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Attention-based modulation of tactile stimuli: A comparison between prefrontal lesion patients and healthy age-matched controls

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ABSTRACT

Objectives: To investigate the role of the prefrontal cortex in attention-based modulation of cortical somatosensory processing.
Methods: Six prefrontal stroke patients were compared with eleven neurologically intact older adults during a vibrotactile discrimination task. All subjects attended to stimuli on one digit while ignoring distracter stimuli on a separate digit of the same hand. Subjects were required to report infrequent targets on the attended digit only. Throughout testing electroencephalography was used to measure event-related potentials for both task-relevant and irrelevant stimuli.
Results: Prefrontal patients demonstrated significant changes in cortical somatosensory processing based on attention compared to age-matched controls. This was evident both in early unimodal somatosensory processing (i.e. P100) and in later cortical processing stages (i.e. long-latency positivity). Moreover, there was a tendency towards a tonic loss of inhibition over early somatosensory cortical processing (i.e. P50).
Conclusions: The attention-based modulation noted for neurologically intact older adults was absent in prefrontal lesion patients.
Significance: The present study highlights the important role of prefrontal regions in sustaining inhibition over early sensory cortical processing stages and in modifying somatosensory transmission based on task-relevance. Notably these deficits extend beyond those previously shown to occur as a function of age.

1. Introduction

The prefrontal cortex (PFC) influences distributed neural networks and is critically involved in the top-down modulation of sensory signals both at the unimodal sensory processing level, and in higher order association regions (Fuster, 2008; Knight, Staines, Swick, & Chao, 1999). Notably, this modulation has been demonstrated across different sensory modalities including visual, auditory and somatosensory processing (Knight et al., 1999). Numerous lines of evidence including animal models of selective attention (Artchakov et al., 2009; Bartus & Levere, 1977), lesion studies in humans (Chao & Knight, 1995, 1998) and imaging work (Dolcos, Miller, Kragel, Jha, & McCarthy, 2007) have established clear links between prefrontal activity, the suppression of distracters and subsequent cognitive performance. Indeed, PFC acts to suppress irrelevant information early in the processing stream, including at the earliest cortical stages of sensory processing and even at the thalamus prior to cortical entry (Cao, Wang, Bai, Zhou, & Zhou, 2008; Yamaguchi & Knight, 1990; Yingling & Skinner, 1976; Zikopoulos & Barbas, 2006). Due to this capacity to gate out irrelevant sensory information, the PFC has a critical role in providing resistance to distraction and in sparing limited cognitive resources from becoming overwhelmed by a surplus of sensory input. This role has been probed more directly in a recent study where single-pulse transcranial magnetic stimulation (TMS) was applied over the PFC during a tactile working memory task (Hannula et al., 2010). The results from this study demonstrated greater suppression over irrelevant/unattended stimuli, as measured by somatosensory-evoked potentials, and a concomitant increase in performance. Given that a major key to optimal cognitive function is the ability to maintain relevant data in working memory while preventing interference from irrelevant sources of information (Bancroft, Hockley, & Servos, 2012), any impaired filtering may result in a greater propensity to encode unwanted information and overwhelm neural processing networks (Awh & Vogel, 2008; McNab & Klingberg, 2008).

Event-related potentials (ERP) following somatosensory stimulation (either electrical or mechanical) provide a useful electroencephalographic probe into cortical processing of somatosensory

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information. The ensuing ERP offers a measure of both early sensory processing such as the P50 or P100 components which reflect unimodal somatosensory generators (Allison, McCarthy, Wood, & Jones, 1991; Hamalainen, Kekoni, Sams, Reinikainen, & Naatanen, 1990), and/or later components originating from neural generators not limited to unimodal sensory processing sites (Hamalainen et al., 1990; Mauguiere et al., 1997). Given the sensitivity of somatosensory ERP measures to attentional manipulation (Adler, Giabbiconi, & Muller, 2009; Bolton & Staines, 2011; Eimer & Forster, 2003b; Gillmeister, Sambo, & Forster, 2010; Iguchi, Hoshi, Tanosaki, Taira, & Hashimoto, 2005), they provide an ideal means of exploring changes in signal processing that may follow from the loss of top-down modulation via prefrontal regions.

The main purpose of the current study was to investigate changes in somatosensory gating during a tactile discrimination task in individuals with prefrontal damage compared to age-matched healthy controls. Furthermore, we wished to explore how these changes may relate to recent findings in our lab where transient suppression of the dorsolateral prefrontal cortex (DLPFC) was used to investigate the role of this region in attention-based sensory gating (Bolton & Staines, 2011). In our previous study, subjects performed a within-hand vibrotactile discrimination task where they were required to attend to targets on one digit, while ignoring distracter targets on another digit. Following the application of continuous theta burst stimulation (cTBS) over DLPFC, subjects demonstrated a loss of attention-based modulation over tactile evoked-potentials that reflected unimodal somatosensory processing. These results supported the view that prefrontal areas regulate somatosensory signal transmission at an early cortical processing stage based upon task-relevance. Consequently, it is important to investigate if the cTBS-induced suppression of DLPFC holds any physiological relevance to a patient population with prefrontal damage. In addition to applying transient suppression to healthy young adults during a tactile discrimination task, we have recently found evidence of losses in attention-based somatosensory modulation purely as a function of age (Bolton & Staines, 2012). An important observation from both studies was that the loss of modulation appeared to result from elevated (i.e. less attenuated) amplitudes with ignored stimuli. This suggests a specific loss in the capacity to filter out unwanted sensory input, consistent with a prefrontal role in attention-based sensory gating. In light of these recent findings, the present study aims to explore attention-based sensory gating in a prefrontal lesion population and compare this with normal age-related changes.

To investigate the impact of prefrontal damage on tactile spatial attention, we used the same vibrotactile discrimination task described above where subjects attended to stimuli delivered to one of two stimulated digits in the same hand. Patients with prefrontal brain lesions were compared with neurologically intact older adults to provide an age-matched control group. As mentioned, many ERP components can be modulated by attention and this has been shown even with components representing early stages of somatosensory cortical processing (Bolton & Staines, 2011; Eimer & Forster, 2003b; Schubert et al., 2008). Moreover, imaging work has shown a strong link between prefrontal activity and activity at these somatosensory processing stages (Staines, Graham, Black, & McIlroy, 2002) suggesting a prefrontal or top-down gating system based upon attention to task-relevant stimuli. In accordance with this we hypothesised that prefrontal lesion participants would show diminished attention-based modulation of ERPs during a tactile discrimination task compared with age-matched control subjects. Such disrupted modulation would be indicated by a loss in the difference between attended and unattended ERP components. Moreover, we postulated that this would most likely occur via reduced suppression of irrelevant stimuli and this effect would be evident early in the somatosensory processing stream. This would suggest reduced or absent attention-based modulation of early somatosensory processing within the cerebral cortex. Finally, we hypothesised that prefrontal lesion patients would demonstrate a lower success rate with target detection.

2. Material and methods

2.1. Participants

Eleven neurologically normal volunteers and seven post-stroke patients (at least 5 months post-stroke) with evidence of damage to the prefrontal cortex participated in the study after providing written informed consent. Testing groups were as follows: (a) older adults OA (mean age 73; range 62–89) and (b) prefrontal lesion subjects PFx (mean age 66; range 56–84). Data from one patient was excluded due to excessive artefacts. The final sample size for each group was as follows: PFx ($n=6$) and OA ($n=11$). All prefrontal lesion subjects were recruited from the Neurological Patient Database (funded through the Heart and Stroke Foundation of Ontario). The patient group was selected from this database on the basis of having a unilateral prefrontal lesion (determined by CT scan or MRI) with no history of sensory deficits by history or clinical examination and no patients were included with evidence of parietal damage. Further, all participants were screened prior to testing with Semmes Weinstein mono-filaments to ensure sensory thresholds were within normal ranges (e.g. no evidence of peripheral neuropathy). Description of the location and extent of each patient's brain lesion is provided in Table 1 and representative lesion images are shown in Fig. 1. The older adults were recruited from a separate research database (Waterloo Research in

Table 1.
Lesion description and demographics.

Subject	Gender	Age (yrs)	Hand stimulated	Report hand/foot	Description of frontal lesion
1	M	56	Left	Left foot	Central left frontal lobe (acute)/almost complete obliteration of left lateral ventricle anterior horn and body from mass effect/overlying sulci also effaced
2	F	84	Left	Right hand	Left frontal lobe haemorrhage (3.9×3 cm^2)/mass effect on anterior horn of left lateral ventricle
3	F	64	Right	Right foot	Right internal carotid artery aneurysm and stroke on right side after surgery/several foci decreased attenuation inferior portion of right frontal lobe, medial portion right temporal lobe and extending up along temporal tip to level of internal capsule. *Note – surgical clips prevented subsequent MRI in this subject*
4	M	62	Right	Left hand	Posterior medial aspect of right cerebellar hemisphere/periventricular white matter, more predominant in the right frontal regions/old infarct: right basal ganglia and anterior to right frontal horn
5	M	69	Right	Left hand	Right frontal and medial temporal lobes and right caudate head extend to cortex/infarct involves peripheral cortex of right frontal lobe, including Insular cortex/internal, external and extreme capsules
6	M	58	Right	Left hand	Haemorrhagic infarct at right frontal and left cerebellar hemisphere/small foci subdural hyperdensity along falx and right frontal extra-axial space/2 indeterminate hypoattenuated foci in skull right frontal and left parietal, parasagittal/re-demonstration of sphenoid sinusitis