Biological Psychology 152 (2020) 107865

Contents lists available at ScienceDirect

Biological Psychology

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

"Does attention bias modification induce structural brain changes? A commentary on Abend et al. (2019)" – Response

Rany Abend[a,*], Ariel Rosenfelder[b], Dana Shamai[b,d], Daniel S. Pine[a], Ido Tavor[d,e], Yaniv Assaf[c,d], Yair Bar-Haim[b,d]

[a] Section on Development and Affective Neuroscience, National Institute of Mental Health, 9000 Rockville Pike, Bethesda, MD, USA
[b] School of Psychological Sciences, Tel Aviv University, P.O. Box 39040, Tel Aviv, 69978, Israel
[c] Department of Neurobiology, George S. Wise Faculty of Life Sciences, Tel Aviv University, P.O. Box 39040, Tel Aviv, 69978, Israel
[d] Sagol School of Neuroscience, Tel Aviv University, P.O. Box 39040, Tel Aviv, 69978, Israel
[e] Department of Anatomy and Anthropology, Sackler Faculty of Medicine, Tel Aviv University, P.O. Box 39040, Tel Aviv, 69978, Israel

In a commentary to our paper recently published in this journal (Abend et al., 2019), Dr. Parsons questions whether five sessions of attentional bias modification (ABM) training can indeed induce changes in brain structure. We welcome this critique and offer responses to the 5 points it raised.

1. Attention bias modification (ABM) reduces anxiety via attention training tasks

Parsons argues that we "…portray an optimistic representation of the ABM literature" (p. 3). We agree with Parsons that the evidence concerning the clinical efficacy of ABM is not unequivocal. However, we could find no claims regarding ABM efficacy in our paper, nor could we find evidence of selective citation. In fact, our paper focused on ABM training effects on brain structure rather than clinical efficacy, and we discuss the literature on mechanistic studies of ABM that is most relevant to this focus. Importantly, our reference to the meta-analysis by Hakamata et al. (2010) in this context was to support our statement that linked the number of ABM training sessions to changes in symptoms. We did not cite it to support a general claim that ABM has "robust clinical effects" as stated in Parsons' comment.

2. We mapped ABM-induced (vs control) short- and longer-term structural changes

Parsons suggests that the presence of low statistical power due to limited sample size makes it likely that our reported findings are false positives. We agree that the sample size is small, as we discuss in our paper, and that small sample sizes could create risks for Type I errors. Our study was not designed to provide definitive evidence but rather to lay the groundwork for more powerful, and perhaps more focused, tests of our preliminary conclusions. Our study, like other early-phase research, fulfills a valuable niche in science, particularly in expensive science, where preliminary data provide clues for larger, more definitive future efforts. We apologize for readers who read our paper as suggesting that our findings be viewed as providing definitive or even particularly strong support for the hypothesis that ABM causes changes in brain structure. We also leave it to readers to decide whether new efforts, with larger potentially clinically-affected populations, are warranted.

3. ABM led to specific longer-term structural changes in inferior temporal cortex

We thank Parsons for identifying the mismatch between the reported F statistic and p-value for the interaction effect in our results. We repeated this analysis, and, indeed, identified a typographical error in reporting the F statistic; thus, instead of $F(2,54) = 12.76$, it should be $F(2,54) = 14.33$, matching the reported p-value of .0001. The results of the study are therefore as originally reported, with the only change being the value of the F statistic for this interaction effect. We apologize for the typographical error and appreciate the opportunity to correct it. As noted in the text, this effect survives a whole-brain FDR correction. Of note, the FDR correction is not just a function of the pre-determined number of possible comparisons (as in the Bonferroni correction), but rather also accounts for the number of tests that are found significant in the specific analysis (Genovese, Lazar, & Nichols, 2002). This number changes for each analysis and dataset, naturally, and is not typically reported by statistical programs. Nevertheless, the reported cluster survives this correction performed on the entire voxel space.

Next, we address Parsons' inquiry regarding the direction of change in absolute FA values in the inferior temporal cortex. Indeed, as Parson identified, the ABM group showed mean FA values of 0.136 and 0.128 during Scan 1 and Scan 3, respectively, whereas the control group

* Corresponding author at: Section on Development and Affective Neuroscience, National Institute of Mental Health, 9000 Rockville Pike, Bldg. 15K, Bethesda, MD 20892, USA.
E-mail address: rany.abend@nih.gov (R. Abend).

https://doi.org/10.1016/j.biopsycho.2020.107865

Available online 11 February 2020
0301-0511/ Published by Elsevier B.V.

showed mean values of 0.125 and 0.127, respectively (Table 2 in the original article). Parsons posits that this change could reflect regression to the mean, rather than a true effect of training, in the active arm. With this possibility, the higher value in the ABM group in Scan 1 would reflect a chance finding, which is no longer present at Scan 3 due to regression to the mean, unrelated to ABM. While this explanation is plausible, it is important to remember that FA was also assessed in Scan 2, where the ABM group exhibited a mean value of 0.136, the same value as measured in Scan 1. Thus, we view it as more plausible to consider the change from Scans 1 and 2 to Scan 3 as arising from an effect of ABM than to view the pattern as reflecting an effect of identical chance sampling at both Scans 1 and 2, with regression to the mean following the two scans. Of course, reasonable people can disagree.

Finally, Parsons notes that "…no evidence is provided that other areas did not change - i.e. absence of evidence is not evidence of absence" (p. 6). We fully agree with this statement but are unaware of appropriate analytic methods for differentiating absence of evidence from evidence of absence. Such methods would prove useful, as this problem plagues many scientific experiments. As Parsons notes, "A well-powered, pre-registered, replication with the aim of testing region specific brain changes is needed" (p. 6); indeed, one motivation for our study was to provide support and preliminary evidence for implementing such a better-powered, pre-registered study.

4. Temporal changes in prefrontal, occipital cortices were noted across groups

Parsons inquires whether it is plausible to conclude that structural brain changes would occur in the course of a single testing session (pp. 6–7). We refer him to prior DTI work in humans and rodents that demonstrates structural changes after one training session, some already referenced in the text (e.g., Brodt et al., 2018; Hofstetter, Tavor, Tzur Moryosef, & Assaf, 2013; Sagi et al., 2012; Tavor, Botvinik-Nezer, Bernstein-Eliav, Tsarfaty, & Assaf, 2020; Tavor, Hofstetter, & Assaf, 2013).

Parsons further notes that inferences from a correlation analysis that we report, $r = -0.53$, $p = 0.003$, may not be stable due to the small sample size, urging for samples that include hundreds of subjects to achieve adequate precision. Indeed, as noted before, we fully agree with the ideal goal of conducting MRI studies on hundreds of subjects in order to generate more confidence in results. Unfortunately, such studies are not easy to perform. Our study, for example, despite its modest sample size, included over 90 MRI scans. We would refer readers to our original report, where we acknowledge the sample size as a primary limitation and call for cross-site collaborations to generate larger sample sizes (p. 6). We hope that preliminary, early-phase studies such as ours can continue to guide future endeavors, and we appreciate the opportunity to re-emphasize the appropriate manner in which to view results from such studies.

5. ABM training induces structural changes; these may relate to clinical effects

Again, we apologize for any unintended suggestions in our text that our findings be viewed as definitive. Moreover, it is important to note that we did not study subjects with clinical problems. Therefore, our study provided no new information on clinical effects but rather evaluated the possible effects of ABM on brain structure. Again, readers can decide how such possible effects in healthy subjects relate to studies evaluating aspects of ABM in patients with clinical problems.

In summary, we thank Dr. Parsons for taking the time to comment on our work, for the opportunity to correct a typographical error, and for the chance to address the questions raised. We agree with Dr. Parsons that our study does not support definitive conclusions regarding the effects of ABM on brain structure. However, we do view the data as providing meaningful support for more research on the topic, ideally using larger samples in pre-registered reports. Finally, we agree with many of Dr. Parson's other remarks on ABM research. Anxiety and related disorders are severe and debilitating, and current first-line treatments leave many patients insufficiently improved. As such, alternative treatments are of great importance. We encourage others to pursue research that addresses this need in the best way possible, towards the common goal of reducing patient suffering.

References

Abend, R., Rosenfelder, A., Shamai, D., Pine, D. S., Tavor, I., Assaf, Y., et al. (2019). Brain structure changes induced by attention Bias modification training. *Biological Psychology,* 146.

Brodt, S., Gais, S., Beck, J., Erb, M., Scheffler, K., & Schonauer, M. (2018). Fast track to the neocortex: A memory engram in the posterior parietal cortex. *Science, 362,* 1045-+..

Genovese, C. R., Lazar, N. A., & Nichols, T. (2002). Thresholding of statistical maps in functional neuroimaging using the false discovery rate. *Neuroimage, 15*, 870–878.

Hakamata, Y., Lissek, S., Bar-Haim, Y., Britton, J. C., Fox, N. A., Leibenluft, E., et al. (2010). Attention bias modification treatment: A meta-analysis toward the establishment of novel treatment for anxiety. *Biological Psychiatry, 68*, 982–990.

Hofstetter, S., Tavor, I., Tzur Moryosef, S., & Assaf, Y. (2013). Short-term learning induces white matter plasticity in the fornix. *Journal of Neuroscience, 33*, 12844–12850.

Sagi, Y., Tavor, I., Hofstetter, S., Tzur-Moryosef, S., Blumenfeld-Katzir, T., & Assaf, Y. (2012). Learning in the fast lane: New insights into neuroplasticity. *Neuron, 73*, 1195–1203.

Tavor, I., Botvinik-Nezer, R., Bernstein-Eliav, M., Tsarfaty, G., & Assaf, Y. (2020). Short-term plasticity following motor sequence learning revealed by diffusion magnetic resonance imaging. *Human Brain Mapping, 41*, 442–452.

Tavor, I., Hofstetter, S., & Assaf, Y. (2013). Micro-structural assessment of short term plasticity dynamics. *Neuroimage, 81*, 1–7.