*Neuroscience* 263 (2014) 96–110

# INVESTIGATING A RACE MODEL ACCOUNT OF EXECUTIVE CONTROL IN RATS WITH THE COUNTERMANDING PARADIGM

**J. BEUK,[a] R. J. BENINGER[a,b,c] AND M. PARÉ[a,b,d]***

[a] *Centre for Neuroscience Studies, Queen's University, Kingston, Ontario K7L 3N6, Canada*

[b] *Department of Psychology, Queen's University, Kingston, Ontario K7L 3N6, Canada*

[c] *Department of Psychiatry, Queen's University, Kingston, Ontario K7L 3N6, Canada*

[d] *Department of Biomedical & Molecular Sciences, Queen's University, Kingston, Ontario K7L 3N6, Canada*

**Abstract—The countermanding paradigm investigates the ability to withhold a response when a stop signal is presented occasionally. The race model (Logan and Cowan, 1984) was developed to account for performance in humans and to estimate the stop signal response time (SSRT). This model has yet to be fully validated for countermanding performance in rats. Furthermore, response adjustments observed in human performance of the task have not been examined in rodents. Male Wistar rats were trained to respond to a visual stimulus (go signal) by pressing a lever below that stimulus, but to countermand the lever press (25% of trials) subsequent to an auditory tone (stop signal) presented after a variable delay. We found decreased inhibitory success as stop signal delay (SSD) increased and estimated a SSRT of 157 ms. As expected by the race model, response time (RT) of movements that escaped inhibition: (1) were faster than responses made in the absence of a stop signal; (2) lengthened with increasing SSD; and (3) were predictable by the race model. In addition, responses were slower after stop trial errors, suggestive of error monitoring. Amphetamine (AMPH) (0.25, 0.5 mg/kg) resulted in faster go trial RTs, baseline-dependent changes in SSRT and attenuated response adjustments. These findings demonstrate that the race model of countermanding performance, applied successfully in human and nonhuman primate models, can be employed in the countermanding performance of rodents. This is the first study to reveal response adjustments and AMPH-induced alterations of response adjustments in rodent countermanding.** 

**Key words: behavioral inhibition, stop task, inhibition function, impulsivity, response adjustments, amphetamine.**

*Correspondence to: M. Paré, Centre for Neuroscience Studies, Queen's University, Kingston, Ontario K7L 3N6, Canada. Tel: +1-613-533-3107; fax: +1-613-533-6840/6880.
E-mail address: martin.pare@queensu.ca (M. Paré).

*Abbreviations:* AMPH, amphetamine; ANOVA, analysis of variance; CV, coefficient of variation; FR1, fixed-ratio 1; RT, response time; SD, standard deviation; SEM, standard error of mean; SSD, stop signal delay; SSRT, stop signal response time; ZRFT, Z relative finishing time.

## INTRODUCTION

In a dynamically changing environment, executive processes are internally generated acts of control that allow an organism to adapt to changing situations and bring courses of thought and action in line with current goal sets (Logan, 1994). The executive system requires the ability to inhibit thoughts or actions no longer appropriate in light of new goals. Thus, inhibition of action, or countermanding, is one important aspect of behavioral control that can be studied to elucidate executive functions (Logan and Cowan, 1984). Furthermore, impairment of inhibitory control characterizes several human psychopathologies, including attention deficit/hyperactivity disorder, obsessive compulsive disorder, and schizophrenia (Alderson et al., 2007; Chamberlain and Sahakian, 2007; Crosbie et al., 2008; Lipszyc and Schachar, 2010).

The countermanding task, also known as the stop task, was specifically designed to investigate inhibitory control. Subjects are given a primary response to perform at the onset of a go signal. On a small subset of trials a stop signal is presented at a variable stop signal delay (SSD) following the go signal, requiring inhibition of the primary task (Lappin and Eriksen, 1966). Logan and Cowan (1984) developed a horse-race model to account for countermanding performance, positing independent go and stop processes racing toward a finish line. The first process to cross its finish line wins the race and determines the behavioral outcome (Fig. 1A).

To validate the race model for human countermanding task performance, Logan and Cowan (1984) predicted and accordingly demonstrated that inhibiting a response was less probable as SSD lengthened and that non-canceled responses on stop trials were generally faster than go trial responses and approached mean go trial response time (RT) as SSD lengthened. Furthermore, the race model allowed fairly precise estimations of mean non-canceled RT at different SSDs given the observed go trial RTs and probability of responding at that SSD, although predicted non-canceled RTs tended to underestimate the observed ones at shorter SSDs. The power of the race model is that it permits estimation of the time required to cancel a response – the stop signal response time (SSRT) – a variable that is not directly observable (Band et al., 2003). Confirming these specific predictions of task performance is necessary to validate the assumptions underlying the race model (Logan, 1994). The SSRT estimate is only valid if race model predictions of performance are

0306-4522/13 $36.00 
http://dx.doi.org/10.1016/j.neuroscience.2014.01.014

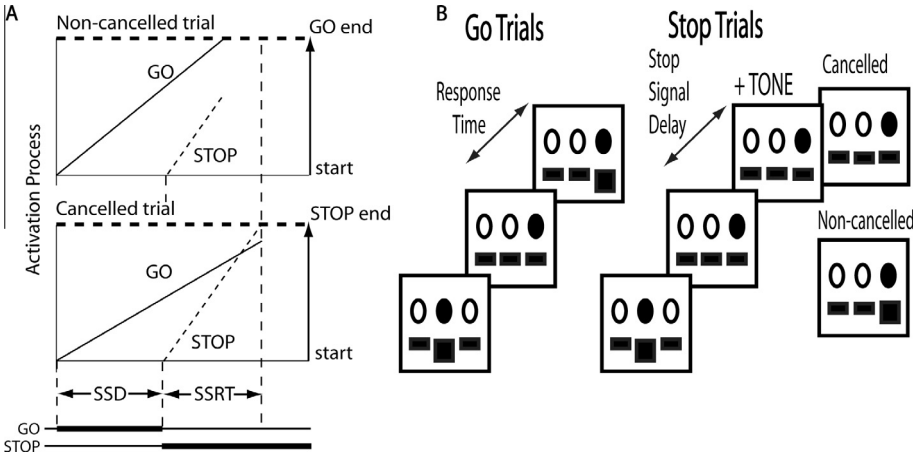


**Fig. 1.** (A) The race model of countermanding performance proposes that two sets of processes, one initiated by a go signal and one by a stop signal after a variable stop signal delay (SSD), race toward a threshold whereby the winner of the race determines the behavioral outcome. The stop signal RT (SSRT) can be estimated as the time between stop signal onset and the point where the stop process crosses the threshold to countermand the response (adapted from Paré and Hanes, 2003). (B) Before a trial, the center light is illuminated. A center lever press begins a trial and a light is immediately illuminated randomly above the left or right lever (i.e., the go stimulus). On go trials (75%), pressing the lever directly below the illuminated light results in reward. On stop trials (25%) an auditory tone (i.e., the stop stimulus) is presented at varying delays from go stimulus onset (SSD) and canceling the lever press results in reward, whereas a non-canceled lever press results in a timeout period.

respected. Consequently, these predictions were replicated to account for both human saccade (Hanes and Carpenter, 1999) and macaque monkey (Hanes and Schall, 1995; Hanes et al., 1998; Paré and Hanes, 2003) countermanding task performance.

The application of the countermanding task to investigate inhibitory control with rats has grown rapidly (e.g., Feola et al., 2000; Eagle and Robbins, 2003a,b; Pattij et al., 2007; Eagle et al., 2009; Kirshenbaum et al., 2011). Yet, there has been sparse systematic investigation into the validity of a race model account of rodent stop task performance. Rats have been omitted in previous reports for performing the stop task outside the framework of the race model, namely generating unstable go trial accuracy or non-increasing probabilities of response inhibition as SSD lengthened (Eagle and Robbins, 2003a,b, 2008; Pattij et al., 2007, 2009; Robinson et al., 2008; Bari et al., 2009, 2011; Eagle et al., 2011); however, these data were not explicitly displayed. Additionally, a number of these studies noted that rats included in analysis performed the task according to the assumptions of the race model. This was partially demonstrated with increased probability of non-canceled responding as SSD increased, although these inhibition functions never spanned the full range from 0% to 100% inhibition. Eagle et al. (2007) reported that mean non-canceled stop trial RT was faster than mean go trial RT in a group of control rats. To date, this is the only evidence directly confirming the race model predictions of stop task performance outlined by Logan (1994). Thus, it remains to be established whether this crucial prerequisite is fully met in rats.

Rat models allow behavioral and invasive investigations in large samples of animals and, ipso facto, the study of inter-individual variability in the control of behavior. Inter-individual differences in executive control are particularly significant given the non-linear role of catecholamine systems in this function (Lidow et al., 1998). For example, amphetamine (AMPH) increased or decreased SSRT in rats, dependent on fast or slow baseline performances respectively (Feola et al., 2000; Eagle and Robbins, 2003a). Important inter-individual differences in adaptive response adjustment have also been documented in humans and macaque monkeys performing the countermanding task; slower responses usually following successfully canceled responses (Emeric et al., 2007), but have not been observed in rats. In addition, there exists several rat models of neuropsychiatric symptoms (Nestler and Hyman, 2010; Sontag et al., 2010; Bari and Robbins, 2011) for which the assessment of executive control deficits would benefit from the rigorous testing offered by the countermanding paradigm.

Here, we demonstrate that the race model does account for performance of rats in a countermanding task closely resembling tasks used in humans and monkeys. Rats adjusted their responses in this task, primarily by slowing responses following non-canceled stop trial responses. Administration of AMPH attenuated these response adjustments.

## EXPERIMENTAL PROCEDURES

### Animals

Behavioral data were collected from two cohorts of male albino Wistar rats. The first cohort ($n$ = 8) was used to test race model predictions, while the second cohort ($n$ = 16) was added to test the effects of AMPH. 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 Animals for Research Act. Rats bred by Charles River Laboratories