FUNCTIONAL MRI STUDY OF NEGATIVE PRIMING IMPLICATIONS FOR FRONTAL DISINHIBITION

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Introduction

It is widely accepted that the prefrontal cortex plays a crucial role in the process of inhibitory control. Evidence from clinical observation of behavioural changes after frontal lobe lesions, Metzler & Parkin (2000), physiological studies of event related potentials (ERP), Knight et al. (1981,1984) and functional MRI studies, Aron, et al. (2003), Bellgrove et al (2004), all support a frontal disinhibition hypothesis. However it remains poorly understood how the frontal cortex mediates inhibitory control of irrelevant information and how interference or perseveration effects are related to inhibition. Metzler & Parkin (2000) study reported that patients with uni- and bilateral frontal lobe damage were impaired on an identity negative priming task (NP) involving letter naming compared to all control groups who demonstrated robust negative priming and distracter interference. The majority of patients in there study showed positive instead of negative priming and not all of them were more susceptible to interference. They concluded that frontal lobe lesions disrupt distracter inhibition and cannot be explained by a retrieval deficit. Although the NP paradigm, has been shown to be a useful tool in linking frontal dysfunction to inhibitory impairments, to the best of our knowledge it has not been applied in an fMRI study to precisely localise the frontal regions involved in this form of `inhibition' that counteracts distracter interference. Using the NP paradigm our fMRI study aims to elucidate whether the frontal lobe is responsible for inhibitory processes or a wider network is implicated, in healthy volunteers, given that human lesions are rarely discrete and the neuropsychological literature still lacks evidence that a definitive brain area is necessary for inhibitory control.

Methods & Materials

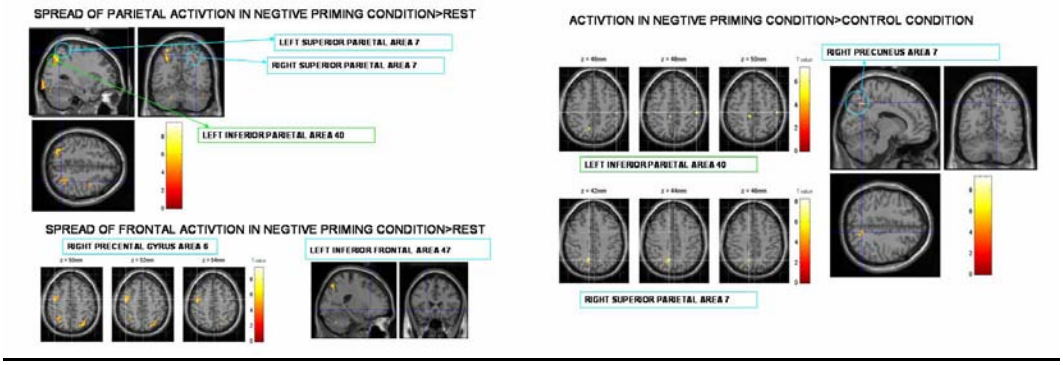
Participants: 15 right handed volunteers ranging in age from 19-36 years gave informed consent to participate in the experiment, which was approved by the School of Psychology ethics committee. 4 participants were excluded from the fMRI data analysis because they did not show a behavioural effect.

fMRI data acquisition: Scanning was performed on a 1.5T Philips Gyroscan magnet at the *Peninsula MRI research centre, University of Exeter, UK.* A T2*-weighted echo planar sequence was used (TR = 3000ms, TE = 50ms, flip angle 90°, 32 transverse slices, 3.6 x 3.6 x 4mm, ascending acquisition). 294 volumes were acquired in each of the 2 runs per subject.

Negative priming paradigm: Visual stimuli were presented on a back projection screen positioned at the foot end of the MRI scanner and viewed via a mirror mounted on the head coil. The screen subtended 16 degrees of visual arc. Button press responses and reaction times were measured using a fibre optic button boxes held in the participants' right or left hands (counterbalanced between subjects). A set of 10 capital letters were used (the five vowels and the 5 consonants K, L, N, R and S). At the beginning of each trial a fixation cross was presented for a random duration of 300, 400 or 500 ms and followed by the two overlapping letters (one green and one red) which were presented for 500ms. The letters were followed by a white screen presented for 1500 ms to allow for longer than 500 ms RTs. Participants were asked to decide whether the red letter was a vowel or a consonant, and to press the corresponding response button. The need for accuracy and speed were equally emphasized in the instructions that participants read. The experimental session consisted of two blocks presented in a fixed order among participants and separated by a short break. Each block consisted of 180 stimuli divided into 4 sub-blocks of 45 stimuli presented in a fixed order. Two of these sub-blocks were NP sub-blocks (where the distracter on trial n becomes the target on trial n+1) and 2 sub-blocks were control sub-blocks (where the distracter on trial n is different from the target on trial n+1). The order of sub-blocks and trials within the sub-blocks was fixed. At the end of the task participants were asked whether they had noticed any relationship between consecutive trials.

fMRI Data Analysis: 11 subjects showing the behavioural effect of NP were included in the fMRI dta analysis. The data analysis was performed in SPM2, each subject was realigned, normalised to the MNI template and smoothed with a Gaussian filter with a 6mm FWHM. The following planned t-contrast were then entered into a group random effect analysis, NP >REST, CONTROL>REST and NP>CONTROL, with P<0.001 uncorrected.

Results



Conclusion The present study provides evidence that in a pure NP task, the effect of negative priming, i.e. distracter information, is not exclusively the domain of the frontal cortex but perhaps involves a frontal-parietal network. Further investigation would be necessary to establish whether this frontal-parietal system could be a top-down epiphenomenon in executive control of the frontal regions over parietal processes in patients with frontal lesions.

References

Aron A. R., Fletcher, P. C., Bullmore, E. T., Sahakian, B. J., & Robbins, T. W. (2003). Stop-signal inhibition disrupted by damage to the inferior from gyrus in humans. *Nature Neuroscience*, **6**, 115 - 116

Bellgrove, M. A., Hester, R., &Garavan H. (2004) The functional neuroanatomical correlates of response variability: evidence from a response inhibition task. *Neuropsychologia*, **42**, 1910-1916

Knight RT. Decreased response to novel stimuli after prefrontal lesions in man. *Electroencephalography and Clinical Neurophysiology* , *59*, 9-20.

Knight RT, Hillyard SA, Woods DL, Neville HJ. The effects of frontal cortex lesions on event-related potentials during auditory selective attention. *Electroencephalography and Clinical Neurophysiology*, **52**, 571-82.

Metzler C., & Parkin A. J. (2000) Reverse negative priming following frontal lobe lesions. *Neuropsychologia*, **38**, 363-379.