Neuroimaging somatosensory perception and masking

Kimford J. Meador[a,*], Kathleen Pirog Revill[b], Charles M. Epstein[c], K. Sathian[c,d], David W. Loring[c], Chris Rorden[e]

[a] Neurology & Neurological Sciences, Stanford University, Stanford, CA, United States
[b] GT/GSU Center for Advanced Brain Imaging & Emory University, Atlanta, GA, Unitet States
[c] Neurology, Emory University, Atlanta, GA, United States
[d] Rehabilitation R & D Center for Visual and Neurocognitive Rehabilitation, Atlanta, VAMC, United States
[e] Department of Psychology, University of South Carolina, Columbia, SC, United States

ARTICLE INFO

ABSTRACT

The specific cortical and subcortical regions involved in conscious perception and masking are uncertain. This study sought to identify brain areas involved in conscious perception of somatosensory stimuli during a masking task using functional magnetic resonance (fMRI) to contrast perceived vs. non-perceived targets. Electrical trains were delivered to the right index finger for targets and to the left index finger for masks. Target intensities were adjusted to compensate for threshold drift. Sham target trials were given in ~10% of the trials, and target stimuli without masks were delivered in one of the five runs (68 trials/run). When healthy dextral adult volunteers (n=15) perceived right hand targets, greater left- than right-cerebral activations were seen with similar patterns across the parietal cortex, thalamus, insula, claustrum, and midbrain. When targets were not perceived, left/right cerebral activations were similar overall. Directly comparing perceived vs. non-perceived stimuli with similar intensities in the masking task revealed predominate activations contralateral to masks. In contrast, activations were greater contralateral to perceived targets if no masks were given or if masks were given but target stimulus intensities were greater for perceived than non-perceived targets. The novel aspects of this study include: 1) imaging of cortical and subcortical activations in healthy humans related to somatosensory perception during a masking task, 2) activations in the human thalamus and midbrain related to perception of stimuli compared to matched non-perceived stimuli, and 3) similar left/right cerebral activation patterns across cortical, thalamic and midbrain structures suggesting interactions across all three levels during conscious perception in humans.

1. Introduction

Our knowledge of the physiological mechanisms underlying conscious awareness is limited. Understanding these mechanisms is critical to delineation of this important brain function central to many cognitive processes. Clinical studies have demonstrated that global loss of consciousness can occur from lesions or dysfunction of the cerebral hemispheres bilaterally or from thalamic or midbrain lesions (Plum and Posner, 1980). Functional imaging studies have shown consistently reduced resting brain activity for patients with disorders of consciousness in bilateral dorsomedial thalamus, precuneus, cingulate, middle frontal gyri, and medial temporal gyri (Hannawi et al., 2015). In patients with focal seizures, loss of awareness is related to spread of seizure activity to the thalamus/midbrain and disruption of corticotha-

lamic interactions and cortical function (Lee et al., 2002; Blumenfeld, 2012).

The specific roles of cortex, thalamus, and brainstem in consciousness remain poorly delineated (Boly et al., 2013). Several prior studies have emphasized various regions as crucial for conscious perception including primary sensory areas, specialized cortical processing regions for specific tasks (e.g., fusiform gyrus for face perception), and regions in the frontoparietal attentional network (Bar et al., 2001; Vuilleumier et al., 2001; Marois et al., 2004; Haynes et al., 2005a, 2005b; Hirvonen and Palva, 2016). In addition, activities in the cingulate, claustrum, insula, precuneus, and thalamus have been related to conscious perception (Marois et al., 2004; Crick and Koch, 2005; Boly et al., 2007; Sadaghiani et al., 2009, 2015).

The thalamus and midbrain have been traditionally viewed as

simply providing sufficient arousal for consciousness. However, thalamocortical interactions appear to be critical for cognitive processing (Ward, 2011; Saalmann et al., 2012; Saalmann, 2014; Saalmann and Kastner, 2015; Sherman, 2007, 2012; Wimmer et al., 2015; Zhou et al., 2016). In addition, there is clear evidence that the midbrain network plays a critical role in controlling selective spatial attention (Knudsen, 2011), although its role in humans has been inadequately studied.

During conscious wakefulness, only a subset of external stimuli reaches conscious awareness. Access to conscious awareness is affected by stimulus saliency, intensity, duration and novelty as well as focused attention, task demands, competing stimuli, stimulus location in space or on the body, and the presence of brain lesions/dysfunction (Desimone and Duncan, 1995; Teixeira et al., 2014). Prior studies have examined sensory awareness using perceptual threshold level stimuli in the auditory (Sadaghiani et al., 2009, 2015), somatosensory (Meador et al., 2002b; Linkenkaer-Hansen et al., 2004; Monto et al., 2008; Hirvonen and Palva, 2016), and visual (Aru et al., 2012; Pins and Ffytche, 2003) modalities. These studies have variably highlighted gamma band activity, prestimulus or background activity, phase locking event-related activity, primary/secondary network nodes, and functional connectivity.

How competing stimuli mask or extinguish perception of target stimuli remains unclear. Imaging studies examining masking in humans are inconclusive. In the visual modality, functional imaging revealed masking effects in the occipital cortex, although effects have also been reported in some studies in the inferior parietal region, anterior cingulate, and thalamus (Green et al., 2005; Tsubomi et al., 2009; Lee et al., 2014; Vidal et al., 2014). In the auditory modality, results have emphasized masking effects in the auditory cortex, but some studies have reported effects in other regions (e.g., temporal and frontal cortex, insula, thalamus, and inferior colliculus) (Hwang et al., 2006; Wiegand and Gutschalk, 2012; Wack et al., 2012, 2014; Uppenkamp et al., 2013). An event-related study of somatosensory perception in a masking paradigm found that early potentials (P60, N80) were found in the contralateral S1 irrespective of whether stimuli were perceived or not, but that consciously perceived stimuli were associated with enhanced later potentials over parietal (P100) and frontal regions (N140) (Schubert et al., 2006). There are no prior fMRI studies of masking in the somatosensory modality in healthy humans to allow examination of subcortical processes. In the present study, we examine the topography of activations for perception and masking of somatosensory stimuli by comparing perceived vs. non-perceived somatosensory stimuli in healthy volunteers using functional magnetic resonance (fMRI). We were particularly interested in the role of subcortical structures and their relationship to cortical activations.

2. Methods

2.1. Study design

A repeated measures design was used comparing fMRI activation for perceived vs. non-perceived tactile stimuli with or without a contralateral mask.

2.2. Subjects

17 healthy dextral adults (mean age 21.9, range 18–28; 6M/11F) were recruited as paid volunteers. Handedness was determined by the Edinburgh inventory (Oldfield, 1971). No subject had major systemic or neurological diseases, or centrally active medications. Informed consent was obtained in accordance with the principles of the Declaration of Helsinki and was approved by the Georgia Institute of Technology Institutional Review Board.

2.3. Task

We used a task involving perception and masking of somatosensory stimuli similar to those developed and employed in our prior behavioral studies (Meador et al., 1998, 2000). In this study, we were particularly interested in differences between perceived and non-perceived target stimuli that were delivered with matched stimulus intensities during the masking task. On each trial, participants reported if they detected a target electrical stimulus delivered to the right index finger. There were five runs, each consisting of 68 trials with randomly jittered intertrial intervals (4.5–6 s; mean=5.2 s). Target stimuli were delivered without masks on one of the five runs. A red light was illuminated prior to stimulation onset to signal trial onset, remaining on for 2 s. Since stimuli were delivered to the hands, participants responded via MRI-compatible foot pedals. Participants pressed the right foot pedal if they detected a target stimulus on the right index finger, and the left foot pedal if no target stimulus was detected. Prior to the test session, participants completed an initial training session, which included one run without a mask to estimate their initial perceptual threshold by the method of incremental titrations (as previously described) (Meador et al., 1998), and 1–2 additional masked runs where mask strength was adjusted until the threshold for targets was increased relative to the unmasked threshold.

2.4. Stimulation Parameters

Stimulus and mask strengths were established during training were used as the initial stimulation and constant mask strengths for the test session. Mask strength was approximately 2.2 times the unmasked stimulation detection threshold (range 1.4–3.3x). Since stimulus detection thresholds drift over time, target strength was varied from trial to trial according to a staircase procedure. Across trials, stimulus strength was changed by a randomly selected amount +0−20% of the initial stimulation strength. If the participant detected a stimulus on trial n, stimulus strength on trial n+1 was decreased by 0−20%, but if the participant failed to detect the stimulus on trial n, stimulus strength was increased by 0−20% on trial n+1. On approximately 10% of trials, no target stimulation was presented (i.e., sham condition). Stimulus strength was not adjusted following sham trials or trials where the participant failed to respond during the 2 s response window. Strength of mask stimuli was constant across each run. The target stimulus was a 7-pulse train of 5 ms square wave electrical pulses at 10 Hz. Mask stimuli were similar except that they had greater intensity and consisted of an 8-pulse train shifted in time relative to the target stimulus so that the first mask pulse occurred 50 ms before target onset, and the last mask pulse occurred 50 ms after target offset.

2.5. Stimulus response classification

Responses were characterized as Hits (i.e., correct target perceptions) or Misses (i.e., non-perceived targets) or Shams (no targets given). Hit and Miss stimuli were further categorized as Near Threshold (i.e., a perceptual zone where both Hits and Misses occurred without differences in target intensities), Strong Stimulus Hits (i.e., targets with intensities that were nearly always perceived), and Weak Stimulus Misses (i.e., targets with intensities that were almost never perceived).

2.6. Neuroimaging

T1-weighted MP-RAGE images (TR=3200 ms, TE=354 ms, 256×256 matrix scan with 160 slices and 1×1×1 mm^3 resolution), homogeneity field maps, and standard resolution functional MRI (T2* EPI scan: iPAT =2, 90-degree flip angle, TE=35 ms, TR=2000 ms, 64×64 matrix, 192×192 mm FOV, 36 ascending 3 mm thick slices with 20% slice gap (effectively 3×3×3.6 mm between voxel centers) with