

Early attentional processes distinguish selective from global motor inhibitory control: An electrical neuroimaging study

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The rapid stopping of specific parts of movements is frequently required in daily life. Yet, whether selective inhibitory control of movements is mediated by a specific neural pathway or by the combination between a global stopping of all ongoing motor activity followed by the re-initiation of task-relevant movements remains unclear. To address this question, we applied time-wise statistical analyses of the topography, global field power and electrical sources of the event-related potentials to the global vs selective inhibition stimuli presented during a Go/NoGo task. Participants ($n = 18$) had to respond as fast as possible with their two hands to Go stimuli and to withhold the response from the two hands (global inhibition condition, GNG) or from only one hand (selective inhibition condition, SNG) when specific NoGo stimuli were presented. Behaviorally, we replicated previous evidence for slower response times in the SNG than in the Go condition. Electrophysiologically, there were two distinct phases of event-related potentials modulations between the GNG and the SNG conditions. At 110–150 ms post-stimulus onset, there was a difference in the strength of the electric field without concomitant topographic modulation, indicating the differential engagement of statistically indistinguishable configurations of neural generators for selective and global inhibitory control. At 150–200 ms, there was topographic modulation, indicating the engagement of distinct brain networks. Source estimations localized these effects within bilateral temporo-parieto-occipital and within parieto-central networks, respectively. Our results suggest that while both types of motor inhibitory control depend on global stopping mechanisms, selective and global inhibition still differ quantitatively at early attention-related processing phases.

Introduction

Inhibitory control refers to the ability to suppress planned or ongoing cognitive or motor processes (Aron, 2007; Zheng et al., 2008). Converging evidence indicate that when the need for inhibitory control cannot be anticipated, the suppression of specific components of ongoing or prepotent movements is not achieved by selectively stopping the irrelevant parts of the movements, but rather depends on global inhibitory mechanisms with widespread effects on motor activity (e.g. Aron and Verbruggen, 2008). Current data indeed suggest a sequential model of selective inhibition wherein selective-stop signals trigger a global stopping mechanism suppressing all motor activity and subsequently, the parts of the movement that participants still have to execute are re-initiated (so-called 'Combination model', e.g. Coxon et al., 2007, 2009).

Support for this model for instance comes from Coxon et al. (2007), who instructed participants to respond to visual stimuli by pressing two

buttons, each with one hand. During the task, stop signals sometimes prompted participants to withhold the response from one (selective inhibition condition) or the two hands (global inhibition condition). The results showed that the responses in the selective inhibition condition were slower than when participant responded with their two hands. The authors advanced that this 'stopping-interference effect' followed from the fact that selective inhibition was achieved by first stopping responses from the two hands with a global inhibition mechanism, and then re-initiating the movement of one hand (see also Coxon et al., 2006). Supporting that global inhibition mechanisms are not only involved when all motor responses must be suppressed but also for selective inhibitory control, Badry et al. (2009) observed a reduced motor evoked potentials of leg muscles in successful stop trials during a manual Stop Signal Task (SST; see also e.g. Cai et al., 2012 or Macdonald et al., 2012 for supporting data).

Further corroborating the Combination model of selective inhibitory control, functional neuroimaging studies revealed that selective inhibition is supported by the same neural pathway as involved in global inhibition: The so-called 'hyperdirect pathway' enables inhibiting motor activity via monosynaptic projections from prefrontal areas to the basal ganglia (Aron, 2007; Nambu et al., 2002). However, because the hyperdirect pathway inhibits large areas of the thalamus, it

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suppresses altogether task-relevant and -irrelevant movements. Thus, in selective inhibition conditions, the movements that participants had to execute to their end have to be re-initiated after the global inhibition. Consistently, functional studies showed that the patterns of brain activity associated with selective vs. global inhibition differ only at the level of the regions involved in programming and executing new movements (notably including the supplementary motor cortex), but not within the inhibitory fronto-basal network. For example, [Coxon et al. \(2009\)](#) used a SST task and contrasted fMRI responses to trials in which participants had to withhold the movements of either one (selective inhibition condition) or two fingers (global inhibition) in a context where most of the trials required responding with two fingers. The authors showed that while the right inferior frontal gyrus (IFG), inferior parietal and middle frontal cortices were engaged in both the selective and global inhibition conditions, the medial frontal cortex was specifically recruited for selective inhibition. Studies on response switching, in which participants had to modify their response schemes according to imperative cues, also speak in favor of the Combination model. [Kenner et al. \(2010\)](#) showed that switching consists of stopping the response based on the global inhibitory control network (IFG and midbrain), and then activating a new response based on the same network as in simple 'go' responses (i.e. the pre-supplementary motor area; see also [Isoda and Hikosaka, 2007](#)).

However, the precise spatio-temporal brain dynamics underlying the sequence of motor inhibition and activation processes posited in the Combination model remains unclear. To address this question, we recorded high-density EEG during a modified visual Go/NoGo task in which participants had to respond as fast as possible with their two hands to Go stimuli and to withhold the response from the two hands (global inhibition condition, GNG) or from only one hand (selective inhibition condition, SNG) when specific NoGo stimuli were presented. We contrasted electrical neuroimaging responses to the global vs selective NoGo stimuli using time-frame wise global analyses of the topography and strength of the scalp-recorded electric potential field, as well as time-frame wise statistical analyses of distributed electrical source estimations. According to the Combination model, because the same inhibitory process support selective and global inhibition, the two conditions should differ only when and where the manual response required in the SNG but not GNG condition is initiated, i.e. within the pre-supplementary motor area, at a delay corresponding to the brain-hand conduction time (ca. 150 ms) before the SNG response time. Electrophysiologically this effect should manifest as a topographic modulation because a different configurations of intracranial generators should be engaged between the two conditions.

Methods

Participants

From an initial sample size of 21 participants, eighteen right-handed young adults (9 males; aged 25 ± 3 years, mean \pm SD, range: 21–29) were included in the study (see the [Results](#) section for details). Handedness was assessed using the Oldfield-Edinburgh inventory ([Oldfield, 1971](#)). Participants reported no history of neurological illness and none was under medication at the time of testing. Each participant provided written, informed consent to participate in the study. The local Ethics Committee approved all experimental procedures.

Stimuli

The stimuli were presented at the center of a computer screen at 60 cm from the participants. Stimuli were displayed in black on a gray background. A trial consisted of the presentation of a warning stimulus (empty circle) during a fixed duration of 500 ms, followed by the presentation of an imperative stimulus during 1000 ms. The imperative stimulus was either a filled circle (Go condition: 'G'; 67% of the trials),

a cross in a circle (Global NoGo condition: 'GNG'; 17%), or a half right filled circle (Selective NoGo condition: 'SNG'; 17%). Then, an inter-stimulus-interval (ISI) ranging from 1500 to 2000 ms was presented ([Fig. 1](#)). Stimuli delivery and response recording were controlled with the E-prime 2.0 software.

Procedure and task

The task was a modified Go-NoGo paradigm designed to assess both selective and global inhibitory control. There were three randomly presented conditions: In the Go (G) condition, participants had to press two response buttons at the same time, one with the index of the left hand and the other with the index of the right hand. In the Selective inhibition (SNG) condition, participants had to withhold responding with the left index while responding with the right index. In the Global inhibition (GNG) condition, participants had to withhold the response from the two hands. For conditions where a button press was required (G and SNG), participants were instructed to respond as fast as possible.

Participants completed a twenty trials (12 G, 4 GNG, and 4 SNG) familiarization block before starting the main experiment. The main experiment consisted of 4 blocks of 60 trials (40 G, 10 GNG, and 10 SNG). A calibration phase of 18 trials (12 G, 3 GNG, and 3 SNG) was presented before each block. The calibration enabled inducing additional time pressure and adjusting individually the difficulty of the task (see [Manuel et al., 2012](#); [Vocat et al., 2008](#) for similar procedures). During the calibration phase, the maximal response time threshold (mRTT) to the Go stimuli was determined. The mRTT was calculated as 80% of the mean response time to the Go stimuli presented during the calibration phase. A feedback "Faster" was displayed when the response time was above the mRTT. At the end of each block, the percentage of response faster than the mRTT was displayed on the screen. A rest period about 60 s was proposed to the participant between each block. The experiment lasted a total of about 45 min. Two participants completed a 5th block because of difficulties in understanding the task at the beginning of the experiment.

Electrophysiological recording and data pre-processing

Continuous EEG was recorded at a sampling rate of 2048 Hz with a 64-channel Biosemi Active two amplifier system (Biosemi, Amsterdam, Netherlands). Offline analyses were performed with

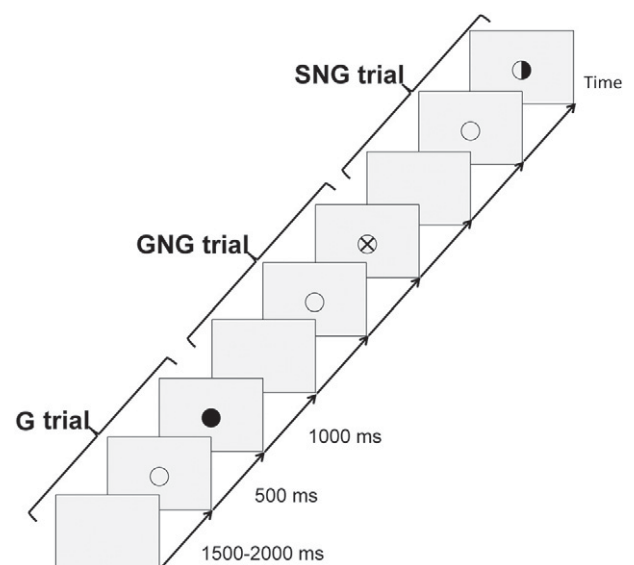


Fig. 1. Go/NoGo paradigm. Stimuli were a filled circle for the Go condition (G), a cross in a circle for the global inhibition condition (GNG) and a half right filled circle for the selective inhibition condition (SNG).

Cartool software (Brunet et al., 2011). The raw EEG data were first down-sampled to 512 Hz to reduce computational load and bandpass filtered (0.31–40 Hz, Notch 50 Hz and DC removed). Epochs from 100 ms pre-stimulus to 500 ms post-stimulus onset were averaged across trials for the GNG and SNG conditions. Only successful GNG and SNG trials were considered in the event-related potentials (ERPs) averaging. We analyzed only GNG and SNG trials because the current study focused on conditions involving motor inhibition. In addition, the Go trials were much more frequent than the inhibition trials, and thus any difference between the brain responses to the Go and the SNG or GNG conditions could be due to differences in their frequency of occurrence (Nieuwenhuis et al., 2003).

In addition to a $\pm 80 \mu\text{V}$ artifact rejection criterion, epochs containing eye blinks or other noise transients were rejected. This procedure resulted in the inclusion of a mean of 32 ± 5 epochs (6.5% rejection) for GNG and 36 ± 4 epochs (5.4% rejection) for SNG condition. Artifacts electrodes were interpolated using a spherical spline interpolation (Perrin et al., 1987). On average, 4% of the 64 electrodes were interpolated. Participants were included when a minimum of 20 trials were accepted by condition during the averaging, leading to the exclusion of 2 participants. Another participant was excluded from the study due to bad EEG signal. Eighteen out of 21 recorded participants were thus eventually included in the study.

Statistical analyses

Behavior

The percentage of false alarms (i.e. incorrect response in NoGo trials; FA) in GNG and SNG conditions and the average response time in the G and SNG conditions were compared using paired *t*-tests.

Global electric field analyses

Global electric field analyses were carried out using the Cartool software (Brunet et al., 2011). By contrast to local, single-electrode level analyses of the ERP, the analysis of the global field power (GFP) and of the ERP topography (Global Map Dissimilarity, GMD) is reference-independent and enables disentangling if the observed effects follow from change in responses gain and/or change in the configuration of brain networks across experimental conditions (e.g. Michel and Murray, 2012; Murray et al., 2008; Tzovara et al., 2012). These two analyses enable a neurophysiological interpretation of the ERP modulations: topographic changes indeed necessarily follow from changes in the configuration of the underlying active brain generators (Lehmann, 1987), while GFP modulations follow from changes in the strength of the same brain generators. Thus, GMD modulations can be understood as reflecting qualitative changes in the underlying brain networks. In contrast, GFP modulations without concomitant topographic modulation suggest a quantitative change in the response strength of statistically indistinguishable configurations of neural generators.

Modulations in the strength of the electric field at the scalp were assessed using the global field power (Koenig and Melie-Garcia, 2010; Koenig et al., 2011; Lehmann and Skrandies, 1980). The GFP represents the spatial standard deviation of the electric field at the scalp. Differences in GFP were calculated as a function of peri-stimulus time between the two conditions using paired *t*-tests.

Topographic modulations were identified using randomization statistics applied to the GMD (Lehmann and Skrandies, 1980; Tzovara et al., 2012). GMD is calculated as the root mean square of the difference between strength-normalized vectors (here the instantaneous voltage potentials across the electrode montage). We analyzed GMD values between the GNG vs. SNG conditions as a function of peri-stimulus time using the following approach: GMD at each time point was compared with an empirical distribution derived from a bootstrapping procedure (1000 permutations per data point) based on randomly reassigning each participant's data to either of the two conditions (see details in Brunet et al., 2011).

The results of the GFP and GMD analyses are displayed as the *p*-value (Y-axis) as a function of time (X-axis). For both GFP and GMD analyses, the threshold for statistical significance was set at $p < 0.01$. Correction was made for temporal autocorrelation through the application of a > 11 contiguous data-point (~ 21 ms at our 512 Hz sampling rate) temporal criterion for the persistence of significant differential effects (Guthrie and Buchwald, 1991).

Electrical source estimations. We estimated electric sources underlying scalp-recorded data using a distributed linear inverse solution based on a local autoregressive average (LAURA) regularization approach (Grave de Peralta Menendez et al., 2001; Grave-de Peralta et al., 2004, also Michel et al., 2004). LAURA selects the source configuration that better mimics the biophysical behavior of electric fields (i.e. activity at one point depends on the activity at neighboring points according to electromagnetic laws). The solution space is based on a realistic head model and included 3005 solution points homogeneously distributed within the gray matter of the average brain of the Montreal Neurological Institute (courtesy of R. Grave de Peralta Menendez and S. Gonzalez Andino, University Hospital of Geneva, Geneva, Switzerland). Intracranial sources were estimated for each participant across the whole epoch and then statistically compared using paired-sample *t*-tests at each time-frame and each node between the GNG and SNG conditions. Correction was made for temporal autocorrelation through the application of a > 11 contiguous data-point temporal criterion (~ 21 ms) for the persistence of significant differential effects (Guthrie and Buchwald, 1991). The results of this analysis of source estimations are presented as plot depicting the percentage of solution nodes showing a significant ($p < 0.05$) difference as a function of peri-stimulus time.

Results

Behavior

There were more false alarms (FA, incorrect responses in NoGo trials) in the GNG (mean percentage \pm SD: $16.2\% \pm 9.7$) than in the SNG condition ($8.0\% \pm 7.4$; $t(17) = -3.74$, $p < 0.01$; Cohen's $d = 0.91$).

Mean response times (\pm SD) were slower for the SNG condition ($374 \text{ ms} \pm 50$) than for the G condition ($303 \text{ ms} \pm 51$; $t(17) = -13.6$, $p < 0.01$; Cohen's $d = 3.3$).

Event-related potentials

The ERP waveforms from four exemplar electrodes and the superimposed ERPs waveforms from the GNG and the SNG are depicted in Figs. 2a and b to help the reader in assessing the quality of our signal. Interpretations are based only on the global, reference-independent analyses of the ERPs.

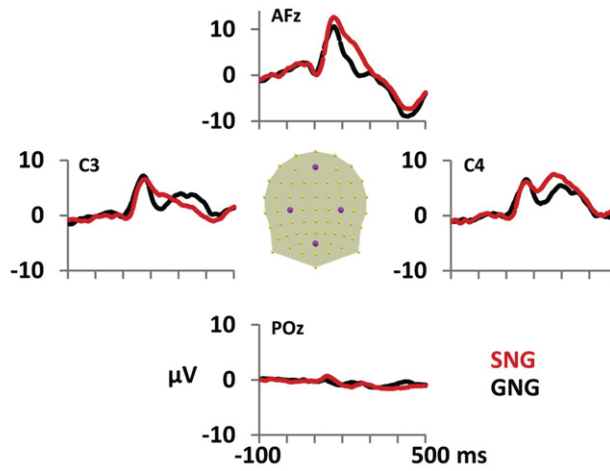
Global field power

The global field power analysis identified three periods of significant ($p < 0.01$) differences between the GNG and SNG conditions. There was a first GFP modulation from 110 ms to 150 ms post-stimulus onset with higher GFP in the GNG than SNG condition. Then, between 200 and 280 ms, the GFP was higher in the SNG than GNG condition, and between 400 and 500 ms, the GFP was higher in the GNG than SNG condition (Figs. 2c & d).

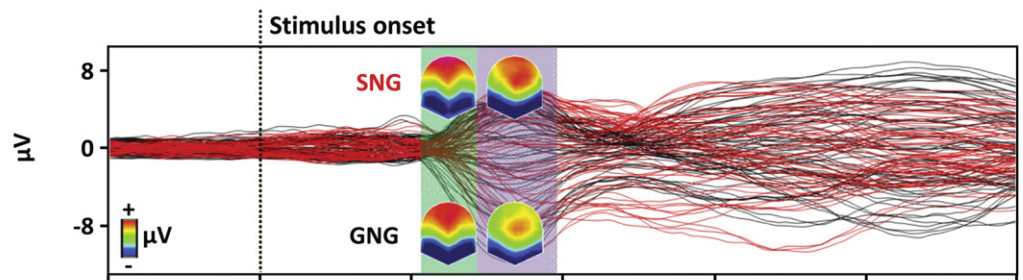
Global map dissimilarity

The topographic analysis identified three time periods of significant ($p < 0.01$) topographic modulation between the GNG and SNG conditions: 130–220 ms, 230–300 ms and 330–500 ms (Fig. 2e).

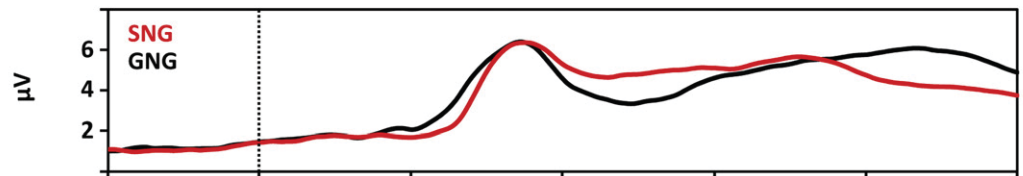
a. Exemplar ERP Waveforms



b. Superimposed ERP waveforms



c. Global Field Power waveforms



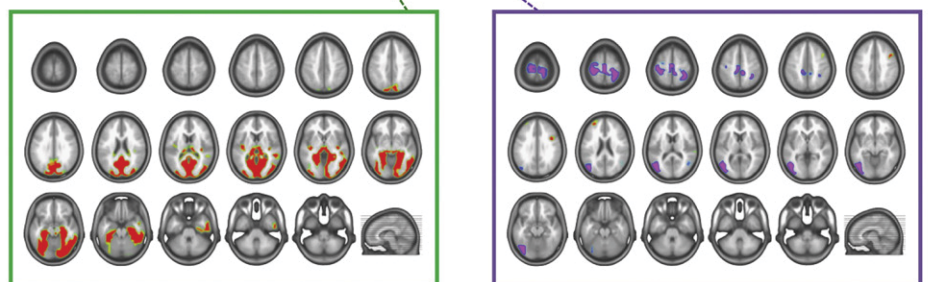
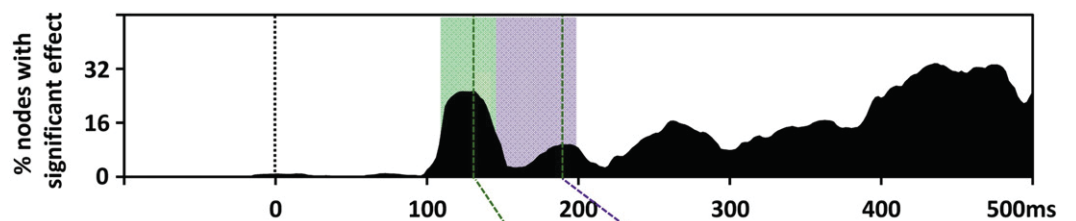
d. Global Field Power: GNG vs SNG t-tests



e. Global Map Dissimilarity: GNG vs SNG



f. Source estimations time-wise GNG vs SNG t-tests



GNG > SNG
 P < 0.05
 GNG < SNG

The time frame-wise analysis of the source estimations revealed three main periods of widespread significant ($p < 0.05$) differences between the GNG vs. SNG conditions peaking at 130 ms and 190 ms (Fig. 2f, upper panel). The significant solution points are represented on a template brain for the time-frames when the number of solution points showing a significant difference was maximal (Fig. 2f, bottom panels).

The significant difference at 130 ms showed higher activity in the GNG than SNG within the bilateral temporal, occipital and posterior parietal regions.

The significant difference at 190 ms showed higher activity in the SNG than GNG condition in the bilateral postcentral gyri. Sparse evidence for lower activity in the SNG than GNG was observed in the right inferior and middle frontal gyri.

Discussion

We examined the spatio-temporal brain mechanisms of selective vs global inhibition of motor action. Behaviorally, we replicated the stopping interference effect: Response times in the selective inhibition condition were slower than in the Go condition. Electrophysiologically, we observed two distinct periods of ERP modulation between the selective (SNG) vs. global inhibition conditions (GNG). Between 110 and 150 ms post stimulus onset, the two conditions differed at the level of the strength of the electric field at the scalp without concomitant topographic modulation. This pattern of result suggests that statistically indistinguishable configurations of neural generators were engaged in the GNG vs. SNG condition, but stronger for global than for selective inhibition. Statistical analyses of electrical source estimations over this period revealed that the global field power (GFP) modulation followed from higher activity in the GNG than SNG condition within bilateral temporal, occipital and posterior parietal regions. Subsequently, between 150 and 200 ms, the response to the selective and global inhibition stimuli differed topographically, indicating the engagement of distinct configurations of neural generators. The topographic modulation followed from higher activity in the SNG than GNG condition within the pre-supplementary motor area (preSMA), SMA and primary somatosensory area (S1), and lower activity in the SNG than GNG in the right inferior and middle frontal gyri.

At the behavioral level, we observed slower RT in the SNG condition than in the Go condition, replicating the well-established stopping interference effect (e.g. Aron and Verbruggen, 2008; Coxon et al., 2006, 2007). Previous studies advanced that the response delays observed in selective reactive inhibition conditions followed from the fact that the global, hyperdirect inhibitory neural pathway was involved even when only parts of the ongoing motor action had to be suppressed: Because the hyperdirect pathway links prefrontal cortices to subthalamic nuclei with very few synapses (Nambu et al., 2002), it is fast and thus helps in preventing commission errors. However, because the hyperdirect pathway leads to a global reduction of thalamocortical outputs and in turn to a widespread inhibition of the motor activity (e.g. Aron, 2007; Aron and Poldrack, 2006; Nambu et al., 2002),

task-relevant movements are also inhibited and must be re-initiated, which delays the response in the selective inhibition condition.

Electrophysiological responses to the GNG and SNG stimuli differed over two distinct stimulus processing phases. First, there was a global field power modulation without concomitant change in topography over the 110 to 150 ms post-stimulus onset period, indicating a change in response strength of the same configuration of brain network between the selective and global inhibition conditions (e.g. Michel and Murray, 2012). This pattern of results suggests that the very initial stage of the inhibitory process was qualitatively similar between the two inhibition conditions but that the supporting brain networks were more strongly activated for global than selective inhibition.

Because all movements have to be suppressed in the GNG condition, participants could have used less cautious inhibition strategy in the GNG than in the SNG condition. This difference in (no) response strategy could be mediated by a modulation in attentional processes, which manifested as changes in the global field power. Modulation in attentional processes during early processing of the inhibition stimuli could have helped speeding up the triggering of prefrontal top-down inhibitory processes to reach fast global inhibition (Heekeren et al., 2008). In contrast, inhibitory processes had to be engaged with more restraint in the SNG condition to reduce the amount of interference induced by global inhibition on the execution of the response from the right hand. Consequently, the early latency modulation could have influenced inhibitory and/or response selection processes.

Supporting this hypothesis, previous evidence indicates that modulation in attentional demand typically manifests as changes in GFP (Hillyard and Anllo-Vento, 1998; Luck et al., 2000). Moreover, converging data indicate that the 130 ms latency of the GFP modulation corresponds to a period when early attentional processes take place in inhibitory control tasks, subsequently to the very initial stage of the perceptual analyses of the stimuli (see Benikos et al., 2013; Roche et al., 2005; Thomas et al., 2009). The ERP components at this latency have further been shown to modulate with the difficulty of the inhibition task (Benikos et al., 2013). Also supporting that attentional processes may differ between global and selective inhibition during early sensori-cognitive processing of the inhibition-stimuli, source estimations revealed that the change in GFP followed from modulations within the right fusiform gyrus, the cuneus, the middle occipital gyrus, and the precuneus. Corresponding bilateral occipito-parietal networks have been related to the allocation of attentional resources (Ramautar et al., 2006) and to visual discrimination processes (Kiviniemi et al., 2009; Smith et al., 2009; Stillova et al., 2013; Zhang and Li, 2012).

Over the 150–200 ms time period, there was a topographic modulation without change in global field power. Because a change in the topography necessarily follows from a change in the configuration of the underlying neural generators (Lehmann, 1987; Tzovara et al., 2012), this result indicates that different brain networks were engaged between the SNG and GNG conditions.

In line with previous neuroimaging data on selective inhibitory control (e.g. Dove et al., 2000; Rushworth et al., 2002), we hypothesize that this topographic modulation reflects differences in response selection and programming between the two inhibition conditions. Indeed, while the global inhibition required the suppression of all prepotent motor responses, the selective condition required a response of the

Fig. 2. Electrical neuroimaging results. a. Group averaged ($n = 18$) event-related potentials (ERPs) to the NoGo stimuli for four exemplar electrodes (AFz, POz, C3 and C4) in the Global inhibition (GNG; in black) and the Selective inhibition (SNG; red) conditions. b. Superimposed ERP waveforms across all electrodes for the two experimental conditions with the topography of the potential field for the SNG (up) and GNG (bottom) over the periods of significant global field power (GFP, green) and topographic modulations (global map dissimilarity (GMD), purple; nasion upward). c. Global field power waveforms across time in the SNG (red) and GNG (black) conditions. d. Time-wise t -tests on the GFP revealed significant ($p < 0.01$; in green) modulations between the GNG and the SNG conditions at 110–150 ms, at 200–280 ms and at 400–500 ms. e. The Global Map Dissimilarity (GMD) analysis revealed significant ($p < 0.01$; in purple) topographic modulations between the GNG and the SNG conditions at 130–220 ms, 230–300 ms and 330–500 ms. f. Time-wise t -tests on the source estimations. The total number of solution nodes showing a significant ($p < 0.05$) difference at each TF is plotted. The periods of significant GFP (green) and topographic (purple) modulation are superimposed on the plot. The dashed lines indicate the two time-frames with the maximal number of solution points showing a significant difference (130 ms and 190 ms) during the periods of GFP and GMD modulation. The results of the t -tests (significant t -values) are projected on a template brain for these two time-frames. The negative t -values (purple color) indicate the regions more activated in the SNG than in the GNG condition; the red values indicate the regions more activated in the GNG than SNG condition. TF: time-frame.

right hand to be executed. The 190 ms post stimulus onset latency of the topographic modulation corresponds to a period 180 ms before the actual response in the SNG condition. Conduction time between the motor cortex and response execution being about 100 ms (Thorpe and Fabre-Thorpe, 2001), the topographic modulation occurred when the response of the right hand in the selective inhibition condition was selected and programmed within the cortical motor areas (e.g. Mostofsky and Simmonds, 2008).

Source estimations further support that the topographic modulation reflects differences in response selection and programming. The topographic difference indeed stemmed from a modulation within regions involved in motor control, including the left frontal (SMA, pre-SMA), the left parietal (S1), the left occipital area (middle and inferior occipital gyri), and in the right pre-frontal cortex (PFC: inferior and middle frontal gyri, for a review, see Ridderinkhof et al., 2004).

The involvement of the pre-SMA in the selective but not the global inhibition condition corroborates previous functional neuroimaging studies on selective inhibition or on task switching involving initiating new movements after the interruption of ongoing movements (Dove et al., 2000; Rushworth et al., 2002). During selective inhibition trials, the SMA/pre-SMA would support the reshaping of excitatory motor pathway to enable the production of the new movement, a process including the inhibition of inappropriate ongoing movements as well as the selection and execution of new motor programs (Cai et al., 2012; Isoda and Hikosaka, 2007; Mostofsky and Simmonds, 2008; Picton et al., 2007). Right PFC activity has been reported during global inhibition in Go-NoGo (Chikazoe et al., 2007; Liddle et al., 2001; Menon et al., 2001; Ridderinkhof et al., 2004; Rubia et al., 2001; Swick et al., 2011; Wager et al., 2005; Watanabe et al., 2002; Zheng et al., 2008) and in stop-signal tasks (Aron, 2007; Aron and Poldrack, 2006; Coxon et al., 2009; Matthews et al., 2005; Swick et al., 2011). As discussed above, higher activity in the rPFC in the GNG than SNG condition might reflect a cruder inhibition strategy when all movements have to be suppressed than when other movements have to be re-initiated right after the global inhibition. The differential activity within the rPFC in our study was, however, limited to very small areas and should thus be interpreted with caution.

Importantly, the GFP and topographic modulations overlap, suggesting that the occipito-parietal process differing between the two conditions largely interact with the SMA processes. The initial attention-related ERP modulation might thus be considered as a first phase of motor or inhibitory modulation between the selective vs global inhibition mechanisms rather than as a functionally distinct process.

Taken together, our data corroborate and extend current models on selective inhibitory control. The Combination model indeed suggests that in conditions where participants cannot predict if selective or global inhibition is going to be required, selective inhibition consists of a combination between a global inhibition and the re-initiation of task-relevant movements (e.g. Coxon et al., 2007). In line with this model, we showed that 190 ms post-stimulus onset, the two inhibition conditions differ at the level of the pre-SMA, supporting that a new movement was initiated in the SNG but not GNG condition.

Critically, the two inhibition conditions also differed at an earlier latency: The same attentional network was engaged in both conditions at 130 ms, but more strongly in the GNG than SNG condition. Evidence for dissociations between selective and global inhibition were so far reported only when participants knew in advance which kind of inhibition to engage (e.g. Aron and Verbruggen, 2008; Claffey et al., 2010; Greenhouse et al., 2012; Majid et al., 2012). These data indicate that specific inhibition mechanisms support selective inhibition only when the need for selective inhibition can be predicted (Cai et al., 2011). By contrast, while our results largely support the current “global stopping plus movement re-initiation” model of reactive selective inhibition, they extend this Combination model by suggesting that the inhibition mechanism may differ during its very early phase when global or selective inhibition is required in unpredictable conditions.

We would note that the present study differs from previous studies on selective and global stopping notably because it is based on a Go/NoGo task and not on a stop-signal tasks (SST) requiring stopping a single response when one of several stop-signals is delivered. The main difference between SST and Go/NoGo tasks is that in Go/NoGo tasks, a prepotent but not an ongoing response has to be inhibited, which may impact on the nature of the inhibitory process engaged to withhold the response (e.g. Rubia et al., 2001 for a comparative study). In contrast to previous studies involving SST task, our results may thus be more directly related to the inhibition of earlier preparatory stages of motor responses. Further studies are required to elucidate potential differences between selective and global inhibition in SST vs Go/NoGo tasks. Furthermore, whether differential brain processes underlie selective vs global inhibition when the type of inhibition being required is predictable and whether such differences would correspond to the effects found in the current study should be investigated. Foreknowledge has indeed been shown to prevent stopping interference effects and is thought to lead to the recruitment of differential neural mechanisms for global and selective inhibition (e.g. Aron and Verbruggen, 2008).

Acknowledgments

This work was supported by a grant from the Swiss National Science Foundation (Grant #320030-143348) to LS. Cartool software has been programmed by Denis Brunet, from the Functional Brain Mapping Laboratory, Geneva, Switzerland, and supported by the Center for Biomedical Imaging (CIBM) of Geneva and Lausanne. We thank Andres Posada for his help in programming the experimental design.

References

- Aron, A.R., 2007. The neural basis of inhibition in cognitive control. *Neuroscientist* 13, 214–228.
- Aron, A.R., Poldrack, R.A., 2006. Cortical and subcortical contributions to Stop signal response inhibition: role of the subthalamic nucleus. *J. Neurosci.* 26, 2424–2433.
- Aron, A.R., Verbruggen, F., 2008. Stop the presses: dissociating a selective from a global mechanism for stopping. *Psychol. Sci.* 19, 1146–1153.
- Badry, R., Mima, T., Aso, T., Nakatsuka, M., Abe, M., Fathi, D., Foly, N., Nagiub, H., Nagamine, T., Fukuyama, H., 2009. Suppression of human cortico-motoneuronal excitability during the Stop-signal task. *Clin. Neurophysiol.* 120, 1717–1723.
- Benikos, N., Johnstone, S.J., Roodenrys, S.J., 2013. Varying task difficulty in the Go/NoGo task: the effects of inhibitory control, arousal, and perceived effort on ERP components. *Int. J. Psychophysiol.* 87, 262–272.
- Brunet, D., Murray, M.M., Michel, C.M., 2011. Spatiotemporal analysis of multichannel EEG: CARTOOL. *Comput. Intell. Neurosci.* 2011, 813870.
- Cai, W., Oldenkamp, C.L., Aron, A.R., 2011. A proactive mechanism for selective suppression of response tendencies. *J. Neurosci.* 31, 5965–5969.
- Cai, W., George, J.S., Verbruggen, F., Chambers, C.D., Aron, A.R., 2012. The role of the right presupplementary motor area in stopping action: two studies with event-related transcranial magnetic stimulation. *J. Neurophysiol.* 108, 380–389.
- Chikazoe, J., Konishi, S., Asari, T., Jimura, K., Miyashita, Y., 2007. Activation of right inferior frontal gyrus during response inhibition across response modalities. *J. Cogn. Neurosci.* 19, 69–80.
- Claffey, M.P., Sheldon, S., Stinear, C.M., Verbruggen, F., Aron, A.R., 2010. Having a goal to stop action is associated with advance control of specific motor representations. *Neuropsychologia* 48, 541–548.
- Coxon, J.P., Stinear, C.M., Byblow, W.D., 2006. Intracortical inhibition during volitional inhibition of prepared action. *J. Neurophysiol.* 95, 3371–3383.
- Coxon, J.P., Stinear, C.M., Byblow, W.D., 2007. Selective inhibition of movement. *J. Neurophysiol.* 97, 2480–2489.
- Coxon, J.P., Stinear, C.M., Byblow, W.D., 2009. Stop and go: the neural basis of selective movement prevention. *J. Cogn. Neurosci.* 21, 1193–1203.
- Dove, A., Pollmann, S., Schubert, T., Wiggins, C.J., von Cramon, D.Y., 2000. Prefrontal cortex activation in task switching: an event-related fMRI study. *Brain Res. Cogn. Brain Res.* 9, 103–109.
- Grave de Peralta Menendez, R., Gonzalez Andino, S., Lantz, G., Michel, C.M., Landis, T., 2001. Noninvasive localization of electromagnetic epileptic activity. I. Method descriptions and simulations. *Brain Topogr.* 14, 131–137.
- Grave-de Peralta, R., Gonzalez-Andino, S., Gomez-Gonzalez, C.M., 2004. The biophysical foundations of the localisation of encephalogram generators in the brain. The application of a distribution-type model to the localisation of epileptic foci. *Rev. Neurol.* 39, 748–756.
- Greenhouse, I., Oldenkamp, C.L., Aron, A.R., 2012. Stopping a response has global or nonglobal effects on the motor system depending on preparation. *J. Neurophysiol.* 107, 384–392.
- Guthrie, D., Buchwald, J.S., 1991. Significance testing of difference potentials. *Psychophysiology* 28, 240–244.

- Heekeren, H.R., Marrett, S., Ungerleider, L.G., 2008. The neural systems that mediate human perceptual decision making. *Nat. Rev. Neurosci.* 9, 467–479.
- Hillyard, S.A., Anllo-Vento, L., 1998. Event-related brain potentials in the study of visual selective attention. *Proc. Natl. Acad. Sci. U. S. A.* 95, 781–787.
- Isoda, M., Hikosaka, O., 2007. Switching from automatic to controlled action by monkey medial frontal cortex. *Nat. Neurosci.* 10, 240–248.
- Kenner, N.M., Mumford, J.A., Hommer, R.E., Skup, M., Leibenluft, E., Poldrack, R.A., 2010. Inhibitory motor control in response stopping and response switching. *J. Neurosci.* 30, 8512–8518.
- Kiviniemi, V., Starck, T., Remes, J., Long, X., Nikkinen, J., Haapea, M., Veijola, J., Moilanen, I., Isohanni, M., Zang, Y.F., Tervonen, O., 2009. Functional segmentation of the brain cortex using high model order group PICA. *Hum. Brain Mapp.* 30, 3865–3886.
- Koenig, T., Melie-Garcia, L., 2010. A method to determine the presence of averaged event-related fields using randomization tests. *Brain Topogr.* 23, 233–242.
- Koenig, T., Kottlow, M., Stein, M., Melie-Garcia, L., 2011. Ragú: a free tool for the analysis of EEG and MEG event-related scalp field data using global randomization statistics. *Comput. Intell. Neurosci.* 2011, 938925.
- Lehmann, D., 1987. Principles of spatial analysis. In: Gevins, A.S., Remond, A. (Eds.), *Handbook of Electroencephalography and Clinical Neurophysiology. Methods of Analysis of Brain Electrical and Magnetic Signals*, vol. 1. Elsevier, Amsterdam, pp. 309–354.
- Lehmann, D., Skrandies, W., 1980. Reference-free identification of components of checkerboard-evoked multichannel potential fields. *Electroencephalogr. Clin. Neurophysiol.* 48, 609–621.
- Liddle, P.F., Kiehl, K.A., Smith, A.M., 2001. Event-related fMRI study of response inhibition. *Hum. Brain Mapp.* 12, 100–109.
- Luck, S.J., Woodman, G.F., Vogel, E.K., 2000. Event-related potential studies of attention. *Trends Cogn. Sci.* 4, 432–440.
- Macdonald, H.J., Stinear, C.M., Byblow, W.D., 2012. Uncoupling response inhibition. *J. Neurophysiol.* 108, 1492–1500.
- Majid, D.S., Cai, W., George, J.S., Verbruggen, F., Aron, A.R., 2012. Transcranial magnetic stimulation reveals dissociable mechanisms for global versus selective corticomotor suppression underlying the stopping of action. *Cereb. Cortex* 22, 363–371.
- Manuel, A.L., Bernasconi, F., Murray, M.M., Spierer, L., 2012. Spatio-temporal brain dynamics mediating post-error behavioral adjustments. *J. Cogn. Neurosci.* 24, 1331–1343.
- Matthews, S.C., Simmons, A.N., Arce, E., Paulus, M.P., 2005. Dissociation of inhibition from error processing using a parametric inhibitory task during functional magnetic resonance imaging. *Neuroreport* 16, 755–760.
- Menon, V., Adelman, N.E., White, C.D., Glover, G.H., Reiss, A.L., 2001. Error-related brain activation during a Go/NoGo response inhibition task. *Hum. Brain Mapp.* 12, 131–143.
- Michel, C.M., Murray, M.M., 2012. Towards the utilization of EEG as a brain imaging tool. *NeuroImage* 61, 371–385.
- Michel, C.M., Murray, M.M., Lantz, G., Gonzalez, S., Spinelli, L., Grave de Peralta, R., 2004. EEG source imaging. *Clin. Neurophysiol.* 115, 2195–2222.
- Mostofsky, S.H., Simmonds, D.J., 2008. Response inhibition and response selection: two sides of the same coin. *J. Cogn. Neurosci.* 20, 751–761.
- Murray, M.M., Brunet, D., Michel, C.M., 2008. Topographic ERP analyses: a step-by-step tutorial review. *Brain Topogr.* 20, 249–264.
- Nambu, A., Tokuno, H., Takada, M., 2002. Functional significance of the cortico-subthalamic-pallidal 'hyperdirect' pathway. *Neurosci. Res.* 43, 111–117.
- Nieuwenhuis, S., Yeung, N., van den Wildenberg, W., Ridderinkhof, K.R., 2003. Electrophysiological correlates of anterior cingulate function in a go/no-go task: effects of response conflict and trial type frequency. *Cogn. Affect. Behav. Neurosci.* 3, 17–26.
- Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh Inventory. *Neuropsychologia* 9, 97–113.
- Perrin, F., Pernier, J., Bertrand, O., Giard, M.H., Echallier, J.F., 1987. Mapping of scalp potentials by surface spline interpolation. *Electroencephalogr. Clin. Neurophysiol.* 66, 75–81.
- Picton, T.W., Stuss, D.T., Alexander, M.P., Shallice, T., Binns, M.A., Gillingham, S., 2007. Effects of focal frontal lesions on response inhibition. *Cereb. Cortex* 17, 826–838.
- Ramautar, J.R., Slagter, H.A., Kok, A., Ridderinkhof, K.R., 2006. Probability effects in the stop-signal paradigm: the insula and the significance of failed inhibition. *Brain Res.* 1105, 143–154.
- Ridderinkhof, K.R., van den Wildenberg, W.P., Segalowitz, S.J., Carter, C.S., 2004. Neurocognitive mechanisms of cognitive control: the role of prefrontal cortex in action selection, response inhibition, performance monitoring, and reward-based learning. *Brain Cogn.* 56, 129–140.
- Roche, R.A., Garavan, H., Foxe, J.J., O'Mara, S.M., 2005. Individual differences discriminate event-related potentials but not performance during response inhibition. *Exp. Brain Res.* 160, 60–70.
- Rubia, K., Russell, T., Overmeyer, S., Brammer, M.J., Bullmore, E.T., Sharma, T., Simmons, A., Williams, S.C., Giampietro, V., Andrew, C.M., Taylor, E., 2001. Mapping motor inhibition: conjunctive brain activations across different versions of go/no-go and stop tasks. *NeuroImage* 13, 250–261.
- Rushworth, M.F., Hadland, K.A., Paus, T., Sipila, P.K., 2002. Role of the human medial frontal cortex in task switching: a combined fMRI and TMS study. *J. Neurophysiol.* 87, 2577–2592.
- Smith, S.M., Fox, P.T., Miller, K.L., Glahn, D.C., Fox, P.M., Mackay, C.E., Filippini, N., Watkins, K.E., Toro, R., Laird, A.R., Beckmann, C.F., 2009. Correspondence of the brain's functional architecture during activation and rest. *Proc. Natl. Acad. Sci. U. S. A.* 106, 13040–13045.
- Stillova, K., Jurak, P., Chladek, J., Halamek, J., Telecka, S., Rektor, I., 2013. The posterior medial cortex is involved in visual but not in verbal memory encoding processing: an intracerebral recording study. *J. Neural Transm.* 120, 391–397.
- Swick, D., Ashley, V., Turken, U., 2011. Are the neural correlates of stopping and not going identical? Quantitative meta-analysis of two response inhibition tasks. *NeuroImage* 56, 1655–1665.
- Thomas, S.J., Gonsalvez, C.J., Johnstone, S.J., 2009. Sequence effects in the Go/NoGo task: inhibition and facilitation. *Int. J. Psychophysiol.* 74, 209–219.
- Thorpe, S.J., Fabre-Thorpe, M., 2001. Neuroscience. Seeking categories in the brain. *Science* 291, 260–263.
- Tzovara, A., Murray, M.M., Michel, C.M., De Lucia, M., 2012. A tutorial review of electrical neuroimaging from group-average to single-trial event-related potentials. *Dev. Neuropsychol.* 37, 518–544.
- Vocat, R., Pourtois, G., Vuilleumier, P., 2008. Unavoidable errors: a spatio-temporal analysis of time-course and neural sources of evoked potentials associated with error processing in a speeded task. *Neuropsychologia* 46, 2545–2555.
- Wager, T.D., Sylvester, C.Y., Lacey, S.C., Nee, D.E., Franklin, M., Jonides, J., 2005. Common and unique components of response inhibition revealed by fMRI. *NeuroImage* 27, 323–340.
- Watanabe, J., Sugiura, M., Sato, K., Sato, Y., Maeda, Y., Matsue, Y., Fukuda, H., Kawashima, R., 2002. The human prefrontal and parietal association cortices are involved in NO-GO performances: an event-related fMRI study. *NeuroImage* 17, 1207–1216.
- Zhang, S., Li, C.S., 2012. Functional networks for cognitive control in a stop signal task: independent component analysis. *Hum. Brain Mapp.* 33, 89–104.
- Zheng, D., Oka, T., Bokura, H., Yamaguchi, S., 2008. The key locus of common response inhibition network for no-go and stop signals. *J. Cogn. Neurosci.* 20, 1434–1442.