In the present study magnetoencephalographic recordings were performed to investigate the neural mechanisms underlying the stopping of manual responses. Subjects performed in a Stop-signal task in which Go-stimuli (S1), requiring a rapid motor response, were sometimes rapidly followed by a Stop-stimulus (S2) indicating to withhold the already initiated response to S1. Success of stopping strongly depended on the early perceptual processing of S1 and S2 reflected by the magnetic N1 component. Enhanced processing of S1 facilitated the execution of the movement, whereas enhanced processing of S2 favored its inhibition. This suggests that the processing resources for the subsequent stimuli are limited and need to be shared. This sharing of resources appeared to arise from adjustments made on a trial-by-trial basis, in that systematic reaction time prolongations on Go-trials following Stop-trials versus following Go-trials were accompanied by attenuated sensory processing to the Go-stimulus similar to that that systematic reaction time prolongations on Go-trials following appeared to arise from adjustments made on a trial-by-trial basis, in that systematic reaction time prolongations on Go-trials following Stop-trials versus following Go-trials were accompanied by attenuated sensory processing to the Go-stimulus similar to that

**Keywords:** executive function, inhibition, MEG, posterior cingulate gyrus, stop-paradigm, visual attention

**Introduction**

Everyday motor behavior requires the complex coordination of movement initiation and inhibition. Such inhibition can either be gradual as in the case of fine-tuning movements or maximal when a movement needs to be aborted. One way to investigate processes that underlie movement inhibition is the so-called Stop-paradigm (Logan et al. 1984; Logan 1994). In this type of paradigm a Go-stimulus (S1) requiring a choice-reaction is infrequently and rapidly followed by a Stop-stimulus (S2), requiring the subject to withhold the just initiated response. Usually, subjects need approximately 200 ms to stop their responses irrespective of the response modality (like button-presses, verbal report or eye movements; Logan and Cowan 1984; Logan et al. 1984; Curtis et al. 2005).

Numerous studies have demonstrated that the outcome of this Stop-process can be predicted quite adequately based on a simple race model which assumes that Go- and Stop-processes both evolve independently over time (Logan et al. 1984; de Jong et al. 1990; see also Boucher et al. 2007). Depending on whether the Stop-process can be implemented rapidly enough to enable withholding of the possibly already initiated response to S1 (called the point of no return; e.g., de Jong et al. 1990), the inhibition will succeed or not. According to this model the success of response inhibition will critically depend on the stimulus onset asynchrony (SOA) between S1 and S2, with short SOAs leading to a higher probability of successful inhibitions than longer SOAs (Logan 1994). An important merit of the race model is that it provides a means to estimate the time required for the Stop-process to come up to the Go-process in order to successfully inhibit the response. This time—referred to as Stop-signal response time (SSRT)—has to be estimated due to the obvious lack of an overtly measurable index (i.e., no response is given when inhibition succeeded). SSRT can be calculated from the mean Go-trial reaction time (RT) minus the mean SOA in which subjects succeed to inhibit their response in 50% of the trials (Logan 1994).

To date, a large number of experiments have investigated the neural mechanisms underlying this process of stopping. In the case of inhibiting manual responses, several functional magnetic resonance imaging (fMRI)-studies suggest the right medial and inferior prefrontal cortex (PFC) to be a key structure in these processes (e.g., Garavan et al. 1999; Rubia et al. 2001, 2003; Aron et al. 2007). The PFC is, however, not the only structure implicated in stopping. For example an fMRI study by Li et al. (2006) reported stronger activation in a network also comprising occipital areas and the posterior cingulate gyrus (PCG) for successful versus unsuccessful stopping. Consistent with the interplay of different areas, the performance of patients with lesions in frontal brain areas in the Stop-paradigm is impaired but not entirely disrupted (Aron et al. 2003; Dimitrov et al. 2003; Picton et al. 2007). The knowledge about the brain regions involved in the processes related to stopping is, however, not sufficient to interpret their functional role. The knowledge of the respective time course of their activation is mandatory for understanding the role areas might play in the Stop-process. Note, that a region can only be directly involved in the process of actual stopping, if it impacts neural processing within the critical time-window for stopping (i.e., between the presentation of the Stop-stimulus and the end of the SSRT (Schall et al. 2002). Several event-related potential (ERP) studies have been conducted to gain insights into the temporal organization of the processes that lead to either successful or unsuccessful stopping.

Research on children with attention-deficit hyperactivity disorder (ADHD; a condition characterized by a severe impairment in motor control) has linked a medium-latency ERP component, the N2, to stopping, which is much more prominent for healthy controls than for the ADHD group (Pliszka et al. 2000; Dimoska et al. 2003). This so-called Stop-N2 arises approximately 200 ms after the presentation of the Stop-stimulus and has a right-frontal maximum. Consistently, in healthy subjects a larger amplitude of this component for successful as compared with unsuccessful stopping has been reported (Schmajuk et al. 2006), and it has been demonstrated to be larger for subjects that display better inhibition...
performance (van Boxtel et al. 2001). Other studies investigating the Stop-signal task also found the Stop-N2 to be related to stopping but failed to establish a clear relationship between the size of this component and stopping success (e.g., Dimoska et al. 2005, 2006; Ramautar et al. 2004). Additional support for the notion that the frontal N2 is related to response inhibition comes from studies investigating the Go-NoGo task, which demonstrated larger frontal N2 components for NoGo- than for Go-stimuli (e.g., Eimer 1993; Bokura et al. 2001; van Boxtel et al. 2001). In addition to the intensely studied Stop-N2 component, one study reported an enhancement of the sensory N1 component of an acoustical Stop-stimulus for successful versus failed response inhibition (Bekker et al. 2005). This component peaked approximately 100 ms after the presentation of the Stop-stimulus, and is probably related to a stronger sensory processing of the Stop-stimulus.

In sum, although studies are pointing to key components of the neuroanatomical network underlying the process of stopping, the exact timing of the involved areas still needs to be studied. We therefore investigated stopping in human participants by means of high-resolution magnetoencephalography (MEG). Using individually determined SSRTs we were able to directly relate the neurophysiological responses to their temporal extent, focusing exclusively on effects within the SSRT. The paradigm consisted of a standard visual Stop-paradigm with 2 important modifications. First, 2 additional conditions were introduced that mimicked the visual stimulation of Stop- and Go-trials but did not necessitate any response. This was done to provide an estimation of the visual processing of S1 and S2. This activity will then be subtracted from that elicited in Stop- and Go-trials, to provide a measure of the motor-related activity. Second, the SOA between the Go- and the Stop-stimulus was adapted using an online staircase-procedure, which has been successfully applied by some earlier studies (e.g., Li et al. 2006). This was done to ensure comparable numbers of trials for successful and unsuccessful stopping for each subject, as well as a minimal difference in SOA between the 2 conditions.

Materials and Methods

Subjects

Nineteen healthy subjects (mean age 24.2 years, SD 3, 7 men) took part in the experiment. They gave their written informed consent and were paid for participation. All subjects were neurologically intact and had normal or corrected-to-normal visual acuity. The experiment was approved by the ethics committee of the Otto-von-Guericke University Magdeburg.

Stimuli

On each trial, an array of 5 traffic light symbols was presented 1° above a central fixation dot within a white box (14.5° × 3.6°) on a gray background (Fig. 1A). The stimuli were 2.5° high and 2.5° wide. Three different shapes of traffic light symbols were used: a "go left sign" (LEFT), a "go right sign" (RIGHT), and a "stop sign" (STOP). All signs could appear either in red or in green. The central symbol was the actual target, whereas the flashing stimuli were irrelevant for the task and each flashing stimulus was randomly varied to be a green LEFT or RIGHT. LEFT as the target symbol required a button press with the right index finger, whereas RIGHT required a response with the right middle finger. This choice-reaction stimulus either lasted for the full stimulus duration (Go-trials, GT) or was rapidly followed by a Stop-stimulus (Stop-trials, ST) that informed the subject to immediately withhold the response (see the left part of Fig. 1A). Stop-trials were later separated into trials in which subjects succeeded in stopping their response (successful Stop-trials, SST) and those in which they failed (unsuccessful Stop-trials, UST). For Stop-trials the SOA between the S1 and the S2 was adapted individually using a staircase-procedure in which the SOA was increased by 1 stimulation-frame (17 ms) after SST and reduced by 1 frame after UST. The initial SOA was always 150 ms.

A further idea was to estimate the sensory activity per se elicited by S1 and S2 in the absence of a motor response. This activity can be subtracted from activity elicited by trials with the same S1-S2 timeframe that do require a motor response, resulting in a simplified magnetic field reflecting motor-related processes (see below).

To this end, 2 conditions served as sensory baselines mimicking the visual stimulation sequence of Go- and Stop-trials without requiring

**Figure 1.** Schematic of the trial-types and RT-data. (A) On Go-trials an array of 5 symbols was presented for 800 ms, with the center one being the target. On Stop-trials the green (depicted in gray) symbol in the center (S1) was substituted by a red (depicted in black) STOP (S2) after an SOA set by a staircase-procedure. The total stimulus duration was 800 ms. Stop-trials were later classified as SST, where subjects successfully inhibited their response, and UST where they did not succeed. In NoGo-trials a display with 5 symbols was presented for 800 ms, of which the center stimulus was a green colored STOP. Control-trials started identically to NoGo-trials, but after SOAs corresponding to those of the Stop-trials the green STOP was replaced by a red stimulus (LEFT or RIGHT), mimicking the visual stimulation timeframe of a Stop-trial. (B) Reaction times were faster for UST than for Go-trials (GT). Reaction times to Go-trials also differed with respect to their trial history (GT + 1 = Go-trial following on another Go-trial; UST + 1 = Go-trial following on an unsuccessful Stop-trial; SST + 1 = Go-trial following on a successful Stop-trial; error bars depict standard error).
motor-related processes (see the right part of Fig. 1A). These trials always started with the presentation of a green STOP that either lasted for the whole presentation duration (NoGo-trials, NT) or was rapidly replaced by a red LEFT or RIGHT sign (Control-trials, CT). For both, NoGo-trials as well as in Control-trials, subjects were instructed to give no response. Importantly, the SOAs for the Control-trials were chosen to match those of the Stop-trials so that visual stimulation was comparable under the 2 conditions. Therefore, Control-trials were very similar to Stop-trials concerning their visual stimulation (i.e., a green stimulus followed by a red stimulus in rapid succession set by the staircase used for Stop-trials), whereas NoGo-trials resembled Go-trials in terms of their sensory stimulation timeframe.

Procedure
Visual presentation was carried out, using a back projection screen at a viewing distance of 120 cm. Total stimulus presentation duration was 800 ms for each trial interleaved by intertrial intervals that varied randomly between 1300 and 1500 ms. In Go-trials and NoGo-trials the stimulation stayed constant for the whole 800 ms, whereas in Stop- and Control-trials it changed at a time point obeying the previously described staircase-procedure. Go-trials were presented in 60% of the trials, Stop-trials in 20%, NoGo-trials and Control-trials in 10% each. Separated by 10 experimental runs, a total of 1600 trials were presented, yielding 360 Go-trial, 320 Stop-trials, 160 NoGo-trials, and 160 Control-trials for each subject. The sequence of the stimulus conditions was randomized and subjects were instructed to keep accurate fixation during the task which was monitored by electrooculogram (EOG, see below).

Recording and Analysis
The MEG and EOG signals were registered simultaneously using a 148-channel Bri Magnes 2500 whole-head magnetometer (Biomedical Technologies Inc., San Diego, CA) and a Synamps amplifier (Neuroscan, Inc., Herndon, VA). The signals were digitized at a rate of 254 Hz and band-passed from 0.1 to 50 Hz. Both the horizontal and the vertical EOG were recorded bipolarly, using 2 electrodes behind the lateral orbital angles for the horizontal EOG, whereas the vertical EOG was recorded from an electrode below the right orbital rim and one above the right eye. Impedances were kept below 5 kΩ and an electrode placed at FPZ served as ground. MEG signals were submitted to online and offline noise reduction (Robinson 1989), and an artifact rejection was applied with peak-to-peak limits of 3 pT for the MEG and 100 µV for the EOG signal. For the analysis responses were considered as valid if the button-presses occurred between 200 and 1700 ms following the presentation of S1. Trials that exceeded the average of 2.5 standard deviations in the first 100 ms will be subject to the analysis. Epochs containing artifacts or incorrect button-presses were excluded from the further analysis. To coregister anatomical and functional data, anatomical landmarks (left and right preauricular points, nasion) were digitized using a Polhemus 3Space Fastrak system (Polhemus Inc., Colchester, VT). These landmarks were then brought into reference with magnetic marker fields generated by 5 spatially distributed coils attached to the subjects’ head.

Two sets of averages were calculated for the different conditions, one time-locked to the onset of the display (S1) and a second time-locked to the time point when the center stimulus was substituted (S2). In order to be able to compare all conditions at both S1 and S2, S2-averages were also calculated for Go- and NoGo-trials (irrespective of the completely unchanged display) using the SOAs of the Stop-trials. To summarize, separate averages to S1 and S2 were generated for Go-trials (GT), Control-trials (CT), NoGo-trials (NT), SST, and UST. Afterward, group-averages over subjects were calculated for the respective conditions.

Statistical analysis of the behavioral data and event-related magnetic fields (ERMFs) was performed using within-subjects repeated analyses of variance (ANOVAs, Greenhouse-Geisser correction was applied when necessary). Data reported for the S1-time-range were quantified as the mean magnetic field response with respect to a 100 ms baseline directly preceding the onset of the display, data reported for the S2-time-range with respect to a 100 ms baseline between 400 and 300 ms before the onset of S2 (and thus well before S1). For statistical comparisons of the N1 component ERMF amplitudes across hemispheres absolute values were used.

Source analysis was carried out using the multimodal neuroimaging software Curry 4.0 (Neuroscan, Inc., see e.g., Hopf et al. 2006 for a similar approach), using the Montreal Montreal Neurological Institute brain (average of 152 T1-weighted stereotaxic volumes from the ICBM project, see www.bic.mni.mcgill.ca/cgi/ibcm_view/). To approach maximum precision in source analysis, a 3-D reconstruction of the head, cerebrospinal fluid space, and cortical surface was created using the boundary element method (Hämäläinen and Sarvas 1989). For the source analysis this realistic volume conductor was used and possible source locations were restricted to the cortical surface. A model of distributed sources was then estimated by means of the minimum norm least square method (Hämäläinen and Ilmoniemi 1994; Fuchs et al. 1999), yielding a model of the distribution of currents over the cortical surface, called source density estimates (SDEs).

For the analysis of motor-related activity in the S2-time-range, differences between conditions with the same S1-S2 timeframes were calculated. Specifically, the magnetic activity for Control-trials (not requiring motor responses) was subtracted from SST (SST-minus-CT), and UST (UST-minus-CT), whereas NoGo-trial activity was subtracted from Go-trials (GT-minus-NT). This was done to obtain a simpler magnetic field reflecting motor activity by attenuating the predominant sensory activity. Note that although NoGo-trials and Control-trials are not necessarily entirely neutral in terms of motor activity, the subtracted magnetic activity should still be similar for all 3 conditions. For a general estimate of the strength of motor activity the average ERMF data over subjects of these differences was used and submitted to source analysis. Additionally, individual current source estimations were performed for each subject. This yielded a better estimate of motor activity as compared with a simple analysis of the ERMF because individual differences in source orientation would lead to different ERMFs, whereas SDEs are unaffected. After estimation, the SDE values were quantified in a 10-mm spherical region of interest (ROI) surrounding the activation maximum of the difference GT-minus-NT for each condition (GT-minus-NT, SST-minus-CT, and UST-minus-CT). Afterward, activity was normalized to the maximum SDE value of GT-minus-NT for each subject. This individual estimation was performed to gain estimates of the exact time course of motor-cortex activity. Importantly, this dataset was used to estimate the onset of motor activity under the different conditions. The onset was defined as the time point when 50% of the individual SDE maximum for GT-minus-NT was reached.

Results

Behavioral Performance
Apart from failures of stopping (which are inherent to the paradigm) subjects committed very few errors. Incorrect responses during Go-trials were given only in 0.9%, false alarms in NoGo-trials in 1.1% of the respective trials. SSRT were on average 241 ms (SD 28). Subjects responded faster during UST (416 ms, SD 40) than during Go-trials (GT: 454 ms, SD 52; F1,18 = 78.1; P < 0.001). In addition, reaction times (RT) to Go-trials were analyzed as a function of trial history (Fig. 1B). RTs in Go-trials following another Go-trial were significantly faster than in Go-trials succeeding a Stop-trial (GT after GT: 452 ms; GT after ST: 467 ms; F1,18 = 12.5; P = 0.002). This slowing did not depend on the success of response inhibition (GT after SST: 468 ms; GT after UST: 466 ms; F1,18 < 0.1; P = 0.846).

On the whole, the proportion of SST and UST was nearly identical (49.4% SST vs. 50.6% UST). An analysis of the SOAs between the Go- and the Stop-stimulus revealed that the SOAs for SST (203 ms, SD 60) and UST (221 ms, SD 60) differed by only 18 ms.

Electrophysiological Effects Related to the Go-Process (S1)
In Stop-trials, Go-stimuli preceding the Stop-stimuli elicited prominent ERMF responses in the N1-time-range that peaked
around 160 ms after the onset of the display (Fig. 2A). Its
distribution centered bilaterally over occipito-temporal cortex
with a prominent "efflux" maximum laterally over the left
hemisphere and the corresponding "influx" over left posterior
areas (note that magnetic fields measured with magnetometers
display an efflux-/influx-constellation that surrounds the
current source). Over the right hemisphere, an influx
maximum over the right occipito-temporal cortex was
accompanied by the corresponding efflux over right posterior
areas. This constellation is consistent with 1 source in the left
and 1 in the right occipito-temporal cortex (see below), whose
respective field components over posterior areas are attenu-
ated by partly canceling each other (Hopf et al. 2002;
Schoenfeld et al. 2007). Taking this cancellation into account,
the further analysis was restricted to sensors measuring the
magnetic efflux over the left and the magnetic influx over the
right hemisphere. For the statistical analysis 3 sensors over the
right and 3 over the left temporal cortex were averaged
(shown in Fig. 2A). The mean amplitude of the N1 component
was quantified in a time window between 130 and 180 ms,
which yielded a larger effect in UST than SST both over the left
(123 vs. 96 fT) and over the right hemisphere (107 vs. 90 fT).
This difference was statistically confirmed by a 2-way
rANOVA with factors condition (UST vs. SST) and sensor-site
(left side vs. right side), showing a significant main effect of
condition ($F_{1,18} = 9.4; P = 0.007$). The difference between the
2 conditions appeared to be larger over the left (27 fT)
than over the right (17 fT) hemisphere. However, the corresponding
condition x sensor-site interaction was not statistically signif-
ient ($F_{1,18} = 1.8; P = 0.2$).

**Sensory Enhancement versus Attenuation of the Go-
Stimulus Processing**

The larger N1-amplitude for UST compared with SST could
either reflect a relative attenuation of the N1 component in SST
or alternatively a relative enhancement in UST. Therefore, both
patterns were compared with Go-trials that do not differ from
Stop-trials before the presentation of the Stop-stimulus with
respect to the sensory input. As Go-trials constituted the
majority of trials, they can be considered as the "standard-case"
of Go-stimulus processing and therefore as a reasonable
sensory baseline-condition. The N1 component to Go-trials
(left hemisphere: 122 fT; right hemisphere: 109 fT) was about
as large as that to UST and thus larger than that to SST (Fig. 2B).
rANOVA investigating these differences yielded a significant
effect for the comparison Go-trials versus SST ($F_{1,18} = 13.3; P =
0.002$), whereas no significant difference was observed for the
corresponding comparison between Go-trials and UST ($F_{1,18} <
0.1; P = 0.908$). This pattern indicates that the difference in N1-
amplitude between UST and SST stems from an attenuated
response to S1 for SST.

**Source Analysis**

The field distribution of the N1 component suggests bilateral
sources in the ventral visual processing stream. Indeed, SDEs
yielded neural sources in these regions (Fig. 2C). Previously,
ERP and MEG studies on visual attention have reported that N1
modulations index the discrimination process at an attended
location (e.g., Vogel and Luck 2000; Hopf et al. 2002). The
locations of the neural sources observed here are similar
to those obtained by this previous attention-related work.
Maximal source strength was seen bilaterally in the inferior
occipito-temporal cortex with a slightly stronger response in
the left hemisphere in both, SST and UST (Fig. 2C). Consistent
with the difference in magnetic field strength, source strength
estimates were higher for UST than for SST in both hemi-
spheres. These findings suggest that the N1 modulation reflects
intermediate levels in the ventral visual processing stream,
indexing the degree of discrimination dedicated to the Go-
stimulus.

![Figure 2.](image-url)

**Figure 2.** ERMF and SDE results to the Go-stimulus (Average over subjects; S1-time-range). (A) ERMF distributions for SST and UST averaged between 130 and 180 ms after the Go-stimulus are displayed in the middle (azimuth projection of the whole sensor array; upper side corresponds to frontal). Additionally the ERMF time course of 3 sensors averaged for each hemisphere (highlighted by black dots in the ERMF distribution) is depicted. Time-course results for the left hemisphere are colored blue, those for the right hemisphere green. Dashed lines depict UST, solid lines SST. The maximum amplitude is reached around 160 ms after display-onset (see arrowheads). (B) The ERMF activity at the selected sensors (average of responses over the right and the left hemisphere) was smaller for SST than for UST and GT (error bars depict standard error). (C) SDE results are displayed at 160 ms poststimulus. Maxima are observed in the inferior occipito-temporal cortex. Both ERMF response and SDE were stronger for UST than for SST.
Electrophysiological Effects Related to the Stop-Process (S2)

Turning to S2, a magnetic field distribution was observed arising approximately 140 ms after the presentation of the Stop-stimulus (Fig. 3A), that was very similar to that elicited by the Go-stimulus before (see Fig. 2A). Again, strong magnetic efflux was detected laterally over the left hemisphere and strong influx over the right. The respective opposite field components can be seen over posterior areas again, but are more strongly attenuated than in the S1-time-range. For further analysis 3 sensors located in the efflux-zone and 3 in the influx-zone (as depicted in Fig. 3A) were averaged. For the statistical analysis the mean amplitudes at these average sensors were quantified between 140 and 200 ms which yielded a larger effect in SST than UST both over the left (186 vs. 162 fT) and over the right hemisphere (147 vs. 101 fT). A 2-way rANOVA with factors condition (SST vs. UST) and sensor-site (left vs. right) yielded a significant main effect of condition ($F_{1,18} = 20.4; P < 0.001$), confirming the larger amplitude for SST than UST.

The observation that this difference was larger on the right side (46 fT) than on the left (24 fT) was statistically confirmed by a significant condition*sensor-site interaction ($F_{1,18} = 4.9; P = 0.041$).

Source localization analysis indicated that the field distribution is generated by 2 different source configurations (Fig. 3B,C). In congruency with the results for S1, the field distribution was very similar to that of the N1 component elicited by the Go-stimulus (see also Fig. 2A). Consistently, clear estimates of activity were observed in bilateral ventral occipito-temporal cortex, but this time larger for SST than UST (Fig. 3B). However, a different field configuration was observed in the posterior part when the field distributions in response to S1 and S2 were compared. Specifically, the respective opposite field components (influx for the left hemisphere and efflux for the right) were attenuated beyond the respective cancellation observed for S1. This posterior field difference evident in the response to S2 was not accounted for by the previously described bilateral ventral occipito-temporal estimates. Additional bilateral estimates of activity were found in the PCG, which is in accord with the remaining posterior field distribution (Fig. 3C). Again, the strengths of the sources were substantially higher for SST than for UST.

Taken together, the ERMF response in the 140 to 200 ms time range appears to contain overlapping activity from a sensory N1 component to the Stop-stimulus localized in intermediate areas of the ventral visual processing stream, and a response from the posterior cingulate cortex. This activity accounts for the difference in N1-field distribution between S1 and S2 (compare Figs 2A and 3A). It appears that both subcomponents are stronger when stopping is successful. Most importantly, these differences of activity between SST and UST occurred before the end of the SSRT.

Interaction of Processes Related to Successful and Unsuccessful Stopping

The rationale of the Stop-paradigm design is to investigate the differential processes of executing a motor response versus withholding it. Therefore, the motor cortex can be regarded as an indicator for the readiness to actually respond or not (Band and van Boxtel 1999; van Boxtel et al. 2001; Coxon et al. 2006). For the analysis of motor-related activity, sensory activity was subtracted from the conditions of interest. Specifically, Control-trial activity was subtracted from UST (UST-minus-CT) and SST (SST-minus-CT) and Nogo-trial activity from Go-trials.

Figure 3. ERMF and SDE results related to the Stop-stimulus (average over subjects; S2-time-range). (A) ERMF distributions for SST and UST averaged between 140 and 200 ms after the Stop-stimulus presentation. Additionally, the time course of 3 neighboring sensors averaged for each hemisphere is illustrated (highlighted by black dots in the ERMF distribution). Time-course results for the left hemisphere are colored blue, those for the right hemisphere green. Dashed lines depict UST, the solid lines SST. The maximum amplitude is reached around 160 ms after the onset of S2 (see arrowheads). (B) SDE results at 160 ms postsimulus. Strong activity is observed bilaterally in ventral occipito-temporal cortex. (C) Additionally strong estimates of activity are found in the PCG. Both ERMF responses and SDE in ventral occipito-temporal cortex and the PCG are stronger for SST than for UST.
(GT-minus-NT; note that GT and NT were also analyzed in S2-time-range, although there was no S2 for these conditions, by adopting the SOA-values from the Stop-trials). This yielded a good estimate of motor-related activity for all 3 conditions. Approximately 100 ms after the presentation of the Stop-stimulus, a field distribution appeared that was focused over the left fronto-parietal cortex (Fig. 4A) that was consistent with a source in the left motor-cortex (i.e., right hand, which was used in the experiment). The signals of channels representative for the magnetic efflux and influx related to this source (as depicted in Fig. 4A) were averaged and afterward subtracted from each other. For the statistical analysis the mean amplitudes of this difference were quantified between 100 and 300 ms for each condition. Both UST-minus-CT and GT-minus-NT resulted in much stronger ERMF responses than SST-minus-CT (UST-minus-CT: 94 fT, GT-minus-NT: 75 fT, SST-minus-CT: 35 fT). A one-way rANOVA with factor condition (GT-minus-NT vs. UST-minus-CT vs. SST-minus-CT) validated the presence of a statistically significant difference between the 3 conditions ($F_{1,18} = 25.6; P < 0.001$). Pair-wise comparisons validated a significant difference when comparing UST-minus-CT and SST-minus-CT ($F_{1,18} = 32.9; P < 0.001$) and in the comparison between GT-minus-NT and SST-minus-CT ($F_{1,18} = 65.9; P < 0.001$). Additionally, the amplitude difference between UST-minus-CT and GT-minus-NT reached statistical significance ($F_{1,18} = 4.6; P = 0.046$).

The source localization results displayed strong estimates of activity in the motor cortex (Fig. 4A). Congruent with the ERMF response, current sources were maximal for UST-minus-CT, followed by GT-minus-NT. Importantly, the source strength in the motor cortex was largely attenuated for SST-minus-CT.

**Relative Timing of Motor-Cortex Activation**

In addition to the investigation of the amplitudes, the relative timing of motor activity under the different conditions is of great importance. To this end, we estimated the time course of the current source underlying the magnetic field for each subject individually and quantified these estimates in a 10-mm spherical ROI around the activation maximum for GT-minus-NT (Fig. 4B). An analysis of the source strength revealed that

![Figure 4. ERMF and SDE results from the motor cortex (average over subjects; S2-time-range). (A) The upper panel displays the SDE results averaged between 200 and 240 ms after S2. The lower part illustrates the corresponding ERMF distributions. Black dots depict the positions of the sensors that were averaged for the statistical analysis. The ERMF activity represents the average over all subjects, that was also used for the source density estimation. (B) SDE time course of the average of individual SDE normalized to the maximum SDE value for GT-minus-NT (error bars depict standard error). Consistent with the ERMF and with the average SDE results, the strongest activation of the motor-cortex was found for UST-minus-CT followed by GT-minus-NT and SST-minus-CT. Additionally estimates of activity in the motor-cortex were found earlier for UST-minus-CT and the activation maximum occurred earlier.](Cerebral Cortex January 2009, V 19 N 1 139)
Go-trials following a Stop-trial. We therefore sought to identify the neural correlates of this behavioral effect.

In the ERMF response trial-by-trial adaptation effects were observed in the amplitude of the N1 component in Go-trials analogous to the behavioral effects. Specifically, the N1 component in Go-trials was larger when the preceding trial was a Go-trial compared with a Stop-trial (Fig. 5). To avoid low-level visual stimulation confounds this analysis was performed on Go-trials only, which ensured that the observed differences can be attributed to the different types of preceding trials. The N1 to Go-trials following either a Stop-trial (ST + 1) or a Go-trial (GT + 1) was quantified as the average of 3 sensors over the right and 3 over the left occipito-temporal cortex (shown in Fig. 5) over a time window of 140–170 ms. This yielded an N1 component that was attenuated for Go-trials following a Stop-trial (left hemisphere: 113 fT; right hemisphere: 55 fT) as compared with Go-trials following another Go-trial (left hemisphere: 127 fT; right hemisphere: 63 fT). A 2-way rANOVA with factors hemisphere (left/right) and condition (GT + 1/ST + 1) yielded significant main effects for hemisphere ($F_{1,18} = 14.6; P = 0.001$) and condition ($F_{1,18} = 8.1; P = 0.011$), whereas there was no significant interaction between the 2 ($F_{1,18} = 0.7; P = 0.424$).

Source localization analysis yielded maximal source strength estimates bilaterally in the inferior occipito-temporal cortex (Fig. 5), with a very similar distribution to the N1 modulations described earlier. Furthermore, the source strength estimation paralleled the ERMF observations in that it yielded slightly stronger estimates for Go-trials following on another Go-trial, than in the case of Go-trials directly following a Stop-trial.

**Discussion**

The present study investigated the spatio-temporal correlates of inhibitory motor control in the human cortex using a Stop-paradigm. There, a first stimulus (S1) is employed to initiate a motor response that subsequently has to be inhibited whenever a second stimulus (S2) is presented in rapid succession. In our experiment, a special procedure ensured that subjects only succeeded to inhibit the response in 50% of the cases. This permitted the direct comparison of processes involved in the successful versus unsuccessful inhibition of the initiated movement, while holding trial numbers and the Stop-stimulus delay almost identical. The inhibition of a planned movement required approximately 240 ms (SSRT), which is in line with previous reports (Logan and Cowan 1984; Logan et al. 1984; Curtis et al. 2005). Both S1 and S2 elicited a “classical” N1 component indexing the perceptual analysis of the visual stimulus within ventral occipito-temporal visual areas. The amplitudes of the N1 components elicited by S1 and S2 displayed an inverse relationship in that the N1 to S1 was more pronounced for unsuccessful stopping whereas the N1 to S2 was more pronounced for successful stopping. This inverse relationship might stem from the differential allocation of processing resources on S1 and S2 (see below). Furthermore, this resource allocation may arise from strategic adaptations that adjust attentional weights between trials, as it could be demonstrated that prolonged reaction times to Go-trials after Stop-trials were paralleled by attenuated amplitudes of the N1 component in response to S1. Moreover, it has been demonstrated that this component is subject to top-down modulations (e.g., Barcelo et al. 2000; Hopf et al. 2002). Finally, shortly after the presentation of S2, estimates of activity were located in the PCG that also indexed the inhibition success by exhibiting higher amplitudes for SST than for UST.

**Sensory Processing of the Go-Stimulus**

The N1 component elicited by the Go-stimulus was larger in UST compared with SST. Importantly, this differential processing of the Go-stimulus took place considerably before the processing of the Stop-stimulus (that was on average presented over 200 ms after S1), indicating that the success of stopping already relies at least in part on the perceptual processing of the Go-stimulus. A comparison with Go-trials, in which no Stop-stimulus occurs, revealed that this difference was probably due to an attenuation of the N1 component for

---

**Figure 5.** ERMF and SDE results to Go-stimuli (average over subjects; S1-time-range) with different trial history. ERMF distributions for Go-trials averaged between 140 and 170 ms after the Go-stimulus are displayed in the upper panel separately for Go-trials that either followed a Stop-trial (ST + 1) or another Go-trial (GT + 1). Additionally, the ERMF time course of 3 sensors averaged for each hemisphere (highlighted by black dots in the ERMF distribution) is displayed. Time-course results for the left hemisphere are shown in blue, those for the right hemisphere in green. Dashed lines depict GT + 1, solid lines ST + 1. The maximum amplitude is reached around 160 ms after display-onset (see arrowheads). Black dots in the field distribution mark the locations of the averaged sensors. The lower panel depicts the SDE results at 160 ms poststimulus. Maxima are observed in the inferior occipito-temporal cortex. Both ERMF response and SDE are stronger for GT + 1 than for ST + 1.
SST, whereas UST and Go-trials had similar N1-amplitudes. Source analyses of the N1 component revealed bilateral sources in the inferior occipito-temporal cortex. Previous studies have shown that attention-related N1 modulations scale with the degree of discrimination devoted to an attended location (e.g., Vogel and Luck 2000; Hopf et al. 2002). Consequently, the N1 modulation observed in the present study is generated at intermediate levels of the ventral visual processing stream, indexing the degree of discrimination dedicated to the Go-stimulus. A down-modulated processing of the Go-stimulus therefore appears to be advantageous for later stopping the initiated response. As at this time, it is not clear whether the trial is actually going to be a Stop-trial at all, this difference must be linked to modulations preceding the trial, that determine the outcome of the race between the Go- and the Stop-process. These modulations are either random or at least in part under top-down control. We favor the second notion (see below).

**Sensory Processing of the Stop-Stimulus**
The N1 component elicited by S2 had a similar field distribution to that elicited by S1 and had comparable sources. In contrast to that modulation, however, the N1 component to S2 was larger for SST. Thus, enhanced sensory processing of the Stop-stimulus was associated with stopping success. This is in line with an earlier report of enhanced sensory processing of the Stop-stimulus where a sound was used as the Stop-stimulus (Bekker et al. 2005). Furthermore, Schmajuk et al. (2006) reported an enhanced negativity over parieto-occipital cortex with a similar latency as our N1-effect, when comparing Stop-trials from trials where Stop-stimuli were relevant as compared with a control trial-block where Stop-stimuli were irrelevant. These observations also indicate that differential sensory processing of the Stop-stimulus is relevant to stopping success.

The present results appear to indicate that stopping success relies on the interplay of attenuated sensory processing of S1 and enhanced sensory processing of S2. Thus, not only the response to the Stop-stimulus indexed the inhibition success, but already the amplitude of the N1 component to the previous Go-stimulus. A likely explanation is that suppressed sensory processing of S1 would slow down the initiation of the movement and increase the probability of stopping successfully. Independent of this, enhanced sensory processing of S2 would speed up the inhibition process and also increase the probability of stopping successfully. Thus, both the down-modulation of the sensory processing of S1 and the up-modulation of the processing of S2 could be independent processes that the system employs with the aim of stopping successfully. Note however, that at the time when the system processes the S1 stimulus it is reasonable to generally prepare the motor execution because only 20% of the trials are Stop-trials. In the majority of the trials subjects need to initiate the movement as quickly as possible. Therefore it is highly unlikely that the differential modulations of the sensory processing of S1 and S2 are independent and unrelated. It is consequently possible that common sensory processing resources are split between the 2 stimuli presented in rapid succession. Thus, the sensory processing of S2 could be enhanced at the cost of an attenuated S1 processing. It therefore appears that in the context of a stop-paradigm with 2 stimuli in rapid succession perceptual processing of the first stimulus has to be reduced in order to favor the second stimulus.

**Source of the Neural Stop-Signal**
Even if sensory processing of S1 and S2 is of importance for the success of stopping, some process still has to signal the need of canceling the already initiated response. As mentioned above, the magnetic field response to the Stop-stimulus was much stronger for SST than for UST between 140 and 200 ms poststimulus. In addition to the sources in bilateral occipito-temporal cortex, source localization revealed sources located bilaterally in the PCG. Consequently, the activity of this source was stronger during SST. Several studies that investigated aspects of motor control have reported compatible activations in the PCG. The most direct demonstration comes from an fMRI experiment that also employed the Stop-paradigm (Li et al. 2006). There, a substantial cluster in the right PCG was activated more strongly for successful than for unsuccessful inhibition. Moreover, a number of other studies have also related PCG activation to successful motor-inhibition (Lee et al. 2001; Hester, Murphy, Garavan 2004; Garavan et al. 2006; Stevens et al. 2007). The PCG therefore appears to generally play a role in inhibiting the initiated response. The exact mechanism remains to be determined. It could either directly inhibit the motor cortex, or indirectly by influencing the sensory processing of the Stop-stimulus (Li et al. 2006). We review evidence for both notions.

The PCG comprises the Brodmann areas 23, 29, 30, and 31 (Vogt, Vogt, Laureys 2005). In general, different areas within this region have been described to have characteristics qualifying them as motor areas (Vogt et al. 1992; Picard and Strick 1996; Fink et al. 1997; Vogt, Vogt, et al. 2005). Furthermore, extensive connections to sensory and motor areas, including the primary motor-cortex (MI), have been described in different species (Shima et al. 1991; Wang et al. 2001; Shibata et al. 2004; Vogt, Vogt, Laureys 2005). In addition the PCG is directly connected to the PFC, the anterior cingulate cortex, the basal ganglia, and the spinal cord (Vogt et al. 1992; Barbas 2000; Takada et al. 2001). Injecting a tracer into the digit finger area in M1 of primates yielded strong labeling in SMA and the PCG (Shima et al. 1991). Furthermore, the PCG has also been directly linked to the control of eye movements (Olson et al. 1996; Berman et al. 1999; Pierrot-Deseilligny et al. 2004). The pattern of anatomical connections by itself suggests a role of this region in motor control. Moreover, a functional demonstration closely linking PCG to motor control has been provided by Shima and colleagues investigating monkeys (Shima et al. 1991). They described a region in the PCG with cells active during movements, whose electrical stimulation however did not lead to overt behavior. It is therefore likely that the PCG is rather involved in the monitoring of movements than in their direct execution. In this context, Li and colleagues have pointed out that a direct comparison between successful and unsuccessful stopping is not sufficient to directly relate differential effects to response inhibition (Li et al. 2006). This certainly applies to our data. Therefore, the PCG activity observed in the current work might not directly relate to response inhibition but rather reflect an attentional process that influences the success of stopping.

As reported above, PCG also has anatomical connections to sensory areas and it has recently been related to attentional processing. Most prominently, it has been related to the default mode network, whose activity is reduced during active
task-performance (e.g., Shulman et al. 1997; Raichle et al. 2001). In accordance with that, greater activity was reported for performance lapses in an attentional task (Weissman et al. 2006). Furthermore, enhanced activity during one trial in a Stop-signal task has been directly linked to failures of motor-inhibition in the consecutive trial (Li et al. 2007). In that respective trial, on the other hand, activity in PCG was larger for successful than for unsuccessful stopping (Li et al. 2006). Taken together, this indicates that the activity to the Stop-stimulus in PCG we found might indeed be related to attentional processing of that stimulus as well. We however note, that for the processing of the Go-stimulus (that was also modulated by attention as indicated by the N1 component), no estimates of activity were found in the PCG. Therefore, PCG activity might be rather related to the specific property of the Stop-stimulus of having immediate consequences on an ongoing behavior.

The present data does not entirely clarify which region is responsible for the direct inhibition of the initiated response. fMRI studies (e.g., Garavan et al. 1999; Rubia et al. 2001, 2003; Aron et al. 2007) as well as ERP research (e.g., Pliszka et al. 2000; van Bokxel et al. 2001; Schmajuk et al. 2006) relate this function to PFC activation. PFC activity that has been reported in fMRI studies has been linked to the so-called Stop-N2 component in ERP research. This component typically arises around 200 ms after the presentation of the imperative Stop-stimulus and has a topographical distribution with a minimum over the right frontal cortex. Importantly, this component has been demonstrated to be larger for successful as compared with unsuccessful stopping (Schmajuk et al. 2006). The analysis of the magnetic field in the corresponding time range in our study did not yield a clear magnetic correspondent of this component. The fact that we did not observe an analog of the Stop-N2 component has been previously associated with successful stopping (e.g., Pliszka et al. 2000; Schmajuk et al. 2006). Such a source would be difficult to detect using MEG that only measures the tangential momentum (e.g., Hämäläinen et al. 1993). Additionally, other brain areas that might not be visible with MEG such as the basal ganglia have been previously associated with successful stopping (e.g., Aron and Poldrack 2006; van den Wijdenberg et al. 2006). In summary, we suggest that the activity in the PCG is rather related to attentional processing of the Stop-stimulus, whereas stopping per se appears to be linked to the PFC.

Site of Stopping

Another central question in the research on the Stop-paradigm is where the race between the Stop- and the Go-process ends, resulting in a motor response or not. Different methodological approaches have generally led to the notion that the primary motor-cortex (M1) is a very suitable candidate (Band and van Bokxel 1999; van Bokxel et al. 2001; Coxon et al. 2006). In the present study we found robust estimates of activity in the motor cortex that were significantly reduced for SST. These findings are consistent with the idea of M1 activity reflecting the degree of response-suppression.

The activation pattern found in the motor cortex provides a very convincing demonstration of a close link between the activation of the motor cortex and the behavior in a Stop-paradigm. Indeed, in this region not only the activity is minimal during SST, but the maximum of the activity for UST is also reached earlier than for regular Go-trials (here by 36 ms). This nicely dovetails with the observation that responses are given faster in UST than in regular Go-trials (here by 38 ms). Additionally, the analysis of the onset-times revealed that during UST the motor cortex became active about 50 ms earlier than during SST or Go-trials. The estimated onset-time following very rapidly the presentation of S2 (by only 13 ms), further highlights the importance of S1 processing on the later execution vs. withholding of the response.

Top-Down Control as Reflected by Sequential Effects

Longer reaction times to simple Go-trials have been reported in previous studies, when the preceding trial was a Stop-trial (e.g., Rieger and Gauggel 1999; Li et al. 2006). Such between-trial adaptations have been suggested to reflect top-down modulations (e.g., Laming 1979; Botvinick et al. 2001; Fecteau and Munoz 2003). A response-prolongation of this kind was also observed in our behavioral data. Reaction times to Go-trials following Go-trials were significantly faster than to Go-trials following a Stop-trial. Importantly, this slowing did not depend on the success of the inhibition of the response (i.e., no difference for UST vs. SST as the preceding trial). Therefore, it probably reflects a general mechanism of conflict detection independent of error-processing.

This behavioral effect was reflected in the electrophysiological correlates of the sensory response in the respective trial. The N1 component to a Go-stimulus was larger when the preceding trial was a Go-trial than when it was a Stop-trial. This suggests that the detection of conflict leads to a strategic adaptation in order to be prepared for the next trial. This will result in an attenuated sensory response to the next stimulus, which in turn will render successful stopping more probable in that trial (if this trial turns out to be a Stop-trial). Importantly, we have demonstrated that the smaller N1 component to the Go-stimulus for regular SST was realized by actively attenuating the response to S1 as compared with both UST and Go-trials. As the N1 components for Go-trials following a Stop-trial were again attenuated, behavioral adaptation paralleled an attenuated sensory processing. Therefore, it is probable that this attenuation of sensory processing is an active process that is prepared between trials. Nevertheless, random fluctuations in attentiveness might not be completely ruled out in explaining the differential degrees of sensory processing of S1 and S2. As we have demonstrated that attenuated processing of a Go-stimulus leads to enhanced processing of the following Stop-stimulus (in the case of a Stop-trial), we suggest that this adaptation also affects the processing of the Stop-stimulus. This could, however, not be investigated in the current study, as Stop-trials were rarely followed by another Stop-trial. In general, the adaptation of sensory processing across trials can most probably be attributed to attentional mechanisms, as it has been frequently demonstrated that attention can also operate in the time-domain (e.g., Bertelson and Boons 1960; Kingstone 1992; Coull and Nobre 1998). Yet, setting up a trade-off between 2 stimuli favoring the second (that furthermore only appears infrequently) is a mechanism not described before.

Despite the independence of RT-slowing following a Stop-trial from stopping success, the underlying mechanism might be related to posterror-slowing. Interestingly, it has been proposed that posterror-slowing relies on active suppression of
the processing of the subsequent stimulus (Ridderinkhof 2002; Marco-Pallares et al. forthcoming). This active suppression is apparent in our attenuated N1 component that indexes visual processing in Go-trials following a Stop-trial. Although the present results do not speak to the origin of these adaptation processes, it is reasonable to assume they might be accomplished by PFC areas. There is abundant literature linking this region to modifications on an intermediate time-scale (i.e., either between different trials or within trials in tasks that permit a relatively late influence; e.g., Egner and Hirsch 2005; Weissman et al. 2006). Moreover, numerous demonstrations of prefrontal influence on sensory processing have been provided (Knight 1994; Barcelo et al. 2000; Miller and Cohen 2001; Egner and Hirsch 2005). Consistent with an involvement between trials, it has been demonstrated that the PFC is already active in a cue-period preceding a NoGo-trial, whereas PCG is only active within it (Hester, Murphy, Foxe, et al. 2004). Importantly, recent fMRI work indicates that stopping and adaptation processes related to posterror-slowing between trials share the same neural machinery within PFC (Marco-Pallares et al. forthcoming). This might be taken as an indication that in the case of motor control the function of PFC is at least in part to set the stage for an upcoming trial. This is accomplished by modulating the sensory processing of that trial.

Implications on Theoretical Models of Stopping

The stopping process has often been conceptualized as a race, with independent processes of going and stopping competing for earlier completion (Logan et al. 1984; de Jong et al. 1990). As this model is not a process-model it only describes the finishing times of the 2 processes, whereas it cannot give insights into the processes themselves (Logan 1994). The present results bear on the issue in 2 ways. On the one hand, we showed that the success of stopping is at least partially determined at a very early level namely already during the perceptual analysis of the Go-stimulus (S1). Therefore, the outcome of the race appears to depend at least in part on the speed of the Go-process. Additionally, the differential sensory response to S2 indicates that the Stop-process might also run with different speeds. On the other hand, it gives insights into the question at which level the race can be affected in order to adapt behavior in response to the current situation. Whereas it has been proposed that this might be accomplished through adjustment of the response-criterion (e.g., Emeric et al. 2007), the current results indicate that the race can also be influenced at the very early stage of the perceptual analysis of the Go- and the Stop-stimulus.

Taken together, a complex pattern of coordinated neural activity within and between trials emerges, that explains the performance in inhibitory motor control. Although the actual neural Stop-signal might stem from the posterior cingulate cortex or the PFC, it appears that the success of stopping depends on the allocation of attentional resources onto the Go- and the Stop-stimulus already. In SST the sensory processing of the Go-stimulus is attenuated, whereas it is enhanced for the following Stop-stimulus. The system needs to cope with the high demands of the task succeeding in only 50% to stop an initiated response. Here not only the recruitment of attentional resources but even more importantly the distribution of these resources over time appears to be crucial. In the case of the Stop-paradigm fewer resources are devoted to the sensory processing of S1 advantaging the sensory processing of S2 when stopping is successful. This appears to be the most efficient trade-off chosen by the system to reach the maximal behavioral performance. Thus, the neural mechanism of trial-by-trial strategic adaptations due to high task demands is reflected by the distribution of attentional resources over time.

Funding

Bundesministerium für Bildung und Forschung (contract no. 01GO0202) to the Center for advanced Imaging, Magdeburg; and by Deutsche Forschungsgemeinschaft (MU1311/11-3) to T.F.M within the priority program "Executive Functions."

Notes

Conflict of Interest: None declared.
Address corresponding to C. Nicolas Boehler, Leibniz Institute for Neurobiology, Brennekstr. 6, 39118 Magdeburg, Germany. Email: boehler@neuro2.medi.uni-magdeburg.de.

References

Coull JT, Nobre AC. 1998. Where and when to pay attention: the neural systems for directing attention to spatial locations and to time intervals as revealed by both PET and fMRI. J Neurosci. 18:7426--7435.

Cerebral Cortex January 2009, V 19 N 1 143


