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CONTEXTUAL RESPONSE TIME ADAPTATION IN THE COUNTERMANDING PERFORMANCE OF RATS

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Abstract—Humans and non-human primates are known to lengthen their response time (RT) to a go signal when they occasionally must cancel their responses following a stop signal in a countermanding task as well as to adjust their RT adaptively on a trial-by-trial basis. Less is clear regarding the adaptive RT adjustments in the countermanding performance of rodents. To investigate this question, male Wistar rats (*N* = 12) were trained with food reward to press a lever directly below an illuminated light (go signal), but to countermand the lever press subsequent to a tone (stop signal) presented infrequently (25% of trials) at variable delays. Rats were then tested in a standard responding task (0% stop trials) or a countermanding task with a 10-s or 1-s TO interval following errors. Rats exhibited significant RT lengthening in the countermanding task, compared with the standard responding task, and RT shortening following consecutive correct go trials. They also show RT lengthening following both error trials in the standard responding task and unrewarded, non-canceled stop trials in the countermanding task. RT lengthening following erroneous stop trials was observed in sessions with a 10-s TO interval, but not with a 1-s TO interval. Analyses of RT distributions suggest that RT lengthening results largely from reduced sensitivity to the go signal, but also from reduced readiness. These findings indicate that rats exert control in the countermanding task by lengthening RT in anticipation of stop trials to avoid long, unrewarded TO intervals.

Key words: stop-signal, timeout interval, response adjustment, post-error slowing, performance monitoring, proactive slowing.

INTRODUCTION

The countermanding task was designed to investigate behavioral inhibition as a measure of executive function, the cognitive abilities that allow organisms to make flexible and goal-directed decisions in a changing and dynamic environment (Lappin and Eriksen, 1966; Verbruggen and Logan, 2008b). The task requires inhibition of a primary, pre-potent response following an infrequently presented stop-signal. Logan and Cowan (1984) developed a horse-race model of countermanding behavior, positing that go and stop signal presentation initiates independent neural go and stop processes respectively, which race toward a threshold whereby the first process to cross the threshold wins the race and determines the behavioral outcome. One important aspect of the race model is that it permits estimation of the amount of time required to inhibit a response, the stop signal response time (SSRT), a measure that is not directly observable. The race model has been verified to account for countermanding task behavior in humans (Hanes and Carpenter, 1999), non-human primates (Hanes and Schall, 1995; Hanes et al., 1998; Paré and Hanes, 2003) and rats (Beuk et al., 2014).

Performance monitoring, the rapid adjustment of ongoing behavior in an effort to optimize performance, has also been investigated as an instance of executive function in the countermanding task (Rabbitt, 1966; Schachar et al., 2004). Humans and non-human primates adaptively adjust their response time (RT) on a trial-to-trial basis during countermanding task performance depending on trial and performance history. For example, humans exhibited RT shortening following consecutive go trials and RT lengthening following a stop trial (Enticott et al., 2009; Boehler et al., 2011; Thakkar et al., 2011; Bissett and Logan, 2012; Corneil et al., 2013; Chang et al., 2014). While some studies have demonstrated greater RT lengthening following canceled stop-trials (Cabel et al., 2000; Emeric et al., 2007), others have reported more RT lengthening following non-canceled stop trials or errors (Li et al., 2008; Thakkar et al., 2014). Non-human primates have similarly been observed to shorten go-trial RT after consecutive go trials and lengthen RT following a stop trial (Kornylo et al., 2003; Nelson et al., 2010). Non-human primates have typically demonstrated greater RT lengthening following canceled than non-canceled stop trials (Emeric et al., 2007; Pouget et al., 2011; but see Chen et al., 2010). Evidence of adaptive RT adjustments has brought into question the notion that neural go and stop processes

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Abbreviations: ANOVA, analysis of variance; CV, coefficient of variation; RT, response time; SD, standard deviation; SE, standard error of the mean; SSD, stop-signal delay; SSRT, stop signal response time; TO, timeout.

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responsible for countermanding task behavior are entirely independent, prompting recent development or updating of modeling accounts (Boucher et al., 2007; Matzke et al., 2013; Logan et al., 2014). Importantly, neither the context independence (the assumption that the RT distribution is the same for both go and stop trials) nor the stochastic independence (the assumption that RT and SSRT are independent for each given trial) of the race model is violated if RT is adjusted in the same manner regardless of whether upcoming go or stop trials are predicted (Verbruggen et al., 2013).

For rodents performing the countermanding task, Bari and Robbins (2013) reported adaptive RT adjustments in the form of shorter go-trial RT following failed stop trials, contrary to the adaptive RT adjustments witnessed in human and non-human primates. Alternatively, Beuk and colleagues (2014) demonstrated significant go-trial RT shortening after consecutive go trials and RT lengthening following non-canceled, but not canceled stop trials for rats performing the countermanding task. Similarly, Mayse and colleagues (2014) demonstrated RT shortening after consecutive go trials and RT lengthening following failed, but not successful stop trials. One key inconsistency among rodent countermanding tasks has been the length of the timeout (TO) interval that occurs following errors, which has varied from 0 to 10 s for rats but is very short or non-existent in human and non-human primate countermanding experiments. A longer TO interval could lead to less post-error slowing, as inhibitory after-effects or conflict monitoring activity may decrease with longer inter-trial intervals (Rabbitt and Rodgers, 1977; Rieger and Gauggel, 1999; Emeric et al., 2007). On the other hand, rats have been observed to actively avoid long timeout periods (Richardson and Baron, 2008). Therefore, a longer TO interval should increase post-error slowing by shifting goal priority to caution over speed (Bissett and Logan, 2011).

Humans have been observed to adjust response time in the countermanding task in comparison to a standard responding task or when go-related stimuli indicate a 0% likelihood of stop signal presentation by lengthening RT (Lappin and Eriksen, 1966; Rieger and Gauggel, 1999; Akerfelt et al., 2006; Mirabella et al., 2006; Chikazoe et al., 2009; Zandbelt et al., 2013). Non-human primates have similarly displayed longer responding in the countermanding task as opposed to a standard responding task (Stuphorn and Schall, 2006). It has been suggested that humans strategically slow responses to increase the likelihood of successful performance in the expectation of a stop signal (Verbruggen and Logan, 2008a). It is not known whether rats lengthen their responses in the countermanding task when compared to a standard responding task.

The primary goal of the present experiment was to investigate the underlying behavioral nature of adaptive RT adjustments of rats performing the countermanding task. We hypothesized that similar to humans and non-human primates, rats would proactively and strategically lengthen their responses in countermanding sessions compared to a standard responding task. We further hypothesized that rats would exhibit RT shortening after consecutive go trials and post-error slowing in the countermanding task when presented with a 10-s TO interval, but that adaptive RT adjustments would be attenuated in sessions with a 1-s TO interval. Findings supportive of these hypotheses would suggest that rats exhibit adaptive RT adjustments in the countermanding task in order to prioritize either caution and accuracy or speed depending upon performance history and task demands. The similarities or differences in human and rat adaptive RT adjustments have important implications regarding the application of rodent countermanding as a model of behavioral control.

EXPERIMENTAL PROCEDURES

Animals

Male Wistar rats (N = 12) were bred by Charles River Laboratories (St. Constant, QC) and weighed 150–250 g at the start of training. Animals were approximately 5 months of age at the time of testing. Subjects were kept in an environmentally controlled colony room with a reversed 12-h light–dark cycle (lights off at 0700 h). Rats were pair-housed in clear plastic cages (50.0 × 40.0 × 20.0 cm high) with woodchip bedding (Beta Chip; Northeastern Products Corp., Warrensberg, NY, USA). Food (LabDiet 5001; PMI Nutrition Intl, Brentwood, MO, USA) was restricted (see procedure), while water was freely available in the home cage. All animal care and experimental protocols were approved by the Queen's University Animal Care Committee and were in accordance with the guidelines of the Canadian Council on Animal Care and the Ontario Animals for Research Act.

Apparatus

Four identical operant chambers (30.5 × 24.1 × 21.0 cm high; ENV-008, Med Associated Inc., St. Albans, VT, USA) were employed for data collection. Each chamber was enclosed in a sound-attenuating cubical (55.9 × 40.6 × 55.9 cm high) with 1.9 cm thick wood composite walls and a ventilation fan. Operant chambers contained a transparent polycarbonate door, rear wall and ceiling. The floor consisted of stainless-steel parallel rods (0.5 cm diameter) separated by a 1.0-cm gap. On both side walls of each chamber, 2 aluminum vertical posts divided the wall into 3 panels. On 1 side wall, the far panel housed a 2.8-watt incandescent house light that was 1.0 cm below the ceiling and 5.0 cm above a tone generator, which emitted a tone with a chamber-specific frequency ranging from 2400 to 3400 Hz at an intensity of 75 dB. The middle panel included a food pellet receptacle (5.1 × 5.1 × 2 cm deep) 3.0 cm above the grid floor. Dustless precision food pellets (45 mg) from Bio-Serv (Frenchtown, NJ; product number: F0021) were delivered into the food pellet receptacle from a pedestal mounted pellet dispenser housed outside the chamber. On the opposite side wall, each of the 3 panels was identically outfitted with a 2.5-cm diameter LED stimulus light located 4.5 cm below the ceiling and 5.0 cm directly

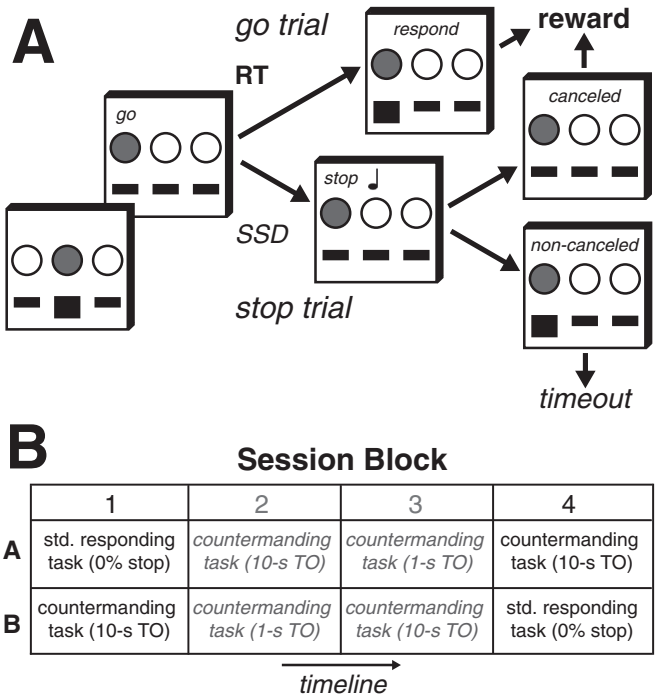

Fig. 1. (A) In the countermanding task, trials were initiated by a center lever press (indicated by the black square), which immediately illuminated the light above the left or right lever, acting as the go signal. In go trials (75%), rats were required to press the lever directly below the illuminated light within a time limit (1.0–1.4 s) to receive food reward. The amount of time between lever presses was recorded as the response time (RT). In stop trials (25%), a tone, acting as the stop signal, was presented following a varying stop-signal delay (SSD) from go signal onset and instructed rats to cancel the lever press for food reward. Non-canceled lever presses (or incorrect go-trial responses) resulted in a timeout (TO) interval. (B) Male Wistar rats were assigned to 2 groups, A ($n = 6$) and B ($n = 6$), to be tested in 4 blocks with 3 consecutive test days per block and 1 or 2 days off before the next test block was administered. In the first block, group A was tested in a standard responding task (1 h) that consisted of 0% stop trials, whereas group B was tested in the countermanding task (1 h) with a 25% stop trials (10-s TO interval) following incorrect responses. For data analysis, these sessions were combined with sessions from the fourth block, in which group A was tested in the countermanding task and group B was tested in the standard responding task (black comparisons). In the second block, group A was tested in the countermanding task (1 h) with a 10-s TO interval following incorrect responses, whereas group B was tested in the countermanding task (1 h) where incorrect responses resulted in a 1-s TO interval. For data analysis, these sessions were combined with sessions from the third block, in which group A was tested in the 1-s TO interval version of the countermanding task, whereas group B was tested in the 10-s TO interval version of the countermanding task (gray comparisons).

above a retractable response lever (4.8 × 1.7 × 1.3 cm thick). Programing and data analysis were controlled by MED-PC® IV software (Med Associated Inc.).

Procedures

Food and water were initially available *ad libitum*. For days 3–7, rats were handled in pairs for approximately 5 min/day. On the 7th day, food access was restricted to 1-h of free-feeding/day for the rest of the experiment.

Following 2 days of food restriction, animals were behaviorally shaped in 30-min sessions to make a lever press for sucrose pellet reward on a fixed-ratio 1 schedule until the behavior was acquired. The behavioral acquisition criterion for all training sessions was correct responding on $\geqslant$80% of the final 100 trials in a session. Following lever press acquisition, rats were trained in once-daily 60-min sessions to press only the lever directly below an illuminated light-emitting diode stimulus light to receive sucrose pellet reward until criterion was reached. Finally, rats were trained in once-daily 60-min sessions to withhold lever press responding in the presence of a tone (acting as the stop signal) in order to obtain sucrose pellet reward. See Beuk and colleagues (2014) for a more detailed description of the training methods.

Countermanding sessions (60 min) included random presentations of 75% go trials and 25% stop trials, as displayed in Fig. 1A. In countermanding sessions, the house light was always illuminated except during TO intervals (see below). To begin all trials, animals were required to press the center lever, directly below the illuminated center light. Immediately following a center lever press, the center light was turned off and the light directly above either the left or right lever was randomly illuminated, acting as the go signal. This signal indicated the lever below the illuminated light as the target lever. The amount of time the target lever was active was restricted to a time limit that was previously established for each individual rat in countermanding task training to eliminate approximately the slowest 10% of responses (1.0–1.4 s). This time limit was imposed to encourage fast responding.

In go trials, rats were required to press the target lever before the end of the time limit to receive the reward. Go-trial RT was recorded as the elapsed time from center to target lever press. The response was considered incorrect if the target lever was not pressed within the time limit, or a non-target lever was pressed. Incorrect

responses resulted in a 10-s TO interval, whereby all lights in the chamber, including the house light, were turned off. In stop trials, a tone, acting as the stop signal, was presented following a predetermined stop-signal delay (SSD) from go signal onset for the length of the time limit plus an additional 300 ms. The stop signal instructed subjects to countermand a lever press to receive reward. Lever presses during stop trials resulted in a 10-s TO interval, whereby all lights in the chamber, including the house light, were turned off. A 5-s intertrial interval was presented before the start of each trial.

Countermanding sessions initially began with a SSD of 100 ms. SSD was adjusted throughout the session by a staircase procedure with 100-ms steps. That is, on the subsequent stop trial within a session, SSD lengthened by 100 ms if a lever press was correctly inhibited or shortened by 100 ms if a non-canceled lever press was made on the current stop trial. This procedure achieved approximately 50% stop trial inhibitions. If a lever press occurred on a stop trial before the SSD, the trial was recorded as a non-canceled response and SSD was reduced by 1 step; however the animal was rewarded as if it had correctly performed a go trial and no TO interval occurred. Immediately prior to all countermanding task sessions, rats completed training blocks of 10 go trials followed by 10 stop trials with a trial time limit of 1.5 s. Subjects were trained until they could consistently meet performance criteria (SSRT > 50 ms, > 100 total trials, < 30% go-trial errors) in countermanding task sessions. From the start of lever press training to test sessions, approximately 62 training sessions were conducted for each animal over 10 weeks.

Following training, rats were randomly assigned to 2 groups (A and B) and tested in a counterbalanced design with 4 blocks of 3 consecutive test days with 1–2 off days between blocks, as illustrated in Fig. 1B. Overall, all rats were administered 3 consecutive 1-h test sessions for each of: 1) the countermanding task described above with a 10-s TO interval following incorrect responses compared to a standard responding task consisting of 100% go trials; and 2) the countermanding task with a 10-s TO interval following incorrect responses compared to the countermanding task with a brief 1-s TO interval following incorrect responses.

Data analysis

SSRT was estimated with the integration method, derived from Logan and Cowan's (1984) horse-race model of stop-task performance, which was recently validated in rats (Beuk et al., 2014). The mean of the peaks and valleys of each SSD run and midpoint of every second SSD run were averaged to estimate the SSD where the probability of making a non-canceled response was 0.5 (Levitt, 1971). The distribution of go-trial RT was then integrated until it was equal to the RT where the probability of making a non-canceled response was 0.5. As illustrated in Fig. 2A, SSRT can be estimated as this instant (i.e., the end of the stop process) minus the SSD where the probability of making a non-canceled response was 0.5 (i.e., the beginning of the stop process). Behavioral data were analyzed to confirm race model predictions of countermanding task performance in order to validate SSRT estimations (for a more complete description, see Logan, 1994; Beuk et al., 2014). Briefly, race model predictions were tested, namely that non-canceled responses that escape inhibition on stop trials: 1) Should be shorter than responses made in go trials on average

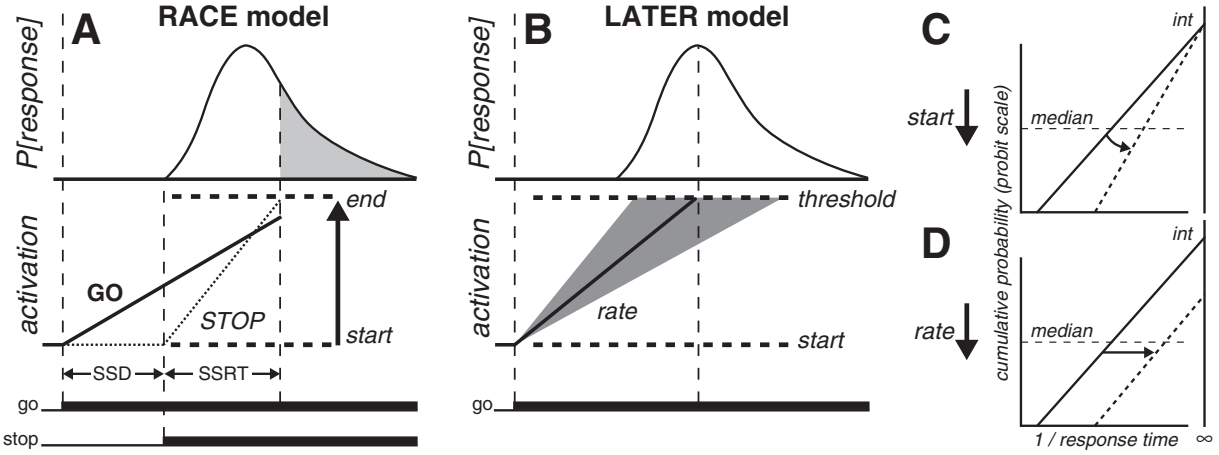

Fig. 2. (A) The race model of countermanding performance (Logan and Cowan, 1984) proposes that independent go and stop processes, initiated by a go and a stop signal respectively, race toward a finish line, whereby the first process to cross it wins the race and determines the behavioral outcome. Assuming that stop signal response time (SSRT) is constant, SSRT can be estimated by integrating the RT distribution from go trials until the integral equals the point at which a response would be canceled (i.e., the end of the stop process) given a particular stop signal delay (SSD). (B) The LATER model proposes that a process rises from an initial, start level at a linearly rate to a threshold level, at which point the response is initiated. The rate of rise varies randomly from trial to trial in a Gaussian manner, thus yielding a response distribution that is skewed to the right and a reciprocal that is Gaussian. (C, D) Reciprobit plots showing how linear is the distribution of response time when the cumulative distribution is plotted on a probit scale as a function of the reciprocal of response time. These linear curves intersect the P[*response*] = 0.5 ordinate at the median response time and their intercept is when they cross the t = infinity axis. Changes in parameters of the LATER model produce distinctive changes in RT. Lowering the start level (or increasing the threshold) causes the curve to swivel about a fixed intercept, whereas lowering the rate shifts the curve horizontally without a change of slope. Both changes produce longer RT.

because the stop signal should truncate the RT distribution when presented, and 2) should lengthen with increasing SSD, because more responses can gradually escape inhibition as the stop signal is delayed.

The Inhibition Function for each session represents the number of non-canceled responses at each SSD divided by the total number of stop trials at that SSD. To account for the potential that failed go responses were represented in the proportion of correctly inhibited stop trials, the inhibition probability data were corrected using a procedure modified from Tannock and colleagues (1989): $Y = (X - O)/(N - O)$, where for a given SSD, Y is the corrected proportion of non-canceled stop trials, X is the observed number of non-canceled stop trials, N is the total number of stop trials and O is the proportion of omissions that occurred on all go trials.

As in Beuk et al. (2014), we excluded individual sessions where animals did not display at least an increase of 0.5 in their inhibition function as SSD increased, as this is a prerequisite of correct countermanding task performance (cf. Kapoor and Murthy, 2008). Individual sessions were also omitted from analysis if they did not meet behavioral criteria (i.e., < 100 total trials, > 30% go-trial errors, SSRT < 50 ms) any of which are suggestive of improper task performance (e.g., Ghahremani et al., 2012). If SSD increased by more than 2 consecutive steps later in 1-h sessions and did not normalize, all trials following the initiation of the run were excluded from analysis, as increased SSD later in sessions may be indicative of decreased motivation or attentiveness and lead to notable SSRT miscalculation (Verbruggen et al., 2013).

We analyzed RT distributions with reciprobit plots and interpreted those with the LATER model (Linear Approach to Threshold with Ergodic Rate) of Carpenter and colleagues (Carpenter and Williams, 1995; Reddi and Carpenter, 2000; Reddi et al., 2003). This model builds on the recinormality of RT. In response to a go signal, a process is activated and rises linearly from an initial start level until it reaches a final threshold level, at which point the response is initiated (Fig. 2B). The typically skewed RT distribution is simulated by having the rate of rise of this process varying randomly between trials in a Gaussian fashion. As a result, the RT distribution is recinormal when the cumulative RT distribution is plotted on a probit scale as a function of the reciprocal of RT. Such recinormal distributions can then be fit with a linear regression model and quantified by its three parameters: slope, intercept and median RT (Fig. 2C, D). The median RT is when these linear curves intersect the P[*response*] = 0.5 ordinate and the intercept is when they cross the t = infinity axis. Characteristic changes in RT can be related to distinct changes in the three variables of the LATER model, also related to three fundamental decision variables: prior probability or readiness (start level; Carpenter and Williams, 1995), criterion (threshold; Reddi and Carpenter, 2000; Reddi et al., 2003), and information supply or sensitivity to go signal (rate of rise; Reddi et al., 2003). In brief, changes in either the start or threshold level causes the recinormal curve to swivel about a fixed intercept, whereas changes in the rate of rise shifts the curve horizontally without a change of slope.

Once each RT distribution was plotted on reciprobit plots, we fitted the data within the 10th percentile to the 90th percentile of the distribution, because data from the tails tend to vary somewhat idiosyncratically. The parameters of the best-fit linear regression model (median RT, intercept, slope) were then analyzed separately and differences between experimental conditions assessed with paired *t*-tests. We also conducted multiple regression analyses to assess the relationship between the changes in median RT observed between conditions $[(RT_1 - RT_2)/RT_2]$ and the changes in intercept and slope.

In the countermanding vs. standard responding task comparison, countermanding sessions were omitted from analysis for containing < 100 trials (1/36 = 2.8%), SSRT < 50 ms (5/36 = 13.9%) and go-trial errors > 30% (11/36 = 30.6%) while standard responding task sessions were omitted for > 30% go-trial errors (6/36 = 16.7%) and equipment malfunction (1/36 = 2.8%). This necessitated the removal of 28 total sessions (38.9%), leaving 9 or 10 animals for subsequent investigation; 1 animal produced adequate countermanding task performance but not standard responding task performance and could therefore only be included in countermanding task-specific analyses.

In the 10-s vs. 1-s TO interval study, 10-s TO sessions were omitted from analysis for containing < 100 trials (3/36 = 8.3%), SSRT < 50 ms (3/36 = 8.3%) and go-trial errors > 30% (4/36 = 11.1%) while 1-s TO sessions were omitted for exhibiting < 100 trials (1/36 = 2.8%), SSRT < 50 ms (3/36 = 8.3%) and > 30% go-trial errors (4/36 = 11.1%). This resulted in the omission of 18 total sessions (25%) and 1 rat, allowing 11 rats to subsequently be examined.

The ratio of the standard deviation (SD) to the mean of the RT distribution was calculated as the RT coefficient of variation (CV) (Bellgrove et al., 2004). If an animal met criteria on more than 1 session for any particular testing condition, overall mean number of trials per session, go-trial RT, CV, go-trial errors and SSRT were averaged from the means of all valid sessions within that testing condition for that subject.

Adaptive response adjustments were computed in the countermanding task from blocks of 3 consecutive trials where correct go trials started and ended sequences interleaved with either: 1) a correct go trial, 2) a non-canceled stop trial or 3) a canceled stop trial. Three trial sequences where correct go trials started and ended sequences interleaved with an incorrect go trial were computed from the standard responding task, as substantially more instances of these 3 trial sequences were observed in these data sets. RT varied substantially among different animals; therefore the adjustments in RT were standardized for each individual trial sequence by computing a Z-score: $Z = [\,go2RT_{(trial)} - go1RT_{(mean)}]/go1RT_{(SD)}$.

For each rat, the response adjustments and Z-scores from each session within a particular testing condition were combined with the other sessions from that condition to determine overall mean RTs and Z-scores. Rats were excluded from RT adjustment analysis if less

than 4 instances were observed for any of the interleaved trial sequences within a particular analysis. This occurred for 1 rat in the 10-s vs. 1-s TO interval comparison and 1 rat from the countermanding task analysis in the countermanding vs. standard responding task study.

In theory, estimated adaptive response adjustments could be biased if an animal displayed differences in response speed for the two go-trial choice directions and the proportion of go-trial choice directions following a particular interleaved trial type was not equal. To account for this possibility, we computed Z-scores for sequences of 3 consecutive trials where the first and third trials of the sequence were correct go trials that were in the same choice direction. This was done separately for left and right go trials. Left and right Z-score distributions were then combined into one distribution of same-direction Z-scores. Same-direction Z-scores from each session within a particular testing condition were combined with other sessions from that condition to determine overall mean same-direction Z-scores. Rats were excluded from same-direction Z-score analysis if less than 4 instances were observed for any of the 3 interleaved trial sequences, leaving 9 animals for subsequent analysis in the 10-s vs. 1-s TO interval study and 9 or 8 animals for subsequent analysis in the standard responding task or the countermanding task respectively.

Stop trials in which animals made the go response before stop signal presentation were recorded as non-canceled stop trials for estimation of SSRT, as the inclusion of these instances is important in the formation of full inhibition functions. Alternatively, these particular trials were omitted from the analysis of adaptive RT adjustments, as these instances appeared to the animals to be correctly performed go trials. For all sessions that were analyzed, the mean (±SE) proportion of non-canceled stop trials in which a response was made before stop signal presentation compared to all non-canceled stop trials was 0.31 ± 0.02.

Countermanding task performance variables were calculated with custom written MATLAB scripts (The MathWorks Inc., Natick, MA, USA). Paired samples *t*-tests were conducted to analyze differences in go-trial RT, errors, CV and SSRT. Analysis of Variance (ANOVA) was conducted to analyze adaptive RT adjustments. Follow-up paired samples *t*-tests compared the average RTs and Z scores for each adaptive response adjustment interleaved trial sequence. Statistical analyses were conducted with SPSS software (IBM SPSS Statistics for Windows, Armonk, NY, USA). Partial eta squared ($\eta p2$) and Cohen's *d* were used to estimate effect sizes (Cohen, 1988). For within-subjects tests, the effect size was corrected for dependence among means (Morris and DeShon, 2002; Eq. 8). All analysis was conducted using a significance level of 0.05.

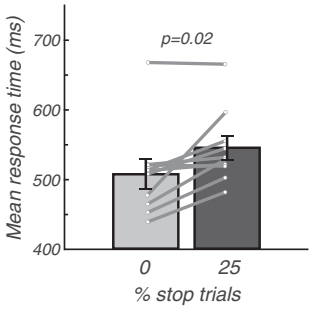

Fig. 3. Performance in standard responding and countermanding tasks. Mean (±SE) go-trial RT for 9 rats performing 1-h sessions of either the standard responding task (0% stop trials) or the countermanding task (25% stop trials). Gray lines show data from individual rats.

RESULTS

Influence of stop-trial presence

Total number of trials. The overall average (±SE) number of total trials performed within 1-h sessions did not differ significantly for rats ($n = 9$) during performance of standard responding task (314 ± 19) or countermanding task (336 ± 18) sessions (paired samples *t*-test, $t(8) = -1.00$, $p = 0.35$, Cohen's $d = 0.33$).

Go-trial accuracy and RT. Mean proportion (±SE) of go-trial errors for rats ($n = 9$) when comparing performance in countermanding (0.12 ± 0.02) and standard responding task (0.13 ± 0.02) sessions did not differ significantly (paired samples *t*-test, $t(8) = 0.38$, $p = 0.71$, Cohen's $d = 0.13$). As Fig. 3 illustrates, animals exhibited significantly longer mean go-trial RT in the countermanding task in comparison to the standard responding task (546 ± 18 vs. 507 ± 23 ms; paired samples *t*-test, $t(8) = -2.85$, $p = 0.02$, Cohen's $d = 0.99$). The average (±SE) CV of within session go-trial RT did not differ significantly for rats between countermanding (0.29 ± 0.02) and standard responding task (0.29 ± 0.03) performance (paired samples *t*-test, $t(8) = -0.22$, $p = 0.83$, Cohen's $d = 0.08$).

Go-trial RT distributions. The mean number of go trials across all available sessions for the 9 rats for which we could make that comparison was 255 (SD 65). Fig. 4A, illustrates the distributions of go-trial RT in standard responding and countermanding sessions from one rat. Each RT distribution was additionally projected on a reciprobit plot (Fig. 4B). Data within the 10th percentile to the 90th percentile of the distribution were fitted with a linear regression model, captured by the three parameters of the best-fit model: its slope, intercept and the median RT. The R^2 of these best-fit functions averaged 0.98 (range 0.84–1.0). We took the weighted average of these parameters across all available sessions in each rat. Fig. 4C shows the average median RT observed in the standard responding task plotted against that in countermanding task; these were found to be statistically different (486 vs. 524 ms; paired *t*-test, $p = 0.02$, $d = -0.58$). Fig. 4D, E, plot the corresponding average intercepts and slopes. The average intercepts were found to decrease significantly (5.0 vs. 5.7; $p < 0.001$, $d = 0.71$), but no significant change was found in the average slopes (2.6 vs. 2.7

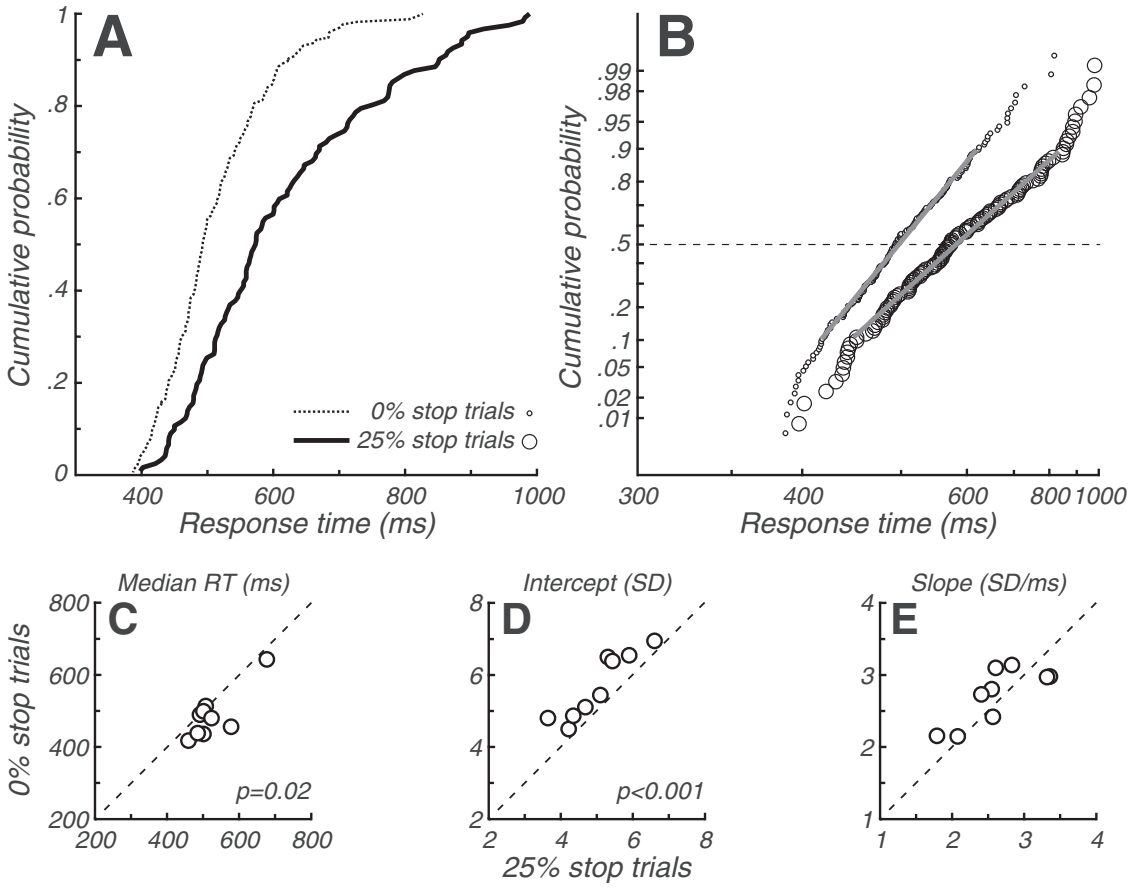

Fig. 4. Cumulative distribution (A) and reciprobit plot (B) of go-trial RT observed in one rat performing the standard responding task (0% stop trials) and the countermanding task (25% stop trials). Data within the 10th percentile to the 90th percentile of the distribution were fitted with a linear regression model. The distribution was captured by the three parameters of the best-fit model: median RT, intercept and slope. Average median RT (C) intercept (D) and slope (E) observed for the 9 rats in the standard responding task are plotted against that observed in the countermanding task.

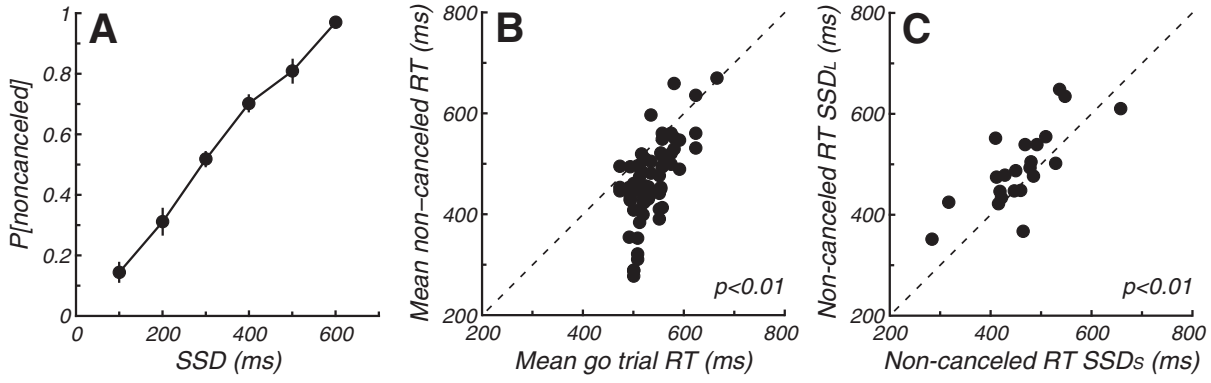

Fig. 5. Inhibition functions in the countermanding task (25% stop trials). (A) Average (±SE) probability of non-canceled responses as a function of the stop signal delay (SSD). Data are shown from 10 rats across 22 sessions. Following the race model predictions, mean non-canceled RT in a session was shorter than mean go-trial RT (B), and RT of non-canceled stop trials with long SSD (SSD_L) was longer than non-canceled RT at short SSD (SSD_S) in the same session (C).

SD/ms; $p = 0.37$, $d = 0.2$). These results suggest that the increase in RT observed between standard responding and countermanding sessions is primarily related to a decrease in the intercept of the linear best-fit functions. Such a change would be predicted by a decrease in the rate of rise in the LATER model (see Fig. 2D), which is interpreted as reduced sensitivity to the go signal. Indeed, a multiple regression analysis revealed that the change in median RT between standard responding and countermanding sessions was

significantly related to the change in intercept and slope (R^2 = 0.89, F = 24.3, p = 0.001) with the following weights: −0.95 (change-in-INTERCEPT), 0.74 (change-in-SLOPE) and 0.016. The sizeable weight of the change-in-SLOPE suggests that the increase in RT that we observed in the countermanding task would be better accounted for by a decrease in both the rate of rise and the start level in the LATER model. In other words, longer RT would result from lower sensitivity to the go signal as well as lower readiness.

Inhibition functions. From each countermanding task session, we also generated an inhibition function from the corrected proportions of non-canceled responses made on stop trials. Fig. 5A shows the average function across tested sessions (N = 22). These proportions spanned nearly the whole range (mean 0.86, SD 0.15, range 0.54–1) and increased significantly with increasing SSD for all rats (n = 10; χ^2 test, p < 0.01). The nearly perfect monotonicity of the inhibition function demonstrates that rats were sensitive to the stop signal, a prerequisite for the application of the race model. Across sessions, the lowest proportions of non-canceled responses averaged 0.12 (SD 0.15) and were observed at SSDs ranging from 100 to 200 ms (mean 118, SD 39). The highest proportions averaged 0.98 (SD 0.06) and were observed at SSDs ranging from 400 to 800 ms (mean 564, SD 85).

Race model compliance and SSRT estimates. We tested race model predictions of countermanding task performance for rats (n = 10) with data from SSDs having at least 6 trials. To determine whether responses that escaped inhibition on stop trials were generally shorter than go-trial responses, the mean non-canceled RT of a particular SSD in each session was compared to overall mean go-trial RT for that session (N = 67 comparisons). As displayed in Fig. 5B, non-canceled RTs were found to be significantly shorter than their corresponding mean go-trial RT (paired t-test, p < 0.01). They were shorter in 90% (60/67) of the comparisons. The mean (±SD) of these RT differences was 69 ± 62 ms. There was on average 11 trials for each SSD that was tested.

To test whether responses that escaped inhibition on stop trials lengthened as SSD increased, within each session we compared the average of the mean non-canceled RT observed in two consecutive SSDs (SSD*long*) with the average of the mean non-canceled RT observed at the immediately shorter two SSDs (SSD*short*), each weighted by the number of trials for each SSD. Combining two SSDs allowed better RT estimates and all sessions to have two mean RTs from at least 6 trials for comparison. As displayed in Fig. 5C, we found that the mean non-canceled RTs at the longer SSDs were significantly longer than those at the corresponding shorter SSDs (paired t-test, p = 0.005). They were longer in 77% (17/22) of the comparisons. The mean ± SD of these RT differences was 33 ± 55 ms. There were, on average, 18 trials for each SSD doublet (min 10, max 32).

For rats that met criteria in the countermanding task sessions that were conducted in the standard responding task comparison blocks (n = 10), mean (±SE) SSRT was estimated to be 258 ± 23 ms.

Adaptive response adjustments. Mean go-trial RT beginning and ending each interleaved trial type for rats (n = 9) performing the countermanding task are illustrated in Fig. 6A. The mean (±SE) number of 3-trial sequences observed were 254 ± 27 for go, 41 ± 4 for canceled and 28 ± 4 for non-canceled interleaved trials. A two-way ANOVA, with interleaved-trial type and go trial as factors did not reveal any significant main effects or interactions. Since it was expected that rats would provide evidence of RT adjustments, planned paired-samples t-tests compared mean RT for go trials prior to and following each interleaved trial type. Overall, animals demonstrated significant mean RT shortening following correct go trials (t(8) = 2.37, p = 0.045, Cohen's d = 0.79) and significant mean RT lengthening following non-canceled stop trials (t(8) = −2.29, p = 0.05, Cohen's d = 0.77). A significant difference was not found for go-trial RT recorded immediately preceding and following canceled stop trials (t(8) = −0.79, p = 0.45, Cohen's d = 0.26).

Mean adaptive RT adjustment Z-scores are displayed in Fig. 6B for each individual animal, along with the average across animals. A one-way ANOVA with the 3 different interleaved trial types as the dependent variable did not reveal a significant main effect (F(2,16) = 2.91, p = 0.08, η_p^2 = 0.27); however, the 7% shortening in mean Z across three consecutive go trials was significantly different from 0 (one-sample t-test, t(8) = −2.73, p = 0.03, Cohen's d = −0.91). The 29% mean Z lengthening following non-canceled stop trials just failed to reach statistical significance (t(8) = 2.14, p = 0.07, Cohen's d = 0.71). The change in mean Z following a canceled stop trial was not statistically significant (t(8) = 1.13, p = 0.29, Cohen's d = 0.38).

To ensure that a difference in response speed to either go choice would not bias RT adjustments, we computed Z scores for the change in go-trial RT following correct go, canceled stop, or non-canceled stop interleaved trials where the first and third correct go trials of the sequence were both in the same direction. The mean (±SE) number of 3-trial sequences observed for rats (n = 8) when the two go choice directions were the same were 132 ± 15 for go, 22 ± 2 for canceled and 16 ± 2 for non-canceled interleaved trials. A one-way ANOVA with the 3 different interleaved trial types as the dependent variable revealed a significant main effect (F(1.06,7.45) = 9.50, p = 0.02, η_p^2 = 0.58). A post hoc pairwise comparison with Sidak adjustment revealed that the main effect was driven by a significant difference in mean (±SE) Z shortening (−0.09 ± 0.03) following go trials and lengthening (0.92 ± 0.26) following non-canceled stop trials (p = 0.03). The 9% shortening in RT across three consecutive go trials when the go choice direction was the same was significantly different from 0 (one-sample t-test, t(7) = −2.84, p = 0.03, Cohen's d = −0.95). The 92%

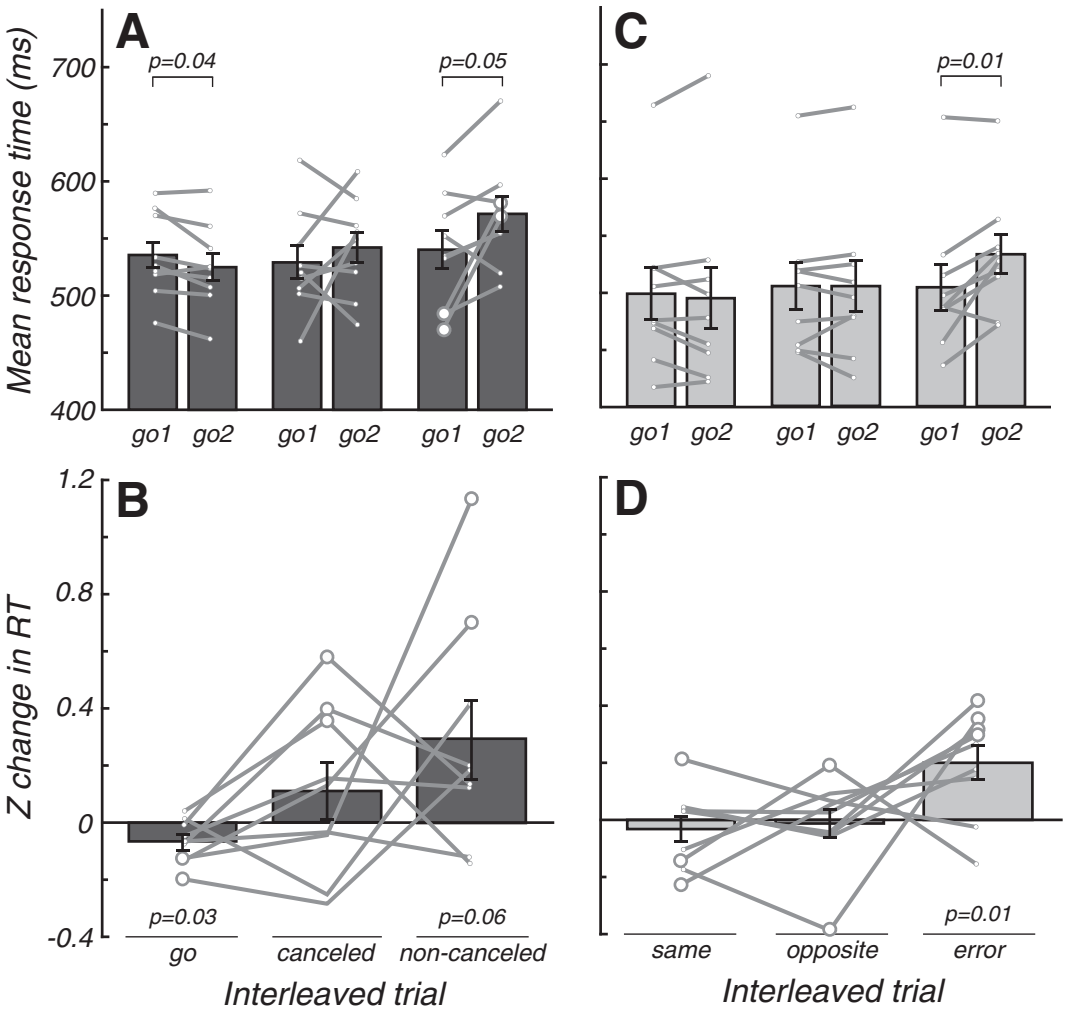

Fig. 6. (A and B) Adaptive response adjustment for the 9 rats performing the countermanding task (25% stop trials). (A) Bar graph showing mean (±SE) RT for the first (*go1*) and third (*go2*) trials from sequences of 3 consecutive trials where 2 correctly performed go trials were interleaved with either: 1) a correct go trial, 2) a canceled stop trial or 3) a non-canceled stop trial. Gray lines show data from individual rat; lines with large white circles indicate cases where *go1* and *go2* were significantly different (paired *t*-tests, $p < 0.05$). (B) Bar graph showing mean (±SE) standardized change (Z score) in go-trial RT for trials following, compared to trials preceding, an interleaved correct go, canceled stop or non-canceled stop trial; one-sample *t*-test *p* value for difference from 0 are shown. Lines indicate Z scores for each individual animal with each interleaved trial type. Lines with large white circles indicate cases with significant difference from 0 (one-sample *t*-test, $p < 0.05$). (C and D) Adaptive response adjustments for the 9 rats performing the standard responding task (0% stop trials). (C) Bar graph showing mean (±SE) go-trial RT for the first (*go1*) and third (*go2*) trials in sequences of 3 consecutive trials where 2 correct go responses made on the same lever were interleaved with either: 1) a correct go response made on the same lever; 2) a correct go response made on the opposite lever; or 3) an incorrect go response. (D) Bar graph showing mean (±SE) Z change in go-trial RT for correct go trials in the same direction following, compared to preceding, an interleaved correct go response made on the same or opposite lever, or an incorrect response. Lines represent each animal's data.

RT lengthening following non-canceled stop trials when the go choice direction was the same also reached statistical significance ($t(7) = 3.52$, $p = 0.01$, Cohen's $d = 1.17$). The change in RT following a canceled stop trial when the go choice direction was the same was not statistically significant ($t(7) = 0.31$, $p = 0.77$, Cohen's $d = 0.10$).

To further examine adaptive RT adjustments for rats ($n = 9$), we examined sequences of 3 consecutive trials in the standard responding task where the first and third trials were correct go-trial responses in the same direction and the interleaved trial was either: 1) a correct go response in the same direction, 2) a correct go trial in the opposite direction, or 3) a go-trial error. The mean (±SE) number of 3-trial sequences observed was 163 ± 24 for same direction, 151 ± 21 for opposite direction and 63 ± 5 for go-trial error interleaved trials. Fig. 6C shows the mean (±SE) RT immediately prior to and following each interleaved trial type. A two-way ANOVA with interleaved-trial type and go trial as factors revealed a significant main effect of the go trial ($F(1,8) = 8.02$, $p = 0.02$, $\eta_p^2 = 0.50$) and a significant interaction ($F(2,16) = 5.56$, $p = 0.02$, $\eta_p^2 = 0.41$). The main effect of the interleaved trial type approached significance ($F(2,16) = 3.42$, $p = 0.06$, $\eta_p^2 = 0.30$). Paired samples *t*-tests revealed that there was a significant lengthening of mean RT on trials that followed, compared to trials that preceded errors

($t(8) = -3.24$, $p = 0.01$, Cohen's $d = -1.16$). A significant difference in mean RT was not discovered for go trials that were interleaved with go trials in the same ($t(8) = 0.64$, $p = 0.54$, Cohen's $d = 0.28$) or the opposite direction ($t(8) = 0.02$, $p = 0.99$, Cohen's $d = 0.01$).

A one-way ANOVA was conducted to compare mean adaptive RT adjustment Z-scores in the standard responding task for 2 correct go responses made in the same direction that followed, compared to preceded a correct go responses in the same or opposite direction or following errors. These results are displayed in Fig. 6D. A significant main effect was revealed ($F(2,16) = 4.46$, $p = 0.03$, $\eta_p^2 = 0.36$), which was supported by a near-significant difference in the Z shortening following a go trial in the same direction and lengthening following a go-trial error (Pairwise comparison with Sidak adjustment, $p = 0.06$). Follow up one-sample t-tests revealed that the 20% lengthening in RT following errors was statistically significantly ($t(8) = 3.18$, $p = 0.01$, Cohen's $d = 1.06$). The 3% RT shortening following go trials in the same direction was not significant ($t(8) = -0.70$, $p = 0.51$, Cohen's $d = -0.23$), nor was the 1% RT shortening following go trials in the opposite direction ($t(8) = -0.23$, $p = 0.82$, Cohen's $d = -0.08$). Finally, Z scores were computed from the standard responding task for the change in go-trial RT following either correct or incorrect go trials in either direction in sequences of 3 consecutive trials where the first and third trials of the sequence were correct go trials both made in the same choice direction. The mean (±SE) number of 3-trial sequences observed for rats ($n = 9$) when the two go choice directions were the same were 315 ± 44 for interleaved correct go-trial responses and 31 ± 3 for interleaved go-trial errors. The 31% mean Z lengthening following interleaved go-trial errors was found to be significantly different from the 2% mean Z shortening following interleaved correct go-trial responses (paired samples t-test, $t(8) = 3.66$, $p = 0.01$, Cohen's $d = 1.24$). Mean Z lengthening following interleaved go-trial errors was also found to be significantly different from 0 (one-sample t-test, $t(8) = 4.63$, $p < 0.01$, Cohen's $d = 1.54$).

Influence of timeout interval

Total number of trials. It was expected that rats ($n = 11$) would perform significantly less total trials on average in 1-h countermanding task sessions with a 10-s TO interval than in sessions with a 1-s TO interval, because the time spent in TOs should limit the opportunity to perform more trials. Thus, sessions with longer TO intervals should have resulted in less total trials performed. That animals performed less total trials on average (±SE) in sessions with a 10-s (270 ± 22), compared to a 1-s (319 ± 16) TO interval was supported by the results of a paired samples t-test ($t(10) = -3.11$, $p = 0.01$, Cohen's $d = -1.00$). To further support this hypothesis, the total amount of time spent in TO for each session with either a 1-s or a 10-s TO interval was estimated from the number of incorrect responses that would have resulted in TOs. This estimate, the amount of time spent in TOs, was subtracted from the total session time (1-h) in order to adjust the total number of trials that would be performed in a 1-h session based on the rate of trials that were performed during active session time. The adjusted mean (±SE) total number of trials performed was not significantly different for sessions with a 10-s TO interval (318 ± 27) compared to sessions with a 1-s TO interval (324 ± 16; $t(10) = -0.31$, $p = 0.76$, Cohen's $d = -0.11$), suggesting that the amount of time spent in the TO interval accounted for the difference in the total number of trials performed in 1-h sessions.

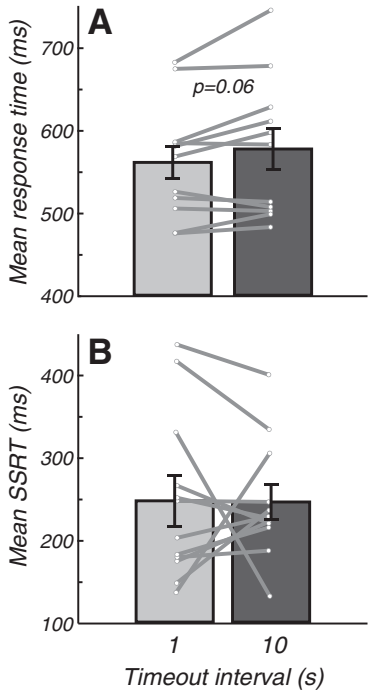

Fig. 7. Performance in countermanding task sessions with the timeout interval following incorrect response being either 1-s and 10-s. Bar graphs showing mean (±SE) go-trial RT (A) and estimated stop signal response time (SSRT) (B) for 11 rats. Gray lines show data from individual rats.

Go-trial accuracy and RT. The mean (± SE) proportion of errors committed by rats ($n = 11$) on go trials in the 10-s (0.16 ± 0.02) or 1-s (0.14 ± 0.02) TO interval versions of the countermanding task did not differ significantly (paired samples t-test, $t(10) = 1.38$, $p = 0.20$, Cohen's $d = 0.42$). Mean go-trial RT are displayed in Fig. 7A for animals ($n = 11$) performing either the 10-s or 1-s TO interval versions of the countermanding task. Animals performing the countermanding task with a 10-s TO interval were on average (±SE), 16 ± 8 ms longer to respond on go trials than in sessions with a 1-s TO interval. The longer mean go-trial RT that was observed for rats in sessions with 10-s, compared to 1-s TO intervals approached statistical significance (paired samples t-test, $t(10) = 2.13$, $p = 0.06$, Cohen's $d = 0.79$). The mean (±SE) CVs for rats ($n = 11$) performing the task with a 10-s (0.31 ± 0.03) compared to a 1-s (0.31 ± 0.02) TO

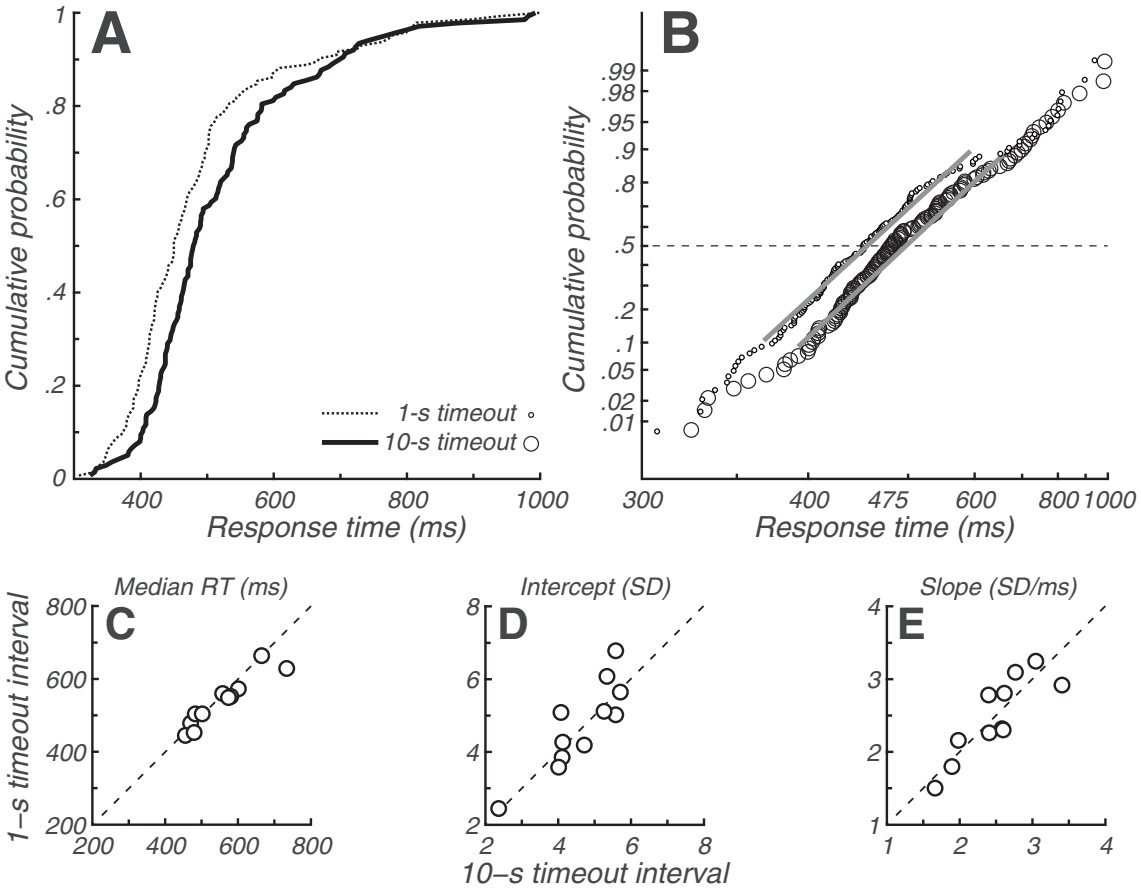

Fig. 8. Cumulative distribution (A) and reciprobit plot (B) of go-trial RT observed in one rat performing the countermanding task with a 1- and 10-s timeout interval. Data within the 10th percentile to the 90th percentile of the distribution were fitted with a linear regression model. The distribution was thus captured by the three parameters of the best-fit model: median RT, intercept and slope. Average median RT (C) intercept (D) and slope (E) observed for the 11 rats in sessions with a 1-s timeout interval are plotted against that observed in sessions with a 10-s timeout interval.

interval were not significantly different (paired samples *t*-test, $t(10) = 0.42$, $p = 0.68$, Cohen's $d = 0.14$).

Go-trial RT distribution. The mean number of go trials across all available sessions for the 11 rats for which we could make that comparison was 194 (SD 62). Fig. 8A, B, illustrates the distributions of go-trial RT from one rat with single 10-s and 1-s TO sessions. Each RT distribution was additionally projected on a reciprobit plot and the data within the 10th percentile to the 90th percentile of the distribution were fitted with a linear regression model. The R^2 of these best-fit functions averaged 0.98 (range 0.85–1.0). We then took the weighted average of these parameters across all available sessions in each

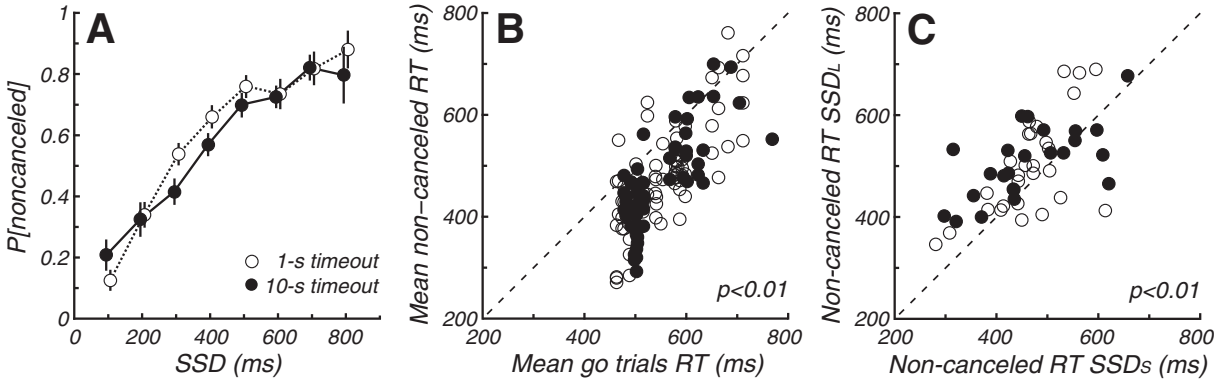

Fig. 9. Inhibition functions in countermanding task sessions with timeout interval following incorrect response being either 1-s (*white circles*) or 10-s (*dark circles*). (A) Average (± SE) probability of non-canceled responses as a function of the stop signal delay (SSD). Data are from 11 rats across 28 and 24 sessions, respectively. Following the race model predictions, mean non-canceled RT in a session was shorter than mean go-trial RT (B), and RT of non-canceled stop trials with long SSD (SSD_L) was longer than non-canceled RT at short SSD (SSD_S) in the same session (C).

rat. Fig. 8C shows the average median RT of the 1-s TO sessions plotted against the 10-s TO sessions; these were not statistically different (537 vs. 555 ms; paired *t*-test, $p = 0.105$, $d = -0.20$). Fig. 8D, E, plot the corresponding average intercepts and slopes, which were also not statistically different from each other: $p = 0.58$ ($d = 0.11$) and 0.85 ($d = -0.03$), respectively. Nevertheless, a multiple regression analysis revealed that the change in median RT between 1-s and 10-s TO sessions was significantly related to the change in intercept and slope ($R^2 = 0.76$, $F = 12.9$, $p = 0.003$) with the following weights: −0.66 (change-in-INTERCEPT), 0.72 (change-in-SLOPE) and 0.009. These results suggests that any increase in RT in rats performing the countermanding task can be accounted for by a decrease in both the rate of rise and the baseline level in the LATER model, i.e., from reduced sensitivity to the go signal as well as reduced readiness.

Inhibition functions. From each individual session, we also generated an inhibition function from the corrected proportions of non-canceled responses on stop trials. Fig. 9A shows the average function across tested sessions ($N = 26$ and 28). These proportions increased significantly with increasing SSD for all rats ($n = 11$; χ^2 test, $p < 0.01$) and spanned nearly the whole range (10-s TO: mean 0.86, SD 0.14, range 0.55–1; 1-s TO: mean 0.85, SD 0.18, range 0.53–1). Across 10-s TO sessions, the smallest proportions of non-canceled responses averaged 0.07 (SD 0.11) and were observed at SSDs ranging from 0 to 400 ms (mean 154, SD 86). The highest proportions averaged 0.93 (SD 0.10) and were observed at SSDs ranging from 300 to 900 ms (mean 650, SD 145). Across 1-s TO sessions, the smallest proportions of non-canceled responses averaged 0.10 (SD 0.16) and were observed at SSDs ranging from 0 to 400 ms (mean 125, SD 75). The highest proportions averaged 0.96 (SD 0.07) and were observed at SSDs ranging from 300 to 900 ms (mean 611, SD 142).

Race model compliance and SSRT estimates. To determine whether responses that escaped inhibition on stop trials were generally shorter than go-trial responses for rats ($n = 11$) performing the countermanding task, the mean non-canceled RT of a particular SSD in each session was compared to overall mean go-trial RT for that session (10-s TO: $N = 55$ comparisons; 1-s TO: $N = 75$ comparisons). As displayed in Fig. 9B, non-canceled RTs were found to be significantly shorter than their corresponding mean go-trial RT (paired *t*-test, $p < 0.01$). Non-canceled RTs were shorter in 87% (48/55) and 85% (64/75) of the comparisons. The mean ± SD of these RT differences for 10-s and 1-s TO was 76 ± 64 and 77 ± 66 ms, respectively. There was on average 10 trials for each tested SSD.

To test whether responses that escaped inhibition on stop trials lengthened as SSD lengthened, within each session we compared the average of the mean non-canceled RT observed in two consecutive SSDs (SSD*long*) with the average of the mean non-canceled RT observed at the immediately shorter two SSDs (SSD*short*), each weighted by the number of trials for each SSD. This provided two mean RTs from at least 6 trials for comparison in each session, with the exception of two 10-s TO sessions. There were 24 comparisons for 10-s TO sessions and 28 for 1-s TO sessions. As shown in Fig. 9C, we found that the mean non-canceled RTs at the longer SSDs were significantly longer than those at the corresponding shorter SSDs (paired *t*-test, $p < 0.001$). Non-canceled RTs at the longer SSD were longer in 75% (18/24) of 10-s TO sessions and 79% (22/28) of 1-s TO sessions. The mean ± SD of these RT differences for 10-s and 1-s TO was 45 ± 77 and 24 ± 75 ms, respectively. There were, on average, 14 and 16 trials for each SSD doublet in sessions with a 10-s or 1-s TO interval respectively.

Mean SSRT are displayed in Fig. 7B for animals ($n = 11$) performing either the 10-s or 1-s TO interval versions of the countermanding task. The mean SSRT for countermanding sessions with a 10-s was not significantly different from that estimated in the sessions with 1-s TO interval (247 ± 22 vs. 248 ± 32 ms; paired samples t-test, $t(10) = -0.52$, $p = 0.96$, Cohen's

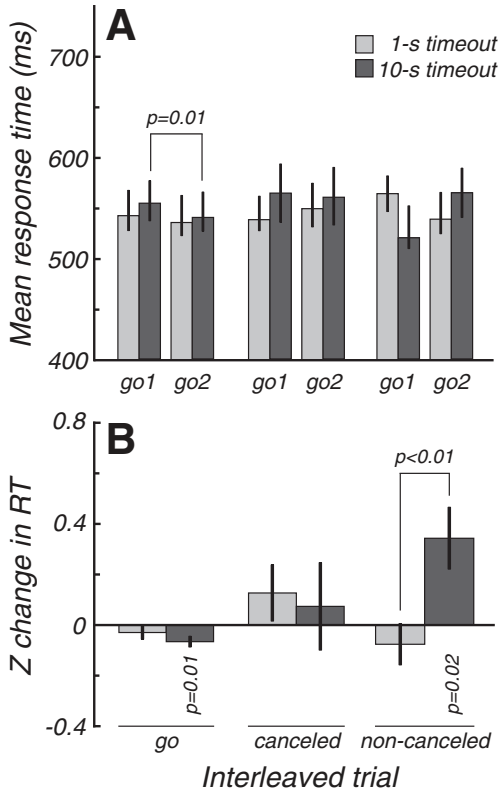

Fig. 10. Adaptive RT adjustment for the rats ($n = 10$) performing the countermanding sessions with timeout interval following incorrect response being either 1-s (*white circles*) or 10-s. (A) Bar graph showing mean (± SE) RT for the first (*go1*) and third (*go2*) trials from sequences of 3 consecutive trials where 2 correctly performed go trials were interleaved with either: 1) a correct go trial, 2) a canceled stop trial or 3) a non-canceled stop trial. (B) Bar graph showing mean (± SE) Z change in go-trial RT for trials following, compared to trials preceding, either an interleaved correct go, canceled stop or non-canceled stop trial. One-sample *t*-test *p* values for significant differences from 0 are indicated vertically; pairwise comparisons with Sidak adjustment *p* values (as a follow up for a significant ANOVA interaction) are indicated horizontally.

$d = -0.02$). For the 10 rats also tested in the countermanding task sessions in the previous comparison, mean SSRT was not significantly different from that estimated in the sessions with 10-s TO interval (258 ± 23 vs. 260 ± 33 ms; paired samples t-test, $t(9) = -0.06$, $p = 0.95$, Cohen's $d = -0.02$).

Adaptive response adjustments. To compare adaptive RT adjustments for rats ($n = 10$) in the 10-s and 1-s TO interval versions of the countermanding task, we isolated sequences of 3 consecutive trials and compared the 2 correctly performed go trials that were interleaved with either: 1) a correct go trial, 2) a canceled stop trial, or 3) a non-canceled stop trial. The mean (±SE) number of 3-trial sequences observed for the 10-s or 1-s TO interval respectively, were 205 ± 28 or 258 ± 30 for go, 35 ± 5 or 40 ± 3 for canceled and 20 ± 4 or 30 ± 5 for non-canceled interleaved trials. As depicted in Fig. 10A, animals demonstrated adaptive RT adjustments in sessions with a 10-s timeout interval following errors, but not a 1-s TO interval. A mixed-design ANOVA with TO interval (10-s, 1-s), interleaved trial type (go, canceled, non-canceled) and go trial (go1RT, go2RT) as within subjects factors did not reveal any significant main effects or interactions. Since RT adjustments were predicted, independent paired samples *t*-tests compared the mean go-trial RT preceding and following each interleaved trial type for sessions with both TO intervals. These analyses revealed that, for sessions with a 10-s TO interval, animals exhibited significant go-trial RT shortening for sequences of 3 consecutive go trials ($t(9) = 3.21$, $p = 0.01$, Cohen's $d = 1.04$).

To better account for the variability of RTs within individual sessions, we computed mean Z scores for the change in go-trial RT following correct go, canceled stop, or non-canceled stop trials for countermanding task sessions with both 10-s and 1-s TO intervals. As illustrated in Fig. 10B, a 2×3 repeated measures ANOVA with TO interval (10-s, 1-s) and interleaved trial type (go, canceled, non-canceled) as within-subjects factors revealed that the main effects of interleaved trial type ($F(2,18) = 1.16$, $p = 0.34$, $\eta_p^2 = 0.11$) or TO interval ($F(1,9) = 3.71$, $p = 0.09$, $\eta_p^2 = 0.29$) were not significant, but there was a significant interaction ($F(2,18) = 4.48$, $p = 0.03$, $\eta_p^2 = 0.33$). Paired samples *t*-test comparing Z scores from 10-s and 1-s TO interval sessions for each interleaved trial type revealed that this interaction may have been driven by the significantly greater RT lengthening that occurred following non-canceled stop trials in sessions with a 10-s, compared to a 1-s TO interval ($t(9) = 3.85$, $p < 0.01$, Cohen's $d = 1.29$). For sessions with a 10-s TO interval, the 7% shortening in Z score RT following correct go trials was significantly different from 0 (one-sample *t*-test, $t(9) = -3.05$, $p = 0.01$, Cohen's $d = -0.97$). The 34% lengthening in Z score RT following non-canceled stop trials was also significant (one-sample *t*-test, $t(9) = 2.80$, $p = 0.02$, Cohen's $d = 0.89$). The 7% lengthening of RT following canceled stop trials was not significant (one-sample *t*-test, $t(9) = 0.42$, $p = 0.68$, Cohen's $d = 0.13$). For countermanding sessions with a 1-s TO interval, mean Z scores did not differ significantly from 0 for interleaved go trials (one-sample *t*-test, $t(9) = -1.10$, $p = 0.30$, Cohen's $d = -0.35$), canceled stop trials (one-sample *t*-test, $t(9) = 1.13$, $p = 0.29$, Cohen's $d = 0.36$), or non-canceled stop trials (one-sample *t*-test, $t(9) = -0.91$, $p = 0.39$, Cohen's $d = -0.29$).

To test whether a difference in response speed to either of the two go choice directions could bias the RT adjustment analysis, we computed Z scores for the change in go-trial RT following correct go, canceled stop, or non-canceled stop interleaved trials where the first and third correct go trials of the sequence were both in the same direction. The mean (± SE) number of 3 trial sequences observed for rats ($n = 10$) when the first and third trials were in the same direction were, for the 10-s or 1-s TO interval respectively, 111 ± 14 or 145 ± 11 for go, 18 ± 3 or 22 ± 2 for canceled and 12 ± 3 or 19 ± 3 for non-canceled interleaved trials. A 2×3 repeated measures ANOVA with TO interval (10-s, 1-s) and interleaved trial type (go, canceled, non-canceled) as within-subjects factors revealed a significant main effect of interleaved trial type ($F(2,16) = 3.85$, $p = 0.04$, $\eta_p^2 = 0.33$). The main effect of TO interval was not significant ($F(1,8) = 2.80$, $p = 0.13$, $\eta_p^2 = 0.26$). The interaction of TO interval and interleaved trial type was also not significant ($F(2,16) = 1.40$, $p = 0.27$, $\eta_p^2 = 0.15$). The main effect of interleaved trial type was mainly driven by a near-significant difference in mean (±SE) Z shortening (−0.01 ± 0.03) following go trials and lengthening (0.41 ± 0.16) following non-canceled stop trials (Pairwise comparison with Sidak adjustment, $p = 0.07$).

Since we expected adaptive RT adjustments when the go-trial direction was the same for the first and third of the 3 trial sequences, we conducted one-sample *t*-tests for each interleaved trial type for both 10-s and 1-s TO interval data sets. For sessions with a 10-s TO interval, the 57% lengthening following non-canceled stop trials was significant ($t(8) = 2.44$, $p = 0.04$, Cohen's $d = 0.81$). The 5% shortening following correct go trials was not significantly different from 0 ($t(8) = -1.14$, $p = 0.29$, Cohen's $d = -0.38$). The 58% lengthening of RT following canceled stop trials was not significant ($t(8) = 1.98$, $p = 0.08$, Cohen's $d = 0.66$). For sessions with a 1-s TO interval, mean Z scores did not differ significantly from 0 when the go choice directions were the same for interleaved go trials ($t(8) = 0.61$, $p = 0.56$, Cohen's $d = 0.20$), canceled stop trials ($t(8) = 1.17$, $p = 0.28$, Cohen's $d = 0.39$), or non-canceled stop trials ($t(8) = 1.44$, $p = 0.19$, Cohen's $d = 0.48$).

DISCUSSION

In the present experiment, rats exhibited the ability to flexibly adapt their responses in a context-dependent manner. First, rats demonstrated longer RT in the countermanding task in comparison to the standard responding task. Second, RT shortening was observed following consecutive correct go trials in the

countermanding task, whereas RT lengthening was observed following both non-canceled stop trials in the countermanding task and error trials in the standard responding task when a 10-s TO interval was administered following errors. RT lengthening following erroneous stop trials was not observed in sessions with a 1-s TO interval. Overall, these findings support the hypothesis that rats display caution in the countermanding task by strategically lengthening their RTs, particularly following errors, possibly to avoid long TO intervals. Further analyses of RT distributions suggest that RT lengthening results largely from reduced sensitivity to the go signal, but also from reduced readiness.

Longer go-trial RT in the countermanding task in comparison to standard responding tasks has commonly been reported in human studies (Rieger and Gauggel, 1999; Cavina-Pratesi et al., 2004; Verbruggen et al., 2004; Akerfelt et al., 2006; Mirabella et al., 2006). Similarly, in studies using the conditional version of the countermanding task, go-trial RT is longer in trials in which the go signal indicates a probable stop signal presentation compared to when there is no possibility (De Jong et al., 1995; Aron et al., 2007; Chikazoe et al., 2009; Jahfari et al., 2010, 2012; Obeso et al., 2011, 2013). In studies varying the probability of stop trials, go-trial RT has been shown to increase with increasing stop-trial probability (Logan, 1981; Logan and Burkell, 1986; Ramautar et al., 2004, 2006; Vink et al., 2005, 2006, 2014, 2015; Verbruggen and Logan, 2009; Bissett and Logan, 2011; Zandbelt and Vink, 2010; Zandbelt et al., 2011, 2013; Poitou and Pouget, 2012). Monkeys also showed go-trial RT in a countermanding (saccade) task that was longer than in a standard responding task (Stuphorn and Schall, 2006) and increased with increasing stop-trial probability (Emeric et al., 2007; Poitou and Pouget, 2012). These findings have been interpreted as evidence of proactive inhibitory control (active response suppression) in the countermanding task. The present study is the first to suggest that rats are also capable of proactive inhibitory control.

That this contextual effect on go-trial RT reflects proactive inhibitory control has been supported by the work of Verbruggen and Logan (2009), whose diffusion model simulation showed that RT lengthening can be generally explained by an increased response threshold (see also Jahfari et al., 2012). This proactive inhibitory control and RT lengthening may thus result from a decrease in readiness, which is simulated by lowering the start level of the go process in the LATER model; the same outcome is obtained by increasing the threshold. However, our RT distribution analyses suggest that the observed RT lengthening is primarily captured by a decrease in the rate of rise of the go process in that model, which suggests a reduced sensitivity to the go signal instead. It is important to note that the modeling work of Verbruggen and Logan (2009) did not rule out strategic effects on drift rate. Moreover, the best-fit diffusion model identified by Logan et al. (2014) to account for the RT lengthening with increasing stop-trial probability observed by Bissett and Logan (2011) suggests a reduced drift rate as the main factor. Altogether, this modeling work makes testable predictions for neural recording experiments. While the cortical network implicated in proactive inhibitory control in fMRI studies (Zandbelt and Vink, 2010; Vink et al., 2015) most likely has no homolog in the rat, the reported striatum activation in the expectation of a stop signal suggests the striatopallidal pathway as a likely substrate for active response suppression in the rat (Freeze et al., 2013; Mallet et al., 2016).

Bissett and Logan (2011, 2012) have suggested that stop signals shift goal priority to caution and that post-stop RT slowing is an explicit strategy adjustment of behavior, reporting significant post-stop slowing in countermanding sessions where stop trials or failed inhibition were more frequent, or when stop trials were not presented on back-to-back trials, but not when participants were informed of this rule. Post-error slowing has been suggested as most prevalent in tasks requiring a brief response window where accuracy is emphasized and where errors are infrequent and consciously perceived, as opposed to unperceived (Danielmeier and Ullsperger, 2011). Our finding that adaptive RT adjustments are eliminated in sessions with a brief 1-s TO interval following errors suggests that rats make a strategy adjustment in the countermanding task, lengthening RTs in sessions with longer 10-s TO intervals to avoid punishment and increase reward likelihood.

The consistent convergence of evidence supporting RT shortening following consecutive go trials and RT lengthening following non-canceled stop trials in countermanding task sessions with a post-error 10-s TO interval that were compared to sessions with a 1-s TO interval or standard responding task sessions supports the hypothesis that rats do adaptively adjust RT in the countermanding task. These observations were revealed in the analyses of RT, Z-score RT and sequences of 3-consecutive trials instructing responses in the same direction, indicating that the adaptive RT adjustments that were hypothesized were a reliably observable behavior. Significant adaptive shortening of RT following consecutive go trials and lengthening of RT following non-canceled stop trials in the countermanding task with a post-error 10-s TO interval also replicated observations from previously tested rats (Beuk et al., 2014).

Humans performing the countermanding task have demonstrated RT shortening following consecutive go trials in both manual (Thakkar et al., 2014) and saccade tasks (Cabel et al., 2000; Emeric et al., 2007; Corneil et al., 2013). In manual countermanding tasks, studies have revealed RT lengthening following all stop trials (Rieger and Gauggel, 1999; Enticott et al., 2009; Boehler et al., 2011; van de Laar et al., 2011; Beyer et al., 2012; Anguera et al., 2013; Chang et al., 2014), but RT lengthening in particular following non-canceled stop trials (Schachar et al., 2004; Li et al., 2008; Verbruggen et al., 2008; Verbruggen and Logan, 2008a; Chevrier and Schachar, 2010; Chen et al., 2014; Thakkar et al., 2014). Saccadic countermanding investigations have reported significant RT lengthening following all stop trials (Thakkar et al., 2011), or following primarily canceled stop trials (Cabel et al., 2000; Emeric et al., 2007). Non-human primates have exhibited RT lengthening following stop tri-

als in comparison to go trials in both manual (Chen et al., 2010) and saccade countermanding tasks (Kornylo et al., 2003; Nelson et al., 2010), although Emeric et al. (2007) reported greater RT lengthening in a saccade countermanding task following canceled, as opposed to non-canceled stop trials. Thus, there may be an important distinction between post-error and post-stop RT lengthening for manual and saccadic countermanding tasks.

The view that performance adjustment in the countermanding task reflects executive control has been supported by evidence of frontal cortex-related activity in this behavior (Stuphorn and Emeric, 2012). In human countermanding studies, fMRI activation is heightened and correlated within the ventrolateral prefrontal cortex and supplementary motor area during post-error RT slowing (Li et al., 2008; Ide and Li, 2011). In non-human primates, neurons in the supplementary motor area and pre-supplementary motor area signaled information about expected reward, actual outcome and the difference in expected and actual reward in the countermanding task (Scangos et al., 2013). Furthermore, Pouget and colleagues (2011) demonstrated that go trials preceded by stop trials, as opposed to go trials, elicited a slower average onset of accumulation in the activity of movement-related neurons in both the frontal eye fields and the superior colliculus. In rats, Narayanan and Laubach (2008) reported RT lengthening following errors in a standard responding task requiring animals to release a held lever within a particular time frame that was evident in sessions with or without a 4–8-s TO interval following errors. Neurons in the dorsomedial prefrontal cortex, but not the motor cortex, exhibited increased post-error activity persisting into the following trial, while post-error slowing was attenuated by dorsomedial prefrontal cortex inactivation with muscimol. In the same task, Narayanan and colleagues (2013) showed an enhancement of low-frequency oscillations originating from the medial frontal cortex in rats following errors that was disrupted by muscimol infusion in the medial frontal cortex. It is possible that this standard responding task, requiring accurate go responses in a short time frame, employed different behavioral control mechanisms that supported post-error slowing even in sessions with brief TO intervals following errors. Nevertheless, these findings provide evidence for top down control of adaptive behavior in rats that could be further elucidated by correlating frontal cortex activity with adaptive RT adjustments in the countermanding task.

Mayse and colleagues (2014) reported adaptive RT adjustments in rats performing a countermanding task with no apparent TO interval following errors. In this task, all trials required go responses for reward presentation, but not until after the end of the hold duration on stop trials. Two separate categories of stop trial errors were identified with this task: 1) failure-to-stop errors, whereby subjects failed to stop the go response and 2) failure-to-wait errors, whereby subjects appeared to stop the go response but then failed to wait until the end of the stop trial hold duration before responding for reward. This study found adaptive RT lengthening following failure-to-wait errors, but not following failure-to-stop errors. Interestingly, rats in this experiment exhibited a significantly greater proportion of responding for reward in failure-to-wait, compared to failure-to-stop errors, suggesting that animals behaved as if they expected reward for correctly stopping in failure-to-wait instances. Thus, it seems possible that animals in this study did not exhibit post-error slowing following failure-to-stop trials with no TO interval, as would be suggested by the results of the present experiment, but did display post-error slowing following failure-to-wait trials in which a reward was expected but not delivered, making the error more salient and emphasizing accuracy in the following trial.

RT shortening following consecutive correctly performed go trials in the countermanding task with a post-error 10-s TO interval has been reported previously with rats (Beuk et al., 2014). Alternatively, Mayse and associates (2014) reported significant RT shortening in rats following consecutive go trials in their stop task without an apparent post-error TO interval. This was not observed in sessions with a 1-s TO interval presently. In the investigation by Mayse and colleagues, RT shortening following consecutive go trials seemed to be primarily driven by significantly longer go trial RT observed in trials preceding a correct go trial and not by significantly shorter RTs on trials immediately following them. Our results suggest that in countermanding sessions with a post-error 1-s TO interval, rats displayed less cautious go-trial behavior in general, leading to shorter overall go-trial and an attenuation of adaptive RT adjustments. The near-significant shortening of mean go-trial RT observed in sessions with a 1-s, as opposed to a 10-s TO interval supports this hypothesis.

Contrary to the findings observed presently, Bari and Robbins (2013) reported go-trial RT shortening following a failed stop trial as a measure of performance adjustment in their stop task, which has been reported in human saccade countermanding (Curtis et al., 2005). Citing evidence from Rabbitt and Rodgers (1977), indicating that less post-error slowing occurs with longer inter-trial intervals, they hypothesized that the 5-s TO interval following errors that was utilized in their experiment may have been responsible for a post-error speeding effect, as human and non-human primate studies reporting post-error slowing typically had not implemented a TO interval following errors (Schachar et al., 2004; Li et al., 2008). Of note, the intertrial intervals in the Rabbitt and Rodgers study were either 20- or 200-ms, small enough that participants reported not perceiving the difference. With longer TO intervals, it would be expected that subjects would perceive the substantial lengthening of time between trials that followed errors and adjust their behavior in a way that actively avoided receiving TO intervals, particularly in sessions where correct responses are directly rewarded and motivationally salient. Observations from the present study appear to support this conclusion.

Bari and Robbins (2013) estimated post-error RT adjustment as a difference value by subtracting RT in go trials preceding an error from RT in go trials following an error, which was different than the analysis of adaptive RT adjustments in the present investigation. Their method of estimation does not include potentially valuable information about variation in RT on trials preceding stop trial errors. It is possible that post-error RT shortening was

observed not due to shortening in RT following stop trial errors per se, but due to significantly longer RTs in go trials immediately preceding stop trial errors. Mayse and colleagues (2014) do not provide support for this hypothesis as evidenced by significantly shorter RT on go trials immediately preceding a failure-to-stop trial that manifested as post-error slowing when comparing only the go trials immediately before and following stop trial errors. Beuk and colleagues (2014), as well as the present investigation, did not observe significantly different go-trial RT immediately preceding stop trial errors. Thus, it is unlikely that variability in RT preceding stop trial errors contributed to the post-error RT shortening found in the Bari and Robbins study; however it is recommended that future experiments studying adaptive RT adjustments in rodents examine RTs of go trials preceding, as well as following different interleaved trial types.

It is possible that post-error RT speeding observed by Bari and Robbins (2013) resulted from differences in countermanding task experimental design. For one, the 5-s TO interval that they utilized may not have been long enough to promote caution on the subsequent trial, similar to the present finding of attenuated post-error slowing with a 1-s post-error TO interval. Moreover, their task did not entail a choice response on go trials, only requiring subjects to press 2 levers in quick succession. The countermanding task employed presently required an accurate choice response on go trials (i.e., choosing the correct target lever from 2 alternatives). It is possible that a task that does not require an alternative choice decision on go trials, but instead a more automated response, required less cautious behavior before a correct go response could be made on the following trial, leading to attenuated post-error slowing. In the present investigation, we aimed to directly test whether utilizing a longer TO interval (10 s) was a critical factor in the previously reported adaptive RT adjustments of rats performing our choice response countermanding task (Beuk et al., 2014). We did not examine the effects of a 5-s TO interval, as a comparison to Bari and Robbins may be inappropriate due to differences in task design and estimation methods; however, future studies should examine varying effects of the full range of TO intervals on behavioral adjustment in the countermanding task.

A number of sessions were omitted from analysis in the present investigation because behavioral performance did not meet particular criteria, which suggested that animals were not following task instructions. A major strength of the countermanding paradigm is that models have been developed to account for countermanding task performance and permit estimation of SSRT (Logan and Cowan, 1984; Matzke et al., 2013; Logan et al., 2014). It is therefore critically important that animals meet performance criteria, which suggests they followed task instructions, in order for these models to be applied appropriately. Examination of data in which animals are not performing the task properly could lead to spurious conclusions. Thus, restricting analysis to sessions in which rats were performing according to task instructions strengthens the validity of the current investigation and it is important that data collection for future rodent countermanding experiments is carefully considered. To account for sessions potentially being excluded from analysis in a small cohort presently, repeated administration of each test session was conducted to augment the data. While this approach may be practical in a behavioral study, the use of repeated test sessions may not be ideal in all countermanding experiments, for example in the investigation of acute drug effects.

Small sample size, in both the number of animals that performed the task appropriately and the number of 3-trial sequences with a particular interleaved trial type that were obtained may be underlying reasons why observed RT shortening following consecutive go trials or RT lengthening following non-canceled stop trials did not always reach statistical significance. Subjects with less than 4 observed 3-trial sequences with a particular type of interleaved trial were excluded from adaptive RT adjustments analysis due to the fact that a small sample size could artificially inflate the observed change in RT. This was especially true for interleaved non-canceled stop trials, which only accounted for approximately half of all stop trials due to the staircase procedure. Moreover, animals responded prior to stop signal presentation on approximately 31% of non-canceled stop trials, requiring these trials to be omitted from adaptive RT adjustment analysis. Furthermore, stop trials only accounted for approximately 25% of trials within a session, which is an important aspect of the countermanding task that ensures subjects are biased toward responding as quickly as possible (Logan and Cowan, 1984; Bissett and Logan, 2011). Future experiments of adaptive response adjustments in rats could consider altering task parameters to allow more instances of non-canceled stop trials (e.g., pre-determined SSDs or a higher proportion of stop trials within the session).

CONCLUSIONS

Post-error RT slowing involves adaptively adjusting behavior by lengthening RT following errors in comparison to correctly performed trials and has long been considered evidence of executive control of behavior (Rabbitt, 1966). In the present study, rats exhibited proactive RT lengthening in the countermanding task in comparison to a standard responding task. Rats demonstrated reactive RT lengthening following non-canceled stop trials in the countermanding task and go-trial errors in a standard responding task in sessions with a 10-s, but not a 1-s post-error TO interval. RT distributions suggest that this RT lengthening was associated with reduced sensitivity to the go signal, as well as reduced readiness to respond. Together, these results suggest that rats engaged executive control networks to employ performance monitoring and adjustment in the countermanding task to reduce the likelihood of receiving a long, unrewarded TO interval and recommends that future experiments examine the potential role of the rodent medial frontal cortex in mediating this behavior.

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