Meta-analysis of fMRI activation associated with response inhibition during performance of Go/Nogo tasks.

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Objective: FMRI studies of response inhibition consistently reveal frontal lobe activation. Localization within the frontal cortex, however, varies across studies and appears dependent on the nature of the task. Activation likelihood estimate (ALE) meta-analysis (Turkeltaub et al., 2002 *NeuroImage*) is a powerful way of establishing concurrence of activation across functional neuroimaging studies. It is made possible by the use of standardized coordinate reporting. In ALE, foci are plotted as the center of a three-dimensional (3D) Gaussian distribution, and pooled to create a new statistical whole-brain image. One previous study performed an ALE meta-analysis of Go/Nogo tasks (Buchsbaum et al., 2005 *Hum Brain Mapp*); however, they included a large number of studies with block-designs that may highlight regions not involved in response inhibition. They also included studies directly contrasting Nogo and Go trials, which potentially masks regions that are critical to response inhibition but also involved in response selection. For this study, ALE was used to investigate concurrence of Nogo-activation in healthy adults during event-related fMRI Go/Nogo tasks that contrasted Nogo with baseline activation, to reveal all regions involved in response inhibition.

Methods: Studies were selected by searching the Pubmed database. Selection criteria were that all studies used event-related fMRI and reported activation for correctly rejected No-go trials against a general task baseline in healthy adults. After these criteria were applied, six studies remained (studies) for a total of 145 subjects and 68 foci. Coordinates were entered and processed using the Brainmap Search&View program (Laird, Lancaster & Fox, 2005 *Hum Brain Mapp*). The ALE analysis was run using a FWHM of 15mm. 5000 permutations using the same FWHM and number of foci were generated in order to assess statistical significance. The ALE map was thresholded at $p=10^{-3}$. ALE values were imported into AFNI and overlaid onto an anatomical template normalized to Talairach space.

Results: Concurrence of activation was lateralized to the right-hemisphere, with the highest concurrence in the rostral supplementary motor area ("pre-SMA";BA6). Concurrence was also seen in bilateral inferior parietal regions (BA40), right middle frontal gyrus (BA9/46), right inferior occipital gyrus (BA19), left precentral gyrus (BA6) and left posterior cerebellum (declive).

Fig. 1: Studies and coordinates entered into ALE meta-analysis

- Bellgrove et al, 2004 *Neuropsychologia*
- Garavan et al, 1999 *PNAS*
- Kiehl et al, 2000 *Psychophysiology*
- Liddle et al, 2002 *Hum Brain Mapp*
- Mostofsky et al, 2003 *Cog Brain Res*
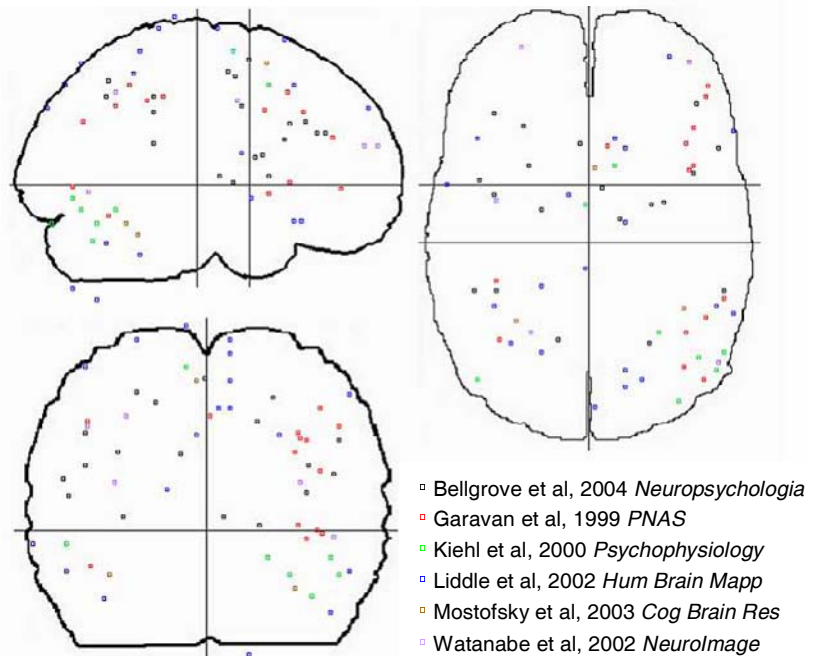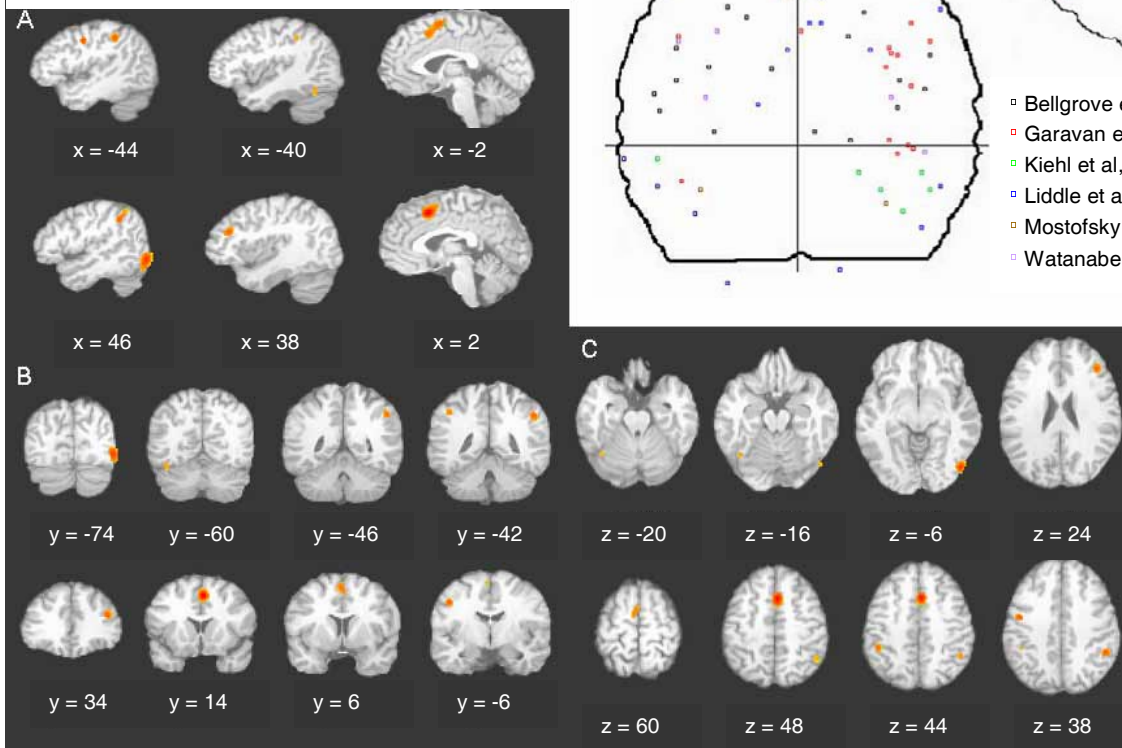- Watanabe et al, 2002 *NeuroImage*

Fig. 2: Sagittal, coronal and axial views of ALE results

Discussion & Conclusions: The ALE meta-analysis indicates that a predominantly right-lateralized network is involved in motor response inhibition. Although much attention has been focused on the involvement of right inferior prefrontal regions in response inhibition, the ALE findings suggest greater concurrence in the pre-SMA, important for motor response selection (including selecting not to respond), and inferior parietal regions important for processing the behavioral relevance of stimuli.