

Chronic Cigarette Smoking in Healthy Middle-Aged Individuals Is Associated With Decreased Regional Brain *N*-acetylaspartate and Glutamate Levels

Timothy C. Durazzo, Dieter J. Meyerhoff, Anderson Mon, Christoph Abé, Stefan Gazdzinski, and Donna E. Murray

ABSTRACT

BACKGROUND: Cigarette smoking is associated with metabolite abnormalities in anterior brain regions, but it is unclear if these abnormalities are apparent in other regions. Additionally, relationships between regional brain metabolite levels and measures of decision making, risk taking, and impulsivity in smokers and nonsmokers have not been investigated.

METHODS: In young to middle-aged (predominately male) nonsmokers ($n = 30$) and smokers ($n = 35$), *N*-acetylaspartate (NAA), choline-containing compounds, creatine-containing compounds (Cr), *myo*-inositol (ml), and glutamate (Glu) levels in the anterior cingulate cortex and right dorsolateral prefrontal cortex (DLPFC) were compared via 4-tesla proton single volume magnetic resonance spectroscopy. Groups also were compared on NAA, choline-containing compounds, Cr, and ml concentrations in the gray matter and white matter of the four cerebral lobes and subcortical nuclei/regions with 1.5-tesla proton magnetic resonance spectroscopy. Associations of regional metabolite levels with neurocognitive, decision-making, risk-taking, and self-reported impulsivity measures were examined.

RESULTS: Smokers showed lower DLPFC NAA, Cr, ml and Glu concentrations and lower lenticular nuclei NAA level; smokers also demonstrated greater age-related decreases of DLPFC NAA and anterior cingulate cortex and DLPFC Glu levels. Smokers exhibited poorer decision making and greater impulsivity. Across the sample, higher NAA and Glu in the DLPFC and NAA concentrations in multiple lobar gray matter and white matter regions and subcortical nuclei were associated with better neurocognition and lower impulsivity.

CONCLUSIONS: This study provides additional novel evidence that chronic smoking in young and middle-aged individuals is associated with significant age-related neurobiological abnormalities in anterior frontal regions implicated in the development and maintenance of addictive disorders.

Keywords: Brain metabolites, Cigarette smoking, Decision making and impulsivity, Magnetic resonance, Neurocognition, Spectroscopy

<http://dx.doi.org/10.1016/j.biopsych.2015.03.029>

Chronic cigarette smoking in adults is associated with multiple neurobiological and neurocognitive abnormalities (1–3). The majority of earlier [see (1)] and recent (4–10) studies on smoking-related neurobiological abnormalities employed magnetic resonance imaging (MRI)-based morphologic measures (i.e., volume and cortical thickness). Overall, the findings indicated that smokers demonstrate widespread structural abnormalities that are particularly prominent in anterior frontal lobe subregions (11).

Although MRI morphometry provides fundamental information on the macroscopic viability of regional brain tissue, magnetic resonance spectroscopy enables a more direct interrogation of the functional integrity of brain tissue. Single volume proton magnetic resonance spectroscopy (SVS) and spectroscopic imaging (SI) methods allow the noninvasive and concurrent quantitation of several brain metabolites that collectively

provide information regarding the neurophysiologic viability of tissue (12,13). Abnormalities in certain metabolite concentrations (e.g., *N*-acetyl aspartate [NAA], choline-containing compounds [Cho]) may precede macroscopic morphologic or neurocognitive changes associated with some diseases or conditions (13). The brain metabolites most commonly quantitated via SVS and SI methods include biomarkers of neuronal integrity (i.e., NAA), cell membrane turnover and synthesis (i.e., Cho), cellular bioenergetics (i.e., creatine-containing compounds [Cr]), astrogliosis and inflammation (i.e., *myo*-inositol [ml]), and excitatory neurotransmitter and neuromodulator pools (i.e., glutamate [Glu]) (13,14). Higher regional NAA and Glu levels are associated with better function in multiple neurocognitive domains (15,16), and both of these metabolites show age-dependent decreases in concentration across adulthood (13). The few proton magnetic resonance spectroscopy studies of “healthy” chronic smokers

primarily employed SVS at 3 tesla (T) and focused on anterior frontal regions (e.g., anterior cingulate cortex [ACC], dorsolateral prefrontal cortex [DLPFC]) and the hippocampus in young or middle-aged adults; anterior frontal subregions and the hippocampus were emphasized because neurobiological abnormalities in these regions are implicated in the development and persistence of addictive disorders (17,18).

Gallinat *et al.* (19) reported that smokers showed lower NAA levels than nonsmokers in the left hippocampus, and higher pack-years were related to higher Cho levels in the anterior cingulate gyrus; however, in a subsequent study, the same investigators found no differences between active smokers, former smokers, and nonsmokers on Glu levels in the ACC and left hippocampus (20). O'Neill *et al.* (21) found no differences between smokers and nonsmokers in thalamic Glu concentration, but among smokers, more cigarettes smoked per day and pack-years of smoking were strongly related to lower thalamic Glu level. Mennecke *et al.* (22) reported higher left anterior cingulate Glu/glutamine and Cho concentrations in smokers than nonsmokers; after 3 days of smoking cessation, anterior cingulate glutamine decreased to nonsmoker levels, but no changes were observed for Cho. In the sole SI study, Durazzo *et al.* (23) observed that a small group of smokers had lower Cho concentrations in the cerebellar vermis than nonsmokers. Taken together, these studies provide evidence that chronic smoking is associated with regional derangements of cortical NAA, Cho, and glutamine levels. However, a limitation of the SVS method is that it does not simultaneously measure metabolites across a large number of brain regions; the regional specificity of the metabolic findings in chronic smokers (e.g., anterior vs. parietal, temporal, or subcortical) and their tissue specificity (i.e., gray matter [GM] vs. white matter [WM]) is unclear. Additionally, previous studies did not assess associations between the regional brain metabolite levels and measures of neurocognition, decision making, risk taking, or impulsivity; consequently, the functional relevance of the metabolite abnormalities observed in smokers is uncertain.

This study compared regional brain metabolite levels in healthy middle-aged smokers and nonsmokers. Imaging with SVS at 4T measured NAA, Cho, Cr, ml, and Glu levels in the right DLPFC and the bilateral ACC; studies at 4T facilitate more accurate quantitation of the Glu signal than lower field strengths because of greater spectral dispersion and increased signal-to-noise ratio (13). Additionally, SI at 1.5T simultaneously measured NAA, Cho, Cr, and ml (but not Glu) concentrations in the GM and WM of the bilateral frontal, parietal, and temporal lobes; occipital WM; and lenticular nucleus, thalamus, and cerebellar vermis. Associations of SVS and SI metabolite levels with performance on a comprehensive neurocognitive battery and on measures of impulsivity, decision making, and risk taking were examined.

Chronic smoking, independent of common smoking-related diseases (e.g., cerebrovascular disease, chronic obstructive pulmonary disorders), appears to affect adversely the integrity of brain neurobiology (1). Additionally, we observed that smoking is associated with greater age-related brain volume loss than observed in morphological studies with healthy individuals (9) and individuals with an alcohol use disorder (24,25). Therefore, we predicted the following: 1) Compared with nonsmokers, smokers demonstrate lower NAA and Glu

levels in the DLPFC and ACC and lower NAA concentrations in the frontal, parietal, and temporal lobes; lenticular nuclei; and cerebellar vermis and smokers evidence significantly greater age-related decreases of regional NAA and Glu levels. 2) Smokers show greater levels of risk taking, impulsivity, and poorer decision making. 3) Across smokers and nonsmokers, higher regional NAA and Glu levels are related to better neurocognition, whereas higher NAA and Glu concentrations in DLPFC and ACC are specifically associated with better decision making and with lower risk taking and impulsivity.

METHODS AND MATERIALS

Participants

Healthy, community-dwelling participants were recruited via posters, electronic billboards, and word-of-mouth. Participants were between the ages of 24 and 69 and gainfully employed at the time of the study (Table 1). Before engaging in procedures, participants provided written informed consent according to the Declaration of Helsinki, and the consent document and procedures were approved by the University of California San Francisco and the San Francisco Veterans Administration Medical Center. For SVS, there were 35 current smokers (4 smokers were female) and 30 nonsmokers (4 nonsmokers were female); for SI, there were 28 current smokers (2 smokers were female) and 36 nonsmokers (3 nonsmokers were female). The SI data were gathered from 2001–2012, and the SVS data were obtained from 2005–2014. Approximately 50% of participants with SI data also had SVS data; smokers and nonsmokers with both SVS and SI data were equivalent in number. The SI and SVS samples were equivalent on demographic, cigarette use, and alcohol consumption variables.

Table 1. Demographic and Clinical Measures^a

Variable	Nonsmokers (n = 30)	Smokers (n = 35)
Age (Years)	49.1 ± 12.0	48.6 ± 10.1
Education (Years)	16.5 ± 2.1	14.9 ± 2.1 ^a
AMNART	119 ± 9	117 ± 6
Male (%)	87	89
Caucasian (%)	63	71
Body Mass Index	25.5 ± 3.7	26.4 ± 3.8
Beck Depression Inventory	3 ± 3	5 ± 4
STAI Score	31 ± 8	35 ± 9
Average Drinks/Month in 1 Year	14 ± 14	22 ± 20
Average Drinks/Month in Lifetime	19 ± 12	26 ± 20 ^a
Biological Mother/Father Positive History of Problem Drinking (%)	28	37
FTND	NA	5 ± 2
Cigarettes/Day	NA	18 ± 6
Total Lifetime Years of Smoking	NA	29 ± 11
Pack-Years	NA	27 ± 15

Data are presented as mean ± SD unless otherwise indicated.

AMNART, American National Adult Reading Test; FTND, Fagerstrom Test for Nicotine Dependence; NA, not applicable; STAI, State-Trait Anxiety Inventory.

^ap < .05.

Download English Version:

<https://daneshyari.com/en/article/6226431>

Download Persian Version:

<https://daneshyari.com/article/6226431>

[Daneshyari.com](https://daneshyari.com)