

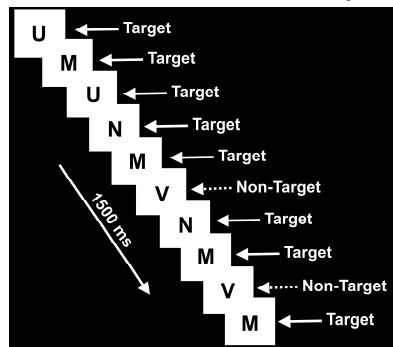
# Dynamic response inhibition network in heroin addicts brain: evidence from functional neuroimaging with Go/Go-nogo task

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**Introduction:** Reduction in the inhibitory control plays an important role in drug addiction. Recently, task-dependent neuroimaging studies have identified several brain regions involved in the response inhibition, including bilateral inferior frontal gyrus (IFG), bilateral dorsolateral prefrontal cortex (DLPFC), medial frontal cortex (MeFG), and cingulate cortex(1). However, little is known about the changes within the response inhibition network while performing a specific task in subjects with heroin addiction. In this study, we investigated the changes of the response inhibition network during Go/Go-nogo task in heroin addicts. We hypothesized that task-induced dynamic reconfiguration of the response inhibition network will be found in subjects with heroin addiction.

**Methods: fMRI measurement:** 30 heroin-dependent subjects and 18 age-matched cognitively normal (CN) subjects participated in this study. Written consent was obtained from each subject. The Go/Go-NoGo association block-design paradigm was utilized to probe response inhibition (Figure 1). MRI



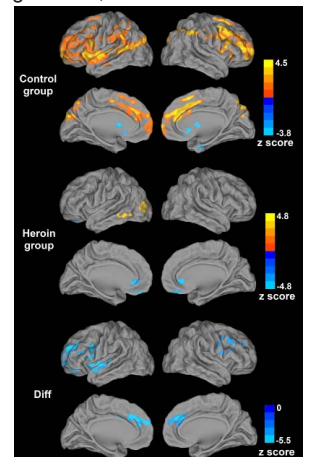
**Figure 1. (Left) Go/Go-nogo paradigm:** Subjects were presented with 0.5Hz serial alternating characters, all of which except for character 'V' were responded to with a button press. Character 'V' (NoGo stimuli) required an inhibition of a response. The upper 5 stimuli composed Go condition and the lower 5 stimuli composed of Go-nogo condition.

scans were obtained in a GE 3.0T Signa LX scanner. 3D high-resolution anatomical images were acquired prior to functional scans. The fMRI data were obtained by using single-shot EPI sequence (TE=25ms, TR=2s, FOV=24×24 cm, matrix=64×64, slice thickness=5 mm, space=1.0 mm). Foam pads were used to reduce head motion during EPI data acquisition. **Data preprocessing:** The fMRI datasets were analyzed with AFNI. The first five data points of each dataset were discarded to obtain the stable state. Physiological motion correction, volume registration, and head motion correction were performed to correct tolerable motions during the scan. For Go/Go-nogo task analysis, a general linear model was employed to obtain the individual signal change percentage maps. These maps were transformed into Talairach space for further group analysis. The detailed

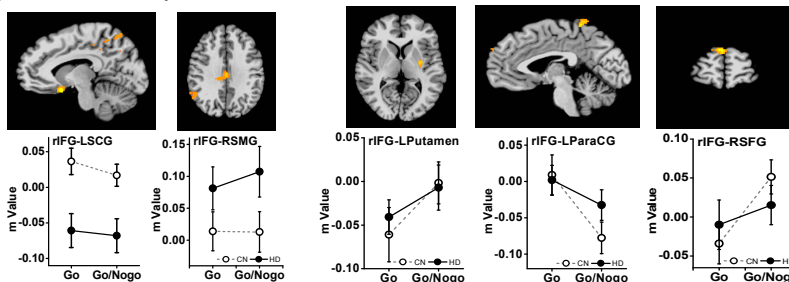
procedure was described in reference (1). According to the results from group-level comparison (Figure 2), we selected right inferior frontal gyrus (RIFG) as the seed region for the functional connectivity analysis of the response inhibition network, as described below. **Functional connectivity analysis:** After regressing out possible contamination from the white matter, cerebral spinal fluid, global signal, and six motion vectors signals in addition to physical noise (respiratory and cardiac rate), task-induced effect was also removed from the functional EPI dataset by using the general linear model (2). We then separated the Go condition and Go-nogo conditions for detecting the response inhibit network alterations across all subjects. A band-pass filter was applied to keep only low frequency fluctuations (0.015-0.1 Hz). The cross-correlation coefficient (CC) maps of individual subjects were generated by cross-correlating each voxel time course with the average time course of seed voxels. 2\*2 analysis of variance (ANOVA) was performed for identifying the RIFG functional network alterations in control and heroin addicted subjects during different tasks. Additionally, we quantitatively measured the altered RIFG response inhibition network from the ANOVA findings between CN and heroin subjects.

**Results:** When performing Go/Go-nogo task, compared to CN subjects, heroin dependent subjects showed significantly decreased activation in multiple brain regions, including bilateral dorsolateral prefrontal regions (DLPFC), inferior frontal gyrus, opercula, and dorsal anterior cingulate cortex (Figure 2). Further, the main effects of subjects (CN vs Heroin) on the RIFG network were located in the left subcallosal gyrus (L SCG) and right superior marginal gyrus (R SMG) (Figure 3); the main effects of Task (Go vs Go-nogo) on the RIFG network were found in the left putamen, paracentral gyrus (L ParaCG), and right superior frontal gyrus (R SFG) (Figure 4); the interactive effects (Subject \* Task) on the RIFG functional network were seen in the right medial frontal gyrus (R MeFG), left DLPFC, left SFG, and right fusiform gyrus (R FFG)(Figure 5). Quantitative data showed dynamic changes within the response inhibition network during different task performances (Figure 5).

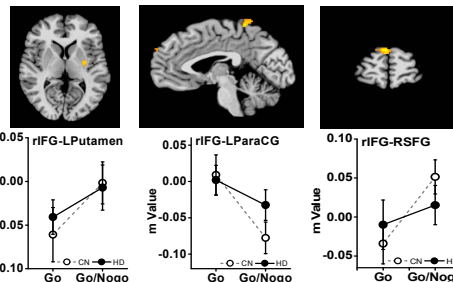
**Conclusions:** Neurocognitive networks with a high-degree connectivity pattern among discrete brain regions are responsible for performance of high-order cognitive behaviors (3). The altered right IFG functional network when performing response inhibition task in heroin dependent subjects may represent the pathophysiological mechanisms underlying heroin addiction. Our study findings extend our understanding of the neural underpinnings of response inhibition dysfunction in heroin addiction.



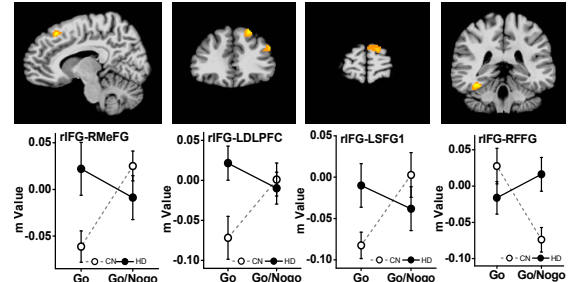
**Figure 2. (Right) Activation map of Go/Go-nogo task induced and group-difference in Controls and Heroin addicted subjects.**



**Figure 3. Main effects of subjects on the Response inhibition network.**



**Figure 4. Main effects of Task (Go vs Go-nogo) on the response inhibition network.**



**Figure 5. Interactive effects of Subjects and Task on the response inhibition network.**

**References:** 1. Fu et al., Neurosci letters. 2008;438: 322-6. 2. Fair et al., Neuroimage. 2007;35(1): 396-405. 3. Mesulam et al., Neuron.2009; 62(1):1-3.

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