Our unrestricted connectivity analysis revealed patterns that were largely in line with what we hypothesized from the visual neuroscience literature. First, significant increases in functional connectivity were observed in brain regions such as the supramarginal gyrus, angular gyrus, and lateral occipital cortex, areas implicated in the categorization of visual information and other higher order visual processes (cannon et al 2007). Similarly, increases in functional connectivity were observed in areas like the precuneous cortex, intracalcarine cortex , brain regions associated with consciousness and visio-spatial imagery (al-ramadhani et al 2021, Nakamura et al 2020) as well as in the cingulate cortex, an area implicated in emotion regulation (stevens et al 2011).

Additionally, we observed that these increases in functional connectivity were significantly correlated to decreases in amygdala reactivity during a fear task as reported in Cushing et al (2023), such that the greater the increase in functional connectivity pre- to post-treatment, the greater the decrease in amygdala reactivity pre- to post-treatment.

In the context of a neuro-reinforcement trial, these results are unsurprising considering the reinforcement of the Ventral Temporal Cortex as a target. The repeated rewarding of VTC activation could possibly influence downstream processes, strengthening the connectivity of those areas in the network that we observed. Furthermore, increases in functional connectivity in areas of the brain such as the cingulate cortex provide a potential bridge between VTC reinforcement and amygdala decreases by modulating one’s ability to regulate emotions on a neural level.

Our primary strength in this analysis lies with the sample of participants with clinically diagnosed animal phobias. Even as previous trials (taschereau dumochel, cortese, 2018) have observed reductions in amygdala reactivity from neuro-reinforcement, finding evidence of intermediate changes in a phobic sample further validates the possibility of neuro-reinforcement as an intervention for those struggling most severely from animal phobias and other fear disorders.

The data-driven model-free approach taken in this analysis represents another strength, as despite our power issues, we were still able to observe significant results at a whole brain level. Demonstrating changes in functional connectivity in regions so closely related to the target of the neuro-reinforcement protocol in the absence of a predetermined model further emphasizes the validity of our spontaneous findings.

However, the study is not without limitations. First, our sample was underpowered due to recruitment issues stemming from the COVID-19 pandemic, as well as other technical issues that led to much of the data being excluded. Secondly, the study lacked a control group to compare these changes against. Lastly, these functional connectivity changes are unspecific about the meaning of the observed changes and does not take into account the use of a target vs control animal in the design, leading to alternative explanations for these effects that are unable to be rejected due to the inherent design of the experiment.

Future studies should seek to firstly replicate these analyses with a larger clinical sample. Secondly, these results provide a foundational set of regions of interest for future studies to further investigate in a more focused manner.

These findings from the first randomized clinical trial of multivoxel neuro-feedback for animal phobia also represent the first steps in elucidating mechanisms of change for the black box that is currently neuro-feedback. With further research building atop these results and a greater understanding of its mechanisms, this novel treatment may open up fruitful new approaches to treating phobia and anxiety disorders.