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Impact of alcohol consumption in healthy adults: A magnetic resonance imaging investigation

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ABSTRACT

The impact of alcohol on brain morphology was studied in a large group of cognitively intact people whose consumption of alcohol was below the threshold for abuse. Participants were 367 healthy subjects, aged 18 years or older, who underwent magnetic resonance imaging (MRI) for reasons other than cognitive impairment. MRI analyses were carried out using SPM8 software on the MATLAB 7.9 platform. Gray matter (GM) and white matter (WM) volumes were normalized for intracranial volume. Participants were interviewed about their lifetime consumption of alcohol, nicotine and other available illicit substances. Direct WM and GM comparisons between alcohol users and non-users did not detect significant differences. Differences also did not emerge from multiple regression analyses or in the subgroup aged 65 or older. Based on this study's findings, we cannot infer a detrimental effect of alcohol on the brain of normal adults. These data may be considered to provide reference information for clinical studies.

1. Introduction

Brain imaging is increasingly used to corroborate clinical correlates and gather insight on the etiology of neuropsychiatric disorders. Brain-imaging scans can provide information on brain lesions contributing to the symptoms and affecting the course of different disorders. Recently, advanced algorithms able to quantify subtle morphological details of brain morphology have been used to investigate morphological correlates of both clinical or normal conditions. However, without adequate "normative" data, results from these advanced techniques cannot be used to infer the etiology of neuropsychiatric disorders, besides those secondary to macroscopic brain lesions.

The possible effects of alcohol and substance consumption are often overlooked in "normal" people who are included in control datasets, despite the fact that alcohol consumption, in particular, is widespread in many Western countries (Degenhardt et al., 2008; Merikangas and McClair, 2012). Moreover, studies conducted in large general population samples also show that lifetime cigarette smoking is widespread around the world, and about 15–25% of people have used cannabis or, less often, other illicit psychoactive substances (2–6% according the statistics: Degenhardt et al., 2010; Merikangas and McClair, 2012).

Chronic heavy alcohol use is known to be associated with both direct and indirect brain damage. There is evidence that heavy alcohol consumption causes abnormalities in both white and gray matter, and is associated with enlarged cerebrospinal fluid volume as an effect of brain atrophy (Oscar-Berman and Marinkovic, 2003). Data on the impact on those people who have maintained a moderate, presumably non-pathological level of alcohol consumption are more limited. Even less is known about people who are regular or occasional alcohol consumers (light drinkers).

1.1. Imaging studies of alcohol dependence

Studies in patients with alcohol dependence – also indicated in the literature with the outdated terms "alcohol addicted" or "alcoholics" – show evidence of a general reduction in brain size, with heavy alcohol consumption being associated with greater regional brain damage (Pfefferbaum et al., 2001; Pfefferbaum et al., 1997; Harper, 1998; Visser et al., 1999; Ding et al., 2004). Global atrophy is the most consistently reported finding in patients with alcohol dependence, together with damage in the frontal lobe area (Moselhy et al., 2001; Sullivan and Pfefferbaum, 2001). In severe alcohol dependence, studies with both computed tomography (CT) and magnetic resonance imaging (MRI) have found reduced gray and white matter and marked loss in the frontal lobes, the medial

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temporal and parietal cortices, in the thalamus, caudate and lenticular nuclei and in the cerebellar cortex (Jernigan et al., 1991; Pfefferbaum et al., 1992; Shear et al., 1996; Sullivan, 2003; Sullivan et al., 2003).

Studies based on voxel-based morphometry (VBM), which allows the investigation of the entire brain without restriction to "a priori" defined regions of interest (Ashburner and Friston, 2000), confirm these findings. In a sample including 26 alcohol-dependent patients withdrawn from alcohol and 24 "healthy" men, Chanraud et al. (2007) reported a positive relationship between age at first drink and gray matter decreases in the right middle frontal gyrus, the right brainstem, and bilaterally in the cerebellum. They also found impaired executive functions in alcohol-dependent patients, and the neuropsychological scores of the patients correlated with gray matter volumes in the frontal and temporal cortices, the insula, the hippocampus, the thalami, and the cerebellum, as well as with white matter volumes in the brainstem (pons and midbrain). No similar relationship was found in controls. Jang et al. (2007) found decreased gray and white matter in 20 alcohol-dependent patients compared with 20 matched healthy controls, particularly in bilateral parahippocampal white matter; alcohol-dependent patients also had perseverative responses and errors in the Wisconsin Card Sorting Test that correlated with the decrease of gray matter in the left superior temporal gyri and right postcentral region. Parahippocampal white matter atrophy is often reported among patients with alcohol dependence (Schulte et al., 2004). Fein et al. (2002) found reduced total gray matter, particularly in the prefrontal and parietal cortical gray matter, in 24 young and middle-aged treatment-naïve men with alcohol dependence compared with to 17 age- and sex-matched controls. Prefrontal atrophy is another frequently reported finding in the investigation of brain effects of alcohol dependence. However, no white matter changes were found in the patients study by Fein et al. (2002). Their sample was younger than other clinical samples, and age was found to magnify the effects of alcohol on the brain.

In a study based on a regions-of-interest analysis, Fein et al. (2006) found reduced gray matter bilaterally in the amygdala in 43 long-term (at least 5 years) abstinent patients with past alcohol dependence compared with 58 matched healthy controls, in both the left (cluster size=370) and the right (cluster size=218) hemispheres, with no difference between men and women. Abstinent patients also performed worse than controls on the simulated gambling task of Bechara (Bechara et al., 1994), but there was no correlation between performance on the gambling test and the reduction of gray matter in the amygdala.

1.2. Studies on drinkers who are not alcohol-dependent

Only a few studies have assessed community samples of untreated social drinkers. The Cardiovascular Health Study (Mukamal et al., 2001) and the Atherosclerosis Risk in Communities Study (Ding et al., 2004) found positive associations between low to moderate alcohol drinking and brain atrophy, using ventricular size as a marker of brain atrophy. Comparison of light-to-moderate with heavy alcohol drinkers showed abnormalities in both the gray and white matter volumes (de Bruin et al., 2005a, 2005b; Taki et al., 2004, 2006), albeit less prominent than in individuals with alcohol dependence. In the Taki et al. (2006) study, based on 405 Japanese male individuals with no alcohol dependence (mean=4.8 ± 2.3 drinks per week, range=1–7), the gray matter volumes of the bilateral middle frontal gyri showed a significant negative correlation with lifetime alcohol intake, with greater reduction in those who were heavier alcohol drinkers. However, in a Japanese sample (114 males and 97 females; mean age=37.4, S.D.=13.5, range=21–72) of light to moderate alcohol drinkers (no information was provided on mean number of drinks per week; only the calculated lifetime alcohol consumption was reported), Sasaki et al. (2009) found no significant alcohol-related changes in gray or white matter volume (after normalization with total intracranial volume). Sachdev et al. (2008) found that moderate alcohol drinking (mean 7.04 ± 8.15 drinks per week) was associated with increased cortical gray matter volume, and decreased white matter volume in the right parahippocampal gyrus, in a sample of 211 middle-aged men (age range=60–64 years) with no alcohol dependence.

In studies aimed at detecting etiological markers of neuropsychiatric disorders, lack of information on alcohol and substance use in the comparison group can be misleading, and can lead to incorrect conclusions. Subtle differences might go undetected due to a lack of information on substance consumption in the control sample. The exploration of the effects of alcohol use in putatively healthy people would be preliminary to the establishment of a "normative" dataset to be used for clinical investigation.

It is not easy to collect large samples of MRI scans of subjects who can be considered representative of the general population. A convenient alternative is to collect scans from people who undergo an MRI examination for reasons other than cognitive impairment or suspected organic brain disease, and who are found to be normal after careful clinical, neuropsychological, and radiological investigation.

This paper summarizes data on a normative dataset of brain-imaging scans taken from people who were determined to be free of neurological disorders or impairment and who did not meet diagnostic criteria for any current mental disorder (Riello et al., 2005; Galluzzi et al., 2009). Alcohol and substance use was assessed in this group of people through a detailed interview.

2. Methods

The imaging acquisition was carried out at the Neuroradiology Unit of the "Città di Brescia" Hospital, Brescia (Italy), from March 2001 to December 2008, and includes data from outpatients examined for reasons unrelated to cognition (Riello et al., 2005; Galluzzi et al., 2009).

Reasons for MRI scan included migraine or headache, visual (diplopia and scotoma) and balance or auditory (hypacusia, dizziness, and tinnitus) disturbances, paresthesias, and mixed reasons for referral (suspected cerebrovascular disease, dyslexia, orbital region study, and lipothymia). As for the specific reasons for MRI referral for the patients in this sample, past clinical history analyses showed that those reasons were not unevenly related to specific sociodemographic variables, global cognition, depressive symptoms or other clinical features (Galluzzi et al., 2009).

All scans were obtained during routine procedures of assessment required for the evaluation of the clinical complaints. All subjects gave their informed consent to use the brain scan for research purposes. The study was reviewed and approved by the local ethics committee (Comitato Etico delle Istituzioni Ospedaliere Cattoliche).

2.1. Participants

A priori exclusion criteria were as follows: (i) request of MRI scan for memory problems or cognitive impairment, (ii) request of MRI scan for clinical suspicion of neurodegenerative diseases (e.g., Parkinson's disease, progressive supranuclear palsy, Huntington's disease, and multiple system atrophy), (iii) request of MRI scan for suspected stroke, and (iv) history of transient ischemic attack or stroke, head trauma, and lifetime alcohol dependence according to DSM-IV criteria (American Psychiatric Association, 1994) or past/current substance abuse (according to DSM-IV criteria), cortico-steroid therapy, and loss of weight greater than 5 kg in the last 6 months. All eligible patients were considered for potential inclusion in the study. The a posteriori exclusion criterion was the following: patient's brain scan found positive at visual assessment by the neuroradiologist in charge. In particular, whenever the scan showed brain masses, white matter hyperintensities (in patients undergoing MRI for suspected multiple sclerosis), aneurysm larger than 10 mm, arteriovenous malformations (excluding developmental venous anomalies), or any malformations of the central nervous system, the patient was excluded. Cognitive impairment as determined on subsequent neuropsychological testing was also an exclusion criterion.