LETTER TO THE EDITOR

Reply: No grey matter alterations in longitudinal data of migraine patients

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We thank Mehnert and colleagues (2020) for their interest in our article (Burke et al., 2020). The authors report that they found no longitudinal grey matter changes in a sample of seven migraine patients over a 30-day period. Combined with a previous letter by Sheng et al. (2020), they conclude that ‘there is no robust evidence that migraine patients have structural brain changes’ and prior reports of such changes may be ‘epiphenomena’. Because we used coordinates of structural brain changes as input into our network mapping analysis, they suggest that our network findings may reflect ‘false-positives.’

We agree that it remains unclear whether structural brain changes exist in migraine, under what conditions, and whether such changes are a cause, consequence, or epiphenomenon. As noted by both Mehnert et al. (2020) and Sheng et al. (2020), some studies have reported structural differences in migraine while others have not. Depending on the meta-analysis, there may be no consistent findings across studies (Sheng et al., 2020) or consistency that implicates a variety of different brain regions (Jia and Yu, 2017). This heterogeneity in neuroimaging findings is not unique to migraine, but an issue for neuroimaging studies in general (Darby et al., 2018b).

The goal of our study was to test whether network mapping could help make sense of this heterogeneity, not to determine whether structural neuroimaging abnormalities ‘exist’ in migraine. As such, we used the most recently published meta-analysis of structural changes in migraine (Jia and Yu, 2017). Because this meta-analysis reported coordinates of structural changes, we used those coordinates as input into our network analysis. If no consistent changes had been reported (as in the meta-analysis by Sheng et al., 2020), we would have performed network-mapping at the individual study level (Darby et al., 2018a, b; Weil et al., 2019). If no consistent changes had been reported in any of the individual studies (as in the study by Mehnert et al., 2020) we could have performed network mapping at the individual subject level, using single-subject patterns of brain atrophy (Tetreault et al., 2020). However, it is worth noting that the 30-day time interval used in Mehnert et al. may not be sufficient to detect longitudinal changes in grey matter volume, even at the single-subject level (Obermann et al., 2009; Rodriguez-Raecke et al., 2009; May, 2011).

We disagree with the suggestion of Mehnert et al. that the network mapping results in Burke et al. represent...
‘false-positives’. Rather, we accurately show that the hetero-
genous neuroimaging coordinates reported by Jia and Yu (2017) map to a common brain network. We welcome fu-
ture work applying this network mapping approach to heterogenous findings across individual neuroimaging stud-
ies in migraine (Darby et al., 2018a, b; Weil et al., 2019), or heterogeneous findings across individual migraine patients (Tetreault et al., 2020). These different network mapping
approaches appear to converge on a common brain network in Alzheimer’s disease (Darby et al., 2018b; Ferguson et al., 2019; Tetreault et al., 2020), and it would be interesting to see if they converge on a common network in
migraine.

Finally, Mehnert et al. suggest using coordinates from functional neuroimaging studies rather than structural neu-
roimaging studies as inputs for network mapping of mi-
graine. This is a reasonable suggestion but is likely to be
more complicated than network mapping of structural
differences given the wide methodological heterogeneity of
functional neuroimaging studies of migraine. This includes
variability in data collection (e.g. different modalities, scan-
ing sites, tasks, timing during the migraine cycle, proca-
avtive stimuli for inducing migraine etc.), and analysis
techniques (e.g. different preprocessing protocols, region of
interest analyses etc.). Such issues have impeded the ability
to conduct appropriate functional neuroimaging meta-anal-
yses of migraine, and accordingly systematic reviews of this
literature have largely been qualitative (Schwedt et al., 2015).
Nevertheless, network mapping could be an ideal
technique for linking heterogenous functional neuroimaging
findings in migraine to a common brain network, and we
encourage such efforts.

Data availability

Data sharing is not applicable to this article as no new data
were created or analysed in this study.

Competing interests

M.J.B. has nothing to disclose. M.D.F. has intellectual prop-
erty on using connectivity imaging to guide brain stimulation
but receives no royalties.

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