Sertraline treatment enhances striatum-frontal connectivity without perfusion alterations in major depressive disorder

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Background: Sertraline, an effective antidepressant for major depressive disorder (MDD), is shown to enhance amygdala and striatum connectivity in MDD patients. However, the sertraline effect on brain connectivity could be either from changing cerebral blood flow (CBF) or from changing neuronal connections. To this point, we revisited sertraline treatment effect and acquired both resting-state fMRI (RS-fMRI) and arterial spin labeling (ASL) in MDD patients for its underlying mechanism.

Methods: We studied 24 unmedicated MDD patients with Hamilton depression rating scale (HAM-D) score and 33 healthy control (HC). The fMRI scans were acquired before (Pre), after 6-weeks sertraline treatment (Post) by 3T MR scanner (GE, Discovery MR750) with 8-channel head-neck-spine coil (RS-fMRI with EPI sequence: 200 measurements, TR/TE = 2500/30 ms; ASL settings: pseudo-continuous labeling sequence with TR/TE = 4737/10.528 ms, post-labeling delay=2025 ms). We applied seed-correlation analysis and amplitude of low-frequency fluctuation (ALFF) on those preprocessed fMRI images, and focused on striatum, amygdala and default-mode network (DMN). Group comparisons were conducted by paired t-test (Post vs. Pre) or two-sample t-test (HC vs. Pre) on the Z-map, ALFF and CBF (p<0.001).

Results: Compared with HC group, the MDD patients showed reduced connectivity between the striatum and the medial prefrontal cortex (mPFC) and enhanced after the 6-week treatment. However, such phenomenon was not observed in neither ALFF nor CBF (Figure 1). In contrast, sertraline treatment had no significant impact on amygdala network and DMN, and their perfusion levels remained mostly the same between three groups.

Conclusions: We found that sertraline treatment in MDD patients showed network specificity on the resting-state functional connectivity, and the therapeutic effect is not associated with the resting CBF or ALFF.

Figure 1 Resting state connectivity map of Pre-treatment (A) and Post-treatment (B) in depressed patient. We set the seed regions on striatum and ROI on medial prefrontal cortex (mPFC). ROI quantification was compared between healthy control, Pre-treatment and Post-treatment for patient in correlation coefficient (C), CBF (D) and ALFF (E). The star (*) presented p < 0.05