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A Pilot Study of Neurocognitive Function in Older and Younger Cocaine Abusers and Controls

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Abstract

Objective—This pilot study compared basic neurocognitive functioning among older and younger cocaine abusers and control participants, as a preliminary assessment of whether specific cognitive deficits exist in an aged cocaine-abusing population. We hypothesized an interaction between aging and cocaine abuse, such that older cocaine abusers would exhibit decreased neuropsychological test performance relative to both younger cocaine abusers and older control participants.

Methods—Four groups (n = 20 each) were examined: older cocaine abusers (ages 51-70), younger cocaine abusers (ages 21-39), and two non-illicit-substance-using control groups. Basic neuropsychological and psychiatric measures were administered to all participants.

Results—Older participants performed more poorly than younger participants on the Mini-Mental State Examination (MMSE, $p < 0.01$), Digit Span Backward ($p < 0.01$), and Trail Making Test (TMT) Parts A and B ($p < 0.01$). Cocaine abusers performed more poorly than controls on TMT A ($p < 0.01$). Older and younger cocaine abusers used similar amounts of cocaine ($p > 0.05$). Older cocaine abusers performed more poorly than older control participants and younger cocaine abusers on the Digit Span Forward ($p < 0.0125$). Older cocaine abusers also performed more poorly than younger cocaine abusers on TMT A ($p < 0.0125$).

Conclusion—This study provides preliminary evidence that older cocaine abusers use a significant amount of cocaine and that there is an interaction between aging and cocaine abuse on psychomotor speed, attention, and short-term memory. Future examination of neurocognitive function in older cocaine abusers is clearly warranted.

Keywords

cocaine; abuse; dependence; old; young; geriatric; older; younger; aging; cognition

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Introduction

Substance abuse and its associated consequences, problems typically associated with youth, are increasing in prevalence among older adults ^{1, 2}. Data from the National Survey of Drug Use and Health suggest that the number of older adults (above age 50) using substances will increase in the next two decades ³, along with the number needing treatment projected to increase from 2.8 million in 2002-06 to 5.7 million by 2020 ⁴.

Cocaine use disorders remain a significant public health problem in the U.S. ⁵ and presumably will play a significant role in the increase in substance abuse among older adults as the population ages. Although systematic studies of cocaine abuse in the aging population are limited, some data support concerns about a growing problem of cocaine abuse among older adults. For instance, the Treatment Episode Data Set, which tracks federal- and state-funded substance abuse treatment admissions, shows a gradual overall increase in treatment admissions for older adults primarily abusing cocaine from 2005 (20,649 admissions) to 2007 (24,357 admissions) ⁶⁻⁸. Case reports have described older cocaine abusers with long-term use continued from younger decades, as well as a recent onset of cocaine use ^{9, 10}. Older adults using cocaine have come to the attention of geriatric psychiatry ¹¹, consult/liaison services ¹², emergency rooms ¹³, and veterans' programs ¹⁴.

The growing number of older adults with cocaine use disorders presents challenges for the medical community. Features specific to older adults can potentially impact the presentation, course, treatment outcomes, and prevention strategies for cocaine use disorders. Irrespective of drug use, older adults are likely to differ from younger adults in their cognitive ¹⁵, biological ¹, emotional ¹⁶, and social ¹⁷ functioning.

Of these domains, changes in cognitive functioning are perhaps the most well-known changes with normal aging, as documented by neuropsychological studies. An age-related decline has been found for cognitive abilities such as processing speed, as measured by reaction time tasks ¹⁸, working memory, as measured by reading span and computation tasks ¹⁹ or digit span ²⁰, and mental flexibility, as measured by the Trail Making Test (TMT) Part B ²¹.

Cocaine use disorders in and of themselves have also been associated with cognitive changes, as documented by neuropsychological studies. Cocaine-related impairments have been found for cognitive abilities such as psychomotor speed, as measured by TMT Part A ²², memory, as measured by the logical memory subtest of the Wechsler Memory Scale ²³, and attention and concentration as measured by the Stroop Color Word Interference Test ²⁴. Impairments have also been found in executive functions, such as updating, shifting, decision-making ²⁵, and reasoning ²⁶.

Thus, an issue of particular concern is that older adults with cocaine use disorders may be especially vulnerable to cognitive impairment. The complex interaction of aging and cocaine effects on cognitive functioning requires further investigation. The primary aim of this pilot study was to compare basic neurocognitive functioning among older cocaine abusers, younger cocaine abusers, and control participants, as a preliminary assessment of whether specific cognitive deficits exist in an aged cocaine-abusing population – over and above what would be expected in either an aging population or a younger cocaine-abusing population. Such data can then be used to determine if treatment strategies for cocaine use disorders need to be adapted for use in a growing population of older adults.

We hypothesized that both age and cocaine abuse would be associated with poorer neuropsychological test performance, such that older participants would exhibit decreased neuropsychological test performance relative to younger participants, and cocaine abusers

would exhibit decreased performance relative to control participants. Further, we hypothesized an interaction between aging and cocaine abuse, such that older cocaine abusers would exhibit decreased performance relative to both younger cocaine abusers and older control participants. The secondary aim of this pilot study was to compare cocaine use patterns between older and younger cocaine abusers.

Methods

Study Design and Procedures

While an older adult is commonly considered as someone over 60 or 65, we defined an older adult as an individual over 50, because chronologic age may not reflect biologic age²⁷ especially in adults with a substance use disorder²⁸. This definition is consistent with that of other studies among older adults with substance use disorders²⁹⁻³². Utilizing ongoing recruitment efforts at our institution for non-treatment-seeking cocaine users, advertisement for this study was conducted via flyers, local newspapers, local community internet websites, and word-of-mouth. As the aim of this study was to compare neurocognitive function but not to provide treatment, and as treatment-seekers represent just a minority of substance abusers³³, only non-treatment-seeking participants were recruited. Four groups of 20 were examined: older cocaine abusers (ages 51-70), older control participants, younger cocaine abusers (ages 21-39), and younger control participants.

All candidates were initially administered a telephone screening interview. Criteria used to determine whether any candidate would be scheduled for an office visit were: having current photo identification; adequate English fluency; adequate hearing/vision; no current diagnosis of major depression; no current diagnosis of a learning disorder or a cognitive disorder (e.g., dementia, amnesic disorder); no current psychosis; no severe anxiety; no current suicidal or homicidal ideations; no current use of psychotropic medications likely to cause sedation and/or cognitive impairment (e.g., benzodiazepines, antipsychotics); no current use of stimulants (e.g., methylphenidate) or cognitive enhancers (e.g., donepezil); and none of the following medical or neurological illnesses or traumas: stroke/transient ischemic attack, head trauma/traumatic brain injury, central nervous system infection, seizures, atrial fibrillation, uncontrolled diabetes, uncontrolled hypertension, uncontrolled thyroid abnormalities, or uncontrolled B12/folate deficiency.

Additionally, potential cocaine-abusing participants had to report current use of cocaine and that they were not currently seeking or engaged in treatment. For potential control participants, current or past history of substance abuse/dependence was exclusionary (except nicotine/cafeine). The control groups were frequency-matched on age/education (within 1 year) to the cocaine-abusing groups. Candidates who passed phone screening were instructed to not change any regular habits or routines (e.g., food, drug intake) prior to the scheduled office visit.

During the office visit, after obtaining informed consent, participants were re-interviewed, and discrepancies between responses on this interview and the phone screen were resolved by excluding participants with inconsistent answers. Demographic information, medical history, family history, and other treatment history were collected. Psychiatric measures were then completed. Participants meeting criteria only for major depression or a psychotic disorder based on the Mini-International Neuropsychiatric Interview (M.I.N.I.)³⁴ were excluded at this point; meeting criteria for other psychiatric disorders was not exclusionary. Participants with a Mini-Mental State Examination (MMSE) score <24, a widely used dementia cutoff³⁵, were excluded. Finally, neuropsychological and urine toxicology measures were completed.

Participants in the cocaine-abusing groups were required to meet Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria based on the M.I.N.I. for cocaine abuse or dependence and could not meet dependence criteria for other substances (except nicotine/cafeine). Where cocaine-abusing participants met abuse criteria for more than one drug, cocaine was required to be identified as their primary drug of choice. Control participants whose urine screens were positive for illicit substances were excluded. For cocaine-abusing participants, the urine screen was not used as an exclusion tool, but rather used to document differences between self-reported use and actual use.

This study was approved by the Columbia University/New York State Psychiatric Institute's Institutional Review Board. All participants were compensated for their time.

Measures

The M.I.N.I. is a brief structured clinician interview for the major Axis I psychiatric disorders in DSM-IV, takes approximately 15 minutes, and has been validated to the Structured Clinical Interview for DSM-III-R Patient Version and the Composite International Diagnostic Interview³⁴. The Adult ADHD Self-Report Scale (ASRS version 1.1, Parts A and B)³⁶ is a scale consisting of the 18 criteria for Attention-Deficit/Hyperactivity Disorder (ADHD) as listed in the Text Revision of the DSM-IV (DSM-IV-TR). The ASRS Part A contains the 6 criteria (out of the total 18 criteria) that have been found to be most predictive of ADHD symptoms, such as “how often do you have problems remembering appointments or obligations?” The ASRS part B contains the remaining 12 criteria³⁷. The ASRS Parts A and B were scored as follows: never (0), rarely (1), sometimes (2), often (3), and very often (4). The 10-item McLean Screening Instrument for Borderline Personality Disorder³⁸ is a self-report screening instrument for the presence of DSM-IV borderline personality disorder, which includes questions such as “have you made desperate efforts to avoid feeling abandoned or being abandoned?”

Current life stressors were assessed by using the 10-item self-report Perceived Stress Scale (PSS)³⁹. The PSS is a measure of the degree to which situations in one's life are evaluated as stressful, and the questions ask about feelings and thoughts during the last month, such as “how often have you felt that things were going your way?” PSS items were scored as follows: never (0), almost never (1), sometimes (2), fairly often (3), and very often (4). Stressors were also assessed by a clinician asking each participant if any stresses in the following DSM-IV-TR Axis IV categories were present during the past year⁴⁰: primary support group, social environment, educational, occupational, housing, economic, access to health care services, interaction with the legal system/crime, and other psychosocial/environmental.

The Quantitative Substance Use Inventory (QSUI) and the Drug Use Questionnaire (DUQ), both used in previous substance abuse studies^{41, 42}, are locally derived clinician-administered instruments that were employed to assess patterns of lifetime and current alcohol/drug use. For each substance that a participant endorsed using, the QSUI was used to collect information on the number of days used (in a time period determined by the clinician), average and maximum \$ value used per day of a substance, principal route of use, the number of days on which urge/desire/craving occurred, and a rating of craving (none (0), mild (1), moderate (2), strong (3), and severe (4)). Also for each substance that a participant endorsed using, the DUQ was used to collect information on the age of 1st use, the age of 1st regular use (defined as “getting high or drunk three times a week or more”), the number of days used in the past 7 and 30 days, the average amount used per day in the past 7 and 30 days, and the route of use. The Rohsenow Cocaine Effects Questionnaire for Patient Populations (CEQ-P)⁴³ is a self-report questionnaire that assesses personal experiences while using cocaine in the last year; a list of 33 statements is presented, and the participant

must rate each item on a scale of 1 (Never) to 7 (Always). Statements on the CEQ-P include “cocaine helps me be romantic” and “I become mean when I use cocaine.” Mean scores for each domain of the CEQ-P are calculated. Urine toxicology screening was completed via the iScreen Drug Test 5 Panel Dip Card (cocaine, marijuana, opioids, amphetamines, methamphetamines; Rapid Detect Inc., #IS5-M).

Intellectual function was estimated with the Reading subtest of the Wide Range Achievement Test-Third Edition (WRAT-III)⁴⁴, where the participant is asked to name 15 letters and pronounce 42 individual words; one point is given for each correct letter and word, with a maximum score of 57 points that can be earned. Then, the following clinician-administered neuropsychological measures were employed to assess a range of important neurocognitive functions: the MMSE^{35, 45}, the Wechsler Adult Intelligence Scale Third Edition (WAIS-III) Digit Span Forward and Backward^{46, 47}, and the Trail Making Test (TMT) Part A and Part B⁴⁸.

The MMSE, which provides a general cognitive assessment, is commonly used to screen for dementia; memory, attention, concentration, language, and constructional ability are assessed, and a maximum score of 30 can be earned. The Digit Span Forward assesses attention and short-term memory, and the Digit Span Backward assesses working memory. In each trial, digits are presented orally to the participant in increasing numbers, which have to be repeated by the participant; the number of correctly recalled trials is recorded as the raw score. A maximum score of 16 can be earned on the Digit Span Forward, and a maximum score of 14 can be earned on the Digit Span Backward. The TMT A assesses psychomotor speed and simple attention; participants use a pencil to connect a series of encircled numbers in numerical order. The TMT B assesses alternating attention and cognitive flexibility; participants use a pencil to connect 25 encircled numbers and letters in numerical and alphabetical order, alternating between the numbers and letters. The total time to complete TMT A and B is recorded. For TMT B, response times ≥ 4 minutes were recorded as 240 seconds to avoid skewing the data⁴⁹. Differences between Digit Span Forward and Backward⁵⁰ and between TMT A and B⁴⁸ were also calculated, which may provide a measure of the level of interference by the addition of the Digit Span Backward or TMT B, respectively.

For the medical history, the following medical system categories were used by a clinician to assess for medical disorders in each category: Head/Eyes/Ears/Nose/Throat, Cardiovascular, Respiratory, Gastrointestinal, Musculoskeletal, Genitourinary, Neurological, Hematologic/Lymphatic, Skin, Endocrinological/Metabolic, and Obstetrical/Gynecological. Although a participant could have more than one disorder per medical system, affected medical systems were only counted once towards the total number of medical systems affecting a participant. All participants lived in the community; no participants lived in a nursing home or other medical facility due to any medical reasons.

Exclusion of Potential Candidates

For the older cocaine-abusing group, 46 out of 76 potential candidates were excluded for the following reasons (listed from most to least frequent): failure to pass phone screen for psychiatric reasons (22), failure to pass phone screen for medical reasons (13), seeking treatment (5), missed appointment (4), and age outside of range (2). For the older control group, 33 out of 60 potential candidates were excluded for the following reasons: failure to pass phone screen for psychiatric reasons (26), failure to pass phone screen for medical reasons (6), and age outside of range (1).

For the younger cocaine-abusing group, 34 out of 54 potential candidates were excluded for the following reasons: age outside of range (18), failure to pass phone screen for psychiatric

reasons (11), failure to pass phone screen for medical reasons (3), seeking treatment (1), and missed appointment (1). For the younger control group, 30 out of 87 potential candidates were excluded for the following reasons: age outside of range (17), failure to pass phone screen for psychiatric reasons (9), and failure to pass phone screen for medical reasons (4).

Statistical Analysis

Initial Analyses—For the 80 participants meeting study criteria, all analyses were completed using SPSS version 17 (SPSS Inc., Chicago, IL). Initial analyses assessed for differences in baseline demographic, medical, psychiatric, and substance use variables across the four groups. For continuous variables, one-way Analysis of Variance (ANOVA) was used to compare means across the groups, followed by post-hoc independent *t*-tests when the omnibus *F* tests were significant. Chi-square tests of independence were used to compare categorical variables across groups. Only *p*-values < 0.05 were considered significant.

Main Neuropsychological Outcome Analyses—As differences in baseline variables can potentially impact neuropsychological test performance, we employed a 3-step approach to account for such differences and analyzed the neuropsychological outcomes.

In the first model, we conducted analyses unadjusted for any baseline differences. In the second model, we employed Pearson's and point-biserial correlations to assess for relationships (alpha level set at 0.05) between four selected variables (race, years of education, WRAT-III Reading score, and presence of any comorbid psychiatric or substance use disorder on the M.I.N.I.) and the main neuropsychological outcomes (MMSE total score, Digit Span Forward and Backward raw scores, seconds to complete TMT A and B, difference in raw scores between Digit Span Forward and Backward, and difference in seconds between TMT A and B). We initially assessed whether these four selected variables were significantly different across at least two groups. Then, we included only the variables that were correlated with the neuropsychological outcomes as covariates in this model.

In the third model, all four variables (race, years of education, WRAT-III Reading score, and presence of any comorbid psychiatric or substance use disorder on the M.I.N.I.) were employed as covariates, in order to make parallel comparisons across all neuropsychological outcomes.

For both of the adjusted models (second and third models), we employed two-way independent ANOVAs (linear regression models) to assess the main effects of age (younger vs. older adults) and cocaine-abusing status (cocaine-abusing vs. control) and the interaction between age and cocaine-abusing status, on the neuropsychological outcomes. Where a significant interaction effect was identified, we did a simple main effects analysis (ANCOVA where the omnibus *F* tests included the covariates) stratified by age and by cocaine-abusing status to examine the effect of age in cocaine-abusing groups and control groups separately, and the effect of cocaine-abusing status in younger and older adults separately. Full Bonferroni corrections were employed (*p*-value was set at 0.0125 for post-hoc tests). Omega² was calculated to estimate the effect size of each factor (age, cocaine-abusing status, and the interaction between age and cocaine-abusing status).

Finally, since positive cocaine urine toxicology status has been found to influence neuropsychological test performance⁵¹, we also employed independent *t*-tests to assess for differences on the neuropsychological outcomes between individuals in the cocaine-abusing groups who tested positive versus negative for cocaine on urine toxicology. We collapsed both of the older and younger cocaine-abusing groups and analyzed by urine toxicology result (cocaine positive versus cocaine negative).

Results

Demographics, Medical History, Psychological/Social Stressors

Table 1 presents demographic features, medical history, and psychological/social stressors for all groups. Older participants naturally differed from younger participants on age, but within each age range, cocaine abusers and control participants did not differ in age ($p>0.05$). Older cocaine abusers reported more medical morbidity and current medication use than younger cocaine abusers ($p<0.01$), but not than older control participants ($p>0.05$). No group differences were seen between older and younger cocaine abusers in self-reported stress on the Perceived Stress Scale ($p>0.05$). Four older cocaine abusers and one older control participant were retired.

Details of Cocaine Use

Table 2 reports details of cocaine use by the two cocaine-abusing groups. In the last 30 days, older and younger cocaine abusers were similar on the number of days of cocaine used, the average and maximum dollar value of cocaine used per day, and the number of days on which craving for cocaine occurred ($p>0.05$). Older cocaine abusers reported an older age of first cocaine use and regular cocaine use than did younger cocaine abusers ($p<0.01$). In the older cocaine group, 5 participants used IV as the route when they first tried cocaine, and 1 participant currently used IV. In the younger cocaine group, none used IV at first use, and none currently used IV.

Urine Toxicology

18 of the older cocaine abusers tested positive for cocaine (2 of these tested also positive for marijuana), and 2 were negative for all drugs. Regarding those who tested negative for cocaine, one individual reported using cocaine twice in the last 30 days (\$300/day), and the other individual reported using cocaine once in the last 7 days (\$20/day),

12 of the younger cocaine abusers tested positive for cocaine (5 of these tested also positive for marijuana, and 1 of these tested also positive for opioids), 4 tested positive for marijuana, 1 tested positive only for opioids, and 3 were negative for all drugs; regarding those who testing. Regarding those who tested negative for cocaine: of the individuals who reported use of cocaine in the last 30 days – one individual reported using twice (\$50/day), another individual reported using 16 times (\$20/day), another individual reported using 7 times (\$100/day), and another individual reported using 20 times (\$100/day); for cocaine-negative individuals who reported use of cocaine in the last 7 days – one individual reported using once (\$80/day), another individual reported using once (\$75/day), another individual reported using 4 times (\$40/day), and another individual reported using 5 times (\$50/day).

The number of older cocaine abusers testing positive for cocaine differed from the number of younger cocaine abusers testing positive for cocaine ($\chi^2 (1) = 4.80, p = 0.028$).

Structured Diagnostic Interview Instrument, Rating Scales, Other Substance Use History

Table 3 presents the results of the rating scales and other substance use history for all groups. Diagnoses on the M.I.N.I. among the 20 older cocaine abusers were: cocaine dependence (16), cocaine abuse (4), alcohol abuse (6), marijuana abuse (2), opioid abuse (1), any anxiety disorder (3), antisocial personality disorder (3), past suicide attempt (1). Diagnoses on the M.I.N.I. among the 20 younger cocaine abusers were: cocaine dependence (16), cocaine abuse (4), alcohol abuse (10), marijuana abuse (9), opioid abuse (4), benzodiazepine abuse (2), any anxiety disorder (6), antisocial personality disorder (6), past suicide attempt (2). Two younger control participants had a past suicide attempt.

Neuropsychological Outcomes

Table 4 presents the raw scores of the neuropsychological measures for all groups. The omnibus F tests for all models (unadjusted, adjusted for significantly correlated covariates, adjusted for all covariates) were significant for all neuropsychological measures, except Digit Span Forward-Backward ($p > 0.05$ for all models). Four older cocaine abusers took longer than four minutes to complete the TMT B, and to avoid skewing the data were all recorded as four minutes on the TMT B. The four variables (race, years of education, WRAT-III Reading score, and presence of any comorbid psychiatric or substance use disorder on the M.I.N.I.) included in the adjusted models were significantly different at baseline between at least two groups (Tables 1 and 2). Analyses of main and interaction effects and post-hoc tests were completed using the adjusted models. The effect sizes ranged from small to approaching medium (Table 4).

A main effect of age was identified for MMSE, Digit Span Backward, TMT A and B, and TMT B-A in both adjusted models, with older participants performing more poorly than younger participants. No effect of age was identified for Digit Span Forward.

A main effect of cocaine was identified for TMT A and TMT B-A in the model adjusted only for significant covariates, with cocaine abusers performing more poorly than controls; no effect of cocaine was identified for the remaining neuropsychological measures. In the model adjusted for all covariates, no effect of cocaine was identified for any neuropsychological measure.

No interaction effect was identified for MMSE, Digit Span Backward, TMT B, and TMT B-A in both adjusted models. An interaction effect was identified for Digit Span Forward in both adjusted models. An opposite effect of cocaine was found as a function of age: older cocaine abusers performed worse than older controls, whereas younger controls performed worse than younger cocaine abusers. An opposite effect of age was found comparing within cocaine abusers and controls: older cocaine abusers performed worse than younger cocaine abusers, whereas younger controls performed worse than older controls (the latter finding in the model adjusted only for significant covariates).

An interaction effect was identified for TMT Part A in both adjusted models. An effect of age was only found in cocaine abusers: older cocaine abusers performed worse than younger cocaine abusers, whereas no group differences were seen between older controls and younger controls. No group differences were seen between older cocaine abusers and older controls, and no group differences were seen between younger cocaine abusers and younger controls.

Although the number of older cocaine abusers testing positive for cocaine differed from the number of younger cocaine abusers testing positive for cocaine, for the urine toxicology screen independent *t*-tests analysis, there were no differences on the neuropsychological outcomes between cocaine-abusing individuals who tested positive versus negative for cocaine ($p > 0.05$).

Discussion

This pilot study compared 1) basic neurocognitive functioning among older cocaine abusers, younger cocaine abusers, and control participants, as a preliminary assessment of whether specific cognitive deficits exist in an aged cocaine-abusing population; and 2) cocaine use patterns between older and younger cocaine abusers. Older and younger cocaine abusers reported similar patterns of cocaine use: the number of days of cocaine used, the average and maximum dollar value of cocaine used per day, and the number of days on which

craving for cocaine occurred. Our finding that older participants performed more poorly than younger participants on the MMSE, Digit Span Backward, and TMT A and B, is consistent with the literature on the neurocognitive sequelae of aging^{20, 21}. Our finding that cocaine abusers performed more poorly than control participants on the TMT A is consistent with the literature on the neurocognitive sequelae of cocaine abuse²².

Our older cocaine abusers performed more poorly than older control participants and younger cocaine abusers on the Digit Span Forward and performed more poorly than younger cocaine abusers on the TMT A, but not on the MMSE, Digit Span Backward, and TMT B. These findings may indicate that particular cognitive functions such as psychomotor speed, attention, and short-term memory, and by extension, particular neural pathways in the brain, are especially sensitive to the combined effects of aging and cocaine abuse. However, it is equally important to note that not all of our older cocaine abusers displayed poor cognitive performance. Further work is needed to understand the factors contributing to resilience in those who continue to function well, despite chronic cocaine abuse.

This study focused on non-treatment-seeking participants who passed stringent exclusion criteria, and this may explain the finding of why our older cocaine abusers did not differ significantly from our older control participants in medical morbidity and current medication use. Among drug abusers more generally, cocaine abuse is associated with medical issues such as cardiovascular⁵² and pulmonary complications, trauma, and infections⁵³, but such issues were not captured in our sample. The high prevalence of psychiatric comorbidity among our younger cocaine abusers is consistent with previous findings⁵⁴. One surprising finding was that our younger control participants performed worse than younger cocaine abusers and older control participants on the Digit Span Forward; this may be due to factors not investigated in this study in all four groups, such as other specific medical disorders (e.g., hypercalcemia), more extensive exploration of past history of substance use and non-substance use disorders (e.g., missing concealed drug use in control participants), or other issues related to participation in a non-treatment type of study.

Neuroimaging studies of cocaine-dependent individuals suggest potential substrates for aging-cocaine interactions that could underlie cognitive impairment of the type reported here. Among cocaine users, usual aging effects in frontal, temporal and cerebellar areas appear to be altered as a function of drug use⁵⁵⁻⁵⁷. These areas are involved in mediating numerous cognitive functions, yet the significance of such findings among older cocaine abusers remains largely unexplored.

These findings are also relevant to the question of whether age-specific treatments are indicated for older cocaine abusers presenting with cognitive impairment. Cognitive impairments have been shown to predict poor retention in outpatient cognitive-behavioral therapy in younger cocaine-dependent patients⁵⁸, and age-specific modifications in therapy may be needed for older cocaine abusers with cognitive impairments.

Regarding neuropsychological outcomes between cocaine-abusing individuals who tested positive versus negative for cocaine on urine toxicology, we recognize the literature on neuropsychological deficits being more pronounced in cocaine-abusing individuals with a negative urine status⁵¹. More of the younger cocaine-abusing individuals may have been in early or protracted abstinence, as compared to the older cocaine-abusing individuals. In our sample of individuals not seeking treatment for cocaine abuse, there was no evidence for differences on the neuropsychological outcomes between cocaine-abusing individuals who tested positive versus negative for cocaine. However, this may be a reflection of the basic and brief nature of the neuropsychological measures used in this study, which may not have

captured more subtle neuropsychological deficits. The use of a more comprehensive neuropsychological battery in the future may find results consistent with known literature in this area.

With respect to the second aim of comparing cocaine use patterns between older and younger cocaine abusers, our data indicate that older abusers use as much cocaine as younger abusers. Thus, in this selected sample of individuals not seeking treatment for cocaine abuse, there was no evidence for a decrease in cocaine use with age. Clearly heavy cocaine use can occur for many years and may even occur in individuals older than we had sampled.

This study has a few strengths. First, by recruiting and interviewing our participants in an explicitly non-treatment context, we limited perceptions that may occur in treatment settings which might bias participants to alter or misrepresent their ongoing cocaine use pattern. This approach may have improved the accuracy of self-reports about our aging cocaine abusers' daily function. Second, our study design and group selection allowed for the testing of interaction effects between aging and cocaine abuse. Third, we used established neuropsychological measures that were feasible to administer in a short amount of time.

This study has several limitations. First, only a brief battery of neuropsychological measures was used. A more comprehensive neuropsychological battery will be needed in the future to better capture neurocognitive function in older cocaine abusers. Second, only the last 30 days of substance use was obtained in detail with the QSUI and the DUQ, and only the last year of substance use disorders was formally assessed by the M.I.N.I. Future studies must employ more detailed instruments, such as the Structured Clinical Interview for DSM-IV Axis I Disorders, to assess contributions of past history of substance use and non-substance use disorders. Third, individuals in their 4th decade were not included in the study. With a total of four groups, a 2-decade range was chosen to compare older and younger adults. This range may be too broad to make accurate comparisons, and an option for future studies is to compare individuals in smaller 5-year or 10-year increments. Excluding individuals in their 4th decade prevented the analysis of neuropsychological performance in a continuous manner across several decades. Fourth, although we verbally screened for other abused substances such as methadone, buprenorphine, benzodiazepines, barbiturates, and phencyclidine, we were unable to confirm the presence or absence of these substances with urine toxicology. Due to limited funds for the study, which were used to compensate participants' time, we used a basic model of a drug screen card readily available to us, which did not detect these other substances. Finally, for the participants who tested negative for cocaine in the cocaine-abusing groups, collateral information (e.g., from family or friends, or if applicable, prior treatment programs) could have been an alternative strategy to independently confirm use of cocaine within the last 7 or 30 days.

Conclusion

This study provides preliminary evidence for an interaction between aging and cocaine abuse on psychomotor speed, attention, and short-term memory. If replicated, these findings raise several issues for older cocaine abusers, such as whether specific cognitive domains are particularly at risk for impairment, how such impairments may be targeted with pharmacological and/or non-pharmacological interventions, and whether such impairments may contribute to a future risk for dementia. In our sample, older individuals used as much cocaine as younger individuals, arguing that the impact of continued cocaine use in combination with aging merits further evaluation. The development of treatments for cognitive impairment among older cocaine abusers will benefit from future controlled studies along these lines.

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Table 1

Demographics, Medical History, and Psychological/Social Stressors.

	Age 51-70		Age 21-39		Overall Test Statistic, significance	t-test or χ^2 and significance between Groups
	Cocaine (Group 1)	Control (Group 2)	Cocaine (Group 3)	Control (Group 4)		
	Mean (S.D.) ^a	Mean (S.D.)	Mean (S.D.)	Mean (S.D.)		
Age (years)	56.8 (4.64)	55.4 (3.98)	34.5 (5.40)	31.0 (7.05)	F (3,76) = 126.37 ^{***} Group 2 > 3: t(38) = 13.93 ^{***}	Group 1 > 3: t(38) = 13.96 ^{***} Group 2 > 4: t(38) = 13.64 ^{***} Group 2 > 4: t(38) = 13.48 ^{***}
Education (years)	13.5 (2.01)	14.7 (1.76)	12.9 (1.69)	13.9 (2.02)	F (3,76) = 3.27 [*]	Group 2 > 3: t(38) = 3.30 ^{***}
# of medical systems ^d affected/participant	2.35 (1.50)	2.30 (1.45)	0.75 (0.85)	0.85 (1.23)	F (3,76) = 9.45 ^{***}	Group 1 > 3: t(38) = 4.16 ^{***} Group 2 > 3: t(38) = 4.11 ^{***} Group 1 > 4: t(38) = 3.47 ^{***} Group 2 > 4: t(38) = 3.41 ^{***}
# of current medications/participant	1.50 (1.76)	2.20 (2.19)	0.30 (0.66)	0.50 (1.05)	F (3,76) = 6.69 ^{***}	Group 1 > 3: t(38) = 2.85 ^{***} Group 2 > 3: t(38) = 3.72 ^{***} Group 1 > 4: t(38) = 2.18 [*] Group 2 > 4: t(38) = 3.13 ^{***}
# of Axis IV Categories ^d endorsed in DSM-IV-TR	2.00 (1.62)	1.10 (1.59)	2.30 (1.26)	1.00 (1.03)	F (3,76) = 4.31 ^{***}	Group 1 > 4: t(38) = 2.33 [*] Group 3 > 4: t(38) = 3.58 [*] Group 3 > 2: t(38) = 2.65 [*]
Perceived Stress Scale 10-item Score	17.2 (7.08)	11.3 (5.88)	19.2 (7.91)	8.90 (6.41)	F (3,76) = 9.91 ^{***}	Group 1 > 2: t(38) = 2.87 ^{***} Group 3 > 2: t(38) = 3.58 ^{***} Group 1 > 4: t(38) = 3.86 ^{***} Group 3 > 4: t(38) = 4.50 ^{***}
Frequency (n/20)						
Sex	Male	12	11	18	11	ns
	Female	8	9	2	9	
Race ^b	African-American	18	5	12	13	Group 4 > 2: χ^2 (1) = 6.47 [*] Group 3 > 2: χ^2 (1) = 5.01 [*]
	Caucasian	0	14	2	3	
	Hispanic	2	1	5	3	
	Other	0	0	1	1	
Work Status ^c	Unemployed	11	4	15	8	Group 1 > 2: χ^2 (1) = 5.23 [*] Group 3 > 4: χ^2 (1) = 5.01 [*]
	Employed/Retired	9	16	5	12	
Marital Status ^d	Single/Never Married	4	10	17	17	Group 2 > 1: χ^2 (1) = 3.96 [*] Group 3 > 1 and 4 > 1: χ^2 (1) = 16.94 ^{***} Group 3 > 2 and 4 > 2: χ^2 (1) = 5.58 [*]
	All Other	16	10	3	3	

^a S.D.: Standard Deviation

ns: non-significant (p > 0.05)

* p < 0.05

** p < 0.01.

^a See “Measures” under Methods section for categories used.

^b Although data are presented on all ethnic categories, the χ^2 comparisons were conducted as African-American vs. Non-African-American. Significant χ^2 results reflect African-American > Non-African-American.

^c Significant χ^2 results reflect Unemployed > Employed/Retired.

^d Significant χ^2 results reflect Single/Never Married > All Other.

Table 2

Details of Cocaine Use.

		Age 51-70 Cocaine (Group 1)	Age 21-39 Cocaine (Group 3)	t-test or χ^2 and significance between Groups
		Mean (S.D.)	Mean (S.D.)	
Age of 1 st cocaine use		26.15 (9.91)	19.15 (4.46)	t(38) = 2.88**
Age of 1 st regular cocaine use ^a		29.5 (10.65)	20.4 (6.12)	t(38) = 3.31**
# of days used cocaine in last 30 days		17.3 (9.04)	16.25 (8.37)	ns
Average \$ value of cocaine used per day of cocaine use in last 30 days		81.25 (70.48)	92.75 (124.01)	ns
Maximum \$ value of cocaine used per day of cocaine use in last 30 days		240.75 (269.4)	232 (254.41)	ns
# of days in last 30 days on which urge, desire, or craving for cocaine occurred		20.40 (9.18)	23.45 (9.87)	ns
Cocaine craving in last 7 days [^]		2.25 (0.91)	2.75 (0.97)	ns
Cocaine Treatment History	# of previous detoxes	10.29 (13.5)	7.33 (7.87)	ns
	# of previous rehabs	2.22 (1.48)	3.8 (2.68)	ns
CEQ-P Domain Mean Scores	Enhanced Well-Being	4.01 (1.65)	4 (1.92)	ns
	Sexual Enhancement	3.90 (1.83)	4.37 (1.9)	ns
	Pain Reduction	4.40 (1.63)	4.44 (1.85)	ns
	Increased Aggression	2.93 (1.02)	3.14 (1.52)	ns
	Social Facilitation	4.46 (1.43)	4.75 (1.61)	ns
	Social Withdrawal & Distrust	3.21 (1.28)	3.04 (1.78)	ns
	Increased Tension	3.75 (1.33)	4.15 (1.75)	ns
		Frequency	Frequency	
Route of Use when 1 st Tried	Smoked	2/20	4/20	χ^2 (1) = 0.27, ns
	IN	13/20	16/20	
	IV	5/20		
Current Route of Use	Smoked	15/20	11/20	χ^2 (1) = 2.51, ns
	IN	4/20	9/20	
	IV	1/20		
Cocaine Diagnosis/ Current Route	Number with Cocaine Dependence Diagnosis/Total Smoked	12/15	10/11	χ^2 (1) = 0.58, ns
	Number with Cocaine Abuse Diagnosis/Total Smoked	3/15	1/11	
	Number with Cocaine Dependence Diagnosis/Total IN	3/4	6/9	χ^2 (1) = 0.09, ns
	Number with Cocaine Abuse Diagnosis/Total IN	1/4	3/9	

[^] Scored as: 0 = none, 1 = mild, 2 = moderate, 3 = strong, 4 = severe.

ns: non-significant (p > 0.05)

* p < 0.05

** p < 0.01

^a Regular use – defined in the Drug Use Questionnaire as “getting high or drunk three times a week or more.”

Table 3
Structured Diagnostic Interview Instrument, Rating Scales, and Other Substance Use History.

	Age 51-70		Age 21-39		Overall Test Statistic, significance	t-test or χ^2 and significance between Groups
	Cocaine (Group 1)	Control (Group 2)	Cocaine (Group 3)	Control (Group 4)		
	Mean (S.D.)	Mean (S.D.)	Mean (S.D.)	Mean (S.D.)		
Presence of any comorbid psychiatric or substance use disorder on the M.I.N.I. ^a (n/20)	10	0	16	2	$\chi^2 (3) = 36.04^{**}$	Group 1 > 2: $\chi^2 (1) = 13.33^{**}$ Group 3 > 1: $\chi^2 (1) = 3.96^*$ Group 3 > 4: $\chi^2 (1) = 19.80^{**}$ Group 2 > 1: t(38) = 2.88 ^{**} Group 2 > 3: t(38) = 2.19 [*]
WRAT-III ^b , Reading Score	44.4 (5.68)	49.4 (5.40)	45.2 (6.77)	46.7 (6.04)	F (3,76) = 2.75 [*]	
ASRS ^c , part A Score	6.50 (4.02)	7.20 (4.11)	8.25 (3.89)	4.30 (4.23)	F (3,76) = 3.38 [*]	Group 2 > 4: t(38) = 2.20 [*] Group 3 > 4: t(38) = 3.07 ^{**}
ASRS, Part B Score	14.6 (8.71)	13.1 (6.69)	15.9 (7.90)	8.10 (6.29)	F (3,76) = 4.15 ^{**}	Group 1 > 4: t(38) = 2.70 [*] Group 2 > 4: t(38) = 2.41 [*]
# of Items Endorsed on the MSI-BPD ^d	2.35 (2.74)	0.40 (0.94)	2.55 (2.70)	0.65 (1.39)	F (3,76) = 5.69 ^{**}	Group 1 > 2: t(38) = 3.01 ^{**} Group 1 > 4: t(38) = 2.48 [*]
Alcohol Use in Last 30 Days	n/20 currently using	16	16	4		
	# of days used	12.1 (9.10)	14.3 (6.38)	1.50 (1.00)	F(3,42) = 3.21 [*]	Group 1 > 4: t(18) = 2.27 [*] Group 3 > 4: t(18) = 3.91 ^{**}
	# of drinks/drinking day	3.13 (2.19)	3.88 (2.31)	2.50 (1.29)	F(3,42) = 3.98 [*]	Group 1 > 2: t(24) = 2.70 [*] Group 3 > 2: t(18) = 3.56 ^{**}
Tobacco Smoking in Last 30 Days	n/20 currently smoking	15	3	2		
	# of days used	26.8 (8.6)	30.0 (0)	30.0 (0)	F(3,32) = 0.49, ns	ns
	# of cigarettes/day	8.93 (7.69)	11.0 (8.54)	20.0 (0)	F(3,32) = 1.26, ns	ns
Marijuana Use in Last 30 Days	n/20 currently using	4	15			ns
	# of days used	10.5 (11.0)	10.7 (9.57)			ns
	# of joints/day	1.25 (0.50)	2.00 (1.07)			ns

ns: non-significant (p > 0.05)

* $p < 0.05$
 ** $p < 0.01$

^a Mini-International Neuropsychiatric Interview

^b Wide Range Achievement Test-Third Edition

^c Adult ADHD Self-Report Scale; see "Measures," under Methods section for scoring.

^d McLean Screening Instrument for Borderline Personality Disorder

Table 4

Raw Scores, Main Analyses, and Analyses of Main and Interaction Effects of Neuropsychological Outcomes.

	Group 1	Group 2	Group 3	Group 4	Main Analyses			Analyses Based on Model Adjusted for Significantly Correlated Covariates ^d				Analyses Based on Model Adjusted for All Covariates ^e		
					Unadjusted Model	Model Adjusted for Significantly Correlated Covariates ^d	Model Adjusted for All Covariates ^e	Main Effect of Age, Effect Size ^f	Main Effect of Cocaine, Effect Size	Interaction Effect of Age & Cocaine, Effect Size	Post-hoc Tests [^]	Main Effect of Age, Effect Size	Interaction Effect of Age & Cocaine, Effect Size	Post-hoc Tests [^]
MMSE^a	28.2 (2.04)	29.5 (0.76)	29.3 (1.03)	29.4 (0.81)	F(3,76) = 4.42**	F(6,73) = 8.29**	F(7,72) = 7.53**	F(1,73) = 6.88** 0.262	ns	ns	ns	F(1,72) = 8.79** 0.297	ns	ns
Digit Span Forward^b	9.20 (1.94)	11.4 (2.37)	11.0 (2.29)	10.2 (2.31)	F(3,76) = 3.78*	F(6,73) = 7.04**	F(7,72) = 5.95**	ns	ns	F(1,73) = 5.81* 0.239	Group 2 > 1: F(4,35) = 5.52*** Group 3 > 4: F(4,35) = 5.48*** Group 3 > 1: F(4,35) = 7.09*** Group 2 > 4: F(4,35) = 3.77***	ns	F(1,72) = 5.61* 0.235	Group 2 > 1: F(5,34) = 4.29*** Group 3 > 4: F(5,34) = 4.26*** Group 3 > 1: F(5,34) = 5.60*** Group 2 > 4: F(5,34) = 3.03*
Digit Span Backward	4.70 (1.38)	7.10 (2.40)	7.05 (2.67)	7.20 (2.02)	F(3,76) = 6.21**	F(6,73) = 5.87**	F(7,72) = 5.22**	F(1,73) = 9.81** 0.313	ns	ns	ns	F(1,72) = 7.14** 0.264	ns	ns
Digit Span Forward – Backward	4.50 (2.09)	4.30 (2.27)	3.95 (2.46)	3.00 (1.97)	F(3,76) = 1.82, ns	F(3,76) = 1.82, ns	F(7,72) = 1.59, ns	ns	ns	ns	ns	ns	ns	ns
TMT^c A	61.7 (33.3)	41.3 (11.8)	31.7 (6.51)	35.5 (10.9)	F(3,76) = 10.14**	F(3,76) = 10.14**	F(7,72) = 5.76**	F(1,76) = 3.95*** 0.166	F(1,76) = 18.19** 0.400	F(1,76) = 8.28** 0.260	Group 1 > 2: F(1,38) = 6.68* Group 4 > 3: ns Group 1 > 3: F(1,38) = 15.62*** Group 2 > 4: ns	F(1,72) = 22.64** 0.450	F(1,72) = 7.17** 0.240	Group 1 > 2: F(5,34) = 3.21* Group 4 > 3: ns Group 1 > 3: F(5,34) = 4.34*** Group 2 > 4: ns
TMT^c B	133.5 (65.1)	73.8 (24.6)	78.6 (35.3)	64.8 (17.5)	F(3,76) = 12.07**	F(6,73) = 9.71**	F(7,72) = 8.27**	F(1,72) = 19.64** 0.426	ns	ns	ns	F(1,72) = 17.81** 0.408	ns	ns

	Group ^a 1	Group 2	Group 3	Group 4	Main Analyses			Analyses Based on Model Adjusted for Significantly Correlated Covariates ^d				Analyses Based on Model Adjusted for All Covariates ^e		
	Mean (S.D.)				Unadjusted Model	Model Adjusted for Significantly Correlated Covariates ^d	Model Adjusted for All Covariates ^e	Main Effect of Age, Effect Size ^f	Main Effect of Cocaine, Effect Size	Interaction Effect of Age & Cocaine, Effect Size	Post-hoc Tests [^]	Main Effect of Age, Effect Size	Interaction Effect of Age & Cocaine, Effect Size	Post-hoc Tests [^]
TMT B-A	71.8 (48.6)	32.5 (16.7)	46.9 (34.2)	29.4 (16.0)	F(3,76) = 7.36**	F(5,74) = 7.57**	F(7,72) = 5.33**	F(1,74) = 5.84*, 0.230	F(1,74) = 7.90**, 0.275	ns	ns	F(1,72) = 5.37*, 0.225	ns	ns

Group 1 (Age 51-70 Cocaine); Group 2 (Age 51-70 Control); Group 3 (Age 21-39 Cocaine); Group 4 (Age 21-39 Control);

ns: non-significant (p > 0.05)

* p < 0.05

** p < 0.01

*** p < 0.001

**** p < 0.0125 (Bonferroni corrected p-value)

***** p = 0.0500

^aMini-Mental State Examination, raw score

^bWechsler Adult Intelligence Scale - Third Edition, raw score (larger value = better performance)

^cTrail Making Test, seconds (larger value = poorer performance)

^dSignificantly Correlated Covariates – For MMSE, Digit Span Forward, and Digit Span Backward: Race (African-American vs. Non-African-American), Years of Education, and WRAT-III Reading Score.

^eFor TMT B: Race, WRAT-III Reading Score, and Presence of Any Comorbid Psychiatric or Substance Use Disorder on the M.I.N.I. For TMT B-A: Race and WRAT-III Reading Score. No covariates were significant for Digit Span Forward-Backward and TMT A

^fAll Covariates: Race, Years of Education, WRAT-III Reading Score, and Presence of Any Comorbid Psychiatric or Substance Use Disorder on the M.I.N.I. The main effect of cocaine in this model was non-significant for all neuropsychological outcomes.

^gEffect size = $\sqrt{\omega^2} = \sqrt{\text{omega}^2}$