Published in final edited form as:

Drug Alcohol Depend. 2013 September 1; 132(0): . doi:10.1016/j.drugalcdep.2013.07.009.

Sensitivity to reinforcer delay predicts ethanol's suppressant effects, but itself is unaffected by ethanol

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Abstract

BACKGROUND—Relative preference for smaller, sooner rewards over larger, later rewards (“delay discounting”) is increased by acute ethanol. Additionally, drug-naïve levels of delay discounting can predict subsequent ethanol consumption. However, it is unknown whether these phenomena are driven by a difference in sensitivity to the reinforcer delay or a difference in sensitivity to the reinforcer magnitude, because typical delay discounting tasks manipulate both parameters simultaneously.

METHODS—To disambiguate these factors, two tasks were developed in which animals chose between levers with either different delay contingencies (adjusting delay task) or different magnitude contingencies (adjusting magnitude task). When task performance was stable, rats received ethanol (0, 0.6, and 0.9 g/kg, i.p.).

RESULTS—Ethanol did not affect sensitivity to delay or sensitivity to magnitude. However, responding was suppressed at the highest dose of ethanol (0.9 g/kg). Less suppression was found in animals exhibiting high levels of drug-naïve sensitivity to delay.

CONCLUSION—Thus, this study suggests that ethanol’s effect on standard delay discounting tasks is not due to an alteration in sensitivity to delay or magnitude. Additionally, these data show that animals with high sensitivity to delay are resistant to the behaviorally suppressant effects of ethanol, which suggests that low tolerance for delayed rewards and low sensitivity to the behaviorally suppressant effects of ethanol may partly be driven by the same underlying mechanism.

Keywords

Impulsivity; Ethanol; Intertemporal Choice; Delay Discounting; Low Level of Response to Alcohol

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Contributors. TMM and SHM designed the study, TMM collected the data with help from Alex Murray and Richard Beaumont, data analysis was performed by TMM, and TMM and SHM interpreted the data and prepared the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of Interest. All authors declare that they have no conflicts of interest.

1. INTRODUCTION

Acute ethanol use can lead to many potentially deleterious actions, such as drunk driving, increased aggression, and unprotected sex, which may be markers of increased impulsivity (reduced sensitivity to delayed consequences). Although studies using human subjects have not yielded clear results (Ortner et al., 2003; Richards et al., 1999; Dougherty et al., 2008; Reynolds et al., 2006), the majority of published studies using animal subjects have indicated that acute ethanol increases impulsivity in a delay discounting model (Evenden and Ryan, 1999; Hellemans et al., 2005; Olmstead et al., 2006; Poulos et al., 1998; Tomie et al., 1998; but see Wilhelm and Mitchell, 2012); that is, ethanol increases choice of a small, immediate reward over a larger, delayed reward.

Although ethanol's ability to increase discounting is well reported in animals, mathematical models of delay discounting do not indicate whether increases in delay discounting occur through increases in sensitivity to delay or decreases in sensitivity to magnitude (Ho et al., 1999; Killeen, 2009; Logue et al., 1984), nor do these models address the effects of ethanol. Further, the typical procedure cannot easily dissociate ethanol's effects on sensitivity to reinforcer magnitude and reinforcer delay, because both reward magnitude and delay length differ between choice alternatives.

Consequently, existing theory and data are inconclusive as to whether changes in one or both types of sensitivity are responsible for increases in delay discounting. However, two studies report that ethanol increased choice of the smaller reinforcer when there was no delay for both the small and the large reward, implying decreases in sensitivity to magnitude (Evenden and Ryan, 1999; Tomie et al., 1998). Unfortunately, in most studies examining ethanol's effects on delay discounting, equivalent delay conditions were not assessed.

Determining the effect of ethanol on these two components of delay discounting is important because it could both impact treatment strategy and help identify the brain regions by which ethanol has its effect on discounting. For example, a behavioral treatment focused on changing sensitivity to delay (e.g., Ainslie, 1975; Monterosso and Ainslie 1999, 2007) would be of little help if ethanol only acts on delay discounting by altering sensitivity to reinforcer magnitude. Furthermore, since different brain regions have been implicated in delay and magnitude sensitivity (see Cardinal, 2006 for a review), determining whether ethanol alters sensitivity to delay or magnitude could narrow down which brain regions to target using selective drugs or other procedures. Accordingly, we tested ethanol's effects on these parameters by examining the effects of systemic ethanol on two tasks that manipulate delay or magnitude independently. We predicted that ethanol would increase sensitivity to delay, decrease sensitivity to magnitude, or do both.

Some research has indicated that drug-naïve performance on a typical delay discounting task predicts ethanol's effects on behavior. For example, steep delay discounting predicts increased sensitization to the locomotor activating effects of ethanol in outbred mice (Mitchell et al., 2006). This is relevant because the motor response to ethanol can itself be predictive of subsequent ethanol consumption. For example, in humans, low response to ethanol's effects predicts future alcoholism (Schuckit, 1994). Similar findings have been found in rats: High alcohol drinking and preferring rats are less sensitive to the behaviorally suppressant effects of ethanol than low alcohol drinking and preferring rats, although they are more sensitive to the stimulant effects of low doses of ethanol (Rodd et al., 2004; Waller et al., 1986; for review see Crabbe et al., 2010). Based upon this literature, we hypothesized that either high sensitivity to delay or low sensitivity to magnitude (operationally, low adjusting delay or low adjusting magnitude) would predict resistance to ethanol's behaviorally suppressant effects (operationally, number of trials completed).

2. METHODS

2.1. Subjects

Male Long-Evans rats ($n = 20$) were purchased from Charles River Laboratories (Hollister, CA). Rats were 8 - 9 weeks old and weighed approximately 275-300 g upon arrival. Animals were housed two per cage in a temperature-controlled vivarium at Oregon Health & Science University. A 12:12 light-dark cycle was used (Lights on at 0600 h). All procedures were approved by the Institutional Animal Care and Use Committee and adhered to NIH Guidelines. Animals were acclimated to handling for one week and were subsequently food restricted to approximately 85% of their free-feeding weights for the duration of the study.

2.2. Apparatus

Eight operant chambers (25 x 32 x 26) housed in sound-attenuating cabinets (4 x 64 x 42 cm; Med Associates Inc., St. Albans, VT) were used. Each cabinet contained a fan for ventilation and white noise. The top, back and front panels of the operant chambers were made of clear acrylic; the front panel also served as the door to the chamber. The left and right panels were made of stainless steel. The left panel contained a central houselight (top), as well as left and right cue lights (top), levers (middle), and liquid receptacles (bottom). Between the receptacles there was a center nosepoke with a built-in cue light. The right panel contained a tone generator (not used) and a response clicker. The chamber had a grid floor with a metallic pan underneath filled with bedding. Two computer-controlled pumps filled with 20% w/v sucrose were connected to the liquid receptacles. Input/output was controlled using a program written in MED-PC (Med Associates Inc.).

2.3. Drugs

Ethanol (200 proof) was diluted to 20% v/v in 0.9% saline, and was administered intraperitoneally (i.p.) immediately before the test session (0.0, 0.6, 0.9 g/kg). Each dose was administered 3 times, order counterbalanced. Test sessions occurred on Tuesdays and Fridays, and non-injection sessions occurred on Mondays, Wednesdays, and Thursdays.

2.4. Procedure

2.4.1. Training—All animals were trained in three consecutive phases, and graduated from each phase after obtaining at least 45 reinforcers over two consecutive days. Animals first trained with independent concurrent VT-120 s FR-1 schedules operating for the left and right levers/feeders. Subsequently, the VT-120 s contingency was dropped and animals were required to nosepoke into a center hole before the FR-1 contingency would operate for the left or right levers. Animals then entered a final training phase on which the FR-1 contingency was alternated between left and right levers on each trial.

2.4.2. Adjusting Tasks (Fig. 1)—After completing training, animals entered the experimental phase and were randomly assigned to either the adjusting delay ($n = 9$) or adjusting magnitude task ($n = 9$). Two animals were not assigned: one died for reasons unrelated to the experiment and the other was unable to complete training. The two tasks used were based on those used by Mazur (1984) and da Costa Araújo et al. (2010) and required animals to respond on discrete trials. In these two tasks, increased sensitivity to delay is measured as a decrease in adjusting delay, while decreased sensitivity to magnitude is measured as a decrease in adjusting magnitude (defined below).

Events in each trial were the same for the adjusting delay and adjusting magnitude tasks. Every trial began with the illumination of the center nosepoke (Figure 1c). If the rat poked its nose into the center nosepoke, the light was extinguished and the lights above the left and

right levers were illuminated (free choice trial). For the trial to continue, animals had to press one of the levers. After two consecutive choices of the same lever on free choice trials, a forced choice was introduced such that only the light over the nonselected lever was illuminated. Following a press on an illuminated lever, the lever light was extinguished, the reinforcer was delivered according to the contingencies associated with the specific lever and task, and the intertrial interval (ITI) began. Responses on the non-illuminated lever were recorded but had no effect. The duration of the ITI was adjusted on a trial by trial basis to ensure that the period between lever choice and the start of the next trial always lasted 27 seconds. Animals performed the task until they completed 90 trials or until 90 minutes elapsed, whichever occurred first. The adjusting and variable levers were switched daily according to a pseudorandom schedule, with no lever being on the same side for more than two consecutive days.

2.4.2.1. Adjusting delay task (Figure 1a): A press on the variable lever resulted in a liquid sucrose reinforcer (75 μ l) delivered 18 s or 2 s after the lever press (probability = .5). A press on the adjusting lever resulted in the same size liquid sucrose reinforcer delivered t s after the lever press, where t was equal to the adjusting delay time. The step size by which the adjusting delay altered across trials was calculated based on each animal's choices. Choice of the variable lever decreased the adjusting delay by 10%, while choice of the adjusting lever increased the adjusting delay by 10%. Percentages, rather than fixed values, were used to address the psychophysical relationship between delay length and perceived delay length. The adjusting delay was set to 10 s at the start of each session, and could not go below 0.75 s or above 22 s.

2.4.2.2. Adjusting magnitude task (Figure 1b): A press on the variable lever resulted in immediate delivery of a liquid sucrose reinforcer with a magnitude of 15 μ l or 135 μ l (probability = .5). A press on the adjusting lever resulted in immediate delivery of a liquid sucrose reinforcer with a magnitude of m μ l, where m was equal to the adjusting magnitude. The adjusting magnitude step size was calculated based on each animal's choices. Choice of the variable lever increased the adjusting magnitude by 10%, while choice of the adjusting lever decreased the adjusting magnitude by 10%. The adjusting magnitude was set to 75 μ l at the start of each session, and could not go below 6 μ l or above 165 μ l.

Before testing began, individual animals had to have at least 5 days of stable data (determined by visual inspection).

2.4.3. Contingency Manipulations—Before ethanol administration, we verified the sensitivity of the tasks to manipulation by altering the values of the variable lever reward delays or magnitudes for animals in each task. Contingency manipulations were administered on Tuesdays and Fridays; on all other days animals were run on the normal task. In the adjusting delay task, animals were exposed to 2 s / 2 s, 2 s / 6 s, 6 s / 18 s, and 18 s / 18 s alternatives on the variable lever (order counterbalanced); for the adjusting magnitude task, animals were exposed to 15 μ l / 15 μ l, 15 μ l / 45 μ l, 45 μ l / 135 μ l, and 135 μ l / 135 μ l on the variable lever (order counterbalanced).

2.5. Data analysis

2.5.1. Contingency Manipulations—The contingency manipulations were analyzed with a 4 x 2 ANOVA (Manipulation condition x Session; the former variable compares each manipulation to the others, the latter variable compares each manipulation session to the preceding non-manipulation session).

2.5.2. Effect of Acute Ethanol—The primary dependent variable was the mean adjusting delay or magnitude value for the latter half of each session (last 45 trials). The latter half was used rather than the whole session in order to allow the animal time to achieve a point of indifference between the two levers (although it should be noted that the results did not change if data for the entire session or first half were used). There were a few instances where animals did not complete all of the trials within the 90-min session. If fewer than 45 trials were completed, such sessions were dropped from the analysis (6 out of 162 injection sessions). If more than 45 were completed but animals did not complete the session, adjusting delay or magnitude values were calculated using data from trials after trial 45 (16 out of 162 injection sessions). Data were collapsed across session and analyzed using a 3 x 2 ANOVA (Dose x Injection; the “Injection” variable compared data from the injection days with data from the days immediately prior to the injection days to determine if there were any effects of injection itself). Similar analyses were performed using preference data (proportion choice of the variable lever). An additional series of 3 x 2 x 18 ANOVAs were performed to examine the effect of ethanol on the number of trials completed as a function of dose, injection and time during the session (number of trials completed was averaged into eighteen 5-minute bins). These were followed up with individual ANOVAs for each dose.

To determine the nature of the behaviorally suppressant effect of ethanol, we performed a 3 x 2 x 10 ANOVA (Dose x Injection x Timebin) analysis on the logarithmically transformed reaction times for each animal in each time bin. We examined both reaction time to nosepoke and reaction time to lever press. Only the first 50 minutes of the task were used in this analysis because many animals completed the task shortly after that time, which introduced missing data into subsequent time bins.

2.5.3. Regression Analysis—A linear regression model using the adjusting delay or magnitude values averaged for the 10 days prior to any ethanol exposure was performed to predict the number of trials completed as well as the reaction times after ethanol administration for each dose. Number of trials completed or reaction time on the pre-injection day was also used as a predictor variable in this model to control for differences in baseline responding in the task. Because animals recovered from ethanol’s behaviorally suppressant effects over the course of the session, we only used the total number of trials completed or reaction times in the first 20 min of the session in the analysis. The use of 20 min was based on the duration of the distribution phase seen in rat brain tissue after i.p. ethanol (lasting roughly 20 min; Adalsteinsson et al., 2006, using 1.0 g/kg) as well as the rate of recovery seen in our data (see Fig. 3).

3. RESULTS

3.1. Contingency Manipulations

There were significant effects of the contingency manipulations for both the adjusting delay and adjusting magnitude tasks (Manipulation x Session: delay: $F(3,24) = 9.20$, $p < .001$; magnitude: $F(2.29,18.33) = 10.50$, $p = .001$). Bonferroni post hoc tests found significant effects for the 18 s / 18 s, 15 μ l / 15 μ l, and 135 μ l / 135 μ l conditions compared to the session prior to manipulation, suggesting that these tasks were able to measure acute changes in behavior (see Fig. 2).

3.2. Effect of Acute Ethanol

Animals reached approximate indifference by the last 45 trials in both tasks after injection (magnitude task: $53.2 \pm 1.8\%$ preference for variable lever, one-sample t-test vs. 50%: $t(8) = -1.75$, $p = .119$; delay task: $52.1 \pm 1.5\%$ preference for variable lever, $t(8) = -1.36$, $p = .210$). There were no effects of ethanol on adjusting delay or adjusting magnitude, calculated from

these final 45 trials of the session, at any dose (Dose x Injection, adjusting delay: $F(2,16) = .84$, $p = .450$; Dose x Injection, adjusting magnitude: $F(2,16) = .06$, $p = .946$; see Fig. 3). Ethanol also did not affect preference ratios for either task ($F_s < 1.4$, $p_s > .27$). However, ethanol did dose-dependently decrease rate at which trials were completed early in the session, followed by a compensatory increase later in the session as shown by the Dose x Injection x Time bin analyses (adjusting delay: $F(34,272) = 11.96$, $p < .001$; adjusting magnitude: $F(34,272) = 4.62$, $p < .001$; see Fig. 4). Examining the saline, 0.6 and 0.9 g/kg dose conditions separately revealed that, although this effect was by far the strongest at 0.9 g/kg, all doses had an effect on the number of trials completed per time bin on the adjusting delay task (Saline, $F(17,136) = 1.98$, $p = .016$; 0.6 g/kg, $F(17,136) = 4.41$, $p < .001$; 0.9 g/kg, $F(17,136) = 26.04$, $p < .001$). Only the effects of the 0.6 and 0.9 g/kg dose conditions were significant for the adjusting magnitude task (Saline, $F(17,136) = 1.21$, $p = .267$; 0.6 g/kg, $F(17,136) = 4.24$, $p < .001$; 0.9 g/kg, $F(17,136) = 10.55$, $p < .001$). Bonferroni post hoc tests comparing pre-injection day to injection day only found significant differences in individual time bins at the 0.9 g/kg dose. In the adjusting delay task, trials completed were significantly different from pre-injection in the 5 – 30 min time bins and in the 65 – 75 min time bins. In the adjusting magnitude task, trials completed were significantly different from pre-injection in the 5, 15, and 85 min time bins. Additionally, ethanol dose-dependently increased time to initiate the trial early in the session in the adjusting magnitude task (Dose x Injection x Time bin, $F(18,144) = 2.40$, $p = .002$) and for the entire first 50 min of the adjusting delay task (Dose x Injection, $F(2,16) = 9.92$, $p = .002$). Ethanol also dose-dependently increased lever choice reaction time for the entire first 50 min of the adjusting magnitude task (trend, Dose x Injection, $F(2,16) = 2.91$, $p = .084$) and early in the session in the adjusting delay task (Dose x Injection x Time bin, $F(18,144) = 1.92$, $p = .019$). These effects were primarily restricted to 0.9 g/kg ($F_s > 2.71$, $p_s < .021$), although modest effects at other doses were seen (adjusting delay, trial initiation, saline: Time bin x Injection: $F(9,72) = 2.29$, $p = .025$; adjusting magnitude, trial initiation, 0.6 g/kg: Time bin X Injection: $F(9,72) = 2.79$, $p = .007$). This shows that 0.9 g/kg generally slowed both trial initiation and choice.

3.3. Regression Analysis

The average adjusting delay on the 10 days before ethanol administration was significantly predictive of the number of trials completed in the first 20 min of 0.9 g/kg ethanol sessions when the number of trials completed on pre-injection days were statistically controlled ($t = -2.62$, $p = .040$; see Fig. 5). No significant relationships were seen for any other dose, for any of the adjusting magnitude data, or for any of the reaction time data.

4. DISCUSSION

In the current study we found that ethanol had no effect on sensitivity to delay or sensitivity to magnitude. Our findings are surprising given the previous literature showing that ethanol can affect delay discounting. However, although many published studies have reported an effect of ethanol on delay discounting, these effects are typically fairly small (e.g. Evenden and Ryan, 1999; Hellemans et al., 2005; Olmstead et al., 2006; Tomie et al., 1998) and at least one published study has failed to find any effect (Wilhelm and Mitchell, 2012). It may be that the procedural differences between our tasks and those used in other studies are sufficient to obscure such modest effects. For example, in our tasks the value of the delay or magnitude changed as a function of the animals' choices, whereas in the aforementioned studies they did not (with the exception of Wilhelm and Mitchell, 2012, which also found no effect of ethanol). If such a procedural difference is sufficient to alter the effect of ethanol, then it may suggest that performance in our task relies on different neural substrates, or that ethanol's effects on delay discounting in other tasks are via a means other than delay or magnitude sensitivity. However, further work would be needed to test these hypotheses.

While we found no effects of ethanol on delay or magnitude sensitivity, we did find that rats with high sensitivity to delay were resistant to ethanol's behaviorally suppressant effects. We did not see a similar relationship in the adjusting magnitude task. The relative specificity of this effect may have implications for other studies showing delay discounting to be predictive of drug effects, since our study suggests that it is sensitivity to delay, rather than sensitivity to magnitude, that is particularly important.

The fact that high sensitivity to delay predicts low response to ethanol's behaviorally suppressant effects may add to the larger literature on high and low responders to ethanol (for reviews of this literature, see Crabbe et al., 2010; Schuckit et al., 2004). It has previously been shown that rats selectively bred for high alcohol consumption exhibit higher ethanol-induced locomotor activity than their low-consuming counterparts (Agabio et al., 2001; Krimmer and Schecter, 1991; Quintanilla, 1999; Rodd et al., 2004; Waller et al., 1986). Furthermore, two of the aforementioned studies also examined doses high enough to result in activity suppression; in both cases the low-consuming lines were more suppressed by ethanol than the high-consuming lines (Rodd et al., 2004; Waller et al., 1986). Thus, there appears to be a strong link between locomotor response to ethanol and consumption of ethanol, and our study suggests that at least the former may be related to sensitivity to delay (although it should be noted that the Long-Evans strain we used only exhibits ethanol-induced decreases in locomotor activity, not biphasic increases and decreases; Duncan and Cook, 1981). Supporting this idea is a previous study in our lab (Mitchell et al. 2006), which found that steep delay discounting predicted stronger sensitization to ethanol's locomotor-enhancing effects in mice.

Complementing our findings are several other studies that have linked delay discounting to ethanol *consumption* (for reviews of this literature see Mitchell, 2011; Lejuez et al., 2010). In humans, individuals dependent upon alcohol show steeper delay discounting than controls (Bjork et al., 2004; Mitchell et al., 2005; Petry, 2001). In animals, steeper delay discounters subsequently consume more ethanol (Poulos et al., 1995; but see Diergaarde et al., 2012). Along similar lines, animals that have been bred for high alcohol consumption also show steeper delay discounting than their low alcohol consumption counterparts (Oberlin and Grahame, 2009; Wilhelm and Mitchell, 2008; but see Wilhelm et al., 2007; Wilhelm and Mitchell, 2012). Indeed, both replicates of the high alcohol drinking [HAD] rat lines have steeper discounting (Wilhelm and Mitchell, 2008), are less sensitive to the locomotor suppressing effects of ethanol (Rodd et al., 2004), and, of course, drink more ethanol than their low alcohol drinking [LAD] counterparts (McKinzie et al., 1998). It may therefore prove fruitful for future studies to examine the direct contributions (and degree of overlap) of these different traits to ethanol consumption in both selectively bred and outbred animals.

This study has a number of limitations. First, while animals in our task were able to appropriately react to most contingency manipulations, there was no significant effect of reducing the length of the variable adjusting delay (Fig. 2). Although we suspect this reflects a lack of power rather than a true lack of effect ($p = 0.027$ before Bonferroni correction), we acknowledge that animals may have had difficulty decreasing adjusting delay in response to manipulations. Second, the relationship we report between adjusting delay and trials completed did not reach significance between adjusting delay and reaction time. Nonetheless, we feel that number of trials completed captures more of ethanol's behaviorally suppressant effects than reaction time because five of the nine adjusting delay animals had sessions in which they did not respond for the entirety or majority of the 20 min period (and thus had no measurable reaction time). Therefore, while ethanol clearly reduced trials completed during this time, its effect on reaction time was unknown for a portion of the data. Third, the tasks incorporate probability to dissociate delay and magnitude. Thus, it is difficult to completely dissociate the effects we see from sensitivity to probability.

However, it seems unlikely that the effects we see rely on sensitivity to probability alone, because increased preference for the probabilistically variable option in the adjusting delay task (lower adjusting delay) predicted resistance to ethanol's effects (Fig. 5a), while preference for the variable option in the adjusting magnitude task (higher adjusting magnitude) was not related (Fig 5b). Furthermore, a previous study using these tasks found that the nucleus accumbens core had higher c-fos counts in animals exposed to the adjusting delay but not adjusting magnitude task, further suggesting that probability alone was not responsible for the differences seen (da Costa Araújo et al., 2010). Nonetheless, it is still possible that an interaction between delay and probability is at work here, and additional studies would be needed to fully disentangle this.

In summary, we report two primary findings. First, ethanol did not affect sensitivity to delay or magnitude in two independent tasks. We believe this suggests that our measures of delay and magnitude sensitivity are differentially affected by ethanol than others, and may therefore be regulated by different neural substrates. Our second finding showed that animals more sensitive to delay are less sensitive to ethanol's behaviorally suppressant effects. This finding fits with and expands existing literature, and supports the idea that sensitivity to delay and sensitivity to ethanol's behaviorally suppressant effects may be driven (at least in part) by the same underlying process.

Acknowledgments

We thank Alex Murray and Richard Beaumont, who assisted with data collection.

Role of Funding Source. TMM was supported by NIAAA grant T32 AA007468 and F31 AA020741, SHM was supported by Portland Alcohol Research Center grant P60 AA10760. The funding sources had no further role in study design, data collection, analysis, interpretation, manuscript preparation or the decision to submit the paper for publication.

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Figure 1. Description of the adjusting delay and adjusting magnitude tasks. **A)** Schematic of the adjusting delay task. **B)** Schematic of the adjusting magnitude task. **C)** Components of an individual trial.

Figure 2.

a) Effect of delay manipulations on adjusting delay. Baseline days used 2 / 18 s for the variable lever (dashed lines, open circles). The manipulation days used 2 / 2 s, 2 / 6 s, 6 / 18 s, and 18 / 18 s (solid lines, closed circles). Only the 18 / 18 s manipulation had a significant effect on adjusting delay, although the 2 / 2 s manipulation was significant before Bonferroni correction. **b)** Effect of magnitude manipulations on adjusting magnitude. Baseline days used 15 / 135 μl for the variable lever (dashed lines, open circles). The manipulation days used 15 / 15 μl, 15 / 45 μl, 45 / 135 μl, and 135 / 135 μl (solid lines, closed circles). Both the 15 / 15 μl and 135 / 135 μl manipulations had a significant effect on adjusting magnitude.

Figure 3.
Ethanol did not affect adjusting delay (**a**) or adjusting magnitude (**b**).

Number of trials completed after ethanol administration

Figure 4.

Ethanol dose-dependently decreased the number of trials completed per time bin (with a subsequent rebound later on) in both tasks. On the days before ethanol injection, animals typically finished the task within 75 min (dashed lines). Both doses of ethanol reduced the number of trials completed and delayed the amount of time it took animals to complete the task; this effect was particularly strong for the 0.9 g/kg dose (**b,e; c, f**).

Figure 5.

Relationship between average adjusting value and number of trials completed or reaction time in the first 20 min after 0.9 g/kg ethanol. Animals with high sensitivity to delay (low adjusting delay) were resistant to ethanol's effects on responding (a), but there was no relationship with reaction time (b). There was no relationship between sensitivity to magnitude and ethanol's behaviorally suppressant effects or effects on reaction time (c, d).