The influence of mindfulness on pain perception

Mindfulness training decreases the automatic orientation towards nociceptive stimuli

Sabine Ströfer

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1st supervisor: Dr. Rob van der Lubbe

2nd supervisor: MSc. Jorian Blom

Abstract

Objective: Determine the influence of mindfulness training and spatial attention on pain perception, by examining the early sensory processing (N1) of and the orienting response (P3a) towards nociceptive stimuli.

Methods: Separate- sample pretest-posttest design was used. The treatment consisted of the mindfulness based stress reduction program (MBSR). Electrical stimuli of low (two pulses) or high intensity (five pulses) were presented on the right or left wrist. The stimulated wrist varied randomly from trial to trial. The to-be-attended site remained the same half of the experiment and varied randomly from trial to trial in the other half. Participants got the instruction to press a foot pedal when a stimulus of relevant intensity (varied between participants) occurred at the attended hand. EEG was recorded to extract the ERPs N1 and P3a, evoked by the electrical stimuli. ERPs and task performance were compared between the treatment and control group.

Results: N1 was enhanced for attended as compared to unattended stimuli and P3a was enhanced for unattended as compared to attended stimuli. Both ERPs were enlarged for five-pulse stimuli as compared to two-pulse stimuli. P3a was higher in the control group than in the treatment group. Although this enhancement was most seen at unattended stimuli, the interaction between attention and group did not reach significance. No group difference was found on task performance.

Conclusion: Mindfulness training reduces the automatic orientation towards pain stimuli. The attention capturing effect of pain stimuli thus can be reduced by mindfulness training. However, mindfulness does not affect early sensory processing of pain. Unlike expected, also spatial attention towards the pain stimuli was unrelated to these finding.

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1. Introduction

The treatment of chronic pain with psychological therapies has had limited effectiveness until now (e.g. Eccleston, Williams, Morley, 2009).

But a meta analysis by Bear (2003) revealed promising results for mindfulness therapy in chronic pain treatment. In the reviewed studies, patients showed significant improvements in pain ratings after having participated in mindfulness trainings. However, these findings were based on self-reports and often even did not use randomized trials. Little is known about mindfulness on a neuropsychological basis (Shapiro, Carlson, Astin, & Freedman, 2006). Hence, this study uses EEG to examine how mindfulness training influences the attentional orientation towards nociceptive stimuli.

Attentional orientation was chosen because the central idea of mindfulness is a change in the orienting of attention by learning to attend to stimuli in a neutral way. This is often taught through meditation exercises which lay their emphasis on paying attention on purpose, the present moment and non-judgmentally (Kabat-Zinn, 2003).

The international association for the study of pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (Merskey & Bogduk, 1994). On a neurological basis, the somatosensory cortex (S1, S2) and the anterior cingulated cortex (ACC) have been consistently shown to respond to nociceptive stimuli (Iannetti and Mouroux, 2010).

It is assumed that the somatosensory cortex is involved in nociception; the detection of (potential) tissue damage by A- δ Delta and C fibers in the tissue. Due to their noxious nature, nociceptive stimuli are very salient, which means that they contrasts with their surrounding input and draw attention (Iannetti and Mouroux, 2010; Itti and Koch, 2001). Recent review papers on nociception argue that activity in the ACC reflects an attentional orientation

towards this stimulus salience, which enables the perception of nociception (Iannetti and Mouroux, 2010; Legrain, Iannetti, Plaghki, Mouraux, 2011). Based on this, we assume that the somatosensory cortex is involved in detection and the ACC in the perception of nociceptive stimuli through orienting attention. A crucial key role in pain perception thus is attention, the mechanism by which sensory events are selected and enter awareness (Legrain, Damme, Eccleston, Davis, Seminowicz, Crombez, 2009).

The effect of attention on pain often has been described by the limited capacity model of human cognition which differentiate top-down and bottom-up attention. The involuntary capture of attention by pain is called bottom-up attention (see e.g. Eccleston and Crombez, 1999). However, attention also can also be directed away from nociceptive stimuli by top-down attention. Studies have shown that this weakens the involuntary capturing effect and reduces the pain experience (e.g. Van Damme, Crombez, Eccleston, 2008). This top-down effect already affects the early sensory processing of pain by biasing activity in the somatosensory cortex (Legrain, Guérit, Bruyer, Plaghki, 2002). Consequently, also the orientation towards the nociception is attenuated. On the other hand, directing attention towards nociceptive stimuli facilitate the attentional capture of pain (Legrain et al., 2009).

At this point, mindfulness training becomes important since it teaches to regulate the focus of attention. On a behavioral level, it is already shown that mindfulness improves focusing on relevant information (Top down) while attenuating the orientation reflex towards task-irrelevant information (Bottom-up) (e.g. Jha, Krompinger & Baime, 2007; Hodgins and Adiar, 2010; Slagter et al., 2007). We assume that this also applies for the processing of pain.

This study examines the above assumption on an electrophysiological basis through examining changes in N1 and P3a as function of nociceptive stimulation. These ERP components are thought to originate from respectively the somatosensory cortex and the ACC, the two brains which are activated in response to nociceptive stimuli. This makes N1 and P3a good indicators for the early sensory processing of nociceptive stimuli and the

orientation towards them. N1 is rather an automatic response to sensory stimulation but can also be moderated by top-down attention (Fabiani, Gratton, Federmeier, 2007). P3a is a more endogenous component and occurs when the subject shift orientation towards a salient stimulus (Nieuwenhuis, De Geus, Aston-Jones, 2011).

Our experimental design is based on a recent EEG study by Van der Lubbe, Buitenweg, Boschker, Gerdes and Jongsma (2012). They studied the effect of transient spatial attention on the processing on intracutaneous electrical stimuli, using a Posner-like visual cueing task (Posner & Snyder, 1980). In our study, some adoptions were made.

First of all the effect of mindfulness was investigated by a separate-sample pretest-posttest design (Campbell & Stanley, 1963). As treatment, the mindfulness-based stress reduction program (MBSR) is used. MBSR is tailored towards the treatment of chronic pain and lays the emphasis in its meditation exercises on somatic attention (Veehof, Oskam, Schreurs, Bohlmeijer, 2011; Kerr et al., 2011).

We also use another stimulation method: small planar concentric electrodes by Inui, Diep Tran, Hoshiyama, Kakigi (2002). These intracutaneous electrodes limit depolarization to the superficial layer of the epidermis, providing that activation is limited to the nociceptive A-δ fibers. In contrast, Van der Lubbe et al. (2012) used intracutaneous stimulation according to the method of Bromm and Meier (1984). This method stimulated also the deeper non-nocicepetive A- β fibers and thus could not assure purely by nociception evoked ERPs.

Furthermore, we added to the existing transient attention manipulation task, a task version of sustained spatial attention. This version is different in that the to-be-attended hand remains the same throughout the experiment. The rationale behind this choice lies in the study of Eimer and Forster (2003). They found an earlier effect of spatial attention in sustained than in transient attention (activity in S1 occurred only in a sustained attention manipulation). Seemingly, attention can be focused more efficiently when it is maintained at

one location. It would be interesting to see whether this moderates the effect of mindfulness on pain processing.

Moreover, both kinds of spatial attention apply to mindfulness training. Techniques as e.g. the body scan learn to maintain attention to a single part of the body (sustained attention) and disengage from irrelevant feelings or thoughts, affording transient attention (Kerr et al., 2011; Bishop, 2004).

In our study we expect that N1 and P3a, evoked by pain stimuli, will be modified by the mindfulness training. This would respectively indicate effects on early sensory processing and orientation aspects of pain. Because mindfulness is supposed to facilitate the ability to orient attention, we expect superiority in suppressing the orientation reflex towards unattended pain stimuli. This should be displayed by lower N1 and P3a amplitudes for unattended stimuli. On the other side, we expect that they also are better in voluntary orienting their attention. This would imply that they have higher N1 and P3a amplitude on attended pain stimuli. The findings on the neuropsychological basis should also be seen in the participant's behavior. For this purpose we instructed participants to react only on relevant stimuli which occur at the cued side by pressing a foot pedal. For half of the participants high, and for the other half low stimuli were relevant. We expect that the MBSR group outperforms the control group. As indicators for task performance serve the sensitivity measure d' and response strategy measure C which are based on the Signal detection theory (Abdi, 2007).

Independent from the mindfulness effect, we expect to verify the results of Van der Lubbe et al., (2012). They found and enhanced N1 for attended compared to unattended stimuli, indicating that spatial attention intensify early sensory processing of pain. However P3a was higher for unattended pain stimuli, indicating that spatially unattended pain induces a stronger orientation reflex. These findings were based on the transient version of the Posner task. We expect the same pattern within the sustained attentional manipulation even though there are studies which found the opposite for P3a (e.g. Blom, Wiering, Van der Lubbe,

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submitted; Legrain et al., 2002). However, these studies differ in stimulation method as well as task design which makes it difficult to build up our hypotheses on them. Furthermore we expect N1 and P3a to be enhanced for high pain stimuli, as both are known to increase with stimulus intensity (Nakajima & Imamura, 2000).

2. Method

2.1. Participants

34 students from the Faculty of behavioral sciences of the University of Twente took part in the experiment (5 male and 29 female). The age ranged from 20 to 34 years ($M =$ 23.74, $SD = 3.27$). Handedness was assessed with Annet's handedness inventory (Annet, 1970). One participant was left-handed and one was ambidexter. All other participants were right-handed. Two participants respectively had a weak form of the red-green color blindness and dyslexia. All participants received an eight -week long mindfulness training in exchange for their participation. Prior to the study, participants signed an informed consent. They agreed to take part in two EEG sessions in which they received nociceptive stimuli embedded in attention- related tasks. The study was approved by the medical ethical commission of the 'Medisch Spectrum Twente' (NL 37791.onn.II).

2.2. Exclusion criteria

The participants in this study had to be aged between 18 and 65 years. Following prerequisites had to be met: No alcohol or drugs consumption in the 24 hours prior to experiment and no coffee or nicotine consumption one hour before the experiment as they can influence attention (Moore, Keogh, Eccleston, 2009). Furthermore, participants with mental or physical disorders, poor visual capacity or physical pain complaints were excluded.

2.3. The Mindfulness-based stress reduction (MBSR) training

The MBSR training lasted eight weeks. In this time span, the participants attended weekly group sessions (n = 10-40) of 2.5 hours. These sessions were led by an experienced meditator who daily practices meditation/yoga. At the end of each session, the participants got homework assignments to carry out daily for 20-45 minutes. Participants received training in

informal and formal exercises. The former includes training which aims to develop attentiveness in daily activities. The latter is supposed to let people become increasingly present in each moment in everyday life. The formal meditative exercises consisted of the body-scan, sitting mindfulness meditation, Hatha-yoga exercises and meditative walking (Hulsbergen, 2009). During the body- scan, the participant progressively moves the attention through the body from toes to head. At each body part, any sensation felt at that moment is noticed without judging it. This practice is supposed to increase body –consciousness and concentration and aims to foster the participant's ability to anchor in the present moment. The sitting mindfulness meditation involves awareness of body sensations, thoughts and emotions while focusing the attention to the breath. Again, it is important to experience all sensations, thoughts and emotions without judging them. A variation of this exercise, the free- choice sitting mindfulness meditation is also contained in the MBSR program. Instead of focusing attention solely to the breath, the object of mediation is anything that appears in consciousness. A further practice is the Hatha- yoga exercise which strives to attain a balance between body, mind and soul through combining physical postures with breathing and meditation. In another practice, called meditative walking, the feet/legs are the object of meditation. It can be practiced in different ways, from alert fast walking to slow walking. All mentioned formal exercises have in common that attention can flow away easily. If this happens, attention needs to be directed back.

2.4. Experimental design

"Seperate –sample pretest- posttest" design is used (Campbell & Stanley, 1963). Participants were randomly assigned into a control and MBSR group. Both consisted of 17 participants, received the MBSR training as described under 2.3 and start and finish the eight week long program concurrently. The control group took part in the EEG experiment before and the MBSR group after having received the MBSR training. This design allows examining

the effect of the mindfulness training through comparing the EEG data of both groups (see figure 1). For half of the participants within each group, 'high intensity' and for the other half 'low intensity' stimuli were relevant during the EEG experiment (see 2.7 for more detail).

Figure 1: Study design

Control group:	R	O	X
MBSR group:	R	X	O

Note: Rows present randomly equivalent groups, X represents the treatment. O stands for the EEG measurement. One group is measures prior and the other the after the treatment.

2.5. Procedure

One experiment session lasts three hours and took place at the University Twente. Participants were seated 60 cm in front of a 17 inch CRT monitor. Before starting the experiment, participants indicate their handedness (Annet, 1970) and filled in Thayer's mood scale (Thayer, 1989) and the Five Facet Mindfulness Questionnaire – short form (FFMQ- SF) (Bohlmeijer, ten Klooster, Fledderus, Veehof, Baer, 2011).

The former assesses the current mood state and the latter the degree of mindfulness. Furthermore we checked for neurological illness and motorical problems. Both could influence task performance. After completing the initial questionnaires, the EEG and stimulation electrodes on the right and left forearm at the dorsal wrists were attached. The employed stimuli intensities during the experiment were individually determined in a pre-test. Finally the room was darkened and the experiment (duration: one hour) started. After the experiment, the participants filled in Thayer's mood scale again to assess possible changes in mood.

2.6. Stimuli

'Pulse train modulation' was used to create different stimulus intensities. Instead of modulating the current, this method varies the number of successively occurring pulses at a

constant current. This leads to changes in pain perception through influencing the number of generated action potentials. The same fibers are recruited for all stimuli intensities. This is desirable, because it minimizes uncontrolled variety (Van der Heide, Buitenweg, Marani, Rutten, 2009).

Before varying the impulses, the employed current had to be determined for each participant. This allows us to account for inter- subjective differences in pain perception and recruited skin fibers.

The used current was calculated in a pre –test in which three intensity thresholds were set. To determine these thresholds, a series of stimuli in ascending intensity were administered. The series started at 0 mA and subsequently rise with steps of 0.1 mA. Stimuli existed of five pulses with a pulse duration of 1 ms and a pulse interval of 5 ms. Participants indicated when they reach a certain intensity-threshold through pushing a key. First we assessed the 'pain threshold' (PT) which describes the transition from a mild to a stimulating displeasure sensation. Then we determined the 'detection threshold' (DT) which indicates the point at which the subject start sensing something. Finally, the 'pain-tolerance threshold' (TT) was determined which indicates the maximal intensity a participant will accept during the experiment. After this, the level of the current was no longer heightened. Each threshold was determined three times for both arms to obtain an average per threshold and arm.

In the experiment, the current for all stimuli was the attained average of the TT-threshold (five pulses). To establish stimuli of high and low intensity, the number of pulses was manipulated without changing the individually determined current. Low intensity stimuli existed of two pulses, which caused that the pain perception lies beneath the TT -threshold. High intensity stimuli in contrast existed of five pulses and thus equaled the TT - threshold.

2.7. Task

In the visual cueing Posner task, participants were instructed to shift their attention to one side, indicated by a visual arrow. After that cue, participants receive a painful stimulus on their left or right forearm of either low or high intensity. The cue predicts for 50% the side on which the stimuli will appear. One experiment consists of four blocks. Two blocks contain the 'sustained attention' version and the other two blocks the 'transient attention' version of the task. In the 'sustained attention' version the visual arrow points to the same direction during the whole block whereas in the 'transient attention' version the position of the visual arrow switched pseudo randomly from trial to trial.

The experiment consisted of four blocks of 96 trials. Prior to the first block the agreement between the computed stimuli intensities (two and five pulses) and the subjective pain perception were assessed. This was done using a digital continuous VAS scale which ranges from '0' (no perceived stimulus) to '10' (extreme painful stimulus). The participant consecutively received eight stimuli in a random order (Pulses: two/five, arm: left/right). Each stimulus combination had to be rated twice. The differences of two pulse and five pulse stimuli are supposed to be reflected in the VAS-scale ratings.

After the stimuli ratings, the participant received a high (five pulses) and low stimulus (two pulses) on each arm which served as examples. At the end of each block participants rated again the eight stimuli on the VAS-scale to control for habituation effects on pain perception.

Figure 2 shows the task design employed in all blocks. Participants were instructed to hold their gaze at the screen center during the task. At the screen center a fixation cross appeared. After 1200 ms it is replaced by a cue for 400 ms. This cue existed of a red and green triangle which point into opposite directions. Subjects were instructed to attend but not look to the arm, towards the red or either the green triangle is pointing to. Whether this is

green or red varied per block. The order of the color instruction was counterbalanced to make sure that each color became relevant in two blocks. After the cue, the fixation cross appeared again for 600 ms. Then the pain stimulus was delivered of either a high (five pulses) or low intensity (two pulses) on either the left or right forearm. Each stimulus combination (two/five pulses, right/left arm, attended/unattended) occurred equally likely and varied pseudo randomly from trial to trial. Both groups were divided into the 'high intensity' and 'low intensity' condition. For the first condition, stimuli of five pulses and for the latter stimuli of two pulses were relevant. Participants only had to give a response when the relevant intensity occurred at the wrist on the attended site. We will call these trails 'Go-trials' and all other trials 'No-Go trials'.

Figure 2: Posner task design
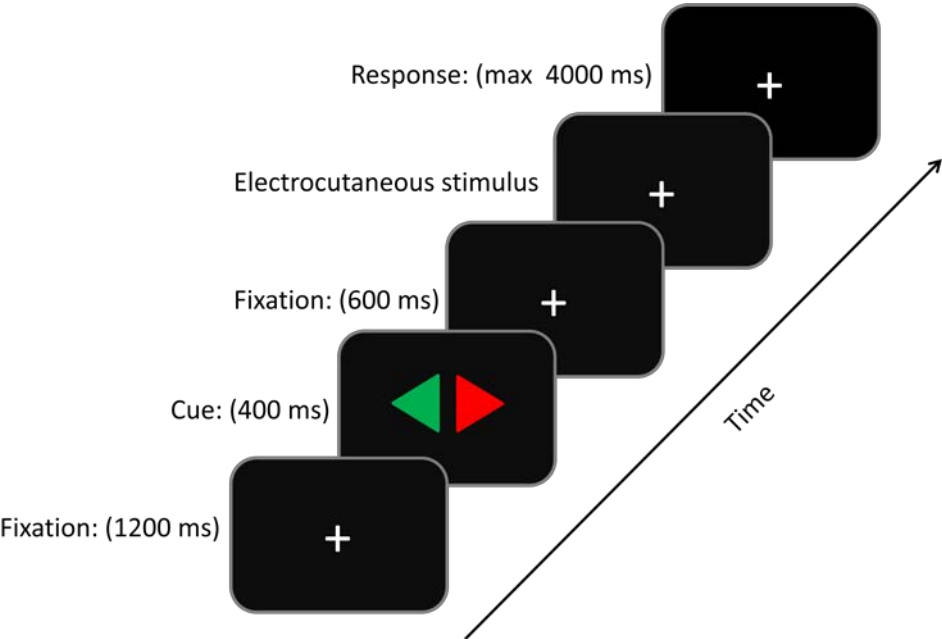
Note: Trials begin with a fixation-cross, presented in the center of the screen for 1200 ms. Then a cue is presented for 400 ms. The electrocutaneous stimulus is presented 600 ms after the disappearance of the cue. The electrocutaneous stimulus can be of high or low intensity and can administered to the cued location or to the other location. Participants are instructed to react only to stimuli which occur at the cued side of the relevant intensity (high or low) by pressing the right foot-pedal.

2.8. Apparatus and programs

The Posner –task was programmed with E- prime ® software. Two 'DS5 isolated bipolar constant current stimulators' (Digitimer, Welwyn Garden City, UK) were used for the intracutaneous electrical stimulation. The stimuli were delivered through two stainless steel concentric bipolar needle electrodes which were attached on both forearms (Inui et al., 2002). Depending on the stimulus intensity, the electrical stimulus consists of either two block- wave or five consecutive block –wave pulses. EEG data was recorded and analyzed with brain vision analyzer (2.0.1). The statistical tests were conducted with SPSS (statistical package of the social sciences) 18.

2.9. Recordings

EEG data was acquired at 500 Hz through Brain Vision recorder. 61 passive Ag/AgCl ring electrodes were used at locations in line with the extended international 10-20 system. To account for eye movements, bipolar electrodes were used 1cm lateral to the outer canthi to measure horizontal EOG (electrooculogram). Similarly, bipolar electrodes 1 cm above and below the left eye were used to record vertical EOG. The data were corrected for EOG artifacts by using the method by Gratton, Coles and Donchin (1983). For all participants, the impedance was set lower than 10 KΩ. The ground electrode was placed at the center of the forehead. All channels were referenced to the common average reference online. The raw data was digitally filtered offline with a 0.159 Hertz, 12-dB/octave low-cutoff filter and a 30 Hz 12-dB/octave high cutoff filter. For the behavioral analysis, pedal presses and digital codes related to stimulus events were recorded and registered.

2.10. Data analysis

2.10.1 Behavioral measures

Performance comparison between the MBSR and control group were based on discrimination capability and response strategy. Both were respectively measured by the parameters d' and C from the Signal detection theory (SDT). d' indicates how well a participant discriminates between Go- and No Go trials whereas C reveals the participant's bias to rather react or not react on a given stimulus.

Both parameters where based on hit- rate (H) and false- alarm rate (F). The hit-rate is calculated by dividing the number of correct reactions (hits) on Go trials by the total number of Go-trials. The false- alarm rate is determined by dividing the number of false alarms (reaction on No-Go trials) by the total number of No-Go trials.

To attain d', the standardized false- alarm rate has to be subtracted from the standardized hit-rate by using the formula d' = z (H) – z (F). High d' values indicate a good discrimination capability. C is calculated by using the formula $C = -\frac{1}{2}[z(H) + z(F)]$. Negative values indicate a liberal strategy (rather react on a stimulus) and positive values indicate a conservative strategy (rather not react on a stimulus).

Hit- and false-alarm rates of 1 and 0 were corrected respectively to 1/ (2N) and 1- (1/2N). N represents the number of trials on which the Hit and false- alarm rates were based. Through this conversion, infinite z values can be avoided (Macmillian and Creelman, 2005).

A repeated measures ANOVA with within-subject factor task (transient/sustained) and between subject factor group (MBSR/control) was conducted to examine effects on d' and C.

2.10.3 Questionnaire measures

The VAS- scores recording between the blocks served to assess the degree of pain habituation during task performance. A repeated measures ANOVA with the within-subject

factors block (pre- experimental block, first block, second block, third block, fourth block), stimulus (two pulses, five pulses) and hand (right, left) and group (MBSR/control) as between subject factor was used.

Changes in mood during the experiment were checked with Thayer's mood scale which was administered before and after the EEG experiment. Changes in mood could give insight in the task load and complexity of the experiment. On a visual analogue scale the participant indicated how tired, indifferent, anxious, happy, energetic, tense, positive, irritable, agitated and relaxed they felt at that moment. Each scale was 110 mm long. The participant's calculated score for each emotion (0 - 110) corresponds with the distance of the marker (in mm) from the start of the visual line. High values display a high presence of the corresponding emotion. Paired sample t-tests were used to check for differences in mood before and after the experiment.

2.10.4 EEG measures

We segmented the raw data into intervals from -100 to 500 ms relative to the onset of the intracutaneous electrical stimuli. The baseline was set from -100 to 0 ms. Trials with artifacts (voltage step higher than 100 µV/ms) and out of range values (+/- 250 µV for prefrontal electrodes, +/- 200 µV for frontal electrodes, +/- 150 µV for central electrodes, and +/- 100 µV for parietal electrodes) occurring within 200 ms before and after the pain stimulus were excluded from further analyses. The procedure removed 71 trials across all participants which is less than 1 % of all trials (n = 13056). Subjects left over 99.4 % of the trials on average with a minimum of 92.2 % and maximum of 100%.

ERPs were computed per individual as a function of electrode, stimulation side, stimulus intensity, attention, task version, group and instruction. The 0 to 500 intervals again were sub segmented into 25 time windows of 20 ms length each. Relevant time window groups for analysis of the different ERP components were determined after inspection of the

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grand means and topographic maps (figure 3-5). The following time intervals were selected: N100: 160-200 ms on C5 and C6; P300a: 200-240 ms for attended and 280-320 ms for unattended stimuli on FCz. Obtained averages per individual were subjected to ANOVAs as function of task, time window, electrode, attention, stimulus intensity (number of pulses), stimulation site, group and instruction.

3. Results

3.1. Questionnaire data

3.1.1 Mood scale

A comparison between the ratings on the mood scale revealed changes in certain emotions during the experiment. Participants felt significant more indifferent ($t = -2.70$, $p < 0.01$), relaxed ($t = -2.08$, $p = 0.05$) and tired ($t = -5.04$, $p < 0.01$) after the experiment. They felt less happy ($t = 4.14$, $p < 0.01$), less energetic ($t = 5.27$, $p < 0.01$), less tense ($t = 2.29$, $p = 0.03$), less positive ($t = 2.54$, $p = 0.02$) and less agitated ($t = 3.54$, $p < 0.00$) after the experiment.

3.1.2. VAS scale

The ANOVA on the VAS scores revealed a main effect of stimulus intensity ($F_{(1, 32)} = 125.35$, $p < 0.001$) and block ($F_{(4, 128)} = 33.05$, $\varepsilon = 0.69$, $p < 0.001$). As expected, five-pulse stimuli were judged as more painful ($M = 4.5$, $SD = 0.2$) than two-pulse stimuli ($M = 2.9$, $SD = 0.2$). After each block, the perceived pain intensity decreased starting with 4.1 for two-pulse and 5.6 for five-pulse stimuli on the VAS-scale. This habituation effect from trial to subsequent trial was significant between the pre- experimental ($M = 4.8$, $SD = 0.2$) and first block ($M = 4.0$, $SD = 0.2$) and between the second ($M = 3.7$, $SD = 0.2$) and third block ($M = 3.0$, $SD = 0.3$).

Surprisingly, the groups almost differ significantly on pain perception ($F_{(1, 32)} = 2.87$, $p = 0.10$). The control group which had not yet received the mindfulness training had a higher VAS-Score ($M = 4.0$, $SD = 0.25$) than the MBSR group which already received the training ($M = 3.4$, $SD = 0.25$).

Independent sample t- Test revealed that the MBSR and control group differ in their degree of mindfulness ($t = -3.21$, $p = 0.03$). The MBSR group (*M*=87.88, *SD*=9.16) scored higher on the test than the control group (*M*=76.88, *SD*=10.78), indicating that the mindfulness training increased self-reported mindfulness.

3.2. Behavioral Data

Prior to analysis, seven from a total of 136 blocks had to be removed. These were blocks in which participants lost the food pedal or stimulation electrode, misunderstood the task or stated to be unable to discriminate between stimuli.

The ANOVA on d' revealed neither group differences, $F(1, 30) = 1.61$, $p = 0.22$, nor task differences, $F(1, 30) = 0.18$, $p = 0.67$. Also on C no group differences, $F(1, 30) = 0.007$, $p = 0.933$, or task differences were found, $F(1, 30) = 1.00$, $p = 0.325$.

3.3 EEG Data

Grand averages and topographical maps of the ERPs N1 and P3a can be seen in figure 3-5. Both were used to choose appropriate electrodes and time intervals for statistical analyses. The chosen time intervals for N1 and P3a were split into two time windows (2 x 20 ms) which allowed tracing activity changes in time.

Inspection of topographic maps revealed that activity for N100 was maximal at T8, FT6, C6 and T7, FT7, C5 for left and right stimuli respectively (see figure 3). Although activity was higher at the temporal electrodes, inspection of the EEG signal revealed no clear N1 component. It is assumable, that the signal was distorted by movements of the jaw. Therefore C5 and C6 were chosen for further N100 analyses. The grand averages showed that the N100 occurred between 160 and 200 ms (see figure 4). Based on this time interval, a repeated measures ANOVA was conducted for N1 with within-subject factors task (transient, sustained), time window (160-180ms/180-200ms), electrode (C5/C6), attention

(attended/unattended), number of pulses (two/five), side of stimulation (left/right) and between subject factors group (Mindfulness/Control) and instruction (high stimuli/low stimuli).

The choice for the P300a time interval was less straightforward. Inspection of the grand averages revealed that the P300a was shifted in time as function of attention. P3a was expressed between 200-240 ms for attended and between 280-320 ms for unattended stimuli in both task versions (see figure 5). Therefore we conducted the ANOVA twice: one time for attended stimuli between 200 and 240ms and the other time for unattended stimuli between 280 and 320ms.

The AVONAs for attended and unattended stimuli both contained the within-subject factors task (transient, sustained), time window (2x 20 ms), number of pulses (two/five), side of stimulation (left/right) and between subject factors group (Mindfulness/Control). Unlike at N1, instruction was excluded, because it neither revealed a main effect nor interacts with group as factor.

Also attention as factor was excluded. Keeping it would be inappropriate. In the first time interval, the amplitude of attended stimuli would be compared with the slope of unattended stimuli. In the second interval, the amplitude of unattended stimuli would be compared to the maximum of a P3b for attended stimuli. P3b followed both P3a peaks around 60 ms later and was also shifted in time as function of attention. It was classified as P3b according to its more temporal- parietal activity (Polich, 2007).

A final ANOVA for P3a was conducted with within-subject factors attention (attended/unattended) and task (transient/sustained) and between subject factor group. The factor attention in this ANOVA contained as level activity from attended stimuli (between 200-240 ms) and unattended stimuli (between 280-320 ms). This made possible to look for overall effect of attention, group, task and possible interactions between them.
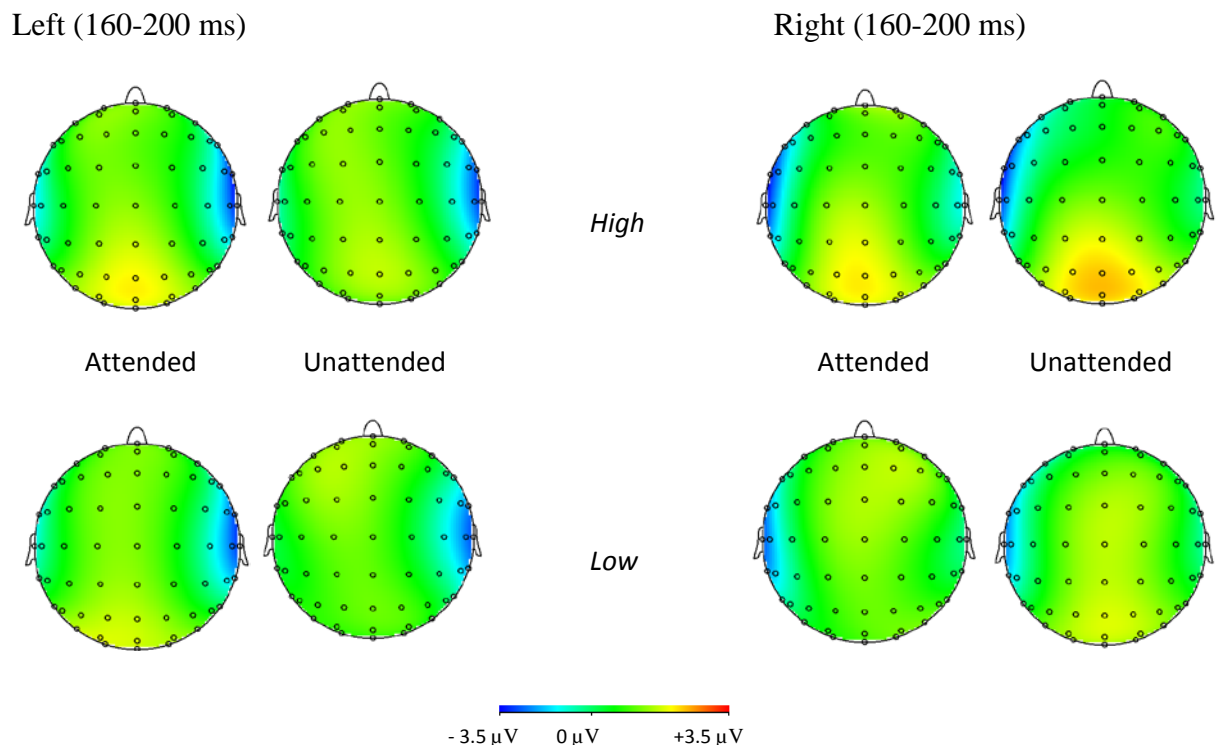
With regard to the electrode, FCz was chosen for the P3a analyses. Pre-analyses including the electrodes FCz, Cz and PCz and inspections of the topographic maps revealed that this was the most appropriate electrode to analyze P3a.

# Figure 3: Topographical maps of P3a and N1 (top view)

A: P3a

Attended (200-240 ms)   Unattended (280-320 ms)
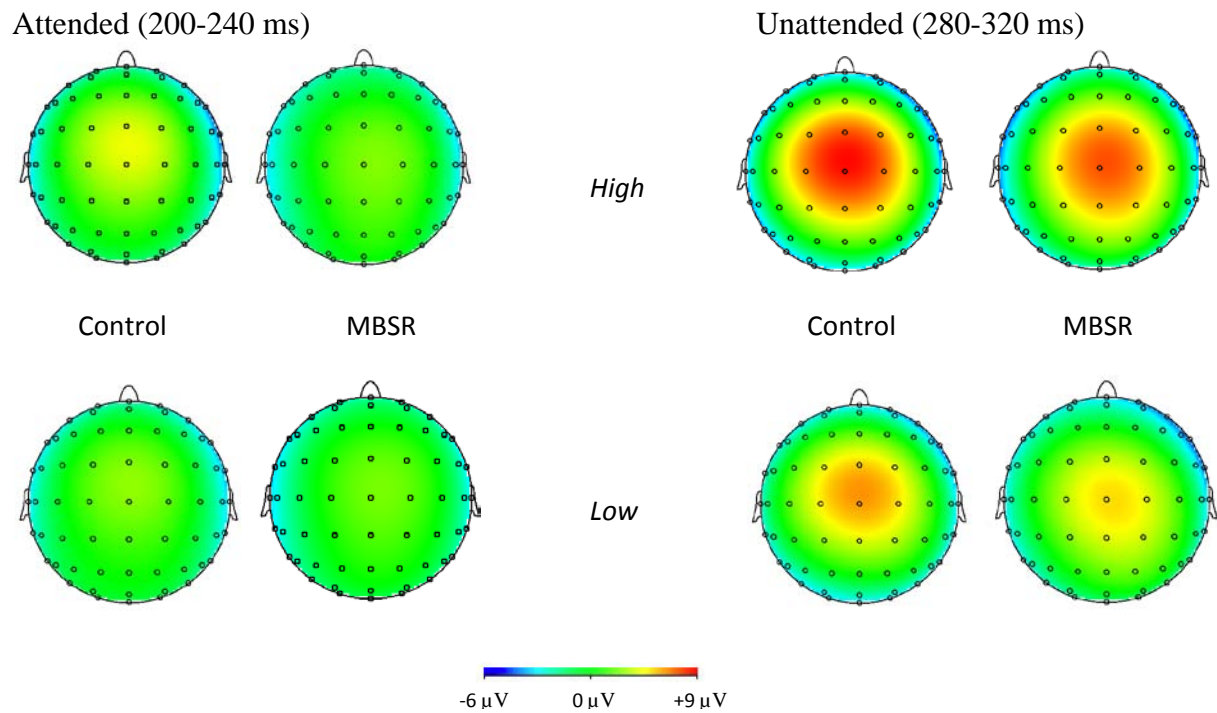
Note: In panel A, topographical maps for P3a (for attended stimuli from 200-240 ms and unattended stimuli 280-320 ms after stimulus onset) as function of group (MBSR or control group), attention (attended or unattended) and stimulus intensity (two pulses or five pulses) are displayed. In panel B, the topographical maps for N1 from 160 – 200 ms after stimulus onset as function of attention (attended or unattended), stimulus intensity (two pulses or five pulses) and site (left/right) are displayed.

Figure 4: N100 at C5 and C6
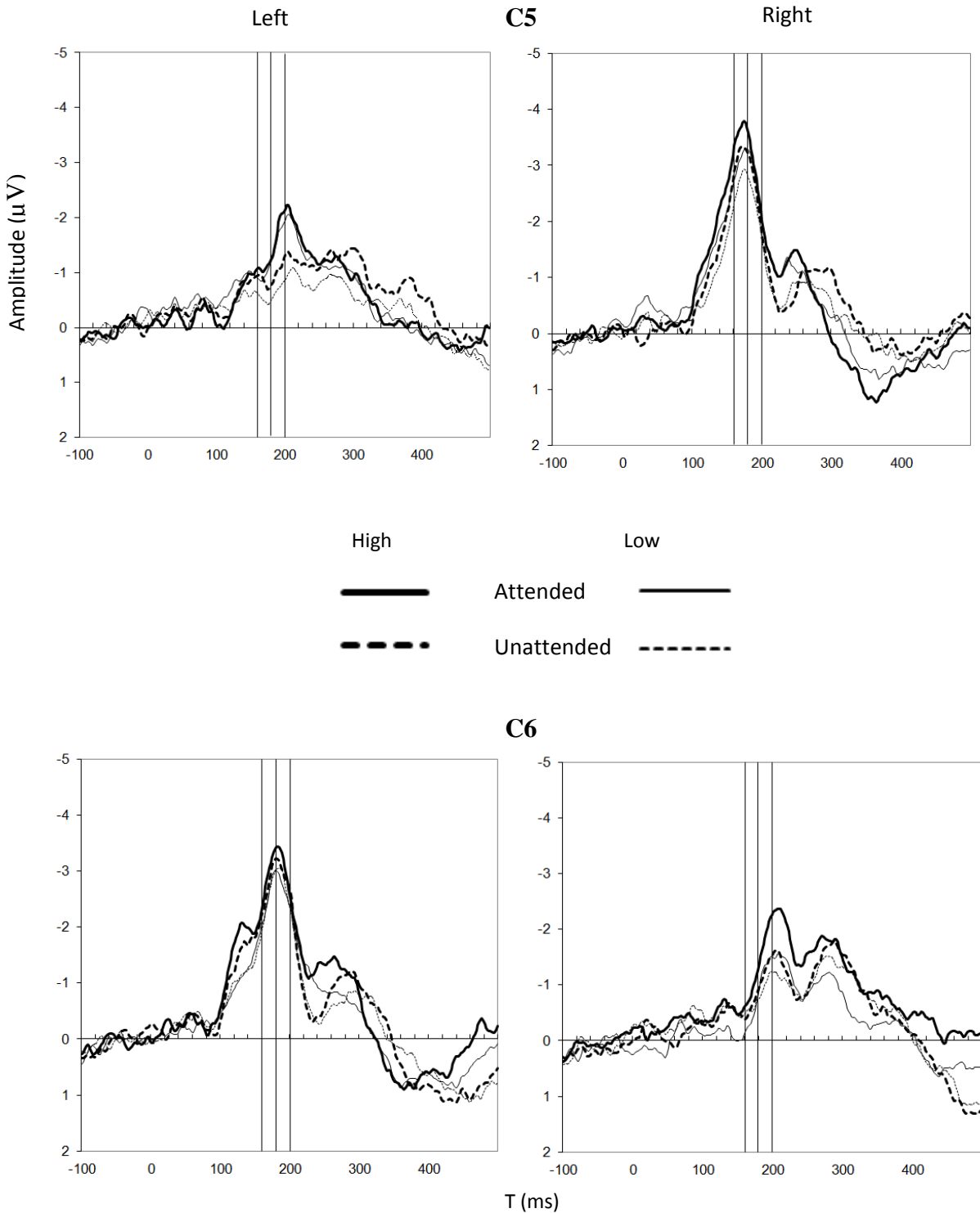
Note: Grand averages of N1 for left (left panel) and right (right panel) stimuli are displayed with time in milliseconds (ms) along the x- axis and amplitude in microvolts (µV) along the y-axis. C5 and C6 are selected for display. Time windows selected for statistical analyses are indicated with solid vertical lines. For both, right and left stimuli, ERP's are displayed as a function of stimulus intensity (two-pulse vs. five-pulse) and attention (attended vs. unattended).

Figure 5: P300a at FCz

Attended   Unattended

Sustained task version

High   Low

Control

MBSR

Transient task version

T (ms)
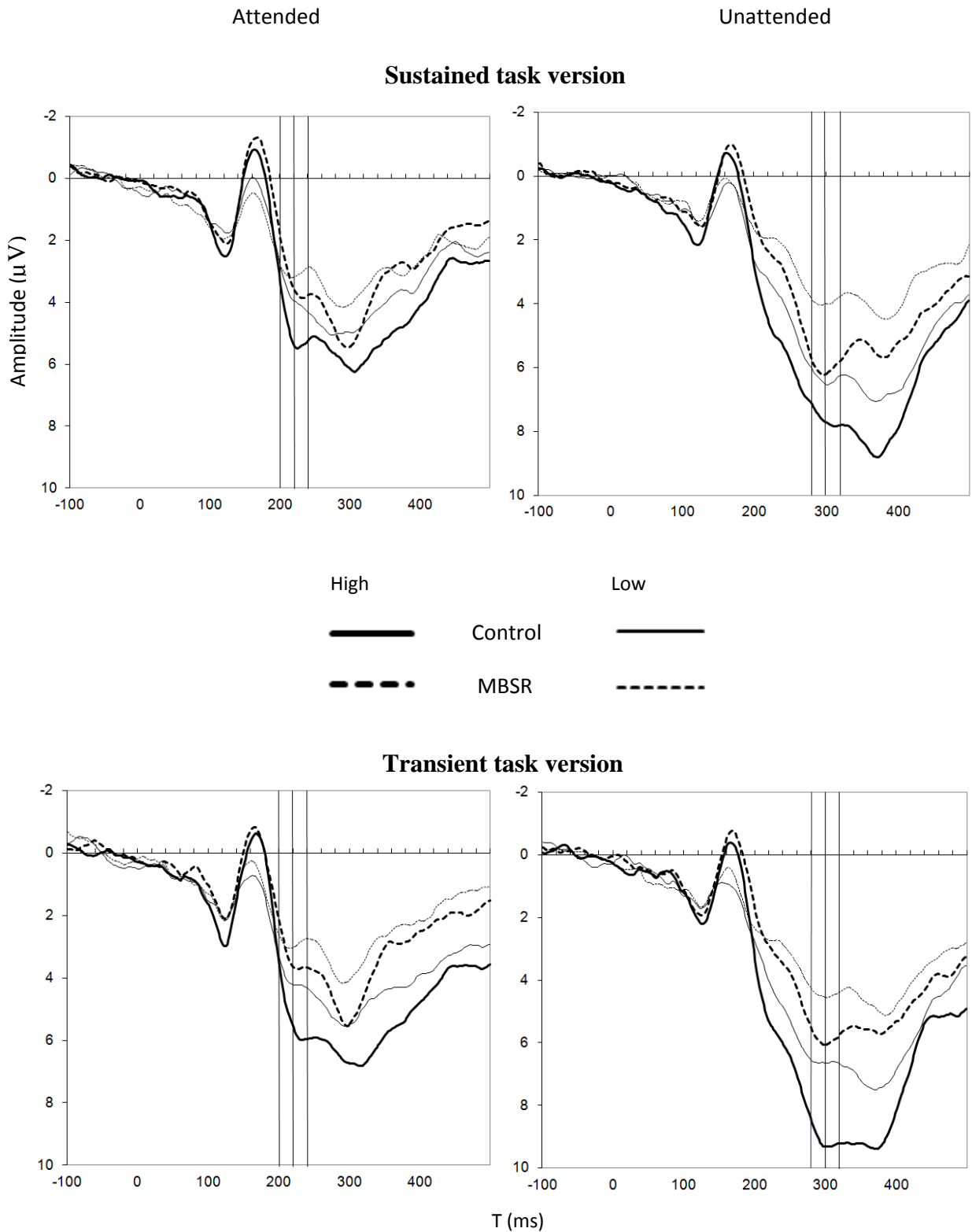
Note: Grand averages of P3a for attended (left panel) and unattended (right panel) stimuli are displayed with time in milliseconds (ms) along the x- axis and amplitude in microvolts (µV) along the y-axis. FCz is selected for display. Time windows selected for statistical analyses are indicated with solid vertical lines. For both, attended and unattended stimuli, ERP's are displayed as a function of stimulus intensity (five-pulse vs. two-pulse) and group (MBSR vs. control group).

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3.3.1 N100

The mindfulness and control group did not differ on the N100 amplitude. Neither a main effect of group nor an interaction between group and attention was found. But an interaction effect between group and time window was found, $F(1, 30) = 4.47$, $p= 0.034$. Separate group analyses revealed that negativity was higher between 180-200 ms than between 160-180 ms within the MBSR group, $F(1, 16) = 9.99$, $p = 0.006$; -2.17 vs. -1.80 µV. In the control group no significant difference between time windows was found (-2.00 vs. -1.89 µV). It seemed that N1 occurs a little bit later in the MBSR than the control group.

Main effects of time window $F(1, 30) = 14.04$, $p = 0.001$, attention $F(1, 30) = 15.74$, $p < 0.001$ and intensity $F(1, 30) = 28.24$, $p < 0.001$ were found. The N100 maximum lied in time interval 180-200 ms. Here, negativity was higher than in time window 160 – 180 ms (-2.09 vs. -1.85 µV). Negativity was larger for attended and high stimuli compared to respectively unattended and low stimuli (-2.13 vs. -1.80 µV; -2.12 vs. 1.81 µV).

An interaction between time window and attention was found $F(1, 30) = 9.86$, $p = 0.004$. In both time windows, attended stimuli were enhanced compared to unattended stimuli, but the difference was highest at the maximum of N1, between 180-200 ms, $F(1, 30) = 17.40$, $p < 0.001$; -2.28 vs. -1.87 µV.

An interaction between electrode and stimulation site, $F(1, 30) =72.86$, $p < 0.001$, confirmed the expected lateralization effect of N100. The electrode contralateral to the stimulated hand was enhanced and the electrode ipsilateral to the stimulated hand was attenuated, $F(1, 30) > 46.02$, $p < 0.001$. Accordingly, activity for left stimuli was higher at C6 (-2.85 vs. -1.01 µV) and higher for right stimuli on C5 (-2.94 vs. -1.06 µV).

An interaction between window and electrode suggested that N100 occurred earlier on C5 than at C6, $F(1, 30) = 11.08$, $p = 0.002$. C5 reached its maximum between 160-180 ms and C6 between 180-200 ms. Only the latter reaches significance in separate electrode analyses, $F(1, 32) = 24.73$, $p < 0.001$. Unexpectedly, we found an interaction between group

and instruction, $F(1, 30) = 6.78$, $p= 0.014$. To examine this effect, separate group analyses were conducted. Within the mindfulness group increased negativity was found when the instruction was given to react on high stimuli (-2.65 vs. -1.32 µV; $F(1, 15) = 52.16$, $p=0.029$). The analysis within the control group reaches no significance, $F(1, 15) = 63.97$, $p= 0.248$. It seemed that in this group the reversed pattern is true, with increased negativity for the instruction to react on low stimuli (-2.24 vs. – 1.65 µV). No difference between the sustained and transient task version was found, $F(1, 30) = 1.43$, $p = 0.241$.

3.3.2. P300a

First we will report the findings within the attended stimuli. Within the attended stimuli, two group differences were detected. At first, P3a on attended stimuli was almost higher for the control than for the MBSR group, $F(1, 32) = 3.46$, $p= 0.072$; 4.53 vs. 3.15 µV. Next, an intensity effect was found, indicating that activity was enhanced for high compared to low stimuli, $F(1, 32) = 15.93$, $p < 0.001$; (4.22 vs. 3.46 µV). This intensity difference was greater in the control (5.12 vs. 3.93 µV) than MBSR group (3.32 vs. 2.98 µV), which was revealed by an interaction effect between group and intensity, $F(1, 32) = 4.88$, $p = 0.035$. Only within the control group, this difference became significant, $F(1, 16) = 19.12$, $p < 0.001$.

Further a main effect was found for time window, $F(1, 32) = 8.54$, $p= 0.006$. Positivity was higher between 220 and 240 ms (4.13 vs. 3.55 µV), indicating that P300a maximum lied in this time window. An interaction between time window and intensity, $F(1, 64) = 23.38$, $p < 0.001$ was found. Separate analyses revealed that the enhancement for high compared to low stimuli was largest at the P3a maximum between 220ms and 240ms (4.69 vs. 3.57 µV). No difference between the sustained and transient task version was found, $F(1, 32) = 0.162$, $p = 0.69$. We will now look at the findings within the unattended stimuli. Again, activity for the control group was almost higher than in the MBSR group, $F(1, 32) = 3.98$, $p= 0.055$; 7.45 vs. 5.09 µV. Also high stimuli were enhanced compared to low ones, $F(1, 32) = 63.96$, $p <$

0.001; 7.18 vs. 5.36 µV). But unlike within attended stimuli, this enhancement was not generally larger in the control than MBSR group. A three way interaction between task, intensity and group revealed that it depended on the task in which group the intensity difference was higher, $F (1, 32) = 6.09$, $p= 0.019$. In the transient task version, the intensity difference was higher for the MBSR group whereas the opposite was found in the sustained task version. No main effect of task was found, $F (1, 32) = 2.6$, $p = 0.117$.

A final analysis was conducted, comparing attended and unattended stimuli, to look for the overall and interaction effects of attention, group and task (see figure 6). This ANOVA revealed a main effect of group, $F (1, 32) = 4.34$, $p = 0.045$ and attention, $F (1, 32) = 35.24$, $p < 0.001$. P3a was higher for the control compared to MBSR group (5.98 vs. 4.12 µV) and higher for unattended compared to attended stimuli (6.27 vs. 3.84 µV). However, an interaction between group and attention was not found, $F (1, 32) = 1.42$, $p= 0.244$. Also no difference between the sustained and transient task was found $F (1, 32) = 1.33$, $p= 0.257$.

Figure 6: P3a as function of attention, group and task

Transient task

Sustained task
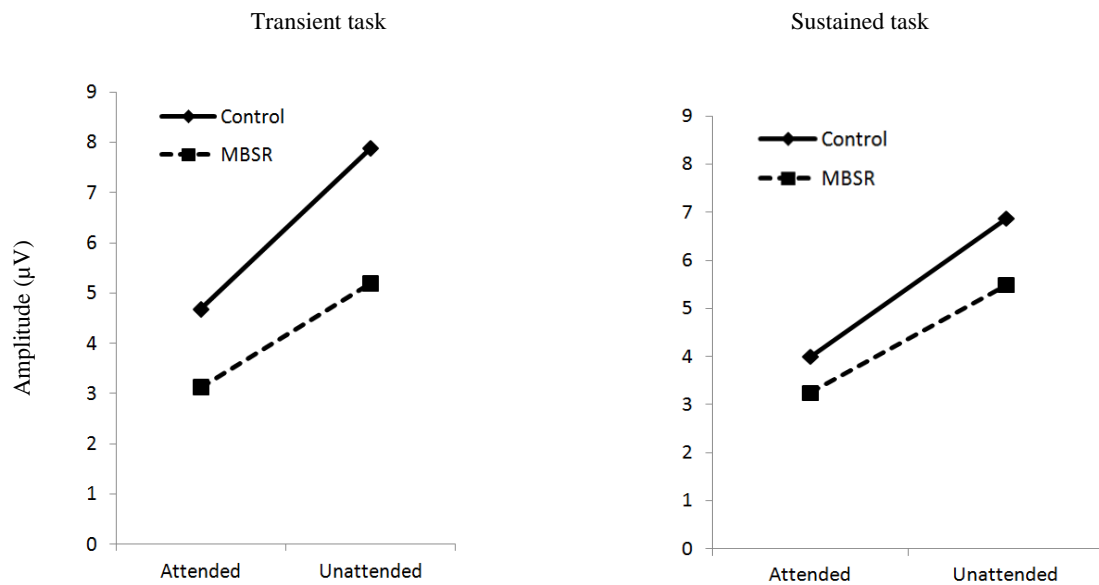
Note: P3 was larger for the control than MBSR group. Unattended stimuli evoked a higher P3a than attended stimuli. Although not significant, following trends could be seen: The group difference in P3 seemed to be larger within unattended stimuli. This difference in turn seemed to be pronounced when attention is manipulated transiently.

4. Discussion

Several studies examined the effect of mindfulness in pain treatment. However, most of them suffer from two limitations: They were not based on randomized trials and/or use self-reports to indicate mindfulness effects (Bear, 2003). The current study aimed to overcome these problems. Participants were randomized into a treatment and control group. The primary aim of this study was to verify the mindfulness effect on a neuropsychological basis. This was done by examining the ERPs N1 and P3a which reflect early sensory processing of pain stimuli and the subsequent orientation towards them.

The early sensory processing of pain was not affected by mindfulness training since no difference in N1 was found between the groups. It seemed that N1 occurred a little bit later in the MBSR group. Unfortunately, the chosen time windows for N1 did not cover the whole N1 component evoked by stimuli ispsilateral to the recorded electrodes (see figure 4). Therefore, it cannot be excluded that this finding is based on an artifact, caused by the time window choice.

Concerning the orienting aspect of pain processing, results were more promising. In line with the central idea of mindfulness, the MBSR training reduced the orienting reflex towards pain sensations. This was indicated by a smaller P3a in response to pain stimuli for the group which followed the MBSR course. So the attention capturing effect of pain stimuli had less impact on this group. This agrees with the idea of mindfulness to pay attention in a "nonjudgmental and accepting" way (Kabat-Zinn, 2003). Thus learning to encounter pain stimuli neutrally can decrease the involuntary orienting towards pain stimuli. This could underlie the effectiveness of mindfulness training in pain treatment. This view is supported when looking at the VAS-scores which revealed the trend that the mindfulness group judged stimuli as less painful than the control group.

Surprisingly, the reduced P3a was independent from whether attention was paid to the pain stimuli or not. Actually, we thought to see this effect only on unattended stimuli. Here, a reduced P3a would apply for a better ability to suppress the automatic orienting towards pain. However, to a lesser degree, this effect was also seen on attended pain stimuli. Here, we rather expected the reversed, since mindfulness is thought to foster the ability to orient attention. This implies a higher P3a on voluntary attended stimuli but seemingly this does not apply for pain stimuli.

A possible explanation could lie in the opposite influences of mindfulness. On the one hand, mindfulness decreases the susceptibility to be detracted by the stimulus driven attention of pain. This reduces the orienting towards pain stimuli, independent of attended or not. On the other hand, mindfulness also improves orienting towards voluntary attended (pain) stimuli. The former implies a decrease and the later an increase in P3a. However, we suppose that the influence of being less captured by pain stimuli is stronger than the general improvement in orienting attention. In this case, the former would overshadow the latter effect and would explain why even on attended pain stimuli, P3a is lower in the MBSR than in control group. This would also explain the trend that the group differences on P3a are higher within unattended stimuli, where voluntary shifting attention plays no role. To examine this assumption the experiment should be repeated with non-painful (less attention capturing) stimuli to test whether stimulus quality (painful, non-painful) functions as moderator variable.

This study also found group differences regarding the stimulus intensity on P3a. Generally, five pulse stimuli evoked a larger N1 and P3a than two pulse stimuli, indicating that high pain stimuli were more obtrusive and attention catching. Yet the intensity difference on P3a on attended stimuli was higher for the control than MBSR group. This again can be explained by the stimulus driven attention of pain which rises with pain intensity. Because the MBSR group is less influenced by this effect, concurrently a smaller discrepancy between high and low stimuli was seen within for the MBSR group. However, within unattended

stimuli, the intensity differences on P3a between the two groups depended on the task version. Whereas in the transient task version, the intensity difference was higher for the control group, unexpectedly the reversed patter was found in the sustained version. Future research should examine this effect.

The group differences on a neuropsychological level were not accompanied by differences on a behavioral level. Perhaps the behavioral measures were not as sensitive as EEG. More assumable is another explanation. Both, reduced orienting towards unattended (always task-irrelevant) and stronger orienting towards attended (half the time task relevant) stimuli improve task performance. Only the first applied for the MBSR group. We think that the benefits of suppressing orientation towards unattended stimuli within this group could not outweigh the costs of a reduced orienting towards attended stimuli. This could explain the absence of performance differences between the groups.

Generally, we were able to verify the findings of Van der Lubbe et al., (2012) on which the current study's task design was based. N1 was higher for attended and lower for unattended stimuli. More importantly, we could confirm that P3 was higher for unattended compared to attended stimuli within both task versions. That unattended pain stimuli form a 'call of attention' agree with the finding from Van der Lubbe et al., (2012) but is new for tasks of sustained spatial attention manipulation (see e.g. Legrain et al., 2002; Blom et al., submitted).

The results of the current study differed by that from Van der Lubbe et al. (2012) in that the latencies for N1 and P3a were different. This could partly be explained by the difference in the used stimulation method. In their study, N1 occurred around 70 ms earlier than in the current study. This could be due to the faster conduction times along non-nociceptive A-β fibers which were stimulated in their study. Conform to that, we did not detect a positive reflection around 60 ms on C5 and C6, which was assumed to indicate the cortical arrival of stimuli along A-β fibers (Van der Lubbe, 2011).

P3a occurred between 240 and 280 ms after stimulus onset in their study. But in our study P3a was shifted in time as function of attention with a maximum of attended stimuli between 220 and 240 ms and that of unattended stimuli between 280 and 320 ms after stimulus onset. Since P3 latency is related to stimulus evaluation time (Mageliero, Bashore, Coles, Donchin, 1984), we assume that pain stimuli were faster evaluated when attention was directed to them. It still remained unclear, why this finding was found in the current study and not in the study by Van der Lubbe et al., (2012). The P3a latency difference as function of attention forced us to make an ANOVA which compared activity from two time intervals to asses main and interaction effects of the factors attention, group and task. It has to be noted that the time window analysis is not the most appropriate method to examine a factor (attention in this case) when its levels are shifted in time. The results regarding the main effect of attention should be verified using peak detection analysis. In this way, also the peak latency could be used as dependent variable to explore the ERP shifts in time.

Finally, this study revealed an unexpected finding concerning the instruction the participants got. The instruction to either react on high or low stimuli was primary given to examine group differences on a behavioral level. We did not expect it to interact with group affiliation. But N1 was enlarged and reduced for respectively the MBSR and control group when the task was to react on high stimuli. Since the instruction was not the main study parameter of this study, it was rather found accidently. This means that the pre-analyses were not done with the aim to clarify this effect. It has to be examined when after stimulus onset the interaction became significant and reaches its maximum. Grand averages and topographical maps as function of group and instruction could further contribute to clarify to this finding. But so far, no inferences can be made yet on the interaction between instruction and group.

Although this study offers valuable clues how mindfulness might work on a neuropsychological basis, it also knows some limitations which could be avoid in future

studies. To begin with, the study design was not optimal. Through using a 'separate-sample pretest-posttest' design, it could not be controlled for specific events, occurring between the first (control group) and second measurement (MBSR group). Unfortunately, the second measurement took place during the examination period of the university. That means that the MBSR group took part under other (perhaps more stressful) conditions than the control group. A solution would be to extend the existing study design and add two further groups from which the MBSR treatment is withheld. One of these groups would participate in the experiment concurrently with the treatment group and the other group concurrently with the control group. The absence of experimental differences between these added groups could exclude the possibility that an observed effect on the MBSR group is due to a specific local trend (examination period) which in fact is unrelated. Such a design is called a separate-sample pretest-posttest control group design (Campbell & Stanley, 1963).

Furthermore, the experiment was vulnerable to demand characteristics and experimenter expectancy. Experimenter expectancy can be defined as "ways (…) by which the researchers influence the subjects to get results consistent with his or her hypothesis" (Dooley, 2001). Since the experiment leaders knew the participant's groups affiliation, expectancy bias could not be fully excluded. Ways to prevent expectancy bias are e.g. to use a naive or blind experiment leader. Demand characteristics, are defined as "subject's beliefs and all the signals in the experimental setting that guide these beliefs" (Dooley, 2001). They could have harmed the internal validity in two ways. Unlike the control group, the treatment group got intensive attention prior to the experiment. This could have increased their willingness to do the best in the experiment. Moreover, participants could have also figured out that they belong to the treatment group and behaved in line with their build up experiment expectations. Demand characteristics can be avoided through giving the control group an equally interesting placebo treatment prior to their participation and keep subjects 'blind' to their condition.

Also the experimental design could be improved through adding practice trials preceding the first block. Participants often were confused and make errors in the first trials. Furthermore, the mood-scale revealed that participants felt less energetic, agitated and more tired after the experiment. In addition to that, they often reported that the pain feeling disappeared towards the end of the experiment. Both point towards a habituation effect which might be avoided through making the blocks shorter (accepting a loss of trials at the expense of more valid ones).

A further consideration has to me made concerning the pre-processing of the EEG data. Eye artifacts are typically larger compared to the ERP signals and may greatly decrease the S/N ratio of the averaged ERP waveform. Instead of removing trials with eye -movements, we corrected for them. Obviously, this method left over more trials. But corrected data is no substitute for good data (Hansen's Axiom) (Luck, 2005). In other words, future studies should remove trials with eye-artifacts instead of correct for them, provided that around 60% of the trials per participant are left over (Utzerath, 2011).

The findings of this study provide a basis for further analyses/ studies. This study has shown that mindfulness training is able to influence pain processing through affecting the orientation of attention. This was indicated by a modified P3a component. It would be insightful to know which aspects of the MBSR training were related to the alteration in P3a. For this purpose, a correlation analysis could be done between the five facets of mindfulness[1] measured by the subscales of the FFMQ-SF questionnaire and the P3a amplitude.

An addition to that, future studies e.g. could also examine the effect of MBSR training on the P3b component, which we detected but not analyzed in this study. Beyond, it would be insightful to look for group differences in 'alertness' by examining the cue-target interval in

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[1] The five facets of mindfulness were observing (noticing internal/external experiences), describing (labeling internal experiences with words), acting with awareness (attending to one's activities of the moment), and being nonjudgmental and nonreactive to inner experience (being neutral towards thoughts and feelings and allow them to come and go) (Baer, 2008). They were measured in this study by the FFMQ-SF from which we only reported the main and not the sub scores.

the visual Posner task. Differences in theta band power at the frontal midline (4-8 Hz) would indicate the influence of mindfulness on focused attention (Pizzagallie, 2007).

4. References

Abdi, H. *(2007).* Signal detection theory (SDT)*.* In Salkind N. J. *(Ed.), Encyclopedia of measurement and statistics.* Thousand Oaks, CA*:* Sage*.*

Annet,M. (1970). A classification of hand preference by association analysis. *British Journal of Psychology, 61*, 303-321.

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

Baer, R. A. (2008). Construct Validity of the Five Facet Mindfulness Questionnaire in Meditating and Nonmeditating Samples. *Assessment, 15,* 329-342.

Bishop, S. R. (2004). Mindfulness: a proposed operational definition. *Clinical Psychology: Science and Practice, 11*, 230-241.

Blom, J.H.G., Wiering, C.H., & Van der Lubbe, R.H.J. (submitted). Distraction reduces early and late electrocutaneous stimulus evoked potentials.

Bohlmeijer ET, ten Klooster PM, Fledderus M, Veehof MM, Baer R. (2011). Psychometric properties of the Five Facet Mindfulness Questionnaire in depressed adults and development of a short form. *Assessment*, *8, 308-20.

Brewer, W. F., & Loschky, L. (2005). Top-down and bottom-up influences on observation: Evidence from cognitive psychology and the history of science. In A. Raftopoulos (Ed.), *Cognitive penetrability of perception: Attention, action, strategies, and bottom-up constraints*. Hauppauge, NY: Nova Science Publishers, pp. 31–47.

Bromm B., & Meier W. (1984). The intracutaneous stimulus: a new pain model for algesimetric studies. *Methods and Findings in Experimental and Clinical Pharmacology, 6,* 405–10.

Campbell, D. T., & Stanley, J. C. (1966). *Experimental and quasi-experimental designs for research.* Boston: Houghton Mifflin company.

Dooley, D (2001). *Social research methods* (4th ed.). New Jersey: Prentice Hall.

Eccleston, C., & Crombez, G. (1999). Pain demands attention: A cognitive-affective model of the interruptive function of pain. *Psychological Bulletin, 125,* 356–366.

Eccleston, C., Williams, A.C., Morley, S. (2009). Psychological therapies for the management of chronic pain excluding headaches in adults (Review). *Cochrane Database of Systematic Reviews, 3,* 1-105.

Eimer, M., & Forster, B. (2003). Modulations of early somatosensory ERP components by

transient and sustained spatial attention. *Experimental Brain Research, 151, 24*–31.

Fabiani, M., Gratton, G., Federmeier, K. D. (2007). Event-Related Brain Potentials: Methods, Theory, and Applications. In J. T. Cacioppo, L. G. Tassinary and G. G. Berntson (Eds.), *Handbook of Psychophysiology* (pp 85 – 119). New York, NY: Cambridge University Press.

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

Hulsbergen, M. (2009). Mindfulness, de aandachtsvolle therapeut. Amsterdam: Boom.

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

Iannetti, G.D,, & Mouraux, A. (2010). From the neuromatrix to the pain matrix (and back). *Experimental Brain Research, 205,* 1–12.

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

Itti, L., Koch, C. (2001). Computational modelling of visual attention. *Nature reviews neuroscience, 2,* 194–203.

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

Kerr, C. E., Jones, S. R., Wan, Q., Pritchett, D. L., Wasserman, R. H., Wexler, A., at al. (2011). Effects of mindfulness meditation training on anticipatory alpha modulation in primary somatosensory cortex. *Brain research bulletin, 85,* 96-103.

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.

Legrain, V., Iannetti, G., D., Plaghki, L., Mouraux, A. (2011). The pain matrix reloaded. A salience detection system for the body. *Progress in Neurobiology, 93,* 111-124.

Legrain, V., Van Damme, S., Eccleston, C., Davis, K. D., Seminowicz, D. A., Crombez, G. (2009). A neurocognitive model of attention to pain: Behavioral and neuroimaging evidence. *Pain, 144,* 230-232.

Luck, S. J. (2005). *An introduction to the event-related potential technique.* London: Mitpress.

Macmillian, N.A., Creelman, C.D. (2005). *Detection Theory: A user's guide (second edition).* Mahwah (NJ): Ehrlbaum.

Mageliero A., Bashore T.R., Coles M.G.H., Donchin E. (1984). On the dependence of P300 latency on stimulus evaluation process. *Psychophysiology, 21,* 171-186.

Merskey, H., & Bogduk, N. (Eds.). (1994). *Classification of chronic pain (2nd ed.). International Association for the Study of Pain (IASP) Task Force on Taxonomy.* Seattle: IASP Press.

Moore, D. J., Keogh, E., Eccleston, C. (2009). Identifying experimental methods to determine the effect of pain on attention: a review of pain, caffeine, alcohol and nicotine studies. *Human Psychopharmacology: Clinical and Experimental, 24,* 601 -618.

Nakajima, Y., Imamura, N. (2000). Relationships between attention effects and intensity effects on the cognitive N140 and P300 components of somatosensory ERPs. *Clinical Neurophysiology 111,* 1711-1718.

Nieuwenhuis S, De Geus E.J., Aston-Jones G. (2011). Anatomical and functional relationship between the P3 and autonomic components of the orientingresponse. *Psychophysiology, 48,* 162–175.

Utzerath, C. (2011). *Electroencephalography for Dummies: Brain Vision Analyzer 2.0.* Cognitive Psychology and Ergonomics University of Twente, The Netherlands.

Pizzagalli, D. A. (2007). Electroencephalography and High-Density Electrophysiological Source localization. In J. Cacioppo, L. G. Tassinary & G. G. Berntson (Eds), *The handbook of psychophysiology* (57 – 84). New York: Cambridge university press.

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

Posner, M.I., Snyder, C.R., and Davidson, B.J. (1980). Attention and the detection of signals. *Journal of experimental psychology,* 109, 160-174.

Slagter, H.A., Lutz, A., Greischar, L.L., Francis, A.D., Nieuwenhuis, S., Davis, J.M., et al. (2007). Mental training affects distribution of limited brain resources. *PLoS Biology, 5,* e138.

Shapiro SL, Carlson L. E., Astin J.A., Freedman B. (2006). Mechanisms of mindfulness. *Journal of clinical Psychology, 62,* 373 -86.

Thayer, R.E. (1989).*The biopsychology of mood and arousal.* New York: Oxford University Press.

Van Damme, S., Crombez, G., Eccleston, C. (2008). Coping with pain: a motivational perspective. *Pain, 139, 1*–4.

Van der Heide E.M., Buitenweg J.R., Marani E., Rutten W.L.C. (2009). Single pulse and pulse train modulation of cutaneous electrical stimulation: a comparison of methods. *Journal of Clinical Neurophysiology, 26,* 54–60.

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,* 947-59.

Veehof, M.M., Oskam, M.J., Schreurs, K.M.G., Bohlmeijer, E.T. (2011). The effects of acceptance-based therapies on mental and physical health in chronic pain patients: results of a meta-analysis. *Pain, 152,* 533–542.