Inhibitory Control Impairment on Somatosensory Gating Due to Aging: An Event-Related Potential Study

Juan L. Terrasa, Pedro Montoya, Ana M. González-Roldán* and Carolina Sitges

Cognitive and Affective Neuroscience and Clinical Psychology, Research Institute of Health Sciences (IUNICS), Balearic Islands Health Research Institute, University of the Balearic Islands, Palma, Spain

The capacity to suppress irrelevant incoming input, termed sensory gating, is one of the most investigated inhibitory processes associated with cognitive impairments due to aging. The aim of this study was to examine the influence of aging on sensory gating by using somatosensory event-related potentials (ERPs) elicited by repetitive non-painful tactile stimulation (paired-pulsed task). Somatosensory ERPs were recorded in 20 healthy young adults and 20 healthy older adults while they received two identical pneumatic stimuli (S1 and S2) of 100 ms duration with an inter-stimulus interval of 550 ± 50 ms on both forefingers. The difference between the somatosensory ERPs amplitude elicited by S1 and S2 was computed as a sensory gating measure. The amplitude and the latency of P50, N100 and late positive complex (LPC) were analyzed as well as the source generators of the gating effect. Reduced sensory gating was found in older individuals for N100 at frontal and centro-parietal electrodes and for LPC at fronto-central electrodes. Source localization analyses also revealed a reduced current density during gating effect in the older group in frontal areas in N100 and LPC. Moreover, older individuals showed delayed latencies in N100. No significant gating effect differences were found between groups in P50. These findings suggest an age-related slowing of processing speed and a reduced efficiency of inhibitory mechanisms in response to repetitive somatosensory information during stimulus evaluation, and a preservation of processing speed and inhibitory control during early stimulus coding in aging.

Keywords: aging, somatosensory gating, paired-pulse task, event-related potential, source localization, inhibitory deficit hypothesis

INTRODUCTION

Physiological aging is associated with functional impairments affecting psychological processes such as memory, executive functions and attention (Hedden and Gabrieli, 2004; Salthouse, 2011). Although the nature and severity of sensory and cognitive decline in older individuals is heterogeneous (Gazzaley and D’Esposito, 2007), aging could be related to reduced efficiency of inhibitory mechanisms (inhibitory deficit hypothesis) (Hasher and Zacks, 1988). Accordingly, age-related decline in early sensory processing has been associated with changes in sensory cortices, including decreased inhibition at the primary somatosensory cortex (SI) during tactile stimulation of fingertips (Brodoehl et al., 2013) and increased excitability in SI after median nerve stimulation in a paired-pulse task (Lenz et al., 2012). Furthermore, several research have examined the influence...
of aging on automatic sensory functions (Bertoli et al., 2002; Cheng et al., 2013; Strömmer et al., 2017). Thus, for instance, it has been demonstrated that elderly adults show smaller ERPs amplitudes to an odd stimulus than young adults indicating an impairment in change-detection efficiency. In this regard, sensory gating protocols have been also used to evaluate age-related changes in ERPs amplitudes.

Sensory gating refers to the ability of the central nervous system to inhibit the processing of repetitive and irrelevant sensory inputs which is an essential protective mechanism that avoids the flooding of higher cortical centers (Freedman et al., 1987; Cromwell et al., 2008). Neurophysiological correlates of auditory and somatosensory gating phenomena have been examined by using event-related potentials (ERPs) elicited by repetitive stimuli in paired S1–S2 tasks with short inter-stimulus time intervals (e.g., 500 ms). Sensory gating is computed as the ratio between ERP amplitudes elicited by S2 and S1 stimuli (S2/S1), or as the amplitude difference between the two stimuli responses (S1−S2). Lower ratios or larger differences may indicate better gating or inhibition of irrelevant inputs (Boutros and Belger, 1999). Sensory gating of P50, N100, and P200 amplitudes of the ERPs elicited by auditory stimuli has received considerable interest because of its possible application in clinical research such as schizophrenia (Brenner et al., 2009) and Alzheimer's disease (Jessen et al., 2001). Moreover, it has been shown that chronic pain patients displayed a reduced sensory gating effect in response to repetitive non-painful somatosensory but not to auditory stimuli (Montoya et al., 2006). These ERPs components has been widely studied. Specifically, P50 represents one of the earliest evoked cortical responses to somatic stimulation (Freedman et al., 1987), N100 is assumed to reflect a trigger to allocate attention (Naätänen and Picton, 1987) and the late positive complex (LPC, 150–350 ms) have been associated with memory and stimulus evaluation (Polich and Herbst, 2000). Nevertheless, the evidences of age-related effects on sensory gating of these components and which variables are involved still limited and unclear (Bolton and Staines, 2012; Cheng et al., 2015a). Previous studies have reported significant age-related impairments of auditory gating (Boutros et al., 2000; Kisley et al., 2005), whereas recent studies failed to replicate this effect (Lijffijt et al., 2009; Gmehlin et al., 2011). Further studies using a paired-pulse electrical stimulation of the left median nerve protocol revealed significant higher S2/S1 ratios (Cheng and Lin, 2013) and a disturbed association between S1 and the motor cortex (Cheng et al., 2018) in an elderly group compared to a younger group, reflecting an age-related decline of somatosensory gating. Finally, Cheng et al. (2015b) pointed to an altered alpha oscillatory activity in response to somatosensory stimulation as a possible explanation to age-related reduced sensory gating.

The present study was aimed at examining possible age-related impairments in the ability of the brain to inhibit irrelevant non-painful somatosensory information in healthy older adults. For this purpose, event-related potentials elicited by repetitive, paired tactile stimulation of the fingertip, as well as source localization of the sensory gating effect were analyzed. We hypothesized that older subjects would show reduced sensory gating and delayed latencies of the P50, N100, and LPC components compared to younger participants.

**MATERIALS AND METHODS**

**Participants**

Twenty healthy young adults (18–30 years old, 8 male) and 20 healthy older adults (65–83 years old, 14 male) participated in the study. All participants were right handed. Upon arrival to the lab, participants were interviewed to exclude those subjects with any neurological or psychiatric disorder. All individuals were naive to the experiment, had no history of drug abuse and gave informed consent after the experimental procedure was explained. Twenty-five percent of the older adults were diagnosed and medicated as hypertensives. The study was conducted in accordance with the Declaration of Helsinki (1991) and was approved by the Ethics Committee of the University of Balearic Islands. Subjects completed the Spanish versions of the Beck Depression Inventory (BDI-II) (Beck et al., 1996), the State-Trait Anxiety Inventory (STAI) (Spielberger et al., 1970) and the Edinburgh Handedness Inventory (EHI) (Oldfield, 1971).

**Measurement of Blood Pressure and Pressure Pain Thresholds**

In order to control confounding variables and based on previous research (Cicconetti et al., 2007; Martinez-Jauand et al., 2013), pressure pain thresholds and blood pressure were measured before starting the main experiment. Blood pressure was measured twice in the right arm with a tensiometer (OMRON MX2, OMRON Healthcare, Hoofddorp, Netherlands) after the participant was seated and after they had rested for 5 min. Pressure pain thresholds were also assessed twice with a digital dynamometer using a flat rubber tip (km², Force One, Wagner Instruments, Greenwich, CT USA) at three body locations: index fingertip, medial area of the ventral surface of the wrist and dorsal area of the shoulder, measured always in this order. All locations were chosen as pain-free sites. The pressure pain threshold was defined as the amount of pressure in Newtons (N) at which participants perceived the pressure stimulus as painful. Participants were asked to rate the subjective pain sensation of the stimulus in a 100-point numerical scale (0: no pain, 100: maximum pain). For safety reasons, the maximal force allowed was 140 N. The mean of the two measurements on each body location was used in the statistical analysis.

**Non-painful Paired-Pulse Stimulation Task**

In the main experiment, subjects received tactile paired-pulse stimulation to analyze the sensory gating mechanism. For this purpose, stimulation consisted of two identical non-painful pneumatic stimuli (S1 and S2) of 100 ms duration that were delivered to both forefingers. Stimulation was applied with a constant pressure of 2 bars, a randomized inter stimulus interval of 550 ms (± 50 ms) and separated by a fixed interval of 12 s. The pneumatic stimulator was used in previous research (e.g., Montoya et al., 2006) and consisted of a small membrane attached to the body surface by a plastic clip and fixated with adhesive strips. Forty trials were presented in a single run session by using
EEG Recording and Data Reduction

EEG was recorded with a commercial amplifier (QuickAmp, Brain Products GmbH, Munich, Germany) at 1,000 Hz sampling rate from 46 Ag/AgCl electrodes placed according to the 10–10 International System. A ground electrode was located at position AFz. A common average reference was used. An electrooculogram (EOG) was also recorded by placing one electrode above and one below the left eye. Electrode impedances were kept lower than 10 kOhm.

During data pre-processing, EEG signals were segmented in epochs of 500 ms (−100 to 400 ms relative to the stimulus onset) and were digitally filtered (high-pass at 0.10 Hz, low-pass at 30 Hz, notch filter at 50 Hz) and baseline corrected (from −100 to 0 ms). Eye movement artifacts were corrected by using Gratton & Coles algorithm (Gratton et al., 1983). Then, an artifact rejection protocol with the following criteria was applied: maximal allowed voltage step/sampling point = 100 mV, minimal allowed amplitude = −100 mV, maximal allowed amplitude = 100 mV, and maximal allowed absolute difference in the epoch = 100 mV. EEG epochs were separately averaged for S1 and S2. In addition, the difference between the amplitude evoked by the first in comparison to the second stimuli (S1–S2) was computed, as gating score measure. Finally, somatosensory ERP amplitudes were determined by using a global maxima detection method and searching separately for each channel in three different time windows after stimulus onset: 20–80 ms (P50), 70–150 ms (N100) and mean amplitude during 150–350 ms (late positive complex, LPC). Peak latencies of P50 and N100 components were calculated for each electrode location.

Data Analyses

Group differences on gender were analyzed with Chi-Squared Test. The rest of sociodemographic data, self-reports, blood pressure and pressure pain thresholds were analyzed with Student t-tests. Regarding EEG, data from 12 electrodes were grouped and statistically analyzed into four regions of interest: frontal (F3, Fz, and F4), fonto-central (FC3, FCz, and FC4), central (C3, Cz, and C4) and centro-parietal (CP3, CPz, and CP4). Two separate multivariate analyses of variance (MANOVA) with repeated-measures were performed using “group” (young vs. older) as between-subject factor and “location” (4 regions) as within-subject factor on P50, N100, and LPC amplitudes. In the first analysis, the “stimulus type” (S1 vs. S2) was used as an additional within-subject factor. In the second analysis, MANOVA were performed on the amplitude difference elicited by S1 minus S2. Greenhouse-Geisser adjustments were applied and post-hoc Bonferroni corrected paired tests were used when necessary. Finally, Spearman’s correlations between age and S1, S2 and S1–S2 amplitude difference for each ERP component were also computed.

Source Localization

Source localization was computed by using sLORETA (Pascual-Marqui, 2002). This software gives a single linear solution to the inverse problem of localization of brain function and produces images of standardized current density with no localization bias. The localization accuracy of sLORETA has been validated in EEG/fMRI studies (Vitacco et al., 2002; Mulert et al., 2004). For sLORETA, the intracerebral volume is partitioned in 6,239 voxels at 5 mm spatial resolution, and the standardized current density at each voxel is then calculated in a realistic head model (Fuchs et al., 2002) using the MNI152 template (Mazziotta et al., 2001). In the present study, the voxel-based data were created from the difference waveforms elicited by S1 and S2 stimuli as a sensory gating measure. Then, the sLORETA images for P50, N100, and LPC were generated by comparing the sensory gating scores (S1–S2) in the young group with respect to the older group (paired-sample t-tests). Voxels with significant group differences (p < 0.01) were located in the MNI-brain and Broadmann areas.

RESULTS

Clinical and Sociodemographic Data

Table 1 displays clinical and sociodemographic data of both groups. Student t-test analyses revealed significant differences on age t(38) = −31.824, p < 0.001 between young (23.14 ± 3.24 years) and older (69.30 ± 5.56 years) groups as expected, but also on gender [Χ²(1, 40) = 4.912, p < 0.05], systolic blood pressure [t(38) = −5.728, p < 0.001] and diastolic blood pressure [t(38) = −3.721, p < 0.01]. Both blood pressure measures were higher in the older group. No significant group differences were found on BDI-II, STAI, pressure pain thresholds or subjective pain ratings.

Somatosensory ERP Amplitudes

Table 2 displays the grand averages of the somatosensory ERPs elicited by the first (S1) and the second stimuli (S2) at the four regions of interest for each group. Figure 1 illustrates these ERPs at Fz and Cz. For P50, a main effect of group [F(1,35) = 11.932, p < 0.01, η² = 0.254] revealed a greater response amplitude in older (1.852 ± 0.596 μV) than in young individuals (1.620 ± 0.548 μV). Furthermore, a significant interaction effect of location × stimuli [F(3,114) = 112.290, p < 0.001, η² = 0.747] were found. Post-hoc analyses revealed that P50 amplitudes to S2 were significantly reduced compared to S1 at the four regions of interest (frontal, fronto-central, central and centro-parietal) (all p < 0.001) in all participants. For N100, significant interaction effects of location × group [F(3,114) = 12.534, p < 0.001, η² = 0.248] and location × stimuli × group [F(3,114) = 12.118, p < 0.001, η² = 0.242] were found. Post-hoc analyses showed that N100 amplitudes to S2 were significantly reduced compared to S1 stimuli in young individuals at the four regions of interest (all p < 0.001), as well as in the older group at fronto-central and central regions (all p < 0.001). Furthermore, N100 amplitudes in response to S1 were significantly reduced in the older when compared to the young group at frontal, central and centro-parietal regions (all p < 0.05); whereas N100 amplitudes in response to S2 were significantly reduced only at the fronto-central region (p < 0.05). Finally, significant differences due to group [F(1,38) = 9.770, p < 0.01, η² = 0.205] and to stimuli × location (4 regions) as within-subject factor on P50, N100, and LPC were generated by comparing the sensory gating scores (S1–S2) in the young group with respect to the older group (paired-sample t-tests). Voxels with significant group differences (p < 0.01) were located in the MNI-brain and Broadmann areas.
TABLE 1 | Clinical and sociodemographic data of the participants in each group.

|                      | Young (n = 20) Mean (SD) | Older (n = 20) Mean (SD) | t-value | p       |
|----------------------|--------------------------|--------------------------|---------|---------|
| Age (years)          | 23.2 (3.318)             | 69.3 (5.564)             | −31.824 | p < 0.001 |
| Gender (males)       | 8                        | 14                       | 4.912†  | p < 0.05  |
| Blood pressure (mm Hg) |                         |                          |         |         |
| Systolic             | 11 (1.379)               | 13.9 (1.771)             | −5.718  | p < 0.001 |
| Diastolic            | 7.2 (1.189)              | 8.5 (0.967)              | −3.721  | p < 0.01  |
| BDI (0–63)           | 6.6 (4.893)              | 10.6 (7.639)             | −1.972  | p = 0.056 |
| STAI (0–60)          | 13.7 (7.419)             | 11.8 (8.475)             | 0.754   | p = 0.455 |
| Trait                | 20.1 (9.349)             | 15.3 (8.738)             | 1.673   | p = 0.102 |
| EHI (10–50)          | 16.7 (3.011)             | 16.4 (3.605)             | 0.238   | p = 0.813 |
| Pain threshold (N)   |                          |                          |         |         |
| Finger               | 107.8 (23.971)           | 111.4 (25.604)           | −0.458  | p = 0.649 |
| Wrist                | 94.6 (27.041)            | 102.1 (24.880)           | 0.913   | p = 0.938 |
| Shoulder             | 91.4 (30.744)            | 105.3 (27.039)           | −1.516  | p = 0.367 |
| Pain rating (0–100)  |                          |                          |         |         |
| Finger               | 29.5 (24.704)            | 30.2 (29.675)            | −0.078  | p = 0.762 |
| Wrist                | 38.6 (25.255)            | 41.2 (29.104)            | −0.305  | p = 0.138 |
| Shoulder             | 42.4 (22.905)            | 35.7 (29.693)            | 0.790   | p = 0.434 |

Means and standard deviations (SD) are shown. BDI, Beck Depression Inventory; STAI, State-Trait Anxiety Inventory; EHI, Edinburgh Handedness Inventory. † Chi-Squared value.

TABLE 2 | Mean amplitude in μV and standard deviation (SD) of the three ERP components in response to the first (S1) and second (S2) stimuli in each region of interest and group.

| Region         | Young (n = 20) Mean (SD) | Older (n = 20) Mean (SD) |
|----------------|--------------------------|--------------------------|
|                | S1       | S2       | S1       | S2       |
| P50            |          |          |          |          |
| Frontal        | −3.18 (1.481) | −1.09 (0.825) | −2.72 (0.964) | −0.68 (0.748) |
| Fronto-central | 1.45 (1.103)  | 0.49 (0.456)  | 1.63 (0.701)  | 0.94 (0.568)  |
| Central        | 1.92 (0.850)  | 0.59 (0.719)  | 2.75 (1.105)  | 1.05 (0.581)  |
| Centro-parietal| 2.07 (1.019)  | 1.01 (0.813)  | 2.76 (1.022)  | 1.28 (0.751)  |
| N100           |          |          |          |          |
| Frontal        | 5.45 (3.233) | 2.40 (1.159)  | 2.20 (1.585)  | 1.73 (0.974)  |
| Fronto-central | −3.52 (2.236) | −1.51 (0.602) | −3.16 (1.939) | −1.01 (0.655) |
| Central        | −5.18 (2.523) | −2.04 (0.994) | −3.39 (2.814) | −1.48 (0.951) |
| Centro-parietal| −4.14 (2.480) | −1.79 (1.037) | −1.54 (2.126) | −1.23 (0.956) |
| LPC            |          |          |          |          |
| Frontal        | 1.61 (1.587)  | 0.28 (0.803)  | 0.30 (1.491)  | 0.51 (0.772)  |
| Fronto-central | 2.55 (1.595)  | 0.64 (0.745)  | 0.86 (1.480)  | 0.61 (0.718)  |
| Central        | 2.24 (1.691)  | 0.66 (0.657)  | 0.90 (1.270)  | 0.41 (0.560)  |
| Centro-parietal| 1.46 (1.575)  | 0.49 (0.678)  | 1.01 (1.182)  | 0.23 (0.706)  |

A second group of analyses was performed by using the amplitude difference elicited by S1 and S2 (S1 minus S2) as a sensory gating measure (Figure 2). No significant effects were found on P50 amplitudes. Post-hoc analyses showed that LPC amplitudes in response to S2 were significantly reduced compared to S1 stimuli only in the young individuals (p < 0.001). In addition, LPC amplitudes in response to S1 stimuli were significantly reduced in the older when compared to the young group (p < 0.01). For LPC amplitudes, a main effect of group [F(1, 114) = 12.220, p < 0.01, ηp² = 0.243] revealed a greater gating effect in young (1.452 ± 1.684 μV) than in older individuals (0.323 ± 1.246 μV). Given that the two groups differed on gender, systolic and diastolic blood pressure, multivariate analyses of covariance (MANCOVAs) with repeated-measures were also performed on ERP amplitudes elicited by the S1-S2 difference (sensory gating measure). Similar results were obtained on N100 and LPC amplitudes after controlling for gender and blood pressure.

Finally, correlational analyses revealed that age was negatively correlated with N100 amplitudes elicited by S1 (r = −0.483, p < 0.01), S2 (r = −0.414, p < 0.01) and S1−S2 (r = −0.438, p < 0.01), as well as with LPC amplitudes elicited by S1 (r = −0.453, p < 0.01) and S1−S2 (r = −0.370, p < 0.05). No
FIGURE 1 | Grand averages of the somatosensory ERPs elicited by S1 and S2 at Fz and Cz for each group as well as topographic maps of P50, N100, and LPC amplitudes at specific latencies.

FIGURE 2 | Waveforms representing the sensory gating (S1 minus S2) at each region of interest for each group.
significant correlations between age and P50 amplitudes were found.

**Somatosensory ERP Latencies**

Regarding peak latencies (Table 3), a main effect of group \( F(1, 38) = 16.948, p < 0.001 \) was found on N100 showing delayed latencies in the older (126.22 ± 8.76 ms) compared to the young group (112.64 ± 5.88 ms). No significant group differences were observed on P50 latencies. Similar results were obtained after controlling for gender, systolic and diastolic blood pressure on P50 and N100 latencies.

**Source Localization Data**

Differences between young and older groups on statistical maps of source analyses of each somatosensory ERP component are displayed in Table 4 and Figure 3. Those analyses revealed a significant higher current density within anterior cingulate cortex (BA 32, BA 33, BA 24), cingulate gyrus (BA 32, BA 24) and medial frontal gyrus (BA 9). LPC component exhibited higher current density within anterior cingulate cortex (BA 25, BA 32, BA 24), precentral gyrus (BA 4, BA 9), insula (BA 9), medial frontal gyrus (BA 6), subcallosal gyrus (BA 25) and postcentral gyrus (BA 40, BA 3, BA 2). No significant group differences were observed on the P50 component.

**DISCUSSION**

The present study was aimed to testing the effects of aging on sensory gating elicited by repetitive tactile stimulation by using a paired-pulse paradigm and the recording of somatosensory event-related potentials (ERPs). As expected, we found that ERP amplitudes were significantly attenuated when the same stimulus was repeated within a short time interval. Although this gating effect was found in both young and older participants, its magnitude was significantly reduced in older compared to young groups, as shown by N100 and LPC results. Furthermore, it is important to take into account that reduced N100 and LPC amplitudes in response to S1 at some regions in the older group could play a role in the gating impairment. These altered amplitudes may be due to an age-related reduced sensory response (Bourisly, 2016) and/or a higher detection threshold for non-painful somatosensory stimuli (electrical and vibration) due to aging (Lin et al., 2005; Leong et al., 2010). In this sense, Strömmer et al. (2017) reported higher P50 and N80 amplitudes in older compared to young adults in response to somatosensory stimulus. However, these differences disappeared after controlling for the individual stimulus intensities, pointing out that the group differences were due to higher stimulus intensities in older than in young adults rather than related to aging. In contrast, we delivered pressure stimuli with the same intensity for all the participants and we reported that the stimuli (S1 and S2 jointly) elicited higher amplitude response in older than in young participants in P50. This might indicate that the age-related effect found in N100 and LPC is indeed related to sensory gating.

Regarding the gating analyses, no age-related effects on sensory gating were found in P50 component (even after controlling by gender and blood pressure). Source localization of P50 component further revealed no group differences. The P50 component represents one of the earliest evoked cortical responses to somatic stimulation (Freedman et al., 1987), and P50 gating is considered an inhibitory filter mechanism that could protect the integrity of higher-order functions (Wan, 2008). Our results are consistent with previous studies about P50 component in auditory paired-click ERPs. For example, (Gmelhin et al., 2011) reported that the inhibition of recurrent acoustic stimuli in
FIGURE 3 | sLORETA results for 3 orthogonal brain slices (horizontal, sagittal, coronal) of N100 and LPC. Colored voxels represent increased ($p < 0.01$) current density of the sensory gating (S1–S2 difference) in young group compared to older group.

this component did not differ between young and older groups. Moreover, another study revealed that no age-related effects on P50 sensory gating in healthy subjects were found (Lijffijt et al., 2009). These findings suggest that physiological aging is not related with a loss of sensory gating capability in preattentive stages of the sensory responses.

By contrast, N100 gating at frontal and centro-parietal locations were significantly impaired in older participants compared to young participants. We also found that response to both S1 and S2 elicited significantly reduced N100 amplitudes in older as compared to young participants over several brain regions. In addition, N100 amplitudes to both single stimuli and to the S1-S2 difference were negatively correlated with age. These results are also in accordance with previous studies using auditory stimulation (Cooper et al., 2006). In auditory protocols, the N100 response is elicited by perceived sensory stimuli regardless of whether they were attended or not (Näätänen and Picton, 1987; Eimer and Forster, 2003). Our results with a passive stimulation task revealed comparable outcome than previous studies using oddball attentional protocols. Thus, it seems that the relation between age-related changes and N100 gating amplitude could be independent of the task complexity and of the attention required. N100 is assumed to reflect a physiological marker of attention and seems to be generated within the secondary somatosensory cortex and distributed mostly over fronto-central regions (Näätänen and Picton, 1987). Our source localization analyses revealed lower current densities during the gating effect in frontal lobe areas as the medial frontal gyrus and in the anterior cingulate cortex in the older than in the young group. Similar results were reported when auditory S1 and S2 amplitude difference were used (Zhang et al., 2011). These regions have been associated with attention and self-related
Moreover, the anterior cingulate cortex participates in a salience network that facilitates the detection of relevant stimuli (Seeley et al., 2007). Therefore, the reduced activity over these brain areas could play a role in the age-related impairment at the attentional component of sensory gating regardless of the used sensory modality.

Similar to our N100 findings, older participants displayed an impaired gating effect on LPC amplitudes. Furthermore, LPC amplitudes in response to S1 as well as to the difference S1–S2 (sensory gating) were negatively correlated with age. This sustained late positive amplitude during the time range around 150–350 ms have been associated with more complex cognitive functioning, such as memory or stimulus evaluation (Polich and Herbst, 2000). Our source localization analyses further revealed reduced current densities during the gating effect in older participants over several brain regions areas (precentral and postcentral gyri, anterior cingulate cortex and insula). It has been previously shown that these regions could be relevant brain generators of LPC (P200, P300) during auditory stimulation (Rusniak et al., 2013; Annic et al., 2016). Again, these findings are in accordance with previous studies with auditory paired-click stimuli demonstrating age-related P200 gating deficits (Boutros et al., 2000; Lijffijt et al., 2009). Our results further suggest that these areas were also associated with age-related gating effects during processing of somatosensory information.

Taking together, our findings about an altered sensory gating effect in healthy older adults compared with younger adults fits with the inhibitory deficit hypothesis, which suggests a reduction in the efficiency of inhibitory mechanisms due to physiological aging (Hasher and Zacks, 1988). These gating impairments were observed during the attentional evaluation of the somatosensory processing and did not appear to be related with early coding of somatosensory information.

Regarding ERP latencies, we found that older participants had longer N100 peak latencies elicited by the S1–S2 difference waves than younger participants at all electrode locations. This finding is in agreement with previous research, showing significant age-related prolongation of N100 latencies and other mid-latency ERP components in auditory (Iragui et al., 1993; Anderer et al., 1996), visual (Dustman et al., 1993; Daffner et al., 2005) and somatosensory processing (Bolton and Staines, 2012). By contrast, we found no significant age-related delays on P50 sensory gating at any electrode locations. Thus, our findings may suggest a significant slowing of attention-related processes due to aging, together with intact early somatosensory processing of repetitive tactile stimulation. This outcome also support the processing speed hypothesis, in which aging-related performance deficits could be attributed to a generalized slowing of processing speed (Salhouse, 1996).

Some limitations of our study merit further consideration. First, 25% of our older participants were diagnosed and medicated as hypertensives. To avoid the possible effects of these drugs on somatosensory ERP response or on the sensory gating process, we repeated the analyses without the hypertensives participants of the older group (see Supplementary Material). The significant effects obtained in the analyses with all the participants were maintained. Thus, hypertension and its medication appear to be irrelevant in the response to stimuli and in the gating effect group differences. Furthermore, although gender and blood pressure differed between groups, the age-related effects of sensory gating on N100 and LPC components were obtained after controlling for those variables. Future research should further explore the role of these variables on brain correlates of somatosensory gating.

In summary, we found a reduced sensory gating to tactile stimuli on mid and late (but not early) stages of information processing in older participants. These findings might indicate: (1) an age-related slowing of processing speed and a reduced efficiency of inhibitory mechanisms in response to repetitive somatosensory information during cognitive evaluation, and (2) a preservation of processing speed and inhibitory control during early stimulus coding in aging.

AUTHOR CONTRIBUTIONS
JT, PM, AG-R, and CS contributed significantly to the design of the study and analysis. JT did the data collection and wrote most of the manuscript but PM, AG-R, and CS critically revised important parts of the manuscript.

FUNDING
This research was supported by grants from the Spanish Ministerio de Economía, Industria y Competitividad (ref: PSI2016-78637-P AEI/FEDER, UE, PSI2015-66295-R AEI/FEDER, UE and PSI2013-48260-C3-1-R), BIAL Foundation Grant (ref: #385/14) and SOIB-Joves Qualificats Program.

SUPPLEMENTARY MATERIAL
The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnhum.2018.00280/full#supplementary-material

REFERENCES
Anderer, P., Semlitsch, H. V., and Saletu, B. (1996). Multichannel auditory event-related brain potentials: effects of normal aging on the scalp distribution of N1, P2, N2 and P300 latencies and amplitudes. Electroencephalogr. Clin. Neurophysiol. 99, 458–472. doi: 10.1016/S0165-4696(96)96518-9
Annic, A., Bourriez, J. L., Delval, A., Bocquillon, P., Trubert, C., Derambure, P., et al. (2016). Effects of stimulus-driven and goal-directed attention on prepulse inhibition of brain oscillations. Front. Hum. Neurosci. 10:390. doi: 10.3389/fnhum.2016.00390.
Beck, A. T., Steer, R. A., and Brown, G. K. (1996). Manual for the Beck Depression Inventory-II. San Antonio, TX: Psychological Corporation.
Bertoti, S., Śmuryński, J., and Probst, R. (2002). Temporal resolution in young and elderly subjects as measured by mismatch negativity and a psychoacoustic gap detection task. Clin. Neurophysiol. Off. J. Int. Fed. Clin. Neurophysiol. 113, 396–406. doi: 10.1016/S1388-2457(02)00015-5
Bourisly, A. K. (2016). Effects of aging on P300 between late young-age and early middle-age adulthood: an electroencephalogram event-related potential study. *NeuroReport*, 27, 999–1003. doi: 10.1097/WNR.0000000000001644

Boutros, N. N., and Belger, A. (1999). Midlatency evoked potentials attenuation and augmentation reflect different aspects of sensory gating. *Biol. Psychiatry* 45, 917–922. doi: 10.1006/biyp.1999.0032

Boutros, N. N., Reid, M. C., Petrikas, I., Campbell, D., Torello, M., and Krystal, J. (2000). Similarities in the disturbances in cortical information processing in alcoholism and aging: a pilot evoked potential study. *Int. Psychogeriatr.* 12, 513–525. doi: 10.1017/S1041610200006621

Brenner, C. A., Kießabfer, P. D., Clementz, B. A., Johannesen, J. K., Shekhar, A.-D., O’Donnell, B. F., et al. (2009). Event-related potential abnormalities in schizophrenia: a failure to “gate in” salient information? *Schizophr. Res.* 113, 332–338. doi: 10.1016/j.schres.2009.06.012

Brodoehl, S., Klingner, C., Steiglitz, K., and Witte, O. W. (2013). Age-related changes in the somatosensory processing of tactile stimulation—An fMRI study. *Behav. Brain Res.* 238, 259–264. doi: 10.1016/j.bbr.2012.10.038

Cheng, C. H., Baillet, S., and Lin, Y.-Y. (2015a). Region-specific reduction of auditory sensory gating in older adults. *Brain Cogn.* 101, 64–72. doi: 10.1016/j.bandc.2015.10.004

Cheng, C. H., Chan, P. Y. S., Baillet, S., and Lin, Y. Y. (2015b). Age-related reduced somatosensory gating is associated with altered alpha frequency desynchronization. *Neural Plast.* 2015, 1–9. doi: 10.1155/2015/302878

Cheng, C.-H., Hsu, W.-Y., and Lin, Y.-Y. (2013). Effects of physiological aging on mismatch negativity: a meta-analysis. *Int. J. Psychophysiol.* 90, 165–171. doi: 10.1016/j.ijpsycho.2013.06.026

Cheng, C.-H., Lin, M. Y., and Yang, S. H. (2018). Age effect on automatic inhibitory function of the somatosensory and motor cortex: an MEG study. *Front. Aging Neurosci.* 10:53. doi: 10.3389/fnagi.2018.00053

Cheng, C. H., and Lin, Y. Y. (2013). Aging-related decline in somatosensory inhibition of the human cerebral cortex. *Exp. Brain Res.* 226, 145–152. doi: 10.1007/s00221-013-3420-9

Cicconetti, P., Ciotti, V., Tafaro, L., Ettorre, E., Chiarotti, F., Priami, C., et al. (2007). Event related brain potentials in elderly patients with recently diagnosed isolated systolic hypertension. *Clin. Neurophysiol.* 118, 824–832. doi: 10.1016/j.clinph.2006.11.001

Cooper, R. J., Todd, J., McGill, K., and Michie, P. T. (2006). Auditory sensory memory and the aging brain: a mismatch negativity study. *Neurobiol. Aging* 27, 752–762. doi: 10.1016/j.neurobiaging.2005.03.012

Cromwell, H. C., Mears, R. P., Wan, L., and Boutros, N. N. (2008). Sensory gating: a translational effort from basic to clinical science. *Clin. EEG Neurosci.* 39, 69–72. doi: 10.1177/155005940803900209

Daffner, K. R., Ryan, K. K., Williams, D. M., Budson, A. E., Rentz, D. M., Scinto, L. F., et al. (2006). Auditory and non-auditory sensory gating in patients with fibromyalgia. *Arthritis Rheum.* 54, 1995–2003. doi: 10.1002/art.21910

Mulert, C., Jäger, L., Schmitt, R., Bussfeld, P., Pogarell, O., Möller, H.-J., et al. (2013). Age-of-onset of menopause is associated with enhanced painful and non-painful sensitivity in fibromyalgia. *Clin. Rheumatol.* 32, 975–981. doi: 10.1007/s10067-013-2212-8

Mazzotta, J., Toga, A., Evans, A., Fox, P., Lancaster, J., Zilles, K., et al. (2001). A probabilistic atlas and reference system for the human brain: International Consortium for Brain Mapping (ICBM). *Philos. Trans. R. Soc. B Biol. Sci.* 356, 1293–1322. doi: 10.1098/rstb.2001.0915

Montoya, P., Sitges, C., García-Herrera, M., Rodríguez-Cotes, A., Izquierdo, R., Truyols, M., et al. (2006). Reduced brain habituation to somatosensory stimuli in patients with fibromyalgia. *Arthritis Rheum.* 54, 1995–2003. doi: 10.1002/art.21910

Mulert, C., Jäger, L., Schmidt, R., Bussfeld, P., Pogarell, O., Möller, H.-J., et al. (2004). Integration of fMRI and simultaneous EEG: towards a comprehensive understanding of localization and time-course of brain activity in target detection. *NeuroImage* 22, 83–94. doi: 10.1016/j.neuroimage.2003.10.051

Nätänen, R., and Picton, T. (1987). The N1 wave of the human electric and magnetic response to sound: a review and an analysis of the component structure. *Psychophysiology* 24, 375–425. doi: 10.1111/j.1469-8986.1987.tb00311.x

Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9, 97–113. doi: 10.1016/0028-3932(71)90067-4

Pascual-Marqui, R. D. (2002). Standardized low resolution brain electromagnetic tomography (SLORETA): technical details. *Methods Find. Exp. Clin. Pharmacol.* 24(Suppl. D), 5–12.

Polich, J., and Herbst, K. L. (2000). P300 as a clinical assay: rationale, evaluation, and findings. *Int. J. Psychophysiol.* Off. J. Int. Organ. Psychophysiol. 38, 3–19. doi: 10.1016/S0167-8760(00)00127-6

Posner, M. I., and Rothbart, M. K. (1998). Attention, self-regulation and consciousness. *Philos. Trans. R. Soc. B Biol. Sci.* 353, 1915–1927. doi: 10.1098/rspb.1998.0344

Qin, P., and Northoff, G. (2011). How is our self related to midline regions and the default-mode network? *NeuroImage* 57, 1221–1233. doi: 10.1016/j.neuroimage.2011.05.028
Rusiniak, M., Lewandowska, M., Wolak, T., Pluta, A., Milner, R., Ganc, M., et al. (2013). A modified oddball paradigm for investigation of neural correlates of attention: a simultaneous ERP–fMRI study. *Magn. Reson. Mater. Phys. Biol. Med.* 26, 511–526. doi: 10.1007/s10334-013-0374-7

Saltz, T. A. (1996). The processing-speed theory of adult age differences in cognition. *Psychol. Rev.* 103, 403–428. doi: 10.1037/0033-295X.103.3.403

Saltz, T. A. (2011). Neuroanatomical substrates of age-related cognitive decline. *Psychol. Bull.* 137, 753–784. doi: 10.1037/a0023262

Seeley, W. W., Menon, V., Schatzberg, A. F., Keller, J., Glover, G. H., Kenna, H., et al. (2007). Dissociable intrinsic connectivity networks for salience processing and executive control. *J. Neurosci.* 27, 2349–2356. doi: 10.1523/JNEUROSCI.5587-06.2007

Spielberger, C. D., Gorsuch, R. L., and Lushene, R. E. (1970). *The State-Trait Anxiety Inventory (STAI): Test Manual.* Palo Alto, CA: Consulting Psychologists Press.

Strömmer, J. M., Pöldver, N., Waselius, T., Kirjavainen, V., Jarveläinen, S., Björksten, S., et al. (2017). Automatic auditory and somatosensory brain responses in relation to cognitive abilities and physical fitness in older adults. *Sci. Rep.* 7:13699. doi: 10.1038/s41598-017-14139-9

Vitacco, D., Brandeis, D., Pascual-Marqui, R., and Martin, E. (2002). Correspondence of event-related potential tomography and functional magnetic resonance imaging during language processing. *Hum. Brain Mapp.* 17, 4–12. doi: 10.1002/hbm.10038

Wan, L. (2008). P50 sensory gating and attentional performance. *Int. J. Psychophysiol.* 67, 91–100. doi: 10.1016/j.ijspsycho.2007.10.008

Zhang, F., Deshpande, A., Benson, C., Smith, M., Eliassen, J., and Fu, Q.-J. (2011). The adaptive pattern of the auditory N1 peak revealed by standardized low-resolution brain electromagnetic tomography. *Brain Res.* 1400, 42–52. doi: 10.1016/j.brainres.2011.05.036

**Conflict of Interest Statement:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Copyright © 2018 Terrasa, Montoya, González-Roldán and Sitges. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.