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Brain Volume Correlates With Duration of Abstinence From Substance Abuse in a Region-Specific and Substance-Specific Manner

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ABSTRACT

BACKGROUND: Human neuroimaging studies indicate that the loss of brain volume associated with substance abuse may be recovered during abstinence. Subcortical and prefrontal cortical regions involved in reward and decision making are among the regions most consistently implicated in damage and recovery from substance abuse, but the relative capacities of these different brain regions to recover volume during abstinence remains unclear, and it is unknown whether recovery capacities depend on the substance that was abused.

METHODS: Voxel-based morphometry was performed in a prison inmate sample (N = 107) of long-term abstinent former regular users (FRUs) and former light users of alcohol, cocaine, and cannabis. Cross-sectional indicators of volume recovery were operationalized as 1) positive correlation between abstinence duration and volume in FRUs and 2) absence of lower volume in FRUs compared with former light users.

RESULTS: In FRUs of alcohol, abstinence duration positively correlated with volume in subcortical regions (particularly the putamen and amygdala) but not prefrontal regions; lower prefrontal, but not subcortical, volume was observed in FRUs compared with former light users. In FRUs of cocaine, abstinence duration positively correlated with volume in both subcortical regions (particularly the nucleus accumbens) and prefrontal regions; lower volume was not observed in either subcortical or prefrontal regions in FRUs. In FRUs of cannabis, abstinence duration positively correlated with subcortical, but not prefrontal, volume; lower prefrontal, but not subcortical, volume was observed in FRUs.

CONCLUSIONS: Subcortical structures displayed indicators of volume recovery across FRUs of all three substances, whereas prefrontal regions displayed indicators of volume recovery only in FRUs of cocaine.

Keywords: Addiction, Brain volume, MRI, Prefrontal cortex, Striatum, Substance abuse

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Neurogenesis and synaptic plasticity confer a capacity for repair and reorganization after certain kinds of neurological damage. A number of studies have investigated the brain's ability to recover from damage resulting from substance abuse. Studies have repeatedly linked substance abuse to decreased gray matter (GM) volume in abusers of alcohol (1,2), cocaine (3,4), cannabis (5,6), and multiple other substances (7) in regions involved in the reward and decision-making circuitry of the brain. These include subcortical structures, such as the striatum (2,3,8), amygdala (1,2,8), and hippocampus (7,8) [but see also (9,10)], as well as prefrontal cortical structures (2,4,5,11). At the same time, there is increasing evidence that abstinence from substance abuse can facilitate the recovery of volume lost during abuse. For instance, there are reported associations between abstinence from abuse and increased volume in regions of the prefrontal cortex (12,13) [but see (2,11,14)], striatum (2), insula (2), and parietal lobe (13).

Yet, owing to the variation in experimental designs and subject profiles among studies and the almost exclusive focus on individuals abstinent from alcohol, a number of important questions regarding abstinence-facilitated recovery still remain unanswered. First, it is unclear whether the capacity for volume recovery is uniform throughout all brain regions affected by substance abuse or if recovery capacities, and perhaps recovery time courses, vary by region. Indeed, a synthesis of the extant literature suggests that the latter alternative may be the case. Though some studies that have examined relatively short periods of abstinence (13,15) have found an association between abstinence and increased volume in the prefrontal cortex, several studies comparing brain volumes between abstinent substance abusers and healthy subjects have found that parts of the prefrontal cortex still display lower volume in abstinent abusers after a period of abstinence (2,11,14). In contrast, findings related to subcortical structures suggest that these regions may have the capacity to recover volume to levels before abuse over a long period of abstinence (16). This pattern of findings suggests regional differences in volume recovery capacities during abstinence.

Furthermore, given that different substances have different modes of neurotoxicity (17,18), it is not known whether recovery capacities might vary depending on the substance that was formerly abused. For instance, whereas cocaine is thought to cause cell death by eliciting uncontrolled autophagy via the nitric oxide–glyceraldehyde-3-phosphate dehydrogenase signaling pathway (17), reports suggest that alcohol causes cell death by increasing levels of proinflammatory cytokines and oxidative enzymes (18). Given the predominant focus on abstinent alcohol abusers, there are presently insufficient data in the literature to address whether recovery depends on the substance abused. The present study uses voxel-based morphometry in a prison inmate sample (N = 107) of long-term abstinent former regular users (FRUs) and former light users (FLUs) of alcohol, cocaine, and cannabis to examine whether recovery capacities may be region specific and substance specific. Because volume recovery cannot be measured directly in a cross-sectional design, we examined two potential indicators of volume recovery: 1) a positive correlation between volume and abstinence duration in FRUs and 2) the absence of lower volume in FRUs compared with FLUs.

METHODS AND MATERIALS

Participants

Participants (N = 124) from a medium-security Wisconsin correctional facility were selected based on the following inclusion criteria: age less than 45 years; IQ greater than 70; no history of psychosis or bipolar disorder; no history of significant head injury or postconcussion symptoms; no current use of psychotropic medications; and completed interview assessments for substance use and psychopathy (see below). Informed consent was obtained both orally and in writing. Of these 124 participants, 15 subjects who reported never having used any of the three substances of interest (alcohol, cocaine, or cannabis) were excluded because they had no history of substance use and thus no period of abstinence. Of the remaining 109 subjects, 2 were excluded because of nonsensical self-report data (i.e., negative abstinence durations), leaving a final sample of 107. Supersets of this sample have been used in previous reports from our group on psychopathy (19,20).

Substance Use and Abstinence Assessment

Substance use and abstinence data were obtained using the Addiction Severity Index (ASI) (21), which measures subjects' histories with a range of substances of abuse. Subjects in this sample were labeled as FRUs of a substance if they met the ASI criterion for "regular use," which constitutes use of a substance at least three times a week (usually to the point of intoxication or to the point where it compromises other normal activities) or use during 2-day binges. Subjects who reported past use of a substance but did not meet the criteria for "regular use" were labeled as FLUs of that substance. Subject characteristics, including substance abuse and abstinence data for the three primary substances of abuse examined, are summarized in Table 1. While the ASI provides data on the history of use of a range of different substances (i.e., alcohol, cocaine, cannabis, heroin, nicotine, methamphetamine,

Table 1. Participant Characteristics

Characteristic	All (n = 107)	Alcohol (n = 107)			Cocaine (n = 45)			Cannabis (n = 97)		
		FRUs (n = 62)	FLUs (n = 45)	p	FRUs (n = 25)	FLUs (n = 20)	p	FRUs (n = 80)	FLUs (n = 17)	p
Age, Years	31.4 (7.4)	31.3 (8.1)	31.5 (6.4)	.93	33.9 (8.0)	29.8 (9.5)	.12	30.2 (6.8)	35.4 (8.3)	< .01
IQ	85.0 (34.7)	85.8 (35.1)	84.0 (35.0)	.80	90.1 (35.6)	91.3 (32.3)	.91	81.9 (37.8)	90.6 (26.3)	.37
Factor 2 Score	13.4 (4.0)	13.7 (3.8)	12.9 (4.3)	.32	14.6 (3.2)	13.4 (4.0)	.27	14.2 (3.5)	10.9 (3.9)	< .01
Abstinence Duration, Months	N/A	72.7 (62.4)	85.4 (77.7)	.35	98.4 (77.5)	95.0 (101.2)	.90	66.9 (60.0)	187.8 (108.3)	< .01
Duration of Abuse, Months	N/A	77.2 (62.6)	N/A	N/A	50.1 (68.5)	N/A	N/A	108.7 (71.3)	N/A	N/A
Age of First Use, Years	N/A	12.4 (3.0)	14.4 (3.4)	< .01	17.4 (3.0)	20.0 (5.3)	.05	12.8 (2.7)	15.4 (1.5)	< .01
Total ICV, mL	1510.9 (129.1)	1514.1 (124.6)	1506.6 (136.4)	.78	1508.2 (108.2)	1514.5 (133.0)	.86	1520.8 (129.9)	1462.0 (135.0)	.10
Race, % (n)										
Caucasian	54 (58)	60 (37)	47 (21)	.10[a]	80 (20)	75 (15)	.84[a]	49 (39)	59 (10)	.68[a]
African American	43 (46)	40 (25)	47 (21)		16 (4)	25 (5)		48 (38)	41 (7)	
Hispanic	2 (2)	0 (0)	4 (2)		0 (0)	0 (0)		3 (2)	0 (0)	
Native American	1 (1)	0 (0)	2 (1)		4 (1)	0 (0)		1 (1)	0 (0)	

All data are mean (SD) except where noted.
FLUs, former light users; FRUs, former regular users; ICV, intracranial volume; N/A, not applicable.
[a]Fisher's exact test.