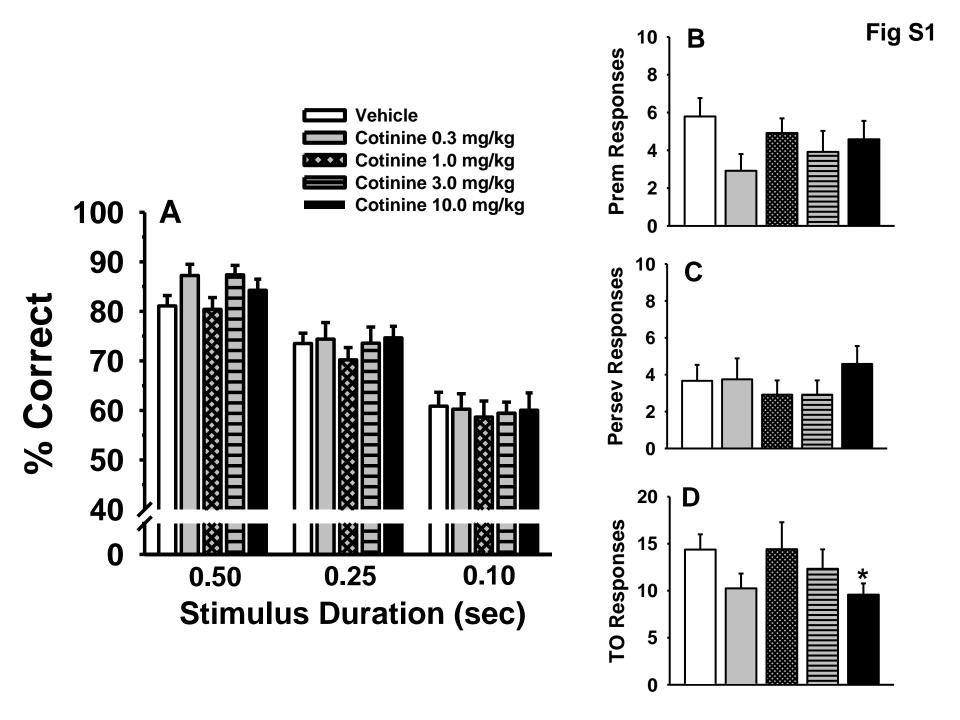
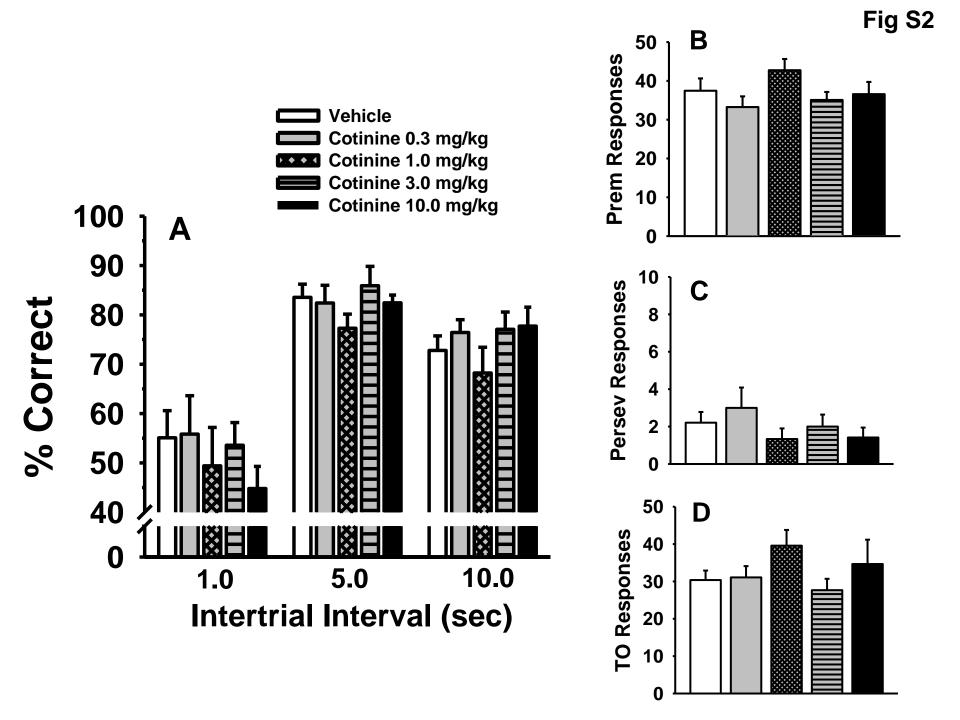
## **Supplemental Files**

The nicotine metabolite, cotinine, attenuates glutamate (NMDA) antagonist-related effects on the performance of the five choice serial reaction time task (5C-SRTT) in rats

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## **Supplemental Figure Legends**

**Supplemental Fig S1.** Dose-related effects of acutely administered cotinine in a variable stimulus duration (VSD) version of the 5C-SRTT. Rats were trained to meet specific performance criterion (described in the Methods section) at a stimulus duration (SD) of 0.5 sec. Subsequently, shorter SDs (0.10 and 0.25 sec) were presented pseudorandomly along with the 0.5 sec SD. Vehicle and four doses of cotinine (administered s.c. 30 min before testing) were evaluated for effects on 5C-SRTT performance. **A.** Percent Correct (accuracy) plotted by individual SD; **B.** Premature Responses (impulsive behavior); **C.** Perseverative Responses (compulsive behavior); **D.** Timeout Responses (compulsive behavior/cognitive inflexibility). Each bar represents the mean ± SEM for each test group. \*=significantly different (p<0.05) compared to vehicle-associated performance level. N=12

Supplemental Fig S2. Dose-related effects of acutely administered cotinine in a variable intertrial interval (ITI) version of the 5C-SRTT. Rats were trained to meet specific performance criterion (described in the Methods section) with a single 5 sec ITI sec. Subsequently, shorter and longer ITIs (1.0 and 10.0 sec) were presented pseudorandomly along with the 5.0 sec ITIs. Vehicle and four doses of cotinine (administered s.c.. 30 min before testing) evaluated for effects on 5C-SRTT performance. A. Percent Correct (accuracy) plotted by individual ITI; B. Premature Responses (impulsive behavior); C. Perseverative Responses (compulsive behavior); D. Timeout Responses (compulsive behavior/cognitive inflexibility). Each bar represents the mean ± SEM for each test group. N=12

**Supplemental Table 1.** Effects of Acute Cotinine on Latencies, % Omissions, and Trials Completed in the Variable Stimulus Duration (VSD) Version of the Five Choice Serial Reaction Time Task

| Treatment           | Latency     | Latency       | Magazine    | %         | Trials      |
|---------------------|-------------|---------------|-------------|-----------|-------------|
|                     | Correct (s) | Incorrect (s) | Latency (s) | Omissions | Completed   |
| Vehicle             | 0.79±0.04   | 1.47±0.11     | 1.48±0.12   | 8.13±2.07 | 96.83±2.99  |
| Cotinine 0.3 mg/kg  | 0.84±0.05   | 1.58±0.08     | 1.49±0.14   | 6.92±1.55 | 100.00±0.00 |
| Cotinine 1.0 mg/kg  | 0.83±0.05   | 1.57±0.11     | 1.51±0.08   | 8.91±2.43 | 98.00±1.35  |
| Cotinine 3.0 mg/kg  | 0.79±0.05   | 1.56±0.13     | 1.47±0.10   | 8.42±2.10 | 99.08±0.92  |
| Cotinine 10.0 mg/kg | 0.82±0.06   | 1.59±0.10     | 1.56±0.14   | 8.40±1.39 | 99.08±0.92  |

All data are presented as the mean  $\pm$  SEM. N=12

**Supplemental Table 2.** Effects of Acute Cotinine on Latencies, % Omissions, and Trials Completed in the Variable Intertrial Interval (VITI) Version of the Five Choice Serial Reaction Time Task

| Treatment           | Latency     | Latency       | Magazine    | %          | Trials      |
|---------------------|-------------|---------------|-------------|------------|-------------|
|                     | Correct (s) | Incorrect (s) | Latency (s) | Omissions  | Completed   |
| Vehicle             | 1.10±0.07   | 1.90±0.18     | 1.39±0.08   | 27.67±2.48 | 64.75±3.99  |
| Cotinine 0.3 mg/kg  | 1.08±0.10   | 1.79±0.15     | 1.97±0.66   | 28.76±3.19 | 57.67±6.11  |
| Cotinine 1.0 mg/kg  | 1.23±0.11   | 1.96±0.18     | 1.50±0.14   | 24.45±3.02 | 43.08±4.21* |
| Cotinine 3.0 mg/kg  | 0.91±0.08   | 1.95±0.20     | 1.48±0.19   | 27.78±2.94 | 67.33±7.66  |
| Cotinine 10.0 mg/kg | 1.19±0.14   | 2.22±0.20     | 1.46±0.15   | 29.70±2.35 | 58.83±6.37  |

All data are presented as the mean  $\pm$  SEM. \* = statistically significant difference (p<0.05) between vehicle and cotinine-treated group at the same stimulus duration. N=12