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Abstract

Advances in non-invasive neuroimaging technology now provide a means of directly observing learning within the brain. Classical conditioning serves as an ideal starting point for examining the dynamic expression of learning within the human brain, since this paradigm is well characterized using multiple levels of analysis in a broad range of species. We used MEG to expand the characterization of conditioned responses (CR) recorded from the human brain with a simultaneous examination of their spatial, temporal and spectral properties. We paired an auditory conditioned stimulus (CS+) with a somatosensory unconditioned stimulus (US). We found that when the US was randomly omitted, presentations of CS+ alone, elicited greater desynchronization of beta-band activity in contralateral somatosensory cortex compared to presentations of an auditory stimulus that was never paired with the US (CS−), and compared the CS+ following a non-reinforced extinction session. This differentiation was largest between 150 and 350 ms following US omission. We show that cross-modal CRs in the primary sensorimotor system are predominantly characterized by modulation of ongoing cortical oscillations.

Keywords: Classical conditioning; Learning; Cross-modal; Somatosensory; Induced responses

Advances in non-invasive neuroimaging technology now provide a means of directly observing learning within the brain. Classical conditioning is a widely studied learning task, which is well characterized using multiple levels of analysis in a broad range of species (e.g. [Antoniadis and McDonald, 1999], [Antoniadis and McDonald, 2000], [Brandon et al., 2003], [Carew et al., 1981a], [Carew et al., 1981b], [Ellison and Konorski, 1964], [Knowlton and Thompson, 1992], [Lennartz and Weinberger, 1992], [Phillips and LeDoux, 1992], [Rescorla, 1988], [Rescorla, 2007], [Solomon et al., 1986], [Sutherland and McDonald, 1990], [Tait and Saladin, 1986], [Wagner, 1981], [Quirk et al., 1997], [Walters et al., 1979] and [Walters et al., 1981]). In classical conditioning, following the pairing of a conditioned stimulus (CS) with an unconditioned stimulus (US), the CS alone comes to elicit the response that is typically associated with the US. This conditioned response (CR) is usually observed as a peripheral response such as salivation and changes in skin conductance. However, there is a growing body of literature that shows robust mapping of CRs in the central nervous system as well.

Invasive recording from non-human animals during classical conditioning demonstrated that primary sensory cortices respond to cross-modal sensory stimulation, and that this cross-modal response is enhanced following classical conditioning training. For example, neurons in the primary auditory cortex responded to tactile stimulation alone prior to conditioning (Dumenko and Sachenko, 1981). Similarly, neurons in the primary somatosensory cortex responded to auditory stimuli alone prior to any training (Oleson et al., 1975). Thus, primary sensory cortical regions show the capacity to respond to cross-modal stimulation. Further, following conditioning training using an auditory conditioned stimulus paired with a somatosensory (electrical

stimulation) unconditioned stimulus, neurons in somatosensory ([Dolbakyan, 1982] and [Oleson et al., 1975]) and motor cortices (Dolbakyan, 1982) showed enhanced responding to the auditory CS with similar firing patterns to those in the auditory cortex. Within a differential conditioning paradigm that incorporated one auditory stimulus that was paired with the somatosensory US (CS+), and one that was unpaired (CS−), neurons in the somatosensory cortex showed increased responses to both auditory stimuli, although the response to the CS+ became significantly greater than to the CS− (Oleson et al., 1975). In a tone discrimination task in which auditory stimuli were preceded by the presentation of a light, activation was found in the auditory cortex following presentation of the light, prior to the onset of the auditory stimuli (Brosch et al., 2005). These conditioned neural responses were not significantly correlated with the acquisition and maintenance of conditioned autonomic responses, such as pupil dilation (Oleson et al., 1975). Thus, CRs can be measured from primary sensory regions, and these CRs behave analogously to those recorded from peripheral tissue. Development and maintenance of neural CRs may occur somewhat independently from other behavioural CRs. These data suggest that CRs in primary sensory regions represent a learned association.

The first non-invasive observations of neural conditioning in humans were made using EEG. Durrup and Fessard (1935) found that after exposure to a click from a camera shutter followed by a camera flash, presentation of the shutter sounds in the absence of the flash elicited an alpha suppression response characteristic of that elicited by presentation of the flash alone. This demonstrated that a neural response typically evoked by a visual stimulus could be elicited by an auditory stimulus. This phenomenon of conditioned alpha suppression has been reliably replicated (e.g. [Harris, 2005], [Putney, 1973] and [Putney et al., 1972]).

Further EEG evidence of neural CRs comes from Skrandies and Jedynak (2000), in which activation topographies of evoked responses from trials containing a visual CS+ followed by the electrodermal US were cross-correlated with data from trials in which the CS+ was presented alone. Significant correlations among somatosensory components were found between the trials containing the US and those with the US omitted, which occurred maximally at 36 ms following US omission. The topography and latency for the somatosensory CR activity found following US omission was similar but not identical to that observed with the US present. In addition, when a conditioned group was compared to a control group of subjects who did not undergo conditioning, the conditioned group showed increases in evoked somatosensory responses following learning, and somatosensory CR topographies differed between groups at 48.8 ms following US omission. Additionally, Wong et al. (1997) found a CR that was greater for a visual CS+ compared to a CS−, just prior to the arrival of an electrodermal US. This differentiation was not present during a pre-conditioning phase.

Advances in non-invasive neuroimaging technologies now allow us to characterize the location of the generators of neural CR in the human brain. Using positron emission tomography (PET), McIntosh et al. (1998) demonstrated that, a tone paired with bilateral visual stimuli, elicited greater activation in primary and secondary visual regions as training progressed. Similarly, McIntosh et al. (1998) reported that by the end of training, presentation of an auditory CS alone elicited activation in left dorsal occipital cortex that was equivalent to that elicited by a visual stimulus.

Functional magnetic resonance imaging (fMRI) studies also localize neural CRs to primary and secondary sensory cortices. Morris et al. (2001) found increased activation in the auditory cortex elicited by presentations of a visual CS+ with the tone US omitted versus a CS−. These activation differences were found predominantly in the left hemisphere, and declined throughout the recording session. Yágüez et al. (2005) paired visual stimuli with painful esophageal distension. Following training, primary and secondary somatosensory regions showed increased activation for the visual CS+ alone compared to the CS−, and this conditioned activation was similar to evoked responses found during US presentations. Following an extinction session, in which the CS+ was presented 20 times in the absence of the US, increased activation of primary sensory regions for CS+ versus CS− was no longer found, although this effect remained in secondary regions. In the same study, this differential pattern of activation for CS+ versus CS− during conditioning was not found for a CS+ paired with an air-puff to the wrist. This could possibly be due to detection failure, since the air-puff elicited a relatively small somatosensory response compared to the painful US, and neural CRs are reported to be smaller in magnitude than unconditioned responses (e.g. Moses et al., 2005).

Although, PET and fMRI can localize the generators of neural CRs, they do so at the expense of a precise characterization of the temporal dynamics of the response. Magnetoencephalographic (MEG) studies that incorporate source localization can provide precise spatial and temporal characterization of generators of neural CRs within the human brain. Wik et al. (1996) paired a visual CS+ with an electrodermal US, and found activation elicited by the visual CS+ within the primary somatosensory cortex just prior to US onset (Wik et al., 1996). This activation was located near that elicited by the US. No similar activation was found during an extinction session involving 120 trials without reinstatement (Wik et al., 1997). When a reinstatement session was introduced every 40 trials, activity was localized to secondary somatosensory cortex 160 ms following US omission (Wik et al., 1997), similar to the results of Yágüez et al. (2005). Thus, these studies suggest that neural CRs are located within primary sensory cortices, and occur around the time that activation elicited by the US would be expected.

Similarly using MEG, Moses, Tesche and colleagues found that when a visual CS+ is paired with a bilateral auditory US, bilateral CRs were found in and near primary auditory cortex elicited by the visual CS+ alone, at approximately 50 ms following US omission ([Moses et al., 2005] and [Tesche et al., 2007]). This auditory activation was stronger than that elicited by the CS−, than the same CS+ following an extinction session without reinstatement, as well as than a visual stimulus prior to training (Moses et al., 2005). Two additional MEG studies similarly report that a stronger CR is elicited by a visual CS+ versus a CS− ([Dolan et al., 2006] and [Moratti and Keil, 2005]). However, these two studies did not co-register MEG data with individuals' structural MRIs for source localization, as did Moses, Tesche and colleagues, and therefore the precise origin of the CRs is unclear. Pizzagalli et al. (2003) co-registered EEG data with a standardized structural MRI for source localization, and thus were able to provide approximate location information. They reported that a CS+ elicited increased activation of the primary auditory cortex 100 ms following onset, and shortly before delivery of the US auditory activation was centered on middle and inferior temporal gyrus.

We used MEG to expand the characterization of neural CRs with a simultaneous examination of their spatial, temporal and spectral properties. We used electrical median nerve stimulation as an

US, since localization of the cortical responses within the contralateral primary somatosensory (SI) and motor (MI) cortex to this type of stimulation is extremely robust, and the temporal and spectral characteristics of this activation are well characterized. Specifically, synchronous neuronal firing in contralateral SI peaking 20–60 ms following stimulation – termed the somatosensory evoked response – represents a cortical response to the primary afferent volley ([Allison et al., 1989], [Hashimoto et al., 2001], [Gaetz and Cheyne, 2003], [Huttunen et al., 2006], [Karhu and Tesche, 1999], [Korvenoja et al., 2006], [McLaughlin and Kelly, 1993] and [Theuvenet et al., 2006]). In addition, median nerve stimulation modulates ongoing beta-band (15–30 Hz) cortical rhythm characteristic of neuronal populations in the primary somatosensory cortex (Penfield, 1954). The beta rhythm in bilateral SI is suppressed for the duration of 200 ms beginning 200 ms after stimulus onset. This event-related desynchronization (ERD) is followed by a one-second interval of increased beta activity to above baseline levels — termed event-related synchronization (ERS; [Della Penna et al., 2004], [Dockstader et al., 2008] and [Houdayer et al., 2006]). It is posited that the induced responses (ERD and ERS) represent changes in the functional connectivity of the underlying networks responsible for generating cortical rhythms (Pfurtscheller and Lopes da Silva, 1999). We hypothesized that activation changes in the SI-region of contralateral postcentral gyrus would be greater following presentation of an auditory CS+ with a somatosensory US omitted as compared to a CS− that was never paired. Furthermore, since induced responses indicate activity in the sensorimotor network (Bardouille et al., 2010), we speculated that the difference between conditions would be mainly expressed in the induced response.

Materials and methods

Participants

Participants consisted of 11 right-handed individuals (9 female) with no known pathology from the volunteer pool at the Rotman Research Institute, Baycrest Centre for Geriatric Care. Ages ranged from 22 to 37 (mean = 26). Informed written consent was obtained from each subject before participating in the experiment according to the protocol established by the Research Ethics Board at Baycrest, which approved the study.

Stimuli and procedures

Participants were exposed to four MEG recording sessions. In each session, participants heard two tones of different frequency, duration of 250 ms, and intensity of 85 dB sound pressure level, which were presented in random order with the inter-stimulus interval uniformly distributed between 1000 and 1500 ms. The first session entailed a classical conditioning in which the onset of auditory Tone A (CS+) was followed, with 50% probability, by a unilateral median nerve pulse (US) of 20 ms duration (15–25 V). The intensity of the US was adjusted for each individual subject to just above the threshold to elicit a mild thumb twitch. The US was presented 150 ms after tone onset (Fig. 1). Tone B (CS−) was never paired with the US. Two-hundred trials of each auditory stimulus type (CS+ paired, CS+ unpaired and CS−) were performed, for a total of 600 trials. The second session entailed an extinction session consisting of 200 presentations each of only the CS+ unpaired (Tone A) and the CS− (Tone B); the US was never presented. The third session was a conditioning session identical to the first session, except

the US median nerve stimulation occurred on the opposite wrist and Tone C and D (of different frequencies) served as the CS+ and CS−, respectively. The fourth session was an extinction session identical to the second, except Tones C and D were used. The order of left/right median nerve stimulation was counterbalanced across subjects. Two pairs of tones (250 Hz and 2000 Hz; 780 Hz and 4000 Hz) were counterbalanced across participants as CS+/CS− pairs for Sessions 1 and 2, or 3 and 4.

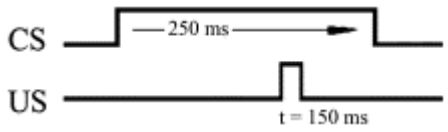

Fig. 1.

Relative timing of stimuli used for conditioning. Presentation of the somatosensory US (20 ms duration) followed the onset of the auditory CS onset by 150 ms.

Data collection

All MEG recordings were performed in a magnetically shielded room at the Rotman Research Institute using a 151-channel whole-head first order axial gradiometer system (VSM-Med Tech Inc., Coquitlam, BC, Canada) with detection coils uniformly spaced 31 mm apart on a helmet-shaped array. Head position within the MEG was determined by monitoring the position of indicator coils on the nasion and bilateral preauricular points, at the start and end of each recording session. Participants sat in a comfortable chair with a screen 28 inches away, and watched a subtitled movie of their choice. Auditory stimuli were presented using pressure transducers (Etymotic Research, Elk Grove, USA) and reflectionless plastic tubes of 2.5 m length connected to foam ear inserts. Median nerve stimulation was administered using a GRASS stimulator device via pairs of electrodes attached to participants' wrists (Grass Technologies, West Warwick, RI, USA). MEG data were collected continuously for 10–15 min with a bandwidth of 0–800 Hz, at a sampling rate of 2500 Hz.

A structural magnetic resonance image (MRI) was obtained for each participant in order to specify/constrain the sources of activation as measured by MEG. Structural MRIs were obtained using standard clinical procedures with a 1.5 T MRI system (Signa EXCITE HD 11.0; GE Healthcare Inc., Waukesha, WI) located at Sunnybrook Health Sciences Centre, or a 3 T MRI system (Siemens Magnetom Trio whole-body scanner) located at Baycrest Centre.

Data pre-processing

Continuously recorded MEG data were parsed into single trials synchronized to the onset of the auditory stimulus. Each trial was 1000 ms in duration and contained a 200 ms pre-stimulus interval. MEG data were baseline corrected based on the pre-stimulus interval. For the conditioning sessions, trials were separated into three datasets based on trial type: CS+ paired, CS+ unpaired, and CS−. For the extinction sessions, trials were separated into two datasets based on trial type CS+ and CS−.

Source analysis

Source activity was estimated using a spatial filtering algorithm called synthetic aperture magnetometry (SAM; [Robinson & Rose, 1992], [Robinson & Vrba, 1999] and [Van Veen et al., 1997]). For a given location in the brain, the SAM spatial filter estimates the time course of source activity within a user-defined frequency band. Based on these band-filtered estimates, the change in source power between two different time intervals ("active" and "control") can be calculated as a pseudo-t statistic (Robinson and Vrba, 1999). This process is repeated across the whole brain on a user-defined grid size to generate a volumetric map of source power change. Alternatively, temporal (Cheyne et al., 2006) and/or spectral ([Bardouille et al., 2006] and [Bardouille and Ross, 2008]) analysis of the estimated source activity can be completed at one location, or in a region of interest, as "SAM virtual channels". The extension of such concepts into five dimensional data analysis, i.e. obtaining time–frequency representations of brain source activity for all volume elements, has been proposed by Dalal et al. (2008). We implemented these approaches when analyzing our data.

We analyzed changes in the cortical beta rhythm during and after the US applied to each wrist in the trials with CS+ paired stimuli. For this analysis, we generated a volumetric SAM pseudo-t map of beta-band power change (15–30 Hz) between a 200 ms interval beginning 50 ms prior to US onset ("active") and an equivalent time interval of the same length immediately prior to auditory stimulus presentation ("control"). A similar volumetric map of changes in beta activity following the US was based on the active interval 150–350 ms after US onset. The individual functional maps were overlaid on the individual participant's structural MRI based on co-registration with the indicator coils placed on the nasion and bilateral preauricular points. The functional data were then transformed to the standard Talairach–Tournoux space, using the same transform applied to the structural MRI (AFNI software, NIMH, Bethesda, MD, USA; Cox, 1996). The resulting spatially normalized volumetric maps of signal power change in the beta frequency band were averaged across the group of subjects. The volume element with global minimum in the group-averaged signal identified the location of beta-band ERD at contralateral SI. The location of maximal effect size in a similar area of the individual's functional map served as a location of interest for estimating the time course of the source activity. These activation time courses, termed virtual channels, were generated for individual CS+ paired trials in the 0–50 Hz frequency range on a subject-by-subject basis.

Time–frequency analysis was performed to examine the temporal dynamics of the estimated source activity. Time–frequency maps were based on a Morlet wavelet with constant number of cycles. This means that the temporal resolution of the spectral analysis was adapted according to the frequency bins respectively. The half intensity width of the wavelet was 208 ms at 10 Hz and 52 ms at 40, which are estimates of the temporal resolution at lower and upper limits of our analysis. These time–frequency maps were calculated in the 10–40 Hz frequency range for each single trial virtual channel data, and then averaged across trials. The signal power change in each time–frequency bin was expressed as the ratio between the averaged power in that bin and the mean spectral power in the baseline interval. These maps of normalized power change at each time–frequency bin were averaged across subjects to estimate a group-averaged normalized spectrogram.

Group-averaged normalized spectrograms at the location of interest identified for CS+ paired were also generated for CS+ unpaired and CS− trials using the same method described above. The spectro-temporal dynamics were compared between CS+ unpaired and CS− trials to identify the time–frequency interval of interest (TFOI) that exhibited the largest difference based on trial type. For CS+ unpaired and CS− trials separately, we generated SAM volumetric maps of source power change comparing the TFOI. Similar maps were generated for the unpaired CS+ trials from the extinction session. The functional data were then transformed to the standard Talairach–Tournoux space. We performed *t*-tests across the group comparing cortical source power between CS+ unpaired and CS− trial types in the conditioning sessions to identify locations that were differentiated by conditioning. We also completed one sample *t*-tests across the group to determine if cortical source power in CS+ and CS− trials in the extinction sessions was significantly different from zero.

Results

Response to CS+ paired with US

SAM analysis revealed prominent desynchronization of beta-band oscillations overlying contralateral postcentral gyrus[1] during the 300–500 ms latency interval following CS+ presentation (150–350 ms following US onset; Fig. 2A). This effect was not as robust during the 100–300 ms latency interval (− 50–150 ms surrounding US onset). Time–frequency analysis revealed that beta ERD began at approximately the time of CS onset (150 ms prior to US onset), and continued to 350 ms following US onset. The epoch containing the largest beta ERD was between 300 and 500 ms following CS onset (150–350 ms following US onset; Figs. 2B,C).

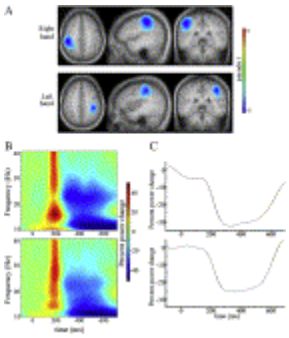

Fig. 2.

Spatial, spectral, and temporal properties of response to CS+ paired with the US (onset = 150 ms following CS onset). A, SAM volumetric maps depicting desynchronization of beta-band activity (15–30 Hz) during the 150–350 ms epoch following US onset (threshold: pseudo-t = ± 2.5); B, Spectrogram depicting the time courses of spectral power changes relative to baseline at the location of peak activation determined from the SAM volumetric analysis. Zero time relates to the onset of the CS. The power increase after US onset (around 200 ms) relates to the somatosensory evoked response; C, Time courses of induced beta-band power changes with evoked responses subtracted out.

The time–frequency analysis also revealed ERS overlying the contralateral postcentral gyrus during the 100–300 ms epoch (− 50–150 ms surrounding US onset; Fig. 2B). This activation was most prominent between 150 and 250 ms following CS onset, or for the first 100 ms following US onset, and corresponds to the somatosensory evoked response (Gaetz and Cheyne, 2003). The waveforms of the evoked response demonstrate that this type of activity was elicited only when the US had been presented (Fig. 3).

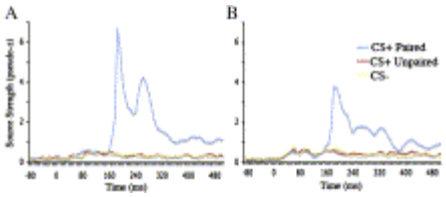

Fig. 3.

Evoked responses within the same location shown in Fig. 2 as determined from the SAM volumetric analysis of the CS+ paired response (time 0 corresponds to auditory CS presentation; time 150 ms corresponds to somatosensory US presentation/omission). Waveforms for CS+ paired, CS+ unpaired and CS− for A, left hand stimulation (right hemisphere), and B, right hand stimulation (left hemisphere).

The signal power of the evoked response was subtracted from the spectrogram (Fig. 2B) in order to separate the time courses of beta desynchronization shown in Fig. 2C (Ross et al., 2005. The interval containing the largest beta ERD was between 300 and 500 ms following CS onset (150–350 ms following US onset).

Event-related beta desynchronization to unpaired stimuli (CS+ unpaired, CS−)

Based on the spatial locations obtained for the CS+ paired, we conducted additional time–frequency analyses for the CS+ unpaired and the CS−. These analyses revealed that beta ERD was present for the CS+ unpaired, with the greatest effect occurring at the same time as found for the CS+ paired, 300–500 ms following tone onset (150–300 ms following the omission of the anticipated US; Fig. 4). We subsequently created SAM volumetric maps of beta ERD during this time interval. *T*-tests revealed greater beta ERD for the CS+ unpaired compared to the CS− overlying both left and right postcentral gyrus (*p*'s = 0.01; Fig. 5).

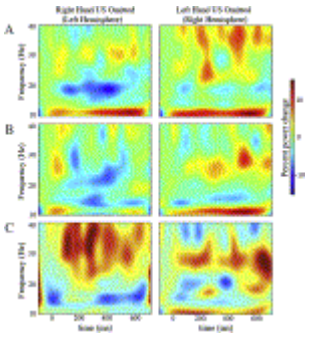

Fig. 4.

Spectrograms depicting time courses of spectral power changes within the same location shown in Fig. 2 as determined from the SAM volumetric analysis of the CS+ paired response (time 0 corresponds to auditory CS presentation; time 150 corresponds to somatosensory US presentation/omission). A, CS+ unpaired during training B, CS− during training and C, CS+ unpaired during extinction.

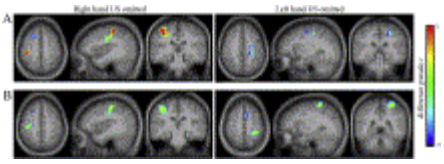

Fig. 5.

T-tests between SAM volumetric maps compare power changes within the 300–500 ms epoch following CS onset (150–350 ms following omission of US). A, training session: CS+ unpaired (US omitted) vs. CS−; B, CS+ unpaired during training session vs. CS+ unpaired during extinction session.

We subsequently created additional whole-head SAM volumetric maps, using the same time interval of 300–500 ms following tone onset for the CS+ unpaired during the extinction session. *T*-tests revealed greater beta ERD for the CS+ unpaired during the conditioning compared to the extinction session overlying both left ($p = 0.003$) and right ($p = 0.006$) postcentral gyrus (Fig. 4).

Comparison between the spectrograms for the CS+ paired with the US in Fig. 2B and the spectrograms for the unpaired stimulus in Fig. 3 reveals that the power change around 200 ms (after US onset) associated with the somatosensory evoked response is absent for the responses to the unpaired stimulus, and the evoked-response waveforms illustrate no differentiation between CS+ unpaired and CS− (Fig. 3).

Discussion

We used MEG to characterize the spectro-temporal dynamics of the neural basis of learning related neural activation within the human somatosensory cortex during classical conditioning. We found that presentations of the auditory CS+ alone, with the somatosensory US omitted, induced greater desynchronization of beta-band activity in contralateral SI compared to presentations of the never-paired CS−. This differentiation between the unpaired CS+ and the CS− was largest between 150 and 350 ms following the omission of the US. The CR was also diminished following an extinction session without reinstatement, as greater beta ERD in contralateral SI was found for presentations of the CS+ alone during the conditioning session compared to during the extinction session. ERS was found only following presentation of the paired CS+ followed by the US, and not following presentation of the unpaired stimuli. These findings were replicated within subjects with two separate unilateral conditioning sessions on opposite body sides.

Our results support and extend the growing body of literature on CRs measured non-invasively directly from the human brain. The occurrence of anticipatory activation within SI elicited by an auditory CS+ adds to the MEG findings of Wik et al. (1996) who demonstrated the presence of SI activation elicited by a visual CS+ just prior to the anticipated arrival of the US, although, in their study the US was never omitted on any CS+ trials. Yágüez et al. (2005), on the other hand, presented CS+ trials with the US omitted in a differential conditioning paradigm, and in agreement with our study, demonstrated that a visual CS+ alone could elicit greater activation within SI compared to a never-paired CS−. However, as this study was conducted using fMRI, the temporal dynamics of this CR following US omission were unavailable.

We found that the differentiation between the unpaired CS+ and CS− occurred during the same time epoch as the maximal response to the US in the paired condition. The timing of this CR is in concert with previous MEG studies demonstrating a greater CR within auditory cortex elicited by a visual CS+ alone compared to a CS−, which occurred at the expected time of a response to the US ([Moses et al., 2005] and [Tesche et al., 2007]). Additionally, the reduction of the CR in our study following an extinction session without reinstatement is similar to previous MEG and fMRI reports ([Moses et al., 2005], [Wik et al., 1997] and [Yágüez et al., 2005]) and the timing of this differentiation between conditioning and extinction, during the epoch of the expected response to the US, is analogous to previous MEG findings within the auditory cortex (Moses et al., 2005).

The presence of activity in SI following omission of a median nerve stimulus is also consistent with previous reports of SI activation following omission of an expected median nerve stimulus during a repeated train of such stimulation (Tesche and Karhu, 2000). However, our study extends these findings by demonstrating that such omission-related SI activation can be elicited by stimulation within a different sensory modality.

Our work also expands the characterization of the neural CR within SI, with the addition of frequency-domain information. We found that the CR was most clearly characterized by beta ERD peaking between 150 and 350 ms after the expected US, rather than the early (20–60 ms) evoked onset response. Both somatosensory evoked responses and ERD are evident in CS+ paired trials, but there is no apparent evoked response in CS+ unpaired and CS− trials. In contrast, the induced response (beta ERD) appears in CS+ unpaired trials, and is diminished in CS− trials. Thus, we found that the cross-modal CR in the sensorimotor system was predominantly characterized by changes in ongoing cortical oscillations in SI, rather than by the early evoked response.

The absence of an evoked response following presentation of the unpaired stimuli found in this study, in contrast to previous reports of evoked CRs following US omission or in anticipation of the US ([Moses et al., 2005], [Tesche et al., 2007] and [Wik et al., 1996]) may be because the attention of the participants in the current study was captured by watching a subtitled movie, whereas in these previous studies the CS employed were visual in nature and hence a movie could not be shown. Thus, in contrast to the current paradigm, in previous work participants were focusing only on stimulus presentation. Evoked responses in multiple sensory modalities have been shown to be substantially larger under conditions of direct attention ([Di Russo et al., 2003], [Giabbiconi et al., 2007], [Kida et al., 2004], [Martínez et al., 2006] and [Poghosyan and

Ioannides, 2008]), and as mentioned previously, the evoked neural CR is smaller than the response to the US, even under conditions of direct attention (Moses et al., 2005). These observations may account for the lack of an evoked CR found in the current study. This pattern of results suggests that induced responses may be more robust indicators of conditioning, and by extension, learning than evoked responses. Future work will examine the differential effects of modulating attention to the stimulus on the evoked and induced CR.

Acknowledgments

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[1] The resolution of the spatial filter of the beamformer may not allow us to dissociate different sources emanating simultaneously from within postcentral vs. precentral gyrus or from within adjacent fissures.