

# Moderate acute alcohol intoxication has minimal effect on surround suppression measured with a motion direction discrimination task

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A well-studied paradox of motion perception is that, in order to correctly judge direction in high-contrast stimuli, subjects need to observe motion for longer in large stimuli than in small stimuli. This effect is one of several perceptual effects known generally as “surround suppression.” It is usually attributed to center-surround antagonism between neurons in visual cortex, believed to be mediated by GABA-ergic inhibition. Accordingly, several studies have reported that this index of surround suppression is reduced in groups known to have reduced GABA-ergic inhibition, including older people and people with schizophrenia and major depressive disorder. In this study, we examined the effect on this index of moderate amounts of ethanol alcohol. Among its many effects on the nervous system, alcohol potentiates GABA-ergic transmission. We therefore hypothesized that it should further impair the perception of motion in large stimuli, resulting in a stronger surround-suppression index. This prediction was not borne out. Alcohol consumption slightly worsened duration thresholds for both large and small stimuli, but their ratio did not change significantly.

## Introduction

In 2003, Dujé Tadin and coworkers demonstrated an interesting effect in motion perception (Tadin, Lappin, Gilroy, & Blake, 2003). They showed subjects a drifting Gabor patch, a set of stripes moving either left or right on a computer monitor, and measured how long subjects needed to view this stimulus in order to correctly report its direction of motion (duration threshold). For low contrast patterns, subjects needed to view a small patch for longer than a large one. This is not surprising, since a large patch stimulates a larger area of the retina and thus provides the visual system with more information on which to base its decision. However, for high contrast patterns, subjects needed to view a *larger* patch for longer than a small one. This effect can be quantified by the Surround Suppression Index (SSI), defined as the  $\log_{10}(\theta_{\text{large}}/\theta_{\text{small}})$ , where

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$\theta_{\text{large}}$ ,  $\theta_{\text{small}}$  are the duration thresholds for a large and small stimulus respectively. Positive values of the Surround Suppression Index indicate that subjects need to see larger stimuli for longer.

In their original paper, Tadin et al. (2003) proposed that this effect is a perceptual correlate of center-surround antagonism in neurons in visual cortex. This interpretation has broadly been supported by subsequent research (Churan, Khawaja, Tsui, & Pack, 2008; Glasser & Tadin, 2010; Neri & Levi, 2009; Pack, Hunter, & Born, 2005; Peterson, Li, & Freeman, 2006; Schwabe, Ichida, Shushruth, Mangapathy, & Angelucci, 2010; Tsui & Pack, 2011). Additionally, the effect has been repeatedly linked to alteration in GABA-ergic inhibitory cortical function. Betts and coworkers (Betts, Sekuler, & Bennett, 2009, 2012; Betts, Taylor, Sekuler, & Bennett, 2005) found much lower Surround Suppression Indices in older observers (mean age 68). Given that center-surround antagonism is thought to be mediated by inhibitory interneurons (Angelucci & Bressloff, 2006), they suggested that this was due to a decline in the efficacy of GABA-ergic cortical inhibitory mechanisms with age (Casparly, Hughes, & Ling, 2013; Leventhal, Wang, Pu, Zhou, & Ma, 2003; Poe, Linville, & Brunso-Bechtold, 2001). Golomb et al. (2009) found that the Surround Suppression Index was reduced in patients with major depression, and linked this to dysfunction of GABA-ergic inhibition in this group (Luscher, Shen, & Sahir, 2011). Similarly, Tadin et al. (2006) found that Surround Suppression Index was reduced in patients with severe schizophrenia, again linking this to GABA-ergic dysfunction (Wassef, Baker, & Kochan, 2003). In indirect support of the GABA-ergic hypothesis, GABA concentration measured with magnetic resonance spectroscopy is significantly correlated with a different psychophysical measure of surround suppression (Yoon et al., 2010).

In all these studies, a reduction in surround suppression index has been linked to reduced efficacy of GABA-ergic inhibition. It would therefore be interesting to examine what happens when GABA-ergic inhibition is potentiated. Consumption of ethanol alcohol potentially provides a convenient way to do this. Among its many effects, alcohol affects GABAergic inhibition in many cortical areas (Deitrich, Dunwiddie, Harris, & Erwin, 1989). Low to moderate concentrations of alcohol enhance GABAergic inhibition, specifically by enhancing GABA<sub>A</sub> receptor function (Harris et al., 1995). Conversely, GABA agonists and reuptake inhibitors enhance the effects of alcohol, whereas GABA antagonists reduce it (Lobo & Harris, 2008).

We therefore hypothesized that moderate concentrations of alcohol should alter surround suppression. By potentiating inhibitory mechanisms, it should increase the Surround Suppression Index. Alcohol may

produce generalized deficits in performance, but these deficits should be particularly strong for large, high-contrast stimuli, where GABA-ergic inhibition is believed to weaken the available motion signal. To test this hypothesis, we ran the task of Tadin et al. (2003) in 56 healthy subjects. We used a within-subjects design in which the value of the Surround Suppression Index was measured before and after subjects consumed a moderate amount of alcohol. To control for changes due to practice or fatigue, we compared these subjects to a control group who consumed a nonalcoholic drink.

## Methods

### Subjects

The 56 subjects were university students and members of the Newcastle University Institute of Neuroscience research volunteer participation scheme. Subjects completed a questionnaire before participating in the study, and those who reported problematic drinking or a health condition which could make drinking alcohol inadvisable did not proceed to participate in the study. All subjects were fully informed about the study protocol before giving their written consent to participate. Participants were paid £8 at the end of the experiment. The study was approved by the Newcastle University Faculty of Medical Sciences Ethics Committee, approval number 00320-1/2012 and complied with the declaration of Helsinki.

Subjects were randomly assigned to the alcohol or control condition. In all, 26 subjects were included in the alcohol condition (17 males, 10 females, age 19 to 58) and 29 in the control condition (11 males, 18 females, age 17 to 58).

### Equipment

The experiment was performed in a room with dim lighting. A computer running Windows 7, Intel® Core™ i7-2600 CPU @ 3.40 GHz with a NVIDIA Quadro FX380 graphics card was used to generate the visual stimuli and record subjects' responses. Stimuli were displayed on a cathode-ray tube computer monitor, model Diamond Pro 2045u, at a frame rate of 160 Hz. The screen size was 39 cm wide × 30 cm high. Subjects viewed it from a distance of 98 cm. The display was gamma-corrected with a value of  $\gamma = 2.27$ . A Minolta LS-100 photometer was used to measure luminance and confirm linearity. The mean luminance

of the screen during experiments was 45 cd/m<sup>2</sup>. The maximum brightness was 90 cd/m<sup>2</sup>.

A DATAPixx Lite visual stimulator from VPixx Technologies (<http://www.vpixx.com/products/visual-stimulators/datapixx-lite.html>) was used to generate the visual stimuli with 12-bit pixel depth. A RESPONSEPixx Tabletop (<http://www.vpixx.com/products/response-boxes/tabletop.html>) was used to record subject responses. All code was programmed in Matlab ([www.mathworks.com](http://www.mathworks.com)) using the Psychophysics Toolbox (Kleiner, Brainard, & Pelli, 2007; Pelli, 1997; Watson & Pelli, 1983). The Procedural Gabor functionality of the Psychophysics Toolbox was used to display the drifting Gabor patch.

The breathalyzer AlcoHawk Pro ([http://www.q3i.com/alcohawk\\_series\\_pro.php](http://www.q3i.com/alcohawk_series_pro.php)) was used to estimate subject' blood alcohol concentrations by asking them to take a deep breath and blow in the breathalyzer for 5 s. AlcoHawk Pro claims a semiconductor sensor accuracy of  $\pm 0.015\%$  at 0.10% blood alcohol concentration. The accuracy with which it reports blood alcohol concentration is presumably far lower, but our conclusions do not depend critically on the accuracy of the breathalyzer.

## Measurement of duration threshold for direction discrimination

The stimuli were drifting Gabor patches based on those of Tadin et al. (2003), i.e., a drifting sine grating displayed within a spatial and temporal Gaussian window. The sine grating was vertical, with a spatial frequency of 1 cycle/° and a horizontal speed of 2°/s either to the left or right. The contrast of the grating at the center of the Gaussian window was 92%. The standard deviation of the spatial Gaussian was either 0.35° (small grating) or 2.5° (large grating). The standard deviation of the temporal Gaussian,  $\tau$ , was varied from trial to trial. We will refer to  $2\tau$  as the *stimulus duration*. The subject's task was to indicate whether the grating was drifting to the left or right. Early on in the study, no feedback was provided as to correctness of response. For later participants, auditory feedback was provided: a short, high beep (pure tone of 600 Hz presented for 100 ms) for a correct response and a longer, lower tone (pure tone of 200 Hz presented for 200 ms) for an incorrect response. In all, 15 out of 29 control subjects and 14 out of 26 in the alcohol condition received feedback. One might expect slightly better thresholds with feedback, but in fact there was no evidence of this. For small stimuli, the mean duration threshold was 38 ms averaged over 126 measurements taken without feedback, and 39 ms over 100 measurements with feedback. For the large stimuli, these were 94 ms and 88 ms respectively.<sup>1</sup> A

two-sample *t* test indicated no difference between measurements with and without feedback for either stimulus size.

We aimed to measure the duration threshold at which they could perform this task with 82% accuracy. Subjects performed the task in blocks of 150 trials. Within each block, the stimulus size was constant (small or large grating), and only the stimulus duration and direction were varying. We will refer to each 150-trial block as one *measurement* of duration threshold.

The stimulus duration was chosen on each trial according to a staircase procedure as described in Serrano-Pedraza, Hogg, and Read (2011). The staircase used the logistic psychometric function described in the following section. Three staircases, each containing 50 trials, were randomly interleaved to make up the 150 trials in a single measurement. The minimum/maximum temporal *SDs* were  $\tau = 10$  ms and 400 ms; if the staircase tried to choose values outside this range,  $\tau$  was clipped to this range. Independent of the temporal *SD*  $\tau$ , the stimulus was always displayed for 700 ms, with the peak contrast occurring at 350 ms after stimulus onset. For stimulus durations below about 233 ms ( $\tau < 116$  ms), the stimulus was in a Gaussian temporal window, i.e., it gradually became visible, rose to a peak contrast of 92%, and then faded away again. For longer stimulus durations, the stimulus already had a central contrast of about 1% at onset, so the Gaussian temporal window was truncated. Duration thresholds larger than 233 ms were unusual: In 476 measurements made from 60 subjects, only seven exceeded 233 ms.

## Data analysis

To obtain an estimate of duration threshold from a single measurement block, data from all 150 trials were fitted with a single psychometric function. We model the probability that the subject correctly discerns the direction of motion as a logistic function:

$$F(\tau) = \left[ 1 + \exp\left(b(a - \ln\tau)\right) \right]^{-1}$$

This tends to zero as the stimulus duration tends to zero, and to unity as the stimulus duration tends to infinity. The function crosses 0.5 at  $\ln\tau = a$ , and the parameter  $b$  controls how steeply it rises.

We allow for a lapse rate  $\lambda$ . That is, on a proportion  $\lambda$  of trials the subject hits the wrong button even if they could correctly discern the direction of motion (Wichmann & Hill, 2001). Overall, their probability of answering correctly is therefore the sum of the probability that they discern direction,  $F(\tau)$ , and do not lapse ( $1-\lambda$ ), and the probability that they do not discern

direction,  $1-F(\tau)$ , but guess correctly (with probability  $g = 0.5$  in our two-alternative forced-choice design):

$$P(\tau) = F(\tau)(1 - \lambda) + (1 - F(\tau))g$$

and so

$$P(\tau) = g + (1 - \lambda - g) \left[ 1 + \exp(b(a - \ln\tau)) \right]^{-1}$$

We define the *duration threshold*  $\theta$  as being the stimulus duration at which the subject has probability  $\pi = 0.82$  of answering correctly:

$$\pi = g + (1 - \lambda - g) \left[ 1 + \exp(b(a - \ln\theta)) \right]^{-1}$$

This rearranges to

$$b(a - \ln\theta) = \ln \left[ \frac{1 - \lambda - \pi}{\pi - g} \right]$$

Each data set consisted of  $N = 150$  pairs:  $(\tau_j, A_j)$ , where  $\tau_j$  is the stimulus duration on the  $j^{\text{th}}$  trial and  $A_j$  is the subject's answer, which could be correct ( $A = 1$ ) or wrong ( $A = 0$ ). The likelihood of this data set is

$$L = \prod_{j=1}^N \left[ A_j P(\tau_j) + (1 - A_j) (1 - P(\tau_j)) \right]$$

We used the Matlab function `FMINSEARCH` to find the value of  $a$ , and hence of threshold  $\theta$ , which maximized this likelihood for the given data set. In both the staircase procedure and the subsequent fitting, chance performance  $g$  was 0.5, threshold performance was defined as  $\pi = 0.82$  and we further fixed the steepness parameter to  $b = 11$  and the lapse parameter to  $\lambda = 0.05$ . Where the psychophysical data constrained the threshold well, the choice of  $b$  and  $\lambda$  was immaterial to the fitted threshold. (Where the data did not constrain the threshold well, this was a problem that could not be overcome by altering  $b$  and  $\lambda$ .)

We used bootstrap resampling to estimate the confidence interval on the fitted threshold. That is, we generated a new “resampled” data set by making  $N$  choices from the original  $N$  trials, with replacement. We then fitted threshold  $\theta$  to this resampled data set. We did this 10,000 times for each data set and estimated the 95% confidence interval on  $\theta$  from the 2.5% and 97.5% percentiles in the set of resampled fits.

## Alcohol dose

All subjects consumed a glass of orange juice. For subjects in the alcohol condition, the juice was mixed with 1.25–5 fluid ounces of vodka containing 40%

alcohol. The volume of vodka was calculated for each subject as being likely to result in a blood alcohol concentration of around 80 mg/100 ml, which is the legal alcohol limit for driving in the UK. We chose this as being an alcohol concentration which is clearly intoxicating, but likely to be safe for both subject and experimenter. To estimate the appropriate dose for each subject, we used Widmark's (1932/1981) basic formula:

$$B = 5.14A / (Wr) - 0.015H$$

where

$B$  = estimated blood alcohol concentration in %, in our case 0.08% (80 mg/100 ml).

$A$  = number of fluid ounces of alcohol consumed.

$W$  = weight of the subject in pounds.

$r$  = alcohol distribution ratio, 0.73 for males and 0.66 for females.

$H$  = time in hours since consumption of alcohol, in our case 0.33 (20 min).

Thus for example a 100-lb female would be given two shots; a 200-lb male would be given 4.5 shots. The breathalyzer was used to estimate the blood alcohol concentration actually obtained. Using the breathalyzer earlier than 20 min after drinking can give inaccurate readings and harm the sensor. Therefore, subjects waited at least 20 min after consuming the drink before using the breathalyzer. Results from two subjects in whom the breathalyzer never reported a blood alcohol level of more than 10 mg/100 ml were removed before analysis, in order to avoid confounds if the dose administered was for some reason insufficient to produce significant intoxication. The sample size of 26 given above for the alcohol condition already excluded these two subjects, i.e., 28 subjects were tested.

## Experimental protocol

We began by weighing the subject and calculating the appropriate dose of alcohol. Subjects initially completed at least one, sometimes two, measurements of the duration thresholds with large and small stimuli. They then drank a small glass of orange juice, either on its own (control condition) or mixed with vodka (alcohol condition). They then waited at least 20 min, before repeating the measurements. Subjects repeated the measurements usually four times over the next hour. They used the breathalyzer before and after each measurement; the mean of the two readings was taken as being the estimated blood alcohol concentration during that measurement.

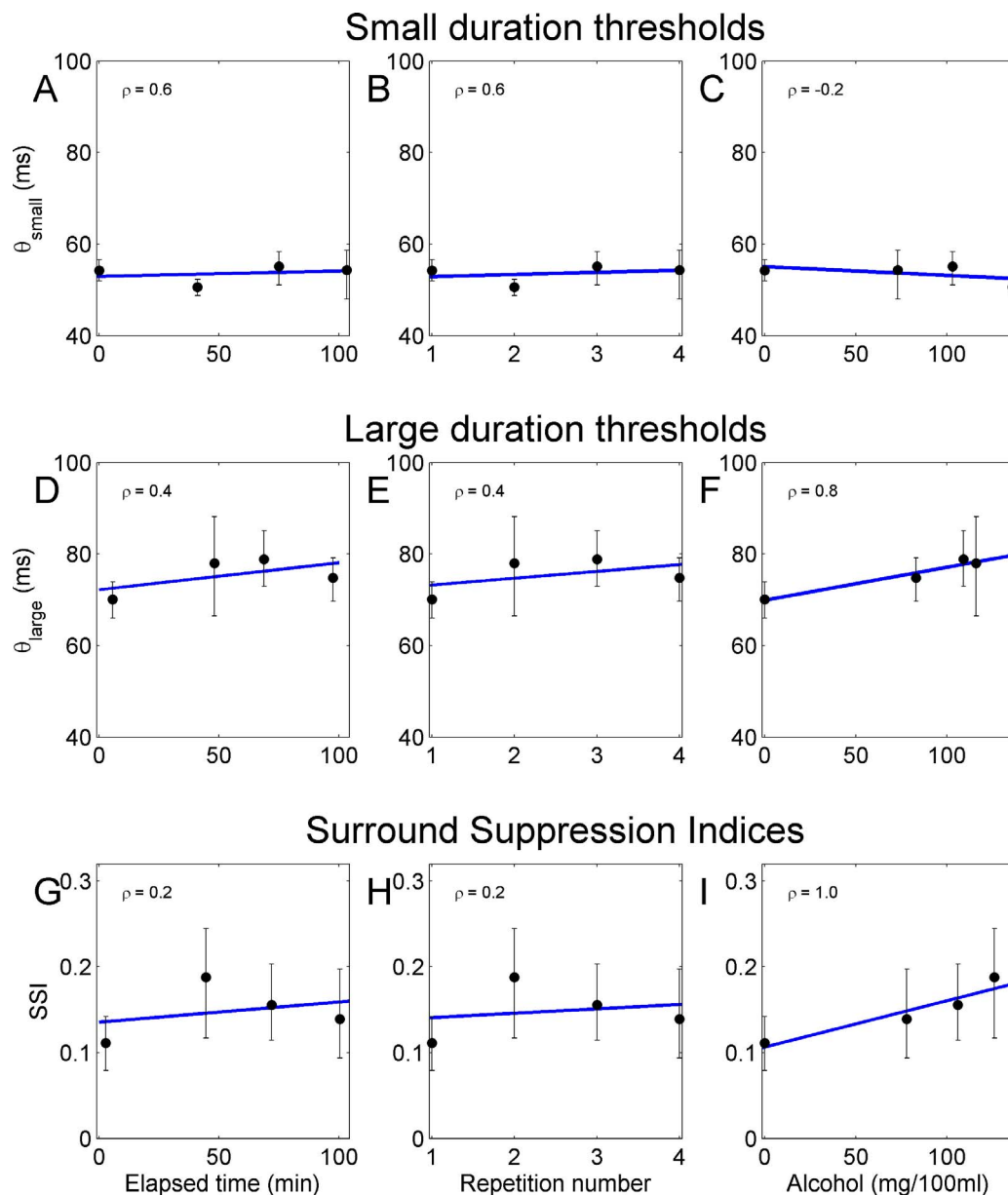


Figure 1. Complete results for an example subject in the alcohol group, subject A1. Black symbols show the results of individual measurements; error bars are 68% confidence intervals from resampling. Blue line is a linear fit to the results as a function of the parameter on the horizontal axis: (ADG) time elapsed since first measurement; (DEH) number of times this quantity has been measured; (CFI) blood alcohol level estimated by the breathalyzer. Spearman's  $\rho$  is shown in the top left of each panel.

## Results

### Example subject: Results and analysis

Figure 1 shows a complete set of data for subject A1 in the alcohol group, a 26-year-old male. At time 0, this subject completed the small-stimulus task, with a fitted duration threshold of 54 ms (first data-point in panels ABC). Immediately afterwards, at time 6 min, he completed the large-stimulus task, with a fitted duration threshold of 71 ms (first point in panels DEF).

He then consumed vodka and orange juice. At time 41 min, the breathalyzer estimated his blood alcohol concentration as 166 mg/100 ml. He repeated the small-stimulus task, obtaining a threshold of 50 ms; immediately afterwards the breathalyzer reported his mean blood alcohol as 106 mg/100 ml. This threshold was therefore assigned a blood alcohol of 133 mg/100 ml, the mean of the two measurements (rightmost data-point Figure 1C). At time 48 min, subject A1 repeated the large-stimulus task, with a threshold of 82 ms. His blood alcohol was estimated at 106 mg/100 ml before the task, and 126 mg/100 ml afterwards, so this

threshold was assigned a blood alcohol of 116 mg/110 ml (rightmost data-point in Figure 1F). Subject A1 repeated both tasks twice more, for a total of four measurements, with breathalyzer readings before and after each measurement.

To estimate the Surround Suppression Index, we took each measurement of the small-stimulus threshold,  $\theta_{\text{small}}$ , and found the measurement of the large-stimulus threshold,  $\theta_{\text{large}}$ , which was closest in time. We then computed the log-ratio,  $\log_{10}(\theta_{\text{large}}/\theta_{\text{small}})$ , as the estimate of the Surround Suppression Index, SSI. We assigned the time/blood-alcohol of this Surround Suppression Index estimate to be the mean of the values for the two large- and small-stimulus measurements which went into that estimate of Surround Suppression Index. The four estimates of Surround Suppression Index are plotted in the bottom row of Figure 1.

We then considered the thresholds and SSI as a function of time since the first measurement (Figure 1ADG), number of times each quantity had been measured (BEH), and blood alcohol (CFI). For each panel, we computed Spearman's  $\rho$  correlation coefficient, shown in the top left of each panel, and also fitted a straight line to the four data-points, shown in blue. In Figure 1G, Surround Suppression Index shows no systematic dependence on elapsed time, but in Figure 1I, it shows a monotonic increase with blood alcohol concentration, reflected in a Spearman's  $\rho$  of 1. With only four data-points, even  $\rho = 1$  is not significant. To assess significance, we used bootstrap resampling. For each data-point, we had 10,000 resampled values, whose 16% and 84% percentiles were used to obtain the error bars. We used these to generate 10,000 sets of four data-points, and computed  $\rho$  and regression gradient for each resampled data set. Finally, we examined the 2.5%–97.5% percentile range of the 10,000 values. If the 2.5% and 97.5% percentiles had the same sign, the gradient would be significantly different from zero. In fact, this percentile range spanned zero for both  $\rho$  and gradient for all nine relationships considered in Figure 1. In subject A1, therefore, there is no evidence that duration thresholds or Surround Suppression Index are affected by time elapsed, repetition, or by alcohol consumption.

### Population: Alcohol impairs performance but without affecting surround suppression

Figures 2 and 3 summarize similar analyses for all subjects in both groups. Spearman's  $\rho$  correlation coefficients are shown with a blue symbol for each subject. The red error bars show the 68% confidence intervals estimated from resampling. In each figure, the top row shows the correlation for  $\theta_{\text{small}}$ , the duration

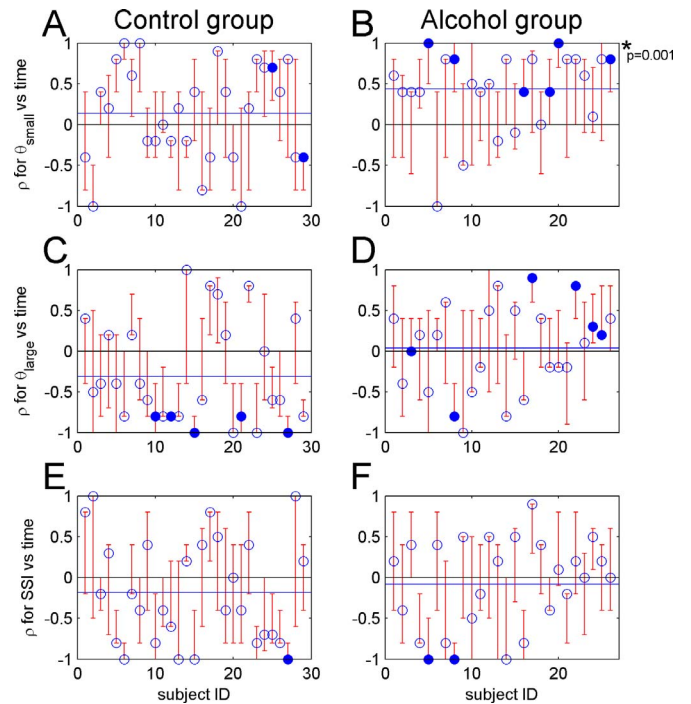


Figure 2. Rate of change with time. For each subject, symbols show Spearman's  $\rho$  between the time that has elapsed since the first measurement and the given metric (AB: duration thresholds for small stimuli; CD: durations thresholds for large stimuli; EF: Surround Suppression Index). In each panel, horizontal black line shows  $\rho = 0$ ; blue line shows the mean across subjects; error bars show the 68% confidence intervals estimated from resampling; filled symbols show individual subjects where  $\rho$  was significantly different from zero (95% confidence intervals did not span 0). The asterisk marks the panel where the population  $\rho$  differed significantly from zero according to the sign test. ACE: Results from 329 control subjects. BDF: Results from 26 subjects who consumed alcohol (for whom elapsed time is confounded with alcohol level).

threshold for the small stimulus, the middle row  $\theta_{\text{large}}$ , the bottom row Surround Suppression Index. In Figure 2, this correlation is computed between each metric and elapsed time, for both groups, while in Figure 3, it is computed between the metric and blood alcohol level, for the alcohol group only. Any effect of practice, task familiarity, or fatigue would be expected to manifest as a change with one of these in the control group. The filled symbols show subjects where the correlation is significantly different from zero, in that the 95% confidence interval estimated from resampling did not span zero. To assess the significance of any trend across the population, we ran a sign test on each set of correlation coefficients. The only significant result was for small-stimulus thresholds in the alcohol group.

For the alcohol group, the duration thresholds for small stimuli tended to increase slightly over time (Figure 2B). In all six subjects where  $\rho$  was significantly

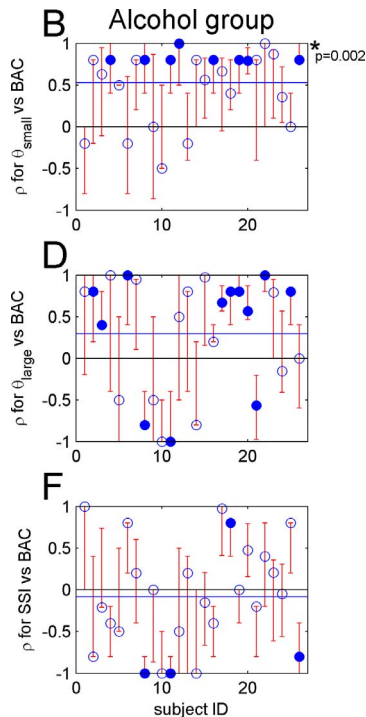


Figure 3. As for Figure 2, but shows Spearman's  $\rho$  for the specified metrics versus estimated blood alcohol concentration (BAC in mg/100 ml), rather than time elapsed, for the alcohol group only.

different from 0 for that individual,  $\rho$  was positive, and across the population, Spearman's correlation coefficient  $\rho$  was positive for 21/26 subjects ( $p < 0.001$ , sign test). Of course, in the alcohol group, time is confounded with blood alcohol concentration. Figure 3B shows that thresholds on the small stimuli also tended to increase with blood alcohol concentration; now  $\rho$  was individually significant in 8/26 subjects, again positive in all 8, while across the population it was positive for 20/26 subjects ( $p = 0.002$ , sign test). We do not see any effect of time in the control group, so we conclude that this increase was due to the alcohol consumption. To quantify the increase, we considered the gradients. Statistically, we found the same results as with  $\rho$ : Across subjects in the alcohol group, the gradient of small-stimulus duration thresholds was positive when  $\theta_{\text{small}}$  was plotted as a function of elapsed time ( $p = 0.001$ ), repetition index ( $p = 0.002$ ), or blood alcohol ( $p = 0.001$ , all sign test). Although significant, this effect was very small; on average, duration thresholds increased by just 1 ms each time subjects repeated the task, and the maximum gradient in any subject was only 4 ms per repetition.

When considering gradients instead of correlation coefficients, we also detected a marginally significant tendency for alcohol to impair performance on the large stimulus ( $p = 0.03$ , sign test on gradients for  $\theta_{\text{large}}$  as a function of blood alcohol). Gradients also revealed

a slight tendency for control subjects to improve on the large stimulus on repeated tests. This effect was small (the average decrease was 2 ms every time the subject repeated the measurement) but marginally significant ( $p = 0.02$ , sign test on gradients computed as a function of repetition index; the gradient was negative in all 5/29 subjects for whom the gradient was individually significantly different from zero). The slight decrease in threshold may represent a practice effect, as subjects become more familiar with the challenging large stimulus. However, this effect is not large enough to result in a significant change in Surround Suppression Index as a function of either time or repetition.

Because alcohol consumption slightly impairs duration thresholds on both the small and large stimuli, it produces no detectable effect on the Surround Suppression index. Changes in Surround Suppression Index are rarely significant for individual subjects, and at the population level there is no consistent trend.

Figure 4 shows an alternative way of approaching the question. Here, results of the second measurement are plotted against those of the first measurement. For the control group, the only difference expected is due to effects such as practice or fatigue. The alcohol group, however, has consumed vodka in between the two measurements. As Figure 4 shows, the two measurements generally agree closely. A sign test indicated significant differences only for the small and large duration thresholds in the alcohol condition ( $p = 0.009$  for  $\theta_{\text{small}}$ ,  $p = 0.001$  for  $\theta_{\text{large}}$ ). This confirms the results of the previous analysis: Alcohol consumption causes a slight increase in duration thresholds for both small and large stimuli, but has no discernible effect on Surround Suppression Index.

## Reliability of duration thresholds and surround suppression estimates

The statistical analysis above has depended on our estimates of confidence intervals obtained by bootstrap resampling, for example in estimating the significance of nonzero gradients. The confidence intervals estimated for Surround Suppression Index are fairly large, especially in percentage terms. This is due predominantly to uncertainties in the duration threshold estimated for the large stimulus. Both the within-subject and between-subject variability are important for the potential clinical applications of this task. The within-subject variability limits our power to accurately assess the true value of the index in an individual, and may mean that multiple measurements are necessary in order to get an accurate estimate. The between-subjects variability further limits our power to detect systematic differences between healthy controls and various clinical populations, a limitation which may be

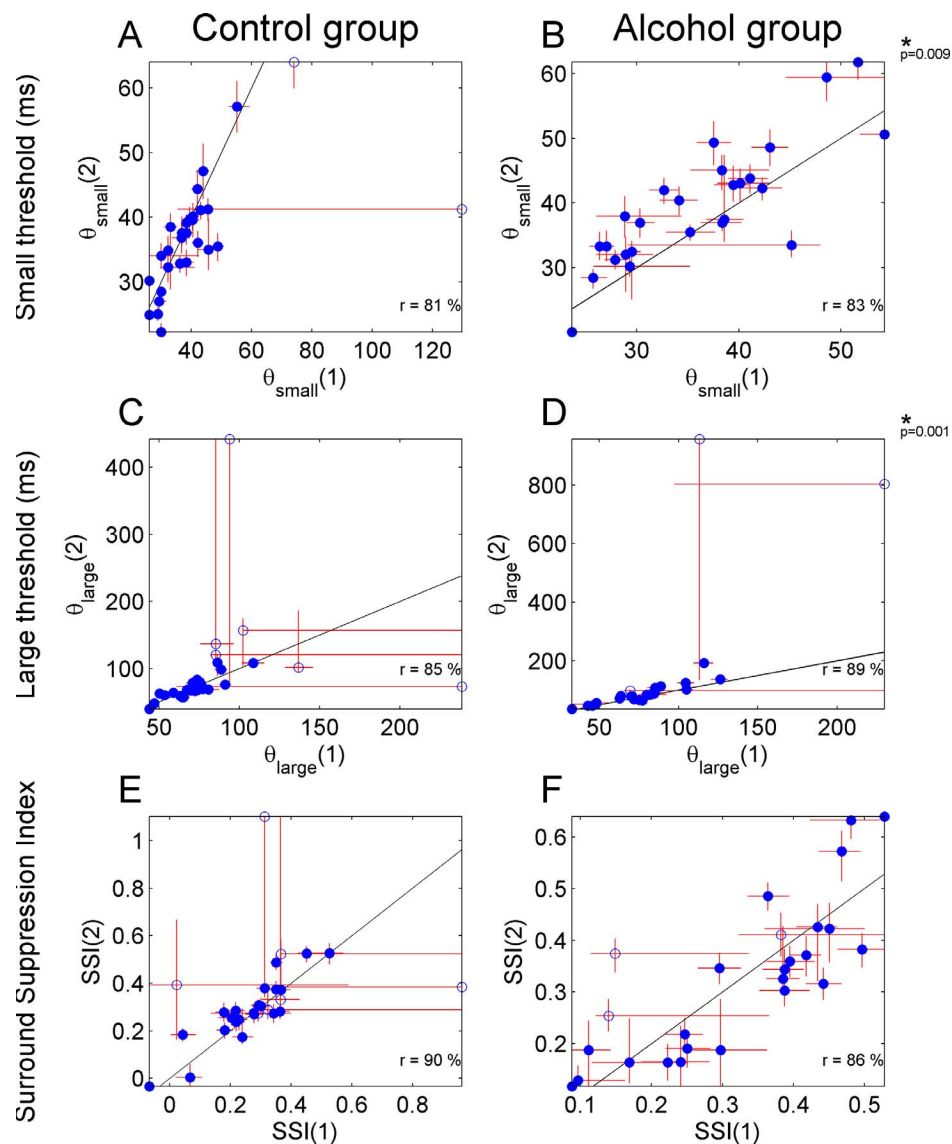


Figure 4. Scatterplots showing the second measurement for each subject plotted against their first measurement. AB: Measurement of small stimulus duration thresholds; CD: large stimulus duration thresholds; EF: Surround Suppression Indices. ACE: Control group; BDF: Alcohol group. Error bars (red) show 68% confidence intervals obtained from resampling. Filled dots are those where both measurements were acceptably precise, defined as 68% confidence interval  $< 20$  ms for small duration threshold,  $< 40$  ms for large duration threshold,  $< 0.2$  for suppression index. Pearson correlation coefficient for filled dots is shown bottom right. Asterisks mark the panels where a sign test indicated a significant difference between the first and second measurements.

important given that this task is being used in clinical studies (Golomb et al., 2009; Tadin et al., 2006). It is therefore important to assess both forms of variability, and our data set allows us to do this.

If factors such as fatigue, practice, and orange juice consumption had no effect on performance, then the measurements in our control group would represent independent samples from the same distribution. We can therefore examine the standard deviation of the sample, and see how it compares to the confidence intervals estimated from resampling. If the noise affecting the measurement is Gaussian with standard deviation  $\sigma$ , then any individual measurement has a

95% probability of lying within  $\pm 2\sigma$  of the mean, and a 68% probability of lying within  $\pm 1\sigma$ . We can estimate  $\sigma$  from the standard deviation of the sample, and test whether  $4\sigma$  agrees with the 95% confidence interval estimates from resampling.

This comparison is presented in Figure 5. For each of our three metrics (duration thresholds for small and large stimuli, and Surround Suppression Indices), we estimated  $\sigma$  from the standard deviation of the different measurements taken. The sample size was usually four, but ranged from three to five. This  $\sigma$  is the horizontal axis in each panel. Each measurement had a confidence interval, estimated from resampling. We took the mean



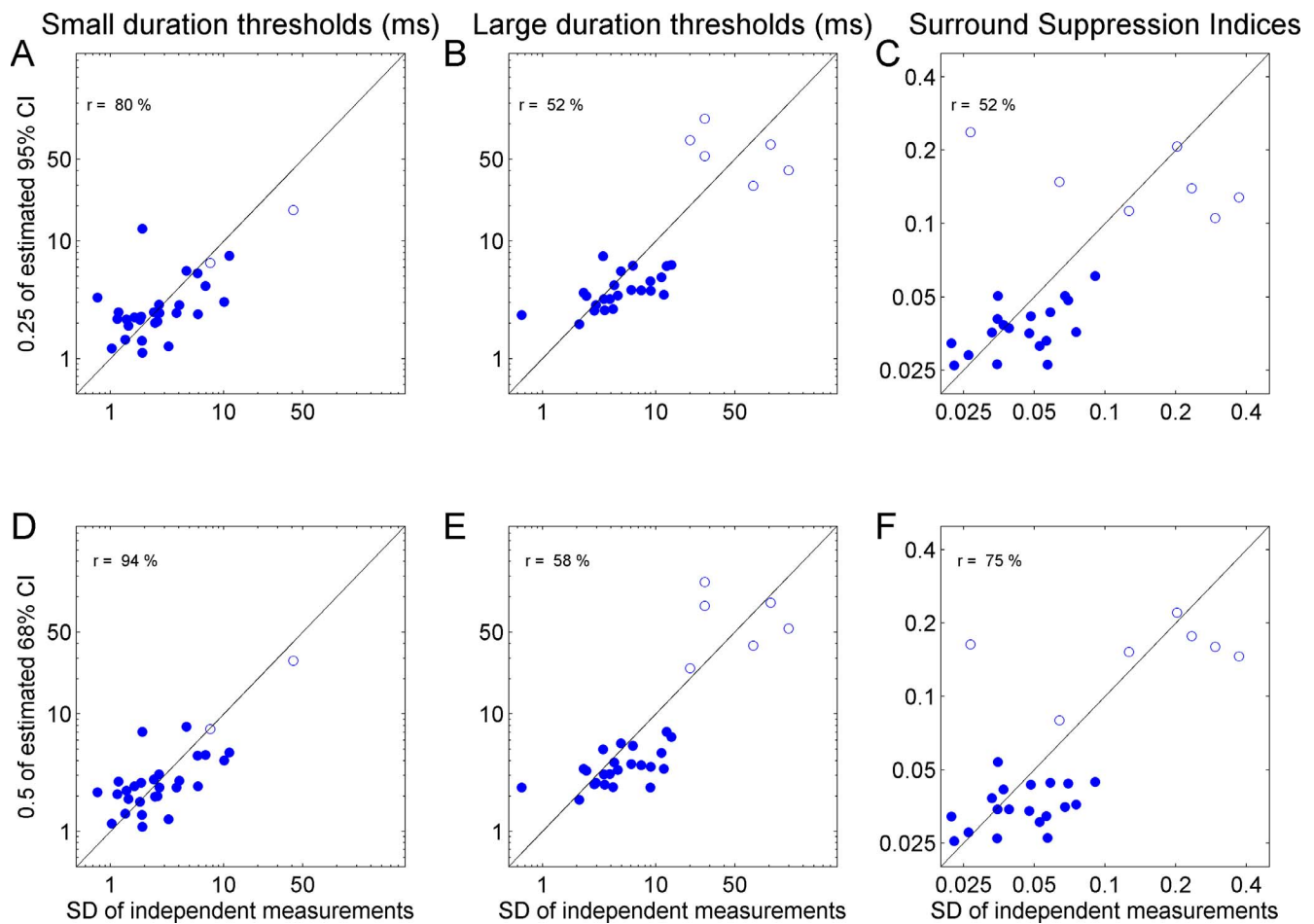


Figure 5. Assessing the accuracy of confidence intervals estimated from resampling (control data only). Each symbol represents data from one subject. For each metric (AD: small-stimulus durations thresholds  $\theta_{\text{small}}$ ; BE: large-stimulus duration thresholds  $\theta_{\text{large}}$ ; CF: Surround Suppression Indices SSI), the horizontal axis shows the standard deviation of the sample of measurements taken for that subject. The vertical axis shows the corresponding fraction of the percentile range of the resamples generated for each individual measurement, averaged over all measurements taken. ABC: one-quarter of the 2.5–97.5 percentile range; DEF: one-half of the 16–84 percentile range.

of the confidence interval across the different measurements taken. We then compared  $\sigma$  with 0.25 of the 95% confidence interval (Figure 5 top row) and with 0.5 of the 68% confidence interval (Figure 5 bottom row). Overall, the agreement is good. The Pearson correlation coefficient  $r$  is shown in the top-left of each panel. For all panels, a paired  $t$  test comparing the two estimates returned  $p > 0.05$ , i.e., consistent with the hypothesis that both estimates are drawn from the same distribution. This reassures us that bootstrap resampling is appropriate for this data set. Another way of approaching this is shown in Figure 4. At the bottom of each panel, we have given the reliability of precise estimates; that is, we have first excluded estimates with excessively large error bars (empty symbols) and then computed the correlation between first and second measurements. In each case, this is over 80%.

Given confidence intervals, we can estimate the within- and between-subject variability. We have used the first measurement from all 56 subjects in both groups (so before alcohol consumption, for the alcohol group). The mean Surround Suppression Index is 0.31, similar to previous reports: 0.45 (Tadin et al., 2006), 0.44 (Golomb et al., 2009), 0.25 (Betts et al., 2005) (younger group). The standard deviation of the sample is 0.16, which we expect to be made up of contributions from both within- and between-subject variability. Given the results in Figure 5, we can estimate the within-subject variability from the mean value of half the 16–84 percentile range of resampled values for each subject, which is 0.07. We can then attribute the remaining variance to between-subject variability, resulting in an estimate for that of 0.14.

Table 1 shows these estimates also for the duration thresholds. Measured thresholds were less precise for the large stimulus, even when confidence intervals are

	Population mean	Within-subject variability, SD (% SD/mean)	Between-subject variability, SD (% SD/mean)
Threshold on 0.7° stimulus, $\theta_{\text{small}}$	39 ms	4 ms (10%)	15 ms (38%)
Threshold on 5° stimulus, $\theta_{\text{large}}$	82 ms	23 ms (28%)	28 ms (34%)
Surround suppression index	0.30	0.07 (24%)	0.14 (47%)

Table. Estimated population mean and variability within and between subjects, for duration thresholds and Surround Suppression Index.

expressed in fractional terms. The mean within-subject standard deviation was just 4 ms for the small stimulus, or 10% of the population mean, whereas it was 23 ms or 28% for the large stimulus. As Tadin et al. (2003) originally reported, subjects find the large stimulus hard and need to see it for longer. Additionally, some subjects appear to experience illusory reversed motion in this stimulus. Glasser and Tadin (2013) have reported that subjects consistently show reversed motion perception in this stimulus at very short durations (Gaussian temporal envelopes with standard deviations < 15 ms). We found that a small minority of subjects seemed confused about stimulus direction even at very long stimulus durations. These were not lapses of concentration, as they were made repeatedly and only for the large stimulus, and some were confirmed verbally to the experimenter. Some subjects reported seeing the envelope and carrier moving in opposite directions, and being unsure which to report. In using a staircase procedure, we followed the methods of previous published studies with this stimulus. However, a staircase assumes a monotonic decrease in task difficulty as stimulus intensity (here, duration) increases. Our observations, together with those of Glasser and Tadin (2013), suggest that this assumption may not always be justified in the large high-contrast stimulus. However, the data collected in this study do not allow us to address this further.

## Discussion

Healthy subjects require longer to discriminate direction of motion in large high-contrast stimuli than in small ones. This is an example of psychophysical surround suppression, and can be quantified with the Surround Suppression Index, defined as the log-ratio of the thresholds for large versus small stimuli. Surround Suppression Indices are affected by age and by several neurological or psychiatric conditions. These differences are generally attributed to alterations in cortical inhibition. However, to our knowledge all human studies to date have simply observed correlations between Surround Suppression Index and various other factors; no one has attempted to manipulate surround

suppression. Ethanol alcohol is a drug which affects cortical inhibitory mechanisms and is widely used for recreational purposes; accordingly, we hypothesized that alcohol ingestion might provide an effective and convenient way of manipulating surround suppression in humans. However, our data revealed no change in surround suppression after alcohol ingestion.

It is always difficult to interpret a null result. One possible explanation is that the dose administered was too small to produce detectable effects. Of course, we cannot exclude the possibility that larger doses would have produced changes in surround suppression. However, the doses we used did produce small but measurable increases in duration thresholds on both large and small stimuli. This increase is not due to a simple effect on contrast sensitivity. Alcohol intoxication does reduce contrast sensitivity (Pearson & Timney, 1998), but the reductions are small at the spatial and temporal frequencies used in our study. Conversely, even major reductions in contrast do not impair performance on the motion-discrimination task used here: Duration thresholds for the small (0.7°) stimulus are unchanged even by a halving of contrast from 92% to 46% (Tadin et al., 2003), whereas for the large stimulus, reducing contrast improves performance. Thus, the increases in duration threshold which we observe following alcohol ingestion cannot solely reflect lower effective contrast after intoxication. They could reflect cognitive effects, e.g., reduced attention or motivation, or some other perceptual effect; our experiment was not designed to discriminate between these possibilities, and further work would be needed to do so. Importantly, however, the increase in thresholds confirms that our experimental dose was large enough to have a detectable effect on subject performance, so the lack of an effect on surround suppression index is not a trivial consequence of limited dose size.

The next obvious question is whether our experiment lacked power to detect a change in Surround Suppression Index. Power reflects both the number of subjects and the variability in the measurement. We will therefore begin by discussing variability in some detail. The fact that several clinical groups show differences in Surround Suppression Index has caused some interest in its possible use in the clinic, for example to track disease progression. For this, it is important to

understand the normal variability. In Table 1, we have reported the within- and between-subject variability for small- and large-stimulus duration thresholds, and for Surround Suppression Index. As far as we are aware, ours is the first study to consider within- and between-subject variability. Melnick, Harrison, Park, Bennetto, and Tadin (2013) reported split-half reliabilities of 98% for duration thresholds averaged over three stimulus sizes. Split-half reliability is the correlation coefficient between estimates obtained using different halves of the data, in their case between the threshold estimates produced by averaging two different staircases per subject. For a variety of reasons, reliability is not a good way of assessing how well two measurements agree (Bland & Altman, 1986). For example, even if the repeatability within in each subject is poor, the reliability will be high if there is enough variability between subjects. However, to compare our results with those of Melnick et al., we computed the reliability coefficients between first and second measurements. Even after excluding measurements with excessive error bars, we obtain much lower reliabilities, around 85% compared to 98%. There are several possible reasons for this. First, Melnick et al. used stimuli with half the contrast of ours (46% vs 92% contrast, also faster at 4 vs 2°/s). This lower contrast produces less surround suppression, thus shorter thresholds and probably less variability (see below). There were also important differences in procedure. To obtain these high reliabilities, Melnick et al. had subjects first complete two practice staircases for each stimulus size, before returning on a later date to complete a further six staircases per size. The highest/lowest threshold estimates were then discarded, and the final threshold taken as the average of the remaining four estimates. Our subjects did not have a practice session beforehand, and our threshold estimates are each based on three staircases, not on six of which the outliers are excluded. It is not surprising, therefore, that we obtain lower reliabilities than Melnick et al. even after excluding measurements which were obviously imprecise. Clearly, researchers should follow the methods of Melnick et al. to obtain the best reliability, but this may not always be practical for clinical groups.

As noted, high split-half reliability does not guarantee good repeatability. To address this, we have estimated within-subjects and between-subjects variability separately. We see much larger variability on duration thresholds for the large stimulus: The within-subject standard deviation was 28% of the population mean for the large stimulus, compared with 10% for the small. For Surround Suppression Index, we find that the within-subjects variability is 0.07. This means that the standard deviation of the difference between two measurements in the same subject is  $\sim 0.1$ , and thus that the repeatability coefficient is 0.2 (Bland &

Altman, 1986). That is, a difference of at least 0.2 between two measurements in the same subject would be required before one can conclude that Surround Suppression Index has genuinely changed in that individual. This is, of course, with the methods used here, where a single estimate of Surround Suppression Index is obtained from duration thresholds each obtained from three 50-trial staircases. Assuming a Gaussian distribution, we can estimate the improvement obtained by using nine staircases per condition: This should reduce the within-subjects standard deviation by a factor of  $\sqrt{3}$  to 0.04, and the repeatability coefficient to 0.1. Armed with this information, we can now assess the power in our study. Given the 26 subjects in our alcohol group, and assuming a within-subject comparison of two measurements before and after alcohol consumption, compared by t-test, our study would have been able to detect a change of around 0.056 in Surround Suppression Index with a power of 80%. This is much smaller than the differences in Surround Suppression Index associated with various neurological conditions (e.g., 0.20 in autism (Foss-Feig, Tadin, Schauder, & Cascio, 2013); 0.14 in depression (Golomb et al., 2009), 0.25 in severe schizophrenia (Tadin et al., 2006), 0.20 for age, 60-year-olds versus 20-year-olds (Betts et al., 2005). Thus, we can safely conclude that acute alcohol ingestion has much less effect on psychophysical surround suppression than the above-mentioned conditions.

The failure of our original hypothesis reflects our lack of knowledge concerning both the effects of alcohol and the neuronal mechanisms which affect psychophysical surround suppression. At a pharmacological level, alcohol affects many neurotransmitter systems, not just GABA (Deitrich et al., 1989). Physiologically, alcohol has many effects on visual pathways; examples include depressed cortical responses following direct optic nerve or lateral geniculate nucleus stimulation (Story et al. 1961). How these physiological changes affect visual perception is less clear; early studies showed reduced, unaffected or increased flicker fusion threshold with moderate alcohol intakes (reviewed in Hill, Powell & Goodwin, 1973). Part of these inconsistencies probably relates to differences in alcohol dose, changes in blood alcohol level during the experiments, and the diversity of stimuli used to investigate visual performance.

More recent studies have converged on the view that alcohol impairs both temporal and spatial visual processing. Increased reaction times to moving stimuli (MacArthur & Sekuler, 1982), impaired depth perception (Watten & Lie, 1996), reduced contrast sensitivity (Pearson & Timney, 1998) and impaired oculomotor control (Hill & Toffolon, 1990) have all been demonstrated at moderate alcohol doses. Not all aspects of visual processing are necessarily impaired; MacArthur

and Sekuler demonstrated improved performance in a direction judgment task with moderate alcohol dose, and no effect on a task requiring attention to two possible directions of motion. Thus the interaction between alcohol and visual processing remains complex. It is possible that our failure to observe changes in surround suppression reflects competing effects of alcohol on different aspects of vision. For example, we argued above that the increases in duration threshold cannot solely reflect reduced contrast sensitivity following alcohol ingestion, because reduced contrast sensitivity should decrease duration thresholds for large stimuli. However, since a reduction in contrast sensitivity and an increase in surround suppression are predicted to have opposite effects on thresholds for large stimuli, it is possible that the former could be masking the latter.

The neuronal mechanisms underlying psychophysical surround suppression are also the subject of ongoing debate. Surround suppression is generally taken to reflect inhibitory mechanisms which become more active at higher contrasts (Tadin & Lappin, 2005). It is usually assumed that these are mediated by GABA. In agreement with this picture, Yoon et al. (2010) found that psychophysical surround suppression on a different task correlated with the GABA concentration in visual cortex, as measured with MR spectroscopy. Surround suppression on the motion discrimination task used here has also often been related to GABAergic inhibition (Betts et al., 2005; Golomb et al., 2009; Tadin et al., 2006). We had therefore reasoned very naively that if alcohol potentiates GABAergic effects, it might increase surround suppression. Our failure to observe this could be because alcohol has a variety of pharmacological actions, and does not simply potentiate GABAergic inhibition in the relevant cortical areas. However, preliminary results from Liu and Pack (2014) suggest that neuronal surround suppression may not reflect GABAergic inhibition in any case. Liu and Pack (2014) studied monkeys performing this motion-discrimination task at fixed duration. Like humans, monkeys found it harder to report the correct motion direction for larger stimuli. This result matched the neuronal response of surround-suppressed neurons in MT. However, MT also contains many non-surround-suppressed neurons, and these consistently outperformed the monkey for large stimuli. Liu and Pack showed that inactivation of MT by the GABA<sub>A</sub> agonist muscimol reduced performance, confirming a causal role for MT on this task. However, local blockade of GABA receptors did not reduce surround suppression in the neurons which showed it. Possibly related to this observation, Ozeki, Finn, Schaffer, Miller, and Ferster (2009) concluded that surround suppression in V1 reflects a decrease in both excitatory and inhibitory

input. Under the circumstances, few would argue with the conclusion of Liu and Pack (2014) that “the contribution of inhibition to surround suppression is more complex and dynamic than previously thought.”

*Keywords:* ethanol, motion perception, vision, psychophysics, surround suppression

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## Footnote

<sup>1</sup> Note that these numbers are slightly different from those in Table 1, since they include subjects in both groups.

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