

ABNORMAL NEUROVASCULAR COUPLING IN THE PRECUNEUS–POSTERIOR CINGULATE CORTEX MAY BRIDGE SIMPLE AND COMPLEX AURA PHENOMENA IN THE MIGRAINE BRAIN: AN ARTERIAL SPIN LABELLING INVESTIGATION

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Background. Migraine aura is a heterogeneous phenomenon in which visual symptoms predominate, while a substantial proportion of patients also experience somatosensory and, more rarely, dysphasic or motor manifestations. While neurovascular coupling (NVC) abnormalities within the primary visual cortices in migraine with aura (MwA) have recently been implicated as a potential mechanism facilitating cortical spreading depression (CSD) ignition, it is still unclear whether impaired NVC extending beyond visual areas may contribute to CSD propagation and, therefore, to the broader symptomatology characterizing complex aura phenotypes.

Methods. Forty patients with MwA (21 simple visual MwA, 19 complex MwA), 30 patients with migraine without aura (MwoA), and 22 healthy controls (HC) underwent multimodal 3T MRI during the interictal period, including resting-state functional MRI and multi-delay arterial spin labeling. Regional NVC was estimated by computing the correlation coefficient between z-scored regional homogeneity (ReHo) maps from resting-state blood oxygen level dependent signals and z-scored cerebral blood flow (CBF) maps from multi-delay arterial spin labeling signals.

Results. Voxel-wise analysis of CBF maps revealed that patients with cMwA showed a significant CBF increase in regions predominantly localized medially, within the precuneus–posterior cingulate cortex region, compared to both patients with MwoA and HC ($p<0.05$, TFCE corrected). Furthermore, a reduced NVC at the left and right precuneus - posterior cingulate cortex (pCUN-PCC-1 parcels) was observed in patients with cMwA compared with patients with svMwA, MwoA and HC (respectively $p=0.004$ and $p=0.048$, FDR corrected).

Conclusions. In patients with complex aura, neurovascular uncoupling extends beyond the visual cortex to involve the precuneus–posterior cingulate cortex, a central hub of the default mode network characterized by exceptionally high baseline metabolic demand and extensive structural and functional connectivity with somatosensory and motor cortices. Such impaired perfusion–function matching within this multimodal hub may reduce network metabolic resilience and facilitate anterior CSD propagation, thereby providing a plausible mechanistic substrate for the broader clinical manifestations of complex aura.