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Galantamine Improves Sustained Attention in Chronic Cocaine Users

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Abstract

Chronic cocaine users are known to have cognitive deficits that are predictive of poor treatment response. Whether these deficits improve with medications targeting specific cognitive functions has not been examined in previous studies. The goal of this study was to evaluate galantamine's efficacy on selected cognitive outcomes, including measures of sustained attention, response inhibition, and attentional bias in recently abstinent cocaine users. Galantamine, a reversible and competitive inhibitor of acetylcholinesterase, is used clinically in the treatment of Alzheimer's dementia. In a randomized, double-blind, parallel-group study, 34 participants were randomized to galantamine (8 mg/day) or placebo treatment for 10 days. Cognitive and self-report mood measures were obtained at baseline and on days 5 and 10 after the initiation of treatment. Galantamine treatment, compared to placebo, improved the reaction time, $F(2,50)=8.6$, $p<0.01$, detection sensitivity (A'), $F(2,50)=4.9$, $p<0.03$, number of hits, $F(2,50)=4.2$, $p<0.04$, and number of correct rejections, $F(2,50)=5.6$, $p<0.02$, on the Rapid Visual Information Processing (RVIP) task. With the exception of speeding the reaction time on the Stroop, galantamine did not affect performance on other tasks, ($p>0.05$). These results demonstrate that medications can enhance cognitive function (e.g. sustained attention) in abstinent cocaine users. The potential efficacy of galantamine as a treatment for cocaine abuse needs to be further evaluated in clinical trials.

Keywords

Galantamine; cholinesterase inhibitor; cocaine; cognitive function

Introduction

Multiple studies have demonstrated that chronic cocaine use is associated with a wide range of deficits in cognitive functioning including decision-making, response inhibition, planning, visual and spatial working memory, and attention (K. I. Bolla, Funderburk, & Cadet, 2000; Fillmore & Rush, 2002; Jovanovski, Erb, & Zakzanis, 2005; Simon et al., 2000; Woicik et al., 2009). These deficits are correlated with the severity of cocaine use, suggesting a dose-related effect (K. I. Bolla, Rothman, & Cadet, 1999). Cognitive deficits are seen as a particular challenge for treatment seeking cocaine users who require intact cognitive functioning in order to engage in treatment and learn new behavioral strategies in order to stop drug use. As demonstrated by Aharonovich and colleagues (Aharonovich et al.,

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2006; Aharonovich, Nunes, & Hasin, 2003), cocaine users who dropped out of treatment had significantly lower performance on attention, memory, spatial ability, speed, accuracy, global functioning, and cognitive proficiency tests at baseline. Similarly, performance in the Stroop color-word interference task, a reliable measure of inhibitory control function, at treatment entry was predictive of treatment retention in cocaine users (Streeter et al., 2008). These preliminary findings are consistent with work in other types of addictions which suggests that deficits in cognitive functioning are associated with higher drop-out rates and poor treatment response (Bates, Pawlak, Tonigan, & Buckman, 2006; Donovan, Kivlahan, & Walker, 1984; O'Leary, Donovan, Chaney, & Walker, 1979). Whether these deficits in cocaine users improve with medications targeting cognitive function has not been examined in previous studies and might represent a new treatment strategy for cocaine addiction (Sofuoglu, 2010).

In this proof-of-concept study, we evaluated galantamine's efficacy on selected cognitive performance measures in abstinent cocaine users. Galantamine, a reversible and competitive inhibitor of acetylcholinesterase (Marco-Contelles, do Carmo Carreiras, Rodriguez, Villarroya, & Garcia, 2006), is used clinically in the treatment of Alzheimer's dementia. Cholinesterase inhibitors work by preventing the breakdown of acetylcholine (ACh), which leads to increased stimulation of nicotinic and muscarinic type of cholinergic receptors (Giacobini, 2004). As a unique feature, galantamine also directly stimulates the nicotinic receptors: it is an allosteric modulator of the α_7 and $\alpha_4\beta_2$ subtypes (Schilstrom, Ivanov, Wiker, & Svensson, 2007). Since nicotine agonists improve cognitive performance, nicotinic effects of galantamine may contribute to its efficacy in Alzheimer's disease and other cognitive disorders. Galantamine and similar cholinesterase inhibitors have shown some promise for stimulant addiction in both preclinical and clinical studies (Hikida, Kitabatake, Pastan, & Nakanishi, 2003; Hiranita, Nawata, Sakimura, Anggadiredja, & Yamamoto, 2006; Sofuoglu & Mooney, 2009). In a human laboratory study with 23 non-treatment-seeking methamphetamine dependent individuals, rivastigmine, a cholinesterase inhibitor, attenuated some of methamphetamine's subjective effects, including "desire" and "anxiety" (De La Garza, Shoptaw, & Newton, 2008). In a small clinical trial, 10 mg/day donepezil, another cholinesterase inhibitor, was well tolerated but did not reduce cocaine use behavior, assessed with urine toxicology results for cocaine (Winhusen et al., 2005). Although, the sample size of the study was small (only 17 subjects assigned to donepezil), those treated with donepezil did show significant reductions in craving for cocaine and other drugs as well as improvements in addiction severity, assessed with the drug subscale of ASI (Addiction Severity Index). Whether galantamine or other cholinesterase inhibitors improve cognitive deficits in chronic cocaine users has not been examined, although a growing body of evidence support disruptions of the cholinergic system function as a result of chronic cocaine use (Williams & Adinoff, 2008). We hypothesized that galantamine would be well-tolerated and improve performance in cognitive functions including attention, working memory, and attentional bias in cocaine users.

Method

Participants

Thirty four abstinent cocaine users were recruited from the New Haven area by word-of-mouth, fliers, and newspaper advertisements. After the initial phone screening, potential subjects underwent a comprehensive evaluation that included medical, psychiatric, and drug use histories as well as physical, psychiatric, and laboratory examinations. Participants included English speaking males and females between the ages of 21 and 50 who met the following inclusion criteria: 1) DSM-IV criteria for past cocaine dependence and history of current or past treatment for cocaine dependence; 2) no cocaine use for the past 30 days, verified by urine toxicology screens; 3) no other current dependence or abuse of other drugs

of abuse or alcohol (except tobacco); 4) no current medical problems and normal ECG; 5) for women, not pregnant as determined by pregnancy screening nor breast feeding, and using acceptable birth control methods. Participants were excluded if they: 1) met DSM-IV criteria for current major psychiatric illnesses including mood, psychotic, or anxiety disorders; 2) had a history of major medical illnesses including liver disease, heart disease, or other medical conditions that the physician investigator deemed contraindicated for galantamine treatment; or 3) had a known allergy to galantamine. This study was approved by the VA Connecticut Healthcare System Human Subjects Subcommittee and all subjects signed informed consent forms prior to their entry into the study. This study was registered at the Clinicaltrials.gov (00606801). Subjects were compensated for their participation in the study.

Procedures

This was a randomized, double-blind, parallel-group study, where abstinent cocaine users were randomized to galantamine (8 mg/day) or placebo treatment for 10 days. Participants were told that this was a study testing a medication that may help their attention, learning and memory. Before initiation of treatment, participants completed an adaptation session, where they were familiarized with the study procedures and baseline measures of cognitive performance and mood were obtained. On day 1 of treatment, participants received their first dose of the medication in the clinic. Participants returned to the clinic for outpatient visits on days 2, 5, 7 and 10 to receive medication treatment and for monitoring of any adverse effects from study medication. Participants received take home bottles to self-administer the assigned study medications. Medication compliance was monitored with pill counts. Cognitive and self-report mood measures were obtained at baseline, during adaptation session, and on test session that were scheduled on days 5 and 10 after the initiation of treatment. The test sessions were conducted around 11 AM, approximately 2 hours after daily medication administration. For the cognitive assessments, subjects were told to respond as fast and as accurately as possible.

Galantamine

We used 8 mg galantamine extended release (ER) capsules or matched placebos administered once daily for 10 days. We chose the 8 mg/day dose since in a previous study, galantamine at 8 mg/day for five days improved cognitive functioning in patients with mild cognitive impairment (Goekoop et al., 2004). The recommended initial dose for galantamine ER for Alzheimer's disease is 8 mg/day, with target dose ranging from 8 to 32 mg. We chose the 10-day treatment duration to allow steady-state plasma levels of galantamine to be reached before the final test session. With once daily dosing of galantamine ER, steady-state plasma levels are reached after one week (Robinson & Plosker, 2006).

Outcome measures

The main outcomes were measures of cognitive performance and self-report mood. In addition, measures of safety and tolerability were also obtained.

Cognitive measures

Cognitive Performance was assessed with 3 tests from the Cambridge Neurological Test Automated Battery (CANTAB): the Rapid Visual Information Processing test (RVIP), the Paired Associates Learning (PAL), and the Pattern Recognition Memory (PRM). In addition, the Sustained Attention to Response Task (SART) and a modified Stroop task (cocaine-Stroop) were also administered. We chose these tests based on the reported cognitive deficits in cocaine users and the pharmacological effects of galantamine. A brief description of the cognitive tests and the rationale for their selection is summarized below.

The RVIP is widely used as a measure of sustained attention with a small working memory component (B. J. Sahakian & Owen, 1992). This task was chosen since chronic cocaine users show deficits in attention and working memory and the RVIP task is sensitive to cholinergic enhancers (Goldstein et al., 2007; Jones, Sahakian, Levy, Warburton, & Gray, 1992; Simon et al., 2002; Wesnes & Warburton, 1984). In this task, subjects are asked to respond to any of three digit sequences in a continuous stream of digits lasting for 7 minutes. A white box appears in the center of the computer screen, inside which digits from 2 to 9 appear in a pseudo-random order at the rate of 100 digits per minute. Subjects are instructed to detect consecutive odd or even sequences of digits (e.g., 2-4-6, 3-5-7, 4-6-8, 5-7-9, etc.) and to register responses using a press-pad.

We also included two other tests from the CANTAB that are sensitive to visual memory and learning (PAL) and visual recognition and memory (PRM). Impairments in visuospatial memory have been demonstrated in cocaine users (Berry et al., 1993; Kubler, Murphy, & Garavan, 2005). In the PAL task, boxes are displayed on the screen and are opened in a random order. One or more of the boxes will contain a pattern. After the subjects have seen the patterns behind each box, the patterns are then displayed in the middle of the screen, one at a time, and the subject must touch the box where the pattern was originally located. An error will cause the test to open the boxes again to remind the subject of their locations. The number of boxes with patterns increases throughout the test. In the PRM, the subject is presented with a series of 12 visual patterns, one at a time, in the center of the screen. These patterns are designed so that they cannot easily be given verbal labels. In the recognition phase, the subject is required to choose between a pattern they have already seen and a novel pattern.

The SART (Robertson, Manly, Andrade, Baddeley, & Yiend, 1997; Sofuoglu, Waters, Mooney, & Kosten, 2008) is a Go/NoGo task which assesses the ability to activate (Go) or inhibit (NoGo) responses. Cocaine users, compared to healthy controls, have been shown to be impaired in response inhibition, measured with Go/NoGo or Stop Signal test (Fillmore, Rush, & Hays, 2002; Hester & Garavan, 2004; Kaufman, Ross, Stein, & Garavan, 2003; Lane, Moeller, Steinberg, Buzby, & Kosten, 2007). In this 4.5 minute task, 225 single digits (25×9 digits) were presented on a computer monitor. Each digit was presented for 250 ms, and was immediately followed by a mask for 900 ms (The time between digit onsets was therefore always 1150 ms). The mask consists of a ring with a diagonal cross in the center. Subjects were instructed to press a spacebar to every digit except the 3, and to give equal importance to speed and accuracy. Responses were allowed during the presentation of both the digit and mask. The digits were presented in a different random order for each subject. There were 18 practice trials, containing 2 no-response targets (3s).

The cocaine-Stroop task assesses attention capture (attentional bias) by cocaine cues. Between-group differences (cocaine users vs. non-users) in attentional bias have been observed using the cocaine-Stroop task (Hester, Dixon, & Garavan, 2006). One study reported that the cocaine-Stroop effect was predictive of treatment outcome (Carpenter, Schreiber, Church, & McDowell, 2006). Participants completed two counterbalanced blocks (150 trials per block). One block contained 15 cocaine-related words (e.g. cocaine) and neutral words presented in a mixed order. The other block contained 15 control words (household words) that were matched in length and frequency to the cocaine-related words, and a different set of neutral words. Participants were required to indicate the colors in which the words were written as quickly and accurately as possible. Reaction times (RTs) to indicate the colors of the words were assessed.

Measures of mood

Measures of mood included the Profile of Mood States (POMS), the Positive and Negative Affect Schedule (PANAS), and the Center for Epidemiologic Studies Depression scale (CES-D). The POMS includes 65 items (rated on a scale from 0, “not at all,” to 4, “very much so” for the past 24 hours) that make up six subscales: tension-anxiety, depression-dejection, anger-hostility, vigor-activity, fatigue-inertia, and confusion-bewilderment. As a global measure of affective state, a total mood disturbance score was calculated by summing the scores on the six subscales, with vigor-activity negatively weighted. The PANAS assesses both negative and positive affective states (Watson, Clark, & Tellegen, 1988). Participants rate 20 adjectives describing affective states on a scale of 1 to 5 at the time of assessment. The CES-D has been shown to be a reliable and valid scale of depressive symptoms (Son, Markovitz, Winders, & Smith, 1997; Weissman, Sholomskas, Pottenger, Prusoff, & Locke, 1977). The CES-D was used to assess the presence of depressive symptoms during the past week.

Measures of safety and tolerability

Safety measures included blood pressure, heart rate, and ratings of adverse events.

Data analysis

The data from the RVIP were analyzed using the principles of Signal Detection Theory, with A' and B'' as the main outcomes (B. Sahakian, Jones, Levy, Gray, & Warburton, 1989). A' is a measure of sensitivity to target sequences and it reflects probabilities of hits and false alarms to provide a score of sensitivity to the target regardless of response tendency. The scores range from 0 (bad) to 1 (good). B'' reflects the probability of hits and false alarms to provide a measure of the participants tendency to respond regardless of whether the target sequence is presented. The scores range from -1 to $+1$ with scores near $+1$ indicative of a subject that gave few false alarms. We also included the mean reaction time, total hits, total correct answers, and total correct rejections in our analysis. Although some of these outcomes were included in the calculation of A' and B'' , they were included to provide outcomes that were easier to interpret (B. J. Sahakian & Owen, 1992).

The outcomes selected for the PAL were the total number of patterns recognized and the mean total trials completed. For the PRM, we used mean total number correct and the mean latency to correct answer (B. J. Sahakian & Owen, 1992).

For the Go/NoGo task, response inhibition was measured as the number of errors on the no-Go trials, with low errors indicating better response inhibition. In contrast, the number of errors on Go trials and the reaction time reflected the response activation function, with fewer errors and faster reaction time indicating greater response activation.

For the cocaine Stroop, we examined RTs over all word types; the difference in RTs to cocaine and control words (cocaine-Stroop effect); and the difference in RTs to words following cocaine and control words (carry-over effect). The carry-over effect has been described in a number of addiction studies (Cane, Sharma, & Albery, 2009; Waters, Sayette, Franken, & Schwartz, 2005) and may capture the difficulty disengaging attention from salient stimuli.

Group differences for baseline characteristics were compared using two sample t-test and Pearson chi-square test when appropriate. For other outcomes, we used a mixed-effect repeated-measures model using Statistical Analysis System, Version 9.1.3. (SAS Institute Inc., 2007). The model included fixed main effect terms for treatment (placebo or galantamine), and time of measurement (day in the study), as well as the interaction of these

two effects, with a random effect for participant. Given the hypothesis generating nature of the study, values of $p < 0.05$ were considered statistically significant, based on two-tailed tests, unless otherwise specified. Significant treatment-by-time effects were followed by Bonferroni post hoc pairwise comparisons: two time points (days 5 and 10) were compared with each other and with the baseline measures separately for each treatment condition. Due to experimenter or computer error, complete data were not available for 4 participants on the SART (3 placebo, 1 galantamine), 3 participants on the cocaine-Stroop (2 placebo, 1 galantamine) and one participant on the CANTAB.

Results

Sample Characteristics

As summarized in Figure 1, of the 34 participants randomized to treatment, 28 (9 female and 19 male) completed the study. The demographic and drug use characteristics of the study completers are shown in Table 1. Most of the participants were currently in treatment ($n=17$) and had no other drug use, except cigarette smoking ($n=21$) and marijuana use ($n=4$). No significant group differences were observed in demographic and drug use characteristics ($p < 0.05$). Those who dropped out did not differ from completers **for demographic and drug use characteristics** ($ps > 0.05$).

Cognitive measures

The results of cognitive performance on the CANTAB, SART, Stroop, and tasks are summarized in Table 2 and Figure 1. Galantamine treatment, compared to placebo, reduced the reaction time, and increased the detection sensitivity (A'), number of hits, and number of correct rejections ($ps < 0.05$). Galantamine treatment, relative to placebo, also reduced the reaction time on the cocaine-Stroop task ($p < 0.05$), but did change the Stroop or carry-over effect ($ps > 0.05$). There were no baseline differences between groups in any of these cognitive measures. No other significant treatment or treatment-by-time interactions were observed.

Subjective measures

No significant treatment-by-time or time interactions were found for the POMS, PANAS, and the CES-D ($p < 0.05$).

Safety measures

There were no significant treatment or treatment-by-time effects for daily heart rate, and systolic or diastolic blood pressure ($p < 0.05$). No adverse events were encountered during the study.

Discussion

This study examined galantamine's effects on multiple cognitive functions including response inhibition, attentional bias, sustained attention, and visuospatial learning/memory in abstinent cocaine users. We found improvement in sustained attention function assessed with the RVIP. However, galantamine did not change the performance in other measures. Overall, galantamine was well-tolerated by abstinent cocaine users without any significant effects on mood, assessed with the POMS, or blood pressure and heart rate measurements. The implications of these findings will be further discussed below.

The selective improvement of the RVIP task performance by galantamine treatment in abstinent cocaine users is consistent with the well-established role of the brain cholinergic system in attentional processes (Everitt & Robbins, 1997; Sarter, Gehring, & Kozak, 2006).

Medications that enhance the cholinergic transmission, like cholinesterase inhibitors, improve performance in the RVIP and similar tasks in patients with compromised cognitive function including Alzheimer's dementia or mild cognitive impairment (Goekoop et al., 2004; Jones et al., 1992; B. J. Sahakian & Coull, 1993; Wesnes & Warburton, 1984). In contrast to the RVIP findings, galantamine treatment did not improve performance in other tasks tapping response inhibition, attentional bias, and visuospatial learning/memory functions in abstinent cocaine users. The role of cholinergic function in these functions, however, is less well established than its role in attentional processes (Furey, Pietrini, Haxby, & Drevets, 2008; Mintzer & Griffiths, 2007; Repantis, Laisney, & Heuser, 2010; Zaninotto et al., 2009). It is also important to note that the dose of galantamine was limited to 8 mg/day, smaller than the average clinical dose for galantamine, which ranges from 8 to 32 mg/day. In addition, the treatment duration was only 10-days. It is possible that longer treatment with higher doses of galantamine might lead to more effective on cognitive enhancement in cocaine users.

This pilot study had other limitations. First, the study included multiple cognitive tests and outcome measures, raising the possibility that some of the significant findings could be due to type I error. However, significant galantamine effects on cognitive performance were largely limited to the RVIP task and these findings are consistent with the role of cholinergic system in attentional processes. Second, since study participants were abstinent cocaine users, the study did not assess galantamine's effects on cocaine use. However, enrolling abstinent cocaine users allowed us to examine galantamine's effects on cognitive function without the confounding influence of ongoing drug use. Third since the study did not have a non-addicted control group, whether galantamine has unique cognitive effects in abstinent cocaine users could not be addressed. Lastly, although we did not have a non-addicted control group for comparison, attentional bias appeared to be of modest magnitude in this study. This may have made it difficult to detect an effect of galantamine on this measure. It is worth noting that a recent study has similarly reported that attentional bias may be reduced in abstinent (treated) opiate/cocaine ex-users, compared to active opiate/cocaine users (Gardini, Caffara, & Venneri, 2009). In addition, the effect of galantamine on attentional bias in active users remains unknown. These limitations need to be addressed in future controlled studies.

In spite of these limitations, our findings may have important treatment implications for cocaine addiction. First, as previously mentioned, cocaine users have deficits in attentional processes. In a meta-analysis of 15 studies, comparing cocaine users (n=481) to healthy controls (n=586), Jovanovski et al. (Jovanovski et al., 2005), reported a large effects size for attentional function, indicating the difference between cocaine users and matched controls. The attentional deficits in cocaine users are consistent with functional imaging studies that demonstrate impaired prefrontal cortex function, or "hypofrontality" in long-term cocaine users (K. Bolla et al., 2004; Volkow, Mullani, Gould, Adler, & Krajewski, 1988; Volkow et al., 2002). Second, attentional processes likely play an important role in optimum cognitive control to drug use behavior (Chambers, Garavan, & Bellgrove, 2009; Posner & Rothbart, 2007). Lapses in attention have been proposed as an important antecedent of the drug-seeking in addicted individuals (Acheson & de Wit, 2008; de Wit, 2009). Thus, among cognitive functions, attentional processes may be a novel treatment target to improve cognitive functioning in cocaine-dependent individuals. Galantamine was well-tolerated by our subjects and can potentially be used to improve the cognitive functioning of cocaine users who are seeking treatment (Sofuoglu, 2010). Cognitive enhancement strategies may especially be important early in the treatment, when stimulant users have greater cognitive impairments following cessation of stimulant use (Woicik et al., 2009). For example, galantamine may augment the efficacy of behavioral treatments in cocaine users, by improving their ability to learn, remember, and implement new skills and coping strategies.

There are examples of augmentation of behavioral treatment with cognitive enhancers. For example, cycloserine is not an effective treatment by itself for the treatment of phobias and other anxiety disorders, but appears to enhance the effectiveness of behavioral treatments for these and other disorders (McNally, 2007; Ressler et al., 2004; Wilhelm et al., 2008). Whether galantamine can augment the efficacy of behavioral treatments for cocaine addiction remains to be determined in future controlled studies.

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Figure 1. CONSORT (Consolidated Standards of Reporting Trials) flowchart of participant recruitment, randomization, and analysis.

Fig 2. Treatment effects on the changes from baseline for the RVIP latency for correct responses and the total number of correct rejections. Both outcomes showed significant treatment-by-time interactions ($p < 0.05$). See text for details.

Table 1

Comparison of demographics and drug use characteristics of study participants.

	Galantamine (n = 14)		Placebo (n = 14)		P-values	
	N	%	N	%		
Race						
African-American	8	57	11	79	0.3	
Caucasian	4	28	3	21		
Hispanic	2	14	0	0		
Sex						
Female	4	29	5	36	0.7	
Male	10	71	9	64		
Employed	4	29	2	14	0.4	
Form of cocaine use						
Snort	1	7	1	7	0.3	
Smoke	12	86	9	64		
IV	1	7	4	29		
Currently in treatment for cocaine addiction	9	64	8	57	0.7	
Current cigarette smoking	10	71	11	79	0.7	
Current marijuana use	3	21	1	7	0.3	
	Mean	SD	Mean	SD		
Age (years)	40.2	7.1	42.3	6.7	0.4	
Years of schooling	11.8	0.5	12.3	1.2	0.2	
Length of cocaine use (years)						
Duration of abstinence (months)	4.5	3.6	4.7	3.5	0.9	

Table 2A

Galantamine vs. placebo treatment on the CANTAB outcomes, mean (SD).

	Baseline	Test Session 1	Test Session 2	F	p	n
RVP						
Mean RT for correct answers						
PLA	407.7 (92.3)	427.4 (35.3)	433.3 (123.6)	8.6	0.006	13
GAL	476.8(119.3)	379.2(71.7) ^a	386.9 (82.9) ^a			13
Total hits						
PLA	16.7 (3.6)	18.0 (5.0)	18.0 (6.8)	4.2	0.04	13
GAL	14.8 (4.7)	16.9 (5.4)	19.7 (4.3) ^a			13
Total correct rejections						
PLA	247.2 (13.7)	247.6 (16.9)	248.2 (23.7)	5.6	0.02	13
GAL	242.4 (15.5)	247.9 (12.9)	253.9 (12.6) ^a			13
RVP A				4.9	0.03	
PLA	0.89 (0.04)	0.90 (0.07)	0.90 (0.1)			13
GAL	0.87 (0.07)	0.90 (0.07)	0.92 (0.04) ^a			13
RVP B						
PLA	0.88 (0.18)	0.82 (0.22)	0.85 (0.25)	0.5	0.5	13
GAL	0.88 (0.25)	0.910 (0.11)	0.88 (0.14)			13
PAL						
Stages completed						
PLA	4.8 (0.4)	4.9 (0.4)	4.9 (0.4)	0.4	0.7	14
GAL	4.9 (0.4)	4.9 (0.4)	4.9 (0.4)			13
Mean number of errors						
PLA	31.1 (22.3)	23.6 (17.7)	17.7 (16.6)	0.8	0.3	14
GAL	25.6 (16.5)	18.1(11.5)	16.8 (13.7)			13

	Baseline	Test Session 1	Test Session 2	F	p	n
PRM						
Mean RT for correct answers						
PLA	2357 (526)	2092 (573)	1995 (479)	0.9	0.3	14
GAL	2439 (685)	2092 (522)	1889 (364)			13
Mean number of correct answers						
PLA	20.8 (3.2)	19.4 (2.9)	21.0 (2.9)	0.8	0.3	14
GAL	20.2 (2.5)	20.6 (2.5)	20.7 (2.2)			13

* F-values reflect treatment x time interaction term.

^a represents significant change from baseline (p<0.01).

Table 2B

Galantamine vs. placebo treatment on the SART outcomes, mean (SD).

	Baseline	Test Session 1	Test Session 2	F^*	p	n
No. errors on No-Go Trials (3s) (/25)						
PLA	12.8 (6.4)	10.7 (6.5)	11.8 (7.7)	0.09	0.9	11
GAL	13.1 (5.8)	10.2 (7.9)	12.2 (8.2)			13
No. errors on Go Trials (non-3s) (/200)						
PLA	14.6 (16.8)	12.0 (19.1)	10.6 (10.6)	0.13	0.8	11
GAL	7.2 (7.4)	3.8 (4.1)	5.1 (7.4)			13
Mean RT for correct presses on Go Trials (ms)						
PLA	399.7 (79.7)	405.4 (81.7)	411.1 (74.2)	0.64	0.5	11
GAL	375.3 (88.5)	382.6 (79.9)	357.8 (109.7)			13

* F^* values reflect treatment x time interaction terms.

Table 2C

Galantamine vs. placebo treatment on the Stroop outcomes, mean (SD).

	Baseline	Test Session 1	Test Session 2	F*	p	n
RT all trials**						
PLA	722 (117)	734 (126)	748 (159)	4.91	0.01	12
GAL	771 (136)	742 (145) ^a	698 (106) ^{a, b}			13
Stroop effect						
PLA	10.5 (66.2)	-19.7 (87.6)	-61.5 (183.9)	0.40	0.6	12
GAL	-13.1 (137.6)	19.6 (149.3)	-33.7 (133.2)			13
Carry-over effect (lag 1)						
PLA	32.4 (95.5)	43.5 (131.2)	-29.8 (179.6)	0.53	0.5	12
GAL	13.4 (131.9)	32.1 (96.2)	18.6 (110.5)			13

* F₂ values reflect treatment x time interaction terms.

** RT all trials = mean RT averaged over all trials; Stroop effect (ms) = mean RT on cocaine words - mean RT on control words; Carry-over effect (ms) (lag 1) = mean RT on words after cocaine words - mean RT on words after control words.

^a significant change from baseline (p<0.01).

^b significant change from test session 1 (p<0.01).