SOMATOSENSORY CHANGE DETECTION IN THE AGING BRAIN

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Master's thesis

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ABSTRACT

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The study examined the brain's automatic somatosensory change detection mechanism using event-related potentials (ERPs) to tactile electrical pulses to fingers in an oddball paradigm. Also the effects of aging to these ERPs were investigated comparing the data of young adults (N = 20, 22–27 years) with the data of aged participants (N = 12, 67–95 years). In the experiment, the participants were instructed to ignore finger stimuli and to be fully involved to a radio play during the electroencephalogram (EEG) recording. The electrical stimulation was delivered to participant's forefinger and little finger in randomized order of standard (P = 0.85) and deviant (P = 0.15) stimuli. The analyzed components were P50 peak (30–80 ms), N80 peak (40–110 ms) and a positive deflection at the latency range of 150–200 ms (the mismatch response, MMR). The results revealed significantly different responses to standards than those to deviants in the young group, indicating the automatic detection of deviant stimuli analogically to mismatch negativity in the auditory and visual modalities. As hypotesized, the MMR was completely attenuated in the aged group. P50 and N80, instead, had prolonged latency in the aged group compared to young adults. The findings suggest that the somatosensory MMR is a good measure of change detection mechanism and age-related changes in it.

Keywords: somatosensory mismatch negativity (sMMN), aging, event-related potential (ERP), oddball paradigm.

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Tutkimuksen tarkoituksena oli selvittää aivojen automaattisen muutoksen havaitsemisjärjestelmän toimintaa sormiin johdettujen sähköisten ärsykkeiden aiheuttamien aivojen tapahtumasidonnaisten jännitevasteiden avulla. Lisäksi tutkimuksessa selvitettiin ikääntymisen vaikutuksia näihin tapahtumasidonnaisiin jännitevasteisiin vertailemalla nuorilta aikuisilta (N = 20, 22–27 vuotta) mitattuja vasteita ikääntyneiltä (N = 12, 67–95 vuotta) mitattuihin vasteisiin. Elektroenkefalografiamittauksen (EEG) aikana koehenkilöä pyydettiin keskittymään kuunnelman seuraamiseen. Samalla koehenkilön etu- ja pikkusormeen johdettiin satunnaisesti säännöllisiä (p = 0.85) ja poikkeavia (p = 0.15) sähköimpulsseja käyttäen oddball paradigmaa. Analysoidut komponentit olivat P50-vaste (30–80 ms), N80-vaste (40–110 ms) ja positiivinen erotusvaste latenssivälillä 150–200 ms (ns. poikkeavuusvaste). Tulokset osoittivat tapahtumasidonnaisten jännitevasteiden säännöllisiin ja poikkeaviin ärsykkeisiin eroavan toisistaan nuorten aikuisten ryhmässä, mikä merkitsee poikkeavan ärsykkeen automaattista havaitsemista samoin kuin on havaittu aiemmin poikkeavuusnegatiivisuuden kohdalla kuulo- ja näköjärjestelmässä. Hypoteesien mukaisesti MMR oli kokonaan vaimentunut ikääntyneiden ryhmässä. P50 ja N80 komponentit sen sijaan olivat latenssiltaan myöhäisempiä ikääntyneillä nuoriin aikuisiin verrattuna. Tulokset osoittavat, että somatosensorinen poikkeavuusvaste on hyvä mittari muutoksenhavaitsemisjärjestelmän toimivuudesta ja sen heikentymisestä ikääntyessä.

Avainsanat: somatosensorinen poikkeavuusnegatiivisuus (sMMN), ikääntyminen, oddball paradigma, tapahtumasidonnainen herätepotentiaali (ERP).

CONTENTS

INTRODUCTION

EEG signal, evoked potential and event-related potential

All human physiological and psychological functions are related to the brain's neural activation. Neuron activation produces currents within the dendrites and simultaneous excitation of the dendrites of many pyramidal neurons in the cerebral cortex generates a flow of currents that generates an electric field (Sanei & Chambers, 2007). This electric field can be measured over the scalp with an *electroencephalogram* (EEG) system. Because of the heavily attenuating effect of the skull, only large populations of active neurons can generate enough potential to be recordable using the scalp electrodes. Therefore part of neural activity is never apparent and recordable at the scalp (e.g. Rugg & Coles, 1995). EEG signals are used to detect varying brain rhythms and evoked potentials induced in the brain. Brain rhythms changing from one state to another and varying in frequency bands from very slow (15–40 s) to ultra-fast (200–600 Hz) are widely used in clinical purposes to diagnose brain disorders by visual inspection of EEG signals as well as in contemporary research of electrical activity in the brain (for a review see e.g. Başar, Schürmann, Demiralp, Başar-Eroglu & Ademoglu, 2001; Penttonen & Busaki, 2003; Sanei & Chambers, 2007;).

Evoked potentials are voltage fluctuations in the EEG signal that occur between 1–1000ms after exogenous stimulus onset (Nyrke, 2006). They can be measured from all sensory systems, but differently from sensations, evoked potentials can be preconscious and they occur after stimulus without any threshold limit unlike sensations. In clinical use evoked potentials can be used as a reliable and objective indicator of occurrence of disturbances in the nervous system, although they do not explain the etiology or age of the pathology. For example, Stephen et al. (2009) recently showed that diverging somatosensory responses of primary and secondary somatosensory cortex to median nerve stimulus might be an early marker of abnormal brain function leading to Alzheimer's disease. In addition, evoked potentials are shown to be affected by normal aging (Ferri et al., 1996; Ziegler et al., 2010). Ferri et al. (1996) measured somatosensory evoked potentials (SEP) to median nerve stimulation in aged participants and dementia patients and found increased amplitude and prolonged latency of middle-latency SEPs (22–65 ms post-stimulus) compared to healthy young controls. In a recent MEG (magnetoencephalography) study with tactile vibration stimuli to fingers, Ziegler et al. (2010) showed similarly that the SEP around 70 ms post-stimulus onset was increased

in magnitude and prolonged in latency in middle-aged participants compared to healthy young controls.

Like evoked potentials, *event-related potentials* (ERPs) are voltage fluctuations in the EEG induced as a sum of a large number of action potentials that are time locked to sensory, motor or cognitive events (Sanei & Chambers, 2007). The ERP waveform can be characterized according to its amplitude (= the extent of neural activity), latency (= the time point at which the peak occurs), scalp distribution (= the pattern of the voltage gradient over the scalp at any time instant) and its sensitivity to characteristic experimental manipulations (Donchin, Ritter & McCallum (1978). The amplitude and shape of each peak are determined by the location and the orientation of the activated neurons as well as by the physical and cognitive properties of the stimulus type (Johnson, 1992). The ERP signals are either positive or negative (Sanei & Chambers, 2007). In literature, peaks are represented like evoked potentials, with the letter P or N representing the peak's polarity and the following number representing its latency in milliseconds (e.g. P300 = positive peak occurring around 300 ms after stimulus onset).

According to their names as cognitive or endogenic evoked potentials, ERPs are evoked potentials related to higher, cognitive or affective brain functions (Partanen et al., 2006). Event-related potentials do not exclusively rely on the physical characteristic of the stimulus, but are determined mainly by the task given to the subject or by the internal state of the subject. Further, earlier classification by Donchin et al. (1978) divides ERP components into exogenous and endogenous ones. Exogenous ERP components are relatively stable regarding their obligatory elicitation by the occurrence of an appropriate stimulus, if the shape of the waveform and the scalp distribution vary as a function of the sensory modality in which the eliciting stimulus is represented (Donchin et al., 1978; Fabiani, Gratton & Coles, 2000). Exogenous ERPs are thus modality specific, representing the activity of the sensory pathways that transmit the signal from peripheral receptors to the central processing system (Fabiani et al., 2000). Endogenous ERP components, instead, vary more according to the subject's mental state and behavior and are nonobligatory responses to eliciting stimuli (Donchin et al., 1978). That is, they are invariant in terms of amplitude, latency and scalp distribution to changes in the physical parameters of the evoking stimulus, but varying by the tasks assigned to the subject. Therefore the same endogenous ERP component can be elicited by different stimuli even in different modalities. However, Rugg and Coles (1995) have argued that almost all exogenous ERP components are actually modifiable by cognitive manipulations (e.g. attention) and many of endogenous ERP components can be influenced by the physical attributes of the evoking conditions (e.g. modality of the stimulus). Thus the classification of ERPs would be more appropriate to consist of an exogenous–endogenous

dimension, in which the ERP components occurring within the first 100 ms after stimulus onset tend to be more exogenous and later occurring ERP components tend to be more endogenous.

ERPs require the use of a signal-averaging procedure for their elucidation, because ERPs are small in amplitude (1–30 μV) relative to their background (Sanei & Chambers, 2007). This can be problematic when using ERPs in individual clinical diagnoses because of their sensitivity to changes in alertness and attention, as well as large variation in ERPs between individuals (Partanen et al., 2006). For research purposes, instead, when ERPs are studied averaging EEG signals among several subjects, ERPs are a valuable tool for studying higher brain functions and their development. However, ERPs are commonly used in psychiatry, and clinical applications of different ERP paradigms might become common in the future (Partanen et al., 2006; Sanei & Chambers, 2007). For instance, Guttorm et al. (2005) showed that the ERPs of newborns might be valid predictors of later language or neurocognitive outcomes.

The mismatch negativity (MMN) and its somatosensory modality

The mismatch negativity (MMN) is an ERP component that occurs when the brain has detected a change in a background of homogenous events (Sanei & Chambers, 2007). The MMN has been originally discovered in its auditory modality in the classic study of Näätänen, Gaillard and Mäntysalo (1978), in which it was elicited at about 100–250 ms after stimulus onset as a response to rare, randomly occurring deviant tones with frequencies higher in relation to repeated standard tones (the so-called oddball paradigm). The MMN response is seen as a negative shift at the fronto-central and central scalp electrodes in relation to reference electrodes in the difference waveform, which is obtained by subtracting the ERP to frequent (standard) stimuli from ERP to rare (deviant) stimuli (Näätänen, Paavilainen, Rinne & Alho, 2007). In the auditory modality, the MMN is found to be elicited by any change or violation in frequency, intensity, spatial locus of origin, rise time, duration, inter-stimulus interval, inter-stimulus relationship, rhythm or phoneme regulation of an auditory stimulus (Näätänen, 1992; Garrido et al., 2009). Similarly, an analogous response occurs in the olfactory modality (for a review see Pause & Krauel, 2000), in the visual modality (for a review see Pazo-Alvarez, Cadaveira & Amenedo, 2003) and in the somatosensory modality (Kekoni et al. 1997; Shinozaki, Yabe, Sutoh, Hiruma & Kaneko, 1998). Due to its frontal location, the MMN is hypothesized to be associated with an involuntary attention orientation process (Näätänen et al.,

2007; Garrido, Kilner, Klaas & Friston, 2009). That is, MMN is elicited when attention is switched towards potentially important events in the unattended environment.

The MMN occurs even in non-attentive states like sleep or coma, which supports the hypothesis of the MMN as an automatic brain process that is not dependent on attention (Garrido et al., 2009). Focused attention outside the stimulus stream, to concurrent stimuli in the same modality with the stimulus stream, seems to be related to attenuated MMN amplitude in the auditory modality, but in contrast, in the visual modality the degree of attention does not seem to influence the occurrence of the MMN (Näätänen et al., 2007; Garrido et al. 2009). However, Näätänen (2000) has argued that directing the subject's attention away from the stimuli, e.g. to a movie or a book, is the best condition to record MMN, because the simultaneous occurrence of the MMN and the overlapping components can thus be avoided. In studies of the visual modality of the MMN the subjects' focus of attention have been directed to auditory stimuli, to simultaneously presented visual stimuli or to some feature of the presented stimuli, while the changes between the standard and deviant stimuli have varied in contrast, shape, colour, size, motion direction, form, orientation or spatial frequency (Pazo-Alvarez et al., 2003).

The fact that attention is automatically switched towards deviant stimuli without focused attention to stimuli is related to sensory memory function. The memory trace explanation, based on auditory experiments, argues that deviant stimuli are compared to representations of standard stimuli that are kept in transient memory (Näätänen, 1992). Consistently with the memory trace explanation, Astikainen, Lillstrang and Ruusuvirta (2008) showed that the visual MMN disappears if the inter-stimulus interval (ISI) is longer than the duration of the sensory memory, or if the deviant stimuli are presented in equal probability with other stimuli, which indicates that the comparison process associated to MMN response uses transient memory contents and is constrained by sensory memory duration. In normal aging the MMN response is shown to have attenuated amplitude and prolonged latency in auditory and visual modalities (Näätänen et al., 2011). These aging-related changes in the MMN seem to be associated with cognitive deterioration and the shortening of sensory memory durations in aging as well as with the lengthening of sensory memory durations in early childhood (Glass, Sachse & von Suchodoletz, 2008; Näätänen et al., 2011).

In *the somatosensory modality,* the mismatch response (sMMR) is less studied than the MMN in auditory or visual modalities. However, the sMMR has been shown to have similar features to its counterparts in other modalities (Spackmann, Boyd & Towell, 2007). Further, positivity seems to be specific to sMMR (Shinozaki et al., 1998; Spackmann et al., 2007). Kekoni et al. (1997) found MMN-like frontal negative deflections as a response to deviant stimuli at the latency range of 100–

160 ms. They used tactile vibration bursts as stimuli, varying the thumb and the middle finger as standards and deviants in an oddball paradigm. In the subsequent study with electrical pulses as stimuli in an oddball paradigm, in addition with consistent results with Kekoni et al (1997), Shinozaki et al. (1998) found change-related frontal positivity at the latency range of 100–200 ms. They also argued that the amplitude of the positive response is reduced with the prolongation of the ISI, supporting the memory trace explanation of MMN. Thus specifically the positive component is more likely the somatosensory counterpart of the auditory MMN. Correspondingly, Akatsuka et al. (2005) reported a large positive component peaking around 100–200 ms as a response to deviant stimuli in an experiment with electrical pulse stimuli pairs as stimuli varying the within-pair ISIs between the conditions. They noted that the mismatch-like response around 100–200 ms elicited only if the within-pair ISI of deviant stimuli were shorter than the within-pair ISI of standard stimuli. Spackmann et al. (2007), for one, found a change-related negative component at the latency range of 100–200 ms and a positive component at the latency range of 170–270 ms as responses to vibration bursts to fingers with varying duration in an oddball paradigm. In reference to Akatsuka et al. (2005), they argued that instead of sensitiveness to within-pair ISI, the positive component is a change-related response that is particularly sensitive to temporal changes. The argument is based on a supposition that the stimuli with the short within-pair ISIs used in Akatsuka et al. (2005) experiment might be perceived as one longer stimulus.

The cerebellar function is shown to be related to the generation of the sMMR in humans (Restuccia, Della Marca, Valeriani, Leggio & Molinari, 2007) and in animals (Astikainen, Ruusuvirta & Korhonen, 2000). Restuccia et al. (2007) measured somatosensory responses to electrical stimuli in oddball in healthy subjects and patients with cerebellar damage and noted that the pre-attentive detection of somatosensory deviant stimuli is impaired in cerebellar patients. Both of the negative components that were analyzed, peaking at the latency range of 60–90 ms and 120–180 ms, were evident in controls, but the latter was almost totally lacking in cerebellar patients. The results indicate that cerebellar processing is required for detecting the novelty of an incoming somatosensory stimulus. Astikainen et al. (2001) found a mismatch negativity-like component in rabbits, comparable to sMMR in humans, as a response to air puffs to the eye in an oddball condition. They found difference between the ERPs to deviants and to standards in the somatosensory regions of the cerebral cortex and in the cerebellar cortex in rabbits. The authors argued, in reference to their earlier work, that the involvement of the cerebellar cortex in the generation of the MMN-like ERPs occurs in parallel with the activation of the sensory specific regions of the cerebral cortex, but is multimodal instead of specific relation to any sensory modality.

The sMMR is suggested to have *clinical applications* for the research of developmental neurology and neurodegenerative diseases (Näätänen, 2009). Restuccia et al. (2009) have recently showed that the sMMR can be reliable obtained in healthy children. They recorded somatosensory ERPs to electrical pulses in an oddball paradigm in children at the age range of 6–11 years and found a negative component peaking at 120–180 ms on parieto-central regions contralateral to the stimulated hand and a negative component peaking at 180–250 ms on the frontal regions contralateral to stimulated hand. Congruently with the theory of auditory MMN, the sMMR thus have both the component on the primary sensory cortex – on the parietal regions for the somatosensory modality – and a frontal component, which seem to be elicited if attention is oriented outside the stimuli and if the deviance detection is difficult. As the growing body of studies in the auditory modality have shown, the mismatch response can be used as an objective index of cognitive decline related to several neuropsychiatric and neurological diseases and aging (Näätänen, 2009; for a review see Näätänen et al., 2011). The somatosensory counterpart of the MMN could be specifically useful in the evaluation of the severity of condition and changes in the condition of several developmental disorders that are related to somatosensory discrimination impairments such as autism, dyslexia and developmental coordination disorder (Näätänen, 2009).

Aims of the study

The first aim of the present study was to examine whether there exists a change detection mechanism in the human somatosensory modality that is analogous to mismatch negativity in the other sensory modalities. Considering the results of the few existing ERP studies that have examined change detection in the somatosensory modality we hypothesized that the change detection can be discerned as the brain's different responses to standard and deviant tactile electrical stimuli in an oddball paradigm. The second and leading aim of the study was to examine conceivable changes in the somatosensory change detection mechanism that are related to aging of the brain. Based on the findings of referred studies of other sensory modalities, we hypothesized that the change detection mechanism is altered by aging and that these alterations might be deteriorative just as the effects of aging to many other brain processes such as cognitive functioning and transient memory functioning. We examined whether the mismatch negativity-like somatosensory ERP components differed between young and aged participants.

MATERIALS AND METHODS

Participants

EEG data was collected from 22 young and 14 elderly Finns during August–November 2010 (Table 1). All participants were volunteers with no known neurological or psychiatric conditions. Four of the participants were discarded due to disrupted data or unfilled requirements of the study (e.g. left-handedness). For the final data analysis there were twenty right-handed participants aged 22–27 years (mean age 25 years, twelve male and eight female) in the young adults group and twelve right-handed participants with the age range of 67–95 years (mean age 75 years, four male and eight female) in the elderly group. Participants in the young adults group were university students recruited via e-mail. Elderly participants were volunteers from the organization of retired people of Jyväskylä recruited at their weekly meeting after an informative presentation of the study. All the participants were informed of the study beforehand and obliged to sign an informed consent before the experiment. During their visit to the laboratory, participants took part in a median nerve stimulation test, a cutaneous finger stimulation test (oddball condition) and a visual stimulation test (oddball condition), from which in this study only the cutaneous finger stimulus procedure is discussed. The ethics committee of the University of Jyväskylä has approved the study.

Procedure and stimuli

During the recording, the subject sat comfortably in a chair in a separated laboratory room. The subjects were instructed to ignore finger stimuli and to be fully involved with a recording of a radio play, about which they were told to ask questions after the recording. The radio play was presented via loudspeaker placed about 50 cm above the subject´s head with a volume comparable to normal speaking voice. The subjects were asked to fix their gaze at the cross in the foot of a screen placed about 1,5 meters in front of the subject's head. The recording was video monitored from the room next to the subject´s room to control the subject's sleepiness and movement during recording.

Electrical stimulation was generated with a Digitimer constant current stimulator (model DS7A). Electrical pulses of 200 ms duration were delivered via conductive jelly moistened flexible metal ring electrodes on the left forefinger and little finger (stimulating cathode electrode above the proximal phalanx and anode electrode above the distant phalanx). A piece of gauze was placed on the finger between electrodes to prevent conductivity between electrodes. A run of 1000 stimuli was delivered with an inter-stimulus interval of 500 ms in randomized order of the stimulus type (85% standard stimuli and 15% deviant stimuli). The target of deviant stimulus finger between little finger and forefinger was changed for every other subject. Thus, 50% of the subjects were given standard stimulation to the forefinger and deviant stimulation to the little finger and 50% of the subjects vice versa. Stimulus intensities were adjusted independently for both fingers to the level of doubled subjective sensory threshold, which was tested before recording. Overall, stimulus intensities were larger in the aged group (forefinger 5.4 mA and little finger 4.1 mA) than in the young group (forefinger 4.0 mA and little finger 3.8 mA). One-way ANOVA showed a significant difference between the age groups in forefinger stimulus intensity ($F(1)=18.372$, $p< .001$) but no significant difference between the age groups in little finger stimulus intensities.

TABLE 1. *The participants of the study.*

YOUNG ADULTS

Subject	Age (years)	Sex (f/m)	Height (cm)	Arm length (cm)
1	26	m	179	57
2	36	f	173	55
3	29	f	158	51
4	27	m	178	58
5	22	f	177	59
6	22	f	160	55
7	23	f	154	48
8	23	m	184	56
9	23	f	172	56
10	25	m	162	51
11	23	m	181	57
12	24	m	177	57
13	24	f	172	54
14	23	m	183	61
15	23	m	179	59
16	26	m	180	59
17	27	m	175	56
18	27	m	181	59
19	27	f	176	66
20	27	f	169	56
21	25	f	160	53
22	25	m	178	55
Mean	**25**	**10f / 12m**	**173**	**56**
SD	**3**	**–**	**9**	**4**
Range	**22–36**	–	**154–184**	**48–66**

AGED

Subject	Age (years)	Sex (f/m)	Height (cm)	Arm length (cm)
23	69	f	164	56
24	66	f	152	49
25	67	f	156	50
26	72	f	154	53
27	77	f	166	56
28	80	m	176	62
29	80	m	172	52
30	76	f	164	55
31	73	f	162	52,5
32	71	f	151	51,5
33	72	m	183	61
34	95	m	179	62
35	69	f	162	55
36	87	m	172	60
Mean	**75**	**9f / 5m**	**165**	**55**
SD	**8**	**–**	**10**	**5**
Range	**66–95**	–	**151–183**	**49–62**

Electroencephalography recording

Electroencephalography (EEG) was recorded with Brain Vision Recorder software (Brain Products GmbH, Munich, Germany) at 30 scalp locations. Ag/AgCl electrodes were placed on the electrode cap (Easy Cap QA40) according to the international 10-20 system at FP1, FP2, Fz, F3, F4, F7, F8, FC1, FC2, FC5, FC6 , T7, T8, C3, C4, Cz, CP1, CP2, CP3, CP4, CP5, CP6, Pz, P3, P4, P7, P8, Oz, O1 and O2. Electrode impedance was kept below 20 KΩ. An average reference was applied and the ground electrode was placed in the middle of the forehead. Eye movements and blinks (EOG) were measured from bipolar electrodes placed one above the left eye and another lateral to the right orbit. The signal was amplified (Brain Vision QuickAmp), filtered with a band pass of 0.1–100Hz and stored on hard disk at a sample rate of 1000Hz.

Data analysis

The data were analyzed with Brain Vision Analyzer 2.0 software (Brain Products GmbH). The signals from the electrodes were first filtered with a band pass of 0.1–32 Hz (24 dB octave roll off) and epochs exceeding ± 90 μV (± 200 ms around the exceeding epoch) were automatically edited out from the averaging in any recording channel. A notch filter was used at the frequency of 50 Hz to delete interference caused by mains current. In addition, the data from three subjects were omitted from further analysis because less than one third of the segments were remaining in the data recorded from these subjects. Thus, an average of 78% (an average of 117 segments of both stimulus types) of the segments for the remaining 32 subjects were included in the analysis (Table 2). Ocular correction (Gratton-Coles method) was used for data from all of the remaining 32 subjects and data at the maximum from two channels from three subjects were corrected with topographic interpolation. At last, the data was segmented to 500 ms periods from 100 ms before stimulus onset to 400 ms after stimulus onset. The 100 ms pre-stimulus period was used as a baseline by averaging its values. Both stimulus types were segmented separately and then averaged consecutively to standards and deviants (standard immediately preceding deviant) for each subject.

TABLE 2. *Accepted deviant segments. Data from the subjects with at least 50 remaining deviant segments after data analysis were accepted into grand-averages.*

Subject	Accepted deviants (max. 150)
1	138
2	134
3	22
4	116
5	92
6	59
7	97
8	65
9	144
10	71
11	118
12	150
13	141
14	117
15	141
16	118
17	97
18	125

Subject	Accepted deviants (max. 150)
19	83
20	140
21	132
22	150
23	81
24	113
25	149
26	126
27	135
28	143
29	27
30	112
31	113
32	47
33	140
34	54
35	123
36	148
Mean	**108**
SD	**36**
Range	**22–150**

Statistical analysis

Visual inspection of the grand-averaged waveforms revealed difference between standard and deviant conditions and difference between the age groups for peak components between 30–80 ms (labeled P50) and 40–110 ms (labeled N80). In addition, a positive deflection between 150–200 ms (labeled mismatch response, MMR) after stimulus onset was chosen for further analysis (Figure 1 and Figure 2). The peak values of P50 and N80 were first detected from C4 in respect of its location on the primary somatosensory cortex contralateral to stimuli and the largest detected responses for both stimulus types. The peak values of other electrodes were then detected at the latency of the peak latency on C4. P50 latency showed variation between subjects from 31 to 77 ms post-stimulus and N80 varied from 45 to 106 ms post-stimulus (Table 3 and Table 4). The amplitude of the MMR was analyzed with average values from the latency range of 150–200 ms. Peak values of P50 and N80 and averaged values from a time window of 150–200 ms post-stimulus (MMR) were analyzed with repeated measures multivariate analysis of variance (MANOVA) with electrode site (C4, Fz, F4, FC2 for P50; C4, FC2, FC6, F4 for N80 and Cz, FC1, FC2, Fz, F3, F4 for MMR) and stimulus type (standard vs. deviant) as factors and age group (young vs. aged) as a grouping factor. Electrode sites used in the analysis for each peak were chosen by visual inspection of a topographic voltage map. The threshold for statistical analysis was $p < .05$.

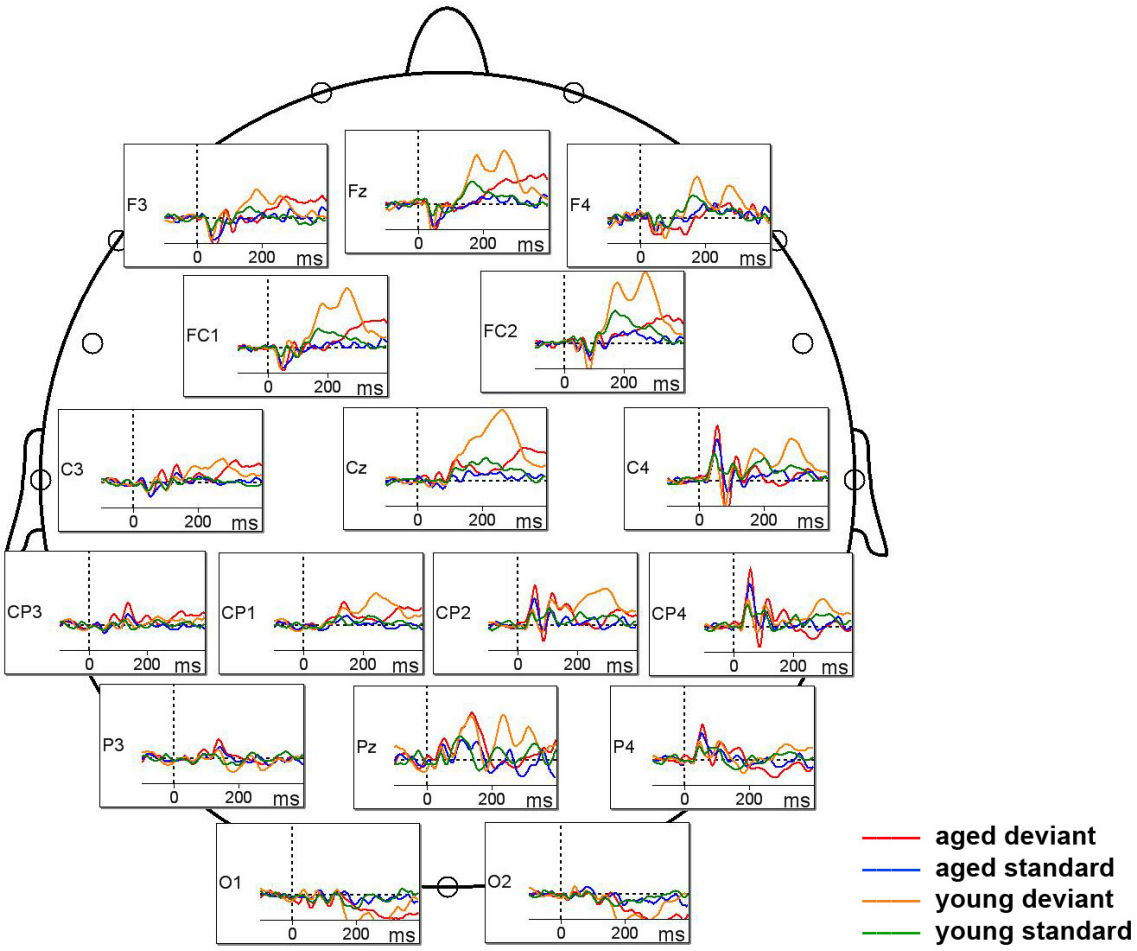

FIGURE 1. *Grand averaged waveforms of both young and aged age groups at 17 electrode sites.*

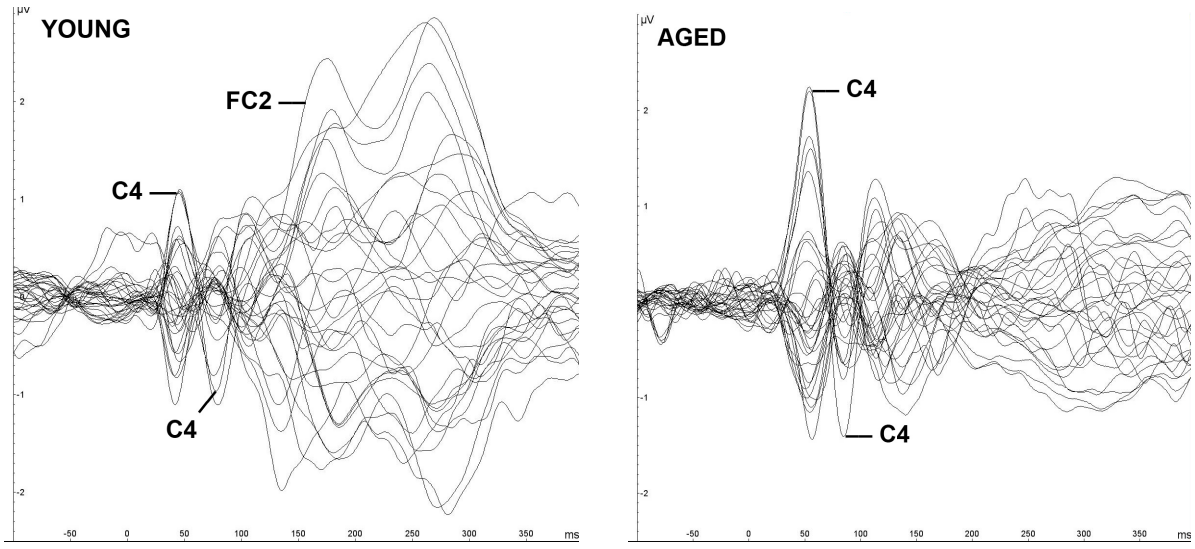

FIGURE 2. *Grand averaged waveforms of responses to deviant stimuli on all 30 electrodes. In the aged group (right) responses at short latency (<100 ms post-stimulus) are larger than in the young group (left), whereas longer latency (>100 ms post-stimulus) responses are considerable larger in the young group compared to the aged group.*

RESULTS

Component P50

3-way MANOVA showed significant interaction between the main effects of *stimulus type* and *electrode site* ($F(3,28)= 3.442$, $p= .030$), which indicates different responses to standard and deviant stimuli in different scalp locations (Figure 1). The responses may have been slightly larger to standard stimuli (mean 0.24 μV) than to deviant stimuli (mean 0.13 μV) ($F(1,31)= 0.774$, $p= .386$). Since the MANOVA did not show significant difference between the age groups, post hoc tests were conducted without the age group as a grouping factor between subjects. 2 × 2 ANOVA with electrode site (C4, FC2, Fz, F4) and stimulus type (standard vs. deviant) as factors showed significant interaction between the *stimulus type* and *electrode site* ($F(3,29)= 3.489$, $p = .028$). In addition, paired samples t-tests were conducted to find out which electrodes the values for deviant and standard stimuli responses did differ in. Paired samples t-tests showed significant difference between standard and deviant stimuli on Fz ($t(31)= 2.544$, $p= .016$) and C4 ($t(31)= -2.503$, $p= .018$).

The latency of the P50 peak on electrode C4 was analyzed by repeated measures MANOVA with *stimulus type* as a factor and *age group* as a grouping factor. The analysis showed a significant main effect for the *age group* ($F(1)= 8.906$, $p= .006$) (Figure 3). Overall, the latencies in the aged group were longer (mean 55 ms post-stimulus) than in the young group (mean 47 ms post-stimulus) (Table 3).

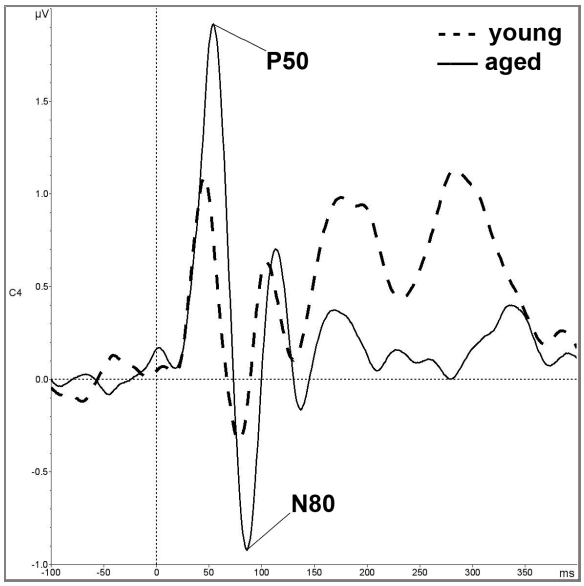

FIGURE 3. *Grand averaged waveforms on C4 electrode in which stimulus type (standard vs. deviant) is averaged into a single waveform. In the aged group (continuous line) the latencies of P50 and N80 peaks are prolonged compared to the young group (dashed line). Also the amplitudes of the peaks appear larger in the aged group compared to the young group, although without statistical support.*

TABLE 3. *P50 peak latencies and amplitudes from C4 electrode.*

Subject	Standard latency (ms)	Deviant latency (ms)	Standard amplitude (µV)	Deviant amplitude (µV)
1	33	33	0,999	0,823
4	58	58	0,686	1,934
5	77	77	1,341	2,548
6	46	46	1,659	1,092
7	45	45	2,554	3,253
8	47	47	0,742	0,913
9	44	44	0,586	0,009
10	42	42	2,049	1,741
11	46	46	1,708	4,835
12	50	50	3,893	1,992
13	55	55	2,525	1,515
14	43	43	1,105	1,389
15	43	43	0,576	0,826
16	46	46	1,607	2,156
17	37	37	0,021	0,481
18	56	56	0,378	0,687
19	51	51	0,936	1,569
20	62	62	0,988	0,38
21	44	44	0,318	1,161
22	36	36	1,017	0,654
23	51	51	1,59	1,668
24	49	49	1,676	3,628
25	47	47	1,401	1,453
26	63	63	1,242	3,024
27	62	62	3,507	3,979
28	47	47	1,459	3,234
30	66	66	0,922	1,146
31	51	51	2,193	1,969
33	59	59	1,604	2,994
34	65	65	0,554	1,509
35	61	61	0,588	1,475
36	53	53	3,896	4,045
Mean	**49**	**51**	**1,45**	**1,89**
Min	**31**	**33**	**0,02**	**0,01**
Max	**68**	**77**	**3,9**	**4,84**
SD	**9,3**	**9,8**	**0,98**	**1,2**

Component N80

3-way MANOVA showed significant main effects of *stimulus type* and *electrode site*. Analysis also showed significant interaction between the main effects of *stimulus type* and *electrode site* ($F(3,28)= 3.544$, $p= .027$), which indicates different responses to standard and deviant stimuli in different scalp locations (Figure 1). The responses were overall larger to deviant stimuli (mean -0.93 µV) than standard stimuli (mean -0.32 µV) ($F(1,30)= 10.619$, $p= .003$). Since the MANOVA did not show significant difference between the groups, post hoc tests were conducted without age group as a grouping factor between subjects. 2 × 2 ANOVA with electrode site (C4, FC2, FC6, F4) and stimulus type (standard vs. deviant) as factors showed significant *stimulus type* ($F(1,31)= 12.981$, $p=.001$) and *electrode site* ($F(3,29)= 6.800$, $p= .001$) main effects and *stimulus type* × *electrode site* interaction ($F(3,29)=3.953$, $p= .018$). Further, paired samples t-tests were conducted to find out in which electrodes values for deviant and standard stimuli responses did differ. Paired samples t-tests showed significant difference between standard and deviant stimuli on C4 ($t(31)= 3.542$, $p= .001$), FC2 ($t(31)= 3.028$, $p= .005$) and FC6 ($t(31)= 2.480$, $p= .019$), but no significant difference between the conditions on F4.

The latency of N80 on electrode C4 was analyzed by repeated measures MANOVA with *stimulus type* as a factor and *age group* as a grouping factor. The analysis proved significant main effect for the *age group* ($F(1)= 5.015$, $p= .033$) (Figure 3). Overall, the latencies in aged group were longer (mean 85 ms post-stimulus) than in young group (mean 76 ms post-stimulus) (Table 4).

TABLE 4. *N80 peak latencies and amplitudes from C4 electrode.*

Subject	Standard latency (ms)	Deviant latency (ms)	Standard amplitude (μV)	Deviant amplitude (μV)
1	85	81	-1,722	-3,618
4	78	88	-0,121	0,563
5	91	101	-0,211	0,547
6	58	61	-0,977	0,189
7	83	80	0,048	-1,99
8	88	80	-0,711	-2,359
9	45	68	-0,064	-1,016
10	63	85	-0,822	-5,819
11	81	75	-0,299	-2,382
12	81	77	0,883	-1,859
13	61	65	0,83	2,169
14	58	73	0,747	0,501
15	64	81	-0,106	-0,969
16	65	81	0,6	-0,402
17	60	71	-0,757	-3,801
18	98	96	-0,239	-0,947
19	91	76	0,376	-0,499
20	72	87	0,162	-0,495
21	86	84	-0,54	-0,461
22	63	76	-0,22	-4,166
23	74	78	-0,765	-1,566
24	69	80	-0,33	-0,83
25	99	85	0,239	-0,136
26	58	88	0,728	0,418
27	91	95	-0,975	-0,923
28	85	81	-0,481	-6,572
30	81	85	0,109	0,556
31	78	82	-1,737	-1,163
33	84	83	-1,184	-2,729
34	89	91	-0,135	-0,084
35	106	92	-1,368	-1,249
36	92	85	-2,036	-3,603
Mean	**77**	**82**	**-0,34**	**-1,4**
Min	**44**	**61**	**-2,03**	**-6,57**
Max	**106**	**101**	**0,88**	**2,169**
SD	**14,6**	**8,7**	**0,76**	**1,9**

Mismatch response (MMR)

The values of the MMR at the time window of 150–200 ms post-stimulus were analyzed by 2 × 6 × 2 MANOVA as stimulus type (standard vs. deviant) and electrode site (Cz, FC1, FC2, Fz, F3, F4) as factors and age group (young vs. aged) as a grouping factor. The analysis showed significant interaction between *stimulus type* and *age group* ($F(1,30)= 5.219$, $p= .030$). The interaction indicated different responses to deviant and standard stimuli and unequal responses between the age groups (Figures 4 and Figure 5). Mean amplitudes for both standard (0.72 μV) and deviant (1.45 μV) stimuli responses were larger in the young group than in the aged group (standard mean 0.20 μV, deviant mean 0.15 μV). None of the other main effects or interactions between main effects were significant. Latencies for MMR were not analyzed because the values used in the analysis were averaged values from the time window of 150–200 ms post-stimulus onset.

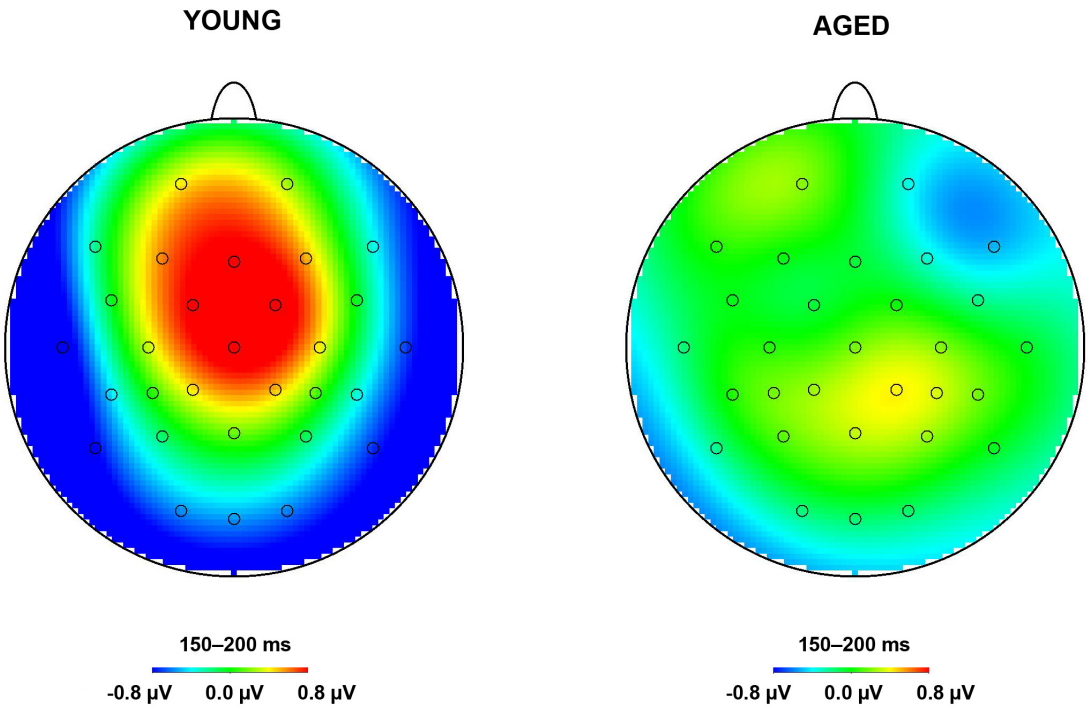

FIGURE 4. *A voltage mapping view of the mismatch response. The values are grand averaged values from the difference wavelet (deviant values minus standard values) from the time window of 150–200 ms after stimulus onset.*

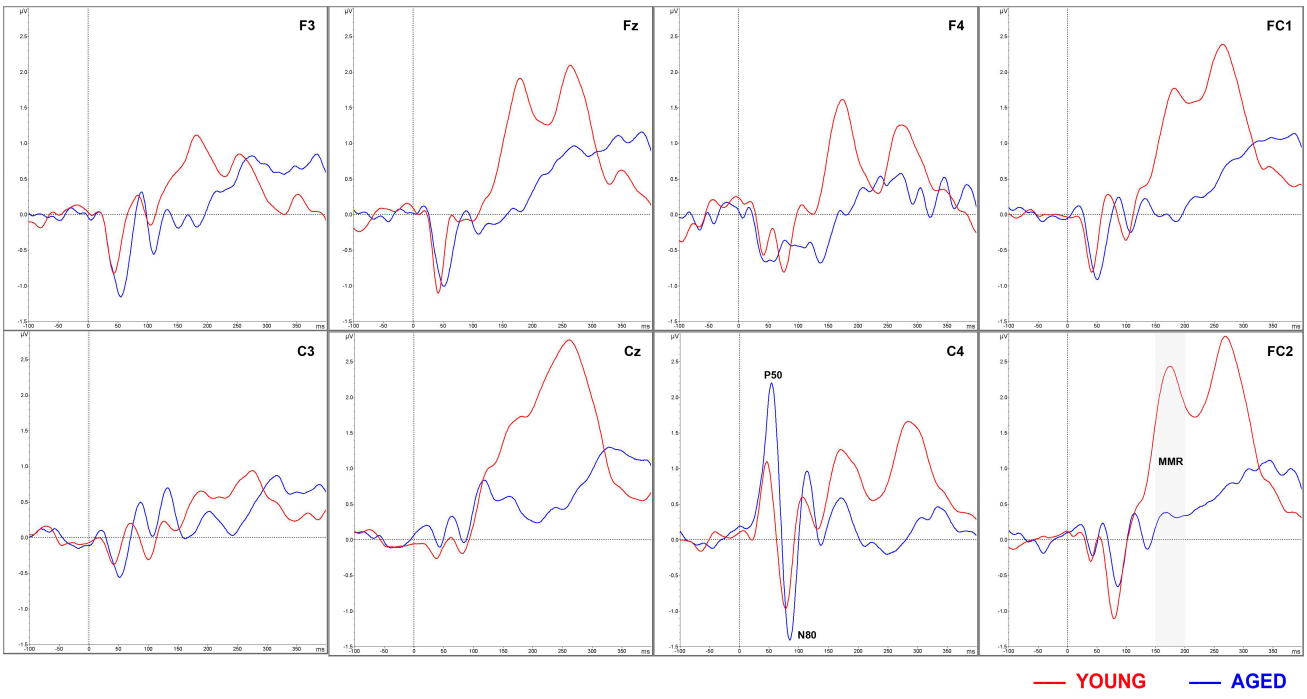

FIGURE 5. *Grand averaged waveforms of the deviant responses on eight electrode sites. The red waveform represents the grand averaged responses to deviant stimuli in the young group and the blue waveform represents grand averaged responses to deviant stimuli in the aged group.*

DISCUSSION

The present study examined the brain's somatosensory change detection mechanism in an oddball experiment, in which ERPs to electrical tactile stimuli were recorded in two age groups. In addition, the effects of aging to these ERP components were studied comparing the data of young adults with an age range of 22–27 with the data of aged participants with an age range of 67–95. Two early ERP components, P50 and N80, and a positive deflection at the latency range of 150–200 ms (MMR) were analyzed.

The results showed that somatosensory ERPs to deviant stimuli differed from the ERPs to standard stimuli supporting the hypothesis about the existence of a pre-attentive change detection mechanism in the somatosensory modality. In both age groups, responses to deviant stimuli were throughout larger in amplitude compared to responses to standard stimuli. In addition, the MMR differed significantly between the age groups indicating that the somatosensory change detection mechanism is affected by aging – confirming the second hypothesis of the present study. Young participants showed significant difference in responses between the conditions in all the analyzed components, P50, N80 and MMR, but aged participants' responses to standard and deviant stimuli differed only in P50 and N80. Early components P50 and N80 were significantly prolonged in latency and showed a tendency to be increased in amplitude in the aged group compared to young adults. Interestingly, the MMR was nearly absent in the aged group. It has been shown by many authors that the auditory MMN is attenuated in amplitude and prolonged in latency with aging (for a review see Näätänen et al., 2011), but to our knowledge, the present study is the first to show this kind of age-related attenuation of the mismatch-like response in the somatosensory modality.

P50 and N80 were located on the fronto-central cortex contralateral to the stimulated hand and the MMR on the frontal and fronto-central cortex with no lateralization (Figure 4). We propose, congruently with other authors (Shinozaki et al., 1998; Spackmann et al., 2007; Restuccia et al., 2009), that like the auditory MMN, the somatosensory mismatch response has a sensory specific subcomponent on the somatosensory cortex and a frontal subcomponent. N80 and MMR might be similar to mismatch negativity components reported by Spackmann et al. (2007), who found a negative peak between 100–200 ms on central and fronto-central regions and a positive peak between 170–270 ms on central and centro-parietal regions. They argued that these two components are separate entities both representing the mismatch response, and that the latter positive peak might be specific to the somatosensory modality. Longer peak latencies compared to our findings might

be due to vibration stimulation versus electrical pulses used in our experiment. However, the scalp distribution of the positive mismatch response reported by Spackmann et al. (2007) rather match with N80 instead of the positive MMR of the present study. Restuccia et al. (2009) studied children aged from 6 to 11 years and found a negative component peaking at about 160 ms on parieto-central regions and another negative component peaking at about 220 ms on frontal regions, both contralateral to stimulated hand. Apart from the longer ISI (1000 ms), they used a similar method to our oddball experiment. Again, the latencies were longer compared to latencies of N80 and the MMR of the present study, and the frontal component was negative versus the positivity of the MMR of the present study. Thus, it can be speculated whether N80 and the MMR are analogous to the mismatch components reported by Restuccia et al. (2009), although the latency differences between the studies might be due to the age of the participants, and the unequal polarities of the frontal components between the studies might be due to different reference electrodes. Interestingly, similar components with the ones analyzed in the present study were found in a MEG study of Akatsuka et al. (2007). They used two-point stimulation in an oddball paradigm and argued, referring to their earlier findings (Akatsuka et al., 2005), that the mismatch magnetic fields, recorded over the time frame of 30–70 ms and 150–250 ms, were noticeable only when the subjects automatically discriminated one-point stimuli from two-point stimuli.

It is, however, possible – considering the present too early peak latencies for cognitive processing – that P50 and N80 are somatosensory evoked potentials that are unconnected to the MMR. Anyhow, the difference between the responses to standard and deviant stimuli were evident at P50 and N80. Also Restuccia et al. (2009), for instance, reported different responses to standard and deviant stimuli at P40, N60, and P100 components in addition to the mismatch components. In addition, Hari et al. (1990), previously proved in an oddball experiment with electrical stimulation to fingers that on the second somatosensory cortex at 100 ms post-stimulus responses to deviant stimuli were three times as high in amplitude as those to standard stimuli. To explain this it is hypothesized that the CABAergic system might be involved in the detection of deviant stimuli (Wikström et al. 1996), which is relevant to our findings of age-related changes of P50 and N80. EEG (Ferri et al., 1996) and MEG (Stephen et al., 2010; Ziegler et al., 2010) studies of median nerve stimulation have shown, corresponding to our findings, that somatosensory evoked potentials are increased in amplitude and prolonged in latency with aging. Ferri et al. (1996) propose that these age-related changes, which are evident also in Alzheimer's disease and specially in vascular dementia, correlate with a structural rearrangement of the cortical connectivity due to neuronal loss and declines in inhibitory function – that is to say, cortical decrease in GABAergic activity – which is a cardinal feature of aging. Moreover, Stephen et al. (2010) argued that larger amplitude

responses on the first somatosensory cortex in patients with mild cognitive impairment compared to normal elderly people and patients with Alzheimer's disease might be an early marker of abnormal brain function leading to Alzheimer's disease. Ziegler et al. (2010), instead, combined the wavelet analysis with the analysis of evoked responses in their MEG study and suggested that an increased amplitude and a prolonged latency of the M70 peak in healthy middle-aged compared to young participants is related to increased pre-stimulus mu power and synchrony in the first somatosensory cortex with aging.

We suggest that the P50 and N80 peaks found in the present study have similarities with P45 and N60 reported by Ferri et al. (1996) and M50 and M70 reported by Ziegler et al (2010), despite the methodological differences between the studies. Since we did not measure GABAergic activation in the present study, we can only assume that the age-related decline in the inhibitory function might explain the differences in P50 and N80 components between the age groups. However, it is noteworthy in the evaluation of P50 and N80 that both the higher sensory threshold and the higher given stimulus intensity in the aged group might have an effect to larger peak amplitudes in the aged group (Appendix 1).

Our main finding of the MMR being nearly absent in the aged group is congruent with the findings of age-related attenuation of the MMN in the auditory and visual modalities (Näätänen et al., 2011). Bertoli, Smurzynski and Probst (2002), for instance, found reduced MMN peak amplitudes, increased MMN latencies and increased threshold limits for elderly compared to young participants in an auditory gap detection task. Further, it has been shown in healthy aged subjects that the amplitude of the auditory MMN correlates with the performance on neuropsychological tests requiring specially the function of the prefrontal cortex, linking the MMN to cognitive functioning (Kisley, Davalos, Engleman, Guinther & Davis, 2005). It is possible that the intense attenuation of the MMR in the aged group is related to the age-related shortening of the sensory memory duration supporting the memory trace explanation of the MMN. Shinozaki et al. (1998), for instance, suggest that a change-related negativity at 60–80 ms and a change-related positivity at 100–200 ms found in their study have different neural generators and that the latter one is related to the duration of sensory memory. Their suggestion was based on the finding that the change related positivity was decreased by a prolonged ISI, whereas the earlier change-related negativity was unchanged by these changes. Our findings congruently indicate that the somatosensory change detection mechanism has an early subcomponent and a late subcomponent. The latter positive component is attenuated with aging whereas earlier components prolong in latency and increase in amplitude with aging, indicating comprehensive age-related changes in the somatosensory change detection mechanism. We propose that the age-related changes in the P50 and N80 might be related

to decline in inhibitory function, but the age-related changes in the MMR might rather be related to the shortening of the sensory memory or transient memory function.

Furthermore, it is possible that the somatosensory change detection mechanism is affected by the age-related changes in the cerebellum. It has been shown that the cerebellar volume decreases by about 30 percent from early adulthood to old age (Anderden, Gundersen & Pakkenberg, 2003). The cell loss is most evident in the anterior lobe of the cerebellum, that is predominantly involved in motor control, where the cell loss of Purkinje and granule cells is about 40 percent from early adulthood to old age. Taking into consideration that Purkinje cells of the cerebellum are GABAergic inhibitory interneurons (Schwartz, 2000), it is possible to speculate about the linkage between age-related decrease in inhibitory function and the changes in the MMN-like ERP components. Congruently with the hypothesis of relationship between cerebellar function and MMN, Restuccia et al. (2007) proved that pre-attentive detection of deviant stimuli is impaired in cerebellar patients. However, the cerebellar function or structural changes of the cerebellum were not studied in the present study and thus it is impossible to make conclusions about the possible connection between the MMR and the cerebellum.

There are other limitations, too, that are considerable when generalizing the findings of the present study. Firstly, the experimental procedure did not include standard-omitted condition in addition to oddball condition. It is thus not possible to ensure that different responses to deviant compared to standard stimuli were due to the change detection mechanism rather than to activation of new afferents. However, it has been proved in previous studies with similar methods with the present study (e.g. Restuccia et al., 2009) that the frontal component that occurs in an oddball condition is fully lacking in the standard-omitted condition. Secondly, since the cognitive abilities of the participants were not evaluated in any behavioral measures, it is not possible to confirm the hypothesized linkage between the age-related cognitive deterioration and the attenuated MMR. Nonetheless, the basis of the present study is reliable, taking into account the methods approved in the previous studies of somatosensory mismatch negativity, the controlled healthiness of the participants and the distance between the age groups. The age ranges of the groups ensure the differences between the groups in the brain's developmental stage; participants in their twenties presumably have full-grown brains, whereas participants in their seventies presumably have some age-related changes in their brain. On the other hand, it is considerable that the young participants were university students, whereas the occupational and educational background of the aged participants were not controlled. The third concern is related to the memory trace explanation of the MMN; the hypothesized connection between the age-related attenuation of MMR and the shortened

sensory memory duration cannot be confirmed since the experimental procedure did not include measures of it, for instance, conditions with varying ISIs.

The connection between the age-related attenuation of MMN-like ERP components and the age-related cognitive deterioration is an important concern for future studies. The findings of the present study show that the pre-attentive processing of deviant stimuli is changed with aging, but its behavioral implications are not clear. That is, the present study confirms the findings from other sensory modalities, that the processing of sensory environment changes with aging (Näätänen et al. 2011). To investigate hypothesized connections of these changes to age-related decrease in inhibitory function, to shortening of sensory memory duration or to cerebellar cell loss will be challenges for future studies. To be exact, the effects of different ISI durations and the effects of increased GABA levels to somatosensory mismatch-like responses could be examined in the future studies. Findings of animal studies and studies with other imaging methods in addition to EEG give necessary additive information for the conclusions of these questions in the future. In addition, it would be interesting to investigate conceivable connections of different ways of life to the brain's change detection mechanism in the old age – even in follow-up studies – and it is thus important that the life background of participants is carefully taken into account in future studies.

The present study strengthens the data basis of the somatosensory MMN. First of all, it confirms the analogy of the somatosensory MMN with the MMN in the other sensory modalities and the definitions of the somatosensory specific features of the MMN. As the first study to show the age-related changes in the somatosensory change detection mechanism it contributes a baseline for future studies that investigate the relationship between aging and the somatosensory MMN. Albeit the clinical applications of the present findings are so far exiguous, at least at the individual level, it is possible that the better understanding of the changes in the attention mechanisms in the old age might help to plan facilities of society to better fulfill the special needs of the elderly. For instance, many everyday tasks, such as driving a car, crossing a street or following a conversation in a group, require fast detection of deviant stimuli that seem to be deteriorated in the old age. Changes in the attention mechanism – particularly in the change detection mechanism – might also have crucial part in age-related cognitive deterioration. In addition, the knowledge of the effects of normal aging to the brain's electrical responses is momentous for the ERP studies that investigate the diseases that often occur along with aging. Näätänen (2009) proposed that the somatosensory MMN could be specifically useful in the evaluation of the severity of condition of several developmental disorders like developmental coordination disorder, autism or dyslexia. Equally, the somatosensory MMN might be valuable in the evaluation of neurodegenerative diseases like

Alzheimer's disease, Parkinson's disease, schizophrenia and aphasia – and even in prognostic purposes of these diseases.

CONCLUSION

The results of the present study indicated that the brain can detect somatosensory deviant stimuli in the background of homogenous (standard) stimuli when attention is directed outside the stimulus stream. The change detection is seen as a mismatch response (MMR): a more positive response to deviant stimuli compared to standard stimuli in averaged waveforms in the latency range of 150–200 ms post-stimuli. In addition, earlier components P50 and N80 reveal the equal difference in the responses to standard and deviant stimuli. The results are in line with the theory of mismatch negativity (MMN) and the findings of previous studies of the MMN in the other sensory modalities, as well as with the somatosensory MMN. The results revealed also that the somatosensory change detection mechanism is affected by aging: the MMR is radically attenuated in amplitude and P50 and N80 have a tendency to increase in amplitude with aging. P50 and N80 are also prolonged in latency in the aged compared to young adults. The age-related difference in the somatosensory change detection mechanism might be due to age-related decrease in the inhibitory function and decreased sensory memory duration. Thus the change detection mechanism might have connections to age-related cognitive deterioration and several neurodegenerative disorders that are common in the old age. More research is needed to investigate the neural and behavioral correlates of the age-related changes in the somatosensory change detection mechanism.

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APPENDIX 1:

YOUNG ADULTS

Notes	Subject number	Age (years)	Sex (f/m)	Dev. seg. (max. 150)	Height (cm)	Arm length (cm)	SI forefinger (mA x 10)	SI little finger (mA x 10)	Include/ count out
	12	26	m	138	179	57	0,44	0,48	
O1, O2, Oz top. Interpol. Left handed su	13	36	f	134	173	55	0,40	0,52	count out
Bad data; few segments	14	29	f	22	158	51	0,42	0,44	count out
	15	27	m	116	178	58	0,28	0,24	
Fp1, Fp2 topographic interpolation	16	22	f	92	177	59	0,36	0,50	
	17	22	f	59	160	55	0,28	0,26	
	18	23	f	97	154	48	0,40	0,40	
	19	23	m	65	184	56	0,54	0,44	
	20	23	f	144	172	56	0,36	0,32	
	21	25	m	71	162	51	0,48	0,40	
	22	23	m	118	181	57	0,46	0,30	
	23	24	m	150	177	57	0,56	0,46	
	24	24	f	141	172	54	0,26	0,30	
	25	23	m	117	183	61	0,42	0,42	
	26	23	m	141	179	59	0,46	0,40	
	27	26	m	118	180	59	0,44	0,44	
	28	27	m	97	175	56	0,48	0,44	
	29	27	m	125	181	59	0,40	0,38	
	30	27	f	83	176	66	0,36	0,30	
	31	27	f	140	169	56	0,30	0,20	
T8 topographic interpolation	32	25	f	132	160	53	0,28	0,24	
	33	25	m	150	178	55	0,46	0,46	
Number / Average	22	25	10f / 12m	111	173	56	0,40	0,38	
N / Average (accepted)	**20**	**25**	**8f / 12m**	**115**	**174**	**58**	**0,40**	**0,37**	

AGED

Notes	Subject number	Age (years)	Sex (f/m)	Dev. seg. (max. 150)	Height (cm)	Arm length (cm)	SI forefinger (mA x 10)	SI little finger (mA x 10)	Include/ count out
	101	69	f	81	164	56	0,50	0,48	
T8 topographic interpolation	102	66	f	113	152	49	0,52	0,46	
	103	67	f	149	156	50	0,52	0,58	
	104	72	f	126	154	53	0,58	0,44	
	105	77	f	135	166	56	0,56	0,34	
	106	80	m	143	176	62	0,78	0,44	
Bad data; few segments	107	80	m	27	172	52	0,30	0,14	count out
	108	76	f	112	164	55	0,56	0,30	
	109	73	f	113	162	52,5	0,48	0,32	
Pz, FC5, FC6 topographic interpolation	110	71	f	47	151	51,5	0,58	0,40	count out
	111	72	m	140	183	61	0,54	0,48	
	112	95	m	54	179	62	0,48	0,38	
	113	69	f	123	162	55	0,48	0,42	
	114	87	m	148	172	60	0,68	0,62	
Number / Average	14	75	9f / 5m	108	165	55	0,54	0,41	
N / Average (accepted)	**12**	**75**	**8f / 4m**	**120**	**167**	**56**	**0,56**	**0,44**	