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Neurocognitive consequences of cigarette smoking in young adults—a comparison with pre-drug performance

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Abstract

The present study examined effects of current and past regular cigarette smoking in young adult subjects. One hundred and twelve 17–21-year-old subjects, assessed since infancy, were evaluated using a battery of neurocognitive tests for which commensurate measures were obtained at 9–12 years of age, prior to the initiation of regular smoking. Smokers, determined by urinalysis and self-report, were categorized as heavy (>9 cigarettes per day) and light (<9 cigarettes per day) current smokers and former smokers, the latter having smoked cigarettes regularly in the past but not for at least 6 months. A third of the subjects were currently smoking cigarettes regularly with half of these being heavy smokers. Among former smokers, the average duration of smoking was slightly less than 2 years. Overall IQ, memory, processing speed, vocabulary, attention and abstract reasoning were the primary outcomes with comparisons being made between each of the three user groups and a control group who never smoked regularly. After accounting for potentially confounding factors including clinical assessment, marihuana use and pre-drug performance in the relevant cognitive domain, current regular smokers did significantly worse than non-smokers in a variety of cognitive areas predicated upon verbal/auditory competence including receptive and expressive vocabulary, oral arithmetic, and auditory memory. This impact of current smoking appears to behave in a dose–response and duration-related fashion. In contrast, former smokers differed from the non-smokers only in the arithmetic task. These results suggest that regular smoking during early adulthood is associated with cognitive impairments in selected domains and that these deficits may be reversed upon cessation. Together, the findings add to the body of evidence to be used in persuading adolescents and young adults against the initiation of smoking and, if currently smoking, the advantages of stopping.

Keywords: Cigarettes; Cognition; Current smoking; Former smoking; Pre-drug performance

1. Introduction

In North America, smoking among adolescents and young adults rose sharply in the 1990s reaching a peak in 1997. Subsequent to that period, although regular tobacco use has declined in these age groups, the rate of decline has decelerated sharply in the past 2 years. Recent observations derived from surveys conducted in both the United States [29] and Canada [4] have indicated that, among older adolescents, the current smoking proportion is 16% and 18%, respectively. The Canadian survey noted that 27% of 20–24-year-olds smoked. For several decades, the perception of risk has been observed to parallel the trends noted in smoking rates [29] suggesting that the perceived dangers play an important role in determining whether this habit becomes part of the lifestyle of the adolescent and young adult. Although there is incontrovertible evidence that smoking is the greatest preventable cause of disease and mortality, the putative impact of cigarette use by adolescents and young adults on cognitive performance is not as clearly defined. If such a relationship could be firmly established it may serve as an important addition to the perception of risk of this habit.

Most studies investigating the association between smoking and cognitive functioning have focused upon the impact of cigarettes in the elderly population using both cross-sectional (e.g., [9,10]) and longitudinal approaches (e.g., [6,31]). Although not entirely consistent [3] current smoking is reported, in the majority of these studies, to affect cognitive function in a

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detrimental fashion. Among 80-year-olds, a recent report [8] noted reduced cognitive scores in current but not previous smokers. In this work, cognitive assessments for the subjects were statistically adjusted for mental abilities assessed at 11 years of age.

A few studies have examined cigarette smoking in relation to cognitive performance in middle age subjects. A battery of tests in a variety of cognitive domains was administered by Kalmijn et al. [30] to 45–70-year-olds using a cross-sectional design. Current smokers were found to have, in a dose–response relationship, reduced psychomotor speed and reduced cognitive flexibility. Former smokers had scores that were intermediate between those of the smokers and non-smokers. In a longitudinal, birth cohort study [40], the association between cigarette smoking and a number of cognitive outcomes was investigated in middle-aged subjects. Smoking more than 20 cigarettes per day was associated with faster declines in verbal memory and slower visual search speeds. The findings were independent of sex, years of education, socioeconomic status and cognitive abilities assessed at age 15.

Information regarding the possible impact of smoking upon adolescents' cognitive performance is limited to the recent observations in 14–18-year-olds reported by Jacobsen et al. [27]. In this cross-sectional study, after controlling for general intelligence, alcohol and marihuana use, adolescent daily smokers, compared to nonsmokers, were found to have impairments in working memory but not aspects of attention or short-term memory irrespective of recency of smoking. Performance decrements were more marked with an earlier age of onset of smoking. In this work presmoking cognitive abilities were not available.

The present study examines the impact of cigarettes upon neurocognitive functioning in young adults. The subjects are members of families recruited in the late 1970s and early 1980s and have been assessed since birth while participating in the Ottawa Prenatal Prospective Study (OPPS). These young adult offspring can now serve as a valuable cohort for the evaluation of the cognitive consequences of their own drug use. The strength of using these subjects includes the rapport established over many test sessions and the extensive background information that has been gathered in a prospective fashion including cognitive abilities prior to the onset of drug use, prenatal exposure to various substances, socioeconomic variables, and other potentially confounding factors.

Recently, we have described the impact of marihuana upon overall IQ [20] and a variety of specific cognitive domains [19] in 17–21-year-olds. In this birth cohort, smoking marihuana five or more times a week was associated with lower scores on global IQ, visual processing speed, and both immediate and delayed memory after controlling for potentially confounding factors and corresponding cognitive measures obtained when the same subjects were 9–12 years of age [17]. Among subjects who were former heavy marihuana users but had not consumed the drug for at least 3 months prior to assessment, no cognitive impairments were observed.

The objectives of the current study are to determine whether, in the same sample with similar prospectively gathered background data, current and former cigarette smoking impacts upon various, specific cognitive domains in young adults.

2. Methods

2.1. Participants

The Ottawa Prenatal Prospective Study (OPPS) began in 1978 with the major objective of examining the effects on children of cigarette smoking, marihuana, and alcohol use by their mothers during pregnancy. The method of recruitment of the pregnant women, the determination of their drug use, and the study results have been reported elsewhere (e.g., [12,16]). Approximately 160 children have been administered neuropsychological tests yearly to age 7 and once during each of the 9–12-, 13–16-, and 17–21-year intervals. In the present report, data from the 9–12-year testing [17] have been used as a measure of predrug performance.

Of the 152 subjects who were tested between 17 and 21 years of age, 122 were available who had also been tested at 9–12 years of age. The 30 unavailable subjects (an average attrition rate of four per year) did not differ from the remaining sample in terms of demographic information (e.g., SES, parental education) and 26 of the 30 were a combination of students unavailable because of attending school out of the area and families who had moved. As in previously based OPPS reports [16–18], no subjects taking psychotropic medications or reporting drug use other than cigarettes, marihuana, and alcohol were included in the analyses. Subsequent exclusions after the 17–21-year testing were one subject on Ritalin, one cocaine user, one amphetamine user, one LSD user, an uncooperative subject, four cases with inconsistent urinalysis and drug self-report, and one subject who quit smoking a week prior to testing. The final sample comprised 112 subjects, 62 males and 50 females. None of the subjects reported smoking cigarettes regularly at the 9–12 testing although four subjects claimed to have tried cigarettes (one in the light, two in the heavy, and one in the former use smoking groups). Two subjects had reported trying marihuana (both in the former use group) and five had tried alcohol (two in the comparison group and one each in the three smoking groups). No use of amphetamines, cocaine, tranquilizers, heroin, LSD, solvents, mushrooms or steroids was reported.

2.2. Procedures

Tests were administered in laboratories at Carleton University in Ottawa from approximately 9:00 AM to 3:00 PM with a supervised lunch break. Subjects were allowed to take breaks from the testing session during which they could smoke if they wished.

Cigarette, marihuana, alcohol, cocaine, opiate and amphetamine use was ascertained by self-report and, except for alcohol use, was validated by urinalysis of samples taken on the day of testing. The urinary level of cotinine, the major metabolite of nicotine, was highly correlated with the self-reported number of cigarettes smoked daily ($r = 0.83$).

For analytical purposes, measures of cigarette use in the present study were the self-reported number of cigarettes smoked daily on a regular basis and the length of time in years of regular smoking. Consistent with government surveys [4], regular use was defined as smoking at least once daily. For the major analysis, cigarette use was categorized into current heavy smokers (>9 cigarettes/day; $n=18$), current light smokers (<9 cigarettes/day; $n=19$), former smokers ($n=11$), and a comparison group who never smoked regularly ($n=64$). Current smoking was divided at the median to create the light and heavy use categories. All of the subjects in the former smoking group had not smoked cigarettes for at least 6 months.

Cognitive tests assessing the domains of intelligence, memory, vocabulary, attention, and concept formation (Table 1) were selected from the battery administered to the 17–21-year-old subjects using commensurate measures from the 9–12-year-old testing and controlling for potential confounds to determine effects of current or former smoking, of the amount smoked daily, and of the number of years of regular smoking (Table 2a).

2.3. Statistical analysis

Using the four smoking groups (current heavy, current light, former, and comparison), the primary analytical procedure consisted of analysis of covariance (ANCOVA) for each cognitive outcome comparing each smoking group with the comparison group by means of an a priori contrast while controlling for potential confounds and premorbid performance.

Potential confounds examined were prenatal exposure to nicotine, marihuana, and alcohol, current marihuana and alcohol use as well as alcohol dependence as defined by DSM-IV [2] criteria. As in previous publications (e.g., [17,19]), any of these variables that satisfied the criteria of association with the cigarette smoking measure ($p<0.1$) (Table 2b) and the outcome

Table 1
Neurocognitive measures administered to young adults, corresponding commensurate tests administered to pre-teens, and the cognitive functions assessed

Young adult tests	Commensurate pre-teen tests	Cognitive functions assessed
Intelligence		
WAIS-III [47]	WISC-III [46]	Full Scale IQ
Verbal IQ composite	Verbal IQ Composite	Verbal knowledge, reasoning, attention
Comprehension	Comprehension	Oral, solutions to common problems, understand rules/concepts
Verbal Comprehension Index	Verbal Comprehension Index	Acquired knowledge, verbal reasoning
Vocabulary	Vocabulary	Oral vocabulary, meaning of words
Similarities	Similarities	Oral vocabulary, state how objects/concepts are alike
Information	Information	General knowledge
Working Memory Index	Auditory Working Memory [41]	Attending, holding and processing information
Arithmetic	Arithmetic	Oral arithmetic
Digit span	Digit span	Oral, repeat number sequence
Performance IQ composite	Performance IQ Composite	Fluid reasoning, spatial processing, attentiveness to detail, visual-motor integration
Picture arrangement	Picture Arrangement	Non-verbal reasoning, spatial processing
Perceptual Organization Index	Perceptual Organization Index	Fluid reasoning, attentiveness to detail, visual-motor integration
Picture completion	Picture Completion	Visual organization, visual memory
Block design	Block Design	Visual organization, visual-motor
Processing Speed Index	Processing Speed Index	Speed and accuracy of visual processing
Digit symbol coding	Coding	Speed of mental visual coding, visual-motor
Symbol search	Symbol Search	Speed of visual scanning and encoding
Vocabulary		
Peabody Picture Vocabulary [44]	Peabody Picture Vocabulary [44]	Vocabulary knowledge
Memory [48]		
Immediate Memory Index		Global immediate memory functioning
Auditory Immediate Index	Sentence Memory [44]	Auditory immediate memory
Visual Immediate Index	TVPS Visual Memory [22]	Visual immediate memory
General Memory Index		Global measure of delayed memory
Auditory Delayed Index	Auditory Working Memory [41]	Auditory delayed memory
Visual Delayed Index	Visual/Tactile Delayed Memory [22]	Visual delayed memory
Auditory Recognition Delayed	Seashore Rhythm [44]	Delayed recognition memory
Working Memory Index	Auditory Working Memory [41]	Attending, holding and processing information
Sustained attention [24,25]		
Auditory omissions [25]	Gordon Vigilance Task omissions [24]	Auditory omissions in sustained attention
Auditory commissions [25]	Gordon Vigilance Task commissions [24]	Auditory commissions in sustained attention
Visual omissions [25]	Gordon Vigilance Task omissions [24]	Visual omissions in sustained attention
Visual commissions [25]	Gordon Vigilance Task commissions [24]	Visual commissions in sustained attention
Concept formation/abstract reasoning		
Adult Category test [44]–total errors	Children's Category test [44]–total errors	Concept formation, non-verbal abstract reasoning, mental flexibility

WAIS = Wechsler Adult Intelligence Scale [47]; WISC = Wechsler Intelligence Scale for Children [46]; TVPS = Test of Visual Perceptual Skills [22]; all memory index tests given to young adults are derived from Wechsler Memory Scale–3rd edition [48]; all attention tests given to young adults are derived from the Test of Variables of Attention (TOVA) [25].

Table 2a
Corresponding commensurate tests at 9–12 years [mean (standard deviation)]

N=112	Controls	>0 and <9 cigarettes per day	≥9 cigarettes per day	Former users	$F(p)$
	n=64	n=19	n=18	n=11	
Intelligence					
WISC-III Full Scale IQ	114.3 (12.5)	111.7 (10.5)	104.1 (8.8)	112.3 (11.4)	3.6 (.015)
Verbal IQ composite	112.2 (12.2)	108.8 (10.7)	104.5 (9.4)	111.7 (12.8)	2.2 (.089)
Comprehension	12.0 (3.0)	11.4 (3.0)	10.8 (3.1)	11.8 (3.3)	0.7 (.554)
Verbal Comprehension Index	111.6 (12.1)	108.5 (9.8)	105.0 (9.5)	110.9 (11.3)	1.7 (.166)
Vocabulary	12.1 (3.0)	10.5 (1.9)	10.4 (2.4)	11.1 (3.2)	2.8 (.046)
Similarities	12.3 (2.3)	12.5 (3.0)	11.9 (2.1)	13.0 (2.3)	0.5 (.670)
Information	11.7 (2.6)	11.4 (1.7)	10.2 (2.1)	11.7 (1.3)	2.1 (.111)
Freedom from Distractibility Index					
Arithmetic	12.1 (3.2)	11.5 (3.0)	10.2 (2.3)	12.0 (3.4)	2.0 (.114)
Digit span	11.4 (2.8)	11.6 (2.8)	11.7 (2.8)	12.2 (3.5)	0.2 (.862)
Performance IQ composite	114.2 (14.3)	112.6 (12.3)	103.4 (10.2)	111.7 (10.1)	3.2 (.026)
Picture arrangement	12.4 (3.5)	11.5 (3.3)	10.4 (3.5)	11.6 (2.3)	1.6 (.191)
Perceptual Organization Index	114.9 (14.3)	112.4 (11.1)	105.9 (11.0)	112.3 (12.4)	2.2 (.090)
Picture completion	12.0 (2.7)	12.1 (3.0)	11.8 (2.5)	11.3 (2.1)	0.3 (.848)
Block design	13.1 (3.4)	12.5 (2.8)	10.6 (3.7)	12.9 (4.3)	2.6 (.060)
Processing Speed Index	110.9 (14.3)	115.2 (16.3)	101.4 (12.9)	108.1 (13.6)	3.1 (.029)
Coding	11.1 (2.9)	11.5 (2.7)	8.9 (2.1)	10.7 (2.1)	3.6 (.017)
Symbol search	12.7 (3.3)	14.1 (4.1)	11.2 (3.3)	12.1 (3.8)	2.3 (.084)
Vocabulary					
Peabody picture vocabulary	114.9 (16.0)	108.5 (12.3)	108.7 (14.1)	11.8 (14.8)	1.4 (.250)
Memory					
Sentence memory	0.19 (1.0)	−0.29 (1.0)	−0.04 (1.0)	0.51 (1.5)	1.6 (.189)
TVPS visual memory	12.3 (2.7)	12.1 (2.3)	11.3 (2.3)	12.0 (2.9)	0.6 (.619)
Auditory working memory	0.80 (1.0)	0.55 (0.8)	0.45 (0.9)	0.85 (1.1)	0.9 (.433)
Visual/tactile delayed memory	−0.02 (1.2)	−0.29 (1.1)	0.01 (1.1)	−0.33 (1.1)	0.5 (.692)
Seashore rhythm	0.70 (0.7)	0.85 (0.7)	0.77 (0.5)	0.67 (0.7)	0.3 (.841)
Sustained attention					
Gordon vigilance task omissions	−0.01 (1.0)	−0.19 (0.4)	0.35 (1.6)	−0.19 (0.6)	1.1 (.347)
Gordon vigilance task commissions	0.69 (1.9)	0.42 (1.2)	2.03 (3.4)	0.17 (0.8)	2.9 (.040)
Concept formation/abstract reasoning					
Children's Category Test (total errors)	−1.32 (1.0)	−0.51 (1.1)	−0.33 (1.4)	−0.76 (0.9)	6.0 (.001)

variable under consideration (p<0.05) [28] were controlled for in the analyses.

Also included as covariates in the analyses were commensurate measures of preteen performance as well as sex, educational attainment and family income (representing SES) identified as important influences on cognition [8,12,40]. The analyses were repeated without control for preteen performance in order to evaluate the importance of its inclusion.

Clinical assessment for the subjects was based on DSM positive criteria for any of the following DSM-IV Axis I [2]: generalized anxiety, major depression, dysthymic disorder, attention deficit/hyperactivity disorder, conduct disorder, oppositional defiant disorder. The automated National Institute of Mental Health Diagnostic Interview Schedule [5] was used to derive the symptom criteria.

The effect of the subject's marihuana use was also evaluated in analyses that included this variable as a covariate. In a previous publication [19], current marihuana use was negatively associated with visual processing mechanisms and the importance of its role in the relationship between smoking and these outcomes will be assessed. If marihuana use proves to be a covariate in the final model which includes presmoking performance, it will be removed to determine whether its exclusion has an effect on the association between smoking and the relevant outcomes.

Although ANCOVA afforded a comparison of former as well as current users with a non-smoking group, hierarchical regression was used in order to investigate further the impact of duration of smoking and the dose–response relationship after controlling for relevant covariates. The full sample of 112 subjects was used for the duration analyses whereas the former use group was omitted from the dose–response analysis since it was considered inappropriate to code the former users as non-smokers.

3. Results

3.1. Sample characteristics

Sample characteristics across the smoking groups are described in Table 2b. Maternal nicotine and marihuana use variables were coded for the analyses, as described in previous publications (e.g., [17]), in order to reduce skewness and outlier

Table 2b
Sample characteristics [mean (standard deviation)]

$N=112$	Controls	>0 and <9 cigarettes per day	≥9 cigarettes per day	Former users	$F(p)$
	$n=64$	$n=19$	$n=18$	$n=11$	
Sex (% female)	45.3	47.3	38.9	41.7	0.1
Family income (×$1000 Cdn)	34.6 (19.6)	24.2 (14.4)	32.6 (13.8)	26.4 (11.0)	2.2 (.098)
Exposed prenatally[a]					
Marihuana (joints per week)	1.6 (4.6)	2.4 (6.2)	8.2 (11.9)	2.6 (4.2)	4.9 (.003)
Nicotine (mg per day)	6.3 (10.8)	7.0 (10.2)	11.6 (13.0)	7.0 (10.2)	1.1
Current cigarette use (cigarettes/day)	0.0 (0.0)	4.9 (2.4)	12.9 (2.3)	0.0 (0.0)	459.2 (.000)
Duration of regular cigarette use (years)	–	2.5 (1.7)	3.7 (1.8)	1.9 (1.7)	3.8 (.031)
Age beginning regular use of zcigarette (years)	–	15.1 (1.5)	14.1 (1.3)	14.5 (2.2)	1.9
Current alcohol use (drinks during week before test)	1.2 (4.7)	2.9 (7.9)	0.4 (1.5)	2.7 (5.1)	1.1
Alcohol dependence DSM (%)	4.7	5.2	11.1	16.7	0.9
Self-reported regular alcohol use (%)	6.3	21.1	5.6	25.0	2.4 (.068)
Current marihuana (joints per week)	0.2 (0.6)	2.0 (3.0)	10.3 (11.7)	2.0 (3.6)	19.7 (.000)
Subject education (years completed)	11.1 (0.8)	11.4 (1.3)	10.3 (1.2)	11.9 (1.6)	6.6 (.000)
Any clinical DSM[b] (%)	12.5	26.3	50.0	25.0	4.3 (.007)

[a] Prenatal drug values were categorized for analysis: Marihuana coded as: 0=no use, 1=>0 to 1 j/week, 2=>1 to 5 j/week, 3=>5 j/wk (F=3.20, p≤0.05); nicotine coded as: 0=no use, 1=>0 to <16 mg/day 2=≥16 mg/day (F=1.23, ns).
[b] Diagnostic and Statistical Manual of Mental Disorders-4th edition: at least one of General Anxiety, Major Depression, Dysthymic, Attention Deficit Hyperactivity, Oppositional Defiant or Conduct Disorder as measured by C-DISC.

effects. The frequency of positive diagnoses for each of the DSM-IV disorders was low and to use this variable as a covariate, a dichotomous measure as described previously [19] was created whereby each subject with one or more positive diagnoses was assigned a '1' or a '0' if no diagnosis.

The subjects in the heavy current smoking group had less education, smoked more marihuana, and displayed more clinical disorders than the other three groups. Although prenatal exposure to marihuana was significantly higher with the heavy current smoking group compared to the control group, exposure to prenatal nicotine did not vary across the smoking groups. Both the light current smoking group and the former user group reported more alcohol use and had lower family incomes than the heavy current smoking group and the comparison group.

3.2. Group differences

The major effects of current smoking were found with the Peabody Picture Vocabulary Test (PPVT), Verbal IQ, Verbal Comprehension, and the Vocabulary, Arithmetic, Information and Comprehension subtests of the Wechsler Adult Intelligence Scale (WAIS) (Table 3). These findings were noted after controlling for presmoking performance and the potential confounds appropriate for each of the outcome variables (determined as described in Section 2.3) but without the control for the clinical data. In all cases, the heavy current smoking group performed more poorly than the control group. When compared with the control group, the light current smoking group had lower scores with the PPVT, the Auditory Recognition Delayed subtest, Full Scale IQ (FSIQ), and the Information and Arithmetic subtests of the WAIS. In contrast to the two current smoking groups, only one test, the Arithmetic subtest, showed a negative impact of former smoking.

The importance of controlling for performance before initiation of cigarette smoking is evident when this premorbid measure was excluded. Conducting the analysis in this fashion revealed a negative association between heavy current smoking and Performance IQ, Processing Speed, and Digit Symbol Coding which was subsequently lost after control for presmoking performance. The premorbid performance also reduced effects found with Full Scale IQ, Verbal IQ, Verbal Comprehension, and the WAIS subtests but these latter relationships remained statistically significant.

In order to examine the independent effect of the computerized derived clinical data, the analyses were repeated with the dichotomous DSM-IV control as described above (Section 3.1). When this measure for clinical disorders was added as a covariate, statistically significant associations with cigarette smoking remained with PPVT and the Vocabulary, Arithmetic, Information, and Comprehension subtests of the WAIS but were reduced with the broader indices of Verbal IQ ($p=0.024$ vs $p=0.08$) and Verbal Comprehension ($p=0.023$ vs $p=0.07$) for the heavy vs. control comparison, and FSIQ ($p=0.046$ vs $p=0.08$) for the light vs. control comparison.

As previous research [19] has described the influence of marihuana use on some of the cognitive outcomes assessed in this report, the possible role of this drug was considered in further detail. Current marihuana smoking, when used as a covariate in the analyses accounted for several relationships. Processing speed, digit symbol coding and symbol search were associated with cigarette use before but not after control for the subject's marihuana use.

3.3. Dose–response and duration effects

The regression analyses examining the impact of cigarette use as a continuous variable (using the current smokers and the control group) revealed a pattern comparable to the categorical analyses as cigarette use was associated with the same outcomes as heavy current use. After controlling for presmoking performance, sex, educational attainment, family income, and other relevant covariates, statistically significant relationships were found between the number of cigarettes smoked daily and the PPVT ($t=-2.3$, $p<0.05$), Verbal IQ ($t=-2.1$, $p<0.05$), Verbal Comprehension ($t=-2.1$, $p<0.05$), and the Vocabulary ($t=-2.5$, $p<0.05$), Arithmetic ($t=-2.5$, $p<0.05$), Information ($t=-2.0$, $p<0.05$) and Comprehension ($t=-2.5$, $p<0.05$) subtests of the

Table 3
Cognitive outcomes adjusted for relevant covariates * [adj. mean (S.E.)]

$N=112$	Controls	>0 to <9 cigarettes per day	≥9 cigarettes per day	Former users	Group comparison
	$n=64$	$n=19$	$n=18$	$n=11$	
Intelligence–WAIS [47]					
Full Scale IQ	115.4 (1.1)	110.6 (2.0)	110.6 (2.2)	114.2 (2.7)	$p=.046$, l vs. c
Verbal IQ	114.0 (1.2)	109.4 (2.2)	107.9 (2.4)	111.6 (2.9)	$p=.024$, h vs. c
Performance IQ	114.5 (1.1)	110.8 (2.1)	111.1 (2.3)	113.8 (2.8)	
WAIS Index scores					
Verbal comprehension	115.8 (1.3)	110.6 (2.5)	108.9 (2.7)	113.9 (3.3)	$p=.023$, h vs. c
Perceptual organization	115.4 (1.3)	112.5 (2.4)	114.5 (2.5)	116.3 (3.1)	
Working memory	106.9 (1.5)	104.8 (2.7)	104.5 (2.9)	102.6 (3.6)	
Processing speed	110.5 (1.5)	107.1 (2.5)	106.8 (3.0)	112.2 (3.3)	
WAIS Subtests					
Picture completion	11.5 (0.3)	10.3 (0.6)	11.3 (0.6)	12.1 (0.8)	
Vocabulary	13.3 (0.2)	12.9 (0.5)	11.7 (0.5)	13.3 (0.6)	$p=.006$, h vs. c
Digit symbol coding	11.6 (0.3)	11.0 (0.6)	10.4 (0.7)	11.8 (0.7)	
Similarities	13.4 (0.4)	12.3 (0.7)	11.7 (0.8)	12.4 (1.0)	
Block design	12.9 (0.3)	13.0 (0.6)	12.9 (0.6)	12.7 (0.7)	
Arithmetic	12.4 (0.3)	10.9 (0.5)	10.6 (0.7)	10.5 (0.7)	$p=.027$, l vs. c $p=.031$, h vs. c $p=.027$, f vs. c
Digit span	10.7 (0.2)	10.5 (0.4)	11.0 (0.5)	10.7 (0.6)	
Information	12.1 (0.3)	10.7 (0.5)	10.7 (0.6)	11.7 (0.7)	$p=.021$, l vs. c $p=.034$, h vs. c
Picture arrangement	11.2 (0.3)	11.1 (0.6)	11.0 (0.6)	10.9 (0.7)	
Comprehension	12.4 (0.3)	11.8 (0.6)	10.4 (0.6)	12.2 (0.8)	$p=.007$, h vs. c
Symbol search	12.4 (0.3)	11.7 (0.6)	11.7 (0.7)	12.5 (0.7)	
Peabody [44]					
PPVT	113.1 (1.4)	105.6 (2.4)	102.8 (2.8)	110.9 (3.1)	$p=.010$, vs. $p=.002$, h vs. c
Memory-WMS [48]					
Immediate memory	101.9 (1.6)	100.1 (3.1)	97.4 (3.2)	96.3 (4.1)	
Auditory immediate	103.6 (1.6)	100.3 (3.0)	99.4 (3.1)	96.9 (3.9)	
Visual immediate	98.9 (1.7)	100.1 (3.2)	96.2 (3.3)	97.3 (4.2)	
General memory	106.8 (1.5)	103.2 (2.8)	102.9 (2.9)	102.8 (3.7)	
Auditory delayed	106.0 (1.5)	102.9 (2.8)	102.5 (2.9)	102.0 (3.6)	
Visual delayed	103.7 (1.6)	102.9 (3.0)	99.5 (3.2)	103.3 (4.0)	
Auditory recognition delayed	108.4 (1.8)	99.6 (3.3)	106.3 (3.5)	102.2 (4.4)	$p=.024$, l vs. c
Working Memory	106.4 (1.6)	110.5 (2.9)	107.6 (3.0)	102.6 (3.8)	
Sustained attention–TOVA [25]					
Auditory omissions	99.2 (2.0)	90.5 (3.6)	91.0 (3.8)	104.1 (4.8)	
Auditory commissions	86.9 (2.7)	77.6 (5.0)	82.3 (5.3)	79.0 (6.6)	
Visual omissions	101.0 (2.3)	92.1 (4.3)	94.2 (4.5)	103.1 (5.7)	
Visual commissions	104.4 (1.3)	104.8 (2.3)	104.2 (2.5)	99.0 (3.1)	
Concept formation/abstract reasoning					
Category Test [44]–*T*-score	52.9 (1.2)	51.3 (2.2)	51.9 (2.3)	49.7 (2.9)	

In all cases, lower scores indicate poorer performance. In significant group comparisons: c = control, l = current light users, h = current heavy users and f = former users.
* Covariates used were preuse performance, sex, educational attainment, family income, and other covariates satisfying criteria as described in the text. DSM not included: see text.

WAIS. After controlling for the clinical data, the number of cigarettes smoked daily remained a significant predictor ($p<0.05$) for the WAIS subtests of Vocabulary, Arithmetic, Information and Comprehension.

Using the entire sample, the duration of smoking was associated with the FSIQ ($t=-3.9$, $p<0.001$), PPVT ($t=-2.8$, $p<0.01$), Auditory Recognition Delayed ($t=-2.1$, $p<0.05$), Verbal IQ ($t=-3.1$, $p<0.01$), Verbal Comprehension ($t=-3.2$, $p<0.01$), and the Vocabulary ($t=-2.0$, $p<0.05$), Arithmetic ($t=-3.2$, $p<0.01$), and Information ($t=-2.3$, $p<0.05$) subtests of the WAIS. These analyses of duration of smoking controlled for presmoking performance, sex, educational attainment, family income, and other relevant covariates including the number of cigarettes smoked daily and the clinical data.

4. Discussion

Using a sample of young adults who have been assessed since birth, the present study offered the unique opportunity of assessing a number of cognitive outcomes in young adult smokers and former smokers for whom evaluation within the same cognitive domains had taken place prior to the onset of regular smoking. Furthermore, the longitudinal, prospective design included assessment of possible confounding variables important in the interpretation of the findings.

The major impact of the quantity and duration of smoking in the present study, after statistically controlling for potentially confounding factors and premorbid performance, was in the area of verbal and aural functioning and noted in the assessment of receptive vocabulary, overall Verbal IQ and Verbal Comprehension. Consistent with the findings of the impact upon verbally mediated cognitive processes was the observation these smoking measures were negatively associated with orally presented arithmetic problems and an auditory based memory test.

In interpreting these findings, the importance of evaluating pre-smoking cognitive functioning within the cognitive spheres assessed is evident. The reported influence of maternal smoking during pregnancy on cognition [11,17,18,34] and early tobacco use [7,26,38] in the offspring are both important in the interpretation of the effects of current smoking. In both the OPPS sample [13–15,17,21,32] and other cohorts [35,42] a recurring theme in the investigation of prenatal exposure to cigarettes is that the primary outcome variables differentiating the children born to smokers compared to those born to nonsmokers are aspects of cognition that placed demands upon auditory processing and verbal comprehension—domains very similar to those associated with current smoking in the young adults. By including pre-smoking cognitive performance as a statistical control in the present work, the putative impact of prenatal tobacco exposure is taken into account in the assessment of the association between current smoking and cognitive performance. Thus, the significantly poorer performances of smokers in several verbal domains represent a further impact over and above the negative consequence of prenatal exposure.

From a second perspective, the importance of the evaluation of presmoking cognitive performance within specific domains was observed in the assessment of Performance IQ, Processing Speed and Digit Symbol Coding which were significantly associated with current smoking prior to premorbid control. If the level of functioning on these specific outcomes prior to the initiation of regular smoking had not been taken into account, an inappropriate attribution of deficits to current smoking in these specific spheres would have occurred.

The negative findings among the heavy cigarette smokers in the group analysis were complemented and extended by using the number of cigarettes smoked daily as a continuous variable. This analysis revealed a dose–response relationship in each of the variables noted to be significantly associated with heavy current smoking. Closely paralleling this dose–response relationship were the observations pertaining to the number of years that the young adults smoked. The outcomes impacted by this duration variable were similar to those observed to be associated both with heavy smoking in the group analysis and with those associated in the dose–response analysis. Furthermore, using duration of smoking as a predictor variable did reveal a negative association with the Full Scale IQ not noted in the other analyses. Although, in the present study, the length of time the young adults smoked was a relatively brief average of less than 4 years, the present findings with young adults are consistent with and extend the observations made with older subjects for whom estimates of presmoking cognitive abilities were available. In the normally aging 80-year-olds [8], current smokers, compared to never smokers and ex-smokers, had significantly lower IQ-type scores after statistically controlling for similar tests administered at age 11. In that study, controlling for sex or years of education did not alter the findings.

The vulnerability of the verbal/auditory domain noted in the heavy smoking group, and analyses of dose–response and duration in the present report is consistent with the one other study in which presmoking cognitive abilities was reported. In this work [40], among middle-aged subjects, cigarette smoking was associated with a faster decline between the ages of 43 and 53 in verbal memory but not visual search with the effects being independent of sex, years of education, socioeconomic status and cognitive ability at 15 years of age.

In the single investigation [27] that examined the putative effect of smoking upon cognition in a somewhat comparable age group to that reported in the present study, no premorbid data were noted. In that recent work, aspects of attention, working memory, verbal learning and memory were examined in 17-year-old smokers and non-smokers. The groups did not differ in terms of gender, years of education, or prenatal exposure to tobacco smoke. Both marihuana and alcohol use, which were higher among the smokers, were statistically controlled. The adolescent smokers were found to have impairments in an auditory, working memory task. In tasks assessing attention, there was a gender effect reported with the male smokers being significantly more impaired on tests of auditory attention than female smokers and non-smokers. The effects were not significant in a visual attention task. Thus, similar to the findings in the young adults of the present report, the cognitive domains which appeared vulnerable were those in which auditory cognitive demands were placed upon the subjects.

The results found in the present work are in contrast to those found, using the same cohort and same battery of cognitive assessments, among current and past marihuana users [19]. Whereas the impact of cigarette smoking was primarily in verbal-related cognitive domains, current regular heavy marihuana users did significantly worse than non-users in overall IQ, visual processing speed, and immediate and delayed memory. This relationship with marihuana, which was most pronounced in tasks with visual processing demands, was observed after accounting for potentially confounding factors including current cigarette use, prenatal marihuana exposure and pre-drug performance. The contrasting findings in the present cigarette study and the earlier marihuana study highlight the different domains of neurocognitive functioning that appear to be vulnerable in the users of these two substances. Furthermore, the importance of controlling for the impact of current marihuana use in the interpretation of the influence of current cigarette smoking on various domains of cognitive functioning is clearly evident. If marihuana use had not been taken into account, an inapt ascription of deficits to cigarette use, particularly in visual processing domains, would have occurred.

In the present study, the testing protocol permitted the subjects to smoke a cigarette, if desired, approximately every 90 min in order to avoid the confound of incipient nicotine withdrawal and to mimic the real world work/study situation in which periodic smoke breaks are the norm in non-smoking environments such as offices and classrooms. Although, because of the procedures followed, it was not possible to examine the immediate consequences of cessation, the effects of abstinence for an extended period of time were considered. Among the subjects who had been regular smokers but had not smoked for at least 6 months there was, with the exception of arithmetic, no association with decreased cognitive scores. Why, among the quitters, arithmetic should remain impacted in contrast to the verbal and memory cognitive domains that did not differ from the control subjects cannot be ascertained at this time.

The apparent recovery of the former smokers must be interpreted cautiously. The sample of such individuals was relatively small and, as young adults, the average length of time the quitters had smoked was limited to approximately 2 years. Although the age of onset of smoking of the quitters was intermediate between the light and heavy current smokers, the amount that they smoked was not ascertained. Because we found no effect for the former users in the group analysis, the duration effect noted is likely due to current smoking habits. It is possible that a longer history of smoking prior to cessation may result in a more lasting impact. However, it is noteworthy that the absence of effect in most cognitive domains seen in the young adult former smokers in the present work is similar to observations reported in both middle-aged [40] and elderly subjects [8] who had stopped smoking and for whom presmoking scores had been available.

Of all the associations observed among the heavy smokers prior to controlling for the DSM scores only the Verbal IQ Index and the Verbal Comprehension composite scores failed to retain their statistically significant relationships but the reduction in effect sizes was small. Thus, although the incidence of a clinical DSM diagnosis is significantly higher among the heavy cigarette smokers, current heavy smoking rather than the clinical symptoms appear to underlie the observed neurocognitive deficits.

The neurophysiological mechanism(s) underlying the association between current regular smoking in the adolescents and performance in the verbal/auditory cognitive area are, at this time, unknown. However, the extant literature suggests a number of potential neurobiological routes whereby smoking may impact upon this cognitive domain. There is incontrovertible evidence that many aspects of brain development including synaptogenesis, cell acquisition, and structural maturation of fiber tracts continue into late adolescence [23,36,45] and perturbation of optimal neurological growth during this period can have long-term consequences. A fundamental tenet regarding the vulnerability of neural development to environmental insults is that susceptibility of specific regional components within the nervous system is maximal during temporal emergence of such systems [39]. Recently, using structural magnetic imaging, evidence was found for significant structural maturation of fiber pathways in the left (but not right) frontotemporal pathway during adolescence [36]. Because of the protracted development of this pathway, critical in speech functioning, it may be particularly vulnerable to the well-established neurotoxic effects of nicotine [43] or other constituents of cigarettes. This possible impact of cigarettes is presently being investigated among adolescent smokers using magnetic resonant imaging procedures [37].

A second putative route whereby smoking may impact upon verbal/auditory based behavior is predicated upon the relationship between nicotinic cholinergic intracellular communication within the auditory system. Nicotinic receptors are directly involved in cholinergic neurotransmission [43] and the cholinergic pathways within the auditory system are well documented [33]. It has been speculated that deficits in auditory related tasks are attributable to the interaction of nicotine with the nicotine acetylcholine receptors within the auditory system [32]. Nicotinic receptors may mediate excitatory electrophysiological activity and changes in these receptors having major consequences for synaptogenesis affecting molecular events and auditory function [33]. Animal models indicate that the adolescent brain is exquisitely sensitive to nicotine neurotoxicity and that nicotine exposure during adolescence, even at plasma levels well below those of regular smokers, is associated with lasting alterations in biomarkers associated with cellular and neuritic damage [1].

In summary, a significant impact of current smoking was noted in a number of spheres requiring aural skills. These included tests of receptive language, the Vocabulary, Arithmetic, Information, and Comprehension subtests of the WAIS, and an auditory memory task. These negative associations, with the exception of Arithmetic were absent among individuals who had ceased regular smoking for at least 6 months. This is the first study evaluating the effects of cigarette smoking in current and former young adult smokers in which a prospective, longitudinal approach was used with known, domain-specific pre-drug cognitive performance levels. By utilizing this premorbid information, an important source of variance is taken into account engendering greater confidence in the interpretation of the findings. Although there is a possibility of Type 1 error with the number of comparisons assessed, the convergence of the effects in the auditory/verbal sphere lends credence to the interpretation.

The demonstration of an impact of heavy current smoking upon aspects of neurocognitive performance and the recovery of the negative impact in most spheres is a previously unrecognized deleterious consequence of smoking among adolescents and young adults. This observation provides a further educational tool in the efforts to persuade adolescents and young adults of the value of not smoking or discontinuing an existing habit.

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