Files).

Author Contributions **H.E.F.**: Conceptualisation, Data curation, Formal analysis, Investigation, Methodology, Visualisation, Writing - original draft, and Writing – review & editing. **P.J.A.**: Conceptualisation, Supervision, and Writing - review & editing.

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