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Increased resting state network connectivity in synaesthesia: Evidence for a neural basis of synaesthetic consistency

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Review of:

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Studying individual differences in conscious awareness can potentially lend fundamental insights into the neural bases of binding mechanisms and consciousness (Cohen Kadosh and Henik, 2007). Partly for this reason, considerable attention has been devoted to the neural mechanisms underlying grapheme-color synaesthesia, a healthy condition involving atypical brain activation and the concurrent experience of color photisms in response to letters, numbers and words. For instance, the letter C printed in black on a white background may elicit a yellow color photism that is perceived to be spatially colocalized with the inducing stimulus or internally in the “mind’s eye”, as for instance, a visual image. Synaesthetic experiences are involuntary, idiosyncratic, and consistent over time (Rouw et al., 2011). To date, neuroimaging research on synaesthesia has focused on brain areas activated during the experience of synaesthesia and associated structural brain differences. However, activity patterns of the synaesthetic brain at rest remain largely unexplored. Moreover, the neural correlates of synaesthetic consistency, the hallmark characteristic of synaesthesia, remain elusive.

Functional imaging studies suggest that grapheme-colour synaesthesia is associated with activation of brain regions specific to relevant visual processes and binding processes (i.e., occipito-temporal, parietal, and frontal brain regions; for a review see Rouw et al., 2011). A popular view is that grapheme-color synaesthesia arises in the fusiform gyrus, more specifically from cross-activation between the visual word form area and the colour area V4 (for an overview see Hubbard et al., 2011). A recent study refined this view and showed that V4 is activated via functional pathways from the superior parietal lobe for synaesthetes who experience colours photisms in the “mind’s eye” but from the letter shape area in the fusiform gyrus for those who experience photisms as spatially colocalized with the inducing stimulus (van Leeuwen et al., 2011).

Structural imaging studies complement the functional studies and suggest morphometric differences in similar brain regions: synaesthetes exhibit increased grey and white matter density in the fusiform gyrus (including V4), and parietal and primary visual cortices (see Rouw et al., 2011). However, on the basis of functional and structural imaging results, Hupé and colleagues (2012) have questioned the role of regional activations and structural changes in the experience of synaesthesia and proposed that synaesthesia may arise from subtle and distributed neural coding. This is in line with the recent finding that synaesthesia is associated with marked differences in global structural brain networks (Hänggi et al., 2011).

In a recent article published in *The Journal of Neuroscience*, Dovern and colleagues (2012) investigated intrinsic (resting) network connectivity, and its relationship to color consistency, in grapheme-color synaesthesia. Using resting-state functional magnetic resonance imaging (rs-fMRI), they sought to identify network differences that would discriminate demographically matched groups of synaesthetes and controls. Synaesthetes exhibited strong consistency when retested on color associations for more than 120 items after a six-month period. The rs-fMRI data were analysed using independent component analysis (ICA). To identify relevant network connections at rest (i.e., intrinsic connectivity networks [ICNs]), independent components were regressed against brain templates containing synaesthesia-specific regions of interest consisting of visual cortex, auditory cortex, and intraparietal cortex. Validation of the ICNs was obtained when ICAs were run separately in each group. Spatial brain maps obtained from the combined group ICA were then used to analyse group differences within ICNs. Finally, the authors calculated correlations between the time course of BOLD signal changes of synaesthesia-relevant ICNs in order to measure functional network connectivity (FNC).

Dovern and colleagues (2012) identified seven synaesthesia-relevant ICNs: medial visual, lateral visual, auditory, left fronto-parietal, right fronto-parietal, lateral parietal, and medial parietal networks. Synaesthetes exhibited greater intranetwork connectivity than controls for regions in each network, whereas controls displayed greater connectivity only in regions of the left and right frontoparietal networks. Relative to controls, synaesthetes also exhibited three-fold more significant connections between the seven ICNs (including all connections found in non-synaesthetes). Moreover, the connections between the medial and lateral visual networks with the right frontoparietal network were stronger in grapheme-color synaesthetes than in controls. Crucially, color consistency in synaesthetes was correlated with connectivity between the lateral visual ICN and both the auditory and right frontoparietal ICNs.

Dovern and colleagues' (2012) results are broadly consistent with previous neuroimaging research on the functional and structural correlates of synaesthesia as outlined above (Hubbard et al., 2011; Rouw et al., 2011; van Leeuwen et al., 2011), as well as with the speculation that synaesthesia is more aptly regarded as arising from distributed neural coding rather than regional differences (Hänggi et al., 2011; Hupé et al., 2012). Furthermore, their results suggest that functional connectivity at rest may underlie the stability of synaesthetic experiences, just as effective connectivity between the letter shape area and V4 in the fusiform gyrus and superior parietal lobe relates to individual differences in the experience of color photisms among synaesthetes (van Leeuwen et al., 2011). However, it should be noted that insofar as resting cognitive and perceptual states (e.g., visual imagery) were not sampled, group differences in task-independent thoughts (e.g., synaesthetic experiences due to lexical imagery) might account for some of the observed effects.

Perhaps the most significant result of Dovern and colleagues' (2012) study was that consistency of synaesthetic associations was related to FNC between the lateral visual network and the right frontoparietal network. This result points to the role of the right frontoparietal network in binding color to phonemes and graphemes (see also van Leeuwen et al., 2011). In the general non-synaesthetic population, frontoparietal connectivity has been hypothesised to be crucial for conscious processing in terms of a global platform for the integration of representations distributed across multiple brain regions (Naghavi and Nyberg, 2005). This is consistent with the idea that synaesthesia is a strong and conscious form of binding that also exists in non-synaesthetes (e.g., letter- and music-color associations), but not to a sufficient degree to breach conscious awareness nor to achieve the level of consistency observed in synaesthetes (see Cohen Kadosh and Henik, 2007). Therefore, consistency may function as an indicator of the level of conscious synaesthetic associations. In contrast, the finding that consistency of synaesthetic associations covaried with connectivity in regions critical to the modality of inducing stimuli (auditory network and lateral visual network) and the modality of synaesthetic concurrent experiences (lateral visual network) may simply reflect the fact that spoken stimuli (auditory network) elicit consistent color experiences (visual network). Hence, repeated, consistent synaesthetic experiences may drive the strength of this connection over time.

A broad implication of Dovern and colleagues' (2012) results is that, in comparison to non-synaesthetes, synaesthetes exhibit marked differences in connectivity when they are not experiencing synaesthesia. These effects may underlie or contribute to enhanced abilities among synaesthetes that are independent of the synaesthetic experience, including visual processing (Barnett et al., 2008) and memory performance (Rothen et al., 2012). More precisely, Dovern and colleagues (2012) reported greater intrinsic network connectivity between medial and lateral visual networks, including fusiform and calcarine gyri, and right frontoparietal network in grapheme-color synaesthetes relative to non-synaesthetes. This is in line with more general differences between synaesthetes and non-synaesthetes related to responsiveness in the parvocellular system (Barnett et al., 2008). Thus, the findings of Dovern and colleagues (2012) support the idea that memory benefits in grapheme-color synaesthesia arise from increased efficiency of visual processing that is specific to the parvocellular pathway (Rothen et al., 2012 and are compatible with contemporary theories of a perception-memory continuum (i.e., emergent memory account, Graham et al., 2010). Crucially, Dovern and colleagues (2012) did not report differences between synaesthetes and non-synaesthetes on an anatomical level or as a functional consequence of task performance but in spontaneously active networks at rest, thereby highlighting the potential of synaesthesia, as a perceptual condition, to affect higher cognitive functions such as memory in interaction with various tasks.

An important question related to abilities in synaesthesia that are independent of the synaesthetic experience itself is whether brain differences among synaesthetes extend beyond the synaesthetic phenotype to influence other cognitive and perceptual functions. The Dovern et al. (2012) study, as well as that by Hänggi and colleagues (2011), suggests broader differences in functional and structural network connectivity. Thus it remains unclear whether these connectivity differences support synaesthesia, in terms of excessive connectivity at an earlier developmental stage, or support other cognitive or perceptual functions, of which synaesthesia is a byproduct. Dovern and colleagues (2012) acknowledge the difficulty of discriminating between network connectivity as a causal antecedent of synaesthesia or a direct consequence of synaesthesia. It is equally plausible that increased structural and functional connectivity produces the experience of synaesthesia and that the repeated experience of grapheme-color binding will over time elicit these changes. As Dovern and colleagues (2012) suggest, a rigorous way of discriminating between these proposals will be longitudinal studies in children. Alternatively, synaesthesia could be induced in non-synaesthetes through suggestion (Cohen Kadosh et al., 2009), which has effectively replicated not only the behavioural markers of synaesthesia, but also associated phenomenological reports. Such studies may be necessary to elucidate the causal relationship between synaesthetic experience and network connectivity. More broadly, they are also likely to have important implications for our understanding of the functional and structural networks that enable visual consciousness.

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