Abstract Preview - Step 3/4

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Topic: 20. Imaging

Title: Hippocampal inflammation and depression in multiple sclerosis: integrating evidence from TSPO PET and resting state fMRI

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Text: Depression is highly prevalent in patients with multiple sclerosis (MS) and is associated more generally with elevated inflammatory markers, suggesting common pathophysiological mechanisms. The hippocampus is implicated in the pathophysiology of depression and is susceptible to neuroinflammation in MS. We hypothesise that the high prevalence of depression in MS is a consequence of the chronic immune activation in the hippocampus.

We characterized the relationship between depressive symptoms and hippocampal microglial activation in MS patients using the 2nd generation TSPO radioligand [^{18}F]-PBR111. To evaluate pathophysiological mechanisms, we explored the relationships between hippocampal inflammation, depressive symptoms and hippocampal functional connectivity as defined by resting state fMRI.

11 patients with multiple sclerosis and 22 healthy controls were administered the Beck's Depression Inventory (BDI) and were genotyped for the SNP rs6971 of the *TSPO* gene, prior to PET and fMRI scanning. The Distribution Volume Ratio (DVR) of [^{18}F]-PBR111 in the hippocampus was estimated as an index of activated microglia density. For the analysis of functional connectivity, the hippocampus was used as the seed region. We compared [^{18}F]-PBR111 uptake in the hippocampus of MS patients relative to healthy controls and examined the correlations between [^{18}F]-PBR111 uptake, BDI scores, and hippocampal functional connectivities in patients with MS.

[^{18}F]-PBR111 DVR was higher in the hippocampus of MS patients relative to healthy controls (F=5.73; p=0.024) and in MS patients the hippocampal DVR was correlated with the intensity of depressive symptoms (r=0.86, p=0.006). The strength of hippocampal functional connectivity to prefrontal regions, including the subgenual cingulate, and parietal regions, such as posterior cingulate and precuneus, correlated with both depressive symptoms and [^{18}F]-PBR111 DVR (p< 0.05 or z=2.3; cluster-corrected for multiple comparisons).

Our results provide evidence that hippocampal microglial activation in MS impairs the brain functional connectivities in regions contributing to maintenance of a normal affective state. They suggest a rationale for the responsiveness of depression in some people with MS to effective control of brain inflammation.

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