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How response inhibition modulates nociceptive and non-nociceptive somatosensory brain-evoked potentials

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Abstract

Objective: To examine and compare the modulation of nociceptive somatosensory laser-evoked potentials (LEPs) and non-nociceptive somatosensory electrically-evoked potentials (SEPs) by brain processes related to response inhibition.
Methods: A warning auditory tone was followed by either an electrical or a laser stimulus. Subjects performed a *Go*/*Nogo* task in which they were instructed to respond to the laser stimulus and refrain from responding to the electrical stimulus in half of the runs. In the other half, they performed the opposite. The paradigm allowed a direct, within-subject comparison of the electrophysiological correlates of brain processes related to the *Go*/*Nogo* task in both somatosensory submodalities.
Results: In the *Nogo*-condition, SEPs displayed an enhanced N120 (early *Nogo*-response), a reduced vertex P240 and enhanced frontal P3 (late *Nogo*-responses). In contrast, LEPs only displayed late *Nogo*-related responses (reduced vertex P350 and enhanced frontal P3).
Conclusions: The early *Nogo*-related enhancement of SEPs may reflect brain processes specific to the processing of non-nociceptive somatosensory stimuli. Later components of the *Nogo*-response may reflect cortical activity common to the processing of both nociceptive and non-nociceptive somatosensory stimuli.
Significance: Response inhibition significantly modulates both LEPs and SEPs. Part of these activities may be specific of the eliciting stimulus modality.

Keywords: Inhibition; Laser-evoked potentials; Somatosensory-evoked potentials; *Go*/*Nogo*; Cerebral processing; Pain

1. Introduction

Response inhibition is the ability to exert high-level voluntary inhibitory control over executive behavior, when there is a change of context. The '*Go*/*Nogo*' paradigm has been widely used to explore brain processes underlying response inhibition (Karlin et al., 1970). In such a paradigm, two physically differing sensory stimuli are presented to the subject which is instructed to respond (e.g. press a button) to one of the two stimuli (the '*Go*' stimulus) and to refrain from responding to the other stimulus (the '*Nogo*' stimulus). Using event-related brain potentials (EPs), the *Go*/*Nogo* paradigm has been explored within auditory, visual and non-painful somatosensory modalities (Pfefferbaum et al., 1985; Eimer, 1993; Falkenstein et al., 1995; Nakata et al., 2004). Whatever the sensory modality or the motor task, the *Nogo*-stimulus may elicit one or both of the following electrophysiological components: (1) a *Nogo*-N2 (a negative potential peaking approximately 150–400 ms after stimulus onset) and (2) a *Nogo*-P3 (a positive potential peaking approximately 300–500 ms after stimulus onset) (Falkenstein et al., 1999; Nakata et al., 2004; Niewenhuis et al., 2004; Van 't Ent and Apkarian, 1999; Yamanaka et al., 2002). Both of these components display a fronto-central scalp distribution. Source analysis studies, relying on either MEG or EEG recordings, have indicated that *Nogo*-related EP responses could be explained by sources located in the ipsilateral and contralateral

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dorso-lateral parts of the frontal lobes: the frontal association cortex and/or the anterior cingulate cortex (Sasaki et al., 1993; Nieuwenhuis and Yeung, 2003; Lavric et al., 2004; Bokura et al., 2001; Bekker et al., 2005).

It is generally assumed that *Nogo*-related EP changes reflect brain processes related to response inhibition (Falkenstein et al., 1999; Lavric et al., 2004; Kopp et al., 1996). However, alternative explanations have been proposed. It has been hypothesized that these responses may reflect brain processes related to the detection of a response conflict occurring when two or more competing response tendencies are simultaneously active (i.e. 'conflict monitoring; Donkers and van Boxtel, 2004; Nieuwenhuis and Yeung, 2003). It has also been hypothesized that these responses may be related to brain processes involved in the activation of a response in the *Go*-condition (i.e. 'response activation'; Bruin et al., 2001), or resultant from working memory-related brain processes (Salisbury et al., 2004).

The aim of the present study was to determine how processes related to response inhibition may affect the brain activity elicited by a specifically nociceptive somatosensory stimulus. Indeed, to our knowledge, no studies have yet explored the influence of response inhibition on nociceptive evoked potentials. In conventional experimental or clinical settings, recording EPs elicited by such stimuli requires the subject to stand still and hold back the motor response that is urged by the salience and nociceptive nature of the evoking stimulus. Therefore, one should consider the possibility that, in such conditions, response inhibition contributes to the recorded EPs. The first objective of this study was to describe the electrophysiological activity related to the occurrence of a nociceptive *Nogo* stimulus and to compare these responses to those recorded in usual experimental conditions. Finally, as a number of studies have shown that a fraction of the brain activity related to the *Go*/*Nogo* paradigm may be specific of the eliciting sensory modality (Nakata et al., 2006; Falkenstein et al., 1999), the Nogo-related EPs elicited by a nociceptive somatosensory stimulus were directly compared to those elicited by a non-nociceptive somatosensory stimulus.

Nociceptive laser stimuli and non-nociceptive electrical stimuli were alternatively delivered to the same skin area of the hand, in random order and with equal probability (Lavric et al., 2004; Legrain et al., 2002; Nakata et al., 2005; Donkers and van Boxtel, 2004; Kanda et al., 1999). In half of the runs, subjects were instructed to respond to the laser stimulus and to refrain from responding to the electrical stimulus. In the other half, they were instructed to respond to the electrical stimulus and to refrain from responding to the laser stimulus. This procedure allowed direct within-subject comparison of the EPs elicited by each of the two types of somatosensory stimulation. A non-specific auditory conditioning stimulus was used to cue the occurrence of the upcoming test-stimulus. This procedure avoided a lack of movement preparation and attention that may have been associated with a specifically primed *Nogo*-trial (Kopp et al., 1996; Bruin et al., 2001).

Although some studies have shown that *Go*/*Nogo* differences may be present even when the task related to the detection of the *Go* stimulus does not require subjects to execute a motor action (Pfefferbaum et al., 1985; Salisbury et al., 2004), a number of investigators have highlighted that motor-related brain processes may contribute to *Go*/*Nogo* differences (Verleger et al., 2006; Salisbury et al., 2004; Kopp et al., 1996; Falkenstein et al., 1999). For that reason, the present study included two control conditions. The first consisted of a simple reaction-time task (*SRT*) which required movement preparation and motor execution. The second was a verbal stimulus-intensity rating task which involved neither motor preparation nor motor execution (No-Movement, *NM*). Additional confounding factors, such as expectancy and enhanced attention (Kopp et al., 1996), may have contributed to observed differences between experimental conditions. Thus, to disambiguate one or several of these confounds, and allow a clearer interpretation of the changes observed in *Nogo* waveforms, difference waveforms (ΔEPs) were computed across all four experimental conditions (*Go*, *Nogo*, *SRT*, *NM*).

A CO_2 laser stimulator was used to produce the nociceptive stimulus. Laser-evoked brain potentials (LEPs) have been widely used to explore the nociceptive system (Treede et al., 1995). Infrared CO_2 lasers can produce brief and intense radiant-heat stimuli which activate selectively and synchronously the thinly myelinated Aδ- and unmyelinated C-fibers located in the superficial layers of the skin (Plaghki and Mouraux, 2003). The most prominent feature of LEPs consists of a large negative–positive complex (N240-P350) which culminates at the vertex (Carmon et al., 1976) and is related to the activation of Aδ-nociceptors (Bromm and Treede, 1987). It is often preceded by an additional negative component (N170) whose scalp topography is maximal at temporal electrodes contralateral to the stimulation site (Kunde and Treede, 1993).

A transcutaneous electrical stimulator was used to produce the non-nociceptive somatosensory stimulus. Non-nociceptive tactile sensations are conveyed by fast conducting Aβ-fibers. Their large diameter is responsible for their low electrical impedance and hence their low electrical activation threshold as compared to thinly myelinated Aδ-fibers and unmyelinated C-fibers (Plaghki and Mouraux, 2003).

2. Methods

2.1. Subjects

Ten healthy volunteers (mean age 27.6 ± 3.3 years; 6 women, 4 men) participated in the study. Nine of these subjects were right-handed. Informed consent was obtained from all subjects. The study was approved by the local Ethics Committee and conducted in accordance with the principles of the Helsinki declaration.

2.2. Stimulus

To avoid possible acoustic or visual clues, equipment associated with the production of the stimulus was kept outside the visual field and subjects wore headphones as ear mufflers.

2.2.1. Electrical stimulus

The electrical stimulus was produced by a constant current generator (Digitimer DS7, Digitimer Ltd., United Kingdom). Two electrodes (inter-electrode distance: 25 mm) were placed 10 cm proximal to the wrist of the non-dominant hand over the *nervus radialis superficialis*. The electrical stimulus consisted of a square-wave pulse of 0.5 ms duration. Stimulus intensity (1.7 ± 0.7 mA) was twice the absolute detection threshold, excluding any discomfort or unpleasant sensation, and set to induce a sensation of non-painful tingling in the first dorsal interdigital space.

2.2.2. Laser heat stimulus

The cutaneous heat stimulus was delivered by a CO_2 laser, designed and built in the Department of Physics of the Université catholique de Louvain. The system generated a highly collimated infrared beam (wavelength 10.6 μm) directed at the first dorsal interdigital space of the non-dominant hand (sensory territory of the *nervus radialis superficialis*). Stimulus duration was 50 ms. Beam diameter at target was 10 mm. Power output was set individually such that stimuli were perceived as clearly pricking, and then kept constant throughout the entire experiment. Before and after each experimental session, the temperature of the non-dominant hand was measured with an infrared thermometer (Tempett, SENSELab, Sweden). Measurement of stimulus energy density was performed at the beginning and end of each experimental session, using an optical power/energy meter (13PEM001, Melles Griot, The Netherlands). Energy density was supraliminal for Aδ-nociceptor activation (8.7 ± 1.1 mJ/mm^2). The laser beam was slightly shifted between each trial to avoid skin overheating and minimize nociceptor sensitization or habituation.

2.3. Experimental design

2.3.1. Experimental paradigm

Two experimental sessions were conducted at 3-month interval. Prior to each experimental session, subjects were familiarized with the experimental surroundings and the two test stimuli. The "*Go*/*Nogo*" paradigm was used during the first experimental session. The "control" conditions were performed during the second experimental session. In both experimental sessions, a warning stimulus (S1)/imperative stimulus (S2) paradigm was used (Fig. 1a). The warning stimulus (S1) was a loud auditory ringing tone lasting 500 ms and presented binaurally through headphones. The imperative stimulus (S2) consisted either of a non-

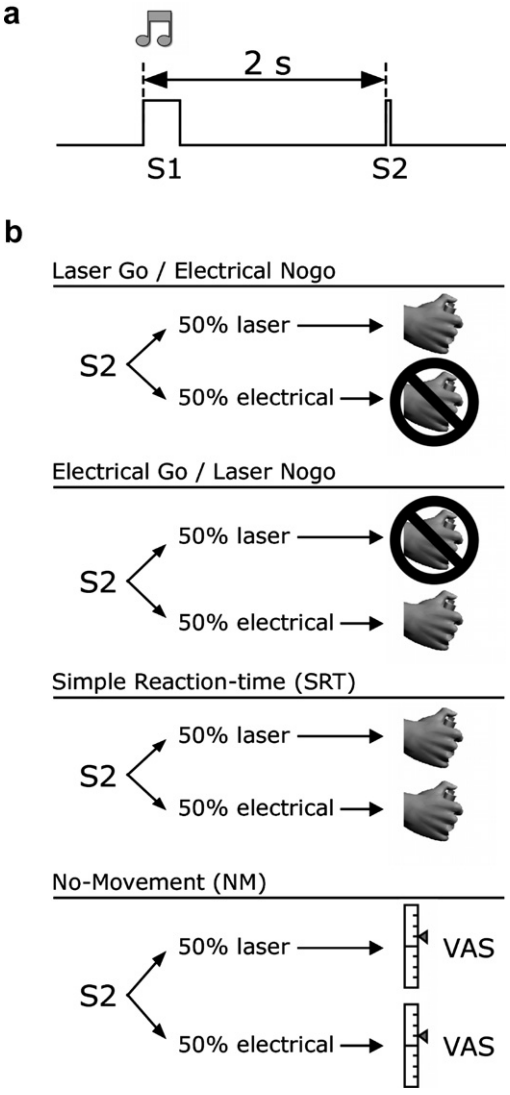

Fig. 1. (a) A warning stimulus–imperative stimulus (S1–S2) was used for the *Go*/*Nogo* paradigm as well as for the control conditions. The warning stimulus (S1) was a loud auditory tone lasting 500 ms. The imperative stimulus (S2) consisted either of a non-nociceptive electrical or a nociceptive laser stimulus that elicited a sensation in the sensory territory of the *nervus radialis superficialis* of the non-dominant hand. The time interval between the onsets of S1 and S2 was fixed at 2 s. The probability that S2 would be an electrical stimulus or that S2 would be a laser stimulus was 50%. (b) In the first experimental session, subjects were requested to perform a *Go*/*Nogo* task by pressing a micro-switch as fast as possible when detecting a *Go* stimulus while refrain from responding when detecting a *Nogo* stimulus. The micro-switch was held in the dominant hand. In two out of the four acquisition blocks, the *Go* stimulus was defined as the laser stimulus (condition 'Laser *Go*/Electric *Nogo*'). In the two other acquisition blocks, the *Go* stimulus was defined as the electrical stimulus (condition: 'Electrical *Go*/Laser *Nogo*'). The second experimental session included two control conditions. In the first control condition (labeled '*SRT*'), subjects were instructed to perform a simple reaction-time task consisting in pressing the micro-switch as fast as possible when detecting the S2 stimulus, this time regardless of its type (laser or electrical). In the second control condition (labeled '*No-Movement*', *NM*) subjects did not perform any stimulus-related motor task. Instead, they were asked to evaluate and verbally report the intensity of the S2 stimulus (laser or electrical), as a value ranging between 0 and 100 on a visual analogue scale ('0' corresponding to the absence of sensation and '100' to the highest level of pain imaginable). The order of presentation of the acquisition blocks was randomized and balanced across subjects.

nociceptive electrical stimulus or a nociceptive laser stimulus. Both stimuli elicited a sensation in the sensory territory of the *nervus radialis superficialis* of the non-dominant hand (see Section 2.2). The time interval between the onsets of S1 and S2 was fixed at 2 s. The inter-trial interval (S1–S1) varied randomly between 10 and 15 s. Each of the two experimental sessions was divided into four successive blocks and lasted approximately 90 min. Each acquisition block included thirty consecutive trials (15 laser stimuli and 15 electrical stimuli) presented in random order. The probability that S2 would be an electrical stimulus or that S2 would be a laser stimulus was 50%. Between acquisition blocks subjects were allowed a 5-min break.

2.3.2. First experimental session: 'Go/Nogo' task

In the first experimental session, subjects were requested to perform a *Go*/*Nogo* task by pressing a micro-switch as fast as possible when detecting a *Go* stimulus while refrain from responding when detecting a *Nogo* stimulus (Fig. 1b). The micro-switch was held in the dominant hand. In two out of the four acquisition blocks, the *Go* stimulus was defined as the laser stimulus (condition 'Laser *Go*/Electrical *Nogo*'). In the two other acquisition blocks, the *Go* stimulus was defined as the electrical stimulus (condition: 'Electrical *Go*/Laser *Nogo*'). The order of presentation of the acquisition blocks was randomized and balanced across subjects.

2.3.3. Second experimental session: 'SRT' and 'NM' tasks

The second experimental session included two control conditions. In both conditions, the stimulation procedure (warning stimulus S1 – imperative stimulus S2) was identical to that of the first experimental session. In the first control condition (labeled '*SRT*'), subjects were instructed to perform a simple reaction-time task consisting in pressing the micro-switch as fast as possible when detecting the S2 stimulus, regardless of its type (laser or electrical). In the second control condition (labeled '*No-Movement*', *NM*) subjects did not perform a motor task. Instead, they were asked to evaluate and verbally report the intensity of the S2 stimulus (laser or electrical), as a value ranging between 0 and 100 on a visual analogue scale ('0' corresponding to the absence of sensation, '100' to the highest level of pain imaginable) (Fig. 1b). Each condition included two acquisition blocks of thirty trials. All four acquisition blocks were presented in random order, and were balanced across subjects.

2.4. Data acquisition

2.4.1. Reaction time

Reaction times to *Go* stimuli in the *Go*/*Nogo* paradigm, and to all stimuli in the *SRT*-condition were measured using an electronic clock (ms resolution) initialized when the laser shutter was opened or the electrical stimulus triggered, and halted when the micro-switch was pressed. If the subject did not react to a stimulus within 2.5 s, the clock was automatically stopped.

2.4.2. Electroencephalogram

EEG was recorded from 19 Ag–AgCl electrodes evenly placed on the scalp according to the International 10–20 system. Linked earlobes (A_1A_2) served as reference. Ground was placed above the wrist contralateral to stimulation site. Impedance was kept below 5 kΩ. Two electrodes, placed at the lower right and upper left side of the right eye, monitored ocular movements and eye blinks. Signals were amplified and digitized (gain: 1000; filter: 0.06–75 Hz, sampling rate: 167 cps) using a PL-EEG recorder (Walter Graphtek, Germany). Epochs extending from 0.5 s before to 2.5 s after stimulus onset (512 bins) were band-pass filtered (0.2–25 Hz) offline. Epochs contaminated by EOG were rejected by visual inspection. After baseline-correction (reference interval −0.5 to 0 s), average waveforms were computed for each subject, experimental condition ('*Go*', '*Nogo*', '*SRT*', '*NM*'), and stimulus type ('Electrical', 'Laser'). All offline signal-processing steps were computed using BrainVision Analyzer® (Brain Products GmbH, Germany) and the Letswave EEG toolbox (Mouraux, Université catholique de Louvain, Belgium).

2.5. Data analysis

2.5.1. Identification of LEP components

For each subject, and within each LEP waveform ('Laser *Go*', 'Laser *Nogo*', 'Laser *SRT*', 'Laser *NM*'), four distinct components (N170, N240, P350, and P3) were individualized. Latencies were measured from stimulus onset to peak. Amplitudes were measured from baseline to peak.

Component P350 was identified at electrode C_Z as a positive component peaking between 300 and 500 ms after stimulus onset. The N240 was then defined at electrode C_Z as a negative component preceding the P350 and occurring between 150 and 300 ms after stimulus onset. An additional negative component N170 was searched for at the temporal electrode (T_3 or T_4) contralateral to the stimulus. It was defined as the negative deflection preceding the N240 and occurring between 120 and 200 ms after stimulus onset. Finally, a later-occurring positive component labeled P3 was identified at midline electrode F_Z, C_Z, and P_Z as a positive peak following the P350 and occurring between 350 and 600 ms after stimulus onset.

2.5.2. Identification of SEP components

For each subject, and within each SEP waveform ('Electrical *Go*', 'Electrical *Nogo*', 'Electrical *SRT*', 'Electrical *NM*'), four distinct late components (P100, N120, P240, and P3) were individualized. First, component P240 was identified at electrode C_Z as a positive component peaking between 150 and 300 ms after stimulus onset. The preceding N120 and P100 peaks were then identified as follows. The N120 was defined as a negative peak preceding the P240 at electrode C_Z and occurring between 80 and 160 ms after stimulus onset. The P100 component was defined as a positive peak preceding the N120 component and occurring between 70 and 130 ms after stimulus onset

at electrodes C_Z and P_4. Finally, a later-occurring positive component, labeled P3, was identified at midline electrodes F_Z, C_Z, and P_Z, following the P240 and occurring between 250 and 500 ms after stimulus onset.

2.5.3. Difference waveforms

In order to identify the differences between the electrophysiological activity elicited by a *Nogo* stimulus and that elicited by a *Go* stimulus, for each stimulus type (electrical, laser), difference waveforms were computed by subtracting the *Go* average waveform from the *Nogo* average waveform ('*Nogo* minus *Go*' waveform). Furthermore, and in order to identify the electrophysiological activity related to the execution of the motor task (button-press), an additional difference waveform (labeled '*NM* minus *SRT*') was obtained, for each stimulus type (electrical, laser), by subtracting the *SRT* average waveform from the corresponding *No-Movement (NM)* average waveform.

2.6. Statistical analysis

Parametric statistical tests were used after confirming that the data were sampled from normal distributions by using the method of Kolmogorov–Smirnov. Central tendencies were expressed by using mean and standard deviation. The peak latency and baseline-to-peak amplitude of each LEP and SEP component were submitted to a two-factor analysis of variance (ANOVA) for repeated measures, with experimental condition and electrode location as factors. Conditions were *Go*, *Nogo*, *SRT*, and *NM*. Electrodes were F_Z, C_Z, and P_Z for all components, except the SEP P100 and the LEP N170. For the SEP P100 the electrodes used were: F_Z, C_Z, P_Z, T_3, T_4, P_3, and P_4. For the LEP N170 the electrodes used were: F_Z, C_Z, P_Z, T_3, and T_4. Differences in topographical distributions of EP components were also assessed using a vector scaling procedure applied "within-subject" (Mc Carthy and Wood, 1985). For each condition, each subject's amplitude was divided by the square root of the sum of the squared mean amplitudes. This method normalized the effects of conditions. When the assumption of sphericity was violated, the Greenhouse–Geisser method was used to correct degrees of freedom. A two-factor ANOVA was used to assess the topographical lateralization of the difference wave components, with electrode location and hemisphere as factors (frontal: F_3, F_4 – central: C_3, C_4 – parietal: P_3, P_4). Significance level was set at $p < .05$. When appropriate, post hoc pairwise comparisons between factors were carried out using a Bonferroni correction.

3. Results

3.1. Reaction times

Mean reaction-times (RT) for each individual subject and experimental condition are displayed in Fig. 2. The means across subjects of RTs obtained in the *Go*- and *SRT*-conditions for laser and electrical stimuli are shown in Table 1.

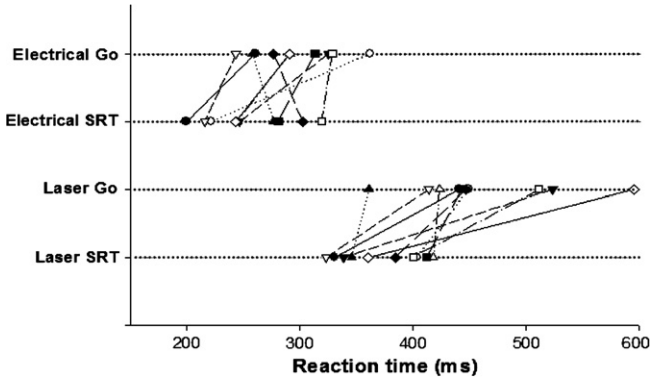

Fig. 2. Mean reaction time (RT) of each of the 10 subjects for laser and electrical stimuli. RTs to laser stimuli were significantly greater than RTs to electrical stimuli, as expected from the difference in nerve conduction velocities of afferent Aδ- and Aβ-fibers. RTs in the *Go*-condition were significantly greater than in the simple reaction time task (*SRT*).

On average, RTs to an electrical stimulus were 150 ms faster than RTs to a laser stimulus. RTs recorded within the *Go*/*Nogo* task were significantly greater than the RTs recorded within the *SRT* task (paired *t*-test; laser *Go* vs. *SRT*: $p = .004$; electrical *Go* vs. *SRT*: $p = .030$). The difference of RTs recorded in the *Go*-condition and in the *SRT*-condition between laser and electrical stimuli was not significantly different ($p = .100$).

3.2. Evoked potentials

Following artifact rejection and exclusion of erroneous responses 92% of epochs remained for further analysis in the laser *Go*-condition, 86% in the laser *Nogo*-condition, 85% in the electrical *Go*-condition and 80% in the electrical *Nogo*-condition. Due to the absence of erroneous responses, a relatively smaller number of trials were rejected in the *SRT*- and *NM*-conditions: 93% of epochs remained for further analysis in the laser *SRT*-condition, 95% in the laser *NM*-condition, 95% in the electrical *SRT*-condition, and 94% in the electrical *NM*-condition.

In the *Go*/*Nogo* task a number of inappropriate reactions were recorded: overall there were more false alarms than misses. The percentage of false alarms was 2.6% in the laser *Nogo*-condition and 5.1% in the electrical *Nogo*-condition. The percentage of misses was 0.3% in the electrical *Go*-condition and 0.0% in the laser *Go*-condition. The low rate of erroneous responses prevented any further analysis.

Table 1
Reaction times (mean ± SD, $n = 10$)

	Laser *Go*	Laser *SRT*	Electrical *Go*	Electrical *SRT*
RT (ms)	461 ± 66	372 ± 36	295 ± 37	255 ± 38

3.2.1. LEP components

Grand-average waveforms of the laser *Go*-, *Nogo*-, *SRT*-, and *NM*-conditions displayed clear N240-P350 late LEP complexes (Fig. 3). At electrode C_Z the mean N240-P350 peak-to-peak amplitude (62 ± 21 μV; mean across experimental conditions) was not significantly different across experimental conditions ($F_{3,54} = 1.259$, $p = .300$).

Table 2 shows the amplitudes of the LEP components as well as their amplitude differences between *Go*- and *Nogo*-conditions, and between *SRT*- and *NM*-conditions.

3.2.1.1. N170. Amplitude of the N170 component was maximal at the temporal electrode contralateral to stimulation side. Amplitudes, scalp topographies, and latencies of the

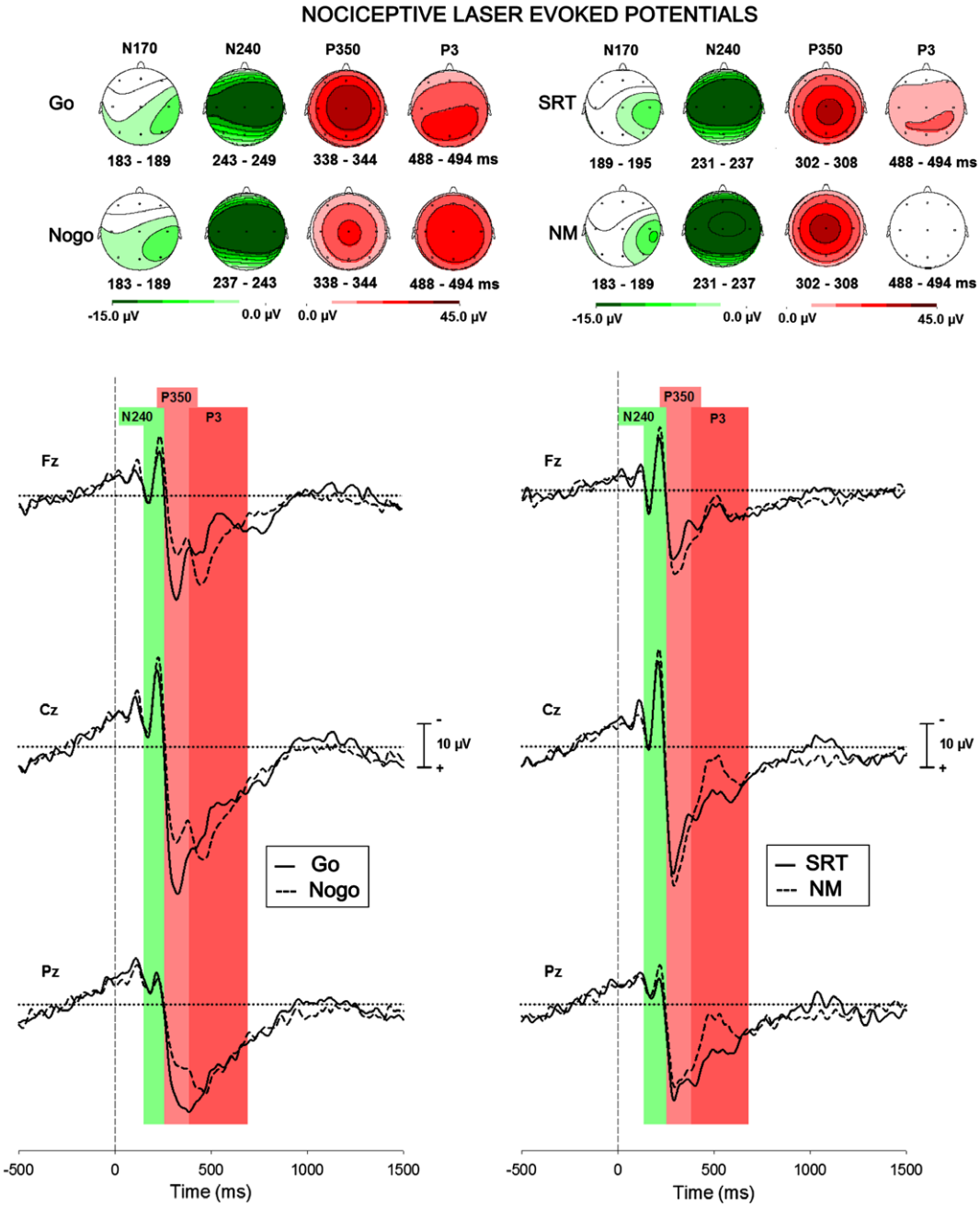

Fig. 3. Grand-averages of laser-evoked potentials (LEPs) recorded from non-dominant hand stimulation at electrodes F_z, C_z, and P_z, and scalp topography of the different LEP components. In the first experimental session (*left column*) a *Go*/*Nogo* paradigm was used in which laser and electrical stimuli were randomized equiprobably. In the *Nogo*-condition the P350 (in red) was significantly smaller, and the P3 (in red) significantly larger and more frontally localised than in the *Go*-condition. In the second experimental session (*right column*) two control conditions were applied: a simple reaction-time task (*SRT*) and a No-Movement condition (*NM*). In the *NM*-condition the LEP component P3 (in red) was significantly smaller than in the *SRT*-condition.

Table 2
Amplitudes of EP components following laser stimuli (mean ± SD in μV): absolute values and paired differences

LEP component	Electrode	*Go*	*Nogo*	Δ(*Nogo–Go*)
N170	T_4	−10.1 ± 5.4	−7.1 ± 5.2	*3.0 ± 5.2*
N240	C_Z	−25.7 ± 13.4	−27.2 ± 10.6	*−1.4 ± 10.6*
P350	C_Z	42.3 ± 10.3	28.1 ± 10.1	*−14.3 ± 13.7*
P3	F_Z	23.0 ± 8.3	26.7 ± 5.7	*3.8 ± 9.7*
	C_Z	34.9 ± 7.6	32.8 ± 9.5	*−2.1 ± 11.0*
	P_Z	33.1 ± 9.1	27.3 ± 10.9	*−5.7 ± 9.3*
LEP component	Electrode	*SRT*	*NM*	Δ(*NM–SRT*)
N170	T_4	−9.0 ± 6.8	−10.3 ± 4.9	*−1.3 ± 5.2*
N240	C_Z	−23.8 ± 11.9	−28.4 ± 15.4	*−4.6 ± 13.6*
P350	C_Z	35.4 ± 10.0	38.9 ± 15.2	*3.5 ± 11.3*
P3	F_Z	12.4 ± 8.6	14.5 ± 11.0	*2.1 ± 11.3*
	C_Z	21.1 ± 9.2	13.3 ± 11.1	*−7.7 ± 12.8*
	P_Z	24.5 ± 8.7	16.7 ± 9.0	*−7.7 ± 10.4*

N170 component were not significantly different across all four experimental conditions.

3.2.1.2. N240. Amplitude of the N240 component was maximal at electrode C_Z and extended bilaterally and symmetrically towards temporal electrodes. Amplitude and scalp topographies of the N240 component were not significantly different across all four experimental conditions.

The mean latencies of the N240 component were, at electrode C_Z: 235 ± 17 ms in the *Go*-condition, 240 ± 13 ms in the *Nogo*-condition, 227 ± 9 ms in the *SRT*-condition and 231 ± 14 ms in the *NM*-condition. Significant differences were found both across experimental conditions ($F_{1,18} = 3.759$, $p = .020$; post hoc *t*-test *Nogo* vs. *SRT*: $p = .020$) and across electrodes ($F_{2,18} = 11.028$, $p < .001$; post hoc *t*-test electrode F_Z vs. C_Z: $p = .001$ and electrode F_Z vs. P_Z: $p = .020$).

3.2.1.3. P350. Amplitude of the P350 component was maximal at electrode C_Z and extended homogeneously on surrounding electrodes. Its amplitude was significantly larger in the *Go*-condition than in the *Nogo*-condition ($F_{1,18} = 9.160$, $p = .010$). The topographical distributions of the *Go*-P350 and the *Nogo*-P350 were compared using a vector scaling procedure which normalized the data for the experimental condition. This analysis showed no significant topographical differences between the *Go*-P350 and the *Nogo*-P350. However, the scalp distribution of the P350 recorded in the *SRT*-condition was significantly more posterior than that recorded in the *Go*-condition ($F_{2,18} = 5.354$, $p = .010$).

The mean latencies of the P350 component were, at electrode C_Z: 343 ± 24 ms in the *Go*-condition, 347 ± 32 ms in the *Nogo*-condition, 317 ± 27 ms in the *SRT*-condition and 329 ± 25 ms in the *NM*-condition. Significant differences were found across experimental conditions ($F_{1,18} = 7.507$, $p < .001$; post hoc *t*-test *Go* vs. *SRT*: $p = .010$ and *Nogo* vs. *SRT*: $p < .001$).

3.2.1.4. P3. In the *Go*-condition, a positive component P3 was individualized at electrode C_Z, with a mean amplitude of 35 ± 8 μV. Its scalp distribution was maximal at electrodes C_Z and P_Z. In the *Nogo*-condition, the amplitude of the P3 component was significantly larger than in the *Go*-condition ($F_{2,18} = 8.388$, $p = .003$) and its topographical distribution was significantly more frontaI ($F_{2,18} = 8.871$, $p = .002$), as assessed with normalized data. In the *SRT*-condition, P3 amplitudes were significantly smaller than in the *Go*-condition ($F_{1,18} = 17.682$, $p = .002$) and its scalp topography was significantly more posterior ($F_{2,18} = 7.630$, $p = .004$). In the *NM*-condition P3 amplitudes were significantly smaller than in the *SRT*-condition, at electrode C_Z ($F_{2,18} = 4.552$, $p < .050$).

The mean latencies of the P3 component were, at electrode C_Z: 422 ± 47 ms in the *Go*-condition, 472 ± 34 ms in the *Nogo*-condition, 451 ± 39 ms in the *SRT*-condition and 449 ± 37 ms in the *NM*-condition. Significant differences were found across experimental conditions ($F_{1,18} = 3.703$, $p = .020$; post hoc *t*-test *Go* vs. *Nogo*: $p = .020$).

3.2.2. SEP components

Grand-average waveforms in electrical *Go*-, *Nogo*-, *SRT*-, and *NM*-conditions are shown in Fig. 4. The late SEP components P100, N120, P240, and P3 could clearly be individualized. Their mean amplitude, as well as the mean amplitude differences between *Go*- and *Nogo*-, and between *SRT*- and *NM*-conditions are shown in Table 3. At electrode C_Z the mean N120-P240 peak-to-peak amplitude (64 ± 19 μV; mean across experimental conditions) was not significantly different across experimental conditions ($F_{3,54} = 2.827$, $p = .060$).

3.2.2.1. P100. Amplitude of the P100 component was maximal at electrodes P_4 and P_Z. P100 amplitude was not significantly different in the *Go*- vs. *Nogo*-conditions. However, amplitude of the P100 recorded in the *NM*-condition was significantly smaller than that recorded in the *SRT*-condition ($F_{1,54} = 25.691$, $p < .001$) and amplitude of the P100 recorded in the *Nogo*-condition was significantly smaller than that recorded in the *SRT*-condition ($F_{1,54} = 12.542$, $p = .006$).

Latencies of the SEP P100 component (91 ± 7 ms in the *Go*-condition) did not significantly differ across experimental conditions.

3.2.2.2. N120. Amplitude of the N120 component recorded in the *Nogo*-condition was significantly greater than that recorded in the *Go*-condition ($F_{1,18} = 6.901$, $p = .030$). Amplitude of the N120 component recorded in the *NM*-condition was significantly greater than that recorded in the *SRT*-condition ($F_{1,18} = 7.806$, $p = .020$). The scalp distribution of the N120 recorded in the *NM*-condition was

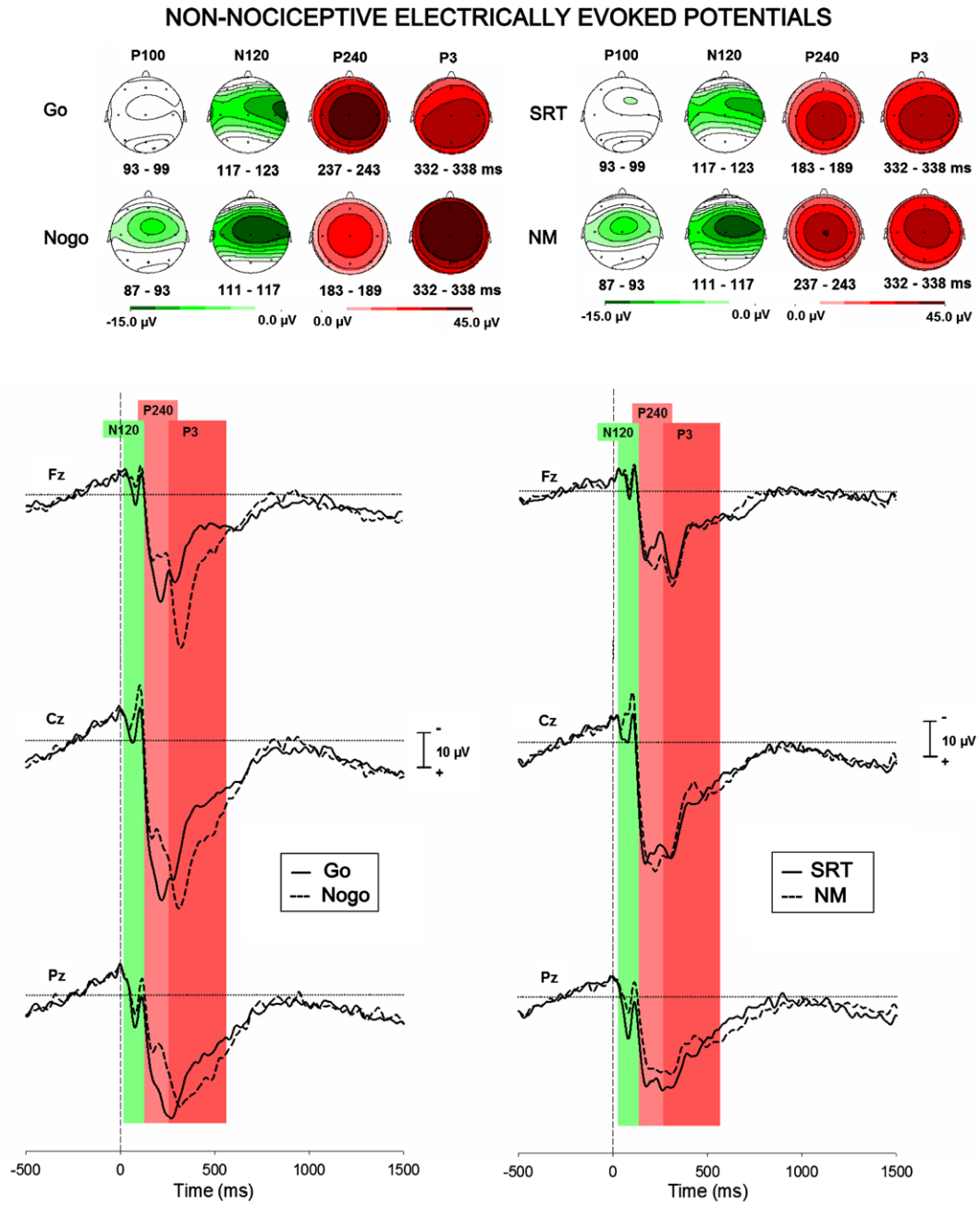

Fig. 4. Grand-averages of electrically-evoked potentials (SEPs) recorded from non-dominant hand stimulation at electrodes F_z, C_z and P_z, and scalp topography of the different SEP components. In the first experimental session (left column) a *Go*/*Nogo* paradigm was used in which laser and electrical stimuli were randomized equiprobably. In the *Nogo*-condition, the SEP components N120 (in green) and P3 (in red) were significantly larger in amplitude and more frontally localised than in the *Go*-condition. The SEP component P240 (*in red*) was significantly smaller in the *Nogo*-condition than in the *Go*-condition. In the second experimental session (right column) two control conditions were applied: a simple reaction-time task (*SRT*) and a No-Movement condition (*NM*). The SEP components P100 (in green) and P3 (in red) were significantly smaller, while N120 (in green) was significantly larger in the *NM*-condition than in the *SRT*-condition.

more frontal than in the *Nogo*-condition ($F_{2,18} = 4.159$, $p = .030$).

Latency of the N120 component was, at electrode C_Z, 117 ± 14 ms in the *Go*-condition. At electrode F_Z, latency of the N120 component was slightly yet significantly shorter in the *NM*-condition than in the *Go*- and *SRT*-conditions ($F_{2,18} = 2.373$, $p = .040$; post hoc *t*-test for electrode F_Z *Go* vs. *NM*: $p = .030$; *SRT* vs. *NM* = .040).

3.2.2.3. P240. In all experimental conditions the positive component P240 was maximal at electrode C_Z and homogeneously distributed among surrounding electrodes. The amplitude of P240 was significantly greater in the *Go*-condition than in the *Nogo*-condition ($F_{1,18} = 7.533$, $p = .020$). The scalp distribution of the *Go*-P240 was significantly more posterior than that of the *Nogo*-P240 ($F_{2,18} = 4.469$, $p = .030$), as assessed with normalized data.

Table 3
Amplitudes of EP components following electrical stimuli (mean ± SD; in μV): absolute values and paired differences

SEP component	Electrode	*Go*	*Nogo*	Δ(*Nogo–Go*)
P100	P_4	10.9 ± 5.0	7.9 ± 9.6	*−3.0 ± 8.3*
N120	C_Z	−14.0 ± 8.6	−21.6 ± 12.8	*−7.6 ± 9.0*
P240	C_Z	53.3 ± 14.2	43.1 ± 16.4	*−10.2 ± 14.5*
P3	F_Z	27.2 ± 9.4	48.6 ± 10.4	*21.4 ± 10.7*
	C_Z	40.6 ± 8.3	52.8 ± 12.4	*12.2 ± 11.9*
	P_Z	40.1 ± 11.3	39.7 ± 13.8	*−0.4 ± 13.0*
SEP component	Electrode	*SRT*	*NM*	Δ(*NM–SRT*)
P100	P_4	14.4 ± 7.8	7.6 ± 8.1	*−6.8 ± 5.7*
N120	C_Z	−12.8 ± 12.5	−19.9 ± 10.9	*−7.1 ± 10.2*
P240	C_Z	43.2 ± 18.4	49.2 ± 13.5	*6.0 ± 15.1*
P3	F_Z	28.2 ± 8.0	29.1 ± 10.0	*0.9 ± 11.5*
	C_Z	38.9 ± 6.8	27.8 ± 19.1	*−11.1 ± 20.9*
	P_Z	35.1 ± 9.1	28.3 ± 13.2	*−6.8 ± 13.9*

Latencies of the P240 component differed significantly across experimental conditions: 232 ± 27 ms in the *Go*-condition, 208 ± 41 ms in the *Nogo*-condition, 195 ± 31 ms in the *SRT*-condition and 220 ± 29 ms in the *NM*-condition ($F_{1,18} = 4.295$, $p = .010$; post hoc *t*-test *Go* vs. *SRT*: $p < .050$ and *SRT* vs. *NM*: $p = .040$).

3.2.2.4. P3. In the *Go*-condition a positive component P3 was individualized with a mean amplitude of 41 ± 8 μV at electrode C_Z. The scalp distribution of the *Go*-P3 was maximal at electrodes C_Z and P_Z. In the *Nogo*-condition the amplitude of P3 was significantly greater than in the *Go*-condition ($F_{1,18} = 9.884$, $p = .010$). The scalp distribution of the P3 component was compared across experimental conditions using normalized data: topography of the *Nogo*-P3 was significantly more frontal than that of the *Go*-P3 ($F_{2,18} = 28.956$, $p < .001$). In the *NM*-condition, P3 amplitudes were significantly smaller than in the *SRT*-condition, at electrode C_Z ($F_{2,18} = 6.269$, $p = .009$; post hoc *t*-test C_Z *SRT* vs. *NM*: $p = .006$).

Latencies of the SEP P3 component were not significantly different across experimental conditions. Latency of P3 for the *Go*-condition was 330 ± 54 ms at electrode C_Z.

3.2.3. Difference waveforms

To highlight the specific effects of the *Go*/*Nogo* task, and those related to the motor task, two difference waveforms (ΔEPs) were computed: "*Nogo* minus *Go*" and "*NM* minus *SRT*" (see Fig. 5).

In "*Nogo* minus *Go*" difference waveforms, two ΔLEP components were individualized: $\Delta N2_{LEP}$ and $\Delta P3_{LEP}$. The scalp distribution of the $\Delta N2_{LEP}$ peak was maximal at electrodes C_Z and C_4. The $\Delta P3_{LEP}$ wave had its maximal scalp distribution at frontal electrodes (F_Z, F_3, F_4, Fp_1, and Fp2). Three ΔSEP "*Nogo* minus *Go*" wave components were visualized: $\Delta N1_{SEP}$, $\Delta N2_{SEP}$, and $\Delta P3_{SEP}$. The topographical maximum of $\Delta N1_{SEP}$ was located at frontocentral electrodes (F_Z, C_Z). $\Delta N2_{SEP}$ was maximally present at central and parietal electrodes (C_Z, C_3, C_4, P_Z, P_3, and P_4). The positivity $\Delta P3_{SEP}$ followed $\Delta N2_{SEP}$ and was maximally distributed among frontal electrodes (F_Z, F_3, F_4). Topographically the $\Delta N2_{LEP}$ and the $\Delta N2_{SEP}$ components of the "*Nogo* minus *Go*" waveform were significantly lateralized towards the contralateral-to-stimulus hemisphere, as shown by two-way ANOVA (electrode × hemisphere) (ΔSEP: $F_{2,18} = 11.492$, $p < .001$; post hoc *t*-tests F_4 vs. F_3, $p = .020$ and electrode C_4 versus C_3: $p = .004$) (ΔLEP: $F_{2,18} = 5.122$, $p = .020$; post hoc *t*-test electrode C_4 versus C_3: $p = .003$). Latencies and amplitudes of these different components are shown in Table 4a.

In "*NM* minus *SRT*" difference waveforms, two ΔLEP components and three ΔSEP components were individualized. Their latencies and amplitudes are displayed in Table 4b.

4. Discussion

Results of the present study showed that both nociceptive and non-nociceptive somatosensory event-related brain potentials were significantly modulated by a *Go*/*Nogo* task. Furthermore, it appeared that brain processes related to response inhibition (as in the *Nogo*-condition) only modulated the later part of the nociceptive-evoked response, and that this modulation did not significantly contribute to the LEPs recorded in standard conditions.

Indeed, as compared to the responses elicited in the *Go*-condition, non-nociceptive electrical stimuli presented in the *Nogo*-condition elicited: (1) an enhanced frontal N120 component, (2) a reduced vertex P240 component and (3) an enhanced frontal P3 component. In contrast, *Nogo* nociceptive laser stimuli only elicited (1) a reduced vertex P350 component and (2) an enhanced frontal P3 component.

As already highlighted in the introduction, interpreting the differences between the evoked potentials elicited by a '*Nogo*' stimulus and those elicited by a '*Go*' stimulus is not straightforward. While these differences may result from the occurrence of brain processes related to response inhibition or conflict monitoring in the '*Nogo*' condition, they may also result from the occurrence of memory-related or motor-related activities in the '*Go*' condition. For that reason, both nociceptive and non-nociceptive SEPs were recorded within two additional experimental conditions. In the first control condition, subjects were requested to perform a simple motor reaction-time task (*SRT*-condition). In the second control condition they were requested to rate the intensity of perception, without performing any motor response (*NM*-condition). How task-related experimental factors may have differentially affected the responses recorded in each experimental condition is outlined in Table 5.

The fact that the *Nogo* task induced an enhancement of the non-nociceptive N120 SEP component, but not of the

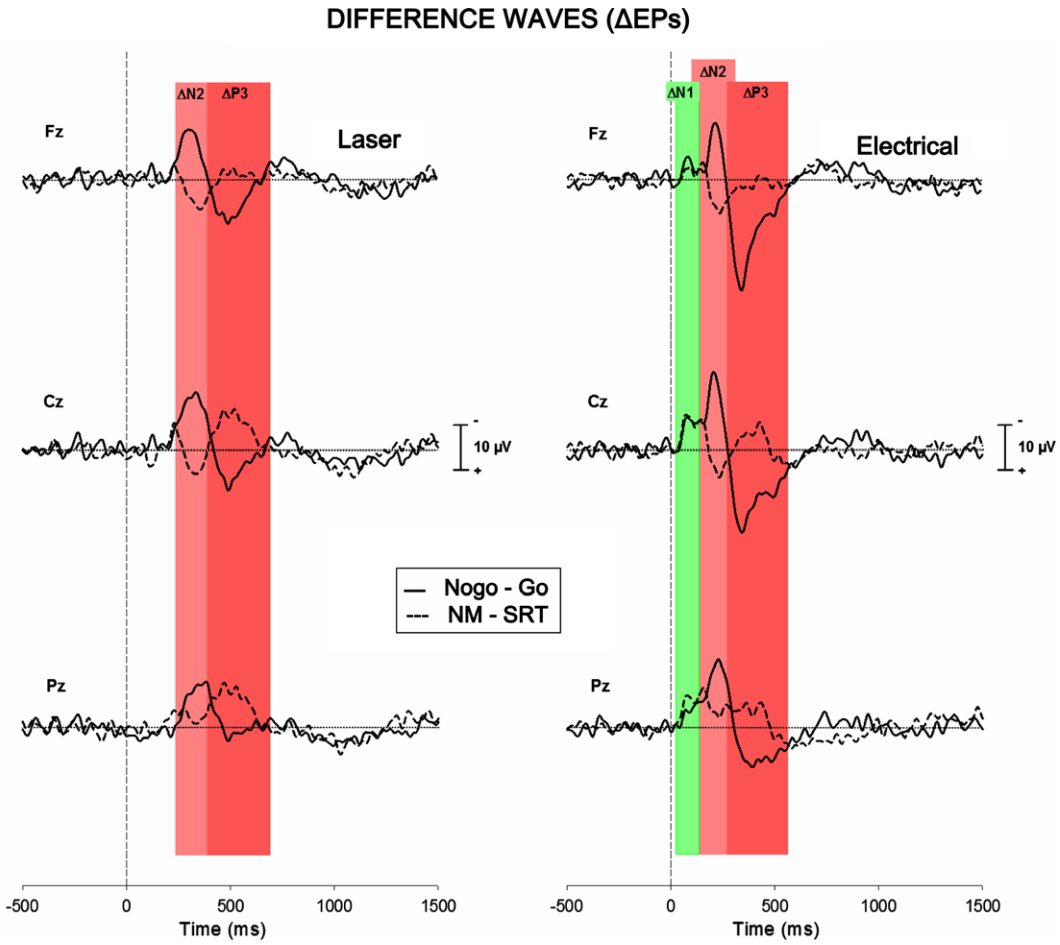

Fig. 5. Grand-averages of the difference waveforms (ΔEPs) for laser and electrical stimuli. For each subject the difference of *Nogo*- and *Go*-EPs, and the difference of *SRT*- and *NM*-EPs were computed. In laser stimuli (left column), "*Nogo* minus *Go*" ΔEPs exhibited a late negative–positive complex "$\Delta N2_{LEP}$–$\Delta P3_{LEP}$" (in red), corresponding to the *Nogo*-related modulation of P350 and P3. In electrical stimuli (right column), "*Nogo* minus *Go*" ΔEPs also showed a late negative–positive complex "$\Delta N2_{SEP}$–$\Delta P3_{SEP}$" (in red), corresponding to the *Nogo*-related modulation of P240 and P3. It was preceded by an early negative wave $\Delta N1_{SEP}$ (in green) in "*Nogo* minus *Go*" ΔEPs as well as in "*NM* minus *SRT*" ΔEPs. The scalp distribution of $\Delta N1_{SEP}$ was significantly more frontal in "*Nogo* minus *Go*" ΔEPs than in "*NM* minus *SRT*" ΔEPs and it corresponded to the enhancement of N120 in *Nogo*- and *NM*-trials.

nociceptive N240 LEP component, raises the possibility that part of the processes underlying 'response inhibition' or 'conflict monitoring' are specific of the eliciting modality or sub-modality. As a consequence, this differential modulation suggests that at least some of the cortical generators underlying *Nogo*-related responses are specifically related to the modality of the eliciting sensory stimulus.

4.1. Early Nogo-related responses

In the visual modality, a *Nogo*-related enhancement of the N2 potential has been consistently reported (Eimer, 1993; Kopp et al., 1996). In contrast, in the auditory modality a similar *Nogo*-N2 potential has been only rarely observed (Falkenstein et al., 1995, 1999). For this reason,

Table 4a
Latencies and amplitudes of "*Nogo* minus *Go*" ΔEP components following laser heat stimuli and following electrical stimuli (mean ± SD) at electrode C_Z

ΔLEP	Latency (ms)	Amplitude (μV)
ΔN2	344 ± 43	−20.4 ± 11.5
ΔP3	501 ± 54	14.1 ± 10.1
ΔSEP	**Latency (ms)**	**Amplitude (μV)**
ΔN1	92 ± 17	−11.0 ± 8.6
ΔN2	229 ± 33	−22.2 ± 12.3
ΔP3	361 ± 32	24.1 ± 11.6

Table 4b
Latencies and amplitudes of "*NM* minus *SRT*" ΔEP components following laser heat stimuli and following electrical stimuli (mean ± SD) at electrode C_Z

ΔLEP	Latency (ms)	Amplitude (μV)
ΔN2	399 ± 60	9.9 ± 9.0
ΔP3	546 ± 81	−12.7 ± 10.9
ΔSEP	**Latency (ms)**	**Amplitude (μV)**
ΔN1	95 ± 33	−13.2 ± 8.0
ΔN2	283 ± 72	13.2 ± 13.8
ΔP3	444 ± 70	−7.7 ± 15.6

Table 5
Characteristics of experimental conditions

	Go	*Nogo*	*SRT*	No-Movement
Stimulus occurrence	50%	50%	50%	50%
Expectation	Yes	Yes	Yes	Yes
Task difficulty	Moderate	Moderate	Low	Low
Attention towards	*Go*-stimulus	*Go*-stimulus	Both laser and electrical stimuli	Both laser and electrical stimuli
Motor preparation	Yes	Yes	Yes	No
Discrimination between stimuli	Yes	Yes	No	No
Motor execution	Yes	No	Yes	No

several investigators have hypothesized that the *Nogo*-related N2 enhancement may reflect modality-specific processes (Falkenstein et al., 1999; Nakata et al., 2006). Niewenhuis et al. (2004) challenged this proposal by showing that the presence or absence of a *Nogo*-related negative potential was dependent on the perceptual overlap existing between each of the two eliciting stimuli. Indeed, stimuli that were easy to discriminate elicited a significantly reduced *Nogo*-related negative potential, and this whatever the sensory modality of the evoking stimuli (auditory and visual). In other words, the difficulty to obtain a consistent auditory *Nogo*-N2 may have resulted from the fact that previous studies relied on the use of easily discriminated auditory stimuli. Yet, this hypothesis cannot explain why, in the present study, the *Nogo* task induced a clear enhancement of the non-nociceptive N120 SEP component, but did not significantly modulate the nociceptive N240 LEP component. Indeed, subjects were to discriminate a nociceptive laser stimulus from a non-nociceptive electrical stimulus in both *Go* and *Nogo* experimental conditions, and the perceptual overlap between a *Go* laser stimulus and a *Nogo* electrical stimulus is identical to the perceptual overlap between a *Go* electrical stimulus and a *Nogo* laser stimulus.

An alternative explanation for the absence of modulation of the N170 and N240 components of the LEPs by the *Nogo*-condition is that evoked cortical responses to thermal, nociceptive stimuli may present more jitter than responses to electrical non-nociceptive stimuli. Theoretically, the smearing of thermally-evoked responses could have interfered with identifying modulations of the LEP components when using peak-to-baseline amplitudes for analysis. Therefore, the mean amplitude of the signal was computed within an arbitrarily defined time-window encompassing the N170 and N240 laser-evoked potentials (data not shown). This additional analysis did not allow to identify a significant modulation of the early LEP components across the experimental conditions, and thus, jitter of LEP responses does not explain the absence of early LEP modulation by the *Nogo*-task.

Several other experimental factors have been shown to condition the occurrence and magnitude of the *Nogo*-related negative potential: probability of occurrence of the *Nogo* stimulus (Nakata et al., 2005), the requesting of a speeded response (Jodo and Kayama, 1992), attention towards the sensory modality (Eimer, 1993; Schröger, 1993), and low false-alarm rate among subjects (Falkenstein et al., 1999). As shown in Table 5, none of these factors may explain the difference between nociceptive and non-nociceptive *Nogo*-related electrophysiological responses that was observed in the present study. For that reason, present results indicate that the *Nogo*-related enhancement of the N120 SEP component may reflect brain processes which are specific of that non-nociceptive sensory submodality.

As compared to the non-nociceptive SEPs recorded in the simple reaction time (*SRT*) task, SEPs recorded in the No-Movement (*NM*) condition also displayed a significant enhancement of the N120 component. The scalp distribution of this enhancement was slightly different from that of the *Nogo*-related N120 enhancement. To explain the presence of this *NM*-related N120 enhancement, two different possibilities were considered: movement related modulation of SEPs (referred to as 'pre-motor gating'), and presence of response inhibition in the *NM*-condition. Several studies have shown that performing a motor action may significantly modulate the amplitude of SEP components. In recent studies, relying on experimental paradigms similar to the *SRT*-condition of the present study, it was shown that a motor action may induce a decrease in magnitude of short-latency N30 and N60 SEP components, and an increase of amplitude of longer-latency P80 (or P100) and N140 (or N120) SEP components (Shimazu et al., 1999; Kida et al., 2004).

In the No-Movement condition, subjects were requested to rate the intensity of perception of the presented stimulus after each trial series. As subjects did not perform any stimulus-related motor response, and as in the previous *Go*/*Nogo* experimental session they had been instructed to respond to stimuli by a button-press, it is possible that this past experience resulted in subjects having to refrain from responding to the presented stimulus. Indeed, it has been shown that inhibiting motor imagery could elicit a negative–positive event-related potential very similar to the *Nogo*-related N2–P3 response elicited by refraining from actually performing a motor task (Burle et al., 2004).

4.2. Late Nogo-related responses

When subjects were requested to refrain from responding to the incoming stimulus (*Nogo*-condition), both the nociceptive laser and the non-nociceptive electrical stimulus elicited an additional positive component, maxi-

mally recorded at fronto-central recording sites. The morphology and topography of this component was very similar to that of the *Nogo*-related P3 component reported in the visual, the auditory and the non-nociceptive somatosensory modality (Falkenstein et al., 1995; Nakata et al., 2004).

In the "*Nogo* minus *Go*" difference waveform (ΔEPs), these later responses appeared as a negative–positive complex (ΔN2–ΔP3). While the activity that is revealed by examining such ΔEPs may result from the occurrence, the enhancement, the attenuation, or the non-occurrence of a component or a subcomponent of the response in one or the other experimental condition, it must also be considered that it may result from a change in the latency of a component or a subcomponent that is equally present in both experimental conditions. Indeed, such a latency-shift would yield a difference waveform consisting of a negative–positive biphasic pattern very similar to the ΔN2–ΔP3 complex observed in the present study. Therefore, it could well be that the non-nociceptive electrically evoked *Nogo*-P3 peak reflects the delayed occurrence of one of the subcomponents which generates the late vertex P240 component in the *Go*-condition, and that the nociceptive laser-evoked *Nogo*-P3 peak reflects the delayed occurrence of one of the subcomponents which generates the late vertex P350 component in the *Go*-condition.

The *Nogo*-related P3 component is generally considered to reflect brain processes related to response inhibition. Nevertheless, a number of investigators have proposed alternative explanations for the occurrence of these *Nogo*-related responses, such as brain activity related to motor inhibition or to the cognitive appraisal of inhibitory response accuracy (Goodin and Aminoff, 1984; Kopp et al., 1996). Other investigators have suggested that the *Nogo*-P3 may reflect a monitoring process implemented to verify that the initial decision to classify some stimulus and act accordingly has led to the appropriate steps of processing (Verleger et al., 2006; Filipovic et al., 1999).

Late P3 components have been reported in experimental paradigms other than the *Go*/*Nogo* task. When a visual or an auditory stimulus is presented within an odd-ball task, provided that the stimulus is both unattended and infrequent, it may elicit a late positive component, often referred to as the P3a component (Courchesne et al., 1975; Squires et al., 1975). The scalp topography of the P3a is very similar to that of the *Nogo*-P3 (Katayama and Polich, 1998). Accordingly, the *Nogo*-P3 component elicited, in the present study, by non-nociceptive electrical stimuli was very similar to the P3a component elicited by a similar electrical stimulus presented within an odd-ball paradigm (Yamaguchi and Knight, 1991). Similarly, the laser-evoked *Nogo*-P3 component resembled the laser-evoked P400 component, described in previous studies (Legrain et al., 2002), and hypothesized to reflect P3a-related processes. The P3a has been hypothesized to reflect cortical activity related to an involuntary switch of attention, elicited by the occurrence of an unexpected deviant event (Halgren and Marinkowic, 1995; Knight, 1996; Escera et al., 2000). For these reasons, investigators have hypothesized that the *Nogo*-P3 component and the P3a component could reflect similar brain processes elicited through different experimental paradigms (Barry and Rushby, 2006). Indeed, one could consider that the occurrence of a *Nogo* stimulus constitutes an unattended, unexpected, and deviant event, interfering with the attended task (i.e. respond to the *Go* stimulus).

4.3. Central processing time of response inhibition to nociceptive and non-nociceptive somatosensory input

The average of reaction-times recorded in the *Go* experimental condition was significantly greater than the average of reaction-times recorded in the *SRT*-condition, and this whatever the nature of the eliciting stimulus. The difference in task difficulty (choice reaction-time task in the *Go*/*Nogo*-condition, requiring that subjects discriminate and decide between perception of a non-nociceptive electrical stimulus and perception of a nociceptive laser stimulus vs. simple reaction-time task allowing subjects to respond to the first-perceived sensation, regardless of its quality) may account for the observed difference in response latencies. Indeed, similar differences have been reported in studies comparing the response latencies to a choice response task to those of a simple reaction-time task (Posada et al., 2003). It is generally assumed that they reflect an increase in the time required for response selection and/or response preparation (Bruin et al., 2001).

In the simple reaction-time task (*SRT*), the difference between the reaction-time to the nociceptive laser stimulus and the reaction-time to the non-nociceptive electrical stimulus was on average 117 ± 39 ms (see also Table 1). These different response latencies may be fully explained by (1) the additional time required for the laser stimulus to actually activate skin nociceptors (i.e. receptor activation time), and (2) the difference between the peripheral conduction time of the thinly-myelinated Aδ-fibers which conveyed the nociceptive input at 10–20 m/s and that of the largely myelinated Aβ-fibers which conveyed the non-nociceptive somatosensory input at 50–100 m/s (Kakigi and Shibasaki, 1991; Desmedt and Cheron, 1983; Kakigi et al., 1982).

In the present study, the increase in response latency related to the *Go*-task was similar for nociceptive laser stimuli and non-nociceptive electrical stimuli (see Fig. 2). Tarkka et al. (1992) provided experimental evidence indicating that the central processing time of a sensory-motor task involving the detection of a nociceptive stimulus was greater than that of a similar task involving the detection of an auditory stimulus. In contrast, Ploner et al. (2006) reported that the central processing of nociceptive sensory information was significantly faster than the central processing of non-nociceptive tactile information. The reaction-times of the present study indicate that the central processing time of a sensory-motor choice task was similar for both nociceptive and non-nociceptive stimuli.

On average, the difference between the latencies of the late *Nogo*-related potentials elicited by a non-nociceptive electrical stimulus and those elicited by a nociceptive laser stimulus was 115 ± 48 ms for ΔN2 and 140 ± 61 ms for ΔP3 (see Fig. 5 and Table 4). This difference, which was very similar to the observed difference in reaction-time, may be entirely accounted for by the fact that the time required for nociceptor activation, and the slower peripheral conduction velocity of Aδ-fibers both delayed the arrival-time of the nociceptive afferent volley. Therefore, it would appear that the time required for the inhibitory processes related to the *Nogo*-condition was similar for nociceptive and non-nociceptive somatosensory input.

5. Conclusion

Event-related brain potentials elicited by a nociceptive laser stimulus or by a non-nociceptive electrical stimulus were both significantly modulated by a *Go*/*Nogo* task. These response modulations were hypothesized to reflect brain processes related to 'response inhibition' or 'conflict monitoring'.

Early components of the *Nogo* response, appearing as a fronto-central enhancement of the somatosensory vertex negativity, were found in response to the non-nociceptive stimulus but not in response to the nociceptive stimulus, thereby indicating that these early activities may reflect brain processes that are specific of the eliciting sensory modality or submodality. In other words, it appears that the short-latency cortical processing of somatosensory input differs significantly between nociceptive and non-nociceptive stimuli.

Late components of the *Nogo* response, appearing as a fronto-central positive component, were found in response to both the non-nociceptive stimulus and the nociceptive stimulus, thereby indicating that these later activities reflect brain processes common to both somatosensory systems.

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