Dissociations between motor timing, motor coordination, and time perception after the administration of alcohol or caffeine

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Abstract
Rationale The impacts of psychoactive drugs on timing have usefully informed theories of timing and its substrates. Objectives The objectives of the study are to test the effects of alcohol and caffeine on the explicit timing involved in tapping with the implicit timing observed in the coordinated picking up of an object, and with the temporal discrimination. Materials and methods Participants in the “alcohol” experiment (N=16) received placebo, “low” (0.12 g/kg or 0.14 g/kg for women/men, respectively) or “high” (0.37 g/kg or 0.42 g/kg, respectively) doses of alcohol, and those in the “caffeine” experiment (N=16) received placebo, 200 or 400 mg caffeine. Time production variability was measured by repetitive tapping of specified intervals, and sources of variance attributable to central timer processes and peripheral motor implementation were dissociated. The explicit timing in tapping was compared with the implicit timing in the coordinated picking up of an object. Time perception was measured as discrimination thresholds for intervals of similar duration. Drug effects on reaction time were also measured. Results For tapping, alcohol significantly increased timer variability, but not motor variability; it did not affect coordination timing in the grip-lift task. Conversely, for time perception, the low dose of alcohol improved temporal discrimination. Caffeine produced no effects on any of the timing tasks, despite significantly reducing reaction times. Conclusions The effects of alcohol argue against a common clock process underlying time interval perception and production in the range below 1 s. In contrast to reaction time measures, time perception and time production appear relatively insensitive to caffeine.

Keywords Caffeine · Alcohol · Reaction time · Psychomotor performance · Timing · Central clock · Time estimation · Time perception · Motor control

Introduction
A number of influential models of timing (e.g., Treisman 1963; Gibbon et al. 1984) assume that a pacemaker-counter (timer) mechanism underlies both the perception and production of time intervals. The basic concept is that randomly occurring neural events generated by the pacemaker are monitored by a counter process through a switch. In time perception, the size of the count occurring in the stimulus interval is taken as an indication of lapsed time,
while, in time production, a timed interval is terminated when a target number of events has been attained. According to such pacemaker-counter models, an increase in the neural event rate should lengthen perceptual judgments of lapsed time, but shorten produced intervals, whereas the converse effects should follow a decrease in the neural event rate. In addition, a faster neural event rate would be expected to improve temporal resolution both in perception (lower thresholds in the discrimination of interstimulus intervals) and production (lower variance in intervals between timed responses), whereas a slower event rate would reduce resolution.

Modulation of the hypothetical neural event rate might be achieved by means of psychoactive drugs: broadly, sedatives should decrease the neural event rate, whereas stimulant drugs should increase it. The limited number of studies that have tested the effects of drugs on timing in people have generally supported the predictions of the pacemaker-counter model. Thus, for example, the sedative gas nitrous oxide alters time estimation and production in a manner consistent with a decrease in the internal timer rate (Adam et al. 1974); alcohol has been shown to predispose the overproduction of time intervals (e.g., Tinklenberg et al. 1972, 1976), and secobarbital promotes the underestimation of stimulus durations (Goldstone et al. 1958; Goldstone and Kirkham 1968). Furthermore, the accuracy of temporal discrimination is impaired by the neuroleptic haloperidol across a range of time intervals (Rammsayer 1989, 1993, 1997, 1999). In contrast, the psychostimulant drug dextro-amphetamine causes overestimation of stimulus durations (Goldstone et al. 1958; Goldstone and Kirkham 1968), and caffeine has been shown to improve the estimation accuracy of durations in the range of seconds (at least at one particular dose in females; Botella et al. 2001). Many studies of timing and its neural substrates have been conducted in laboratory animals, and their results are broadly consistent with those from human research in suggesting that psychoactive drugs can modulate the functioning of an internal clock. Thus, for example, the psychostimulant methamphetamine produces a shortening of the peak-interval response function in rats trained to press a lever at a criterion duration, whereas haloperidol and other neuroleptics have the opposite effect (e.g., Meck 1986; Buhusi and Meck 2002; Cevik 2003; for review, see MacDonald and Meck 2004).

Many drug effects on timing are specific to certain time intervals: for example, the minor tranquilizer midazolam, the atypical neuroleptic remoxipride, and the NMDA receptor antagonist memantine, all reduce estimation accuracy for longer time intervals (in the range of seconds) but not for shorter intervals (in the range of hundreds of milliseconds; Rammsayer 1992, 1993, 1997, 1999, 2006), and the noradrenaline reuptake inhibitor reboxetine improves accuracy only at longer intervals (Rammsayer et al. 2001). These dissociations, together with recent neuroimaging evidence (for a review see Lewis and Miall 2003) suggest that intervals below and above approximately one second are represented by two distinct timing processes that may be differentially sensitive to drug effects. Studies in laboratory animals have also supported the proposal that interval timing may involve different neurobiological mechanisms at different intervals, with perhaps three or four discrete interval ranges (e.g., see Ivry 1996; Gibbon et al. 1997).

In the present study, we tested the effects of caffeine and alcohol on interval timing in the hundreds of milliseconds range and on the very short interval timing (up to tens of milliseconds) that is involved in motor coordination. Interval timing in the hundreds of milliseconds range relates current movement to previous actions and external events, whereas motor coordination in the tens of milliseconds range requires synchrony or very short delays between concurrent actions or events. One reason to expect that the two might be dissociated is that timing in the hundreds of milliseconds range involves timing mechanisms over which we have explicit conscious control of timing as an outcome, whereas timing exhibited in coordination may be considered implicit, in that it is an emergent property reflecting movement skill directed at outcomes defined in spatial rather than temporal terms (see also Zelaznik et al. 2002). We contrasted the explicit timing involved in tapping with the implicit timing observed in coordinated picking up of an object from a support using precision grip. In the latter, the arm provides a lift force that is coordinated with grip force produced by the hand which is needed to generate friction and prevent the object slipping from grasp. Johansson and Westling (1984) have shown that grip force and load force associated with the lift increase in parallel; hence, grip anticipates the lift. To evaluate drug effects on implicit timing in movement coordination, we tested the effects of alcohol and caffeine on the time difference between peak rate of change of grip and load forces during lifting and holding an object.

We also compared the explicit timing involved in tapping with accuracy of time perception by deriving thresholds for perceiving intervals of similar duration. Most drug studies of timing have required participants to signal the end of a stated target interval, report the duration of a given interval, or compare standard and test intervals to derive discrimination thresholds. Measures are typically expressed as performance means. Instead, we examined production and perception of short time intervals (300, 500 ms) measuring changes in variability rather than changes only in mean (or bias) of produced or perceived intervals. Thus, it might be hypothesized that the CNS depressant drug alcohol would reduce the neural event rate,
thereby increasing variance, whereas the stimulant drug caffeine would have the opposite effect. However, the effects of alcohol on performance are not consistently linear in terms of dose–response; at low doses (typically, below 0.3 g/kg), alcohol can elicit performance improvements of the kind commonly associated with stimulant drugs (e.g., Maylor et al. 1987; Lloyd and Rogers 1997). Hence, the present study included not only a high dose condition but also a low dose condition, with the expectation that the latter might produce stimulant-like effects and increase the neural event rate. We examined time production by recording repetitive tapping of equal (isochronous) or alternating intervals (rhythm), and time perception by testing discrimination thresholds for identifying the longer of two intervals. In the case of tapping, we used the VH extension (Vorberg and Hambuch 1978, 1984; see also Vorberg and Wing 1996) of the W-K timing model (Wing and Kristofferson 1973) to determine whether any observed changes in timing variability were attributable to timer processes (i.e., neural event rate) or to peripheral motor implementation sources of variance. We included an alternating “rhythm” condition that required switching between two time intervals. Following recent evidence (Doumas and Wing 2007), we predicted that the increased cognitive load associated with the rhythm condition would render timer variability in this condition especially susceptible to (and so likely to interact with) drug effects. This approach may be seen as having parallels with the use of rhythm to reveal effects of aging on timing which are not apparent in isochronous timing (Krampe et al. 2005).

Finally, two reaction time (RT) tasks were included: a test of simple RT and a test of logical reasoning (the semantic verification test, SVT; Baddeley 1968; Warburton 1995). Caffeine has been shown to reduce simple RT and to improve performance on the SVT (e.g., Warburton 1995; Smith et al. 1992; Smit and Rogers 2000; Hewlett and Smith 1999). Alcohol typically lengthens simple RT (e.g., Carpenter 1959; Sutton and Burns 1971; Franks et al. 1975; Tzambazis and Stough 2000), although doses below 0.3 mg/kg might speed responding (Lloyd and Rogers 1997). Alcohol might be expected to disrupt SVT performance, at least at higher doses. Hence, these tasks provide useful positive controls to evaluate the effectiveness of the doses employed.

Materials and methods

Participants

Twenty-eight women and eight men were assigned to one of two sex-balanced groups for either the caffeine or alcohol experiment. Mean body weight was 66.3 kg (SE=2.4 kg), and all were >18 years old (mean=24.3 years; SE=0.9 years). Participants were employees or students recruited by poster advertisements from the University of Birmingham. Current users of any prescription medication (except the contraceptive pill) were excluded, as were people who smoked more than ten cigarettes per day. In fact, there was only one regular smoker in the caffeine experiment (four cigarettes per day), and only one in the alcohol experiment (ten cigarettes per day). In the caffeine study, the minimum daily caffeine consumption (estimated from self-report) was 125 mg, while the mean intake was 393.4 mg/day (SE=46.4 mg). In the alcohol study, participants were selected with intakes between 5 and 35 U/week; mean intake was 13.8 U/week (SE=1.8 units). Participants were asked to refrain from alcohol and caffeinated products from 1900 hours the evening before testing, and from smoking for at least 4 h before testing. On the morning of each test session, participants were asked to eat a similar breakfast 90–180 min before testing: 2 slices of toast with any kind of spread, and a glass of any kind of juice. None of the volunteers took part in both experiments; they were all paid UK £30, and they provided written, informed consent. The study was approved by the School of Psychology Intramural Ethics Committee.

Experimental design

Both experiments were within-subjects: drug (two doses and placebo) was administered double-blind (order counterbalanced) in sessions separated by at least 48 h. Testing was in one of three consecutive time slots (all in the morning); each participant was tested in the same time slot throughout, and time slots were counterbalanced across the six possible orders of drug exposure. The performance tests were grouped into three sets of similar duration: (1) tapping and grip force (motor coordination); (2) time discrimination; (3) simple reaction time and semantic verification task. The ordering of the three sets of tasks was consistent for each participant but varied randomly (three orders) across participants. The total duration of each test session was approximately 90 min.

Procedure

a) Drug administration

In the caffeine experiment, participants were given a capsule (Qualicaps, Spain) containing either caffeine (200 or 400 mg) or placebo (arrowroot); testing began 45 min later. In the alcohol experiment, a measure of breath alcohol concentration (BrAC) was taken before each session (Lion alcolmeter breathalyzer: model S-D2); all BrAC measures were zero prior to testing. Drink formulations were based
on Wright and Terry (2002): alcohol drinks contained Sainsbury’s Vodka (37.5% alcohol), Schweppes Indian Tonic Water, and 4 ml Angostura Bitters. The placebo drink replaced vodka with tonic water, and 0.25 ml of vodka was floated on the drink surface and around the rim of the glass to mask olfactory cues. In taste comparison tests, the drink formulation has been shown to be effective at concealing the alcohol content of the beverage (Wright 2001). Alcohol was administered at 0.12 or 0.37 g/kg (0.4 ml/kg or 1.2 ml/kg) and 0.14 or 0.42 g/kg (0.46 ml/kg or 1.38 ml/kg) for women and men, respectively. Drinks were given at a constant volume of 240 ml and consumed over 15 min. Testing began 20 min later, immediately following a second BrAC measure. A third BrAC reading was taken at the end of testing.

b) **Performance Tests**

1. **Bimanual Tapping Task.** Responses were recorded using two force transducers (Novatech, Model F241), one for each hand. A metal plate (6.5×2.7×0.3 cm) was attached to each of the transducers, which were fixed 20 cm apart on a rectangular wooden block (26.4×2.5×1.9 cm). Foam pads raised each of the participants’ hands to the level of the metal plate. To ensure that only the two index fingers contributed to responses, the hand positions were specified to limit movement about the metacarpophalangeal joint. At the beginning of each trial, a series of tones was generated (duration, 100 ms; frequency, 750 Hz), consisting of a short (300 ms), long (500 ms) or a rhythmic (alternating short—300 ms and long—500 ms intervals) series. On each session, participants completed nine trials, three of each type: short, long and rhythm. Volunteers were instructed to commence tapping once they were ready to synchronize their responses with the appropriate tones. After ten intervals, the tones were terminated, and participants were required to continue tapping in the unpaced phase by maintaining the target interval as accurately as possible for the rest of the 40 s trial. LabView software (National Instruments) was used to record the force-time waveforms generated during tapping by means of a 16-bit analog-to-digital interface board (National Instruments).

2. **Time Discrimination Task.** A two-interval forced choice duration discrimination task was used. Two durations separated by 1000 ms were presented on each trial, and participants were required to indicate which duration was longer by pressing the left or the right mouse key. Two base durations (300 ms or 500 ms) were employed to create two parallel stimulus staircases in which the longer duration was varied using a 20 ms step size to determine thresholds for 79% correct (MacMillan and Creelman 2005). The number of reversals used to assess the threshold was 12. After each response, participants were given feedback in the form of a high-pitched pulse for a correct response or a low-pitched pulse for an incorrect response. The total duration of the task was approximately 10 min. The means and SDs of the thresholds for the two base pulses were calculated. Participants were given ten practice stimulus presentations.

3. Grip and Lift Task. Participants were required to grasp an apparatus (mass 0.45 kg) consisting of two mechanically linked cylindrical force transducers (Novatech, Model F245). One, oriented horizontally, measured grip force normal to the grasp surfaces, and the other, oriented vertically under the first, measured the load due to the apparatus weight, and hence indicated the lift force tangential to the grasp surfaces. The grip surfaces were made of wood (5.5×4×0.6 cm) and fixed to the grip force transducer; the width between contact surfaces was 5.2 cm. A modified precision grip was used: thumb on one side, and the index plus middle finger on the other side. On each trial, participants lifted the object vertically, approximately 1 cm above the surface, held it in that position for approximately 1 s, and then placed it back on the surface. No specific accuracy criteria were given. Participants performed 20 trials, ten with 100 g weight added load and ten without, in an alternating sequence. Grip and load forces were recorded via a 16-bit analog-to-digital interface board (National Instruments) on a computer running LabView data collection software.

4. Simple Reaction Time Task (SRT). Participants pressed the space bar of a computer keyboard as quickly as possible after a white asterisk appeared in the center of a 17-in. ADI microscan screen. Interstimulus interval varied randomly from 1,000 to 2,500 ms, and each stimulus was on screen for 1,000 ms. There were 160 stimulus presentations, preceded by ten practice stimuli. Responses faster than 100 ms or slower than 900 ms were considered erroneous and omitted from analyses.

5. Semantic Verification Task (SVT). In this task, based on the Baddeley Semantic Verification Task (Baddeley 1968), the letters A and B were presented, one above the other in the center of the screen. Directly below them was a sentence describing the position of the letters relative to each other.
There were eight possible descriptions of the letter arrangement, four positive (“A is above B”, “A is below B”, “B is above A”, “B is below A”) and four negative (“A is not above B” etc.). Participants pressed one of two keys on a PC keyboard (“m” or “z”), counterbalanced for response type to indicate whether the descriptor sentence was correct or not. If the reaction time on a particular trial was less than 500 ms or greater than 10,000 ms, the score was excluded from subsequent analysis. There were 160 consecutive stimuli, with letter arrangement crossed with descriptor type. Stimuli remained on screen until a response was made, and the intertrial interval was 1,000 ms. For each session, eight practice trials were given. The task was presented on the same PC/VDU as for SRT.

c) Data Analyses

For each measure, there were three levels of factor Dose: placebo, low, and high. The analogue force-time functions from the two hands in the tapping task and for the grip and load force data in the lifting task were low-pass filtered at 20 Hz (second order Butterworth dual-pass filter). Interactive feature detection programs written in LabView were used to identify successive interresponse intervals (IRIs) in the tapping task and times of peak load and grip force rates in the lifting task. The two time series of intervals for the left- and right-hand in tapping were then analysed in terms of: (1) average and SD of the intervals for each hand and, in the rhythm condition, for short and long intervals separately; (2) timer SD: square root of the covariance at lag zero between the intervals of each hand; (3) motor SD: asynchrony SD between the hands (for details see Vorberg and Hambuch 1978, 1984; Vorberg and Wing 1996). Two $3 \times 2 \times 2$ within-subjects repeated measures analyses of variance (ANOVARs) were performed on timer and motor variability (SD); factors were Dose, Interval (short, long), and Task (isochronous, rhythm). From the grip and lift task, each participant provided a mean and a standard deviation of (1) the time differences between peak rate of change of grip and load force; and (2) the grip force rise, measured from onset of grip to peak rate of change of force. These four measures were analyzed independently using $3 \times 2$ ANOVAs (factors Dose and Load). Scores for the time discrimination task were logarithm-transformed to normalize the distributions, and data for a single outlier (alcohol experiment) were replaced by group means. SRT data were sorted into four consecutive blocks of 40 trials (factor Time) yielding a $3 \times 4$ within-groups ANOVA. For the SVT, correct and incorrect responses were incorporated into the analyses of RT (factor Correct), yielding a $3 \times 2$ within-groups ANOVA. Scores were also analyzed by stimulus type: positive or negative statements (factor Difficulty), yielding two $3 \times 2$ within-groups ANOVAs, one for RT (correct) and one for errors. RT (incorrect) could not be analyzed reliably in the same way because five (caffeine) or four (alcohol) participants failed to make errors for at least one level of Difficulty, making the analysis unreliable. All data were tested for normality, violations of sphericity, homogeneity of variance, and the presence of outliers using SPSS 10. RT scores for the SVT were logarithm-transformed, and error scores were square root transformed to normalize the distributions. The Greenhouse–Geisser correction was applied to the degrees of freedom in cases of nonsphericity. Planned comparisons were by Bonferroni test (adjusting for multiple comparisons).

In the following, values in parentheses after means are SEs of the means, and for brevity, nonsignificant outcomes are not reported in full.

Results

Breath alcohol concentrations were zero for all participants before they consumed alcohol and at both subsequent timepoints after the placebo drink. After the lower dose of alcohol, mean BrACs were 8.6 (2.7) and 4.1 (1.3) μg/100 ml before and after testing, respectively; after the higher dose, they were 23.3 (5.1) and 18.3 (4.7) μg/100 ml, respectively. The effects of Dose and Time were both significant [respectively, $F(1,17)=162.7, P<0.001$; $F(1,17)=48.1, P<0.001$].

Bimanual tapping task

Alcohol: timer SD

A main effect of Dose was observed [$F(2,16)=5.88, P<0.05$]. Pairwise comparisons indicated that participants exhibited more variable performance after the high dose than after placebo [$P<0.05$] or the low dose [$P<0.05$] at each level of Task × Interval; placebo and low dose estimates of timer variability did not differ significantly at any level (see Fig. 1). A main effect of Interval [$F(1,17)=82.8, P<0.001$] indicated that timer SD increased with the mean, and a main effect of Task [$F(1,17)=31.80, P<0.001$] showed that rhythm performance was more variable than isochronous. An Interval × Task interaction [$F(1,17)=7.66, P<0.05$] indicated that the increase in timer SD with the mean interval was steeper in rhythm performance (Fig. 1). However, neither Task nor Interval interacted with Dose.

Alcohol: motor SD

There were no effects of Dose on motor SD (Fig. 1).
For timer SD, there were main effects of Interval \( F(1,17)=116.26, P<0.05 \), showing that timer SD increased with the mean, and Task \( F(1,17)=14.38, P<0.05 \), showing that rhythm performance was more variable than isochronous, and an interaction between Interval and Task \( F(1,17)=10.48, P<0.05 \) revealing that the increase in SD with the mean was steeper in rhythm performance.

**Caffeine: motor SD**

There were no effects of Dose on motor SD, but there was an Interval × Task interaction \( F(1,17)=14.01, P<0.05 \) with more variability in the isochronous task at the shorter interval (Fig. 1).

**Time discrimination**

**Alcohol** For the average threshold of the logarithm-transformed scores, there was a significant main effect of Dose \( F(2,34)=3.97, P=0.028 \), with the low dose yielding a lower mean threshold (1.88, SE=0.05) than either placebo (1.958, SE=0.04) or the high dose (1.983, SE=0.05) [quadratic trend: \( F(1,17)=6.69, P=0.019 \)]. Planned comparisons showed a significant difference between low and high doses only \( P=0.026 \). There was a main effect of Interval \( F(1,17)=8.14, P=0.011 \), reflecting a higher threshold at the long interval (1.976, SE=0.04) compared to the short (1.904, SE=0.05), but no Dose × Interval interaction \( F(2,34)=1.26, \text{NS} \). The only effect on SD was for factor Interval \( F(1,17)=7.11, P=0.016 \), with average SD greater at the long interval (1.501, SE=0.05) than the short interval (1.380, SE=0.05).

**Caffeine** There were no effects of caffeine on time discrimination, either for average threshold or SD, and no interactions with factor Interval \( Fs<1 \). There was a main effect of Interval only for average threshold \( F(1,17)=11.57, P=0.003 \), reflecting higher values at the longer (2.063, SE=0.05) compared to the shorter (1.927, SE=0.05) interval.

**Grip and lift task**

For this task, the critical score was the SD of the interval between peak grip force rate and peak load force rate. Also measured were mean scores for the same variable, as well as mean scores and SDs for grip force rise (calculated from onset to peak rate of change of force). No drug effects on SD or mean were found for either variable, and there was no effect of weight \( \text{all } Fs<1 \). It is apparent from Table 1 that performance was very similar across all dose condi-
tions for both drugs. As expected, peak grip force preceded peak load force, both with and without an additional weight, hence the negative mean scores.

Simple reaction time

**Alcohol** Mean RTs were 304.1 (4.6), 311.9 (6.5), and 315.2 (6.2) ms for placebo, low, and high doses, respectively. The main effect of alcohol approached significance \([F(2,34)=2.78, P=0.076]\), but a significant linear contrast confirmed a dose-related increase in RT \([F(1,17)=8.29, P=0.01]\), with planned comparisons showing that the high-dose condition differed significantly from placebo \([P=0.03]\). There was a main effect of Time \([F(3,51)=15.9, P<0.001]\) reflecting a linear increase in RT over trials \([\text{linear contrast: } F(1,17)=26.8, P<0.001]\).

**Caffeine** There were significant main effects of Dose \([F(2,34)=9.19, P=0.001]\) and Time \([F(1.81,30.79)=5.55, P=0.011, \text{Greenhouse–Geisser correction}]\), but no Dose \(\times\) Time interaction \([F<1]\). Means for placebo, 200 and 400 mg conditions were: 325.9 (8.7), 308.2 (9.0), and 312.7 (9.3) ms, respectively. Planned comparisons showed that the effects of both caffeine doses differed significantly from those of placebo \([Ps<0.016]\), but not between each other. There was a linear increase in RT over trial blocks \([\text{linear contrast: } F(1,17)=7.86, P=0.012]\).

Semantic verification task

**Alcohol** There was a significant main effect of dose on errors \([F(2,34)=3.30, P=0.049]\), but the linear trend (for errors to increase with dose) only approached significance \([F(1,17)=4.28, P=0.054]\), and Bonferroni tests failed to show significant differences between drug and placebo \([Ps>0.06]\). Means of the square-root transformed scores were: placebo, 1.88 (0.22); low dose 1.88 (0.20); high dose 2.22 (0.23). There were main effects of Difficulty on errors \([Fs(1,17)>17.4, Ps<0.001]\), but no interactions between Dose and Difficulty \([Fs(2,34)<1.8, \text{NS}]\). For RTs, there was no main effect of Dose and no Dose \(\times\) Correct interaction \([Fs<1.4]\), but incorrect RTs were longer than correct RTs \([\text{factor Correct: } F(1,17)=4.72, P=0.044]\).

**Caffeine** Caffeine produced no effects on the various measures derived from the SVT. Incorrect responses were slower than correct responses \([\text{factor Correct: } F(1,17)=7.89, P=0.012]\), and the negative items produced more errors and longer RTs than did positive items \([\text{factor Difficulty: } Fs(1,17)>25.5, Ps<0.001}\).

Discussion

This study was concerned with determining possible effects of alcohol and caffeine on timing behavior. Alcohol significantly increased the variability of performance on the tapping task; more specifically, alcohol selectively affected timer variability in the tapping task, whereas motor variability was unaffected. The alcohol effect did not interact with the isochronous/rhythm factor, even though performance in the rhythm condition was more variable than in the isochronous condition (consistent with recent findings reported by Krampe et al. 2005; Doumas and Wing 2007). As a complement to the lack of alcohol effect on the motor component of tapping, there was no effect of alcohol on coordination timing (variability or mean) in the grip and lift task. In contrast to its effects on the tapping task, there was some evidence that the lower dose of alcohol actually improved the accuracy of temporal discrimination in the time perception task. Caffeine, on the other hand, produced no effects on any of the three timing tasks, despite

### Table 1 Effects of alcohol and caffeine on the grip-lift task: group means of individual means (Mean) and of individual standard deviations (SD), in ms, for (1) interval between peak grip force rate and peak load force rate; and (2) grip force rise, measured from onset to peak rate of change of force

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<td><strong>Interval from peak grip force rate to</strong></td>
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<td><strong>Grip rise (from onset to peak rate of change of force)</strong></td>
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<td><strong>peak load force rate</strong></td>
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<td><strong>Alcohol</strong></td>
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<td>Placebo</td>
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<td>43 (7.5)</td>
<td>119 (6.1)</td>
<td>38 (4.3)</td>
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<td>124 (9.2)</td>
<td>46 (7.5)</td>
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<tr>
<td>High dose</td>
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<td>45 (10.7)</td>
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<tr>
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<td>43 (7.5)</td>
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Data are collapsed across the two conditions of Load (weight present and weight absent), for which there was no effect. SEs of group means are given in parentheses; see “Materials and methods” section for drug doses; \(N=12\) throughout
significantly reducing simple reaction times. By contrast, alcohol tended to increase simple reaction times. Finally, caffeine had no effect on the semantic verification task, whereas alcohol increased error rates without affecting response times (consistent with findings that, in complex tasks, alcohol tends to conserve response speed at the expense of error rates, e.g., Tiplady et al. 2001).

The selective effect of alcohol on timer variability supports the idea that alcohol reduces the neural event rate, thereby affecting the way intervals are generated by the central timer. The effect of alcohol on variability in tapping but not on the grip and lift task indicates that timing of motor control, but not of coordination, was more variable after alcohol. The dissociation of effects between tasks supports the view that the control of interval timing in the hundreds of milliseconds range may be different from that which operates at very short intervals (up to tens of milliseconds). This suggests a contrast between tasks involving conscious control over explicit timing, where timing is the task goal, from motor coordination tasks, in which outcomes are defined in spatial rather than temporal terms and timing is an emergent property. Such a contrast has previously been suggested on different grounds for intervals in the hundreds of milliseconds range depending on whether the movements are smooth and continuous (emergent timing) or whether the movements are discontinuous (discrete, explicit timing; Zelaznik et al. 2002).

Our results may be seen as having parallels with Rammsayer’s (1992, 1993, 1997, 1999, 2006) findings that the timing of longer intervals is more susceptible to drug effects than the timing of shorter intervals. The relative insensitivity of short interval timing to the disruptive effects of drugs has been taken as evidence against a unitary account of timing based on a single timer. Instead, it is suggested that drugs affect longer-interval timing by impacting on selective attentional process; since durations up to around 300 ms are not affected by manipulations that alter selective attention, shorter intervals (perhaps more dependent on sensory–motor, rather than attentional processes) are likely to be more resistant to the effects of drugs that impair selective attention (e.g., Mattes and Ulrich 1998; Rammsayer et al. 2001). Such an account would be consistent with the present findings. Rammsayer (2006) notes that there is no clear agreement on where the transition from one timing mechanism to another may occur; it is most often given as between 300 and 1,000 ms. Our results would be more consistent with the lower boundary.

Differential effects of alcohol on timing have not been demonstrated previously, although there are surprisingly few studies of alcohol’s effects on timing. At doses higher than those used here, Heishman et al. (1997) were unable to demonstrate any effect of alcohol either on time estimation or on time production. However, in a study of time production where undrugged estimates of 1 s intervals tended to be too long, and estimates of intervals of 5 s or more tended to be too short, Lapp et al. (1994) showed that alcohol’s effects seemed to be more selective for the 1 s interval. Such a finding, implying that a short interval is relatively more sensitive to drug effects, might be considered discrepant with the current results, but the short interval in the earlier study was longer than our longest interval. Lapp et al. also adopted a complex design incorporating a variation of the balanced placebo design, and alcohol’s effects at longer durations were not clearly characterized. Rammsayer (1999) showed that midazolam, a benzodiazepine sedative–hypnotic that has neurochemical properties in common with alcohol, disrupted the estimation of durations based on a standard of 1,000 ms but not of shorter durations (based on a 50-ms standard). Many of midazolam’s psychoactive effects, like those of alcohol, have been attributed to agonist activity at GABA<sub>Α</sub>-benzodiazepine receptors (e.g., Grobin et al. 1998). However, Rammsayer (1999), in common with most studies that have reported differential sensitivity to drug effects according to target duration, measured time perception, rather than time production, using discrimination techniques. We, on the other hand, did not find any detrimental effect of alcohol on time discrimination; alcohol’s detrimental effects on timing were only revealed in the time reproduction (tapping) task. We had expected, but did not find, parallel changes across tasks, i.e., more variable timing with larger threshold time discriminations after alcohol. The dissociation between alcohol’s effects on time discrimination and central motor timing might be taken to indicate that separate timing processes are involved in the two skills, and that alcohol’s effect on the former cannot be attributed to a neural event source that is common to all activities that require control of timing. Indeed, there was evidence of a qualitative difference in response to alcohol across tasks, since there was a suggestion of improved accuracy of time discrimination after the lower dose of alcohol. The finding that a low dose of alcohol can have effects that might be considered more typical of a “stimulant” drug is not without precedence. For example, Lloyd and Rogers (1997) showed that, at a similar dose, alcohol can reduce reaction times (however, in the present study, the effect on time discrimination occurred in the absence of any effect on reaction times). The qualitatively different effects of alcohol that have been reported at low and high doses might reflect the preferential activation of different neurochemical systems by different doses. For example, evidence has suggested that the discriminative stimulus effects of alcohol at low-to-moderate doses primarily reflect agonist activity at GABA<sub>Α</sub> and 5-HT<sub>1</sub> receptors, whereas its effects at higher doses are more closely associated with antagonism.
of NMDA receptors (e.g., Grant and Colombo 1993a,b). It is noteworthy that a different sedative–hypnotic drug with activity at GABA$_A$ receptors, the barbiturate secobarbital, can also produce a stimulant-like effect on time estimation: Goldstone and Kirkham (1968) reported that secobarbital produced overestimates of stimulus durations soon after drug administration, a point when drug concentrations in the brain were likely to be low, whereas sedative-like underestimates were made at later test times, when brain concentrations were likely to be significant.

Caffeine at doses of 200 and 400 mg did not affect time reproduction, motor coordination, or time perception. The absence of effects on the timing tasks cannot be attributed to the use of pharmacologically inactive doses, since both doses of caffeine produced highly significant improvements in reaction times as measured using the simple reaction time task. Furthermore, the timing tasks cannot be considered insensitive to drug effects, given the results obtained with alcohol. Hence at behaviorally active doses, caffeine was unable to alter timing as measured across a range of tasks. In studies using similar doses of caffeine that have also produced faster reaction times, there have been reports that the drug increased the rate of unpaced tapping relative to placebo (e.g., Robelin and Rogers 1998; Rogers et al. 2005); clearly, these psychomotor effects do not transfer readily to the paced situation where reproduction of intervals is required. There have been very few studies of caffeine’s effects on timing specifically, but interestingly, the study by Botella et al. (2001) produced a pattern of results that in certain respects demonstrates a dissociation opposite to the one we report here: women (but not men) gave shorter time estimates after 300 mg caffeine compared with placebo, despite showing no speeding of reaction times. The men’s results were more similar to our findings: no effect of caffeine on timing despite faster reaction times. The discrepancy between Botella et al. and the present findings cannot be readily attributed to differences in the sex of the participants, since our sample was also predominantly female. Although caution is needed when considering an outcome that is gender-specific, task-specific, and dose-specific, the discrepancy between studies might again reflect differences in target interval—10 s in the case of Botella et al. It may be noteworthy that Gruber and Block (2003) found effects of caffeine on estimates of a similar time interval, 15 s. Further studies of caffeine’s effects on intervals substantially longer than ours would clearly be useful.

Gruber and Block (2003) also reported that their effects of caffeine on timing cannot be explained easily by recourse to a single timer, since caffeine only affected performance when estimates were requested prospectively, not when requested retrospectively. Relatively, in the present series of experiments, the selectivity of caffeine’s effects for reaction time performance rather than for time production or discrimination seems inconsistent with the idea that time estimation and reaction time are based on a single (or, at least, common) oscillator (e.g., Treisman et al. 1992). If that were the case, the two kinds of task would be expected to exhibit similar changes under the influence of caffeine. Treisman et al. (1992) based their claim of a common oscillator on two experiments with a small number of different subjects in which performance was impaired by a concurrent auditory click sequence. They claimed that this impairment only occurred when the click rate was at certain frequencies and that the frequencies matched in the two experiments. However, the correspondence in frequencies was not strong and was based on group average data, providing only weak support for the hypothesis of a common oscillator. On the other hand, pharmacological studies in nonhuman animals have provided evidence for at least some overlap in the substrates underlying reaction time performance and interval timing, and a number of models have been developed to explain the nature of the link (for review, see MacDonald and Meck 2004). Both processes are similarly amenable to differential modification by dopaminergic agonists and antagonists, and the disruptions to both processes exhibited by patients with Parkinson’s disease have been attributed to degeneration of a common underlying mechanism (e.g., Jahanshahi et al. 1992; Marrow et al. 1993; Brown et al. 1996; Bherer et al. 2003). Caffeine’s primary pharmacological effects are on adenosinergic neurotransmission (e.g., see Fredholm et al. 1999); as such, its enhancement of response speed in the absence of effects on timing would not rule out the possibility of a separate dopamine-sensitive system for which reaction time performance is intimately associated with timing processes. However, caffeine does indirectly facilitate dopaminergic neurotransmission (e.g., Garrett and Griffiths 1997; Okada et al. 1997), and so might have been expected to influence both timing and reaction time performance if it follows the profile of other drugs with dopaminergic effects (which remains to be established), and if the two processes are linked. At the very least, the present results suggest that interval timing and reaction time performance are not always necessarily interdependent.

The selection of particular drugs to investigate timing processes has often been based upon a relatively crude categorization of psychoactive effects as being sedative or stimulant, as initially adopted here. However, the sedative/stimulant distinction is clearly unreliable in terms of predictive power. The “stimulant-like” action of alcohol in the present study and the effects of secobarbital reported by Goldstone and Kirkham (1968) show that properties considered typical of both stimulants and sedatives can be exhibited by the same compound. Also, marijuana is often considered sedative but produces effects that are more
consistent with the speeding of a putative internal timer (e.g., Tinklenberg et al. 1972, 1976). Nicotine’s effects are not easily described as sedative or stimulant, and its effects on timing have been inconsistent: some studies have reported overestimation of time after nicotine (e.g., Agué 1974), but others have reported underestimation (e.g., Leigh and Tong 1976; see Carrasco et al. 1998a,b). Hence, it is not easy to predict how a drug will affect timing processes on the basis of assumptions concerning the drug’s effects on physiological arousal. Nevertheless, regardless of the drugs’ functional classification, the present experiment has demonstrated that alcohol and caffeine can be effective tools for revealing the relationships between different aspects of timing processes in people.

In conclusion, this study has presented a set of tests for evaluating the effect of two psychoactive drugs, alcohol and caffeine, on various aspects of timing in the under 1-s range. While contrasting effects of alcohol and caffeine on reaction time were noted, only alcohol resulted in effects on explicit timing in time interval perception and production. Surprisingly, the effects on time perception and production were not in the same direction, the low dose of alcohol resulting in improved time perception consistent with lower clock variability, whereas clock variability in motor timing increased in proportion with alcohol dose. This suggests a separation of cognitive mechanisms responsible for time interval perception and production.

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