O2024

Distinct white matter tract changes associated with apathy in cerebrovascular small vessel disease

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Abstract

Background and aims:

Clinical apathy is a poorly understood neuropsychiatric syndrome characterised by a significant decrease in goal-directed and motivated behaviour. It occurs in ~30% of patients with cerebrovascular small vessel disease (SVD). With the aim of improving our mechanistic understanding of apathy, we conducted a multimodal investigation combining validated behavioural paradigms and magnetic resonance imaging (MRI) techniques.

Methods:

83 patients with MRI evidence of SVD were recruited from the Oxford Vascular Study (OXVASC) and Oxford neurology clinics. They were investigated using a novel effort-based decision making task3 and the Apathy Evaluation Scale (AES). Structural and diffusion weighted MRI was conducted to measure white matter lesion load (WMLL) and tract integrity, indexed by Fractional anisotropy (FA).

Results:

Patients with apathy demonstrated a significant reduction in motivated behaviour and were significantly less incentivised by low levels of reward (Fig 1). Diffusion weighted imaging demonstrated that apathy was characterised by focal changes to limbic association tracts including the uncinate fasciculus and cingulum bundle, as well as fronto-striatal white matter tracts (Fig 2). Importantly, global measures of disease severity did not independently associate with apathy. Apathy is related to performance on effort-based decision making task a) Severity of apathy predicts motivated behaviour in SVD. b) The greatest differences between motivated and apathetic subjects are shown by the red peaks and occur when the reward levels on offer are low. In other words, apathetic subjects are less incentivised by low reward. Figure 2. Apathy in SVD characterised by reduced Fractional anisotropy in white matter tracts.

Conclusion:

Reduced incentivisation by low reward characterised apathy in SVD, as previously reported in Parkinson's disease, suggesting a common mechanism underlying apathy across diseases. At the network level, the association of apathy with focal white matter tract changes is consistent with disruption to key fronto striatal circuits (linking medial frontal regions to each other and to the basal ganglia) which previously have been implicated in effortbased decision-making for rewards.