Changes in Gray Matter Volumes Induced by Repetitive Transcranial Magnetic Stimulation in Drug-resistant Major Depression

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Introduction
Treatment-resistant depression (TRD), with up to 20% of patients not responding to antidepressant treatment, is a crucial issue 1,2. Add-on repetitive transcranial magnetic stimulation (rTMS), an emerging treatment approach for TRD, has been reported to modulate regional brain activity of the prefronto-thalamo-limbic system in depressed patients 3,4. Whereas how brain structures can be modulated by rTMS in depression remains unclear. This study aimed to investigate, through voxel-based morphometric analysis, the effect of rTMS on gray matter density in TRD patients.

Materials and Methods
Thirty TRD patients and forty age- and gender-matched healthy controls were recruited from the Department of Psychiatry, Taipei Veterans General Hospital. All participants signed the written consent forms approved by the Institutional Review Board at Taipei Veterans General Hospital. Each patient received high-frequency (10 Hz) rTMS over the left dorsolateral prefrontal cortex for two weeks and was assessed the severity of depression using the Beck Depression Inventory and Hamilton Depression Rating Scale (HDRS) before (W0) and after (W2) rTMS intervention. Brain regions with volume changes induced by rTMS (W0 vs. W2) were localized using voxel-based morphometric analysis from T1-weighted magnetic resonance images. A binary logistic regression model based on regional gray matter volumes measured at W0 was constructed to predict clinical outcome.

Results
Seventeen patients were diagnosed as treatment-responders after two-week rTMS therapy (≥50% improvement of HDRS). The responders exhibited rTMS-induced gray matter volume recovered in the regions of bilateral orbitofrontal cortex, right middle frontal gyrus, right inferior temporal gyrus, vermis, and right precuneus (increased volume), as shown in Figure 1, as well as in the left insula, left inferior frontal gyrus, left olfactory, right Rolandic\Heschl gyrus, right superior temporal gyrus, and right cerebellum (decreased volume). However, this effect was not found in the non-responders. Finally, the regression model accurately predicted 93.3% of patients as responders/non-responders.

Conclusions
Our data demonstrated brain plasticity of regional gray matter volumes induced by two-week rTMS treatment. The findings of different patterns of brain volume changes between TMS-responded and TMS-non-responded TRD patients implicate distinct neuropathology between subtypes of depression, suggesting possibility of TMS-induced gray matter recovery in depressive patients.

References