Behavioral Neuroscience
2000, Vol. 114, No. 4, 838–848

0735-7044/00/$5.00 DOI: 10.1037//0735-7044.114.4.838

Effects of *d*-Amphetamine and Alcohol on a Measure of Behavioral Inhibition in Rats

Tyler W. Feola
West Virginia University

Harriet de Wit
The University of Chicago

Jerry B. Richards
West Virginia University

This study was designed to develop a version of the stop task, a putative measure of behavioral inhibition, for use in rats and to assess the effects of *d*-amphetamine (AMP) and alcohol (ALC). The stop task provides a quantitative index of the ability to inhibit a response that has been initiated. Rats ($N = 11$) were tested after intraperitoneal injections of AMP (0.125, 0.25, 0.5, 1.0 mg/kg) and ALC (250, 500, 750 mg/kg). AMP improved the ability to inhibit responses only in rats with relatively poor inhibitory performance at baseline. ALC impaired inhibition at doses that did not affect simple reaction time. The results support the sensitivity, reliability, and validity of the procedure as a measure of behavioral inhibition in rats and are highly concordant with a parallel study conducted with humans.

An established and theoretically well-developed method for studying behavioral inhibition in humans is the *stop task* (Logan, 1994), which measures the ability to stop a motor response after its execution has been initiated. Impairments in the ability to inhibit behavior are characteristic of several psychiatric disorders, most notably attention deficit hyperactivity disorder (ADHD). A large number of studies have shown that stop task performance is impaired in children with ADHD (Brandeis et al., 1998; Jennings, van der Molen, Brock, & Somsen, 1992; Jennings, van der Molen, Pelham, Debski, & Hoza, 1997; Oosterlaan, Logan, & Sergeant, 1998; Oosterlaan & Sergeant, 1996, 1998a, 1998b; Pliszka, Borcherding, Spratley, Leon, & Irick, 1997; Quay, 1997; Rubia, Oosterlaan, Sergeant, Brandeis, & von Leeuwen, 1998; Rubia et al., 1999; Tannock, Schachar, Carr, Chajczyk, & Logan, 1989; Tannock, Schachar, & Logan, 1995). The psychomotor stimulant methylphenidate, a drug commonly used to treat ADHD, has been shown to ameliorate impairments on the stop task in ADHD children (Tannock et al., 1989, 1995). Even among normal healthy volunteers, stop task performance has been reported to be correlated with paper-and-pencil tests of impulsivity (Logan, Schachar, & Tannock, 1997). Barkley (1997) suggested that poor response inhibition in children with ADHD on the stop task may be indicative of the central impairment underlying other deficits of executive functioning such as working memory, internalization of speech, and self-regulation of affect. Thus, the stop task may be an important laboratory model for studying basic behavioral and biological processes that mediate impairments in impulse control.

In this article, we describe a stop task procedure for rats that is modeled after the stop task procedure developed by Logan and colleagues in humans (Logan, 1994). An analogous procedure for use in laboratory animals would enable researchers to study the neural processes underlying this behavior. Development of the stop task in rats may provide an animal model for studying the psychobiological processes that underlie behavioral inhibition and for the identification of potential therapeutic compounds. To our knowledge, only one other study has used the stop task procedure to measure stopping in nonhuman subjects. Hanes, Patterson, and Schall (1998) developed a version of the stop task to measure the ability of monkeys to inhibit eye movements. In the present article, we report on the results of a procedure designed to parallel the human stop task in rats. We examined the relationship between various measures of stop task performance and test–retest reliability of the stop task and investigated the effects of two drugs, *d*-amphetamine (AMP) and alcohol (ALC), on performance. To assess the comparability of results obtained from the rat version of the stop task with results obtained from the human version of the stop task, we compared the results of the present study with those obtained from a similar study done in humans (de Wit, Crean, & Richards, 2000).

The stop task is a discrete-trials reaction time (RT) procedure in which the subject is required to execute a simple motor response (Go response) following the presentation of a stimulus (Go signal). In the human stop task, the Go response was a key press on a computer keyboard following presentation of a visual stimulus on a computer monitor. In the rat stop task, the Go response was inserting the head into a water feeder aperture in response to a

Tyler W. Feola and Jerry B. Richards, Department of Psychology, West Virginia University; Harriet de Wit, Department of Psychiatry, The University of Chicago.

This research was supported by National Institute on Drug Abuse Grants DA-09133 and DA-10588. We acknowledge Gordon Logan for his support and advice on this project. We thank Tammy Wade and Diane Booth for their technical assistance.

Correspondence concerning this article should be addressed to Jerry B. Richards, Department of Psychology, West Virginia University, 114 Oglebay Hall, P.O. Box 6040, Morgantown, West Virginia 26506. Electronic mail may be sent to jrichar7@wvu.edu.

visual stimulus for a water reward. Occasionally and unpredictably, a tone (Stop signal) was presented soon after the Go signal, which signaled the subject to stop the execution of the Go response. In the human stop task, the participants were instructed simply to stop the execution of the Go response when they heard the tone, whereas in the rat version of the stop task the rat was required to stop the Go response and perform an alternative response (i.e., insert its head into an alternative water feeder aperture) to get a water reward. The parameter of interest is the time it takes the subject to inhibit or stop the Go response. Although this inhibition time is not directly measurable, Logan and colleagues (see Logan, 1994, for a review) have developed a theoretical basis for estimating the Stop RT. They characterize stop task performance as a race between a Go process and a Stop process: Whichever process (Go or Stop) completes its execution first wins the race, resulting in either a response or no response. According to the race model, execution of the Go response and stopping execution of the Go response involve identifiably different processes. The speed of the Go process is indicated by the time taken to execute a response to the Go signal ("Go RT"). The speed of the Stop process is estimated by subtracting the stop signal delay (the elapsed time between the Go signal and presentation of the Stop signal [tone]) at which subjects perform with 50% accuracy from the Go RT. Figure 1 illustrates the distribution of the observed Go RTs above the timeline and the hypothetical distribution of the Stop RTs below the timeline. When the stop signal delay is short (top timeline in Figure 1), the subject usually succeeds in stopping the response because the mean of the distribution of the Stop RTs occurs before the mean of the distribution of the Go RTs. When the stop signal delay is long (bottom timeline in Figure 1), the subject usually fails to stop because the mean Stop RT occurs after the mean Go RT. However, if the stop signal delay is adjusted so that the subject fails to stop 50% of the time (middle timeline in Figure 1), then the mean of the distribution of the Stop RTs occurs at the same moment on the timeline as the mean of the distribution of the Go RTs. At the stop signal delay value in which the subject fails to stop 50% of the time, the average time taken to execute the Stop response (Stop RT) is equal to the average time taken to execute the Go response (Go RT) minus the stop signal delay. Thus the procedure described in this article adjusts the stop signal delay for each subject to determine the stop signal delay required to produce 50% stop failures. The stop signal delay that produces 50% failures in each subject can then be used to estimate the subjects' mean Stop RT.

The version of the stop task that we have developed for use with rats not only requires the rats to stop the execution of the Go response but also requires the rats to make an alternative "Change" response. Results from studies that have tested humans on stop task procedures with change requirements indicate that these tasks produce results on the Stop RTs and Go RTs that are similar to those observed on stop task procedures without a change requirement (Logan, 1994). In addition, children with ADHD have im-

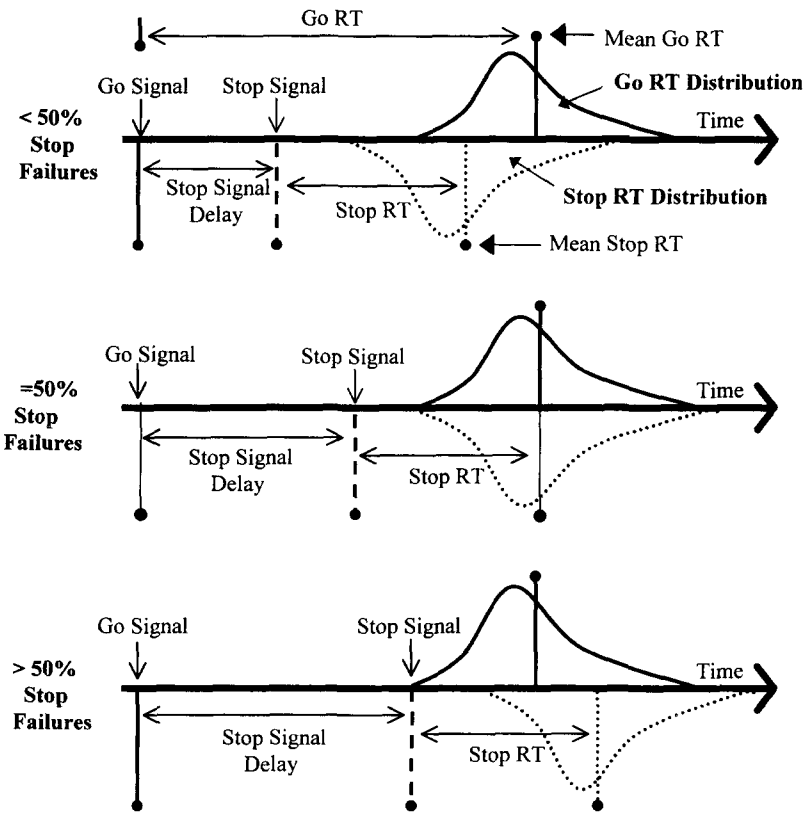

Figure 1. Schematic illustrating how the race model allows determination of the Stop reaction time (RT) using the stop task procedure. See text for details.

pairments on the change version of the stop task that are ameliorated with methylphenidate (Oosterlaan & Sergeant, 1998b; Tannock et al., 1995). An advantage of the change task is that it provides an additional measure (Change RT) that may be an indicator of the rat's ability to switch to an alternative response. In the rat stop task procedure described above, the Change RT is the elapsed time between the onset of the Stop signal (tone) to head entry into the alternative water dispenser aperture.

ALC has been shown to increase RT in both humans (Gustafson, 1986; Maylor, Rabbitt, James, & Kerr, 1992; Young, 1970) and rats (Koob, Percy, & Britton, 1988; Mayfield, Grant, Schallert, & Spirduso, 1992; Spirduso, Mayfield, Grant, & Schallert, 1989). Increases in RT induced by ALC have been explained as a function of both impaired perceptual–motor performance and impaired cognitive capacity. Previous studies in humans with the stop task have shown that ALC impairs the Stop RT performance at doses that do not affect the Go RT, indicating that stopping is more sensitive to the effects of ALC (Fillmore & Vogel-Sprott, 1999; Mulvihill, Skilling, & Vogel-Sprott, 1997). The sensitivity of the Stop RT to ALC may be indicative of a specific effect of ALC on behavioral inhibition. This impairment in behavioral inhibition may underlie the association of ALC intoxication with risky and impulsive behaviors (Baer, Novick, & Hummel-Schluger, 1995; Cherpitel, 1993; Lejoyeux, Feuche, Loi, Solomon, & Ades, 1999; Nagoshi, Wilson, & Rodriguez, 1991). An important aim of the present study is to determine if the Stop RT in rats is also more sensitive than the Go RT to ALC. A differential sensitivity of the Stop RT to ALC would support the hypothesis that the rat and human versions of the stop task measure the same basic behavioral processes.

As was described above, methylphenidate decreases impulsivity, hyperactivity, and Stop RT in children with ADHD. AMP is also an effective treatment for the impulsivity and hyperactivity associated with ADHD (Findling & Dogin, 1998; Gillberg et al., 1997; Solanto, 1998). In normal adults, moderate doses of AMP not only decrease RT (Koelega, 1993) but also improve sustained performance (Caldwell & Caldwell, 1997; Ward, Kelly, Foltin, & Fischman, 1997) and learning and memory (Rapoport et al., 1980; Soetens, Casaer, D'Hooge, & Hueting, 1995; Ward et al., 1997). Given the effectiveness of psychomotor stimulants such as AMP and methylphenidate in both ADHD children and normal adults, it is of interest to determine the effects of AMP on the stop task in both normal adult humans and rats. In this study we examined the effects of AMP on the stop task in rats.

In summary, this study had five main goals: (a) to develop a version of the stop task in rats, (b) to determine if individual differences in stop task performance are stable (test–retest reliability), (c) to determine if the Stop and Go processes are different as predicted by the race model, (d) to assess the effects of ALC and AMP on stop task performance, and (e) to determine if the stop task performance and the effects of AMP and ALC in rats are similar to stop task performance and the effects of AMP and ALC in humans.

Method

Subjects

Eleven Holtzman Sprague-Dawley rats (Harlan Sprague Dawley, Inc., Indianapolis, IN) weighing between 520 and 760 g at the time of testing were used. The rats were housed 2 per cage. Lights were on in the colony room from 7 a.m. to 7 p.m. Food (Harlan Teklab Diet No. 8604, Harlan Sprague Dawley, Inc., Indianapolis, IN) was available without restriction. Following each testing session, the rats received 20 min of access to water. The rats were tested 7 days a week.

Apparatus

Six locally constructed experimental chambers were used. These chambers, which were described in detail by Richards, Mitchell, de Wit, and Seiden (1997), had stainless-steel grid floors, aluminum front and back walls, Plexiglas sides, and a Plexiglas top. The front wall of the chamber served as the test panel and had two water dispensers located on either side of a centrally located snout poke hole (see Figure 2). A stimulus light was mounted above the center snout poke hole. The water dispenser stimulus lights were arranged so that they were level with the rat's eyes when the rat's snout interrupted a photo beam in the center snout poke hole. A Sonalert tone generator with a frequency of 4500 Hz was mounted above the left stimulus light. Snout pokes and head entries into the water dispensers were monitored with infrared detectors. Each water dispenser was calibrated to provide a flow rate of 0.151 μl per millisecond. The amount of water dispensed to the rat was a linear function of the duration for which the solenoid valve was held open. The equation $y = 0.151X - 3.2$ specified the amount of water dispensed, where y was the amount in microliters and X was the duration of the solenoid valve operation. For example, opening the valve for 250, 690, and 1,350 ms dispensed 35, 101, and 201 μl of water, respectively. The six chambers were connected to a Pentium 133 MHz microcomputer using a MED Associates interface (MED Associates Inc., St. Albans, VT). The experimental contingencies were programmed using the MED-PC programming language.

Procedure

Stop task. Each session ended after 30 min or the completion of 60 trials. Each trial began with the chamber's center light illuminated. The rat was required to place its snout in the center snout poke hole, just below the center light, and to hold it there for a varying time period between 0.04 and 4 s after which the center light would be turned off (offset). The required hold time for each trial was randomly selected without replacement from the following list: 0.04, 0.56, 1.12, 1.68, 2.28, 2.88, 3.44, and 4.0 s. The hold time was cumulative; for example, if the hold time was 4 s, the rat could meet this requirement by holding its snout in the hole for 2 s on the two different occasions. Following the offset of the center light (Go signal), the rat was required to remove its snout from the center snout poke hole and go to the right water dispenser for a water reward. The time elapsed from the offset of the center light (Go signal) to the rat breaking the photo beam in the right water dispenser provided the Go RT measure. To induce the rat to make the Go RT as fast as possible, the amount of water the rat received for making the Go response depended on the speed of the rat's Go

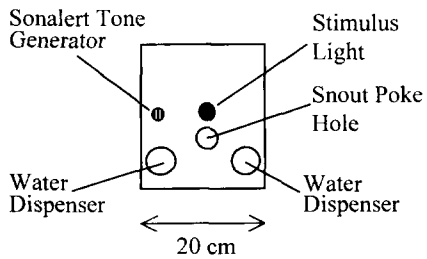

Figure 2. Schematic of the intelligence panel of the experimental chamber, showing the relative locations of the center snout poke hole, the stimulus light, the Sonalert tone generator, and the two water dispensers.

RT. The amount of water the rat received for making the Go response was determined by the equation: valve duration = 2,010 / (1 + 0.01*RT*), where valve duration is the duration that the solenoid valve was open in milliseconds and RT is the Go RT in ms. For example, a 500-ms Go RT would result in the solenoid valve being open for 335 ms, which would produce 50 μl of water (see equation in *Apparatus* section above that describes the relationship between the duration that the solenoid valve is open and the amount of water dispensed), and a 250-ms Go RT would result in the solenoid valve being open for 570 ms, which would produce 84 μl of water.

A tone was presented at random on 4 trials out of every block of 16 trials after the Go signal. The presentation of the tone served as the Stop signal. The Stop signal required the rat to stop the Go response to the right water dispenser and emit a head poke response to the left water dispenser to get water. If the rat failed to stop the Go response (i.e., it interrupted the photo beam in the right water dispenser), it did not receive any water on that trial. If the rat successfully stopped the Go response, it received a water reward when it interrupted the photo beam in the left water dispenser. The amount of water that the rat received for making the Change response to the left water dispenser was equal to the amount of water that it had received for the most recently reinforced Go response. The time elapsed between the presentation of the Stop signal (tone) and the rat breaking the photo beam in the left water dispenser was defined as the Change RT measure.

The elapsed time between the Go signal (offset of the center light) and presentation of the Stop signal (tone) was referred to as the *stop signal delay*. The stop signal delay was increased or decreased by 20 ms depending on the success of the rat on the preceding Stop trial. For example, if the rat successfully stopped, the stop signal delay was increased by 20 ms on the next Stop trial. If the rat failed to stop, the stop signal delay was decreased by 20 ms on the next Stop trial. Adjusting the stop signal delay in this fashion resulted in the rat failing to stop approximately 50% of the time. At the beginning of each session, the stop signal delay was set at the average stop signal value for the preceding day's session (except for sessions following drug tests). As was described in the introduction, determination of the stop signal delay at which the rat failed to stop 50% of the time provided a method for estimating how long it took the rat to stop or "inhibit" an ongoing response. This estimate was referred to as the Stop RT and was calculated by subtracting the average stop signal delay from the mean of the Go RT.

Initial training. The rats were first trained to go to the left water dispenser for water when the light offset occurred simultaneously with tone presentation and to go to the right water dispenser when the light offset was not accompanied by tone presentation. This was accomplished by placing a naive, thirsty rat into the chamber with the center light on. The first center snout poke turned off the center light and resulted in the presentation of the tone on 50% of the trials (there was no center snout poke hold requirement in this initial phase of training). On tone trials, a head insert into the left water dispenser resulted in water presentation, offset of the tone, and onset of the light above the center snout poke hole. In contrast, a head insert into the right water dispenser resulted only in the offset of the tone and onset of the light above the center snout poke hole on tone trials. On no-tone trials, a head insert into the right water dispenser resulted in water presentation and onset of the light above the center snout poke hole. In contrast, a head insert into the left water dispenser resulted only in the onset of the light above the center snout poke hole. During this phase of training, both the left and right water dispensers provided a constant 50 μl of water. Because of the rats' natural tendency to investigate holes with their snouts, they learned the conditional discrimination within five, 1-hr training sessions.

After the rat learned the conditional discrimination, the center snout poke hold requirement was gradually increased over a 2-week period to the training durations listed above. At that point, training on the stop task procedure described above was begun. The rats were trained on different versions of the stop task for 32 weeks before drug testing reported in this article was started. During this training period, parameters of the testing procedure (i.e., magnitude of reinforcement, stop signal delay, and the number of trials) were varied to determine the best procedure for drug testing.

During drug testing (described below), each test session consisted of a total of 192 trials or 30 min, whichever occurred first. Except after the highest doses of ALC and AMP, the rats completed 192 trials in about 15 min. Only Trials 33 through 192 were used for data analysis. Eliminating the first 32 trials helped ensure that the stop signal delay was adjusted to close to the 50% failure point on drug days before data collection was begun.

Drug administration. *d*-amphetamine sulfate (AMP; Sigma Chemical, St. Louis, MO) was dissolved in saline (0.125, 0.25, 0.5, 1.0 mg/kg; doses are expressed in terms of the salt) to form a solution of 1 ml/kg. ALC was mixed with saline (0.25, 0.5, 0.75 g/kg) to form a solution of 3 ml/kg. The drugs were injected intraperitoneally every 3rd day. The sequence of doses for each rat was determined using a balanced Latin square sequence. Each dose of AMP and ALC was administered to each rat on three different occasions, and the mean of the three data points at each dose was used for analysis. AMP was administered first over an 8-week period, followed by ALC, which was administered over a 6-week period. AMP was injected 20 min prior to the start of each session, and ALC was injected 30 min prior to the start of the session.

Data analysis. The dependent measures were the Stop, Go, and Change RT. To determine if the Stop, Go, and Change RTs reflect different or related behavioral processes, we calculated a Pearson product–moment correlation coefficient between each of these measures using baseline data (the 2nd day after a drug injection) collected during the AMP and ALC dose response determinations. To determine if the individual differences observed in the Stop, Go, and Change RT were stable across time and demonstrated test–retest reliability, we calculated a Pearson product–moment correlation for each of these measures between AMP baseline performance and ALC baseline performance.

The effects of AMP and ALC on the Stop, Go, and Change RTs and on the percentage of failures to stop were first analyzed using a one-factor (drug dose) within-subject analysis of variance (ANOVA). If the ANOVA was significant, follow-up post hoc analysis was done using Fisher's least significant difference tests to compare each dose with vehicle. Because of the large intersubject variability in the Stop RT and because inspection of individual subject data seemed to indicate differential effects of AMP, a median split analysis was performed on the AMP data, which analyzed performance of "fast stoppers" and "slow stoppers" separately. The median split analysis was based on the baseline Stop RT. The baseline data were not included in the statistical analysis. Separate one-factor (drug dose) within-subject ANOVAs were performed on the fast and slow stoppers, and follow-up Fisher's least significant difference tests were done if the ANOVA was significant. In all cases, the required significance level was $p < .05$.

Results

Correlations

There was no significant correlation between the Go and the Stop RTs or the Go and the Change RTs, but there was a significant correlation between the Stop and the Change RTs. The Pearson product–moment correlation coefficients between the three measures of Stop performance during the AMP dose response determination were as follows: Stop RT versus Go RT, $r = .064$, $p > .05$; Stop RT versus Change RT, $r = .714$, $p < .05$; and Go RT versus Change RT, $r = -.338$, $p > .05$. The correlation coefficients for the baseline test days during the ALC dose response determination were as follows: Stop RT versus Go RT, $r = .072$, $p > .05$; Stop RT versus Change RT, $r = .832$, $p < .05$; and Go RT versus Change RT, $r = -.122$, $p > .05$.

There were large and reliable correlations between measures of baseline stop task performance during the AMP dose response determination and baseline performance during the ALC dose response determination: baseline AMP Stop RT versus baseline ALC Stop RT, $r = .955$, $p < .05$; baseline AMP Go RT versus baseline ALC Go RT, $r = .969$, $p < .05$; and baseline AMP Change RT versus baseline ALC Change RT, $r = .997$, $p < .05$.

Amphetamine

Stop failures. There was no significant effect of AMP on the percentage of stop trials on which the rats failed to stop. The average percentage (± *SEM*) of the trials on which the rats failed to stop during the AMP dose response determination are shown in Table 1 .

Stop RT. Figure 3A shows the effects of AMP on the Stop RT. The results of the ANOVA indicated no significant effect of AMP on the Stop RT, $F(4, 40) = 2.18$, $p = .09$. A median split analysis was performed on the Stop RT data to examine the performance of fast and slow stoppers separately (see *Data analysis* section above). The median split was based on the baseline Stop RT (see Figure 3B). A significant effect of dose was found in the slow-stopper group, $F(4, 20) = 3.03$, $p < .05$. There was no significant effect of dose in the fast-stopper group. Post hoc tests on the slow-stopper data indicated that, compared with saline, the Stop RT was decreased at the 1.0 mg/kg dose.

Go RT. Figure 3C shows the effects of AMP on the Go RT. The results of the ANOVA indicated a significant effect of AMP on the Go RT, $F(4, 36) = 27.05$, $p < .05$. Post hoc tests indicated a significant effect of AMP at the 0.25, 0.5, and 1.0 mg/kg doses when compared with the Go RT for saline. Figure 3D shows the Go RT data for the fast and slow stoppers from the median split analysis performed on the Stop RT. A significant effect of dose was found in both the slow-stopper, $F(4, 20) = 19.73$, $p < .05$, and fast-stopper, $F(4, 12) = 7.57$, $p < .05$, groups. Post hoc tests indicated a significant effect of AMP on the Go RT in both the fast- and slow-stopper groups at the 0.25, 0.5, and 1.0 mg/kg doses when compared with saline.

Change RT. Figure 3E shows the effects of AMP on the Change RT. The results of the ANOVA indicated a significant effect of AMP on the Change RT, $F(4, 36) = 5.22$, $p < .05$. Post hoc tests indicated that the Change RT was significantly decreased at the 0.25 and 0.5 mg/kg doses when compared with the Change RT for saline. Figure 3F shows the Change RT data for the fast and slow stoppers from the median split analysis performed on the Stop RT that analyzed the performance of fast and slow stoppers separately. A significant effect of dose on the Change RT was found in the slow-stopper group, $F(4, 20) = 5.02$, $p < .05$. There was no significant effect of dose on the Change RT in the fast-stopper group. Post hoc tests on the slow-stopper group indicated that the Change RT was significantly decreased at the 0.5 mg/kg dose when compared with the Change RT for saline.

Alcohol

A median split analysis of the effects of ALC on fast and slow stoppers showed no differential effect (data not shown). The results reported below are for fast and slow stoppers combined.

Stop failures. There was a significant effect of ALC on the percentage of stop trials on which the rats failed to stop, $F(3, 30) = 5.13$, $p < .05$. The average percentage of the trials on which the rats failed to stop during the ALC dose response determination is shown in Table 2 . Post hoc tests indicated that ALC caused a significantly greater percentage of stop failures at the 0.75 g/kg dose.

Stop RT. Figure 4 (top) shows the effects of ALC on the Stop RT. The results of the ANOVA indicated a significant effect of ALC on the Stop RT, $F(3, 30) = 10.86$, $p < .05$. Post hoc tests indicated a significant increase in the Stop RT at both the 0.5 and 0.75 g/kg doses of ALC when compared with the Stop RT for vehicle.

Go RT. Figure 4 (middle) shows the effects of ALC on the Go RT. The results of the ANOVA indicated a significant effect of ALC on the Go RT, $F(3, 27) = 7.30$, $p < .05$. Post hoc tests indicated a significant increase in the Go RT at the 0.75 g/kg dose when compared with the Go RT for vehicle.

Change RT. Figure 4 (bottom) shows the effects of ALC on the Change RT. The results of the ANOVA indicated a significant effect of ALC on the Change RT, $F(3, 27) = 10.19$, $p < .05$. Post hoc tests indicated a significant increase in the Change RT at the 0.75 g/kg dose of ALC when compared with the Change RT for vehicle.

Discussion

The results of this study showed that the measures were stable and reliable and, as in the human version of the stop task, the Stop and the Go RTs measured different processes. The Stop and Go RTs were highly correlated for the same subjects tested at different times, at least 2 weeks apart, showing that the measures have good test–retest reliability. There was no correlation between the Stop and the Go RTs, supporting the assumption of the race model that

Table 1
Effects of Amphetamine on Percentage of Stop Failures in "Slow," "Fast," and "Slow + Fast" Stoppers

			Dose of d-amphetamine (mg/kg)			
Group	Baseline	Saline	0.125	0.25	0.50	1.0
Slow	44.3 ± 3.0	48.8 ± 3.0	45.8 ± 1.6	47.8 ± 1.4	48.6 ± 1.3	50.6 ± 1.5
Fast	46.8 ± 1.9	45.8 ± 2.3	47.6 ± 1.4	47.8 ± 1.4	51.6 ± 1.4	50.0 ± 1.2
Slow + Fast	45.4 ± 1.8	45.6 ± 2.4	45.8 ± 1.3	47.4 ± 0.9	49.5 ± 1.1	51.0 ± 0.9

Note. Values are means (±SEM).

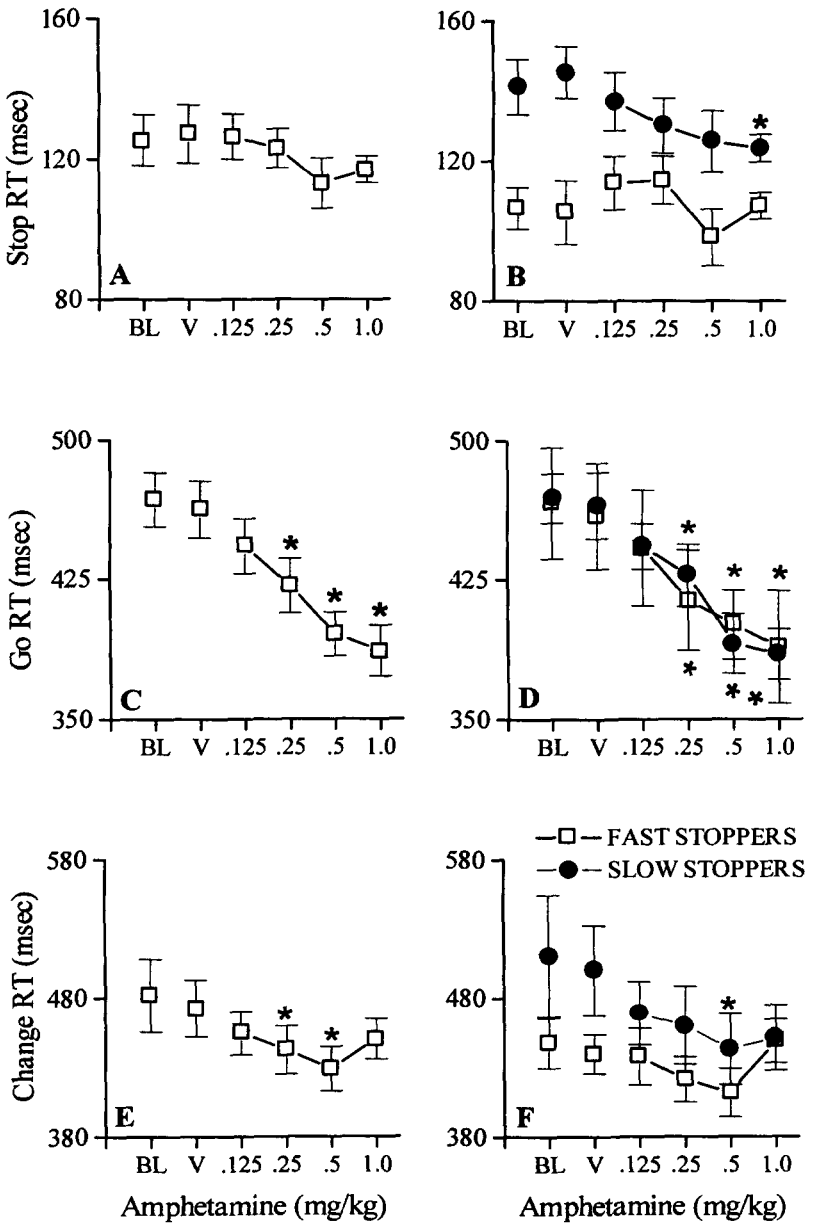

Figure 3. A: Mean Stop reaction time (RT) plotted as a function of amphetamine dose. B: Mean Stop RT in slow and fast stoppers plotted as a function of amphetamine dose. C: Mean Go RT plotted as a function of amphetamine dose. D: Mean Go RT in slow and fast stoppers plotted as a function of amphetamine dose. E: Mean Change RT plotted as a function of amphetamine dose. F: Mean Change RT in slow and fast stoppers plotted as a function of amphetamine dose. Error bars indicate *SEM*. BL = baseline; V = vehicle. * $p < .05$.

the Stop and Go processes are different (Logan, 1994). There was also no significant correlation between the Go RT and the Change RT, indicating that these metrics also measure different behavioral processes. In contrast, there was a significant correlation between the Stop RT and the Change RT, indicating that these two metrics share at least some of the same behavior processes. Indeed, the Change RT is the sum of the time required to inhibit the Go response (Stop RT) and the time required to execute the Change response.

Table 2
Effects of Alcohol on Percentage of Stop Failures

		Dose of alcohol (g/kg)		
Baseline	Saline	0.25	0.50	0.75
45.0 ± 1.7	45.0 ± 1.8	45.0 ± 1.9	45.0 ± 2.5	41.0 ± 2.7*

Note. Values are means (±*SEM*). Asterisk indicates significantly different from saline, $p < .05$.

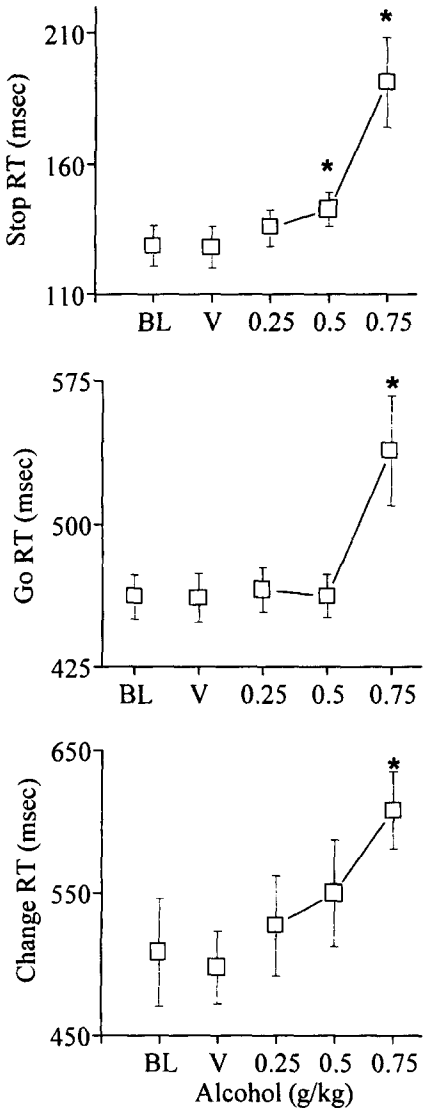

Figure 4. Mean Stop, Go, and Change reaction time (RT) plotted as a function of alcohol dose. Error bars indicate *SEM*. BL = baseline; V = vehicle. * $p < .05$.

Did the Rats Inhibit the Go Response on Stop Trials?

An important assumption in the interpretation of the stop task is that the rats actively inhibit the Go response after it has been initiated. On first examination of the procedure, it may appear that the rats can improve their ability to inhibit responses by learning to slow their initial response to Go signal. However, the procedure is designed specifically to prevent this strategy, and there was no evidence that the rats did so in this study. Several elements of the procedure helped to ensure that the rats did not learn to slow execution of the Go response. First, the stop signal delay was adjusted to compensate for the duration of the Go RT. The stop signal delay was adjusted so that the rats would fail on approximately 50% of the Stop trials no matter how much they slowed the speed of the Go response. The stop signal delay was increased by 20 ms every time a rat successfully stopped. Thus, the rat would have had to constantly slow the Go response throughout the session to increase the percentage of successful Stop trials. Second, the faster the rats made the Go response, the more water they received for both the Go and Stop responses. The amount of water the rats received for successfully completing both Go and Stop trials was contingent on the execution speed of the Go response. On Go trials, the faster the rat completed the Go response, the more water it received. On successful Stop trials, the amount of water the rat received was equal to the amount given on the most recent Go trial. Thus, slowing of the Go response to wait for the possible occurrence (on one out of four trials) of the Stop signal would have resulted in less water for both the Go and Stop responses. In other test procedures, with the same apparatus, we have found that rats are very sensitive to the amount of water (Richards et al., 1997). Third, the rats were rewarded for making the Go response on three out of four trials. Making three of four trials Go trials was designed to bias the rats toward making the Go response by establishing the Go response as the prepotent response in the experimental setting.

Obtained measures of performance on the Stop task indicate that the rats did not slow Go RT to wait for the Stop signal. First, Stop RT was not correlated with Go RT as may have been expected if the rats were following a strategy of slowing execution of the Go RT to wait for the Stop signal. Second, the rats had an average failure rate of approximately 45% (see Tables 1 and 2). This means that out of every 20 Stop trials 11 were rewarded. This represents a very small increase in the number of rewarded Stop trials compared with the ideal failure rate of 50% in which 10 of every 20 Stop trials would have been rewarded.

Figure 5 shows the within-session performance of fast and slow stoppers during amphetamine baseline test sessions. This figure indicates that there was no difference in Go RT between fast and slow stoppers during the experimental sessions, indicating that

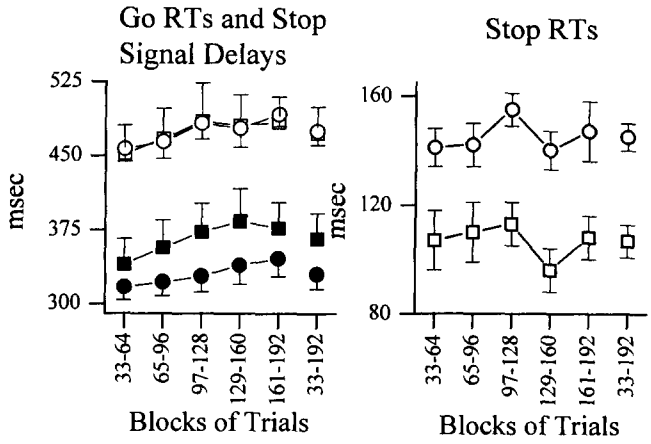

Figure 5. The within-session performance of fast and slow stoppers during amphetamine baseline test sessions. Left: the stop signal delays and Go reaction times (RTs) for Trials 33–192, in 32-trial blocks, and the average stop signal delays and Go RTs for Trials 33–192. Circles indicate slow stoppers, and squares indicate fast stoppers. Open symbols indicate Go RTs, and closed symbols indicate stop signal delays. Right: Stop RTs for the data shown in the left, computed for each rat by subtracting the stop signal delays from the Go RTs shown in the left. The average Stop RT for Trials 33–192 is also shown in the right. Error bars indicate *SEM*.

Stop RT was not a function of the speed of the Go RT. Instead, the difference between fast and slow stoppers resulted from different stop signal delays for fast and slow stoppers as would be predicted by an inhibition interpretation but not a response-slowing interpretation. Figure 5 also shows that Go RT increased slightly across the session (37 ms on average) and that the adjusting stop signal delay tracked this increase so that the difference between Go RT and the Stop signal delay (Stop RT) remained constant, indicating that the observed slowing of the Go RT did not affect the estimated Stop RT. Much larger within-session changes in Go RT than those shown in Figure 5 would have been expected if the rats had followed a strategy of constantly slowing the Go RT to wait for the Stop signal. The observed small increase in Go RT may reflect satiation or perhaps habituation to the experimental stimuli. In summary, the lack of an association between Stop RT and Go RT, the obtained 45% failure rate, and the pattern of within-session changes are consistent with an inhibition interpretation but not with an interpretation based on slowing of the Go response.

Amphetamine

Although AMP did not significantly change the Stop RT when subjects were analyzed as a single group of 11 rats, significant drug effects were obtained when the rats were divided into fast and slow stoppers, with a median split. Slow stoppers showed a dose-dependent decrease in the Stop RT, whereas fast stoppers did not. This effect is probably not due to regression toward the mean because the median split analysis was performed on the baseline data, which were not included in the statistical analysis of the drug effect data. Furthermore, a regression toward the mean effect would predict that the Stop RT should regress toward the mean after vehicle administration, which did not occur (see Figure 3A and 3B). The improvement in the Stop RT observed in slow stoppers after the administration of the stimulant AMP is consistent with findings from ADHD children, in whom the stimulant methylphenidate decreases the Stop RT. ADHD children are also slow stoppers compared with control children (Tannock et al., 1989, 1995).

AMP dose dependently decreased the Go RT in rats, including both fast- and slow-stopper groups (see Figure 3C and 3D). The fact that AMP decreased the Go RT in all of the rats but only decreased the Stop RT in a subset of the rats provides further support for different Go and Stop processes.

AMP at the 0.25 and 0.5 doses significantly decreased the Change RT. The Change RT was decreased more in slow stoppers than in fast stoppers, and AMP had larger effects on the Change RT in the slow-stopper group than in the fast-stopper group (see Figure 3E and 3F). These results and the fact that the Change and the Stop RTs were significantly correlated indicate (as was pointed out above) that the Change and the Stop RTs both reflect the ability to stop. However, in addition to stopping, the Change RT reflects the ability to switch to an alternative response. The fact that there was a significant decrease in the Change RT at doses that did not have significant effects on the Stop RT (0.25 and 0.5 mg/kg) indicates that switching was enhanced at these doses. AMP did not significantly decrease the Change RT at the 1.0 mg/kg dose, indicating that higher doses of AMP may impair switching. An impairment in switching to an alternative response at doses would be consistent with research indicating that AMP increases perseverative responding at doses higher than 1.0 mg/kg (Evenden & Robbins, 1983; Lyon & Robbins, 1975; Ridley, Baker, Frith, Dowdy, & Crow, 1988; Ridley, Baker, & Haystead, 1981). The stimulant methylphenidate has also been observed to decrease the Change RT in children with ADHD (Tannock et al., 1995).

There was no effect of AMP on the percentage of stop failures. Table 1 shows that during baseline and saline conditions the rats had an average failure rate of approximately 45%. This 45% failure rate is less than the ideal failure rate of 50% and may have occurred because of a tendency for the Go RT to increase slightly as the test session progressed. However, a failure rate of 45% represents only a small deviation from the ideal failure rate of 50% (failure on 9 of 20 rather than 10 of 20 trials) and probably does not represent a significant bias of the estimate of the Stop RT.

Interestingly, Table 1 indicates that AMP tended to increase the percentage of stop failures toward the ideal 50% rate, although this effect was not statistically significant. Table 1 also shows that there was no difference between fast and slow stoppers in the percentage of stop failures, so that an increase in the percentage of stop failures does not account for the difference between fast and slow stoppers on the Stop RT.

The effects of AMP on the stop task reported here with rats are similar to the results found using a similar procedure in normal human adult participants (de Wit et al., 2000). In humans, AMP decreased the Stop RT only in participants categorized as slow stoppers by a median split analysis. This striking similarity of the effects of AMP on the Stop RT in rats and humans supports the idea that the stop task procedures in rats and humans are comparable and that cross-species generalizations can be made with the stop task procedure.

AMP decreased the Go RT in rats but not in humans (de Wit et al., 2000). This difference may be accounted for by procedural differences in the Go tasks. In the rat study, the rats were required to perform a vigilance task in which they held their snout in a hole until the imperative stimulus (light offset) was presented. The light offset occurred after an unpredictable interval, and therefore, the rats were required to remain attentive. In the human study, the presentation of the discriminative stimuli (X or O on the screen) was very predictable, occurring every 2 s. These differences in the Go tasks may be responsible for the differential effects of AMP on the Go response in the human and rat stop tasks, especially because it has been shown that AMP decreases the RT in humans performing vigilance tasks (Koelega, 1993).

Alcohol

The Stop RT was increased at the 0.5 and 0.75 g/kg doses of ALC, whereas the Go RT was increased only at the 0.75 g/kg dose (see Figure 4). The finding that the Stop RT but not the Go RT (see Figure 4) was increased at the 0.5 dose of ALC indicates that stopping was more sensitive to the effects of ALC than the Go response. The greater sensitivity of the Stop RT to the effects of ALC in comparison with the Go RT provides further support for separate Go and Stop processes. The differential effects of ALC at the 0.5 g/kg dose also provides some evidence that the effects of ALC are not due to ethanol-induced slowing of motor function. However, it cannot be ruled out that stopping was more sensitive to disruptive motor affects of alcohol.

The Change RT was significantly increased at the 0.75 g/kg dose of ALC (see Figure 4). Although ALC did not have a significant effect at the 0.5 g/kg dose, the patterns of effects of ALC on the Change RT were similar to those observed for the Stop RT. This is not surprising, given the strong correlation between the Stop and Change RTs. However, the lack of a significant effect at the 0.5 g/kg dose indicates that the ability to initiate an alternative response may not be as sensitive as the ability to stop to the effects of ALC.

There was a significant effect of ALC on the percentage of stop failures. Examination of Table 2 shows that during the baseline, saline, 0.25, and 0.5 g/kg conditions, the rats had an average failure rate of approximately 45%. However, only the largest dose (0.75 g/kg) significantly decreased the percentage of stop failures. This result indicates that ALC disrupted the adjusting procedure for determining the Stop RT only at the highest dose.

Stop task studies in humans have also found an effect of ALC on stopping at doses that did not affect the Go RT. Two studies (Fillmore & Vogel-Sprott, 1999; Mulvihill et al., 1997) have reported that ALC decreased the number of successful inhibitions to the Stop signal without affecting the Go RT. We (de Wit et al., 2000) have also found that ALC increased the Stop RT at doses that did not affect the Go RT using an adjusting stop task procedure similar to the one used with rats in the present article. These results, showing that ALC has similar effects in humans and rats, are supportive of the idea that cross-species generalizations can be made with the stop task procedure.

The stop task procedure described in this article measures three different behaviors in rats: (a) the ability to respond to an irregularly presented imperative stimulus (Go RT), (b) the ability to stop a response after its execution has been initiated (Stop RT), and (c) the ability to switch to an alternative response (Change RT). Both AMP and ALC affected all three of these behavioral functions. In general, AMP and ALC had opposite effects: AMP decreased the Go, Stop, and Change RT and ALC increased the Go, Stop, and Change RT. The effects of AMP and ALC on the Stop RT in rats were similar to those reported in humans, indicating that the results from the stop task studies in rats can be generalized to humans.

The data from this experiment and others indicate that Go task requirements do not affect the process of inhibition on the stop task. First, there was no correlation between the Stop and Go processes, and there were differential effects of both AMP and ALC on the Stop RT and the Go RT. Second, research using a variety of different Go tasks (i.e., typing, speaking, and arm movements) has shown that the process of inhibition in the stop task is relatively unaffected by the particular Go response used (see Logan, 1994, for a review).

A major difference between the rat stop task in this article and the human stop tasks, on which AMP and ALC were tested (de Wit et al., 2000; Fillmore & Vogel-Sprott, 1999; Mulvihill et al., 1997), is that the rats were explicitly reinforced for Go and Stop/Change responses whereas the humans were given instructions on how to respond. Fillmore and Vogel-Sprott (1999) reported that explicitly rewarding Stop responses eliminated ALC-induced impairment in stopping. However, this study compared the ALC plus reward group with a control group that was not rewarded. It may have been that, compared with a rewarded control group, the ALC plus reward group was impaired. Other researchers (Oosterlaan & Sergeant, 1998a) have compared explicitly rewarded and nonrewarded (given instructions only) stop task performance in children with ADHD to determine if reward would ameliorate the impairment in the Stop RT typically observed in these children. It was found that explicit reinforcement decreased the Stop RT in both the control and ADHD children, but that the ADHD children were still impaired compared with the controls. These data indicate that the requirement of using explicit contingencies of reinforcement, compared with rule-governed performance, does not affect performance on the stop task when compared with appropriate controls.

The Stop Task as a Measure of Inhibition in Nonhuman Animals

Other behavioral procedures have been used to measure behavioral inhibition in nonhuman animals, such as go/no-go tasks, differential reinforcement of low rates (DRL) schedules, and passive avoidance. However, these lack the solid conceptual and theoretical grounding of the stop task (see Logan, 1994, for a review). The stop task is based on a well-developed theoretical model of behavioral inhibition in humans, the race model, which postulates competing inhibitory stop and noninhibitory go processes. The results of the present study support the existence of these two different processes: The Go and Stop RT were found to be uncorrelated, and the 0.5-g/kg dose of ALC increased Stop RT without affecting Go RT. The inclusion of inhibitory and noninhibitory measures provides a unique within-task control for determining the specificity of the drug effects to inhibitory processes.

The stop task is also different from other putative measures of behavioral inhibition in that it does not require the organism to wait or delay responding. Most of the other measures use the animal's ability to wait or delay responding for a period of time as an indicator of behavioral inhibition. For example, go/no-go tasks require animals to omit a response for the duration of each no-go trial, and on DRL schedules rats are trained to wait between responses to earn a reward. However, these procedures involving the ability to wait may be susceptible to interference from other factors (e.g., general increases in motor output) other than behavioral inhibition. The stop task, in contrast, is less susceptible to the effects of other nonspecific influences. For example, amphetamine at the same doses decreases the time between responses on DRL schedules (Sabol, Richards, Layton, & Seiden, 1995), indicating decreased behavioral inhibition. In contrast, the present results with the stop task indicate that amphetamine increases behavioral inhibition.

In summary, in comparison with other approaches to operationally defining behavioral inhibition in nonhuman animals, the stop task provides a novel approach, which has a well-developed set of theoretical premises. The results observed with AMP and ALC in this study and the similarity of the effects of these drugs on the human stop task performance indicate that the stop task may be a valuable tool for studying behavioral inhibition in animals.

A number of studies from a variety of different laboratories have identified impaired stop task performance in children with ADHD. Drug studies have shown that the stop task is sensitive to the effects of psychomotor stimulants and ALC. The importance of these results is enhanced by the fact that the stop task has strong construct validity as a measure of behavioral inhibition. Development of the stop task in rats and evidence indicating that the stop

task measures similar basic behavioral processes in humans and rats are important because they may provide the basis for establishment of a valid animal model of ADHD and impulsivity in humans. The establishment of the stop task in rats may provide an important approach for studying the neurobiological processes that mediate behavioral inhibition.

Three main goals were accomplished by this experiment. First, we developed a procedure for measuring the Stop RT in rats and demonstrated its reliability and sensitivity. Second, we demonstrated that the Stop and Go processes were different processes as predicted by the race model. And, third, the effects of AMP and ALC on the rat version of the stop task were determined and shown to be parallel to data obtained with human participants.

References

Baer, J. S., Novick, N. J., & Hummel-Schluger, A. O. (1995). Task persistence after alcohol consumption among children of alcoholics. *Alcoholism, Clinical and Experimental Research, 19*, 955–960.

Barkley, R. A. (1997). *ADHD and the nature of self-control*. New York: Guilford Press.

Brandeis, D., van Leeuwen, T. H., Rubia, K., Vitacco, D., Steger, J., Pascual-Marqui, R. D., & Steinhausen, H. C. (1998). Neuroelectric mapping reveals precursor of stop failures in children with attention deficits. *Behavioral and Brain Research, 94*, 111–125.

Caldwell, J. A., & Caldwell, M. A. (1997). An in-flight investigation of the efficacy of dextroamphetamine for sustaining helicopter pilot performance. *Aviation Space and Environmental Medicine, 68*, 1073–1080.

Cherpitel, C. J. (1993). Alcohol, injury, and risk-taking behavior: Data from a national sample. *Alcoholism, Clinical and Experimental Research, 17*, 762–766.

de Wit, H., Crean, J., & Richards, J. B. (2000). Effects of *d*-amphetamine and ethanol on a measure of behavioral inhibition in humans. *Behavioral Neuroscience, 114*, 830–837.

Evenden, J. L., & Robbins, T. W. (1983). Increased response switching, perseveration and perseverative switching following d-amphetamine in the rat. *Psychopharmacology, 80*, 67–73.

Fillmore, M. T., & Vogel-Sprott, M. (1999). An alcohol model of impaired inhibitory control and its treatment in humans. *Experimental and Clinical Psychopharmacology, 7*, 49–55.

Findling, R. L., & Dogin, J. W. (1998). Psychopharmacology of ADHD: Children and adolescents. *Journal of Clinical Psychiatry, 59*(Suppl. 7), 42–49.

Gillberg, C., Melander, H., von Knorring, A. L., Janols, L. O., Thernlund, G., Hagglof, B., Eidevall-Wallin, L., Gustafsson, P., & Kopp, S. (1997). Long-term stimulant treatment of children with attention-deficit hyperactivity disorder symptoms. A randomized, double-blind, placebo-controlled trial. *Archives of General Psychiatry, 54*, 857–864.

Gustafson, R. (1986). Alcohol and simple reaction time in a vigilance setting: a placebo control study. *Perceptual and Motor Skills, 63*(2, Part 1), 385–386.

Hanes, D. P., Patterson, W. F., II, & Schall, J. D. (1998). Role of frontal eye fields in countermanding saccades: Visual, movement, and fixation activity. *Journal of Neurophysiology, 79*, 817–834.

Jennings, J. R., van der Molen, M. W., Brock, K., & Somsen, R. J. (1992). On the synchrony of stopping motor responses and delaying heartbeats. *Journal of Experimental Psychology: Human Perception and Performance, 18*, 422–436.

Jennings, J. R., van der Molen, M. W., Pelham, W., Debski, K. B., & Hoza, B. (1997). Inhibition in boys with attention deficit hyperactivity disorder as indexed by heart rate change. *Developmental Psychology, 33*, 308–318.

Koelega, H. S. (1993). Stimulant drugs and vigilance performance: A review. *Psychopharmacology, 111*, 1–16.

Koob, G. F., Percy, L., & Britton, K. T. (1988). The effects of Ro 15–4513 on the behavioral actions of ethanol in an operant reaction time task and a conflict test. *Pharmacology, Biochemistry, and Behavior, 31*, 757–760.

Lejoyeux, M., Feuche, N., Loi, S., Solomon, J., & Ades, J. (1999). Study of impulse-control disorders among alcohol-dependent patients. *Journal of Clinical Psychiatry, 60*, 302–305.

Logan, G. D. (1994). On the ability to inhibit thought and action: A users' guide to the stop signal paradigm. In D. Dagenbach & T. H. Carr (Eds.), *Inhibitory processes in attention, memory, and language* (pp. 189–236). San Diego, CA: Academic Press.

Logan, G. D., Schachar, R. J., & Tannock, R. (1997). Impulsivity and inhibitory control. *Psychological Science, 8*, 60–64.

Lyon, M., & Robbins, T. W. (1975). The action of central nervous system stimulant drugs: A general theory concerning amphetamine effects. In W. B. Essmand & L. Valzelli (Eds.), *Current developments in psychopharmacology* (Vol. 2, pp. 79–163). New York: Spectrum.

Mayfield, R. D., Grant, M., Schallert, T., & Spirduso, W. W. (1992). Tolerance to the effects of ethanol on the speed and success of reaction time responding in the rat: Effects of age and intoxicated practice. *Psychopharmacology, 107*, 78–82.

Maylor, E. A., Rabbitt, P. M., James, G. H., & Kerr, S. A. (1992). Effects of alcohol, practice, and task complexity on reaction time distributions. *Quarterly Journal of Experimental Psychology, 44*(A), 119–139.

Mulvihill, L. E., Skilling, T. A., & Vogel-Sprott, M. (1997). Alcohol and the ability to inhibit behavior in men and women. *Journal of Studies on Alcohol, 58*, 600–605.

Nagoshi, C. T., Wilson, J. R., & Rodriguez, L. A. (1991). Impulsivity, sensation seeking, and behavioral and emotional responses to alcohol. *Alcoholism, Clinical and Experimental Research, 15*, 661–667.

Oosterlaan, J., Logan, G. D., & Sergeant, J. A. (1998). Response inhibition in AD/HD, CD, comorbid AD/HD + CD, anxious, and control children: A meta-analysis of studies with the stop task. *Journal of Child Psychology and Psychiatry and Allied Disciplines, 39*, 411–425.

Oosterlaan, J., & Sergeant, J. A. (1996). Inhibition in ADHD, aggressive, and anxious children: A biologically based model of child psychopathology. *Journal of Abnormal Child Psychology, 24*, 19–36.

Oosterlaan, J., & Sergeant, J. A. (1998a). Effects of reward and response cost on response inhibition in AD/HD, disruptive, anxious, and normal children. *Journal of Abnormal Child Psychology, 26*, 161–174.

Oosterlaan, J., & Sergeant, J. A. (1998b). Response inhibition and response re-engagement in attention-deficit/hyperactivity disorder, disruptive, anxious and normal children. *Behavioral and Brain Research, 94*, 33–43.

Pliszka, S. R., Borcherding, S. H., Spratley, K., Leon, S., & Irick, S. (1997). Measuring inhibitory control in children. *Journal of Developmental and Behavioral Pediatrics, 18*, 254–259.

Quay, H. C. (1997). Inhibition and attention deficit hyperactivity disorder. *Journal of Abnormal Child Psychology, 25*, 7–13.

Rapoport, J. L., Buchsbaum, M. S., Weingartner, H., Zahn, T. P., Ludlow, C., & Mikkelsen, E. J. (1980). Dextroamphetamine: Its cognitive and behavioral effects in normal and hyperactive boys and normal men. *Archives of General Psychiatry, 37*, 933–943.

Richards, J. B., Mitchell, S. H., de Wit, H., & Seiden, L. S. (1997). Determination of discount functions in rats with an adjusting-amount procedure. *Journal of the Experimental Analysis of Behavior, 67*, 353–366.

Ridley, R. M., Baker, H. F., Frith, C. D., Dowdy, J., & Crow, T. J. (1988). Stereotyped responding on a two-choice guessing task by marmosets and humans treated with amphetamine. *Psychopharmacology, 95*, 560–564.

Ridley, R. M., Baker, H. F., & Haystead, T. A. (1981). Perseverative behaviour after amphetamine: Dissociation of response tendency from reward association. *Psychopharmacology, 75*, 283–286.

Rubia, K., Oosterlaan, J., Sergeant, J. A., Brandeis, D., & von Leeuwen, T.

(1998). Inhibitory dysfunction in hyperactive boys. *Behavioral and Brain Research, 94*, 25–32.

Rubia, K., Overmeyer, S., Taylor, E., Brammer, M., Williams, S. C., Simmons, A., & Bullmore, E. T. (1999). Hypofrontality in attention deficit hyperactivity disorder during higher-order motor control: A study with functional MRI. *American Journal of Psychiatry, 156*, 891–896.

Sabol, K. E., Richards, J. B., Layton, K. E., & Seiden, L. S. (1995). Amphetamine analogs have differential effects on DRL 36-s schedule performance. *Psychopharmacology, 121*, 57–65.

Soetens, E., Casaer, S., D'Hooge, R., & Hueting, J. E. (1995). Effect of amphetamine on long-term retention of verbal material. *Psychopharmacology, 119*, 155–162.

Solanto, M. V. (1998). Neuropsychopharmacological mechanisms of stimulant drug action in attention-deficit hyperactivity disorder: A review and integration. *Behavioral and Brain Research, 94*, 127–152.

Spirduso, W. W., Mayfield, D., Grant, M., & Schallert, T. (1989). Effects of route of administration of ethanol on high-speed reaction time in young and old rats. *Psychopharmacology, 97*, 413–417.

Tannock, R., Schachar, R. J., Carr, R. P., Chajczyk, D., & Logan, G. D. (1989). Effects of methylphenidate on inhibitory control in hyperactive children. *Journal of Abnormal Child Psychology, 17*, 473–491. [Published erratum appears in *Journal of Abnormal Child Psychology, 1990,* Vol. 18, p. 119]

Tannock, R., Schachar, R., & Logan, G. (1995). Methylphenidate and cognitive flexibility: Dissociated dose effects in hyperactive children. *Journal of Abnormal Child Psychology, 23*, 235–266.

Ward, A. S., Kelly, T. H., Foltin, R. W., & Fischman, M. W. (1997). Effects of d-amphetamine on task performance and social behavior of humans in a residential laboratory. *Experimental and Clinical Psychopharmacology, 5*, 130–136.

Young, J. R. (1970). Blood alcohol concentration and reaction time. *Quarterly Journal of Studies on Alcohol, 31*, 823–831.

Received August 13, 1999
Revision received January 24, 2000
Accepted February 11, 2000 ■