UNIVERSITY OF TWENTE

The influence of MBSR-training on attentional subsystems in a sustained attention task.

An ERP study using intracutaneous pain stimuli and a peak detection approach.

Dustin Maser

03/07/2012

1st supervisor: **Dr. Rob van der Lubbe**

2nd supervisor: **MSc. Jorian Blom**

Abstract

Objective: To determine the influence of a mindfulness-based stress reduction (MBSR) training on Event Related Potential (ERP) components that are correlates of sensory processing, attentional orienting, response inhibition, and stimulus evaluation of intracutaneous electrical stimuli in a sustained attention task.

Methods: A separate-sample pretest-posttest design was used. The experimental group took part in an EEG experiment after a mindfulness based stress reduction (MBSR) training. The control group took part only in an EEG experiment. Visual cues directed spatial attention constant to one side (left or right). The side (left or right) and the intensity (high or low) of the intracutaneous stimulation varied from trial to trial. Half of the participants were instructed to respond only to attended high intensity stimuli by pressing a foot pedal. The other half was instructed to respond to low intensity stimuli. The relevant ERP components were the sensory N1, the orienting response P3a, the inhibitory NoGo-P3 and the target sensitive P3b. Only the N1 and P3a components were analyzed using a peak detection approach. The NoGo-P3 and P3b components had to be excluded from detailed analysis because of great individual variation in peak latencies.

Results: No group effects were found concerning the N1 amplitude and latency. The P3a was decreased for the MBSR group at FCz for unattended stimuli, but there was no group difference in latency. The MBSR group reported less perceived pain on the right arm after the last trial of the experiment as compared to the control group.

Conclusions: The results suggested that the positive effects of the MBSR-training in (chronic pain) patients could be explained through an decreased attentional orienting response towards the pain sensation. Additionally, it seemed that the MBSR training could induce a stronger habituation effect concerning pain.

Content

1. Introduction

Chronic pain is a human health problem that has Europe wide social and economic impact (Reid, Harker, Bala, Truyers, Kellen, Bekkering & Kleijnen, 2011). Several studies have shown that chronic pain can have negative effects on the patient's perception of his or her general health, on relationships and other social interactions, it also can interfere with everyday activities and was associated with depressive symptoms (Reid, Harker, Bala, Truyers, Kellen, Bekkering & Kleijnen, 2011). One relatively new intervention to help chronic pain patients is mindfulness-based stress reduction (MBSR). MBSR originated from eastern meditation practices. The central idea of MBSR is "bringing one's complete attention to the present experience on a moment-to-moment basis" (Marlatt & Kristeller, 1999, p. 68), and "paying attention in a particular way: on purpose, in the present moment, and non-judgmentally" (Kabat-Zinn, 1994, p. 4). Several studies with chronic pain patients have shown significant improvements in pain ratings, other medical symptoms, and general psychological symptoms (e.g., Kabat-Zinn, 1994; Kabat-Zinn, Lipworth, & Burney, 1985; Randolph, Caldera, Tacone & Greek, 1999).

A sustained attention task was chosen to operationalize chronic pain conditions. In most chronic pain conditions especially one body area is affected by constant pain sensations and the attention of these patients is constantly drawn to this exact spot. Comparably sustained attention involves directing ones attention continuously to one spatial location. In the current study painful stimuli were used that had to be attended to or ignored. Therefore did the participants have to permanently attend to one body location over many trials. Because of the fact that chronic pain patients have usually pain in a specific part of their body, a sustained attention task using painful stimuli was regarded as a valid operationalization of chronic pain.

The sensory component of pain is called nociception. Nociception works through the activation of the primary afferent axons. There are Aδ fibers and Aβ fibers, but only the slower Aδ fibers are involved in nociception. One of the disadvantages of transcutaneous stimulation is, that besides nociceptive Aδ fibers, somatosensory Aβ fibers are activated as well. Trancutaneous stimulation could therefore lead to multimodal neural activities and somatosensory-specific activity simultaneously. To exclusively activate the Aδ fibers, the method of intracutaneous electrical stimulation was used as decribed by Inui, Tran, Hoshiyama and Kakigi (2002). Because this method is known to activate selectively the slower Aδ fibers (Mouraux, Iannetti & Plaghki 2010) we expected to find greater latencies of the examined components as compared to studies using transcutaneous electrical stimuli.

Mindfulness is a fundamental element in all Buddhist meditation practices (Kabat-Zinn, 2003) and the essence of these practices was often described as attention-control training (e.g. Claxton, 1987). The positive effects of MBSR training could be a consequence of a modification of attentional subsystems (e.g. Jha, Krompinger, & Baime, 2007; van den Hurk, 2010; Hogins & Adjar, 2010). Bishop, Lau, Shapiro, Carlson, Anderson, Carmody, Segal, Abbey, Speca, Velting, and Devins (2004) and Shapiro, Carlson, Astin, and Freedman (2006) proposed that self-regulated attention was one of the core components of mindfulness and consists of three subcomponents; sustained attention, switching attention, and inhibition of secondary elaborative processing of operations and sensations. Jha, Krompinger, and Baime (2007) suggested that concentrative meditation training enhances the functioning of both the dorsal and the ventral attention system. The dorsal attention system sub-serves the voluntary top-down attention and the ventral attention system correlates with exogenous stimulus detection. This enhancement in attentional systems implies reduced interference of irrelevant information, better orientation and restriction to a specific subset of information, and an increased sensory alertness (Jha, Krompinger, & Baime, 2007). Sahara, MacLean, Ferrer, Shaver, Rosenberg, Jacobs, Zanesco, King, Aichele, Bridwell, Mangun, Lavy, Wallace, and Saron, (2011) suggested that the improvement in self-regulation in patients with mindfulness training is an implication of enhanced response inhibition. Sauer (2011) suggested that an enhanced behavioral inhibition system through mindfulness leads to better outcomes.

Most of the findings of the MBSR studies were based on self-reports and thus almost nothing was known about the neuropsychological processes that lie behind these findings (Shapiro, Carlson, Astin, & Freedman, 2006). However, a recent study examined the influence of MBSR training and spatial attention on pain perception, by examining the event-related potentials (ERPs) of attentional subsystems using an electroencephalogram (EEG) (Ströfer, 2012). The ERPs that were examined by Ströfer (2012) were the early sensory component N1 and the orienting response towards attention capturing stimuli P3a. Participants had to execute a sustained and a transient attention task in which they had to respond by pressing a foot pedal to optic cues and intracutaneous nociceptive stimuli. The results of this study showed no MBSR effect on the sensory N1. However, the orienting response P3a was shown to have a lower mean activity in the control group for unattended stimuli. These findings indicated a smaller orienting response induced through the MBSR training. Ströfer (2012) examined mean activity based of the assessment of grand averages and topographical maps. This method could bear some disadvantages because it does not take individual differences in latencies into account. Using the mean activity method a time window was chosen and the mean activity in this time window was taken, but there was no consideration given whether there really was a peak in the chosen time window at a particular participant or not. Furthermore, as discussed later in this chapter, there are more attentional components besides N1 and P3a on which the MBSR training could have an effect. This study used the same methods as Ströfer (2012), but utilized a peak detection approach to account for individual differences in latencies. Furthermore, besides the sensory N1 and the orienting response P3a, the inhibitory NoGo-P3 and the target sensitive P3b were examined.

The N1 component represents an early stage of sensory processing that is directly related to the intensity of the stimulus. Van der Lubbe, Buitenweg, Boschker, Gerdes, and Jongsma (2012) suggested that the nociception related N1 can be explained by combined activity of the contralateral secondary somatosensory cortices (SII) and the insula. Different studies have shown that the N1 component can be modulated by attention. This implies that the N1 arising from an attended body part is increased as compared to the N1 induced through an unattended channel (e.g. Legrain, Guérit, Bruyer, & Plaghki, 2002). As discussed earlier, Jha, Krompinger, and Baime (2007) and Shapiro et al. (2006) suggested an increase in alertness and an enhancement in sustained attention trough MBSR training. These effects were operationalized as a modulation of the N1 wave.

The P3a component is known to reflect an orienting response, which originates from the anterior cingulate cortex (ACC) (Polich, 2007). Van den Hurk, Giommi, Gielen, Speckens, and Barendregt (2010) suggested that a reduced orienting mechanism may lead to more flexibility. Hodgins and Adair (2010) suggested that participants that received MBSR training became better in redirecting or disengaging behavior. In this study this enhanced orienting mechanism and the enhancement in redirecting or disengaging behavior was operationalized as a modulation of the P3a component wave. The P3a component wave was expected to be decreased in participants that received MBSR training.

The NoGo-P3 was mostly studied in other modalities, but Nakata, Sakamoto, Ferretti, Gianni Perrucci, Del Gratta, Kakigi, and Luca Romani. (2003) argued that cortical activities related to response inhibition processes are independent of sensory modality. They suggested that roughly the same ERPs for response inhibition found in auditory and visual modalities can also be found in somatosensory. Kropotov (2011) showed that response inhibition was dissociated in three independent components: action inhibition, conflict monitoring and sensory mismatch. The action inhibition fluctuations were measured at the fronto-central electrodes and were presumably evoked in the supplementary motor cortex. Sahara et al. (2011) and Sauer (2011) suggested that the positive outcomes of MSBR training can be explained in terms of an enhanced response inhibition. An enhancement in response inhibition was operationalized as a modulation of action inhibition fluctuations as described by Kropotov (2011). This component was declared the NoGo-P3.

Finally there is the target P3b which is frequently described as second posterior aspect of the anterior P3a (e.g. Polich, 2003; Friedman, Cycowicz, & Gaeta, 2001) and is thought to be involved in evaluating the painful stimulus (Dowman, 2004). In another study that used a different intracutaneous electrical stimulation this positive component was found around 500ms (Van der Lubbe, Buitenweg, Boschker, Gerdes, & Jongsma, 2012). Here the P3b component had an enhanced amplitude for those stimuli to that the participants had to respond (Van der Lubbe, Buitenweg, Boschker, Gerdes, & Jongsma, 2012). These results suggest that the P3b component indicates a target dependent peak. In the literature it was unclear in which way MBSR training could modulate the P3b.

The main question this study tried to answer was, what the attention modulating properties of mindfulness-based training are. If the MBSR training leads to enhanced alertness and enhanced sustained attention, then the amplitude of the N1 component should be larger in the group that received the MBSR training as compared to the group that did not receive this training. Additionally, if MBSR training leads to a decreased orienting response and more flexibility in allocating attentional resources, then the amplitude of the P3a component should be smaller in the group that received mindfulness training as compared to the group that did not. Furthermore, if MBSR training leads to an enhanced ability to inhibit responses of unimportant information, then the amplitude of the NoGo-P3 should be larger in the group that received mindfulness training as compared to the group that did not receive MBSR training. Finally, if mindfulness training affects the evaluation of painful stimuli, then there should be a difference on the P3b component between the group that received mindfulness training as compared to the group that did not.

2. Methods

2.1. Participants

Thirty-four students from the Faculty of Behavioral Sciences of the University of Twente participated in this study. Five of them were male and 29 were female. Their age ranged from 20 to 34 years. All but two participants were right handed, none suffered from motoric afflictions. One participant had dyslexia. Another participant suffered from dyschromatopsia, but ensured the researchers that he was able to differentiate between the green and the red arrow cues. All participants had normal or corrected-to-normal visual capabilities and signed a written informed consent. The study was approved by an ethical committee.

2.2. Experimental groups and MBSR-training

The thirty-four students were randomly assigned to two different groups. One group was the control group that took part in an EEG experiment. The other group was the experimental group and first took part in a MBSR-training and thereafter took part in an EEG experiment. Accordingly EEG measurements of control group and MSBR-group were compared

The MBSR-training lasted nine weeks and consisted of eight different sessions of two hours. During these sessions the following MBSR-exercises were implemented: sitting mindfulness mediation, meditative walking, body-scan and hatha-yoga exercises. During the sitting mindfulness meditation the participants had to sit on the ground and concentrate on one particular thing at a time. Most often they concentrated on the movement of their own breathing. The second goal of this exercise was to notice the present feelings without judging them. During meditative walking the focus of the concentration lied on the movement of foots and legs. In the body-scan exercise the participants had to alternate their attention from one specific body part to the next while trying to assess what was felt in this specific body part at that moment, again without judging those feelings. In the hatha-yoga exercises physical yoga postures were combined with breathing and meditation techniques. All these methods shared that attention could easily be captured by other stimuli in the environment or simply flow away. It was part of the MBSR-training that, whenever attention was directed away from the exercise at hand, it had to be directed back and refocused at the task again. Furthermore, the participants were asked to exercise the learned methods every day for twenty to forty minutes. During the study the participants were asked to keep a mindfulness journal and report the time spend with the mindfulness exercises at home.

2.3. Stimuli and Procedure

A CRT monitor, with 75 hertz and 17 inches diameter, was located approximately 60 centimeters in front of the participants to present the spatial cues during each trial. At the beginning of each trial a grey fixation cross was presented for 1200 milliseconds. Next the cue was presented for 400 milliseconds . The cue consisted of a red and a green triangle, which pointed to the left and the right. Thereafter the fixation cross was presented once again for another 600 milliseconds. After that an intracutaneous electrical stimulus was presented on the dorsal surface of the left or right forearm. This stimulation could be of high or low intensity. After the stimulus, the participants had 4000 milliseconds to infer whether the inflicted stimulus was a target or non-target and, in case of a target, to respond (see Figure 1). Targets were only those stimuli that were attended, thus on the cued side, and had the relevant intensity. Half of the participants were instructed to respond to low intensity stimuli the other half to high intensity stimuli.

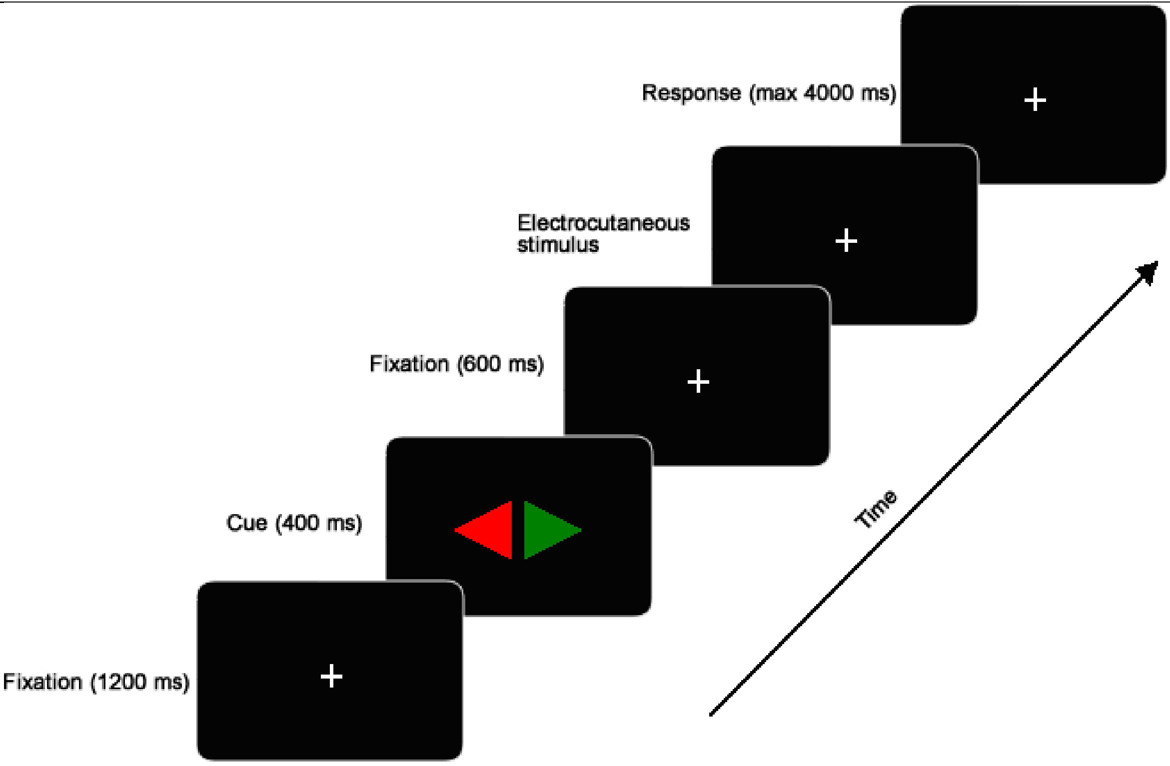

*Figure 1***.** A graphic display of the stimuli sequence that the participants experienced. First a grey fixation cross was presented for 1200ms, then the cue for 400ms, again the cross for 600ms After that the electrocutaneous stimulus was inflicted and the participants had 4000ms to respond while the grey fixation cross was shown.

To determine the current of the high and low intensities of the intracutaneous stimuli, different individual thresholds were determined in a pre-measurement. After the electrodes were placed on the dorsal surface of the left or right forearm, stimuli were presented consecutively. The current of these stimuli began at 0mA and was progressively augmented by 0.1mA. Each stimulus consisted of three pulses and was presented for one millisecond. The first threshold that was determined was the pain threshold, which was reached once the neutral sensation changed into a displeasing sensation. The second threshold that was determined was the detection threshold, which was reached whenever the participant sensed the first just perceivable sensation. The third and last threshold was the pain tolerance threshold, which represented the highest amount of pain the participant would allow to be inflicted upon him or her. The current of the intracutaneous stimuli during the experiment was the individual's pain tolerance threshold. By varying the number of pulses (two and five pulses) and maintaining the current of the pain tolerance threshold, the different intensities were applied. Because the stimuli in the pre-measurement were inflicted in three pulses, the two pulse stimuli were thought to be perceived as a low intensity pain sensation and the five pulse stimuli as a high intensity pain sensation. Before and after the experiment, the participants had to determine values on a visual analog scale (VAS) indicating their perceived pain. The scale ranged from zero to ten with five in the middle. Zero corresponded to no perceived stimuli and ten corresponded to an extreme painful sensation.

2.4. Task

The experiment consisted of two blocks with each containing 96 trials. During the first block half of the participants had to attend to the green cue and during the second block they had to attend to the red cue. These color dependent instructions were counterbalanced in the second half of the participants. The cue predicted for 50% the side where the stimulus would occur and pointed the first half of each block constantly to the left (or the right) and the second half to the right (or left). Each administered stimulus was of either high (five pulses) or low intensity (two pulses). Half of the participants had to respond to attended high intensity stimuli the other half to attended low intensity stimuli. In total, 192 intracutaneous stimuli were administered to each participant.. It was important, and thus pointed out to the participant, that only spatial attention had to be allocated to the hand and not, for example, the eye gaze. In each trial the intracutaneous stimulus could thus differ in the arm that it was administered on (left versus right), in intensity (high versus low) and whether the stimulated side was attended or not. The stimulus was only a target if the stimulus was presented at the attended side and only if it had also the relevant intensity. The participants were instructed to press a foot pedal whenever a stimulus was a target and do nothing if the stimulus was not a target. Therefore, only one quarter of all stimuli were targets and the other three quarters were non-targets. There were three types of non-target. Non-targets that had an irrelevant intensity, non-targets that were on the unattended side and non-targets that were of irrelevant intensity and on the unattended side.

2.5 Apparatus

To deliver the intracutaneous stimuli two “DS5 Isolated Bipolar Constant Current Stimulator” (Digitimer, Welwyn Garden City, UK) were used. The used electrodes were stainless steel concentric bipolar needle electrodes and satisfed the conditions which were established in the norm of Medical electrical equipment (EN-IEC 60601). The anodes of these electrodes were rings of 1.2 mm in diameter with needles that were placed in exactly the middle of the anodes and worked as the respective cathodes.These needles stuck 0.1 mm out from the anodes and were pricked into the uppermost layer of the epidermis on the dorsal surface of each forearm. The reason for this method, which was also implemented by Inui et al. (2002) and Mouraux et al. (2010), was to selectively activate the pain related Aδ fibers and not the Aβ fibers. The stimuli consisted of a constant-block wave of sequential pulses that were five milliseconds away from each other and lasted one millisecond each. The voltage was constantly held at 10mV and the strength of the current was individually appointed through each participant and his pain threshold. The number of pulses differentiated between two pulse for low intensities and five pulses for high intensities. Two battery-driven computer-controlled constant current stimulators were used to deliver the intracutaneous stimuli.

2.6 Recording

To record the EEG and electrooculogram (EOG) a 72-channels Brain Vision Recorder with a Quick Amp 72 amplifier (Brain Products, GmbH, München) was used. An elastic cap (Easy Cap, Falk Minow Services) was used to attach 68 Ag/AgCl electrodes to the head of the participants according to the 10-10 system. Sixty-one of electrodes were used to measure the current differences on the dorsal surface of the head. Four bipolar electrodes were attached around the ocular regions and used to measure the EOG. One electrode was attached to the forehead and served as grounding. For all participants the electrode resistance was kept below 5kΩ.

2.7 Data-analyses

2.7.1. Behavioral Measures

Reaction times (RTs) of responses were measured and analyzed by means of a repeated measures ANOVA with RT as measure, arm (left versus right) as within-subject factor, and group (control versus experimental) as between-subjects factor. Hit rates were calculated by dividing the number of correct hits by the sum of all target trials. The false alarm rates were calculated by dividing the number of the false responses by the sum of all non-target trials. Hit rates and false alarm rates were analyzed by using a repeated measures ANOVA, with hit rates as measure, side of stimulation (left versus right) as within-subject factor and group (control versus experimental) as between subjects factor. Additionally VAS scores were inspected by using a repeated measures ANOVA with measurement (pre-measurement versus post-measurement), stimulus intensity (high versus low) and arm (left versus right) as within-subject factors and group (control versus experimental) as between-subject factor. Furthermore, the percentages of time spend with mindfulness training exercises were calculated in relation to the time the participants were instructed to spend. This was done by counting the minutes each participant reported spending with mindfulness training (minus the weekly group sessions) and dividing them by the number of minutes they were instructed to spend.

2.7.2. EEG Measures

Brain Vision Analyzer Version 2.0.1 (Brain Products, GmbH, München) was used to analyze the EEG data. Some Channels of particular participants had to drop out, because of errors during the experiments. Sixteen channels, distributed over eleven participants, were recalculated using the formula evaluator and the mean activity of the surrounding channels. After that the signals were sampled by employing infinite impulse response (IIR) filters with a low cutoff of 0.16Hz and a high cutoff 0f 30Hz, while using a slope of 12 decibel per octave. Accordingly, the data was segmented from 100ms before the cue to 800ms after the stimulus. This gave intervals of 1900ms. For these intervals level trigger were utilized to mark all activity in the horizontal eye movement channel (hEOG) that was higher than 120µV and lower than -120µV. A baseline was set from 100ms to 0ms before the cue. Trials that were marked for horizontal eye movement were removed. Because of a to high data loss, it was chosen not to filter out horizontal eye movements, but to utilize the ocular correction algorithm instead. After vertical eye movements were filtered out, the data was segmented to an interval that ranged from 100ms before the intracutanous stimulus to 800ms afterwards. A new baseline was set, referencing the activity from 100ms before the stimulus to the moment of the stimulus. EEG artifacts were removed and ocular correction was utilized. This procedure left on average 96.5% of the trials per participant for further analysis.

Through the inspection of the grand averages and their topographical maps, separate components were identified and appropriate time windows and electrodes for peak detection were chosen. A negative component was found peaking approximately 180ms post-stimulus onset contralateral to the stimulated side at C5 and C6. The inspection of the individual averages of each participant showed however that, there were individual differences between participants with the component peaking between 100ms and 200ms. The butterfly views of C5 and C6 of the contralateral, attended and high stimuli condition illustrated these individual differences (see Figure 2). On behalf of further analyzes, this peak was called N180 and a time window ranging from 100ms to 210ms was chosen for a peak detection at the electrodes C5 and C6. This N180 was further analyzed using repeated measures ANOVA with electrode (C5 versus C6), attention (attended versus unattended), intensity (low versus high) and side of stimulation (left versus right) as within-subject factors and group (control versus experimental) as between-subjects factor.

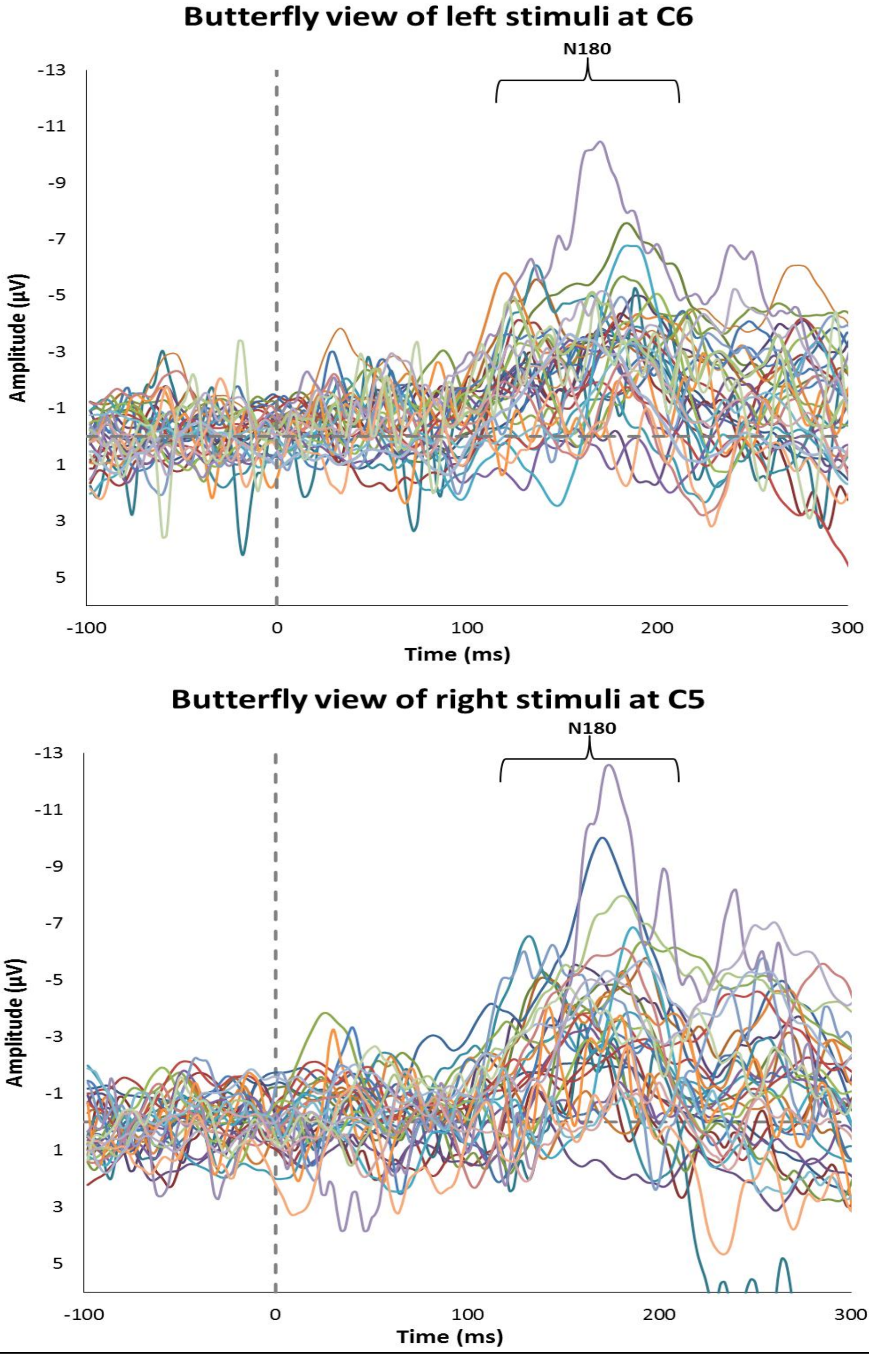

Figure 2. Butterfly views of the ERPs of each participant are shown with time in milliseconds (ms) along the x-axis and amplitude in microvolt (µV) along the y-axis. Butterfly views of the ERPs of each participant at the electrodes C6 for left stimuli (upper panel) and C5 for right stimuli (lower panel), of all attended high intensity stimuli are displayed. The respective contralateral electrode and the attended high stimuli condition were chosen because the N180 seemed to be most pronounced in this combination. This graphic illustrates that most participants had just one peak between 100 and 210 milliseconds, but the latencies of these peaks had a strong variation between individuals.

Furthermore at least three positive components seemed to peak in between 200ms and 400ms after stimulus onset at FCz, Cz and CPz. However, the inspection of the individual averages of each participant did again show that there were significant individual differences between them. The butterfly view of Cz of the unattended high stimuli condition illustrated that most participants had just one peak between 200ms and 400ms with a latency that varied a greatly between participants (see Figure 3). For further analysis this peak was called P300 and, because of the big variation between individuals, a time window ranging from 200 to 400 milliseconds was chosen. The peak amplitudes and latencies were further analyzed by utilizing a repeated measures ANOVA, with electrode (FCz versus Cz versus CPz), attention (attended versus unattended) and intensity (low versus high) as within-subject factors and group (control versus experimental) as between-subjects factor.

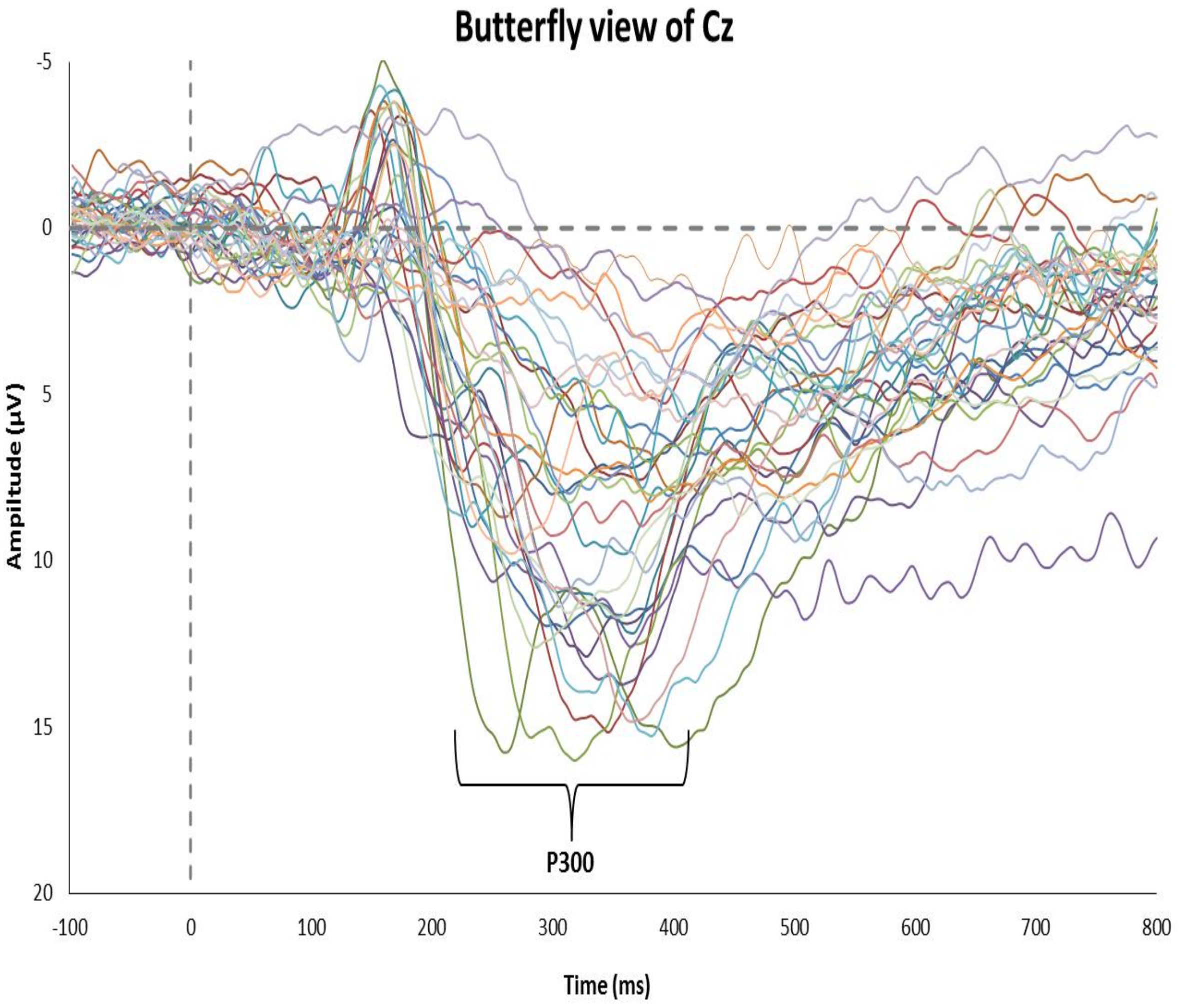

Figure 3. Butterfly view of the ERPs of each participant are shown with time in milliseconds (ms) along the x-axis and amplitude in microvolt (µV) along the y-axis. Butterfly view of the ERPs of each participant, at the electrode Cz, of the averages of all unattended high intensity stimuli are displayed. Cz and the unattended high stimuli condition were chosen because the P300 seemed to be most pronounced in this combination. This graphic illustrates that most participants had just one peak between 200 and 400 milliseconds, but the latencies of these peaks had a strong variation between individuals.

Additionally, two late positive components were found which seemed to be target sensitive. The first one peaked at Cz around 500ms post-stimulus and the second one peaked at Pz around 550ms post-stimulus (see Figure 4). The first one seemed to be more positive in non-target trials than in target trials which suggested that it was associated with response inhibition (NoGo P3). The second one seemed to be more positive in target trials than in non-target trials, which connects it to target identification (P3b). To find an applicable time window for these two components, individual differences in peak latency were considered by means of butterfly views (see Figure 5). These individual differences in P500 and P550 component peaks illustrated that the NoGo-P3 and the P3b were much too instable for the present study to use the method of peak detection and further analyze these components. Because these two components were the target sensitive components and they would not be analyzed any further, the between-subjects factor relevant intensity (high versus low) was not used for further analysis. This was conductive for further analyses, because it increased the numbers of degrees of freedom and thereby increased the power of this study.

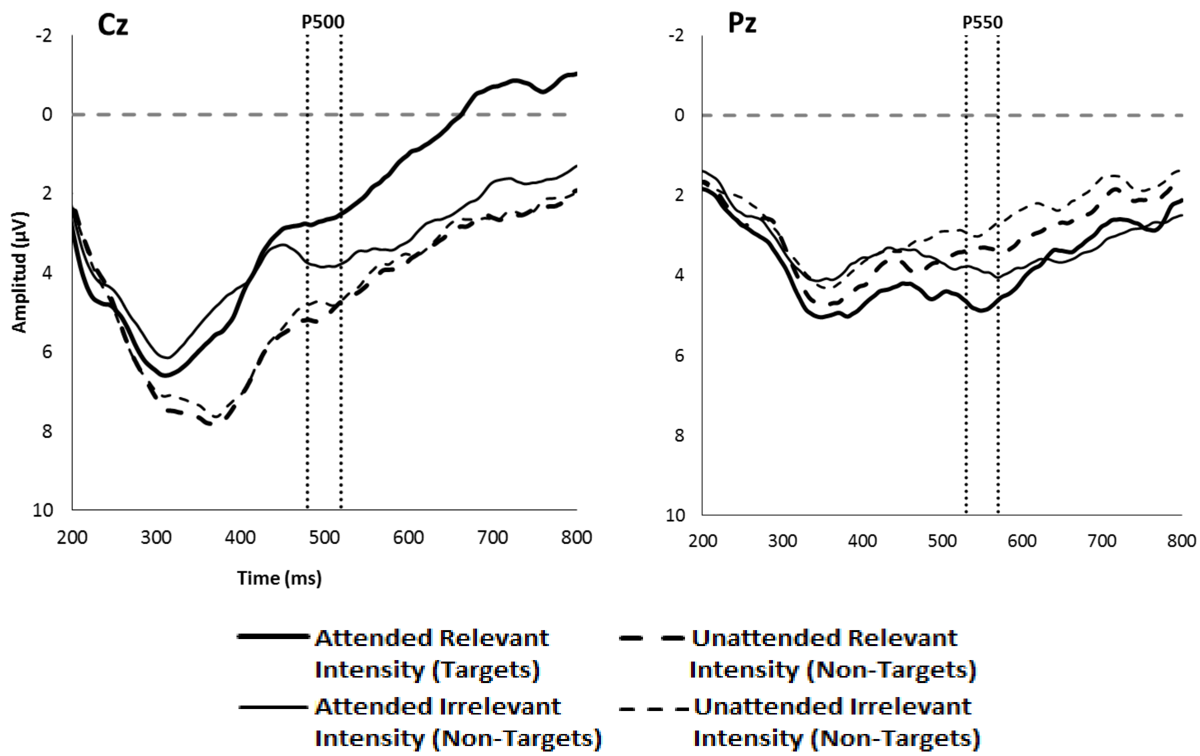

Figure 4. Grand averages of the P500 (left panel) and P550 (right panel) ERPs with time in milliseconds (ms) and amplitude in microvolt (µV). The non-target sensitive P500 component was most pronounced at the electrode Cz (left panel), and the target sensitive P550 component was most pronounced at Pz (right panel). Grand averages are shown as a function of target (targets (attended and relevant intensity), non-targets irrelevant intensity (attended, but irrelevant intensity), non-targets wrong side (unattended, but relevant intensity) and non-targets irrelevant intensity and wrong side (unattended and irrelevant intensity)).

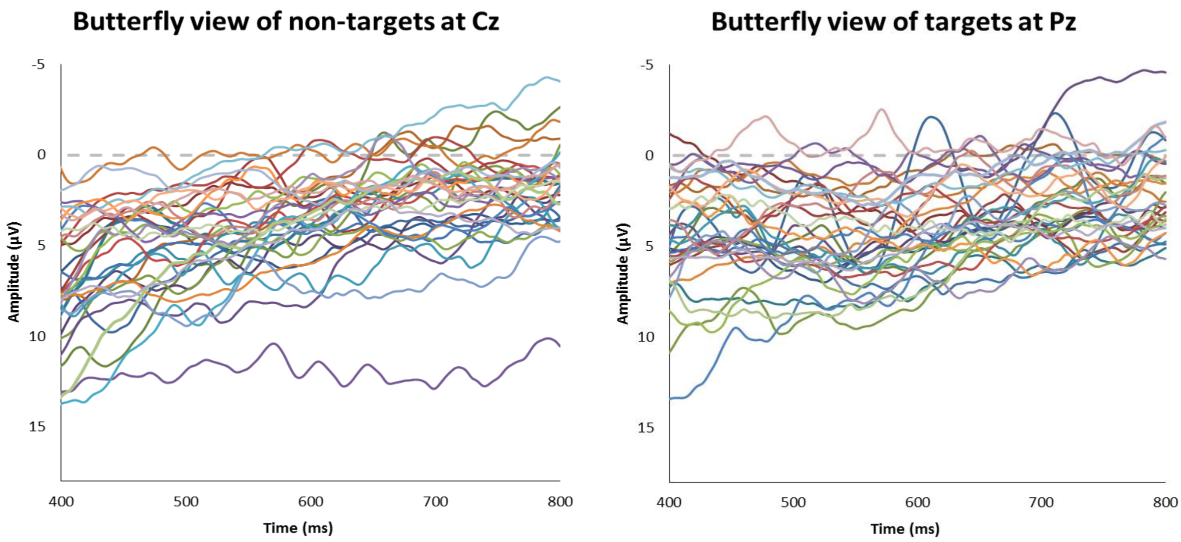

Figure 5. Butterfly views of the ERPs of each participant are shown with time in milliseconds (ms) along the x-axis and amplitude in microvolt (μV) along the y-axis. A butterfly view of the averages of unattended high stimuli of the non-target sensitive P500 component is shown at the electrode Cz (left panel). A butterfly view of the averages of attended stimuli with the relevant intensity of the target sensitive P550 component is shown at Pz (right panel). These butterfly views illustrate that most participants had one peak between 200 and 400 milliseconds, but the latencies of these peaks had a strong variation between individuals.

3. Results

3.1. Behavioral Data

The repeated measures ANOVA that was performed on the RTs showed no significant effect of side of stimulation, relevant intensity or group. The overall mean RT for valid responses was 1062 milliseconds with a standard error of 288 milliseconds. These RTs are relatively slow, which could implicate on the one hand that the participants tried to be most accurate or on the other hand that they had trouble identifying relevant stimuli and were therefore doubtful. The participants responded more than 500ms after the effects this study was looking for. Therefore were the RTs slow enough so that no cognitive motor effects were expected to influence the inspected ERP components.

Another repeated measures ANOVA was performed on the hit and false alarm rates which showed no main effect of group or side of stimulation. The mean hit rate was found to be 73% with a standard error of 4% and the mean false alarm rate was 7% with a standard error of 1%. The mean hit rate is considerable above chance and mean false alarm rate is low enough to assume that most participants no hard time identifying targets.

		Low Intensity		High Intensity	
		Pre-measurement	Post-measurement	Pre-measurement	Post-measurement
Control	Left arm	4.5 (0.2)	2.8 (0.4)	5.7 (0.3)	4.4 (0.4)
	Right arm	4.4 (0.3)	3.5 (0.3)	5.5 (0.3)	5.0 (0.4)
Experimental	Left arm	3.6 (0.2)	2.8 (0.4)	5.2 (0.3)	4.0 (0.4)
	Right arm	4.5 (0.2)	2.4 (0.3)	5.9 (0.3)	3.9 (0.4)

*Table 1***.** Mean visual analog (VAS) scores as a function of time of measurement (pre-measurement and post-measurement), group (control and experimental), intensity of stimulation (low and high intensity) and arm (left and right).

A repeated measures ANOVA was also performed on the VAS-scores (see Table 1) of the participants. This ANOVA used the within-subject factors measurement (pre-measurement versus post-measurement), intensity (high versus low) and arm (left versus right) and the between-subject factor group (control versus experimental). This analysis showed main effects of measurement ($F(1,32) = 35.7, p < 0.001$) and the factor intensity ($F(1,32) = 133.1, p < 0.001$). The VAS scores of the pre-measurement were significantly higher than the VAS scores of the post-measurement (4.9 versus 3.6). Furthermore was the perceived pain found to be higher for high intensity stimuli, than for low intensity stimuli (4.9 versus 3.6). Additionally, an interaction effect between measurement, arm and group was found ($F(1,30) = 8.8, p = 0.006$). Accordingly, the left and right arm were inspected separately, which showed a significant interaction between measurement and group for the right arm ($F(1,32) = 11.9, p = 0.002$), but not for the left arm. Further analyses showed that there was a main effect of group in the post-measurement for the right arm ($F(1,32) = 6.4, p = 0.017$), but not in the pre-measurement. The experimental group reported significantly less pain in the post-measurement at the right arm, than the control group (3.1 versus 4.2).

	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9
Training									
Time	186 (68)	183 (51)	163 (64)	166 (65)	149 (79)	117 (77)	99 (60)	113 (68)	48 (76)
(minutes)	133 %	131 %	117 %	119 %	107 %	84 %	71 %	81 %	35 %

Table 2. Mean times spend training in minutes as function of week (1-9) with standard errors in brackets. Below the means percentage of mean time spend training in relation to minimal instructed training time.

The instructed minimal training time for each participant was twenty minutes per day, which gave 140 minutes per week and 1260 minutes overall. The mean time spend exercising was only from week one through week six above this minimum. From week six to week nine the mean training time was below the minimum and in week nine only 35% of the instructed time was trained (see Table 2). Overall only eight out of seventeen participants (47%) spend the instructed minimal time training of 1260 minutes.

3.2. EEG Data

3.2.1. The N180 Amplitude

A repeated measures ANOVA was performed on the amplitude of the N180 peaks (see Figure 6 and 7) with the within-subject factors electrode (C5 versus C6), attention (attended versus unattended), intensity (high versus low) and side of stimulation (left versus right) and the between-subject factor group (control versus experimental). This revealed a main effects on the N180 amplitude of the within-subject factor intensity ($F(1,32) = 20.8$, $p < 0.001$). An increased negativity for stimuli of high intensity compared to stimuli with low intensity was found (-3.6µV versus -3.1µV). An interaction effect was found between the side of the stimulation and electrode ($F(1,32) = 47.8$, $p < 0,001$). To examine this effect the left and right arms were examined separately. Examination of the left arm showed a main effect of electrode ($F(1,32) = 24.1$, $p < 0.001$) and examination of the right arm showed also a main effect of electrode ($F(1,32) = 20.8$, $p < 0.001$). For stimuli on the left side the amplitude was more negative at C6 than at C5 (-4.1µV versus -2.7µV). Stimuli on the right side showed an inverted effect with more negativity at C5 than at C6 (-4.1µV versus -2.6µV). Thus, the negativity was respectively greater at the contralateral electrode, than at the ipsilateral electrode. Furthermore an interaction effect between attention and arm was found ($F(1,32) = 4.3$, $p = 0,045$). Separate ANOVAS for the left and right arm showed that there was an attentional effect only at the right arm ($F(1,32) = 6.5$, $p = 0,015$). Negativity was greater at the right arm for attended stimuli as compared to unattended stimuli (3.6µV versus 3.2µV).

3.2.2. The N180 Latency

There were no relevant significant main or interaction effects for the N180 Latency. The mean latency was found to be 178ms with a standard error of 1.7ms. The mean standard error of all conditions was found to be 25.5ms.

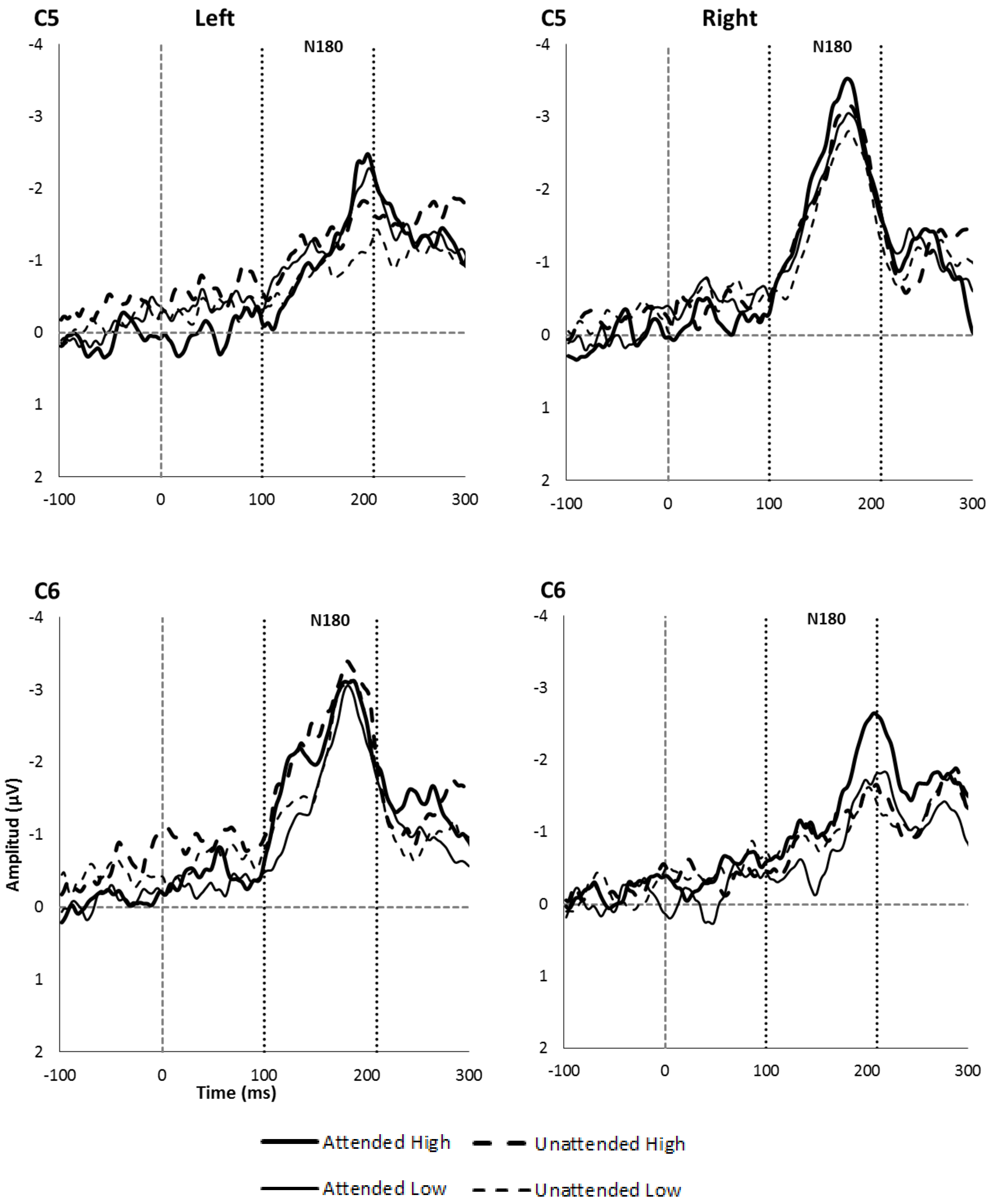

Figure 6. Grand averages of N180 for left stimuli (left panel) and right stimuli (right panel) are displayed with time in milliseconds (ms) along the x-axis and amplitude in microvolts (µV) along the y-axis. C5 and C6 are selected for display. Time windows selected for peak detection are indicated with solid vertical lines. ERPs are displayed as a function of stimulus intensity (low versus high) and attention (attended versus unattended).

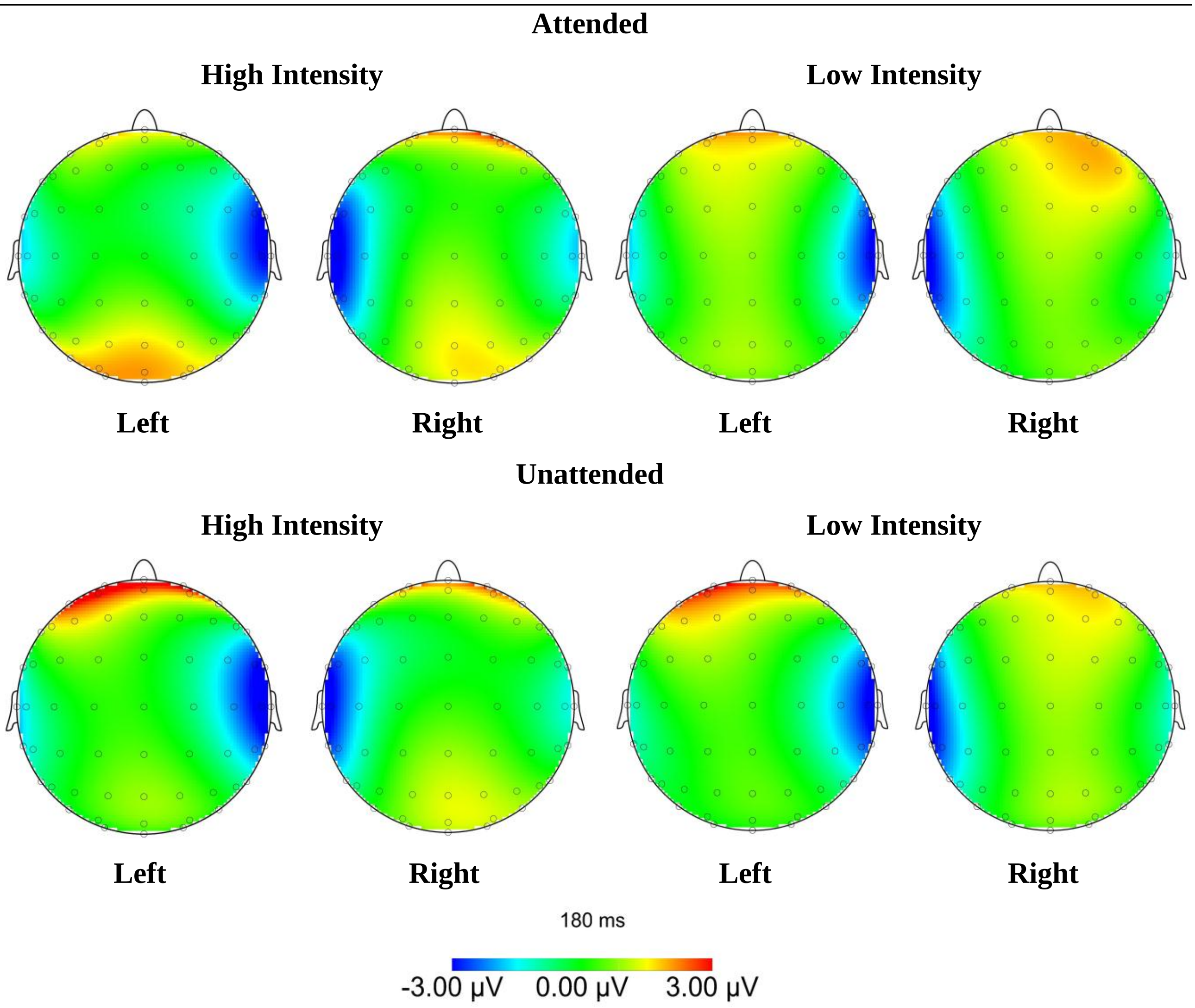

Figure 7. Topview of topographic maps of the grand averages for the N180 component. The upper panel shows the topographic maps of the attended condition and the lower panel shows the topographic maps of the unattended condition. On the left side are the topographic maps of the high intensity stimuli and on the right side are the topographic maps of the low intensity stimuli. These conditions are further split whether the left or right arm was stimulated.

3.2.3. The P300 Amplitude

A repeated measures ANOVA was used on the amplitude of the P300 peaks (see figure 8 and figure 9) with the within-subject factors electrode (FCz versus Cz versus CPz), attention (attended versus unattended) and intensity (high versus low) and the between-subject factor group (control versus experimental). Through the ANOVA the main effects on the P300 amplitude of the within-subject factors electrode ($F(2,64) = 5.6$, $p = 0{,}019$), attention ($F(1,32) = 9.4$, $p = 0{,}004$) and intensity ($F(1,32) = 49.9$, $p < 0.001$) were revealed. An increased positivity was found at electrode Cz as compared to electrode CPz (7.8µV versus 6.7µV), but no difference between electrodes Cz compared to FCz, or FCz compared to CPz was found. Furthermore, a decreased positivity was found for the attended stimuli compared to the unattended stimuli (6.7µV versus 7.6µV). Additionally an increased positivity was found for high intensity stimuli compared to low intensity stimuli (8µV versus 6.3µV). An interaction effect was found between electrode and attention ($F(2,64) = 12.6$, $p < 0{,}001$). One possible explanation for this could be that the main effect of attention was more pronounced at one electrode than at the others. To test this hypothesis separate ANOVAs for each electrode were inspected separately. These ANOVAs showed that the factor attention had a significant main effect at FCz and Cz, but not at CPz. Furthermore did the repeated measures ANOVA reveal an interaction effect between electrode, attention and group ($F(2,64) = 6.4$, $p = 0{,}006$). One possible explanation for this could be that the interaction effect between attention and group was significant at just one electrode but not at the others. Accordingly to test this hypothesis separate repeated measures ANOVA's were made for the different electrodes FCz, Cz and CPz. These ANOVAs showed that there indeed was an interaction effect between attention and group at FCz ($F(1,32) = 5$, $p = 0.032$). Additionally separate repeated measures ANOVAs were made for the attended and unattended condition to check for a group effect,. This ANOVA showed that there was a group effect in the unattended but not in the attended condition at FCz ($F(1,32) = 4.2$, $p = 0.049$). Further analyses showed that the peak amplitude of the P300 component at FCz was significantly lower for the MBSR group than for the experimental group (8.8µV versus 6.4µV) for unattended stimuli.

3.2.4. The P300 Latency

A repeated measures ANOVA was used on the latency of the P300 peaks with the within-subject factors electrode (FCz versus Cz versus CPz), attention (attended versus unattended) and intensity (high versus low) and the between-subject factor group (control versus experimental). The ANOVA revealed main effects on the P300 component latency of the within-subject factors electrode ($F(2,32) = 10$, $p = 0,001$) and attention ($F(1,32) = 21.8$, $p < 0,001$). The P300 peaked earlier at FCz than at Cz (308ms versus 320ms) and later at CPz than at Cz (332ms versus 320ms). Furthermore did the P300 component peak earlier for attended than for unattended stimuli (306ms versus 334ms).

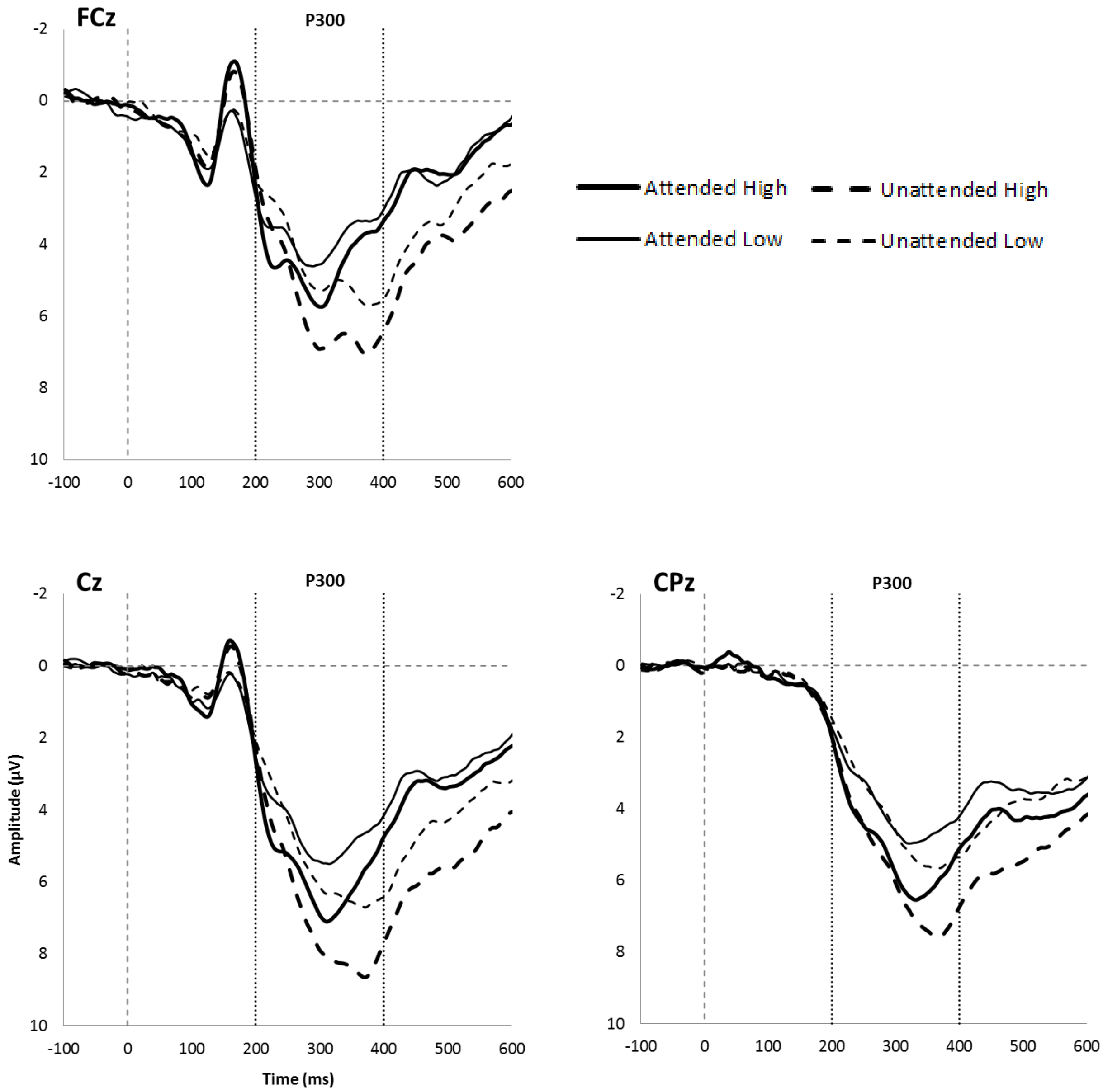

Figure 8. Grand averages of P300 are displayed with time in milliseconds (ms) along the x-axis and amplitude in microvolts (µV) along the y-axis. FCz, Cz and CPz are selected for display. Time windows selected for peak detection are indicated with solid vertical lines. ERPs are displayed as a function of stimulus intensity (low versus high) and attention (attended versus unattended).

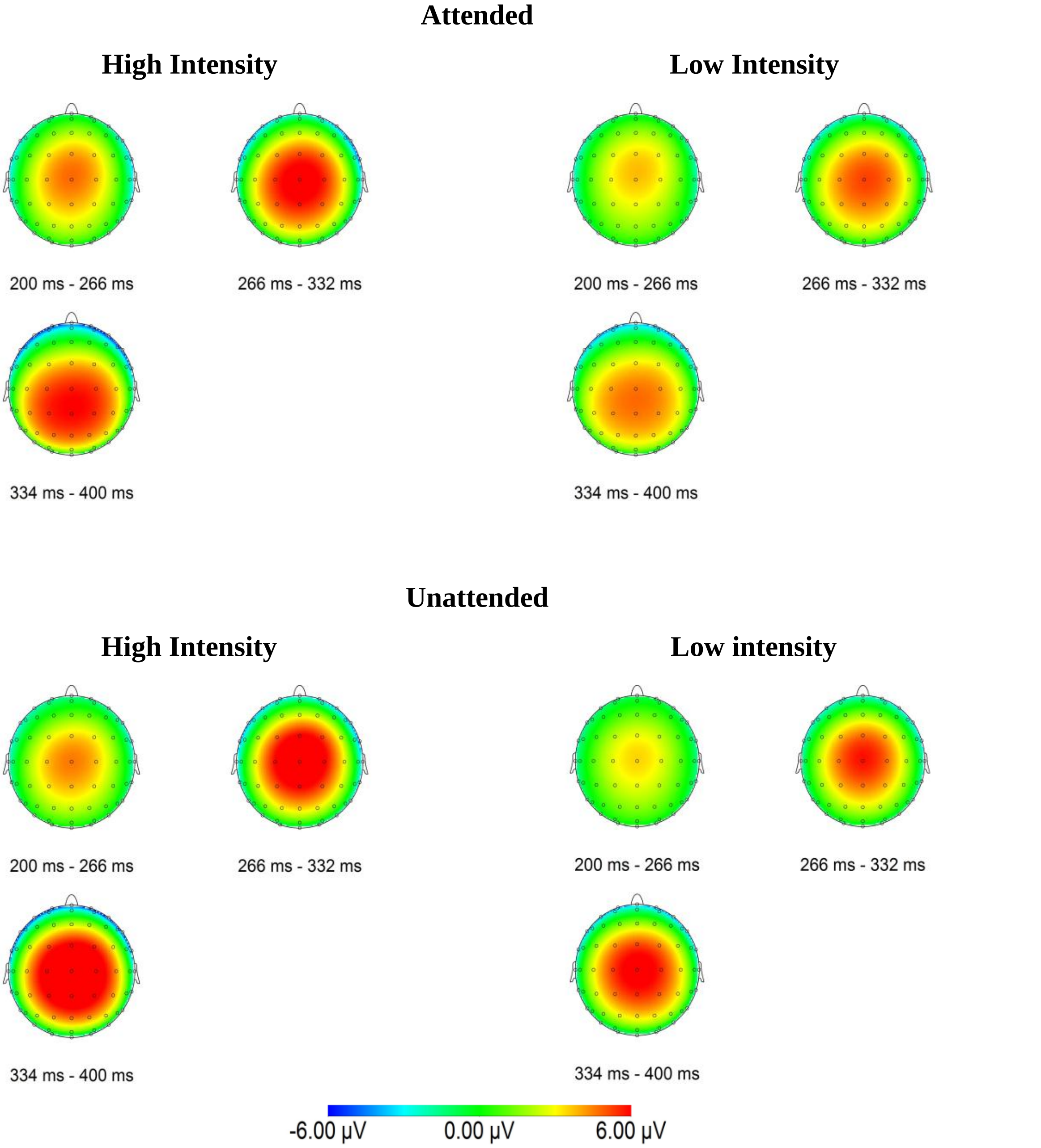

Figure 9. Topographical maps for the P300 component from 200ms to 400ms as a function of attention (attended versus unattended) and intensity (high versus low). P300 component peaks for attended stimuli are shown in the upper panel and for unattended stimuli in the lower panel.

4. Discussion

The main objective of this study was to find the neurological correlates of the changes induced by MBSR-training. MBSR-training had a significant effect on the wellbeing of patients with different kinds of pathology and most prominently patients with chronic pain. A recent study by Ströfer (2012), had the same objective. Ströfer (2012) examined the effect of MBSR-training on the sensory N1 component and the orienting response P3a. This was done by inspecting mean activities in particular time windows. Through this method Ströfer (2012) found for the MSBR-group an attenuated mean activity of P3b for unattended stimuli as compared to the control group. To take individual differences into account this study tried to replicate the study conducted by Ströfer (2012), but using a peak detection analysis. A sustained attention task was chosen, because of the similarity with the situation of chronic pain patients. Furthermore this study was intended to take more components into account on which an effect of the MBSR-training could be expected. These plans had to be discarded after butterfly views showed that the peaks of the P3b and NoGo-P3 components were too instable for the method of peak detection. These butterfly views showed furthermore significant individual differences in latencies between the different participants at the sensory N1 and the orienting response P3a. The implications of these differences will be discussed later in this chapter.

The most important finding of this study was a decreased P3a amplitude at FCz for unattended stimuli of the MBSR group. This finding suggested that the orienting response was less pronounced for the MBSR group as compared to the control group. This replicates the findings of Ströfer (2012) and suggests that the positive effects of MSBR training observed in chronic pain patients could be due to less attentional orientation towards the painful sensations.

The analyses of the VAS-scores suggested that the degree of perceived pain was higher in the pre-measurement than in the post-measurement. This effect is arguably due to a habituation effect (e.g. LeBlanc & Potvin, 1966). Not unexpectedly, an effect of stimulus intensity was found, which showed that the participants perceived the high intensity stimuli as more painful than the low intensity stimuli. Surprisingly, a group effect was found. The perceived pain of the MBSR group was lower than the perceived pain of the control group. This effect was significant only for the right arm during the post-measurement. The mean VAS score of the MBSR-group was also lower for the left arm, but this difference was not significant. It could be argued that the MBSR-training induced a stronger habituation effect to painful stimuli. The difference between the two hands could be explained through a bias for the right hand. Almost all participants were right-handed. This could imply that because the participants are used to focus attention on their right hands, as they perform most actions with this hand, they also could be more accustomed to notice and inhibit pain there. Another possible explanation could be an unreliability in placing procedure of the stimulus electrodes, which is discussed in more detail later in this chapter.

The mean RT for valid stimuli was about 1062 milliseconds and thereby relatively slow. Two possible explanations were that the participants either tried to be most accurate, although they were not instructed to do so, or they had trouble identifying relevant stimuli. Accordingly, hit rates and false alarm rates were examined, which showed a mean hit rate of 73% and a mean false alarm rate of 7%. The mean hit rate is considerably above chance and the mean false alarm rate is low enough to assume that most participants had no hard time identifying targets. This would suggest that participants indeed tried to respond as accurate as possible.

Inspection of the training reports showed that the mean training time after week six was below the instructed minimum. Additionally in week nine only 35% of the instructed time was spend with training. Only 47% of the participants spend the instructed minimal exercising time of 1260 minutes over nine weeks. This could implicate that the found results might be smaller than they could have been. If the MBSR group had exercised the instructed amount of time, the effects of mindfulness on the examined ERP components might have been more explicit, leading to more significant differences between the groups.

A negative component was found peaking roughly around 180 milliseconds post-stimulus at C5 and C6. Inspection of the butterfly views showed that the peak latencies varied between 100ms and 210ms. Therefore a relatively big time window of 110ms had to be chosen. This component's amplitude was more negative for high intensity stimuli than for low intensity stimuli. Furthermore was the amplitude respectively more negative contralateral to the stimulated side. Because of the latency, the topography, and modulation through stimulus intensity, it could be assumed that the found N180 component was the sensory N1. This N1 component represents an early stage of sensory processing and is more directly related to the intensity of the stimulus that is preconscious. The N1 can be explained by combined activity in the contra lateral secondary somatosensory cortices (SII) and the insula (Van der Lubbe et al., 2012). The N180 component seemed to originate from the electrodes C5 and C6, which corresponds with an origin in somatosensory cortices. There was no group difference in the N1 component. Therefore the hypothesis that early sensory processing is modulated by MBSR training had to be discarded. Furthermore, the effect of attention for this component was enhanced for the right arm as compared to the left arm. This finding could be another indicator for the right hand bias, discussed earlier in the context of the VAS scores.

After inspecting the topographic maps and the grand averages it was unclear whether the P300 originates from FCz, Cz or CPz. Furthermore it seemed that there were three different components peaking between 200 and 400 milliseconds, but inspection on individual participant level showed that most participants had just one peak between 200 and 400 milliseconds. As with the N1 component the latencies varied a lot between individuals (see Figure 3). Therefore a big interval, of 200-400ms, had to be chosen to capture all P300 components with peak detection. There was no significant difference between the amplitude at FCz and Cz and between FCz and CPz, but the amplitude was more positive at Cz than at CPz. This finding implies that CPz is not the main locus of the activity of this component. Concerning the factor electrodes, there were also latency differences found. The P300 peaked earliest at FCz, later at Cz and still later at CPz. This delayed peak suggested that the P300 component originated from FCz. This origination corresponds with the ACC, suggesting that the found P300 component corresponds to the P3a component. Stimulus intensity had an effect on the P300 in the form of a bigger amplitude. Furthermore, did unattended stimuli induce a more positive P300 amplitude at FCz and Cz, but not at CPz. All in all, the location and modulation of the found P300 suggested that it is the orienting component P3a, as described by different other studies (e.g. Legrain, Guérit, Bruyer, & Plaghki, 2002; Van der Lubbe, Buitenweg, Boschker ,Gerdes & Jongsma, 2012). Further analyses showed a group effect of mindfulness. The MBSR group had a decreased P3a amplitude at FCz for unattended stimuli. This suggests that the orienting response was less pronounced for the MBSR group than for the control group. Furthermore, an attentional effect on the latency of the P3a was found. The P3a seemed to peak later for unattended stimuli as compared to attended stimuli, which was shown by other studies as well (e.g. van der Lubbe et al., 2012; Ströfer, 2012).

The unexpected and relatively big individual differences in latencies are suspicious. One explanation for these individual differences between participants could be, that the method of intracutaneous electrical stimulation is not as reliable as was thought (Inui, Tran, Hoshiyama & Kakigi 2002; Mouraux, Iannetti & Plaghki 2010). This method should have activated only the Aδ fibers of the primary afferent axons and not the Aβ fibers. Thereby a combination of multimodal neural activities and somatosensory-specific activity should have been avoided. A nociceptive-specific activity should have been induced. Because the Aδ fibers transport the signals slower than the Aβ fibers it was expected that all latencies would be delayed. For example, other studies reported a sensory N1 component peaking around 100-160 ms (e.g. Desmedt & Robertson, 1977; Legrain, Guérit, Bruyer, & Plaghki, 2002; Van der Lubbe, Buitenweg, Boschker, Gerdes & Jongsma, 2012). In the present study most of the N1 peaks were found as late as 180ms post-stimulus. A few other N1 peaks however were found peaking much earlier, as indicated by the butterfly views. These earlier peaks seemed to have a latency that would be expected of Aβ fiber activation. This effect of individual differences was even bigger for P3a and made a peak detection analysis of the later P3b and NoGo-P3 impossible. These individual difference effects made the conclusions about the latency effects unreliable. One possible explanation for these differences could be a unexpected unreliability of the stimulation method. It seemed that the electrodes not just activated Aδ fibers, as was expected, but also Aβ fibers. This unreliability could be due to the not standardized and relatively vague placement method of the stimulus electrodes. Maybe sometimes the electrode needle was in direct proximity of particular fibers and other times not. Further studies are necessary to test the reliability of this method of intracutaneous stimulation.

In summary, the first hypothesis concerning the modulation of the N1 component had to be discarded, indicating that mindfulness had no influence on early sensory processing. MBSR-training seemed to induce a stronger habituation effect concerning pain, which was concluded from lower perceived pain ratings in the right arm of the experimental group. Furthermore, one of the hypotheses could be confirmed through the smaller P3a amplitude at FCz for unattended stimuli in the MBSR-group. This finding suggests that the positive effects of the MBSR-training on (chronic pain) patients could mostly be explained through a decreased attention of these patients on their pain.

References

Baer, R.A. (2003). Mindfulness training as a clinical intervention: A conceptual and empirical review. *Clinical Psychology: Science and Practice,* 10, 125–143.

Bishop, S.R., Lau, M., Shapiro, S., Carlson, L., Anderson, N.D., Carmody, J., Segal, Z.V., Abbey, S., Speca, M., Velting, D. & Devins, G. (2004). Mindfulness: A proposed operational definition. *Clinical Psychology: Science and Practice,* 11, 230–241.

Desmedt, J.E., & Robertson, D. (1977) Differential enhancement of early and late component of the cerebral somatosensory evoked potentials during forced-paced cognitive tasks in man. *Journal of Physiology*, 271, 761-782.

Dowman, R. (2004). Electrophysiological indices of orienting attention toward pain, *Psychophysiology*, 5, 749-761.

Friedman, D., Cycowicz, Y. M., & Gaeta, H. (2001). The novelty P3*:* An event-related brain potential (ERP) sign of the brain's evaluation of novelty. *Neuroscience and Biobehavioral Review,* 25, 355–373.

Hodgins, H.S., & Adair, K.C. (2010). Attentional processes and meditation. *Consciousness and Cognition*,19, 872-878.

Inui, K., Tran, T.D., Hoshiyama, M., & Kakigi, R. (2002). Preferential stimulation of Ad fibers by intra-epidermal needle electrode in humans. *Pain*, 96, 247-52.

Jha, A.P., Krompinger, J., & Baime, M.J. (2007). Mindfulness training modifies subsystems of attention. *Cognitive, Affective, & Behavioral Neuroscience,* 7, 102-119.

Kabat-Zinn, J., Lipworth, L., & Burney, R. (1985). The clinical use of mindfulness meditation for the self-regulation of chronic pain. *Journal of Behavioral Medicine,* 8, 163-190.

Kabat-Zinn, J. (1982). An outpatient program in behavioral medicine for chronic pain patients based on the practice of mindfulness meditation: Theoretical considerations and preliminary results. *General hospital psychiatry,* 4, 33-4.

Kabat-Zinn, J. (1994). Wherever you go there you are (pp. 4). *New York, NY: Hyperion.*

Kabat-Zinn, J. (2003). Mindfulness based interventions in context: Past, present, and future. *Clinical Psychology: Science and Practice,* 10, 144-156.

Kropotov, J.D., Ponomarev, V.A., Hollup, S., & Mueller, A. (2011).Dissociating action inhibition, conflict monitoring and sensory mismatch into independent components of event related potentials in GO/NOGO task. *NeuroImage,* 57, 565-575.

Legrain, V., Guérit, J.-M., Bruyer, R., & Plaghki, L. (2002). Attentional modulation of the nociceptive processing into the human brain: selective spatial attention, probability of stimulus occurrence, and target detection effects on laser evoked potentials. *Pain,* 99, 21-39.

LeBlanc, J., & Potvin, P. (1966). Studies on habituation to cold pain. *Canadian Journal of Physiology and Pharmacology,* 44, 287–93.

Manchikanti (2007). Interventional Pain Management: Past, Present, and Future. The Prithvi Raj Lecture: Presented at the 4th World Congress- World Institute of Pain, Budapest, 2007. *Pain Practice,* 7, 357-371.

Marlatt, G.A., & Kristeller, J.L. (1999). Mindfulness and meditation. In W.R. Miller (Ed.), Integrating spirituality into treatment (pp. 68). *Washington, DC: American Psychological Association*.

Mouraux, A., Iannetti, G.D., & Plaghki, L. (2010). Low intensity intra-epidermal electrical stimulation can activate Ad-nociceptors selectively. *Pain*, 150, 199–207.

Nakata, H., Sakamoto, K., Ferretti, A., Gianni Perrucci, M.,Del Gratta, C., Kakigi,R. & Luca Romani, G. (2008). Somato-motor inhibitory processing in humans: An event-related functional MRI study. *NeuroImage,* 39, 1858–1866.

Polich, J. (2003). Theoretical overview of *P3a and P3b*. In Detection of change: Event-related potential and fMRI findings, *J.Polich* (Ed.) (pp. *83–98). Boston: Kluwer Academic Press.*

Polich, J. (2007). Updating P300: An integrative theory of P3a and P3b. *Clinical Neurophysiology*, 118, 2128-2148.

Randolph, P.D., Caldera, Y.M., Tacone, A.M. & Greek, M.L. (1999). The long-term combined effects of medical treatment and a mindfulness-based behavioral program for the multidisciplinary management of chronic pain in west Texas. *Pain digest*, 9, 103-112.

Reid, K.J., Harker, J., Bala, M.M., Truyers, C., Kellen, E., Bekkering, G.E. & Kleijnen, J. (2011). Epidemiology of chronic non-cancer pain in Europe: narrative review of prevalence, pain treatments and pain impact. *Current Medical Research and Opinion,* 27, 449-62.

Sahdra, B.K., MacLean, K.A., Ferrer, E,. Shaver, P.R., Rosenberg, E.L., Jacobs, T.L., Zanesco, A.P., King, B.G., Aichele, S.R., Bridwell, D.A., Mangun, G.R., Lavy, S., Wallace, B.A., & Saron, C.D. (2011). Enhanced response inhibition during intensive meditation training predicts improvements in self-reported adaptive socioemotional functioning. *Emotion*, 11, 299-312.

Sauer, S., Walach, H., & Kohls, N. (2011). Gray’s Behavioural Inhibition System as a mediator of mindfulness towards well-being. *Personality and Individual Differences,* 50, 506-511.

Shapiro, S.L., Carlson, L.E., Astin, J.A., & Freedman, B. (2006).Mechanisms of mindfulness. *Journal of Clinical Psychology,* 3, 378–386.

Ströfer, S. (2012). The influence of mindfulness on pain perception. Mindfulness training decreases the automatic orientation towards nociceptive stimuli. *Unpublished Master Thesis*, University of Twente.

Van den Hurk, P.A.M., Giommi, F., Gielen, S.C., Speckens, A.E.M. & Barendregt, H. P. (2010). Greater efficiency in attentional processing related to mindfulness meditation. *The Quarterly Journal of Experimental Psychology*, 63, 1168-1180.

Van der Lubbe, R.H.J., Buitenweg, J.R., Boschker, M., Gerdes, B., & Jongsma, M.L.A (2012). The influence of transient spatial attention on the processing of intracutaneous electrical stimuli examined with ERPs. *Clinical Neurophysiology*, 123, 947–959.

Valentini, E., Hu, L., Chakrabarti, B., Hu, Y.. Aglioti, S.M., & Iannetti, G.D. (2012). The primary somatosensory cortex largely contributes to the early part of the cortical response elicited by nociceptive stimuli. *NeuroImage,* 59, 1571–1581.