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RESEARCH ARTICLE

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Inhibitory control of reaching movements in humans

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Abstract Behavioral flexibility provides a very large repertoire of actions and strategies, however, it carries a cost: a potential interference between different options. The voluntary control of behavior starts exactly with the ability of deciding between alternatives. Certainly inhibition plays a key role in this process. Here we examined the inhibitory control of reaching arm movements with the countermanding paradigm. Right-handed human subjects were asked to perform speeded reaching movements toward a visual target appearing either on the same or opposite side of the reaching arm (no-stop trials), but to withhold the commanded movement whenever an infrequent stop signal was presented (stop trials). As the delay between go and stop signals increased, subjects increasingly failed to inhibit the movement. From this inhibitory function and the reaction times of movements in no-stop trials, we estimated the otherwise unobservable duration of the stopping process, the stop signal reaction time (SSRT). We found that the SSRT for reaching movements was, on average, 206 ms and that it varied with the reaching arm and the target position even though the stop signal was a central stimulus. In fact, subjects were always faster to withhold reaching movements toward visual targets appearing on the same side of the reaching arm. This behavior strictly parallels the course of the reaction times of no-stop trials. These data show that the stop and go processes interacting in this countermanding task are independent, but most likely influenced by a common factor when under the control of the same hemisphere. In addition, we show that the point beyond which the response cannot be inhibited, the so-called point-of-no-return that divides controlled and ballistic phases of movement processing, lies after the inter-hemispheric transfer.

Keywords Motor control · Countermanding · Human · Reaching

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Introduction

Considerable efforts has been directed to understanding the neural system underlying the control of reaching movements, and significant advances have been made with respect to the preparation and the execution of these movements (Georgopoulos 1986, 1996; Kalaska et al. 1997; Wise et al. 1997; Caminiti et al. 1998; Graziano et al. 2002). Nevertheless, much less attention has been given to mechanisms subserving the inhibition of these movements. The ability of suppressing an impending action is a fundamental property of executive control, and the quantitative study of the inhibitory control of action was made possible with the introduction of the countermanding paradigm (Logan 1994). This paradigm is a test of a subject's ability to withhold a commanded movement in response to an infrequent stop signal. In practice, stopping becomes increasingly more difficult as the delay between go and stop signals is lengthened, and the inhibition function that describes the probability of stopping across the range of stop signal delays (SSD) can be exploited to estimate the length of time needed to cancel the commanded movement, i.e., the stop signal reaction time (SSRT).

Thus far, the countermanding paradigm has been used for studying the inhibitory control of different motor acts: eye movements (Hanes and Schall 1996; Hanes and Carpenter 1999; Cabel et al. 2000; Logan and Irwin 2000; Asrress and Carpenter 2001; Colonius et al. 2001; Kornylo et al. 2003), eye-head gaze shifts (Corneil

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and Elsley 2005), manual responses (Logan 1981; Logan and Cowan 1984), hand squeezes (De Jong et al. 1990), and simple arm movements (McGarry and Franks 1997; Kudo and Ohtsuki 1998). The results show that the race model applies equally well to all types of responses, suggesting that the inhibitory control of action obeys the same principles across effectors and/or motor systems (Logan and Irwin 2000). In the present report, we adapted the countermanding paradigm to the study of the inhibitory control of visually guided reaching movements. This new experimental approach is the first step toward our general goal of elucidating the neural basis of this executive process, in parallel to efforts directed to understanding the inhibitory control of saccadic eye movements (Hanes et al. 1998; Stuphorn et al. 2000; Ito et al. 2003; Paré and Hanes 2003).

An interesting characteristic of arm movement is how the performance of the left and right arm differs in certain motor tasks. The observation that right-handed subjects produce left-arm movements with shorter reaction times has been presented as evidence that there is a left arm advantage in the preparation of pointing and reaching movements (Velay and Benoit-Dubrocard 1999; Mieschke et al. 2001; Barthelemy and Boulinguez 2002a,b; Neely et al. 2005). This phenomenon has been attributed to a specialization of the right hemisphere for spatial processing and visuospatial attention (Mesulam 1981; Fisk and Goodale 1988; Velay et al. 2001; Barthelemy and Boulinguez 2002a). Furthermore, it has been shown that the reaction times of movements made by both left and right arms are shorter when the go signal appears in the visual field ipsilateral to the arm used by the subject (Velay and Benoit-Dubrocard 1999; Barthelemy and Boulinguez 2002b; Cavina-Pratesi et al. 2004). This asymmetry is thought to reflect the inter-hemispheric transmission of information (Bashore 1981; Marzi et al. 1991; Marzi 1999). By studying right-handed subjects making left- and right-arm reaching movements to left and right visual targets in a countermanding reach task, we wished to determine whether and how the ability to withhold a movement in response to a central stop signal is dissimilar. Given the race model assumption of independence of go and stop processes, we expected stopping ability not to be influenced by performance asymmetries related to either the reaching arm or the target position.

The countermanding reach paradigm can also shed some light onto another important issue, namely, whether the cognitive process underlying the inhibition of action is lateralized. Aron et al. (2003) have shown that human patients with highly selective lesions to the right inferior frontal gyrus (IFG) have defective stopping behavior. The SSRTs of these patients were significantly longer than controls and they correlated with the amount of damage to the right IFG. This study strongly suggests the right hemisphere as exerting a preferential inhibitory control over action. In contrast, Van der Schoot et al. (2003) found that stopping performance was better with a stop signal presented in the right visual field, thereby suggesting a major involvement of the left hemisphere in inhibitory control. Given this clear discrepancy, possibly because of differences in experimental procedures, we wished to examine further this issue.

In this report, we will show that the SSRT associated with human reaching movements is close to that found for hand key-press (Logan and Irwin 2000), but remarkably longer than that of saccades (Hanes and Carpenter 1999; Cabel et al. 2000; Kornylo et al. 2003). We will also show that humans are always faster both to execute and to withhold reaching movements toward visual targets presented on the same side of the reaching arm, even if the stop signal was always presented centrally. In addition, we will present evidence that the inhibition of reaching movement is not lateralized. Lastly, we will address how the inter-hemispheric transmission of motor signals relates to the point of no return, the moment at which the go process leaves its controlled phase, during which movement can be inhibited, to enter its ballistic phase, during which movements cannot be inhibited. As in the classic Poffenberger task (Poffenberger 1912), we found shorter reaction times when the target is presented on the same side of the responding arm (uncrossed combination) than when is presented on the opposite side (crossed combination). This extra time, the so-called crossed-uncrossed-difference (CUD), is attributed to the inter-hemispheric transmission of a signal through the corpus callosum (Marzi et al. 1991; Marzi 1999). In agreement with the findings of Cavina-Pratesi et al. (2004), we will show that the ballistic stage occurs after inter-hemispheric transmission.

A brief report has appeared previously (Mirabella et al. 2004).

Materials and methods

Subjects and apparatus

Ten right-handed subjects between the ages of 22 and 36 years (mean 27.1 ± 4.2), with normal or corrected-to-normal visual acuity were tested. Subjects' handedness was determined using the Edinburgh handedness inventory (Bryden 1977) and only participants with a homogeneous pattern of hand preference were included. Each subject completed two experimental sessions on two different days, one using the right arm and the other using the left arm. The order in which the arm was used in each session was counterbalanced across subjects.

Subjects were seated in a darkened, sound-attenuated chamber with their eyes 40 cm from a 21″ PC monitor (CRT noninterlaced, refresh rate 85 Hz, 800 × 600 resolution, 32 bit color depth) where visual stimuli were presented. Stimuli consisted of red circles (2.434 cd/m^2) of 2.5° diameter against a dark background of uniform luminance (< 0.01 cd/m^2). The PC monitor was coupled with a touch screen (MicroTouch™, sampling rate 200 Hz) for touch positions monitoring. The presentation

of stimuli and data acquisition was controlled by the CORTEX real-time control system (http://www.cortex.salk.edu) running on a PC. The temporal arrangements of stimulus presentation were synchronized with the exact presentation time of the visual stimulus determined by the monitor update rate. All subjects gave their informed consent and they were paid 5 € for each session. The experimental procedures were approved by the local ethics board and performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

Behavioral tasks

Subjects were first made familiar with the apparatus and the primary task of making reaching arm movements to visual targets. Once familiarized, the subjects performed a block of 100 go-trials (go-only task), from which we measured the mean and standard deviation of the individual's RTs in the absence of a stop signal. RT was determined as the time difference between time of the occurrence of the go signal and movement onset. After a short break, they performed the countermanding task. This task consisted of a random mix of 75% no-stop trials (Fig. 1a) and 25% stop trials (Fig. 1b). Each no-stop trial was identical to those in the go-only task and began with the presentation of a red circle at the center of the display. Subjects were required to touch it with the index finger of their reaching hand for a variable period of 500–800 ms (holding time). Then the central red circle disappeared (go signal), and simultaneously a target appeared on the horizontal plane randomly at one of two locations, either 11.3° (8 cm) to the right or the left of the central stimulus. Subjects had to perform a speeded reaching movement toward the peripheral target. The stop trials only differed from the no-stop trial by the reappearance of the central red circle, which acted as the stop signal instructing the subjects to inhibit their movements and which was presented after a variable delay, the SSD. Stop trials in which subjects successfully cancel their movements were defined as stop-success trials, while stop trials in which they fail to cancel, leaving the central position, were defined as stop-failure trials. Subjects were given feedback in the form of a tone when their responses in either no-stop or stop trials were correct.

Each subject performed a total of 1,000 countermanding trials in five blocks of 200 trials, with interleaved resting periods when requested. These experimental sessions included stop trials whose SSD values were previously determined with one or more blocks of 200 countermanding trials (mean 2.8 ± 2.2). Five values of SSD were used and they ranged from 2 to 18 units of refresh rate (or 23.6 and 212.4 ms, respectively). The

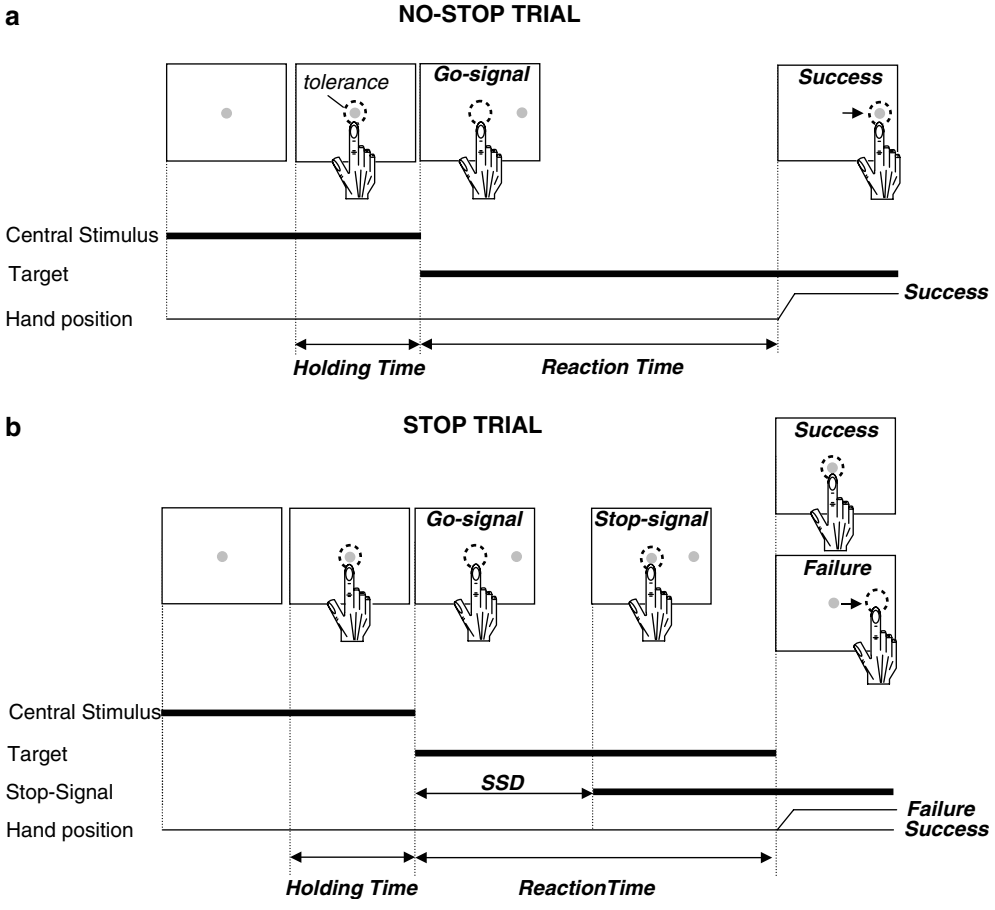

Fig. 1 Schematic of the task. Temporal sequence of the visual displays for no-stop and stop trials. All trials began with the presentation of a central stimulus. After a variable holding (500–800 ms), the central stimulus disappeared and, simultaneously, a target appeared (*go signal*) at one of two locations, either to the right or to the left of the central stimulus. In the no-stop trials subjects had to perform a speeded reaching movement toward the peripheral target within a maximum time (see Methods for further details). On a fraction of interleaved trials (25%) the central stimulus reappeared (*stop signal*) after variable delays (*SSDs*), instructing the subject to inhibit movement initiation. In these stop trials, if subjects countermanded the planned movement keeping the arm on the central stimulus the trial was scored as a success. Otherwise if subjects executed the reaching movement the trial was scored as a failure. *Dotted circle* indicates the size of the tolerance window for the touches (diameter 5°)

actual SSD values were adjusted to the performance of each subject in each experimental session so that movements were successfully inhibited in ~85% of the stop trials with the shortest SSD and in ~15% with the longest SSD. Since each subject performed two experimental sessions—one using the right arm and the other the left arm—on different days, the SSD values were adjusted separately for each arm.

Before performing the countermanding task, subjects were instructed that in some stop trials they would not be able to withhold the movement and that they should not be troubled by their performance. We stressed that the importance was to respond to the visual target as quickly and accurately as possible and not let the stop signal interfere with their performance. At the end of each countermanding block, subjects were informed about the changes in their mean RTs with respect to the mean RT obtained during the initial go-only session, and they were asked, whether necessary, to maintain the same speed level (see also Ozyurt et al. 2003). We also discourage subjects to adopt the strategy of slowing down to cancel more easily their movements by imposing an upper RT limit, defined as the mean RT of go trials during the go-only task plus five SDs. The no-stop trials with RTs higher than the upper RT were thus identified as errors during task performance, but kept for the final analysis. Finally, the peripheral target was present only for 350 ms in stop trials to give additional feedback to the subjects if they failed to cancel (Fig. 1b).

Data analysis

To quantify the inhibitory ability of each subject, inhibition functions were constructed by plotting the probability of stop-failures as a function of SSD. To derive reliable parameter estimates for the inhibition function, the data were fit with a cumulative Weibull function of the form:

$$W(t) = \gamma - (\gamma - \delta)\, e^{-(t/\alpha)\beta},$$

where t is the time after target presentation, α the time at which the inhibition function reaches 64% of its full growth, β the slope, γ the upper limit and δ was the lower limit of the function (Hanes et al. 1998). Since, by definition, the inhibition function could not assume negative values or values bigger than one, the value of γ was set to 1 and the value of δ to 0.

Results

Reaction times of reaching movements

Reaction times of reaching movements made in the no-stop trials were affected by the spatial relationship between target position and the reaching arm. Figure 2a, b contrasts the cumulative distributions of the RTs of reaching movements made by one representative subject with either arm and target. RTs of reaching movements made with the left arm were significantly shorter when directed to targets positioned in the ipsilateral hemifield (260 ± 2.2 vs. 283 ± 1.8 ms; Kolmogorov–Smirnov-test, $p < 0.0001$). The same result was obtained with the right arm (257 ± 1.7 vs. 312 ± 2.1 ms; Kolmogorov–Smirnov-test, $p < 0.0001$).

Figure 2c and Table 1 summarizes the average ($\pm$SE) RTs for reaching movements made by the ten right-handed subjects during the no-stop trials of the countermanding task to the left and right targets with their left and right arms. An analysis of variance on RTs of no-stop trials, with reaching arm and target position as factors, was performed across subjects. This analysis revealed a significant interaction between reaching arm and target position (two-way ANOVA with repeated measures, df = 9, $F = 32.5$, $p < 0.0005$), but no significant main effects (arm: df = 9, $F = 2.72$, $p = 0.13$; target: df = 9, $F = 0.85$, $p = 0.38$). Post-hoc analyses (Newman–Keuls-test) showed that subjects had significantly shorter RTs for targets presented on the same side of their reaching arm (right: $p < 0.005$; left: $p < 0.05$). In addition, right-arm reaches to targets positioned in the left hemifield had RTs significantly longer than left-arm reaches to targets positioned in either the left ($p < 0.001$) or right hemifield ($p < 0.05$). Because of the interaction between reaching arm and target position, all our analyses took into account these factors separately.

We also estimated the CUD by subtracting the mean RT of each subject in the uncrossed conditions (e.g., right arm to right target) from that obtained in the crossed combinations (e.g., right arm to left target). This measure averaged 24 ms ($\pm$4.2) and was positive in all subjects, regardless of the reaching arm, meaning that uncrossed combinations always yielded shorter RTs. Our estimate of CUD exceeds the range (8.1–15.5 ms) reported in studies of pointing movements (Velay and Benoit-Dubrocard 1999; Boulinguez et al. 2001; Barthelemy and Boulinguez, 2002a,b; Velay et al. 2002). The presumably greater cognitive load of the countermanding task, due to the unpredictable presentation of the stop signal, may explain this discrepancy. In this respect, it must be noted that the mean CUD obtained in the block of go-only trials (15 ± 4 ms) was within the range of previously reported values and significantly smaller than that obtained in the no-stop trials of the countermanding task (paired t-test, df = 9, $p < 0.05$).

Contextual influences on reaction times

Motor responses often tend to have longer RTs with the introduction of stop trials in the countermanding task (Lappin and Eriksen 1966; Ollman 1973; Logan 1981; Rieger and Gauggel 1999; Cavina-Pratesi et al. 2004). We also observed this contextual effect in our experiments. In each subject, the RTs of the reaching movements produced during the no-stop trials of the

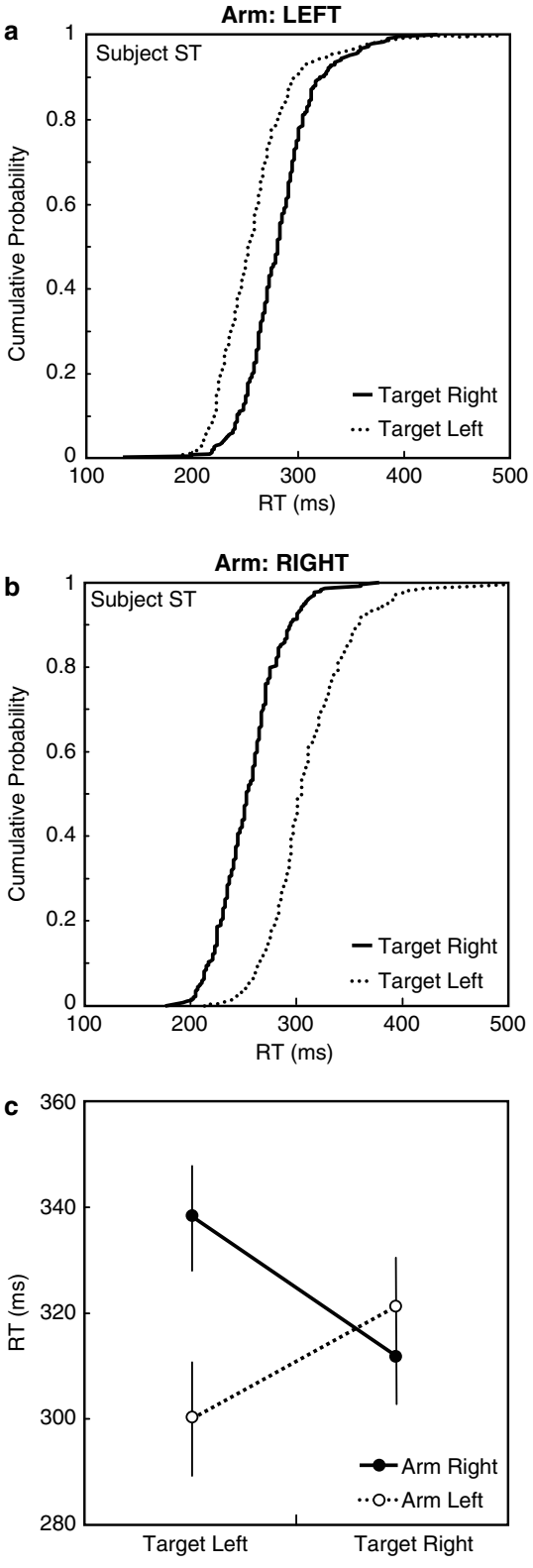

Fig. 2 Reaction times (*RTs*) of no-stop trials for reaching movements in relations to the arm used and target presentation. Panel **a** and **b** show, for an example subject, the cumulative distributions of the RTs of no-stop trials for right (*solid traces*) versus left (*dotted traces*) targets using the left and the right arm, respectively. Panel **c** shows the mean values (± SE) of RTs across all subjects ($n = 10$) for the no-stop trials in the countermanding block for either arm and target position

Table 1 Mean RTs (±SE) and percent correct of no-stop trials in the countermanding blocks across the entire population

	Mean RT		(%) Corr	
	Target right	Target left	Target right	Target left
Right Arm	311 ± 9.1	338 ± 10.5	94.5	93.0
Left Arm	321 ± 8.7	300 ± 9.7	92.9	94.8

countermanding task were significantly longer than those obtained in the initial block of go-only trials, even though our experimental design included a low probability (0.25) of stop signal trials (Logan 1994) as well as detailed instructions and continuous feedback (Ozyurt et al. 2003).

Figure 3a, b contrasts the cumulative distributions of the RTs of reaching movements made by one representative subject in go-only and no-stop trials. The RTs of both left- and right-arm movements produced in the no-stop trials of the countermanding block were significantly (Kolmogorov–Smirnov-test, $p_s < 0.0001$) longer than those observed in the block of go-only trials (left: 271 ± 1.5 vs. 232 ± 3.5 ms; right: 287 ± 1.7 vs. 241 ± 4 ms). A similar increase in RTs for either reaching arm was found to be significant ($p_s < 0.0001$) in all ten subjects. Furthermore, the amount of procrastination for the right (61 ± 4.1 ms) and left arm (76 ± 10.3 ms) was not significantly different (paired *t*-test, df = 9, $p = 0.32$).

To exclude the possible confounding effect of fatigue, we ran two of the subjects in a series of consecutive blocks of 100 go-only trials (six for the first subject, 12 for the second). The mean RTs of both subjects in the last block was significantly shorter than that obtained in the initial block (first subject: 280 ± 2.7 vs. 296 ± 2.1 ms, Kolmogorov–Smirnov-test, $p < 0.001$; second subject: 289 ± 3.2 vs. 328 ± 2.2 ms, $p < 0.0001$). Fatigue was therefore not a factor.

In addition to the global increase in RTs of motor responses in the countermanding task, the occurrence of stop trials has also been reported to have a local effect on the RTs of responses produced in the immediately following no-stop trials (Cabel et al. 2000; Botvinick et al. 2001; Jones et al. 2002; Brown and Braver 2005). Figure 4a, b shows an analysis of the influence of stop trials on the RTs of the left- and right-arm reaching movements made by one subject in the four subsequent no-stop trials. RTs in the first no-stop trial immediately after a stop trial were significantly longer than the following three no-stop trials both for the right arm (one way ANOVA, $df = 3$, $p < 0.0001$; post-hoc Tuckey–Kramer, $p_s < 0.05$) and for the left arm (one way ANOVA, $df = 3$, $p < 0.0001$; post-hoc Tuckey–Kramer, $p_s < 0.05$). The slowing effect of stop-success trials and stop-failure trials did not differ (not shown). We observed a similar sequential effect across all subjects (Table 2). An analysis of variance with RT of the no-stop trial sequence and reaching arm as factors, revealed a main effect of the reaching arm in eight subjects both

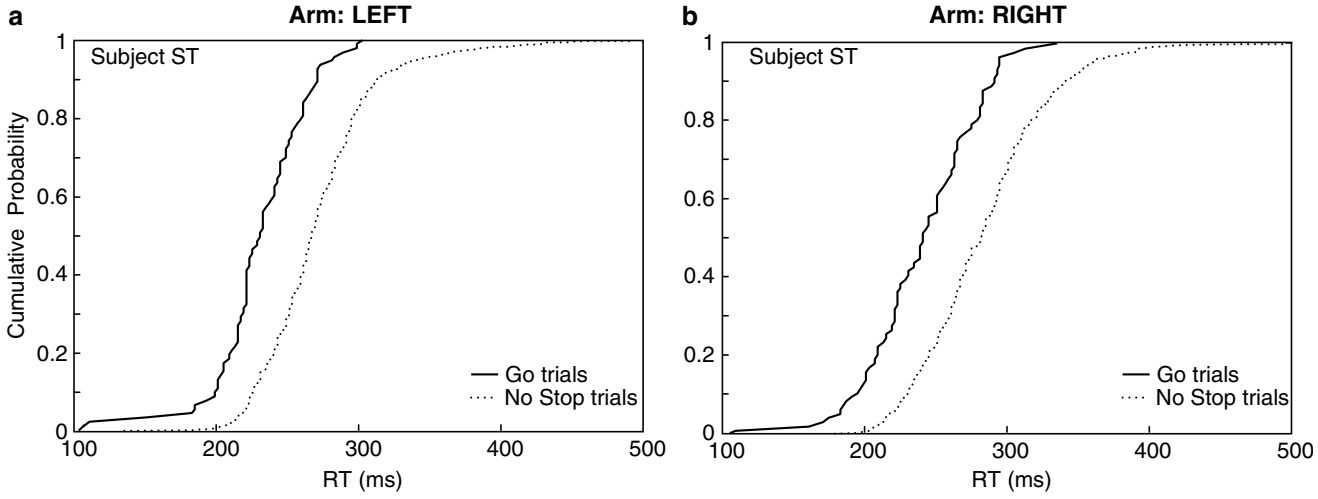

Fig. 3 Reaction times (*RTs*) for reaching movements in the go-only task and in the countermanding task. Panel **a** and **b** show the cumulative distributions of the reaction times (*RTs*) of a block of trials with (no stop trials; *dotted traces*) and without stop trials (go trials; *solid traces*) intermixed for the left and the right arm of one subject, respectively

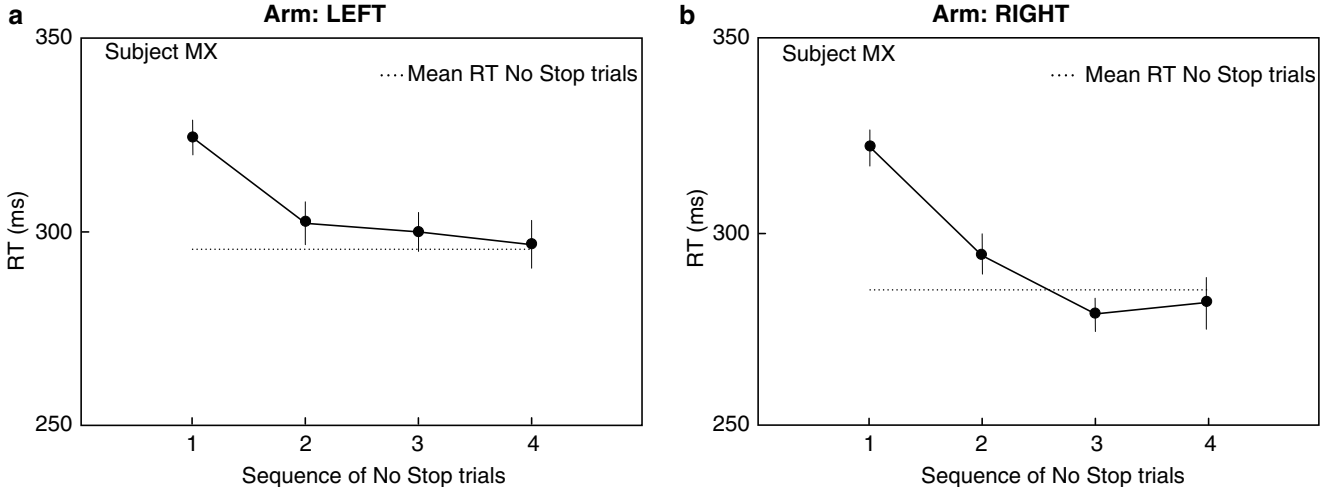

Fig. 4 After-effect of stop signal appearance in the trial sequence. Panel **a** and **b** shows the effect of a stop signal on the RTs of four consecutive no-stop trials for the left and the right arm of one subject, respectively. In each panel the *dotted line* represents the mean RT of no stop trials. The *black dots* represent the mean RT (± SE) for each category of no stop trial

after a correct and wrong stop, with the RTs of six being shorter for left-arm reaches. Most importantly, the main effect of trial sequence on RT was significant in all subjects ($p_s < 0.01$). A significant interaction between the two factors never occurred.

In order to establish the duration of the slowing effect of the stop signal we performed a post-hoc analysis on the RTs of the correct no-stop trial sequence (Newman–Keuls-tests). Separately for each subject-arm combination, we counted the number of times in which the RT of the first no-stop trial was significantly longer ($p_s < 0.01$) than that of the three subsequent trials (three comparisons were made for each subject-arm combination). In the same way we established how many times the second

Table 2 Mean RTs (± SE) of a sequence of four no-stop trials after a correct/wrong stop signal

	First no-stop	Second no-stop	Third no-stop	Fourth no-stop
RT right arm correct trials	350 ± 10.3	332 ± 9.3	322 ± 10.2	315 ± 8.8
RT left arm correct trials	337 ± 8	320 ± 10.3	309 ± 9.9	304 ± 8.2
RT right arm wrong trials	342 ± 10	324 ± 10	318 ± 9.1	316 ± 8.3
RT left arm wrong trials	328 ± 9.3	312 ± 8.8	308 ± 9.8	302 ± 8.6

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trial was slower than the third and the fourth trials in the sequence (two comparisons were made for each subject-arm combination). Finally we counted the number of times in which the third trial was slower than the fourth. Considering all combinations together, the first no-stop trial was slower that the other in the sequence 66.7% (40/60; ten subjects, two arms, three comparisons) of the cases. In contrast the second trial was slower than the third and the fourth trials in the sequence just in the 15% (6/40; ten subjects, two arms, two comparisons) of the cases, while the third and the fourth trials never differed. Similar results have been obtained for wrong no-stop trial sequence (not shown). Overall this result indicates that the effect of a stop trial was generally limited, when present, to the immediately following no-stop trial.

Behavioral estimate of reaching movement cancellation

One of the main goals of the present study was to estimate the length of time required to cancel a commanded reaching movement, the SSRT. This value cannot be measured directly but can be estimated from the behavioral performance in the countermanding task using the race model developed by Logan (Logan and Cowan 1984; Logan 1994).

In the countermanding task, the inhibition of reaching movements depended on the SSD. Subjects successfully canceled their reaching movements to a target when the stop signal was presented after a short SSD, but they increasingly failed with the lengthening of the SSD. Figure 5a, b plots the probability of not canceling a movement as a function of SSD (the inhibition function) for one representative subject reaching with the left and right arm. The three functions in each panel represent the inhibition functions for the crossed combination (e.g., right arm to left target), the uncrossed combination (e.g., right arm to right target), and both combinations pooled together. One can see that the inhibition control of this subject did not depend on the reaching arm: the probability of not canceling the reaching movements was always lowest at the shortest SSD, it increased with the lengthening of the SSD, and was highest at the longest SSD. Nevertheless, the overall ability of this representative subject to cancel a reaching movement in the uncrossed conditions was lower than in the crossed conditions.

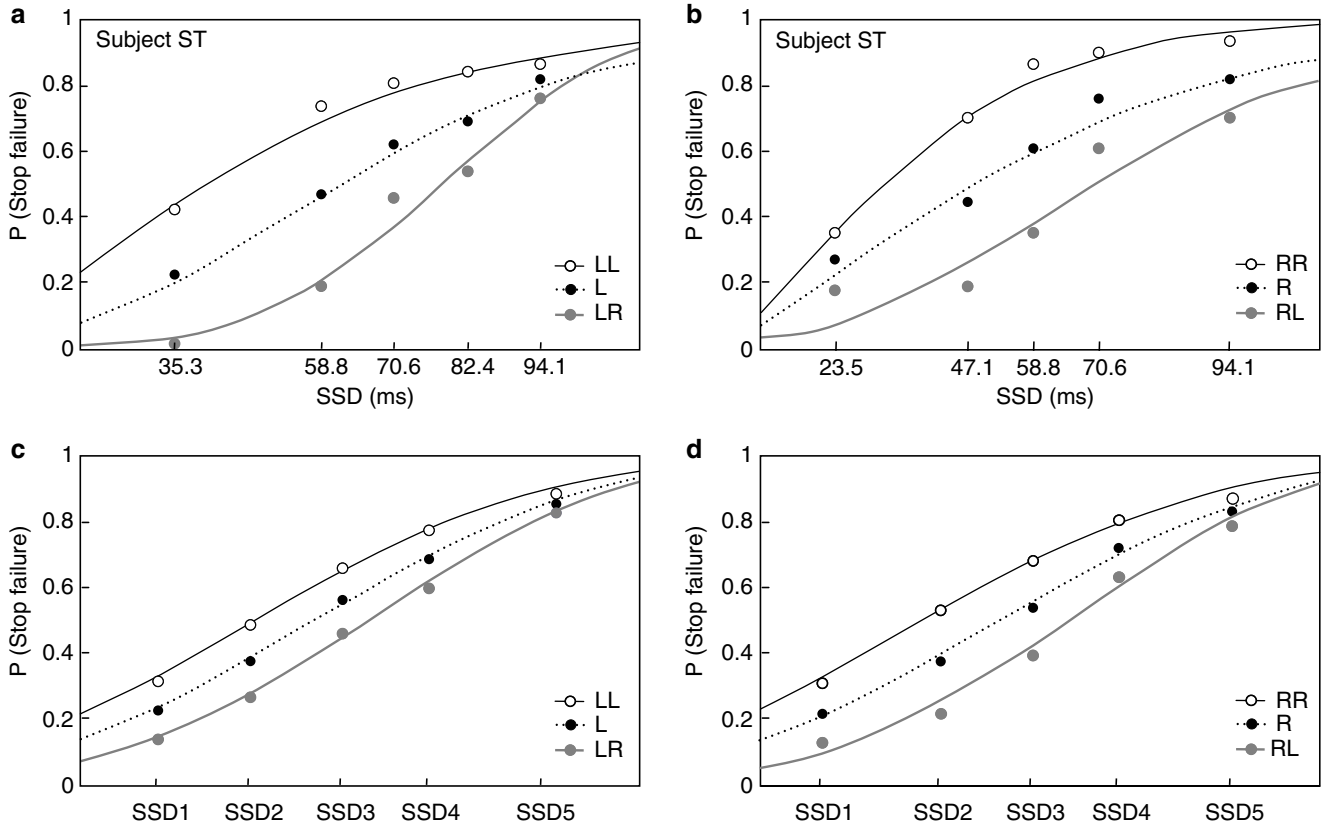

Fig. 5 The inhibition functions (*IF*), represented by the best fit of the Weibull function, (see Results for further details), for one experimental subject are shown for the left (**a**) and the right hand (**b**). In each plot the *solid grey line* represents the IF for crossed conditions, the *thin black line* the IF for uncrossed conditions and the *dotted line* both combinations pooled together. Panels **c** and **d** show the average IF across the entire population ($n = 10$) for the left and the right hand, respectively. Data from individual subjects were combined by averaging for each single SSD the probability of generating a movement even though a stop signal was presented. In all instances the probability of a stop failure increased as a function of the SSD and is consistently higher for crossed than for uncrossed stimuli. *L* left arm, *R* right arm, *LL* left arm left target, *LR* left arm right target, *RL* right arm left target, *RR* right arm right target

The population analysis showed very similar results (Fig. 5c, d). We performed a two-way-ANOVA on the probability of responding, with SSD and target positions as factors. The main effects were significant for both arms. The probability of responding increased with SSD (left arm: $df = 4$, $F = 91.6$, $p < 0.0001$; right $df = 4$, arm: $F = 81.7$, $p < 0.0001$), and its value in the crossed condition was higher than in the uncrossed condition (left arm: 0.64 ± 0.03 vs. 0.43 ± 0.04, $df = 1$, $F = 80.3$, $p < 0.0001$; right arm: 0.63 ± 0.03 vs. 0.46 ± 0.04, $df = 1$, $F = 45.4$, $p < 0.0001$). It is worthy to note that there was no statistical difference in the SSDs across arm used. For instance the mean value (± SE) of the shortest SSD for the right hand across all subjects was 83.5 ± 9.3 while that for the left hand was 70.6 ± 8.6 ($p = 0.12$ $df = 9$ paired t-test). The same holds true for the longest SSD (154.7 ± 10.25 for the right hand vs. 144 ± 10.9 for the left hand; $p = 0.32$ $df = 9$ paired t-test). Furthermore, in most cases, the SSDs of each single subject in the two experimental sessions, showed small if any differences.

Starting from the RT distributions obtained for each subject during no-stop trials (e.g. Fig. 2a, b for subject ST) and inhibition functions (e.g. Fig. 5a, b for the same subject) of each combination of arm used and target presentation, we estimated the corresponding SSRT. We used two estimation methods. The first method of estimating the SSRT assumes that it is a random variable. This estimate relies on the mathematical demonstration that the mean SSRT is equal to the difference between the mean RT during no-stop trials and the mean value of the inhibition function (Logan and Cowan 1984). We computed the mean of the inhibition function from the best-fit of the Weibull functions, $W(t)$, as follows:

$$\text{Mean of inhibition function} = \sum[(W(t) - W(t-1))\cdot t]/[W(t\ \max) - W(t\ \min)],$$

where t ranges from the minimum to the maximum stop signal delay in 1-ms intervals, while $W(t\ \max)$ and $W(t\ \min)$ represent the maximum and the minimum probabilities of responding. Overall, the Weibull function fits had a mean r^2 of 0.74 (± 0.02) and the Chi-squared test was always nonsignificant ($p_s > 0.9$). We computed the SSRT for each subjects and for each combination of reaching arm and target presentation. The average (± SE) SSRT estimated with this approach across all of the subjects was 206 ± 2.7 ms.

The second method of calculating the SSRT makes the assumption that the SSRT is a constant. Although this assumption seems implausible, its violation does not significantly alter the result of the analysis (Logan and Cowan 1984; Band 1997). By this method, the SSRT is estimated by integrating the distribution of RT in no-stop trials, beginning at the onset of the go-signal, until the integral equals the observed proportion of noncancelled trials at that SSD. This point is taken as the finishing line of the stop process, namely the longest RT possible before all reaching movements become inhibited by the stop process. The SSRT at each SSD is then equal to the difference between the finishing line and the given SSD. The mean (± SE) SSRT across all of the subjects with this approach was 208 ± 2 ms.

Since the SSRTs obtained with the two methods were not significantly different (paired t-test, $df = 9$, $p = 0.13$) in the following we will consider just the SSRT estimated with the first method because it is the one that makes the most acceptable assumption, namely, that the SSRT is a random variable. Figure 6a and Table 3 summarizes the mean values of SSRT (± SE) obtained across subjects for each reaching arm and target position.

As we proceeded previously for the analysis of RTs of no-stop trials, we explored the changes of SSRT in relation to both the reaching arm and the target position with a two-way ANOVA with repeated measures. There were no significant main effects (arm: $df = 9$, $F = 0.44$, $p = 0.52$; target: $df = 9$, $F = 1.78$, $p = 0.21$), but the interaction between the two factors was significant ($df = 9$, $F = 10.7$, $p < 0.01$). A post-hoc analysis (Newman–Keuls-test) revealed that the SSRT was significantly shorter in the uncrossed condition, i.e., when the movement was going to be made to a target positioned on the same side of the reaching arm (right arm: $p < 0.01$; left arm: $p < 0.05$). In addition, the SSRT associated with the inhibition of right-arm reaching movements to the left target was longer than that found for left-arm reaches to the same target ($p < 0.005$).

These findings closely resemble the results obtained for the RT of reaching movements. We therefore wondered whether SSRT and RT were related. Figure 6b shows that this was not the case ($r = 0.26$ $df = 38$, $p > 0.05$). Since SSRTs and RTs have a different variability (see Tables 1, 3) we transformed all scores in Z-values. However, even after this procedure the two sets of values did not correlate ($r = 0.27$, $df = 38$, $p > 0.05$; not shown), meaning that there is no linear relationship between the SSRTs and the RTs.

We also computed the CUDs of the SSRT. The average (± SE) CUD was 18 ± 3.4 ms and it was positive for all subjects, meaning that the uncrossed combinations always yielded shorter SSRTs. The CUDs associated with the SSRTs were significantly shorter than those associated with the RTs (paired t-test, $df = 9$, $p < 0.0005$). Figure 6c shows, however, that these two measures were highly correlated ($r = 0.97$, $df = 8$, $p < 0.0001$). The CUDs measured from the RTs of stop-failure trials (26.6 ± 1.1 ms) were also significantly longer than the CUDs of the SSRTs (paired t-test, $df = 9$, $p < 0.05$). These two sets of values were also linearly related ($r = 0.73$, $df = 8$, $p < 0.05$).

Figure 7a shows how variable were the inhibition functions across subjects within a single experimental condition because of the different SSDs that were chosen to account for each subject's RTs. To compensate for that subject-to-subject variability, we normalized the probability at each SSD that subjects fail to cancel successfully their reaching movements into a Z score of the relative finishing time (ZRFT; Logan and Cowan 1984) with the following expression:

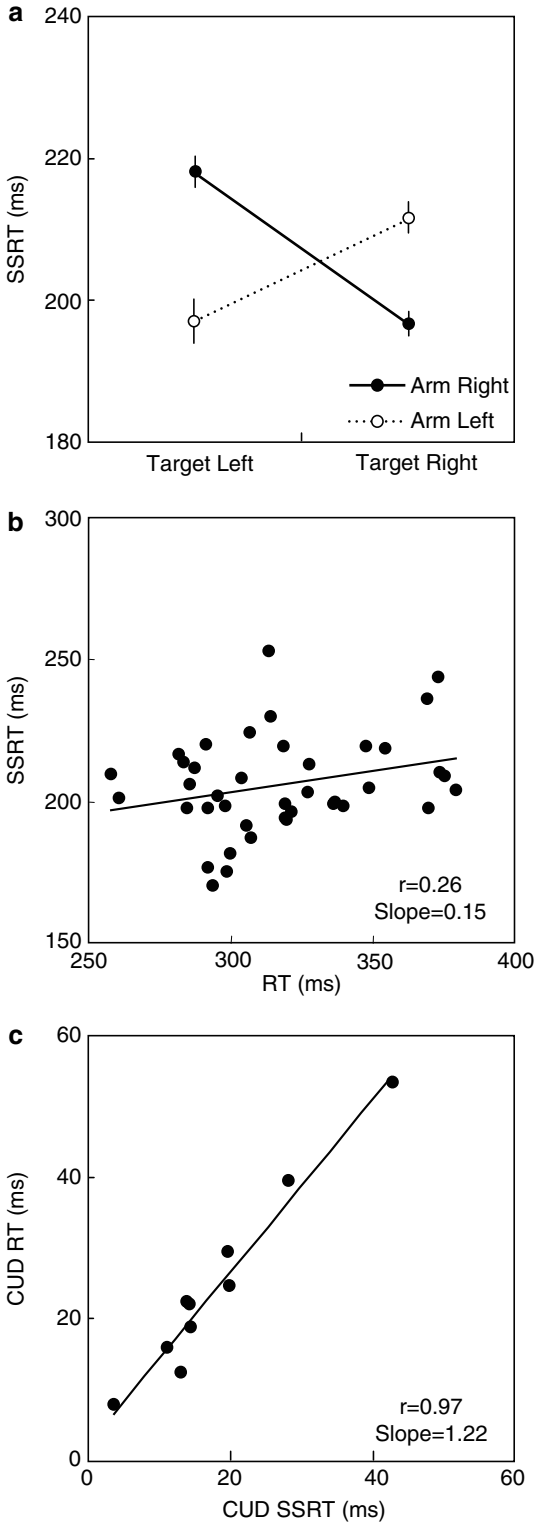

Fig. 6 Estimate of the stop signal reaction time (*SSRT*) and relationship with the reaction times (*RTs*) of no stop trials for reaching movements. Panel **a** shows the mean values of SSRTs (±SE) across all ten subjects, separately for each response arm and for each position of the target. Panel **b** shows the relationship between the RTs of no stop trials and the corresponding SSRT measured separately for each response arm and for each position of the target. Panel **c** shows the relationship between the 'crossed uncrossed difference' (*CUD*, see text for further details) of the RTs of no stop trials and that of the corresponding SSRT

Table 3 Mean SSRTs (± SE) across all subjects for each response arm and for each position of the target

	Target right	Target left
Right arm	197 ± 2.2	217 ± 3.2
Left arm	211 ± 1.7	197 ± 2.2

$$ZRFT = (RT_{no\text{-}stop} - SSD - SSRT)/SD_{no\text{-}stop}.$$

The slope of the resulting inhibition function could be taken as a measure of the inhibitory control of any experimental condition, and any differences in slopes between subjects and/or experimental conditions as evidence of distinct inhibitory processes (Logan and Cowan 1984). Figure 7b shows that, once normalized, the inhibition functions obtained in all our subjects for the right-arm-right- target condition, became closely aligned. Figure 7c shows the average slope obtained after normalization. Comparable alignment was observed in all experimental conditions (not shown). Table 4 reports the average values of the slopes of the inhibition functions across all subjects. An analysis of variance (two-way ANOVA with repeated measure) performed on the slopes of the normalized inhibition functions, with reaching arm and target position as factors, revealed that the slopes did not differ significantly (arm: $df = 9$, $F = 1.32$, $p = 0.28$; target: $df = 9$, $F = 1.05$, $p = 0.33$; interaction: $df = 9$, $F = 1.58$, $p = 0.24$). We conclude from this analysis that the process underlying the inhibition of reaching movements was the same across all conditions and subjects.

Independence of GO and STOP processes

The race model assumes that the behavioral outcome in the countermanding paradigm depends on a race between two independent processes: (1) a *go process* initiated by the go signal that can lead to the execution of the reaching movement; and (2) a *stop process* initiated by the stop signal that can inhibit the commanded movement (Fig. 8a). If the stop process is faster than the go process, the response is inhibited. If not, the response is initiated. Since the duration of the go and stop processes are both random variables the result of the race is stochastic. The proportion of stop trials in which the commanded response is successfully inhibited (stop-success trials) and in which it is not (stop-failure trials) is determined by the distribution of the finishing times of the go and stop processes (Fig. 8b). One of the central assumptions of the race model is that the go and stop processes are stochastically independent, namely, that the finish time of each process is uncorrelated with the finish time of the other process. To test whether the go and stop processes interacted, we considered how well the race model predicted the RTs of the reaching movements that escaped

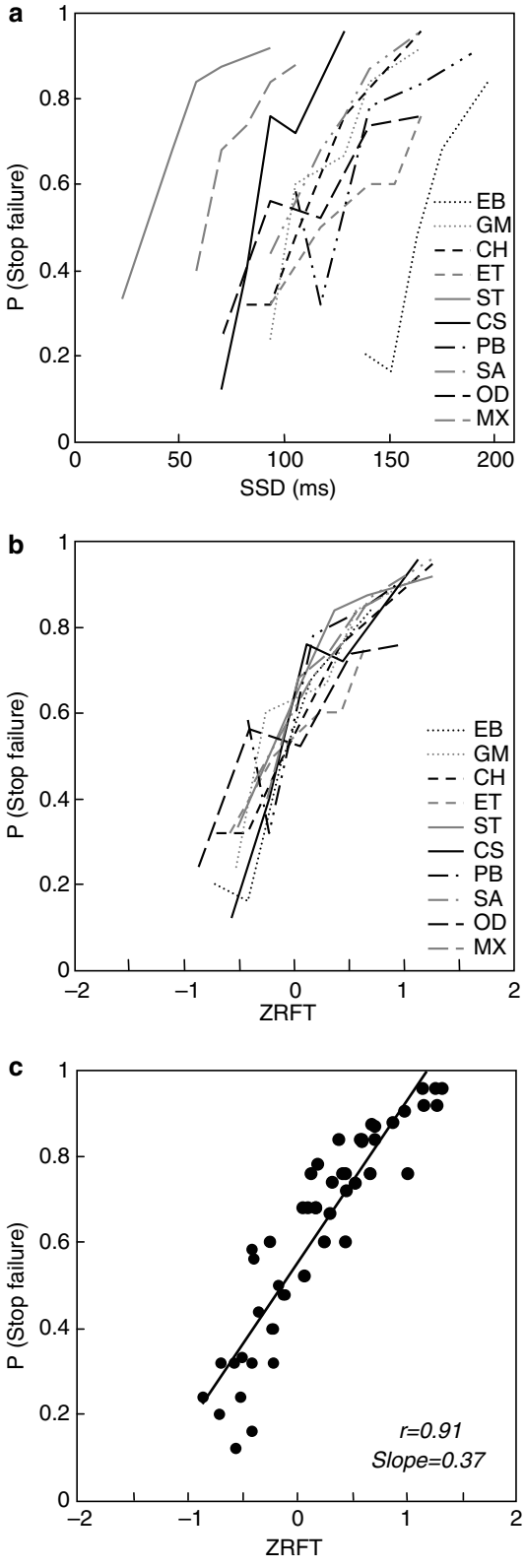

Fig. 7 Normalization of inhibition functions. Panel **a** shows the inhibition functions of each of the ten subjects obtained when they were using the right arm and the target was presented in the right hemi field. Panel **b** shows the same inhibition functions after the normalization of each stop signal delays (*SSDs*) of each subject into *Z* values of the relative finishing time (*ZRFT*). Panel **c** shows the best linear regression fit considering all data coming from the entire population

Table 4 Mean slopes (± SE) across all subjects for each response arm and for each position of the target

	Target right	Target left
Right arm	0.37 ± 0.02	0.43 ± 0.03
Left arm	0.39 ± 0.02	0.38 ± 0.04

inhibition (Logan and Cowan 1984). Reaching movements were produced in both the no-stop trials and the stop-failure trials, but the latter were initiated because the go process finished before the stop process. Therefore, considering the distribution of the RTs of the no-stop trials, the responses that escape inhibition should be those corresponding to reaching movements that had RTs shorter than the SSD plus the estimated SSRT (Fig. 8b, light region of RT distribution).

Given the above reasoning, three predictions should be satisfied (Logan and Cowan 1984; Logan 1994). First, the mean RT in stop-failure trials should never be longer than the mean RT in the no-stop trials. Second, the mean RT in stop-failures trials should lengthen with increasing SSD. Third, the mean RT in the stop-failure trials at each SSD should be equal to those predicted from the race model. Figure 9 shows that these predictions were satisfied. Figure 9a shows the cumulative RT distribution of right-arm reaches to the left target made by a representative subject. This example illustrates that the RTs in stop-failure trials (288 ± 3.3 ms) are significantly shorter (Kolmogorov–Smirnov-test; $p < 0.0005$) than the RTs in no-stop trials (306 ± 3.3 ms). From the same dataset, Fig. 9b shows that the RTs in the stop-failure trials increases as a function of SSD and that they are not significantly different from those predicted by the race model (paired *t*-test; $p_s > 0.05$).

To check if at the population level the predictions were satisfied, we used two different approaches. First of all, we considered how many times each single subject fulfilled each of the three predictions. The RTs in stop-failure trials were significantly longer than the RTs in the no-stop trials (Kolmogorov–Smirnov-test; $p_s < 0.05$) in 168/200 (ten subjects; two arms, two targets; five SSDs) cases (or 84%). In all occurrences the mean RTs in stop-failures trials lengthen with increasing SSD (one way ANOVA, $df = 4$, $p_s < 0.05$). Finally, in the 133 out of 200 (ten subjects, two arms, two targets, five SSD) cases (or 66.5%) the observed mean RTs in the stop-failure trials at each SSD ware equal to those predicted.

As a second approach we considered the population as a whole by collapsing single subjects data together. Figure 9c shows for the condition in which subjects made right-arm reaches to the left target, that the cumulative distribution of the RTs in stop-failure trials across all subjects (316 ± 1.75 ms) is significantly different (Kolmogorov–Smirnov-test, $p < 0.0001$) and shifted to the left with respect to the RT distribution obtained in no-stop trials (338 ± 0.8 ms). Furthermore,

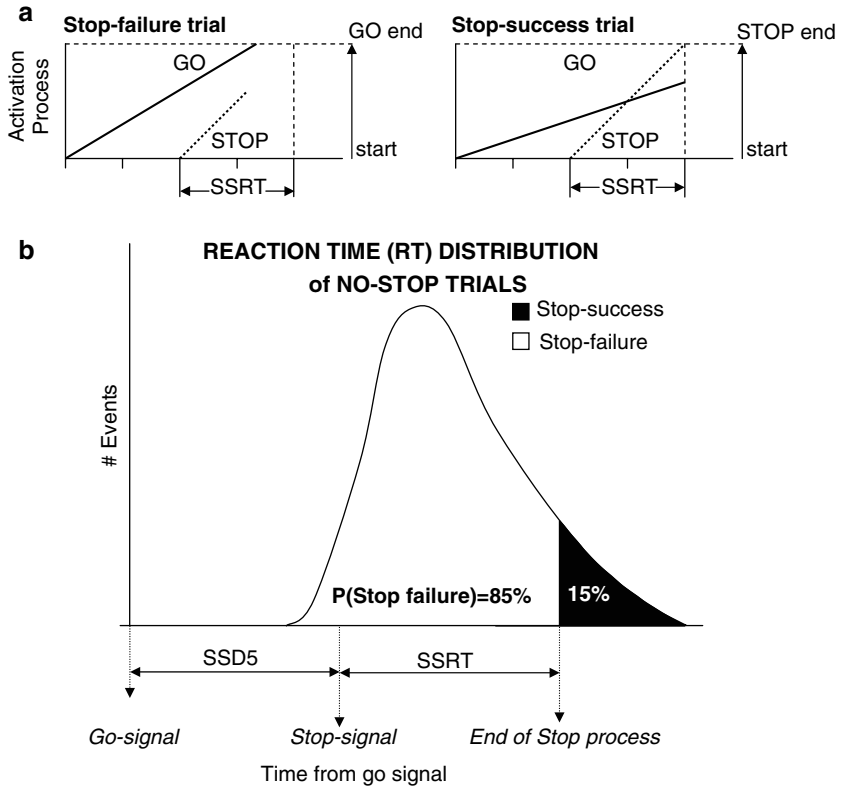

Fig. 8 Logic underlying the race model. The race model represents the performance in the countermanding task assuming that a GO process (*solid line*) independently race against a STOP process (*dotted line*) toward their respective threshold (*broken horizontal line*). The GO and STOP processes are initiated by the presentation of the target and the stop signal, respectively. In no-stop trials, only the GO process is active, and a movement is generated when the GO process finishes. In stop trials, since the stop signal is always presented at variable delays (*SSDs*) after the go signal, the STOP process begins after the GO process has begun. In all instances in which the GO process finishes before the STOP process, the reaching movement is not cancelled (**a**, *left*) and vice versa (**a**, *right*). The time it takes to respond the stop signal is the stop signal reaction time (*SSRT*). In **b** the predictions of the outcome of the race between STOP and GO process for the longest SSD (SSD5) are shown. Considering a hypothetical distribution of the RTs of the no-stop trials, the responses that escape inhibition should be those corresponding to reaching movements that had RTs less than the SSD5 plus the estimated SSRT. In our design, the longest SSD should be such that the subjects could inhibit the movement just 15% of times (*dark region of distribution*)

as shows in Fig. 9d, with the only exception of the shortest SSD, RTs in the stop-failure trials increases significantly along with the SSD (one way ANOVA, $df = 4$, $F = 101.5$, $p < 0.0001$). It has been already shown that at the shortest SSD this prediction can be violated probably because of the very few stop-failure trials (Logan and Cowan 1984; Logan 1994). Similar results were obtained in the other three experimental conditions.

A further evidence of the independence between the go and stop processes comes from the comparison between the CUD values measured for the RTs in the no-stop trials of the countermanding task (when only the go process is activated) and the corresponding values measured for stop-failure trials. If stop-failure trials represent instances in which the responses escaped inhibition, than the CUD in both situations should not differ. In agreement with this prediction, the CUD measured from the stop-failures trials was not significantly different from the CUD measured from no-stop trials (27 ± 3.4 vs. 24 ± 13.4 ms; paired *t*-test, $df = 9$, $p = 0.53$).

Discussion

Using the countermanding paradigm, we showed that the length of time needed for human subject to cancel their reaching movements is about 200 ms. This estimate, however, varies as a function of the reaching arm and target position: subjects always took less time to cancel their reaching movements toward visual targets appearing on the same side of their reaching arm, the same condition that led to shorter reaction times. This new form of spatial compatibility is interpreted as a consequence of the existence of a common factor influencing both the go and the stop processes.

Inhibitory control of reaching movements

Our behavioral estimate of reaching movement cancellation averaged 206 ms, a value close to that reported for manual key presses in several experiments (see for review Logan 1981; Logan and Cowan 1984), but much

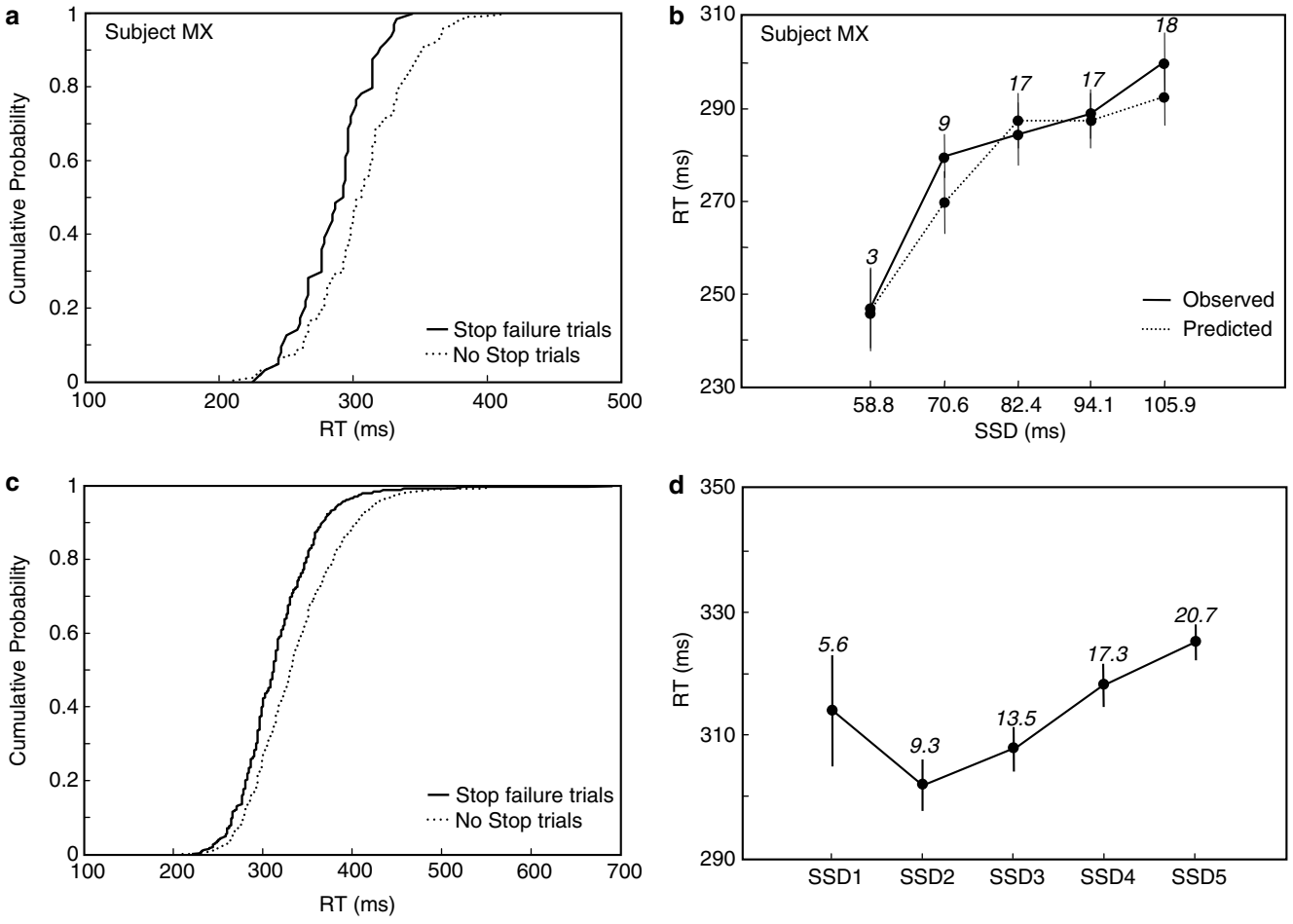

Fig. 9 Independence of go and stop processes. Panel **a** and **c** show the cumulative distributions of the reaction times (*RTs*) of no-stop trials versus that of stop failures trials across all stop signal delays (*SSDs*), for a subject (**a**) and for the entire population (**c**; $n = 10$), respectively in the condition in which they were using the right arm and the target was presented in the left hemi field. The cumulative distribution of the RTs of stop-failure trials is significantly shifted to the left respect to that of the no stop trials in both cases. As far as the population is concerned, the cumulative distributions were obtained by collapsing together the single RTs of no stop- or stop failure-trial of all subjects. Panel **b** shows the actual versus the predicted reaching movement latencies for stop-failure trials in the same subject and condition of **a**. *Vertical bars* at each data point indicate one standard error of the mean. The numbers above the data points indicate the number of stop failure trials at each SSD. The mean values of the RTs of stop-failure trials across all ten subjects are shows in **d**. These values were obtained by collapsing together the single RTs of stop failure trials of all subjects separately for each SSDs. The numbers above the data points indicate the mean number of stop failure trials at each SSD

longer than cancellation estimates (100–150 ms) obtained for saccadic eye movements (Hanes and Carpenter 1999; Cabel et al. 2000; Kornylo et al. 2003). Could the processes inhibiting the production of eye and arm movements be different?

Although our experimental design was comparable to that of Hanes and Carpenter (1999), we cannot address this issue directly because eye movements were not simultaneously recorded. Logan and Irwin (2000) did, however, study the inhibitory control of eye and hand movements under identical conditions. In their experiment subjects were instructed to respond to visual stimuli either with an eye movement or by pressing a key. They found a significant difference between ocular and manual SSRT estimates, a result they interpreted as supporting the hypothesis that separate processes, governed by common principles, inhibit eye and hand movements. One important detail overlooked by this study is that SSRT estimates include the duration of the ballistic phase of movement processing (Logan and Cowan 1984). This is because SSRTs are computed from the reaction times of the no-stop trials, which encompass both controlled and ballistic processes. Differences between SSRT estimates could therefore not only be due to different inhibitory processes at play but possibly to differences between the ballistic processing of ocular and hand movements. If we assume that the ballistic processing of arm movements is longer than that of eye movements, then the controlled processing could be identical and possibly under the control of the same inhibitory process. This hypothesis is, however, mitigated by reports indicating that the point of no return occurs very late in the processing of manual responses (Osman et al. 1990) and that such movements can even be

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inhibited after muscle activation (De Jong et al. 1990) and initiation (Kudo and Ohtsuki 1998). These observations question whether controlled and ballistic processes in the programming of skeletomotor movements can be distinguished. It is, however, possible that reaching inhibition does not entail only the suppression of centrally generated motor commands but that it can also operate (during the ballistic process of the central programming) to suppress issued commands at the level of the periphery (De Jong et al. 1990). These peripheral inhibitory processes may thus participate, downstream of the motor plan, in the online adaptive control of movements that is becoming well documented (e.g., Desmurget and Grafton 2000). Determining whether the reaching SSRT we estimated is longer than the ocular SSRT because of a longer ballistic phase of central motor processing will necessitate further investigations with neurophysiological methods.

An alternative to the hypotheses described above is that the differing ocular and reaching SSRTs obtained with very similar experimental designs arise from differences in the organization of the respective motor systems. In the case of saccade inhibition, a foveally presented stop signal could be sufficient to directly suppress the motor commands of saccade-related neurons in frontal eye field (Hanes et al. 1998) and superior colliculus (Paré and Hanes 2003) via the activation of local neurons with fixation-related activity. Such a local inhibitory network has not been described within the neural system involved in the production of reaching movements. It is thus plausible that reaching inhibition simply requires longer time because the stop process initiated in response to the foveal stop signal can only exert its suppression of central motor commands through rather indirect pathway.

Neural basis of inhibitory control

The neural substrates underlying the countermanding of reaching movements have not been explored. Neural activity involved in the inhibitory control of arm movement has only been studied using the Go/No-Go paradigm. In this paradigm, neurons whose activity was related to the decision to move or not to move have been found in both premotor (Kalaska and Crammond 1995) and motor (Miller et al. 1992; Port et al. 2001) cortices of primates. However, there is an important difference between the countermanding and the Go/No-Go task. In the former, the signal for inhibiting the movement is presented after the go signal, while in the latter the stop signal precedes the go signal. Therefore in the countermanding task it is an ongoing response that has to be inhibited, in the Go/No-Go task it is a potential movement. Likely the neural activity in the two tasks could be very different. It is not clear what are the motor areas involved in regulating the initiation of reaching movements. A good candidate is the dorsal premotor area (PMd) because of the strong presence of set-related activities (Wise 1985; Johnson et al. 1996) involved in the preparation to make the movement and because of the existence of a direct projection to the spinal cord (Dum and Strick 1996). The observation that reaching movements become more impulsive and uncontrolled after lesion of the premotor cortex (Moll and Kuypers 1977) suggests that this cortical area may exert a role in reaching inhibition. Another possibility is that reaching inhibition could involve the primary motor cortex, the main source of movement-related activity to the spinal cord. It would be interesting to compare the discharge properties of motor cortex neurons in the countermanding task with the known properties of neurons within saccade executive centers (Hanes et al. 1998; Paré and Hanes 2003). Other motor areas, including the supplementary motor areas and the cingulated areas of the frontal lobe could be also involved on signaling conflicts and error situations similarly to what observed for the countermanding saccade task (Stuphorn et al. 2000; Ito et al. 2003; Curtis et al. 2005). Finally, different prefrontal areas could be involved at different levels as suggested by the numerous studies in humans (Liddle et al. 2001; Rubia et al. 2001; Watanabe et al. 2002; Aron et al. 2003; Hasegawa et al. 2004).

A new form of spatial compatibility

We found unexpectedly that reaching SSRT depended on which arm was used and within which visual hemifield the target fell. As far as reaching movements is concerned, it is well known that reaction times are shorter when a target is presented on the same (uncrossed) side of the reaching arm than when it is presented on the opposite (crossed) side (Marzi et al. 1991; Velay and Benoit-Dubrocard 1999; Velay et al. 2001; Barthelemy and Boulinguez 2002b; Cavina-Pratesi et al. 2004). This phenomenon most certainly results from the organization of the visual and motor pathways, i.e., each hemifield is represented in the contralateral hemisphere and each arm is controlled by the contralateral hemisphere. Processing would be speeded up when limited to a single cerebral hemisphere in the uncrossed situation, and the necessary inter-hemispheric transfer of information would slow down processing in the crossed situation. In our study, every single subject reacted significantly faster in the uncrossed situation rather than in the crossed one, and no significant difference was observed between left and right arm. We thus found no evidence for any asymmetry in the production of reaching movements.

Because we designed our experiment with a stop signal that was presented at the fovea and did not possess any spatial attribute, we did not expect to find a difference in SSRT between the two different experimental conditions (crossed versus uncrossed). Our prediction rose from the consideration that the stop signal most likely reaches both hemispheres at the same time and, in principle, it should have been equally effective in eliciting the

inhibitory process independently from the arm used and the side of target presentation. The variation in SSRTs paralleled those seen for the RTs of no-stop trials, as if the two processes interacted. In fact, subjects were always faster to withhold as well as to execute reaching movements toward visual targets appearing on the same side of the employed arm. We additionally showed that SSRTs and RTs of no-stop trials were not significantly correlated, but that the SSRT CUD was related with the RT CUD of both the no-stop trials and stop-failure trials. Reaching inhibition thus covaried with the primary task. This observation suggests that the stop and go processes are independently influenced by a common factor. A similar phenomenon was reported by Van den Wildenberg et al. (2002), who concluded that changes in response readiness during a countermanding task equally affected the primary and the secondary task. Logan and Cowan (1984) referred to this type of interaction as functional, not stochastic, dependence and therefore it does not represent a violation of the assumptions of the race model.

How could the go and stop processes be concurrently affected? If the ballistic phase of movement processing in both crossed and uncrossed situation is assumed to be identical, then the duration of the controlled phase of movement processing in the crossed situation must be longer because of the added inter-hemispheric transfer. As a consequence, the probability of stopping would be higher, which is indeed what we observed. Consistent with observations made by Cavina-Pratesi et al. (2004), the point of no return thus likely occurs after the inter-hemispheric transmission.

Since our data confirm the independence of stop and go processes, it is very likely that these two processes are independently influenced by a common factor. What could be the factor affecting both the go and the stop processes? A possible candidate could be the time of the arrival of the go signal to the hemisphere, which control the arm movement. It is assumed that, in stop tasks, subjects continuously monitor for the presence of stop signals by maintaining a tonic readiness for inhibiting movements while responding to the primary task to maximize the number of correct responses to stop trials (Lappin and Eriksen 1966; Ollman 1973; Logan 1981; Kramer et al. 1994; Douglas 1999; Rieger and Gauggel 1999; Cavina-Pratesi et al. 2004). Inhibition is, however, very likely to change during the course of a trial, being maximal just after the presentation of the go signal because the likelihood of a stop signal presentation is highest exactly after this event. As a consequence, the late arrival of the go signal to the hemisphere recruited in the crossed condition would cause a delay both in the movement initiation and in the movement inhibition, resulting in the lengthening of the SSRT. Our results thus extend the current view about spatial compatibility: whenever a single hemisphere is recruited for stimulus detection, response production, and response inhibition, all these processes are faster.

As for movement initiation, we found no clear evidence that movement inhibition is lateralized. The two other studies that have addressed this question have reached contradictory conclusions. On the one hand, Aron et al. (2003) reported that patients with lesions restricted to the right IFG are impaired in their inhibitory control, putting this process under the control of a right-lateralized neural system. On the other hand, Van der Schoot et al. (2003) reported that inhibitory control is enhanced when stop signals are presented in the right visual hemifield, suggesting a left-lateralized neural system. Since the latter study is the only one that has used lateralized stop signals, its results demand to be replicated, especially because they seem to be related more to the processing of the stop signal rather than response inhibition per se. Differences between our results and those of Aron et al. (2003) may also be due to different experimental settings. Subjects in this study responded with both hands and manual key presses instead of single-hand reaching movements. There is nevertheless some indication, albeit not reaching statistical significance, of hemispheric asymmetry in our study, namely that the SSRT for right arm reaching movement toward targets presented to the left side were the longest among the four experimental conditions. Further studies are definitely needed to fully explore this issue.

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