Altered interplay among large-scale brain functional networks underpins multi-domain anosognosia in early-AD

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Background and aims:
Decline in self-awareness (anosognosia) is a prevalent early symptom of Alzheimer's disease (AD). The integrity of the functional hubs of the default mode network (DMN) has been heavily implicated in retained self-awareness abilities in AD patients. Moreover, an early breakdown of this network has been found to be a hallmark feature in the clinical profile of AD. However, the interplay among other large-scale brain networks in support of cognitive awareness in early-AD remains poorly understood.

Methods:
Resting-state functional MRI scans were acquired and pre-processed from fifty-three early-stage AD individuals. An independent component analysis isolated four intrinsic connectivity large-scale brain functional networks, namely left and right central executive fronto-parietal networks (FPN), salience network, anterior and posterior DMN. In addition, hypothesis-driven seed-based connectivity analyses were performed. Multiple regression models were carried out between scores of memory, non-memory (executive) and total anosognosia and large-scale network and seed-based connectivity maps.

Results:
All anosognosia domains displayed consistent lower fronto-temporal connectivity. However, higher connectivity was found between memory anosognosia and parieto-temporal regions. Non-memory anosognosia displayed stronger connectivity between the DMN-cerebellum and the contralateral prefrontal cortices. Finally, total anosognosia yielded increased connectivity between the right FPN and the anterior cingulate.

Conclusions:
Multi-domain anosognosia in early AD is characterised by selective fronto-temporal disconnection. Selectively increased fronto-parietal-subcortical connectivity seems to provide cognitive resources to cope with unawareness, explaining the heterogeneity of the symptom. Therefore, these findings support the hypothesis that alterations in functional connectivity of frontal regions involved in executive related mechanisms represent the neural correlate of domain-specific anosognosia in early AD.