Response to Moreira et al. Journal Club
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In their Journal Club review of our recent article, Moreira et al., cogently summarize our principal findings and make interesting observations linking our large-scale meta-analysis with other recent studies. Here we respond to and clarify two general points raised by Moreira et al.

First, Moreira et al. suggest that the 9-cluster parcellation of medial frontal cortex (MFC) we report may underestimate the number of distinguishable parcels present in MFC– as illustrated by a recent multi-modal parcellation of cerebral cortex (Glasser et al., 2016). We agree with this point, but reiterate that the choice to use nine clusters primarily reflected a pragmatic desire to generate a relatively interpretable meta-analytic functional parcellation. There should be no doubt that other criteria (e.g., based on cytoarchitechtonic or anatomical divisions) could produce higher-resolution parcellations. Indeed, given that association cortex demonstrably contains numerous overlapping neuronal populations with distinct functional profiles (Kvitsiani et al., 2016; Tye and Deisseroth, 2012), it follows that *any* discrete parcellation of voxels into mutually exclusive clusters will necessarily underestimate the complexity of the brain's functional organization. Thus, while we agree with Moreira's suggestion that our 9-clustering solution is relatively coarse, and that large-scale multi-modal parcellations may provide more generalizable clustering solutions, we disagree with the implication that there is a single optimal domain-general MFC parcellation. As such, we provide a set of open source tools (https://github.com/adelavega/neurosynth-mfc) to generate parcellations of MFC– or any other brain region– at any granularity desired.

Second, although Moreira et al. highlight the strength of large-scale meta-analysis for overcoming the so-called 'reverse inference' problem, we disagree with their characterization of our classification based approach as 'forward inference'. For each region, we generated functional association profiles by calculating the log odds ratio of the probability of a given topic in studies that *activated* the region to the probability of the same topic in studies that *did not* activate the region. Critically, although these profiles reveal preferential associations between topics and regions– an informative measure that could not be obtained in smaller meta-analyses that only consider studies that activate a region– this approach does not constitute formal probabilistic inference. Although we agree that performing proper 'reverse inference' (i.e. determining the probability a psychological state given a pattern of brain activity) is a desirable goal, this problem is notoriously difficult to resolve because the prior probabilities of arbitrary psychological states are unknown (see: Wager et al., 2016; Yarkoni, 2015). Thus, although we agree with Moreira et al's suggestion that meta-analytically predicting mental states from brain activity is an important future direction, this goal cannot be accomplished simply by inverting the direction of the prediction, and requires stronger assumptions about base rates than we are currently willing to countenance.

References

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