The effects of Methylphenidate on resting-state brain activity in normal adults: An fMRI study

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1. Objective: Methylphenidate (MPH) is the most common used stimulant for treatment of attention deficit hyperactivity disorder (ADHD). There have only a few studies in which the MPH effects were assessed by using functional magnetic resonance imaging (fMRI)(Vaidya CJ, 1998; Teicher, 2000; Anderson, 2002; Schafritz KM, 2004; Konrad K, 2007). However, most studies utilized cognitive tasks and the MPH effects were evaluated from a baseline state to task state. In contrast to task-based approaches, resting-state brain activity characterizes task-independent patterns. By using resting-state fMRI and analytic approach, regional homogeneity (ReHo)(Zang, 2004), the current study focused on the MPH effect on the intra-regional synchronization of spontaneous brain activity in a group of normal adults.

2. Methods: Eighteen healthy males participated in the study after they given informed consent. A handedness questionnaire and the Wechsler Adult Intelligence Scale were tested before taking any medication. Then the subjects were tested during two counterbalanced sessions, one with a single dose of MPH (20 mg) and the other with placebo. A resting-state fMRI scan was obtained 1 hour after medication. During the scanning, subjects were instructed to close their eyes and not to think of anything particular. 2D, 3D and resting EPI images were obtained. The data was preprocessed by using SPM5. And then a software REST was used for calculation of Kendall's coefficient concordance (KCC) in a voxel-wise way by using ReHo approach. Paired t-test was performed between MPH and placebo conditions.

3. Results: 1) Stronger MPH related activativities are in middle cingulate cortex, bilateral superior temporal lobe, right superior parietal lobe, left precuneus, bilateral cuneus, right supra marginal lobe, bilateral lingual gyrus, bilateral superior occipital lobes, left paracentral lobe, right precentral gyrus, right postcentral gyrus, left supplementary motor area, and right rolandic operculum. 2) Weaker MPH related activativities are in bilateral superior frontal lobes, bilateral orbital-frontal lobes, left middle frontal lobe, right postcentral lobe, right fusiform and left middle occipital lobe.

4. Conclusions: The brain activities affected by MPH in normal adults using ReHo seems to have good match to the activity in four big brain areas which is concluded by Gusnard and Raichle in resting state. They are posterior medial cortices (tonically active region), posterior lateral cortices(conscious awareness), ventral medial prefrontal cortex(intergration), and dorsal medial prefrontal cortex (spontaneous)(Gusnard and Raichle, 2001). Only a single dose of MPH can change the resting activity in most resting-state related areas, and it may help us to know the mechanism of how MPH improves the task performance.

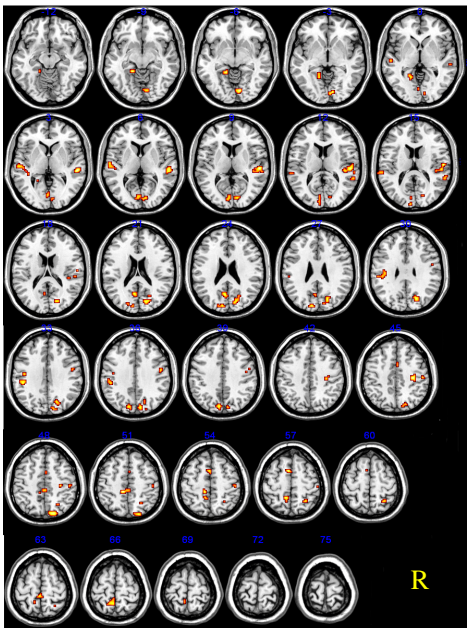

Fig. 1. Map of resting-state brain activity pattern in which the activation of on-MPH is stronger than on-placebo. Maps are superimposed on axial sections from z=-12 mm to z=75 mm in MNI system. Threshold is *P*<0.005, FDR corrected for multiple comparisons.

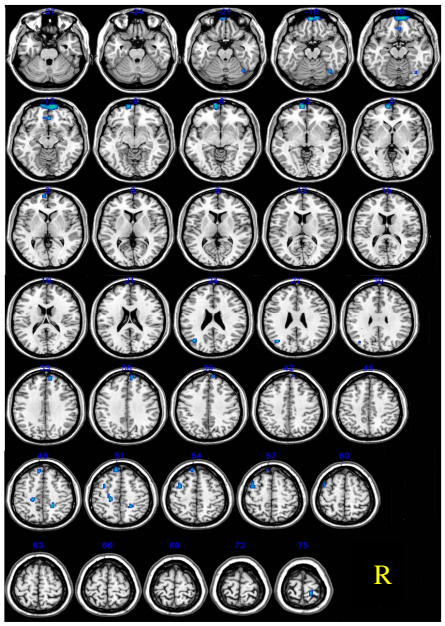

Fig. 2. Map of resting-state brain activity pattern in which the activation of on-MPH is stronger than on-placebo. Maps are superimposed on axial sections from z=-27 mm to z=75 mm in MNI system. Threshold is *P*<0.01, uncorrected.