## Grey matter volume changes in medication-overuse headache before and after medication withdrawal

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Objective: The objective of this article is to investigate neurological substrates associated with medication overuse headache (MOH) in patients with chronic tension type headache (CTTH) before and after medication withdrawal. Methods: We recruited age- and sex-matched CTTH patients with MOH, and healthy controls (HCs). Magnetic resonance T1-weighted images were processed by voxel-based morphometry in MOH patients before medication withdrawal (n=23), MOH patients who withdraw the medication successfully after one month of routine treatment (n=10) and HCs (n=23). SPM8 was used to analyze voxel-based morphometry. The findings were correlated with clinical variables and treatment responses. Results: Patients with MOH compared to HCs showed gray matter volume (GMV) decrease in the right inferior temporal cortex, left insula, right parahippocampal cortex and bilateral anterior cingulum as well as GMV increase in the left temporal cortex. Significantly, we found the decreased and increased GMV of these regions tended to be normal in patients with MOH after medication withdrawal comparing with the MOH patients before withdrawal and HCs, especially in the right inferior temporal cortex and left insula. Conclusions: Our study showed GMV changes in MOH patients before and after medication withdrawal. Abnormalities in these regions in MOH patients may contribute to explaining variance of the analgesics use frequency. These regions may tend to be normal after the medication withdrawal.

Table 1. Regions of gray matter volume change in chronic tension type headache with medication overuse headache and healthy controls

|           | Region          | Hemi | Voxel | Peak voxel MNI coordinates |       |      | T value |
|-----------|-----------------|------|-------|----------------------------|-------|------|---------|
|           |                 |      |       | Χ                          | Υ     | Z    |         |
| Cluster 1 | Temporal_Inf    | R    | 6174  | 40.5                       | -1.5  | -45  | -5.88   |
| Cluster 2 | Insula          | L    | 3964  | -28.5                      | 4.5   | -30  | -5.41   |
| Cluster 3 | ParaHippocampal | R    | 1267  | 21                         | -34.5 | -9   | -5.72   |
| Cluster 4 | Cingulum_Ant    | L/R  | 536   | -1.5                       | 37.5  | 7.5  | -4.16   |
| Cluster 5 | Temporal_Mid    | L    | 187   | -58.5                      | -25.5 | -1.5 | 4.49    |