

# The Effects of Escitalopram Administered Alone and with Alcohol on Cognition and Psychomotor Performance

Candace Jeavons Wilkinson, PhD,<sup>1,2</sup> Grace S. Lee,<sup>3</sup> Chung-Chi Chang, PhD,<sup>3</sup> and Daniel Ventura, PhD<sup>3</sup>

<sup>1</sup>Southern California Research Institute, Los Angeles, CA; <sup>2</sup>UCLA Mood Disorders Research Program, Los Angeles, CA (current address); <sup>3</sup>Forest Laboratories, Inc., New York, NY

## Abstract

**Background:** Escitalopram is a recently approved selective serotonin reuptake inhibitor (SSRI) for the treatment of depression. This study evaluated the effects of escitalopram, given alone and when co-administered with alcohol, on cognitive and psychomotor function in healthy subjects.

**Methods:** This was a double blind, placebo-controlled study with a balanced 4 x 4 Latin square design. Nineteen healthy male subjects were randomly assigned to four sequence groups to receive the following treatments at weekly intervals: escitalopram alone [10 mg escitalopram + placebo alcohol], combination [10 mg escitalopram + alcohol (0.8 g/kg)], alcohol alone [placebo + alcohol (0.8 g/kg)], and placebo [placebo + placebo alcohol]. Cognitive and psychomotor functions were evaluated with a driving simulator, choice reaction time test, memory task, digit symbol substitution test (DSST), serial sevens, finger tapping test (FTT) and field sobriety tests. Subjective effects (e.g., sedation) were rated by both the investigator and subjects. Blood alcohol concentrations (BAC) were measured through breath samples.

**Results:** Sixteen subjects (ages 21-31) completed the study. As expected, nearly all performance measures showed a significant impairment effect by alcohol alone ( $p < 0.05$ ). Escitalopram alone did not impair cognitive or psychomotor function relative to baseline measures and was comparable in effect to placebo on the psychomotor test battery except for the FTT where performance was significantly improved ( $p < 0.05$ ). When co-administered with alcohol, escitalopram did not further impair performance compared to alcohol alone but did significantly improve performance on the DSST, serial sevens and FTT ( $p < 0.05$ ) despite comparable BACs (peak: 0.08%).

**Conclusions:** An acute dose of escitalopram given alone or with alcohol does not impair cognitive or psychomotor function in this study population.

## Introduction

Escitalopram, the therapeutically active isomer of the SSRI citalopram, is effective and well tolerated in the treatment of depression and anxiety disorders. It has been shown in several clinical trials to have antidepressant efficacy at a dose of 10 mg/day.<sup>1,2</sup>

Minimizing impairment of cognitive and psychomotor performance for antidepressants is important for safe and unimpaired performance of activities of daily living, especially where driving or operating machinery is involved. Medications that potentiate alcohol-induced impairment of psychomotor, cognitive, and sensorimotor processing may cause heightened safety concerns.<sup>3</sup> It has been demonstrated previously that citalopram neither impairs psychomotor performance<sup>4</sup> nor potentiates alcohol-induced impairment.<sup>5</sup> This study was designed to investigate the effects of escitalopram, administered alone and with alcohol, on cognitive and psychomotor function, including performance on a driving simulator.

## Methods

### Study Design

- Double-blind, single-dose, 4 x 4 crossover study.

• Following two training visits and a baseline visit, subjects were assigned in random sequence to receive the following four treatments at 1-week intervals:

- **Placebo:** placebo + placebo alcohol
- **Alcohol:** placebo + 0.8 g/kg alcohol
- **Escitalopram:** 10 mg escitalopram + placebo alcohol
- **Combination:** 10 mg escitalopram + 0.8 g/kg alcohol

• Alcohol (or placebo-alcohol) was administered 2 hours and 45 minutes after administration of escitalopram (or placebo) so that the assessments would be timed to capture the peak effects for both the alcohol and drug treatments. Alcohol treatment was given as 3 divided doses, each consumed for a paced 10-minute period in order to provide a steady absorption rate.

• A 75-minute assessment battery was performed at a baseline visit, and 45 minutes after start of administration of alcohol (or placebo-alcohol), corresponding to 3.5 hours post drug dose, at each of the 4 treatment visits.

### Subjects

- 19 male volunteers with a normal physical examination including medical and psychiatric history, laboratory tests and electrocardiogram (ECG).

• Moderate or low-heavy social use of alcohol on the Quantity-Frequency-Variability (QFV) alcohol use questionnaire.

### Assessments

- Pharmacodynamic effects of the four treatments were assessed by measuring changes relative to baseline in the following cognitive and psychomotor tests (given in this order):

- Choice Reaction Test (PC-based task of psychomotor speed and coordination)

- Driving Simulator (20-minute driving task with multiple demands)

- Shopping List Task (immediate memory and delayed recall)

- Digit Symbol Substitution Test (psychomotor and processing speed)

- Serial Sevens Test (attention; subtraction by sevens)

- Finger Tapping Test (motor speed)

- Field Sobriety Tests (horizontal gaze nystagmus, walk-and-turn, and one-leg stand)

• Subjective effects (e.g., coordination, speech, and sedation) were assessed using investigator-rated and subject-rated visual analog scales (100 mm line; 0 = “not at all,” 100 = “extremely”).

### Statistical Methods

- Pharmacodynamic analyses were based on all subjects who completed the study (N=16).

• Comparisons between the four treatments were performed using a two-way analysis of variance (ANOVA) model with sequence, subject within sequence, treatment and period as effects.

## Results

### Subjects

Sixteen subjects completed the study; mean (SD) age = 23.0 ± 2.6 yrs, weight = 168.6 ± 23.8 lbs. Two subjects withdrew due to adverse events, and one subject was dropped from the study due to protocol violations. Peak blood alcohol level was comparable for combination (0.07%) and alcohol (0.08%) treatments.

### Evaluation of Pharmacodynamic Effects

Table 1 shows the mean change from baseline on psychomotor and cognitive tests. As expected, alcohol significantly impaired memory (both for immediate and delayed recall), attention, choice reaction time, psychomotor and processing speed, and behavioral measures of sobriety. Alcohol did not significantly affect motor speed in the Finger Tapping Test. In contrast, escitalopram alone did not significantly affect any of the parameters, except motor speed, which was significantly improved relative to placebo. When co-administered with alcohol, escitalopram did not further impair performance compared to alcohol alone, but did significantly improve performance on the Digit Symbol Substitution Test, Serial Sevens Test, and the Finger Tapping Test ( $p < 0.05$ ).

Table 1. Mean Change (SD) from Baseline on Psychomotor and Cognitive Tests				
Measure (Baseline Mean ± SD)	Placebo	Escitalopram	Alcohol	Combination
Shopping List Task (Delayed Recall, max = 15) 13.8 ± 1.7	-0.2 ± 2.4	0.0 ± 1.8	-2.9 ± 2.7 **	-2.5 ± 2.4
Serial Sevens Test (Number Correct) 11.5 ± 3.3	1.3 ± 2.0	0.9 ± 3.4	-1.6 ± 2.3 **	-0.2 ± 2.1 <sup>†</sup>
Choice Reaction Test (Reaction Time; msec) 1003.0 ± 93.1	-8.4 ± 67.2	14.5 ± 85.2	61.6 ± 122.4 *	47.4 ± 130.7
Finger Tapping Test (Number of Taps) 70.3 ± 11.2	1.9 ± 5.7	5.6 ± 6.2 *	0.2 ± 6.2	3.3 ± 6.4 <sup>†</sup>
Digit Symbol Substitution Test (Number correct) 77.6 ± 6.9	1.6 ± 6.3	3.7 ± 5.7	-7.3 ± 4.8 **	-3.4 ± 4.7 <sup>†</sup>
Field Sobriety Tests (Total score (max = 18) 0.3 ± 0.5	0.1 ± 0.9	0.3 ± 1.0	4.9 ± 2.8 **	4.8 ± 2.9

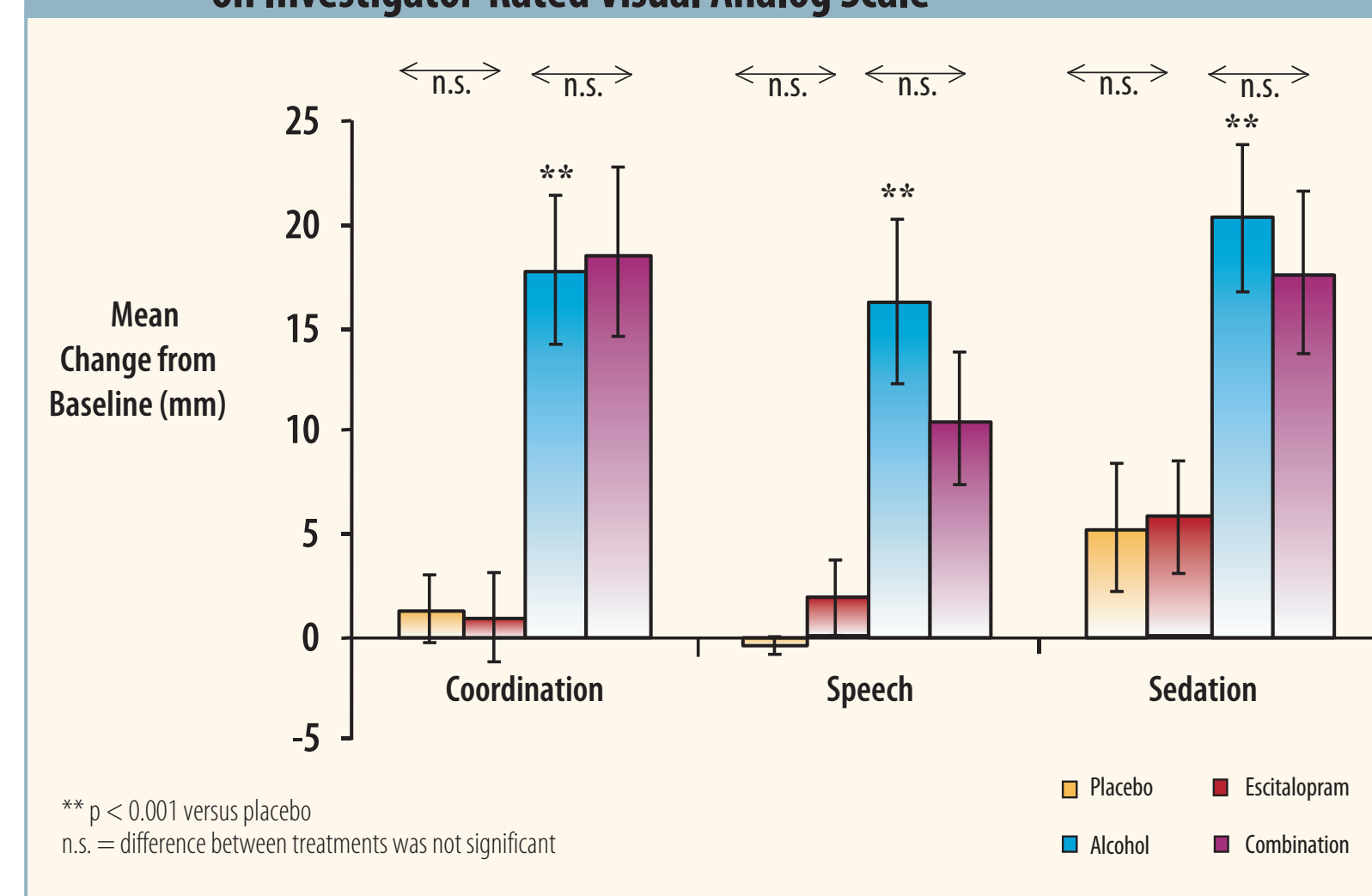
\*  $p < 0.05$  versus placebo

\*\*  $p < 0.01$  versus placebo

<sup>†</sup> $p < 0.05$  versus alcohol

Escitalopram administered alone had no effect on subjects' coordination, speech and sedation as rated by the investigator on the Visual Analog Scale (Figure 1). In contrast, alcohol significantly affected all three measures. Combination treatment did not potentiate the effects of alcohol. With the exception of significantly increased intoxication ratings after alcohol, the subject-rated VAS results showed no other significant treatment effects.

Figure 1. Mean Change from Baseline in Coordination, Speech, and Sedation on Investigator-Rated Visual Analog Scale



Escitalopram alone had no effect on any of the measures of driving simulator performance (Table 2). In contrast, excessive speed and collisions (Figure 2), as well as lane deviation (“weaving”) and reaction time to respond to visual signals, were significantly increased after alcohol, versus placebo ( $p < 0.05$ ). The overall performance index was defined as the average of the standardized scores for the change from baseline score in lane deviation, reaction time, and total driving errors. For each change score and within each period, the standardized score was calculated as the fractional rank score among all subjects. Both the standardized score and the overall performance index range from 0 to 1 where a higher value indicates worse performance. As shown, only alcohol significantly impaired overall performance, and combination treatment did not potentiate the effects of alcohol on driving simulator performance.

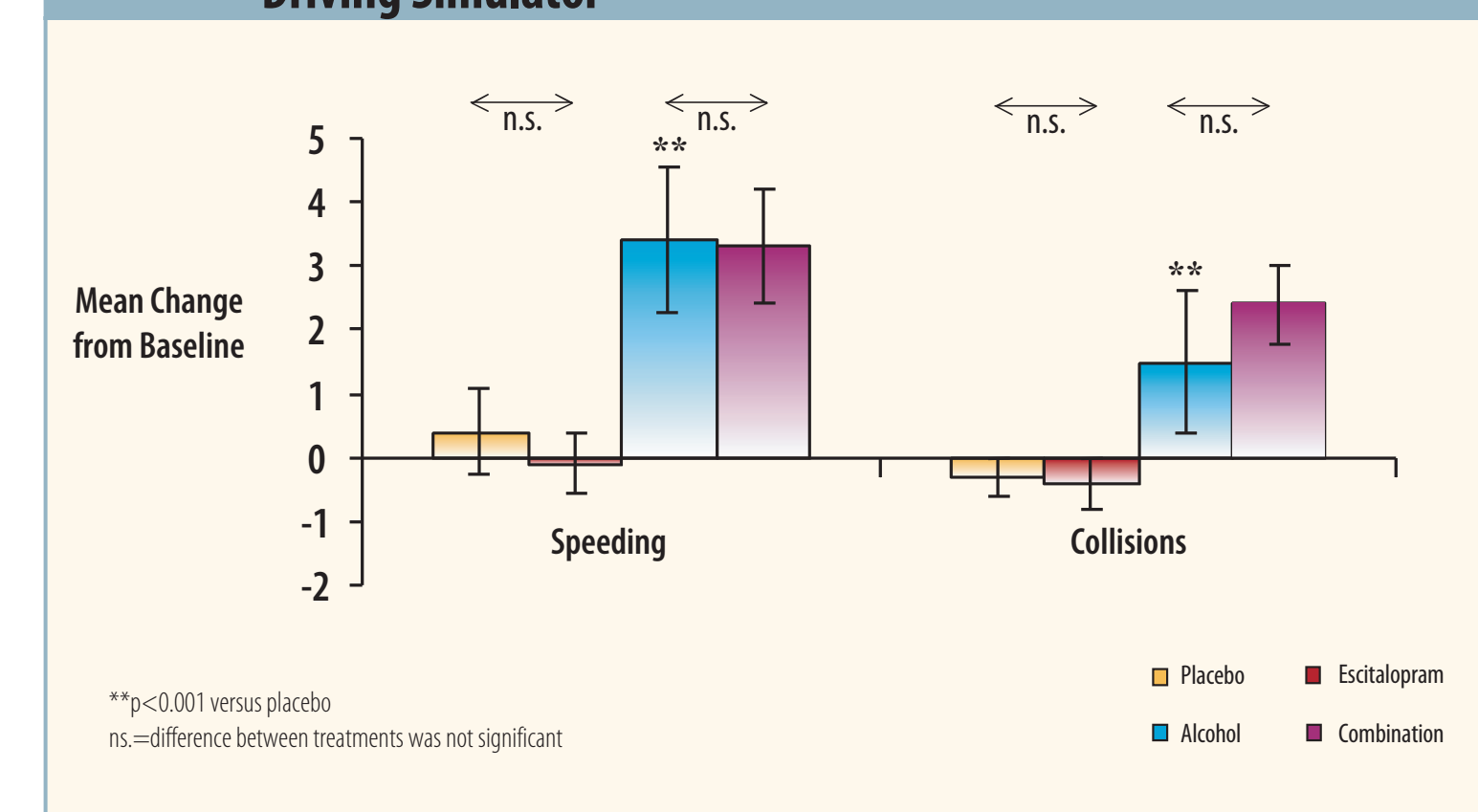
Table 2. Mean Change (SD) from Baseline in Driving Simulator Performance

Measure (Baseline Mean ± SD)	Placebo	Escitalopram	Alcohol	Combination
Lane Deviation (ft) (1.1 ± 0.15)	-0.0 ± 0.12	0.0 ± 0.19	0.2 ± 0.21**	0.2 ± 0.11
Reaction Time to Visual Signals (sec) (1.97 ± 0.19)	0.05 ± 0.17	-0.01 ± 0.18	0.28 ± 0.39*	0.25 ± 0.19
Total Driving Errors (no) (4.6 ± 3.4)	0.3 ± 4.16	-0.5 ± 2.61	5.4 ± 5.34*	6.1 ± 8.48
Speeding (2.3 ± 2.8)	0.4 ± 2.68	-0.1 ± 1.91	3.4 ± 3.58*	3.3 ± 4.51
Collisions (1.2 ± 1.2)	-0.3 ± 1.20	-0.4 ± 1.55	1.5 ± 2.42*	2.4 ± 4.56
Off Road Accidents (0.1 ± 0.3)	0.0 ± 0.37	-0.1 ± 0.25	0.3 ± 0.70	0.3 ± 1.08
Traffic Light Tickets (1.1 ± 1.0)	0.1 ± 1.71	0.1 ± 1.18	0.2 ± 1.38	0.1 ± 1.00
Overall Performance Index	0.39 ± 0.14	0.38 ± 0.18	0.71 ± 0.14*	0.69 ± 0.17

\*  $p \leq 0.05$  alcohol vs. placebo

\*\*  $p \leq 0.001$  alcohol vs. placebo

Figure 2. Mean Change from Baseline in Speeding and Collisions on the Driving Simulator



## Conclusions

• An acute dose of escitalopram, compared to placebo, does not appear to cause any significant impairment for a wide variety of cognitive and psychomotor skills in healthy male subjects.

• Co-administration of escitalopram with alcohol does not appear to potentiate alcohol-induced impairment of cognitive and psychomotor function.

## References

1. Wade AG, Michael Lemming O, Bang Hedegaard K. Escitalopram 10 mg/day is effective and well tolerated in treating patients with depression in primary care. *Int Clin Psychopharmacol.* 2002;17:95-102.
2. Burke WJ, Gergel I, Bose A. Fixed-dose trial of the single isomer SSRI escitalopram in depressed outpatients. *J Clin Psychiatry.* 2002;63:331-336.
3. Wilkinson CJ. The acute effects of zolpidem, administered alone and with alcohol, on cognitive and psychomotor function. *J Clin Psychiatry.* 1995;56:309-318.
4. Fairweather DB, Dal Pozzo C, Kerr JS, et al. Citalopram compared to dothiepin and placebo: Effects on cognitive function and psychomotor performance. *Hum Psychopharmacol.* 1997;12:119-126.
5. Lader M, Melhuish A, Frcka G, et al. The effects of citalopram in single and repeated doses and with alcohol on physiological and psychological measures in healthy subjects. *Eur J Clin Pharmacol.* 1986;31:183-190.

Supported by Forest Laboratories, Inc.

Presented at the 43rd Annual New Clinical Drug Evaluation Unit Meeting

Boca Raton, Florida | May 27-30, 2003