University of Alberta

Electrophysiological Correlates of Multisensory Integration in Peripersonal Space: an Exploration of the Auditory Attention System

by

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Abstract

Neuroscientific investigations of the primate brain point to the presence of multimodal (visual, tactile, auditory) neurons that preferentially code stimuli presented in the space immediately surrounding the body, termed peripersonal space. The activity of these neurons has been shown to facilitate sensory and motor processing to stimuli looming near, or approaching the body. Furthermore, neuropsychological evidence indicates that peripersonal space coding is closely related to the activity of the human attention system. Here we present results from two studies which served to elucidate the differential activity of the auditory attention system in response to peripersonal and extrapersonal stimuli. The data reveal proximity dependent multisensory interactions across early, late, selective and automatic stages of auditory attention processing and further indicate that the peripersonal region of multisensory integration is dynamically linked to the functional (not physical) sphere of the body.

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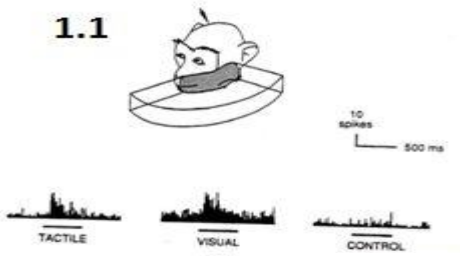
1. The Neurophysiology of Peripersonal Space

Evidence from a variety of fields indicates that the brain represents space in a modular fashion, that is, peripersonal (near) space is coded separately from extrapersonal (far) space (see Holmes & Spence, 2004 for a review). Unlike distant objects, stimuli presented close to the body, within peripersonal space, are coded by a specialized network of multimodal neurons with overlapping tactile, visual and sometimes auditory receptive fields. Single cell recordings in macaque monkeys have identified these “peripersonal space coding” neurons in a variety of brain regions including the premotor cortex, putamen and parietal lobe and have found that the visual and auditory receptive fields extend roughly 10 – 20 cm beyond the somatosensory receptive fields (Graziano, Yap, & Gross, 1994; see figures 1.1 and 1.2). Peripersonal space neurons have been noted for a variety of body parts including the head, arm, shoulder and torso (Fogassi et al., 1996; see figures 1.3 and 1.4). Moreover, many of these neurons have been found to code somatotopically; as the limb moves through space, so too do the visual and auditory receptive fields despite a fixed gaze (Graziano et al., 1994; see figure 1.5). This has also been shown in the absence of vision indicating that many of these neurons integrate proprioceptive (along with visual) cues in order to code the position of the limbs in space (Graziano et al., 1994). By preferentially coding the visual and auditory space immediately surrounding the body in a somatotopic fashion, this fronto-parietal-putamen peripersonal space network mediates attention to near space with the goal of facilitating both sensory processing of near-to-the-body or incoming stimuli and also any responses these stimuli may necessitate. As such, this peripersonal space system provides a neural basis for identifying threats in the environment and defending the body against them (Graziano & Cooke, 2006). Support for this attention mediated multimodal facilitation of sensorimotor processing in peripersonal space has been supported in a wide number or studies using both non-human primates and humans alike (Cooke & Graziano, 2003; Serino, Annella, & Avenanti, 2009).

1.1



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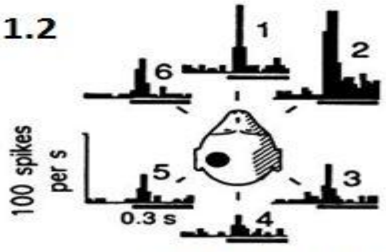

Figure 1.1: Overlapping visual (box) and tactile (shaded area) receptive fields of a peripersonal space neuron found in the macaque putamen. Firing rates are shown below in response to visual stimuli, touch, and visual stimulation while the eyes are closed (control). **Figure 1.2**: Activity of a premotor neuron in response to auditory stimuli presented within peripersonal space of the somatosensory receptive field.

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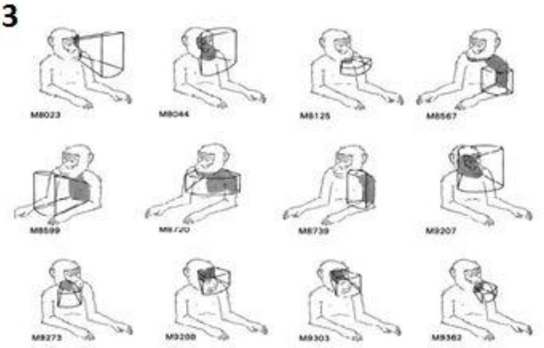

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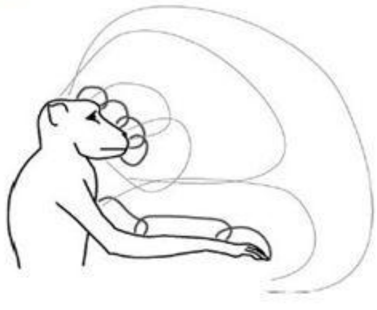


Figure 1.3: Examples of areas for which peripersonal space neurons have been identified. **Figure 1.4:** Peripersonal "bubble" made up of overlapping audio-visual and tactile receptive fields surrounding the monkey.

1.5

Figure 1.5: An example of a visuo-tactile in the macaque putamen showing somatotopic arrangement of the visual receptive field. The visual receptive field moves with the hand regardless of direction of gaze.

While most peripersonal space investigations have been performed in monkeys, in humans, a distinction between peripersonal and extrapersonal space coding has been demonstrated with patients who have parietal cortex damage and present with neglect and tactile extinction (Làdavas, 2002). Neglect is a multisensory disorder of spatial attention where patients have deficits in their awareness of the contralesional side of space. Tactile extinction is a major clinical sign of this disorder where patients are able to feel independently presented tactile stimuli to the hands (for example) but are unable to feel the contralesional stimulus when this stimulus is presented at the same time as a touch to the ipsilesional hand. This extinction effect (inability to feel the contralesional stimulus) is believed to result from unbalanced competition between the left and right hemispheres for limited attentional resources: a touch to the ipsilesional hand captures the bulk of the patient’s attention causing the contralesional stimulus to go unnoticed. While studying this phenomenon, Làdavas and colleagues (Làdavas, di Pellegrino, Farnè & Zeloni, 1998) noted that the extinction effect was not limited to unimodal (tactile-tactile) stimulation; it could, in fact, be replicated by presenting a visual stimulus near to the ipsilesional hand in lieu of a tactile stimulus. Furthermore, they noted that this cross-modal (visuo-tactile) extinction effect was modulated by the stimulus' proximity to the hand: visual stimuli presented at a distance from the hand (30 cm away) were much less likely to overshadow the contralesional touch (Figure 1.6). These effects occur regardless of the position of the hands in space (crossed or otherwise; di Pellegrino, Làdavas, & Farnè, 1997) indicating that the visual-tactile integrative space is anchored to the hands, as it is in monkeys. Overall, this work strongly supports the presence in humans of a multisensory integrative area, or peripersonal space, extending approximately 10 – 20 cm beyond the skin wherein visual stimuli are able to activate a somatosensory representation of the hand. Visual stimuli presented beyond peripersonal space (in extrapersonal space) are coded unimodally and do not activate a somatosensory representation of the hand in the same way that near stimuli can.

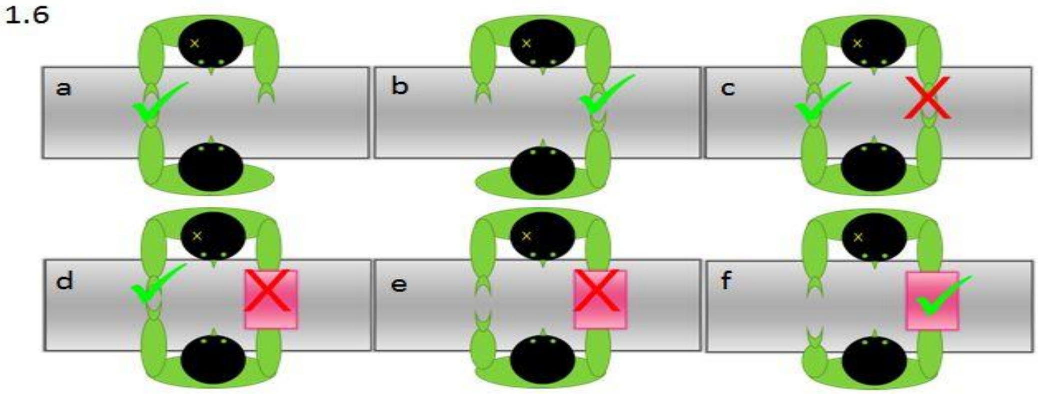


Figure 1.6: Patient (top) and experimenter (bottom) in a typical tactile extinction study. Green checkmark denote perceived touch while red X denotes impaired perception. a) preserved sensation of single touch to the right hand, b) preserved sensation of a single touch to the left hand, c) impaired perception of simultaneously presented touches, d) impaired perception of simultaneously presented touches, e) impaired perception of the left touch when simultaneously presented with a visual stimulus (flexion of the experimenter's left hand towards the patient's right hand) in peripersonal space, f) preserved perception of the left hand touch when simultaneously presented with a visual stimulus in extrapersonal space. Vision of the tactile stimulus was occluded in d, e and f using a shield (red box).

While well established in vision, peripersonal space processing in the auditory modality is less well studied. From work done by Graziano and colleagues (Graziano, Reiss, & Gross, 1999) in macaque monkeys, it is clear that many peripersonal space coding neurons are sensitive to spatial proximity of auditory stimuli. Auditory stimuli presented within 10 cm of the cheek, for instance, result in higher rates of firing in these neurons than stimuli presented in extrapersonal space, regardless of stimulus amplitude. A small number of studies have also noted differential processing to auditory stimuli in peripersonal space in humans. Farnè and Làdavas (2002) for instance found that auditory stimuli presented within peripersonal space of the ipsilesional side of the neck of tactile extinction patients successfully extinguished the perception of a touch to the contralesional side of the neck (Figure 1.7). Despite the relative dearth of research in the auditory modality compared to vision, the available evidence does indicate that auditory cues presented in peripersonal space are able to activate a somatosensory representation of the body in the same way that visual cues can. Peripersonal space therefore can be defined as the space immediately surrounding the body, wherein visual and auditory cues are processed such that they may result in a somatosensory representation of a given body part.

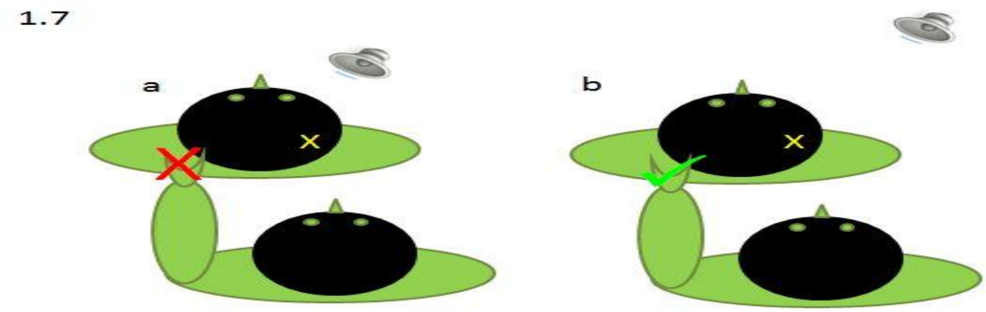


Figure 1.7: a) impaired perception of a contralesional touch to the side of the neck when auditory stimuli are presented within peripersonal space (20 cm) of the ipsilesional side of the head b) preserved perception of a contralesional touch to the side of the neck when auditory stimuli are presented within extrapersonal space (70 cm) of the ipsilesional side of the head.

While peripersonal space processing has been well studied, particularly in monkeys and tactile extinction patients, little is known about the interaction between peripersonal space processing and the intact human attention system.

2. The Attention System

According to Spence & Driver (2004), attention “refers to those processes that allow selective processing of the incoming stimuli, such that those stimuli that are most relevant to current goals or to the on-going task (or those that have the greatest intrinsic salience or biological significance) will get processed more thoroughly than other potentially distracting stimuli” (Spence and Driver, 2004 p.vi). Monitoring the environment in this way can be performed selectively or automatically. Selective attention is considered a controlled, top-down process that permits us to focus on relevant information from the environment while ignoring less relevant information. This is a different process from attentional capture that is more automatic in nature, bottom-up, and allows us to orient to exogenous information (LaBerge, 2002) that is otherwise being ignored. Early research into the nature of attention primarily studied phenomena within a particular sensory modality, such as vision or audition. However, research questions are now being investigated regarding the nature of attention across different sensory modalities. Multisensory integration allows us to identify different sources of input as being associated with a particular object or location. Moreover, it is a process that increases our perceptual sensitivity to stimuli in the environment, and likely operates in a parallel fashion where information from different sensory modalities is integrated at both early and later stages of processing (Driver & Spence, 2000). It is important to note here that early, late, automatic, and selective attention are distinct, yet not mutually exclusive phenomena. For instance, while early sensory responses are oftentimes considered to be automatic in nature, studies have shown that selective attention can modify these processes (Hillyard, Hink, Schwent, & Picton, 1973). Selective attention therefore works at early and later stages of processing and automatic attention may work at early and late stages as well (Näätänen, Kujala, & Winkler, 2011). A major goal of attention research is to reconcile all of these processes into a comprehensive model of human attention.

An important tool in this kind of research has been event-related potentials (ERPs) primarily because their millisecond temporal resolution is well suited to model rapid phenomena that occur at both early and late stages of information processing.

3. Electrophysiological Correlates of Auditory Attention

Derived from averaging together minute changes in electrical activity at the level of the scalp in response to stimuli (events), ERPs offer non-invasive, instantaneous insight into a variety of processes in the brain including memory, language, emotion, sensorimotor integration and attention. Five ERPs are of particular relevance when discussing auditory attention. They are: the N1, P2, N2, the Mismatch Negativity (MMN), and the Negative difference (Nd). Each of these waveforms reflects different levels of attentional processing: The N1 and P2 reflect early more sensory processes, the N2 reflects later, more cognitive processes, the MMN reflects automatic attention and the Nd reflects selective attention. As outlined below in section 4, these waveforms may offer insight into the relationship between the auditory attention system and peripersonal space processing.

The N1 waveform is an early obligatory, stimulus-driven and transient response which results in a negative deflection of the auditory ERP roughly 100 ms post-stimulus. It is indicative of the neural activity underlying the conscious perception of transient sounds in the environment (Näätänen & Picton, 1987) and is sensitive to attentional manipulations (Hillyard et al., 1973). The N1 is believed to consist of 3 separate components, each with its own dedicated neural generator: components 1 and 2 are believed to be generated in the primary auditory and auditory association cortices and mediate attention to the acoustic environment with the goal of creating a sensory memory of incoming auditory stimuli

(Näätänen & Picton, 1987). This sensory memory is crucial in alerting an organism towards what the auditory environment should sound like and acts to filter the passage of auditory information entering conscious awareness. Component 3 on the other hand, is believed to be generated in the premotor cortex and is thought to facilitate motor preparation processes towards auditory, but also tactile and visual stimuli (Näätänen & Picton, 1987). These 3 N1 components can be somewhat distinguished topographically from each other as component 3 is maximally recorded at the vertex while components 1 and 2 are maximally recorded at frontal and temporal sites. The components can be further dissociated by intracranial source localization, as well as their different sensitivities to stimulus features and general state factors of the organism (see Nätäänen & Picton, 1987 for a full and comprehensive review).

The P2 is a positive deflection in the auditory ERP immediately following the N1; it co-varies with the N1 across many stimulus dimensions and was studied as part of a greater N1-P2 complex for many years. More recent research however indicates that the P2 can be distinguished from the N1 under certain experimental manipulations (Oades, Dittmann-Balcar, & Zerbin, 1997). Moreover, while the N1 remains unchanged throughout the life of an individual, the P2 shows age related changes and is influenced by experience such as training (Miller, Rietschel, McDonald, & Hatfield, 2011). The P2 is therefore believed to be influenced by somewhat more cognitive influences than the N1 while still being considered an early exogenous (stimulus-driven) component. Like the N1, its generators are believed to be in the primary and secondary auditory cortices, however the P2 has been dissociated from the N1 both topographically (Roth, Ford, Stephen, & Kopell, 1976; Vaughan, Ritter, & Simson, 1980) and in lesion studies (Knight, Scabini, Woods, & Clayworth, 1988). Compared to the N1, MMN and Nd, little work has been done on the P2 and the functional significance of this waveform remains unclear, however many studies suggest that the P2 reflects auditory sensory discrimination (Novak, Ritter, & Vaughan, 1992), some aspects of stimulus classification (Garcia-Larrea, Lukaszewicz, & Mauguiere, 1992) and overall auditory attentional resource allocation. The P2 is sensitive to attentional load manipulations (Picton & Hillyard, 1974) and is decreased as attentional resources are used up (Miller et al., 2011).

The N2 is a negative deflection in the auditory ERP immediately following the P2. It is a relatively late, endogenous waveform that can be elicited even in the absence of stimulus presentation (when one is expected but does not occur, for instance; Ritter, Simson, Vaughan, & Friedman, 1979). The N2 is associated with categorization and further processing of attended stimulus features (Teder, Alho, Reinikainen, & Näätänen, 1993) and is believed to index pattern recognition (Ritter, Simson, Vaughan, & Macht, 1982), target detection (Ritter et al., 1979) and cognitive control of response inhibition (Kaiser et al., 2006). Like the P2, N2 amplitudes have been shown to increase as task demand increases and it is therefore also believed to reflect auditory attentional resource allocation (Duncan et al., 1994). Its generators are thought to be located in the auditory cortex (Bruneau & Gomot, 1998) but also the anterior cingulate cortex (van Veen & Carter, 2002).

The MMN is closely related to the N1, it reflects the activity of an automatic (outside of awareness) deviance detector in the brain used to update the sensory memory created by components 1 and 2 of the N1 (Näätänen, 2008). Furthermore, upon detecting a change in the auditory environment (a snapping twig in an otherwise quiet forest, for instance) the MMN may create a shift of attention towards the deviant stimulus. These roles are subserved by at least 2 generators, one in the auditory cortex that monitors the environment for change and another in the frontal lobes which mediates the orienting of attention towards the deviant stimulus (Alho, Woods, Algazi, Knight, & Nätäänen, 1994). By monitoring the environment and orienting the organism towards change, the MMN reflects the brain activity underlying the fundamental task of automatically alerting and orienting organisms to potential threat. Studies have even shown that MMN amplitude is enhanced during times when alerting and orienting may need to be facilitated, such as in times stress and in the presence of negatively valenced emotional stimuli (Schirmer & Escoffier, 2010).

The Negative difference (Nd) is a waveform that reflects selectively attending to one’s environment for information pertaining to stimulus parameters such as location, pitch and intensity (Teder et al., 1993). It is reflective of an auditory mechanism that compares the parameters of incoming auditory stimuli to those stored in memory and, unlike the MMN, is not present in cases where attention is directed away from the stimulus of interest.

ERP investigations of the above waveforms and other indicators of the auditory attention system typically employ the auditory oddball paradigm (Figure 3.1). This task consists of a set of non-overlapping, randomly delivered tones presented through 2 speakers placed in front of the participant. Typically, 2 tone types are employed, one standard (90%) and one deviant (10%) that differ from each other in some parameter such as intensity, pitch or location. By designating one speaker to be attended and one to be ignored, 4 discrete tone types are produced (attended and unattended standards as well as attended and unattended deviants) from which we can gain insight into basic auditory processing as well as information pertaining to attentional processes related to overtly orienting to a stimulus as well as processing stimuli that are outside of attentional focus.

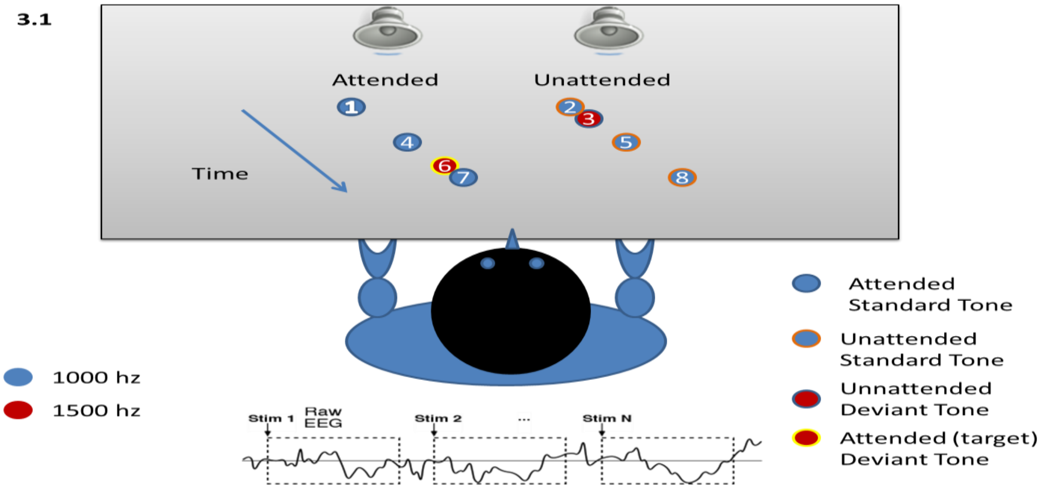


Figure 3.1: Typical auditory oddball paradigm set-up.

4. ERPs and Peripersonal Space

Given the temporal resolution of ERPs and their well-established use as a window into attentional processing, it stands to reason that ERPs may elucidate whether the auditory attention system operates differently to stimuli in peripersonal vs. extrapersonal space. Moreover, given the limitations of studying audition in loud MRI environments, ERP research remains as perhaps the only suitable platform with which to study auditory attention and auditory peripersonal space. Despite this, no experiments to date have employed ERPs to draw connections between attention of any kind (visual or auditory) and peripersonal space processing. In fact, there have only been a few attempts to investigate peripersonal space processing in general using ERPs (Molholm et al., 2002; Sambo & Forster, 2009; Simon-Dack & Teder-Salejarvi, 2008) and these have yet to establish consistent markers of peripersonal space processing. One such attempt was performed by Simon-Dack and Teder-Sälejärvi (2008). In their study, these authors sought to address whether hand position had an effect on auditory processing of stimuli presented in peripersonal space. In order to test this, they had participants sit in a dimly lit room and respond to a fast-paced auditory oddball paradigm similar to that described above. Participants responded to high pitched, attended deviant tones coming from speakers placed on a table at an arm's length away 1) with their hands resting on their lap, 2) with their hands reaching towards (but not touching) the speakers and 3) while holding the speakers. The results indicated an attenuated N2 in the "hold" condition. This finding was explained in terms of proprioceptive (or more accurately, tactile) cues reducing the need for auditory processing that would otherwise be used calculate the spatial coordinates of the stimuli and not in terms of peripersonal space processing *per se*. No other significant differences were found.

The lack of significant ERP differences between conditions in this study is surprising. Given its well established role in indexing activity of the auditory attention system and the known interactions between the attention system and peripersonal space processing, one might expect to see N1 differences between stimuli presented far from the hands (hands down condition) and those presented either near the hands (reach condition) or in the hands. Null results in the N1 may be the result of a number of factors. This experiment, for instance, had no extrapersonal space condition; instead the speakers were placed in the same location throughout all 3 conditions. A lack of N1 effects may therefore be due to the fact that all conditions were technically within peripersonal space of the body. Moreover, the ISI in this experiment (120-360 ms, rectangular distribution) was not ideal for eliciting component 3 of the N1. This component is believed to facilitate motor preparation (Näätänen & Picton, 1987) and could very well index peripersonal space processing in humans under the right experimental conditions. It is known to respond best under conditions of slow rates of stimulation (ideally 4-5 seconds; Nätäänen & Picton, 1987) and thus may have been suppressed under the very rapid stimulus presentation seen in the above study.

This study was also limited in the extent to which it explored the underlying attention mechanisms subserving peripersonal space processing. The MMN and Nd are markers of automatic and selective attention processing respectively and may offer insights into the roles of each type of attention on processing cues in peripersonal versus extrapersonal space. An analysis of these waveforms would be particularly relevant given the dearth of research directly examining the relative contributions of automatic and selective processing in peripersonal space.

The question of whether the deviance detector system reflected by the MMN is preferentially activated by near as opposed to far stimuli, has yet to be investigated but given that stimulus proximity is a likely criterion for appraising the importance of switching attention towards a stimulus (a twig snapping close to you is inherently more important than a twig snapping at a distance), this system may very well be enhanced in response to peripersonal stimuli over extrapersonal stimuli. This idea would fit with work by Farnè, Demattè and Làdavas (2003) who sought to investigate the nature of attentional mechanisms underlying peripersonal space processing using tactile extinction patients. Specifically, they sought to address whether peripersonal space processing was dependent on top-down, selective attention mechanisms, or bottom-up, automatically driven processes. To do this, they used an identical set up to their earlier work investigating crossmodal extinction whereby an experimenter sat across the table from the patient and presented a touch to the left hand at the same time as a visual stimulus (a flexion of the experimenter's finger) towards the right hand (Figure 4.1). The only difference was that in that this case, a clear glass barrier was placed between the visual stimulus and the patient's right hand. In this way, the participant could see the visual stimulus; however, he or she had the conscious understanding that the experimenter's hand could not physically contact his or her own. Despite the explicit understanding that the hand was protected, visual stimuli were still able to activate a somatosensory representation of the hand and produce extinction effects, thus indicating that peripersonal space processing may lie beyond top-down control. Proximity dependent modulations of the MMN would provide strong corroborating evidence for the automatic coding of peripersonal space.

4.1

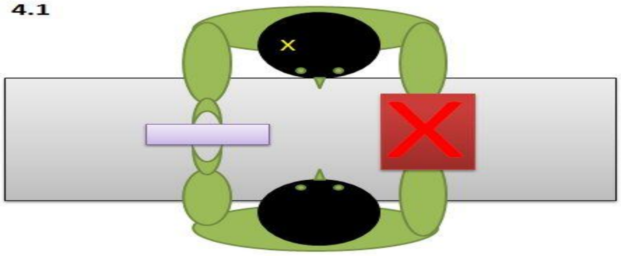


Figure 4.1: Experimental set-up showing the glass barrier between the patient's right hand and the experimenter's left hand.

While Farnè and colleagues (2003) suggest that peripersonal space processing occurs independently of selective attention, it remains unclear whether selective attention plays an important role in peripersonal space processing in neurologically intact persons. As a marker of selective attention that is sensitive to overt spatial orienting of attention (Tata, Prime, McDonald, & Ward, 2001), the Nd stands to inform on this issue. By comparing Nd waveform morphology in response to stimuli presented in peripersonal versus extrapersonal space it may be possible to draw inferences about the role of selective attention during the processing of relevant information in peripersonal space.

Whether the P2 will show any peripersonal space based modulations is difficult to predict given the relative dearth of research specifically exploring this waveform, though a larger P2 in response to peripersonal stimulus presentations would be consistent with early bottom-up processes dominating this type of processing.

Whether the N2 will show any peripersonal space based modulations is also difficult to predict, however, as a more endogenous waveform, we would expect it to be largely resistant to experimental manipulations. One potential difference may be seen in the N2 in response to unattended targets, which is considered to be a reflection of cognitive control of response inhibition (Kaiser et al., 2006). One might expect that given the inherent salience of nearby stimuli, inhibiting responses to tones presented in peripersonal space would be more difficult than to extrapersonal tones. Proximity based modulations of the N2 in response to unattended targets would inform on this issue.

5. General Summary and Primary Research Questions

Based on the forgoing review, the following points regarding the processing of information in peripersonal space have been established. 1) The brain selectively processes the contents of peripersonal space across multiple modalities including audition, vision, and proprioception. 2) The attention system likely plays a primary role in the processing of information within peripersonal space. 3) It is not clear if the voluntary and automatic attention systems are equally implicated in peripersonal space. 4) ERPs may provide a useful means to investigate the nature of peripersonal space processing.

With this in mind, we sought to elucidate the neural mechanisms of multisensory attention in peripersonal space in healthy adult humans using ERP markers of both bottom-up reflexive and top-down voluntary attention recorded during the presentation of auditory stimuli near and far from the body while visual and proprioceptive cues were also varied. This is a novel experimental approach that stands to inform on the nature of visual and proprioceptive influence on early, late, selective, and automatic auditory attention processes. It also stands as one of the first electrophysiological experiments to measure the patterns of activation of the auditory attention system in response to peripersonal and extrapersonal stimulus presentations. These manipulations are based on empirically established properties of both the auditory attention and peripersonal space systems and will offer the first glimpse into the relationship of these two systems.

6. Experiment 1

6.1. Primary Hypotheses

1) Since the auditory attention system interacts with multisensory processing of information in peripersonal space, we expect to see differences in the morphology of the auditory attention ERPs elicited by stimuli in peripersonal space compared to stimuli presented in extrapersonal space. Specifically, we expect that peripersonal stimuli will result in increased N1 and P2 amplitudes as compared to extrapersonal stimuli.

2) Given the strong background support for peripersonal space coding around the hands, we also expect to see differences in the ERPs elicited by stimuli that are near to or far from the position of the participants' hands determined by their own visual and proprioceptive awareness of those positions. Specifically, we expect larger N1 and P2 amplitudes to tones presented next to the hands relative to tones presented far from the hands.

3) Based on previous results with monkeys and neglect patients, we predict that ERP markers of automatic attention will be more sensitive to our manipulations of stimuli within peripersonal space compared to ERP markers of voluntary selective attention. That is, we expect to observe stronger effects in the N1, P2 and MMN waves elicited by unattended stimuli compared to the N1, P2 and Nd waves elicited by stimuli requiring focused selective attention.

4) Given the peripersonal space system's role in facilitating motor responses to stimuli presented near to the body, the final hypothesis of this experiment is that footswitch reaction times to attended target tones will be faster in response to tones presented in peripersonal space relative to those presented in extrapersonal space.

6.2. Methods

Twenty-one healthy right handed volunteer students (12 females, ranging in age from 21 – 27 years) with normal (or corrected to normal) vision and hearing were recruited for this experiment. All participants gave informed consent and ethics approval was obtained from the University of Alberta's Human Research Ethics Committee in accordance with the Declaration of Helsinki. Participants performed an auditory oddball task consisting of 2 pink noise tone types: high pitched infrequent "deviants" (10%) and frequent low pitched "standards" (50 ms bursts, with an average ISI of 700 ms) presented from 2 speakers placed at shoulder's width apart. The speakers were arranged an arm's length away (peripersonal space), or 20 inches beyond this point (extrapersonal space). Participant hand position was manipulated such that they performed the task with each arrangement of the speakers, both with their hands up towards the speakers, and with their hands in their laps (for a total of 4 conditions, see figure 6.2.1). Each condition consisted of 4 blocks of 100 tones. In the 'hands up' conditions participants were instructed to reach towards the speakers as if they were going to grasp them from the outside. To avoid any potential vibrations from the speakers during the 'hands up with speakers in peripersonal space' condition, participants held thin, soft foam pads in their hands throughout the entire experiment. Although each tone type (standard and deviant) was presented through both speakers (though not simultaneously), participants attended only to the left speaker and responded via footswitch to deviant tones presented from that location while ignoring all others. Participants were also asked to fixate on a central point to avoid looking directly at the speakers.

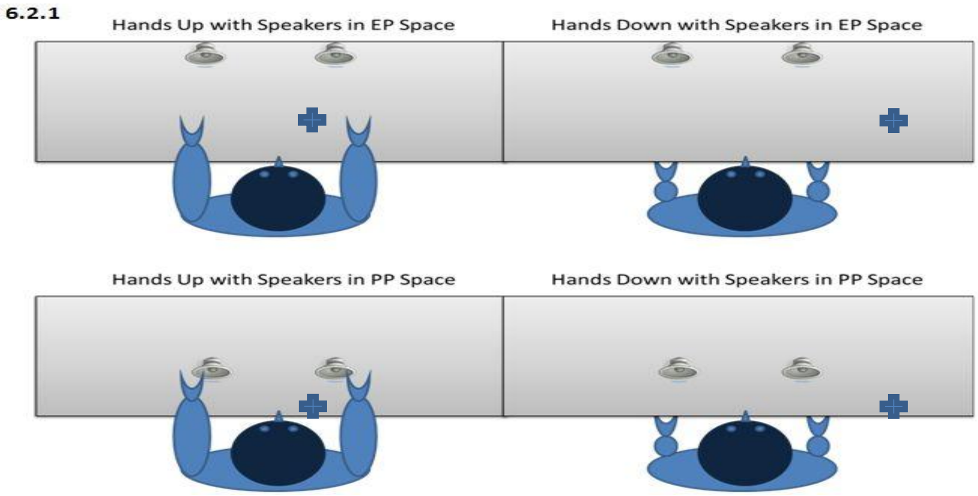


Figure 6.2.1: Experimental set-up for Surdhar and Singhal (in preparation). The '+' notes the area of fixation.

High density ERP recordings were made using the 256 channel Hydrocel Geodesic Sensor Nets® (Electrical Geodesics Inc.) and changes in waveform morphology in response to the auditory stimuli across all 4 conditions were analyzed using Net Station software (version 4.3.1). Data was bandpass filtered from 0.1 hz to 30 hz and was eye corrected using the Gratton method (Gratton, Coles, & Donchin, 1983). Data was collected in 900 ms epochs with a baseline of 100 ms. Impedances were kept below 50 kΩ. Statistical analyses for all electrophysiology and behavioural data consisted of 2 x 2 (space x hand position) repeated measures ANOVAs and all post-hoc planned comparisons were 2-tailed student's t-tests performed between the 'hands up with speakers in peripersonal space' (HUPP) and 'hands up with speakers in extrapersonal space' (HUEP) conditions. It is important to note that sound level was calibrated such that the decibel level registered at the participant's head was the same (64 db) regardless of speaker positioning (peripersonal or extrapersonal space). Differences in tone amplitude were therefore unable to account for any ERP differences found and after reviewing our data we are confident of this.

After visually inspecting the data, ERP time ranges were established for the Net Station “peak picking” software from grand-averaged waveforms. The N1, seen in response to both standard and deviant tone types was defined as the most negative point between 79-179 ms post stimulus. The P2 was identified as the most positive point between 130 - 279 ms and the N2 was identified as the most negative point between 185 - 339 ms. The MMN was isolated by subtracting unattended standard tones from unattended deviant tones and was defined as the most negative peak between 224 – 352 ms post stimulus. The Nd was isolated by subtracting unattended standard tones from attended standard tones and was defined as the most negative peak between 196 – 332 ms post stimulus.

6.3. Results

Figure 6.3.1 shows the mean reaction time (RT), hits and false alarms collected during all four conditions of this experiment. A 2 space (near / far) X 2 hand (up / down) repeated measures ANOVA on these measures revealed no significant differences ($p > 0.05$), however a statistical trend of space ($p = 0.082$) representing decreased RT in the peripersonal conditions was present.

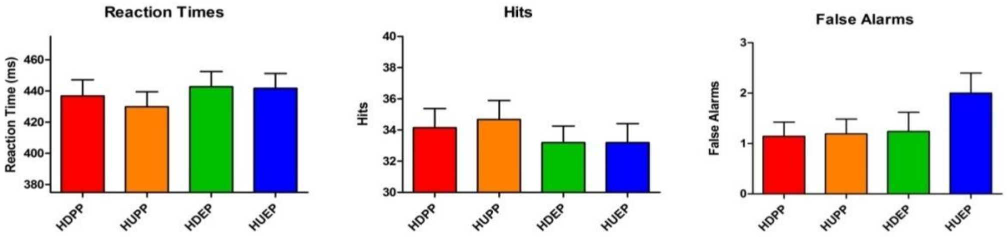
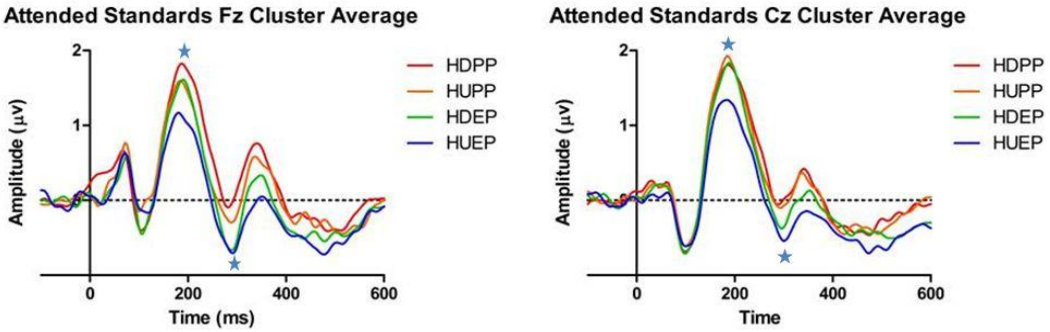


Figure 6.3.1: Mean reaction time (left), hits (centre) and false alarms (right) for footswitch responses across all 4 conditions. Error bars indicate standard error of the mean. Abbreviations: HDPP, hands up with speakers in peripersonal space; HUPP, hands up with speakers in peripersonal space, HDEP, hands down with speakers in extrapersonal space; HUEP, hands up with speakers in extrapersonal space.

The ERP figures below represent grand average data averaged across 3 electrodes. The frontal graph includes the cardinal frontal FZ electrode and adjacent electrodes (left and right) and the central graph includes the cardinal central CZ electrode and adjacent electrodes (left and right).

Attended standards:

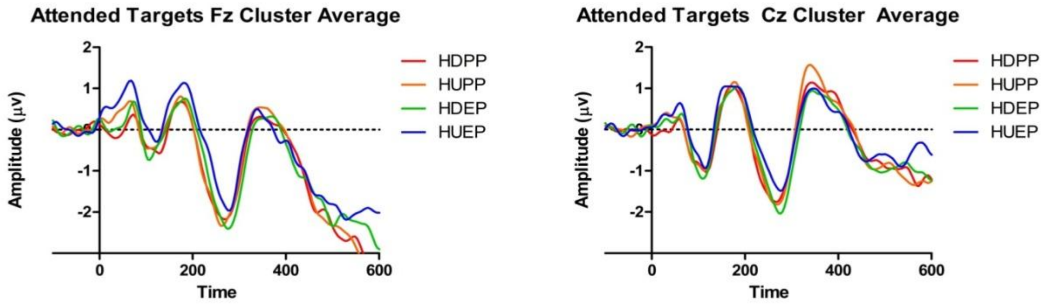
Figures 6.3.2 and 6.3.3 show the grand average waveforms collected at the frontal and central clusters respectively in the four experimental conditions in response to attended standard stimuli. A 2 space (near / far) X 2 hand (up / down) repeated measures ANOVA on these attended standard tones produced no significant N1 effects ($p > 0.05$) at either frontal or central sites. In the P2, a significant effect of space was found both frontally (F (1, 20) = 5.011, p= 0.037) and centrally (F (1, 20) = 8.515, p= 0.009). Post-hoc planned contrasts indicated that these effects were driven by reduced P2 amplitude in the HUEP condition relative to the other 3 conditions, such that the HUEP condition was driving the main effect of space both frontally (p = .015) and centrally (p = .001). In the N2, significant main effects of space were found both frontally (F (1, 20) = 16.595, p = 0.001) and centrally (F (1, 20) =11.887, $p = 0.003$). The N2 was generally larger in response to tones presented in extrapersonal space (FZ: $p = 0.004$; CZ: $p = 0.002$).



Figures 6.3.2 and 6.3.3. Grand averaged data at frontal (left) and central (right) electrode locations in response to attended standard waveforms. * indicates significant differences

Attended targets:

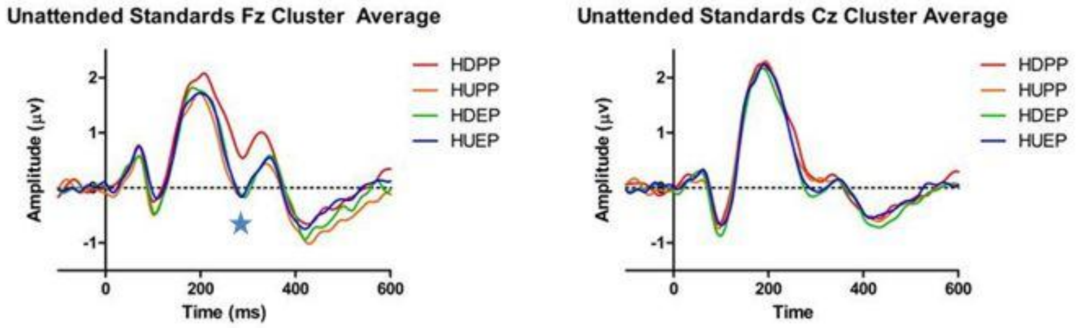
Figures 6.3.4 and 6.3.5 show the grand average waveforms collected at the frontal and central clusters respectively in the four experimental conditions in response to attended target stimuli. A 2 space (near / far) X 2 hand (up / down) repeated measures ANOVA on these revealed no significant effects in response to attended targets at either electrode location, for any waveform of interest ($p > 0.05$).



Figures 6.3.4 and 6.3.5. Grand averaged data at frontal (left) and central (right) electrode locations in response to attended target waveforms.

Unattended standards:

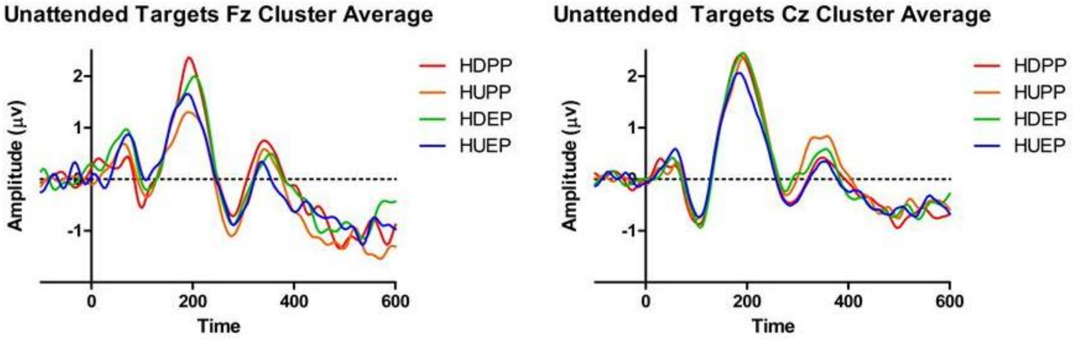
Figures 6.3.6 and 6.3.7 show the grand average waveforms collected at the frontal and central clusters respectively in the four experimental conditions in response to unattended standard stimuli. A 2 space (near / far) X 2 hand (up / down) repeated measures ANOVA revealed a main effect of hands was present in the N2 at the frontal electrode locations (F (1, 20) = 4.554, p = 0.045) as well as an interaction (F (1, 20) = 5.689, p = 0.027). Post-hoc planned comparisons revealed that the interaction was due to a significantly smaller N2 in the HDPP condition relative to the others (p = 0.030). There were no other significant differences in response to unattended standard tones (p > 0.05).



Figures 6.3.6 and 6.3.7. Grand averaged data at frontal (left) and central (right) electrode locations in response to unattended standard waveforms. * indicates significant differences

Unattended targets:

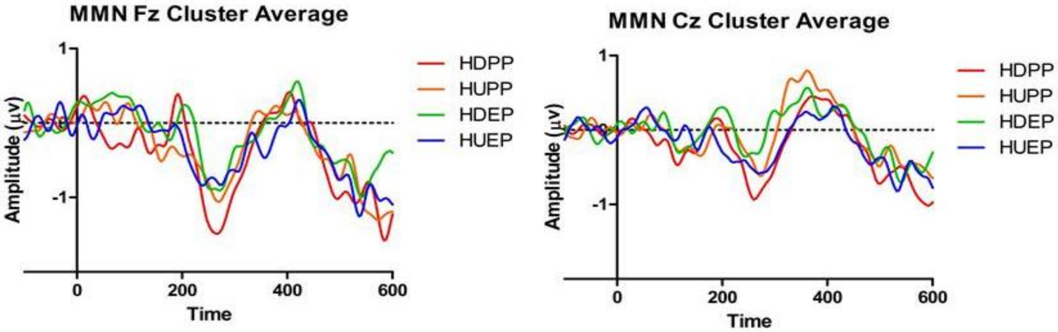
Figures 6.3.8 and 6.3.9 show the grand average waveforms collected at the frontal and central clusters respectively in the four experimental conditions in response to unattended target stimuli. A 2 space (near / far) X 2 hand (up / down) repeated measures ANOVA on these revealed no significant effects (p > 0.05).



Figures 6.3.8 and 6.3.9. Grand averaged data at frontal (left) and central (right) electrode locations in response to unattended target waveforms.

Difference waveforms:

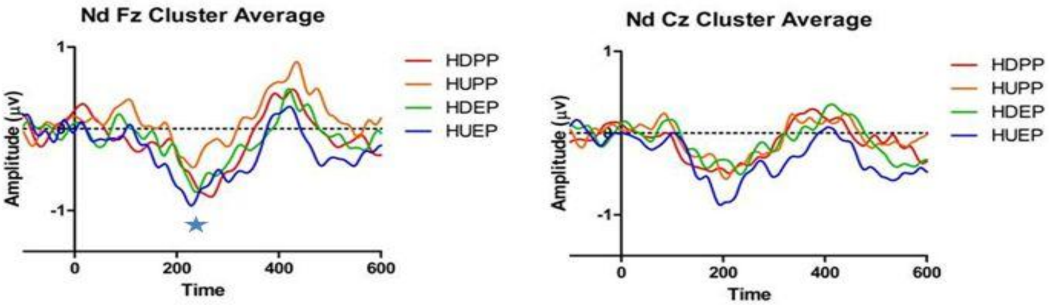
Figures 6.3.10 and 6.3.11 show the grand average Mismatch Negativity waveforms collected at the frontal and central clusters respectively in the four experimental conditions. A 2 space (near / far) X 2 hand (up / down) repeated measures ANOVA on these revealed no significant effects ($p > 0.05$).



Figures 6.3.10 and 6.3.11. Grand averaged Mismatch Negativity data at frontal (left) and central (right) electrode locations.

Figures 6.3.12 and 6.3.13 show the Negative Difference grand average waveforms collected at the frontal and central clusters respectively in the four experimental conditions. A 2 space (near / far) X 2 hand (up / down) repeated measures

ANOVA on these revealed a main effect of space frontally in the Nd (F (1, 20) = 5.203, p = 0.034). Post-hoc planned comparisons revealed that the effect was due to a smaller Nd in response to tones presented in HUPP condition relative to the other 3 (p = 0.014).



Figures 6.3.12 and 6.3.13. Grand averaged Negative difference data at frontal (left) and central (right) electrode locations. * indicates significant differences.

6.4. Discussion

The purpose of this experiment was to explore the activity of the auditory attention system in response to peripersonal and extrapersonal stimuli presentations across, early, late, automatic and selective stages of attentional processing. We further sought to explore whether limb position manipulations would alter the activity of the auditory attention system.

The four main questions addressed were: 1) whether differences in the activity of the auditory attention system can be seen between peripersonal and extrapersonal stimulus presentations 2) whether any differences in the activity of the auditory attention system are further modulated by hand position, 3) whether the engagement of the attention system relies upon selective or automatic mechanisms and 4), whether responses are facilitated to stimuli presented in peripersonal versus extrapersonal space. The data reveal differential activation of early bottom-up and later top-down attentional mechanisms in response to peripersonal vs. extrapersonal stimulus presentations and offer support for some of our hypotheses, but not others.

The P2 is an ERP considered to reflect early selection in the human attention system (Picton & Hillyard, 1974). Larger P2 amplitudes in response to near attended standard tones indicate that peripersonal stimuli recruit more bottom-up attentional resources than do extrapersonal stimuli when the stimuli are attended. This interpretation, however, is complicated by the fact that the effect was seemingly driven by a greatly reduced P2 in response to tones in the HUEP condition. Smaller P2 amplitudes when the hands are up but the speakers are far may represent a tuning of the attention system towards peripersonal space due to hand position thus leaving fewer resources available to process distant tones. This pattern of results suggests that early auditory attentional processes are preferentially engaged to nearby stimulus presentations and suggest further that visual and proprioceptive cues have the ability to modulate these processes. This implies an interesting connection between vision, proprioception and early auditory processing. That is, the auditory attention system is sensitive to sensory input from a combination of visual and proprioceptive sources of information.

The N2 is an ERP that is considered to reflect the voluntary allocation of attentional resources in a top-down fashion (Duncan et al., 1994). While early exogenous auditory responses appear to be preferentially engaged to peripersonal stimuli, these later, more cognitively driven N2 attentional processes seem to be preferentially engaged to extrapersonal stimulus presentations instead, perhaps in order to compensate for reduced bottom-up resource allocation at the level of the P2. Furthermore, while early auditory processing at the level of the P2 appears to be influenced by vision and proprioception, the processes underlying the N2 are seemingly more robust to proprioceptive influence, since in this experiment the N2 effect did not depend on hand position.

In the unattended standards, no significant P2 effects were found, however a smaller N2 at frontal electrodes was noted in response to peripersonal tones while the hands were down. Whether this effect is due to peripersonal space processing *per se*, or a reduction in general arousal is unclear. The N2 is known to fluctuate with task demands (Duncan et al., 1994) and it could be that the HDPP condition is the least taxing. There is no proprioceptive input and (as seen in the attended standard N2) fewer top-down resources are being allocated towards near stimuli.

Our third hypothesis concerned the relative contributions of selective and automatic attentional mechanisms in peripersonal space processing. Derived from subtracting the brain activity in response to unattended standard tones from attended standard tones, the Nd waveform provides a measure of those processes related to selectively attending to a stimulus (Singhal & Fowler, 2004). The Nd analysis revealed a main effect of space driven by smaller amplitudes in the HUPP condition, likely representing a facilitation of selective attention in response to tones that are presented near to the hands. This effect strongly suggests that selective attention mechanisms are relevant in peripersonal space processing.

In order to assess the relative contributions of automatic attention mechanisms, the MMN was investigated. The MMN is derived from subtracting brain activity to unattended standards from unattended targets and likely provides a measure of automatic auditory attention that acts outside of awareness (Näätänen, 1990). A lack of significant MMN effects suggests that (at least in this experimental set-up), automatic processes are not mediating attention to the space surrounding the body. While we can't entirely rule out automatic processes entirely with our experimental set-up, we have demonstrated that peripersonal space processing does involve some selective attention and provides evidence against the prevailing notion of peripersonal space processing as a purely automatic process (Farnè & Làdavas, 2000; Farnè et al., 2003).

Our final hypothesis for this experiment focused on reaction time differences between peripersonal and extrapersonal stimulus presentations. Despite our understanding of peripersonal space processing as a means to facilitate actions to near stimuli, no behavioural effects were evident. The reasons for this are unclear; however we will explore this issue further in section 8.

The results of this experiment were consistent with the premises that auditory peripersonal space processing and attention can be studied using ERPs and that hand position may modulate peripersonal space processing. It shows that stimuli presented in peripersonal space recruit more early attention resources than extrapersonal stimuli and surprisingly that this pattern is reversed once later attention resources are engaged. Moreover, we see that selective attention plays a role in peripersonal space processing. However, our strongest prediction of the N1 as an electrophysiological marker for peripersonal space processing did not bear fruit. The results were also inconsistent with our expectation that automatic attention processes (as indexed by the MMN) would be relevant in peripersonal space processing and that there would be a behavioural facilitation to near tones.

Regardless of these unexpected findings, this study was important for a number of reasons. First, it shows that the pattern of attentional engagement is different in response to extrapersonal vs. peripersonal stimuli and indicates that while others note peripersonal space processing to be an automatic process, selective attention does play a role and is relevant. Moreover, the experimental set-up is novel and potentially relevant for studying auditory spatial attention. A thorough literature review of auditory attention studies that explore the N1, P2, N2, MMN or ND has revealed that the near / far manipulation in this task is unique. The vast majority of studies focusing on auditory spatial attention employ left / right manipulations of attention as opposed to near / far. This may be due to the perceived difficulty of calibrating distant tones to the same dB level as nearby ones, however the morphology of our ERPs suggest that we were successful in doing so using simply an inexpensive handheld sound level meter and a sound attenuating booth.

Overall, our data helps create a model of the human attention system as it relates to peripersonal space processing. This work provides some of the first electrophysiological evidence for differential engagement of the auditory attention system based on stimulus proximity. Moreover, this work provides some support for the notion that selective attention mechanisms are involved in peripersonal space processing at more cognitive stages (though doesn't completely rule out the engagement of automatic processes). This work also serves to establish some methodological and theoretical parameters necessary to study peripersonal space processing in healthy humans. This same method will next be applied to examine new questions pertaining to whether the preferential engagement of attentional resources towards near stimuli is statically confined to the space physically surrounding the body, or whether it is dynamically linked to the functional sphere of the body. This is a particularly relevant question when you consider that humans proficiently alter the functional reach of their limbs using tools such as cooking utensils, musical instruments and sporting equipment every day.

7. Experiment 2

7.1. Investigations of Peripersonal Space Extension

The hallmark study exploring the plasticity of the brain's representation of peripersonal space was performed by Iriki, Tanaka and Iwamura (1996) using single-cell recordings of bimodal visuo-tactile peripersonal space neurons in the intraparietal sulcus (IPS) of Japanese monkeys. These authors sought to explore whether peripersonal space could be extended following goal-directed tool use. They did this by mapping peripersonal space surrounding the monkey’s hands before and after a period of actively using a tool. After identifying the location of somatosensory receptive fields for bimodal visual-tactile neurons in the hand / arm region of the IPS, visual stimuli were presented in the area surrounding these receptive fields such that the location of visuo-tactile integrative space around the hands could be determined. They then had the monkey use a rake to retrieve food pellets placed beyond reach for 5 minutes and re-measured the extent of the visual receptive fields for the same neurons. Prior to tool use, the densest area of excitation closely surrounded the somatosensory receptive field. Following tool use the visual receptive fields were found to enlarge while somatosensory receptive fields remained unchanged. This enlargement occurred along the length of the tool in 29% of the neurons tested (17/59) but lasted only 3 minutes in the absence of active tool use.

Similar effects were found for more proximal neurons with somatosensory receptive fields on the shoulder (as opposed to distal neurons with somatosensory receptive fields on the hands). Prior to tool use the visual receptive fields of these proximal neurons became active when a visual stimulus was presented within reach of the arm. Following tool use, the visual receptive fields of these neurons enlarged beyond the reach of the arm to encompass the entire area within reach of the tool (Figure 7.1). This was found in 25% of the neurons recorded (15/59) and, as with the hand centered neurons, contracted following periods of passively holding the rake. All of these effects occurred regardless of direction of the monkey’s gaze and were independent of any attempt to retrieve the bait. This work provided the first convincing evidence of a tool based extension of peripersonal space.

7.1.1

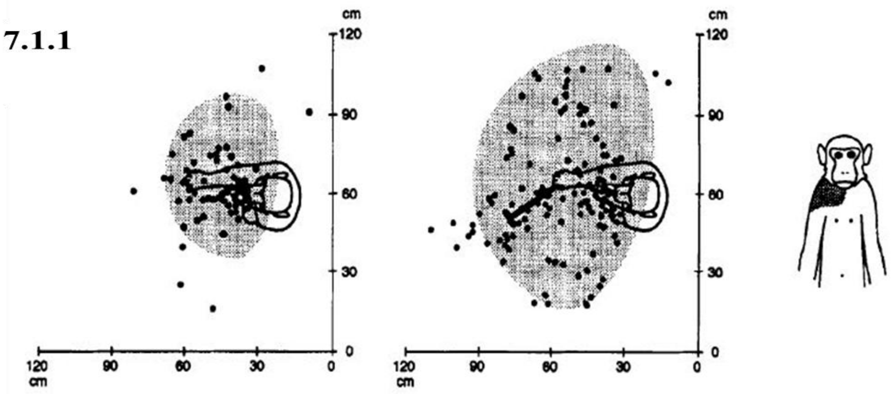


Figure 7.1.1: Peripersonal space for a proximal type neuron prior to tool use (left), peripersonal space for a proximal type neuron, while holding a rake following 5 minutes of actively using the tool (center), somatosensory receptive field (right). Black dots indicate areas wherein visual stimuli were able to elicit firing in the bimodal visuo-tactile IPS neurons.

The first attempt to explore the possibility of peripersonal space extension in humans was performed by Farnè and Làdavas (2000). Given the previously established similarities between monkey and human peripersonal representation around the hand, the authors hypothesized that a dynamic extension of peri-hand space should also be possible in humans. They sought to address this using a modified version of their tactile extinction protocol and hypothesized according to Iriki’s et al.’s (1996) findings that a period of active tool use would extend peripersonal space around the hand such that cross-modal extinction effects could be produced by stimuli presented at a greater distance than previously possible provided the visual stimuli were presented close to the tool (yet far from the hand). Moreover, they hypothesized that any peri-tool crossmodal effects would be short lived, disappearing as the functional manipulation of the environment with the tool ended. As expected, cross-modal extinction was more pronounced in extrapersonal / peri-tool space following 5 minutes of using a rake to retrieve objects placed beyond reach (85 cm) than it was prior to tool use (Figure 7.1.2). In other words, the visual-tactile integrative space surrounding the hand was found to extend following goal-directed tool use. Furthermore, in accordance with Iriki et al.'s work, this effect disappeared within a few minutes of the participant ceasing to use the rake.

7.1.2

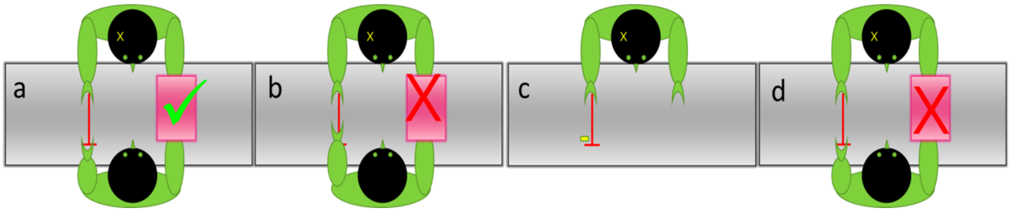


Figure 7.1.2: a) preserved perception of the contralesional touch during simultaneous visual stimulation in extrapersonal / peri-tool space, b) impaired perception of contralesional touch during simultaneous visual stimulation in peripersonal space of the hand while passively holding the tool, c) a 5 minute period of actively using the rake to retrieve blocks placed at 85 cm from the patient, d) impaired perception of the contralesional touch during simultaneous visual stimulation in extrapersonal / peri-tool space following a period of tool use

While this work provides strong evidence for peripersonal space plasticity in humans in the visual modality, it is currently unclear whether auditory attention and peripersonal space processing can also be modified by tool use. Moreover, whether any peripersonal space extension effects are dependent on actively monitoring the proximity of stimuli in relation to the tool being used, or whether these effects are instead mediated by automatic attention mechanisms is uncertain.

7.2. Open Questions and Hypotheses for Experiment 2

Having established that ERPs can be used as a measure of peripersonal space processing in experiment 1, experiment 2 sought to use a variation of the established procedure to explore peripersonal space extension in the auditory modality in a healthy human population. By monitoring auditory attention ERPs in response to tones presented far from the hands compared to tones presented equidistantly from the hands but close to tools (xylophone mallets) before and after tool use, 4 questions were addressed: 1) can auditory peripersonal space be extended by holding tools? 2) Is a period of goal directed tool use necessary to extend peripersonal space? 3) Are extension effects mediated by selective of automatic attention mechanisms? And 4) is there a behavioural facilitation to stimuli presented in peri-tool space?

Specifically, we expected: 1) If the brain considers peripersonal space to be the functional space surrounding the body, as opposed to the space physically surrounding the body proper, then when participants are extending their reach towards speakers using tools, P2 and N2 morphology will be similar to when the tones are being presented within peripersonal space (as seen in experiment 1). Moreover, the relative difference between these conditions and conditions wherein participants are holding their hands out towards speakers that are out of reach will be similar to the differences seen between peripersonal and extrapersonal stimulus presentations in experiment 1. In other words, stimuli presented within peri-tool space are expected to result in larger P2 amplitudes but smaller N2 amplitudes than tones presented at the same physical distance of the hand when tools are not being held.

2) Based on findings by Iriki, Tanaka and Iwamura (1996), and Farnè and Làdavas (2000), we expect that differences between tool and no-tool conditions to manifest only following a period of goal directed use of the tools.

3) Given the selective nature of peripersonal space coding seen in experiment 1, we expect that the Nd will show increased amplitudes to tones presented near the tips of the tools following tool use and that no such changes will be seen in the MMN.

4) Finally, based on the results from experiment 1, we do not expect to see any behavioural differences (RT, hits or false alarms) between tones presented near the tips of the tools versus tones presented at the same physical distance when tools are not being held.

7.3. Methods

Twenty-one healthy right handed volunteer students (12 females, ranging in age from 20 – 28 years) with normal (or corrected to normal) vision and hearing were recruited for this experiment. All participants gave informed consent and ethics approval was obtained from the University of Alberta’s Human Research Ethics Committee in accordance with the Declaration of Helsinki. Participants performed an auditory oddball task consisting of 2 pink noise tone types: high pitched infrequent “deviants” (10%) and frequent low pitched “standards” (50 ms bursts, with an average ISI of 700 ms) presented from 2 speakers placed at shoulder's width apart which were arranged 20 inches beyond arm's reach. Participants performed this task before and after training with their hands held towards the speakers and also with 20 inch long xylophone mallets held towards the speakers. Training involved playing a simple song (happy birthday or twinkle, twinkle little star) on a xylophone for 5 minutes prior to performing the task. Each participant underwent 2 training conditions, one prior to a "hands up" condition and one prior to a "mallets up" condition to ensure that any extension effects were fresh. To avoid the possibility of any lingering extension effects contaminating data following training, the no-training "hands up" and "mallets up" conditions were performed first. The order of these conditions before and after training was counterbalanced. Although each tone type (standard and deviant) was presented through both speakers (though not simultaneously), participants attended only to the left speaker and responded via footswitch to deviant tones presented from that location while ignoring all others. Each condition involved 3 blocks, each consisting of 100 tones. Participants were also asked to fixate on a central point to avoid looking directly at the speakers.

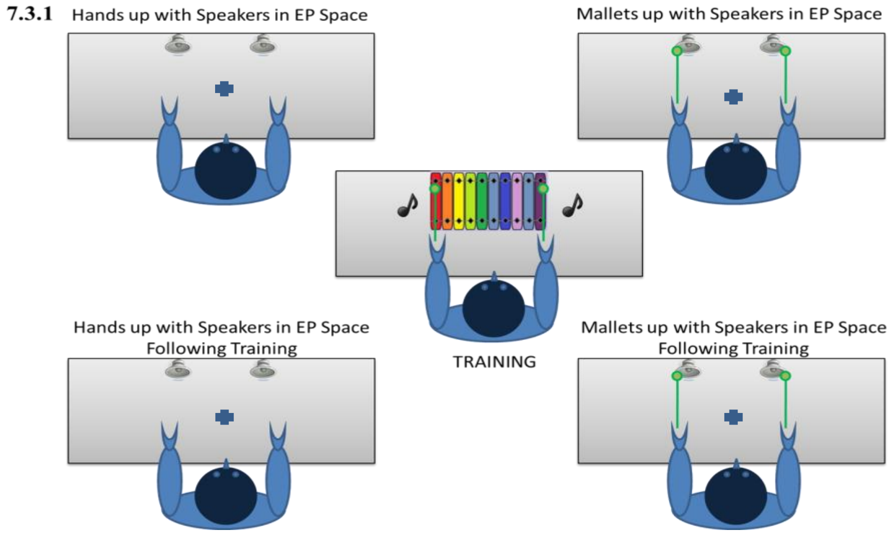


Figure 7.3.1: Experimental set-up for experiment 2. The ‘+’ denotes the fixation point.

High density ERP recordings were made using the 256 channel Hydrocel Geodesic Sensor Nets® (Electrical Geodesics Inc.) and changes in waveform morphology in response to the auditory stimuli across all 4 conditions were analyzed using Net Station software (version 4.4.2). Data was bandpass filtered from 0.1 hz to 30 hz and was eye corrected using the Gratton method (Gratton et al., 1983). Data was collected in 900ms epochs with a 100 ms baseline. Impedances were kept below 50 kΩ. Statistical analyses for all electrophysiology and behavioural data consisted of 2 mallet (mallets / no mallets) x 2 training (training / no training) repeated measures ANOVAs.

After visually inspecting the data, ERP time ranges were established for the Net Station “peak picking” software from grand-averaged waveforms. The N1, seen in response to both standard and deviant tone types was defined as the most negative point between 79-179 ms post stimulus. The P2 was identified as the most positive point between 130 - 279 ms and the N2 was identified as the most negative point between 185 - 339 ms. The MMN was isolated by subtracting unattended standard tones from unattended deviant tones and was defined as the most negative peak between 224 – 352 ms post stimulus. The Nd was isolated by subtracting unattended standard tones from attended standard tones and was defined as the most negative peak between 196 – 332 ms post stimulus.

7.4. Results

Figure 7.4.1 shows the mean reaction time (RT) collected during all four conditions of this experiment, as well as mean hits and false alarms. A 2 mallet (mallets / no mallets) X 2 training (training / no training) repeated measures ANOVA on these measures revealed no significant differences between the conditions ($p > 0.05$).

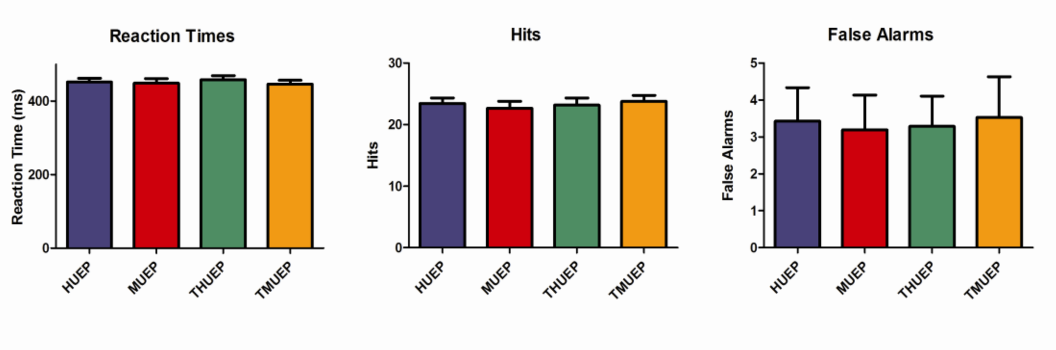
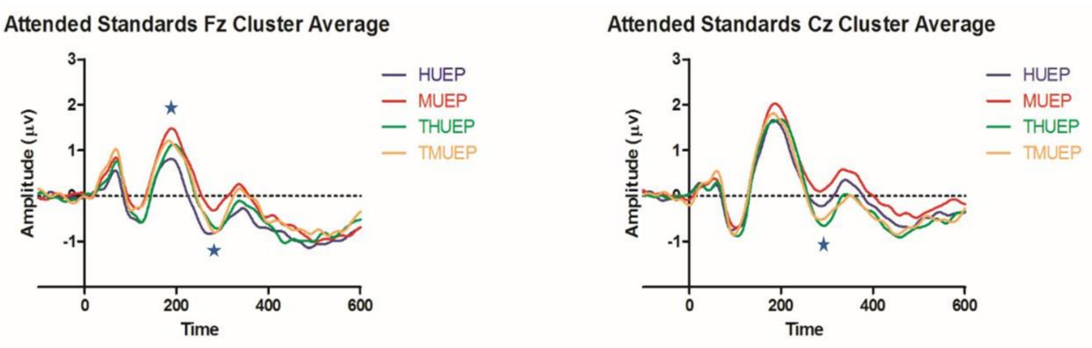


Figure 7.4.1: Mean reaction time (left), hits (centre) and false alarms (right) for footswitch responses across all 4 conditions. Error bars indicate standard error of the mean. Abbreviations: HUEP, hands up with speakers in extrapersonal space; MUEP, mallets up with speakers in extrapersonal space, THUEP, hands up with speakers in extrapersonal space following training; TMUEP, mallets up with speakers in extrapersonal space following training.

The figures below show grand average data averaged across 3 electrodes. The frontal graph includes the cardinal frontal FZ electrode and adjacent electrodes (left and right) and the central graph includes the cardinal central CZ electrode and adjacent electrodes (left and right). ANOVAs performed were 2 mallet (mallet / no mallet) X 2 training (training / no training) repeated measures designs. Post-hoc planned comparisons consisted of 2-tailed student's t-tests.

Attended standards:

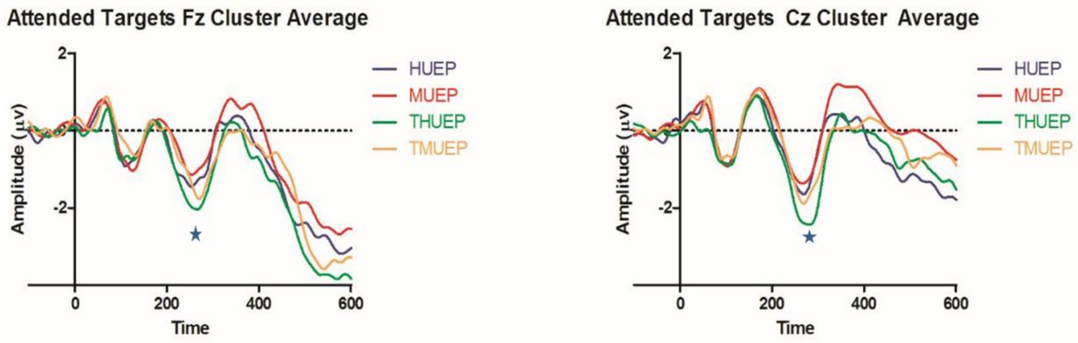
Figures 7.4.2 and 7.4.3 show the grand average waveforms collected at the frontal and central clusters respectively in the four experimental conditions in response to attended standard stimuli. A 2 mallet (mallets / no mallets) X 2 training (training / no training) repeated measures ANOVA on these attended standard tones produced no significant N1 effects ($p > 0.05$) at either frontal or central sites. In the P2, a significant effect of mallets ($F(1, 20) = 4.172$, $p = 0.055$) and an interaction ($F(1, 20) = 5.226$, $p = 0.033$) were found frontally, with no effects at the central cluster ($p > 0.05$). Post-hoc planned comparisons between the HUEP and MUEP conditions indicated that the effects were being driven by a smaller HUEP condition relative to the others ($p = 0.009$). In the N2, a significant main effect of mallets ($F(1, 20) = 7.084$, $p = 0.015$) and an interaction ($F(1, 20) = 5.000$, $p = 0.037$) were found frontally while main effects of mallets ($F(1, 20) = 4.631$, $p = 0.044$) and training ($F(1, 20) = 8.775$, $p = 0.008$) were found centrally. Post-hoc planned comparisons between the HUEP and MUEP conditions indicated that the frontal effects were being driven by a smaller MUEP ($p = 0.003$). At central electrode sites, the main effect of mallets was driven by smaller mallet conditions (p = 0.023) while the main effect of training was driven by larger training conditions (p = 0.001).



Figures 7.4.2 and 7.4.3. Grand averaged data at frontal (left) and central (right) electrode locations in response to attended standard waveforms. * indicates waveforms where significant differences were present.

Attended targets:

Figures 7.4.4 and 7.4.5 show the grand average waveforms collected at the frontal and central clusters respectively in the four experimental conditions in response to attended target stimuli. A 2 mallet (mallets / no mallets) X 2 training (training / no training) repeated measures ANOVA revealed no significant effects in the N1 or the P2 either frontally or centrally (p > 0.05). In the N2, a main effect of training (F (1, 20) = 5.828, p = 0.025) was found frontally while main effects of both mallets (F (1, 20) = 7.355, p = 0.013) and training (F (1, 20) = 6.803, p = 0.017) were found centrally. The frontal effect of training was driven by smaller amplitudes in the HUEP and MUEP conditions relative to the training conditions (p = 0.009). At central electrodes, the main effect of mallets was driven by smaller amplitudes in the mallet conditions relative to the hand conditions (p = 0.048) while the main effect of training was driven by larger amplitudes in the training conditions relative to the no-training conditions (p = 0.013)



Figures 7.4.4 and 7.4.5. Grand averaged data at frontal (left) and central (right) electrode locations in response to attended target waveforms. * indicates waveforms where significant differences were present.

Unattended standards:

Figures 7.4.6 and 7.4.7 show the grand average waveforms collected at the frontal and central clusters respectively in the four experimental conditions in response to unattended standard stimuli. A 2 mallet (mallets / no mallets) X 2 training (training / no training) repeated measures ANOVA revealed no significant differences in any waveforms in response to unattended standard tones ($p > 0.05$), at either electrode location.

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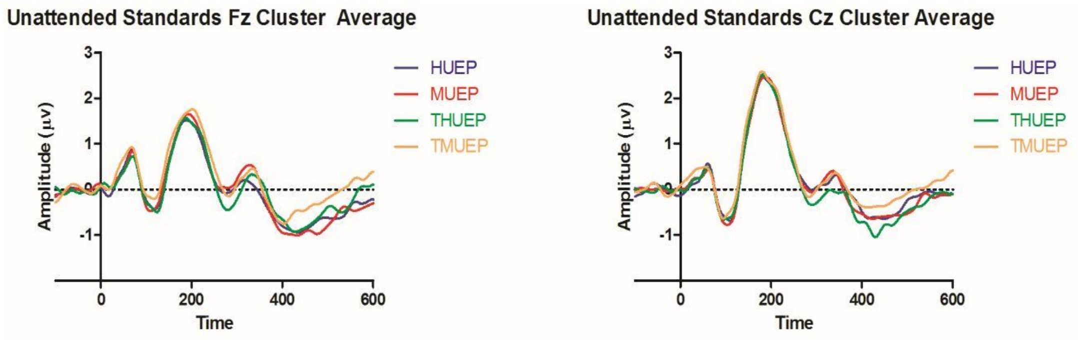
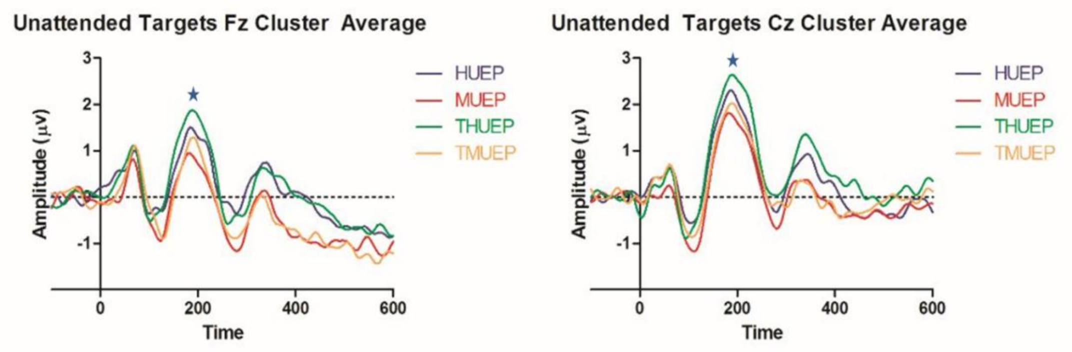


Figures 7.4.6 and 7.4.7. Grand averaged data at frontal (left) and central (right) electrode locations in response to unattended standard waveforms. * indicates waveforms where significant differences were present.

Unattended targets:

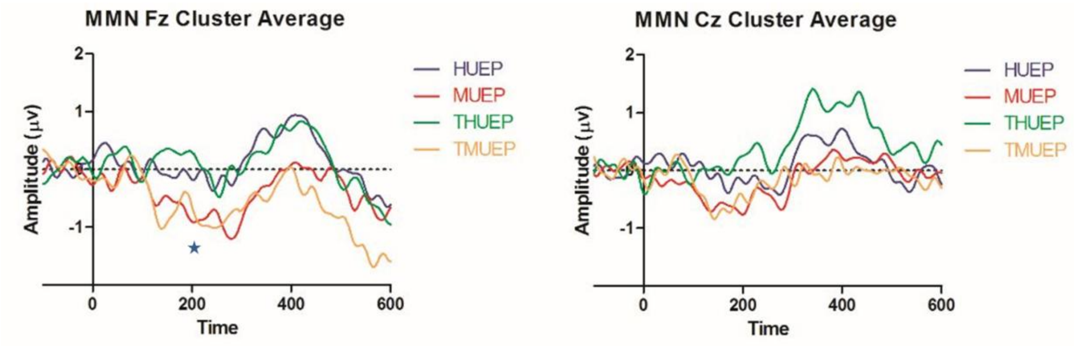
Figures 7.4.8 and 7.4.9 show the grand average waveforms collected at the frontal and central clusters respectively in the four experimental conditions in response to unattended target stimuli. A 2 mallet (mallets / no mallets) X 2 training (training / no training) repeated measures ANOVA on these measures revealed no significant effects in the N1 ($p > 0.05$), however main effects of both mallets ($F(1, 20) = 4.765$, $p = 0.041$) and training ($F(1, 20) = 5.493$, $p = 0.03$) were found in the P2 at frontal locations. Main effects of mallets ($F(1, 20) = 4.569$, $p = 0.045$) and training ($F(1, 20) = 6.73$, $p = 0.017$) were also found centrally. Post-hoc tests reveal that the main effect of mallets at the frontal electrode locations was driven by smaller amplitudes in the mallet conditions relative to the no-mallet conditions ($p = 0.031$) and that the training effect was driven by larger amplitudes in the 'hands up with speakers in extrapersonal space following training' (THUEP) condition relative to the others ($p = 0.004$). Post-hoc tests for the central electrode location reveal identical findings. The main effect of mallets was driven by smaller amplitudes in the mallet conditions relative to the no-mallet conditions ($p = 0.042$) and the training effect was driven by larger amplitudes in the THUEP conditions relative to the others ($p = 0.007$). There were no effects N2 effects in the unattended targets ($p > 0.05$).



Figures 7.4.8 and 7.4.9. Grand averaged data at frontal (left) and central (right) electrode locations in response to unattended target waveforms. * indicates waveforms where significant differences were present.

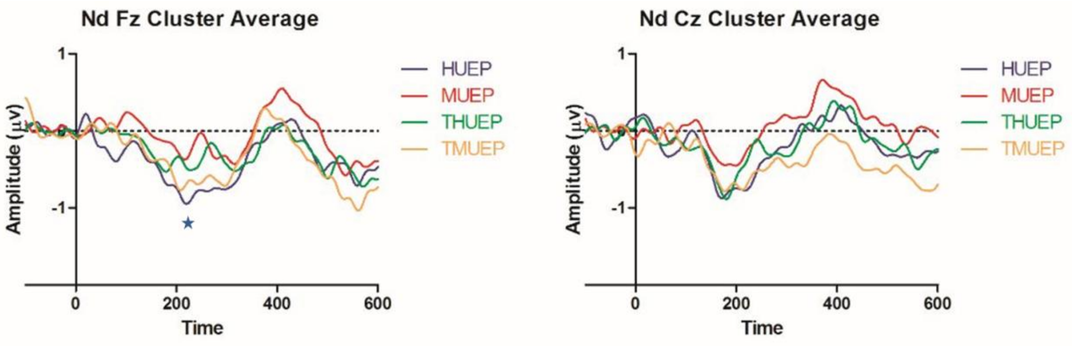
Difference waveforms:

Figures 7.4.10 and 7.4.11 show the grand average Mismatch Negativity waveforms collected at the frontal and central clusters respectively in the four experimental conditions. A 2 mallet (mallets / no mallets) X 2 training (training / no training) repeated measures ANOVA revealed a main effect of mallets was found in the MMN frontally (F (1, 20) = 5.191, p = 0.034) with no effects centrally (p > 0.05). Post-hoc tests reveal that the main effect of mallets was driven by larger MMN amplitudes in the mallet conditions relative to the no-mallet conditions (p = 0.008).



Figures 7.4.10 and 7.4.11. Grand averaged Mismatch Negativity data at frontal (left) and central (right) electrode locations.* indicates waveforms where significant differences were present.

Figures 7.4.12 and 7.4.13 show the Negative Difference grand average waveforms collected at the frontal and central clusters respectively in the four experimental conditions. A 2 mallet (mallets / no mallets) X 2 training (training / no training) repeated measures revealed an interaction frontally in the Nd (F (1, 20) = 4.604, p = 0.044) with no effects centrally. Despite the interaction, 2-tailed student's t-test post-hoc comparisons revealed no significant differences among conditions in the Nd.



Figures 7.4.12 and 7.4.13. Grand averaged Negative difference data at frontal (left) and central (right) electrode locations.* indicates waveforms where significant differences were present.

7.5 *Discussion*

The purpose of this experiment was to explore tool use dependent changes in the activity of the auditory attention system in response to peripersonal and extrapersonal stimuli across, early, late, automatic and selective stages of attentional processing. This experiment built on findings in experiment 1 and specifically sought to explore 1) whether auditory peripersonal space extends following tool use, 2) whether extension is dependent upon a period of active tool use 3) whether extension effects are mediated by selective or automatic attention mechanisms and 4) whether there is a behavioural facilitation to stimuli presented in peri-tool space. Moreover, as in experiment 1, the interaction of attention with information in the auditory, visual and proprioceptive modalities was of particular interest. The present study corroborates many of our findings from experiment 1 and helps inform on the nature of tool based extensions of peripersonal space. The morphology of auditory attention ERPs reveal both peripersonal space extension effects as well as training related plasticity in the auditory attention system.

In experiment 1, we saw that extrapersonal stimulus presentations resulted in less bottom-up attentional resource allocation, but more top-down resource allocation in response to attended standard stimuli. In support of hypothesis 1, similar effects can be seen in the P2 and N2 in experiment 2. Like in experiment 1, we see a main effect of mallets (space in experiment 1) in the P2 driven by smaller amplitudes in the HUEP condition. This identical pattern of effects supports the notion of proprioceptive input tuning the attention system into the space around the hands and suggests that the auditory attention system, at an early level of processing (reflected in the P2), is coding the space surrounding the mallets as it was the space surrounding the hands in experiment 1. This in and of itself supports the notion that peripersonal space can be extended using tools. Moreover, the N2 (a marker of later, more endogenous attention) in response to both attended standards and targets at central electrodes is smaller during the mallet conditions, supporting findings from experiment 1 that extrapersonal stimuli receive greater top-down resource allocation than do peripersonal stimuli.

Interestingly, most early attentional (P2) resources were engaged during the mallets-up condition as opposed to the ‘training mallets-up’ condition. This is incongruent with hypothesis 2 since it suggests that the re-orienting of early auditory attention to peri-tool space is automatic and does not require a period of goal directed tool use. This finding is surprising since the neurophysiological and neuropsychological literature indicates that a period of goal directed tool use is required to extend peripersonal space (Iriki et al., 1996; Làdavas, 2002). Humans are particularly adept at altering the functional region of our bodies; we do so with tools such as rakes, violin bows and hockey sticks on a day-to-day basis. This fact may explain differences between our data and monkey neurophysiology findings given that monkeys do not share this same propensity towards tool use. In our study, it may also be the case that since the mallets are tools that many people have some experience with, there may be some highly automatic extension of peripersonal space that has developed since childhood.

Reconciling our findings with Farnè and Làdavas’ (2000) work is more difficult; however the fact that our data was collected using healthy participants as opposed to patients with a known attentional disorder cannot be overlooked. This is particularly true when you consider the nature of parietal damage induced deficits such as apraxia. It could be that Farnè and Làdavas’ (2000) patients lost the highly automatic peripersonal space extension effects seen in our participants with their brain damage and need to re-establish the functional link between the tool and its affordance before the tool can be integrated into the body schema. To better approximate the neuropsychological patient data, future studies could employ “pseudo-tools” that would require neurologically intact participants to train prior to making a functional connection between the tool and its affordance (a limp tube with which you must move objects placed on a table, for instance). We should also note that peripersonal space extension effects in the monkey and tactile extinction literatures involved visual peripersonal space, whereas our findings were reflected in the auditory domain. However, why training would be necessary to extend visual peripersonal space but not auditory is unclear, particularly when our experiment had such a strong visual component.

Though we weren’t explicitly looking at the impact of training on the auditory attention system, such effects were evident in this experiment. Most notably, we see training effects at the N2 in response to both attended standards and targets. Because of the known lingering of peripersonal space extension effects, the training conditions were always done after the no-training conditions, thus, we can’t be certain whether these training effects are due explicitly to playing the xylophone, or are instead related to practice effects. Disentangling these two possibilities will require future work.

While we can’t definitively establish the extent to which the auditory attention system can be modulated by tool use, a significant interaction in the Nd hints at the possibility that selective attention may be altered by the presence of tools. This remains speculatory however, since a lack of differences across conditions in the ERPs to unattended standards means that the pattern of results in the Nd are being driven almost exclusively by the ERPs in response to attended standard tones. The Nd data therefore becomes simply a restatement of the early attention P2 effects seen in response to the attended standard tones and cannot be used to draw conclusions about those selective attention processes typically associated with the Nd. Future work will be necessary to establish a relationship between the Nd and tool-based extensions of peripersonal space.

Despite a lack of MMN effects in experiment 1, the data from this experiment indicate that extending one's reach with tools may alter automatic attention. Two related results represent this fact. We see a smaller P2 in response to unattended target tones presented near the mallets than the hands, indicating decreased bottom-up attentional resource allocation to unattended tones far from the hands. The fact that this effect is present in an early waveform like the P2 and that there is no such effect in the unattended standard waveforms, implies that this is likely an early, unattended target (or deviance) processing phenomenon, much like that indexed by the MMN. As we look to the MMN, we see that it is indeed preferentially enhanced to tones presented near the tips of mallets. This pattern is consistent with automatic attention processes mediating the identification of the spatial proximity of objects and fits with the previously discussed tactile extinction literature (Farnè et al., 2003) which suggests that peripersonal space is coded without input from top-down processes. Moreover, it is the first electrophysiological evidence to indicate that peri-tool space is coded (at least partially) by automatic mechanisms. The reason for the discrepancy in the MMN between experiments 1 (no effects) and 2 (tool effect) is unclear, but it seems reasonable to assume that the tools are somehow able to draw more automatic spatial attention resources relative to the hands from brain regions underlying the MMN. This may be related to particularly strong visual salience of the tools compared to the hands and we hypothesize that the effect is due to increased activity in the dorsolateral prefrontal cortex (an MMN generator; Alho, et al., 1994), that has been implicated in spatial attention (Hoshi, 2006). Without training effects in the MMN, it follows that these tool based modulations of the deviance detector system indexed by the MMN occurs automatically and is not due to actively manipulating the environment with the tools.

Taken together, the ERP data above demonstrate that the auditory attention system can be modulated at various stages of processing by tool use such that stimuli in peri-tool space are generally processed in a similar manner to peripersonal stimuli. This is particularly evident at early stages of attention (reflected in the P2) and late stages (reflected in the N2). Moreover, strong similarities between peripersonal and peri-tool space processing exist in the activity of the selective attention system. The only major discrepancy in attention activity between peripersonal and peri-tool stimuli occurs in the automatic attention system. Here we see that automatic processes are engaged to a larger extent in response to peri-tool stimuli vs. peripersonal stimuli. Some caveats to this interpretation are presented in section 8, however.

Finally, in support of our 4th and final hypothesis, we did not see any behavioural facilitation towards tones near the tips of the mallets. This is consistent with experiment 1 and bears further explanation below.

8. Final Thoughts and Future Directions

The two studies outlined in this thesis represent 1) one of the first explorations of peripersonal space processing using ERPs, 2) the first experiment to explicitly explore the relationship between the auditory attention system and peripersonal space processing 3) the first experiment to explore the relationship between tool use, peripersonal space processing and the auditory attention system, and 4) a new methodological avenue from which to explore peripersonal space processing in a healthy human population.

Given that this work is novel and relatively untested, the conclusions noted above must be considered as preliminary, however the consistency of results between the two experiments allows us to make reasonable inferences that peripersonal stimuli are allocated more early, bottom-up attentional resources than are extrapersonal stimuli. Extrapersonal stimuli, in turn are allocated more late, top-down attentional processes. Moreover, as seen in experiment 2, these effects are not confined to the space physically surrounding the body, but are instead linked to the functional sphere of the body.

The above experiments also demonstrate that, despite work done with monkeys and tactile extinction patients, selective attention plays a role in peripersonal space processing in healthy humans. From the work of others, we acknowledge that automatic attention processes do play a role in peripersonal space processing, however not exclusively. And while our first experimental set-up showed no automatic attention process engagement in peripersonal space processing, our tool experiment did demonstrate that automatic mechanisms are preferentially engaged to tones presented within peri-tool space. Although MMN differences between the two experiments may be related to tool use, we note that experiment 1 involved both visual (near / far) and proprioceptive (hands up / hands down) signal manipulations while experiment 2 employed no visual manipulations; instead the speakers remained in the same location throughout the task. This meant that in experiment 1, the speakers were placed at a wider visual angle (and therefore more peripheral) in the peripersonal conditions relative to the extrapersonal space conditions, while the visual angle remained constant in experiment 2 and was more central overall. The different MMN effects may thus be related to stronger visual activation in the tool experiment and hence stronger visual influence on the auditory attention system. Whether the MMN effects seen in experiment 2 are related explicitly to differential engagement of automatic mechanisms to peri-tool space as opposed to peri-hand space will therefore require further work using modified methods that will control for visual information.

Despite the potential issue of a visual confound, the main premise that we could examine peripersonal space processing by introducing stimuli in near and far space while controlling stimulus amplitude was successful. While the morphology of our waveforms suggests that the decibel level calibration was very effective in experiment 1, this was only a first step in establishing the use of this experimental protocol in peripersonal space research. Future work will be necessary to determine the optimal experimental protocols which will be able to maximize both attention effects and effects related specifically to peripersonal space processing. Such adjustments will be necessary to properly examine our hypothesis of the N1 being a marker for differential activity in the auditory attention system in response to peripersonal and extrapersonal stimuli. Despite not seeing any significant N1 effects in these experiments, the unattended target data in experiment 2 did show larger N1's in response to peri-tool stimuli, moreover, preliminary data in experiment 1 at times showed a peri-hand effect as well. Since the hypothesis of component 3 of the N1 being a marker of peripersonal space processing is predicated on peripersonal space processing being useful for facilitating behavioural responses, a lack of reaction time differences between peripersonal / peri-tool and extrapersonal conditions may account this null result. Future work will be necessary to alter the experimental protocol in such a way that behavioural differences can be seen. This may involve making the oddball task more difficult, adjusting the ISI to better accommodate the activity of component 3, or perhaps having participants respond using small hand held devices as opposed to responding with the foot. Foot responses are not typically associated with auditory stimuli and the need to activate a large number of muscles (both big and small) in order to push the footswitch introduces response time variability that may have washed out potential ERP effects.

Overall, our data helps create a model of various levels of the human attention system as it relates to peripersonal space processing. This work provides some of the first electrophysiological evidence for differential engagement of the auditory attention system based on stimulus proximity and represents the first human electrophysiological evidence for tool-based extensions of peripersonal space. Moreover, it raises interesting questions about the relative contributions of selective and automatic attention mechanisms in peripersonal space processing. Most importantly though, this work also serves to establish some methodological and theoretical parameters necessary to study peripersonal space processing in healthy humans and will serve as a strong stepping stone for future work of this nature.

9. References

Alho, K., Woods, D. L., Algazi, A., Knight, R. T., & Nätäänen, R. (1994). Lesions of frontal cortex diminish the auditory mismatch negativity. *Electroencephalography and Clinical Neurophysiology, 91*(5), 353-362.

Bruneau, N, & Gomot, M. Auditory evoked potentials (N1 wave) as indices of cortical development throughout childhood. (1998). In N. B. Garreau (Ed.), Neuroimaging in Child Neuropsychiatric Disorders, Springer-Verlag, New-York, pp. 113–124

Cooke, D. F., & Graziano, M. S. (2003). Defensive movements evoked by air puff in monkeys. *Journal of Neurophysiology, 90*(5), 3317-3329.

di Pellegrino, G., Làdavas, E., & Farnè, A. (1997). Seeing where your hands are. *Nature, 388*(6644), 730.

Driver, J., & Spence, C. (2000). Multisensory perception: beyond modularity and convergence. *Current Biology: CB, 10*(20).

Duncan, C. C., Rumsey, J. M., Wilkniss, S. M., Denckla, M. B., Hamburger, S. D., & Odou-Potkin, M. (1994). Developmental dyslexia and attention dysfunction in adults: brain potential indices of information processing. *Psychophysiology, 31*(4), 386-401.

Farnè, A., Dematte, M. L., & Làdavas, E. (2003). Beyond the window: multisensory representation of peripersonal space across a transparent barrier. *International Journal of Psychophysiology : Official Journal of the International Organization of Psychophysiology, 50*(1-2), 51-61.

Farnè, A., & Làdavas, E. (2000). Dynamic size-change of hand peripersonal space following tool use. *Neuroreport, 11*(8), 1645-1649.

Farnè, A., & Làdavas, E. (2002). Auditory peripersonal space in humans. *Journal of Cognitive Neuroscience, 14*(7), 1030-1043.

Fogassi, L., Gallese, V., Fadiga, L., Luppino, G., Matelli, M., & Rizzolatti, G. (1996). Coding of peripersonal space in inferior premotor cortex (area F4). *Journal of Neurophysiology, 76*(1), 141-157.

Garcia-Larrea, L., Lukaszewicz, A. C., & Mauguiere, F. (1992). Revisiting the oddball paradigm. Non-target vs neutral stimuli and the evaluation of ERP attentional effects. *Neuropsychologia, 30*(8), 723-741.

Gratton, G., Coles, M. G., & Donchin, E. (1983). A new method for off-line removal of ocular artifact. *Electroencephalography and Clinical Neurophysiology, 55*(4), 468-484.

Graziano, M. S., & Cooke, D. F. (2006). Parieto-frontal interactions, personal space, and defensive behavior. *Neuropsychologia, 44*(13), 2621-2635.

Graziano, M. S., Reiss, L. A., & Gross, C. G. (1999). A neuronal representation of the location of nearby sounds. *Nature, 397*(6718), 428-430.

Graziano, M. S., Yap, G. S., & Gross, C. G. (1994). Coding of visual space by premotor neurons. *Science (New York, N.Y.), 266*(5187), 1054-1057.

Hillyard, S. A., Hink, R. F., Schwent, V. L., & Picton, T. W. (1973). Electrical signs of selective attention in the human brain. *Science (New York, N.Y.), 182*(4108), 177-180.

Holmes, N. P., & Spence, C. (2004). The body schema and the multisensory representation(s) of peripersonal space. *Cognitive Processing, 5*(2), 94-105.

Hoshi, E. (2006). Functional specialization within the dorsolateral prefrontal cortex: a review of anatomical and physiological studies of non-human primates. *Neuroscience Research, 54*(2), 73-84.

Iriki, A., Tanaka, M., & Iwamura, Y. (1996). Coding of modified body schema during tool use by macaque postcentral neurones. *Neuroreport, 7*(14), 2325-2330.

Kaiser, S., Weiss, O., Hill, H., Markela-Lerenc, J., Kiefer, M., & Weisbrod, M. (2006). N2 event-related potential correlates of response inhibition in an auditory Go/Nogo task. *International Journal of Psychophysiology : Official Journal of the International Organization of Psychophysiology, 61*(2), 279-282.

Knight, R. T., Scabini, D., Woods, D. L., & Clayworth, C. (1988). The effects of lesions of superior temporal gyrus and inferior parietal lobe on temporal and vertex components of the human AEP. *Electroencephalography and Clinical Neurophysiology, 70*(6), 499-509.

LaBerge, D. (2002). Attentional control: brief and prolonged. *Psychological Research, 66*(4), 220-233.

Làdavas, E. (2002). Functional and dynamic properties of visual peripersonal space. *Trends in Cognitive Sciences, 6*(1), 17-22.

Làdavas, E., di Pellegrino, G., Farnè, A., & Zeloni, G. (1998). Neuropsychological evidence of an integrated visuotactile representation of peripersonal space in humans. *Journal of Cognitive Neuroscience, 10*(5), 581-589.

Miller, M. W., Rietschel, J. C., McDonald, C. G., & Hatfield, B. D. (2011). A novel approach to the physiological measurement of mental workload. *International Journal of Psychophysiology : Official Journal of the International Organization of Psychophysiology, 80*(1), 75-78.

Molholm, S., Ritter, W., Murray, M. M., Javitt, D. C., Schroeder, C. E., & Foxe, J. J. (2002). Multisensory auditory-visual interactions during early sensory processing in humans: a high-density electrical mapping study. *Brain Research.Cognitive Brain Research, 14*(1), 115-128.

Näätänen, R. (2008). Mismatch negativity (MMN) as an index of central auditory system plasticity. *International Journal of Audiology, 47 Suppl 2*, S16-20.

Näätänen, R., Kujala, T., & Winkler, I. (2011). Auditory processing that leads to conscious perception: a unique window to central auditory processing opened by the mismatch negativity and related responses. *Psychophysiology, 48*(1), 4-22.

Näätänen, R., & Picton, T. (1987). The N1 wave of the human electric and magnetic response to sound: a review and an analysis of the component structure. *Psychophysiology, 24*(4), 375-425.

Näätänen, R. (1990). The role of attention in auditory information processing as revealed by event-related potentials and other brain measures of cognitive function. *Behavioral and Brain Sciences, 13*(2), 201-288.

Novak, G., Ritter, W., & Vaughan, H. G.,Jr. (1992). Mismatch detection and the latency of temporal judgements. *Psychophysiology, 29*(4), 398-411.

Oades, R. D., Dittmann-Balcar, A., & Zerbin, D. (1997). Development and topography of auditory event-related potentials (ERPs): mismatch and processing negativity in individuals 8-22 years of age. *Psychophysiology, 34*(6), 677-693.

Picton, T. W., & Hillyard, S. A. (1974). Human auditory evoked potentials. II. Effects of attention. *Electroencephalography and Clinical Neurophysiology, 36*(2), 191-199.

Ritter, W., Simson, R., Vaughan, H. G.,Jr, & Friedman, D. (1979). A brain event related to the making of a sensory discrimination. *Science (New York, N.Y.), 203*(4387), 1358-1361.

Ritter, W., Simson, R., Vaughan, H. G.,Jr, & Macht, M. (1982). Manipulation of event-related potential manifestations of information processing stages. *Science (New York, N.Y.), 218*(4575), 909-911.

Roth, W. T., Ford, J. M., Stephen, J. L., & Kopell, B. S. (1976). Effects of stimulus probability and task-relevance on event-related potentials. *Psychophysiology, 13*(4), 311-317.

Sambo, C. F., & Forster, B. (2009). An ERP investigation on visuotactile interactions in peripersonal and extrapersonal space: evidence for the spatial rule. *Journal of Cognitive Neuroscience, 21*(8), 1550-1559.

Schirmer, A., & Escoffier, N. (2010). Emotional MMN: Anxiety and heart rate correlate with the ERP signature for auditory change detection. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology, 121*(1), 53-59.

Serino, A., Annella, L., & Avenanti, A. (2009). Motor properties of peripersonal space in humans. *PloS One, 4*(8), e6582.

Simon-Dack, S. L., & Teder-Sälejärvi, W. A. (2008). Proprioceptive cues modulate further processing of spatially congruent auditory information. A high-density EEG study. *Brain Research, 2008*(1220), 171-178.

Singhal, A., & Fowler, B. (2004). The differential effects of Sternberg short- and long-term memory scanning on the late Nd and P300 in a dual-task paradigm. *Brain Research.Cognitive Brain Research, 21*(1), 124-132.

Spence, C., & Driver, J. (Eds.). (1994). *Crossmodal space and Crossmodal attention.* New York, NY: Oxford University Press

Tata, M. S., Prime, D. J., McDonald, J. J., & Ward, L. M. (2001). Transient spatial attention modulates distinct components of the auditory ERP. *Neuroreport, 12*(17), 3679-3682.

Teder, W., Alho, K., Reinikainen, K., & Näätänen, R. (1993). Interstimulus interval and the selective-attention effect on auditory ERPs: "N1 enhancement" versus processing negativity. *Psychophysiology, 30*(1), 71-81.

van Veen, V., & Carter, C. S. (2002). The anterior cingulate as a conflict monitor: fMRI and ERP studies. *Physiology & Behavior, 77*(4-5), 477-482.

Vaughan, H. G.,Jr, Ritter, W., & Simson, R. (1980). Topographic analysis of auditory event-related potentials. *Progress in Brain Research, 54*, 279-285.