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NEWS

Blood-Brain Barrier Water Permeability Disruption in Major Depressive Disorder

Wednesday 3:40-3:50 PM | SSM19-05 | Room: S501ABC

PURPOSE

Major depressive disorder (MDD) is the most prevalent and disabling form of depression. Blood-brain barrier (BBB) disruption has been implicated in the development and progression of MDD. The purpose of this study was to investigate differences in BBB integrity between patients with MDD and healthy subjects using the recently developed Intrinsic Diffusivity Encoding of Arterial Labeled Spins (IDEALS) MRI technique.

METHOD AND MATERIALS

14 healthy subjects and 14 MDD patients were recruited with IRB approval and informed consent. Depression symptom severity was assessed with the Beck's Depression Index (demographics in Table 1). All studies were performed on a Siemens 3T Prisma MRI with 64-channel head/neck coil. IDEALS images were acquired according to (Wengler et al. NeuroImage, 2019) for mapping of cerebral blood flow (CBF), water extraction fraction (Ew), and water permeability (PSw). High resolution T1w images were acquired for segmentation and spatial normalization. Four regions of interest (ROIs) implicated in MDD were evaluated: anterior cingulate cortex (ACC), amygdala, dorsolateral prefrontal cortex (DLPFC), and hippocampus. ROIs were selected using WFU Pickatlas. Analysis of covariance (ANCOVA) was used to evaluate group differences between BBB water permeability parameters within the 4 ROIs while controlling for age and gender; $p < 0.05$ was considered significant.

RESULTS

Figure 1 displays the group averaged IDEALS parameter maps. Box plots with individual data points for PSw, Ew, and CBF within ROIs are shown in Figure 2. Figure 3 displays the mean values after adjusting for age and gender. No significant differences in CBF between healthy subjects and MDD patients were. Significantly lower Ew was observed in the amygdala, ACC, DLPFC, and hippocampus of MDD patients compared to healthy subjects. Significantly lower PSw was observed in the amygdala and hippocampus of MDD patients compared to healthy subjects.

CONCLUSION

With active trans-membrane water cycling pathways, such as NaK-ATPase, accounting for a large fraction of water exchange, the lower BBB water permeability observed in MDD patients suggests BBB disruption and cerebral metabolic deficits.

CLINICAL RELEVANCE/APPLICATION

Despite its societal impact, the mechanisms underlying major depressive disorder (MDD) are not well understood. This study uses the IDEALS MRI method to probe BBB water permeability disruption in MDD.

Multiscale Modeling of Intra-Regional and Inter-Regional Connectivities and Their Alterations in Major Depressive Disorder

Tuesday 3:30-3:40 PM | SSJ19-04 | Room: S404CD

PURPOSE

Resting-state functional magnetic resonance imaging (rs-fMRI) studies have focused primarily on characterizing the connectivity among discrete brain regions. A major drawback is that it fails to provide a mechanistic understanding of brain cognitive function or dysfunction at cellular and circuit levels. To overcome this limitation, we developed a Multiscale Neural Model Inversion (MNMI) framework that linked microscale circuit interactions with macroscale network dynamics and estimated both local coupling and inter-regional connections based on blood oxygen-level dependent (BOLD) rs-fMRI.

METHOD AND MATERIALS

The fMRI data was obtained from a single-center, large-cohort first-episode, treatment-naïve MDD rs- fMRI database, consisting of 66 MDD adults and 66 matched normal controls (NC). We used biologically plausible Wilson-Cowan oscillators to model the dynamics of local neural circuits consisting of excitatory and inhibitory neural populations (Fig. 1). Different brain regions are connected via long-range fibers with initial strength estimated from their respective structural connectivity. The neural activity of each region was converted to BOLD signals with corresponding functional connectivity (FC) matrix using a hemodynamic model. The local and inter-regional connection parameters were optimized via stochastic optimization procedures to minimize the error between the simulated and the empirical FC matrices.

RESULTS

The recurrent excitation and inhibition within the dorsal lateral prefrontal cortex (dlPFC) were found to be reduced in MDD, consistent with the commonly accepted hypothetical model of MDD. In addition, recurrent excitation in the thalamus was found to be abnormally elevated, which may be responsible to abnormal thalamocortical oscillations often observed in MDD.

CONCLUSION

The MNMI framework was able to characterize potential intra-regional pathophysiological mechanisms of MDD, thus could be better than the conventional inter-regional FC analysis.

CLINICAL RELEVANCE/APPLICATION

Understanding impaired circuit dynamics via multiscale neural modeling helps to identify both biomarkers and pathologies of MDD, which is necessary to develop more effective diagnosis and treatment.