VOLUMES OF ANATOMICALLY DEFINED BRAIN STRUCTURES ON MR IMAGES INCREASE WITH CONTINUED ABSTINENCE FROM ALCOHOL

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Introduction

Previous neuroimaging studies showed volume loss in certain brain regions in alcoholics, which is partially reversible with abstinence. However, these studies had methodological limitations. They estimated regional brain volumes from non-contiguous slices not encompassing the entire brain. In longitudinal studies, the 2D approach, together with different head positions during repeat scans, created a methodological error. Regional volumes were obtained by hand-marking and/or geometrical rules not strictly following brain anatomy. Moreover, most of previous MRI studies segmented MRIs into gray matter (GM), white matter (WM), and cerebro-spinal fluid (CSF) based on pixel intensities. The goal of this study was to use improved accuracy of absolute volume and of volume change measures to quantify volume changes in anatomically defined brain regions of recovering alcoholics (RA) at 1 month and 6 to 9 months of abstinence from alcohol.

Methods

We studied 27 RA in treatment (50±8 years; 270±139 standard alcoholic drinks/month over lifetime) at time-point 1 (TP1, 6±3 days of sobriety) and again at TP2 (32±9 days of supervised abstinence) and 18 light-drinking controls (LD, 48±5; 13±10 drinks/mo) at 1.5T (Vision, Siemens Medical Systems, Iselin, NJ). We used MRI sequences covering the entire brain: 3D MPRAGE (TR/TI/TE=10/300/4ms) and DSE (TR/TE=5000/20/80ms). 16 RA were re-scanned at an average of 221±44 days (TP3). They were grouped into relapsers (n=7, who consumed 6 or more alcoholic drinks over 3 consecutive days at any time between TP2 and TP3) or abstainers (n=9, who remained abstinent or consumed less than 6 alcoholic drinks over 3 consecutive days). Data analysis was performed with automated techniques to improve the accuracy of determination of brain structure volumes. Regional WM, GM and CSF volumetry was performed at all time-points using a) automated probabilistic segmentation of high-resolution ($1x1x1.5mm^3$) T1w images based on a global voxel intensity histogram and the intensity of each voxel and its neighbors, and b) automated atlas-based region labeling of major lobes, cerebellum, brainstem, and subcortical structures. A boundary shift integral method (BSI) yielded overall brain tissue volume changes between pairs of studies, which were converted into monthly rates of overall brain tissue gain over duration of sobriety in 20 RA and 15 LD. Hippocampal volumes were obtained in 15 RA, using surgical navigation technology, a semi-automated method. A brief neurocognitive battery was administered at TP1, and more comprehensive batteries at TP2 and TP3.

Results

Cross-sectional comparison between RA at TP1 and LD showed smaller volumes of frontal, parietal, and temporal WM (all p≤0.01), smaller volumes of parietal and temporal GM (all p≤0.003), as well as smaller thalami (p=0.03). At TP1, visuospatial learning correlated with parietal WM volume (r=0.46, p=0.02) and aural attention/concentration was related to parietal WM, temporal WM, total cerebral WM, and lenticular volumes (all r≥0.38; all p≤0.05).

BSI showed greater overall brain tissue gain (+11.8±9.7cc) in RA during the first month of abstinence compared to LD over 2 years (-2.1±4.0cc, p=0.0001) and a greater rate of overall monthly tissue gain than in LD (+1.1±0.8% vs. –0.01±0.01%, p=0.0001). Region-specific volumetric analyses revealed increases in volumes of frontal WM, parietal WM, thalamus, caudate (all p≤0.01), brainstem and cerebellum (both p=0.04) as well as increases in right hippocampal volume (p=0.03) over the first month of sobriety. Frontal and temporal GM volumes tended to increase (both p=0.09). Monthly rates of volume change for WM structures tended to be greater than those for GM structures, e.g. frontal WM volume increased at a rate of 2.1±4.0% per month and frontal GM volume at 1.7±5.7%. Increases in tissue volumes were accompanied by lobar sulcal CSF decreases (all p≤0.08). At TP2, visuospatial learning correlated with parietal and temporal WM and total lobar WM (all r=0.46, all p≤0.02), while executive skills and general intelligence were inversely related to frontal CSF volumes (r≤-0.38, all p≤0.05).

Between 1 and 6 to 9 months of abstinence, the volumes of frontal GM, parietal GM, thalamus, caudate (all p≤0.04), brainstem and cerebellum (p≤0.02) increased, but additional lobar WM volume increases were non-significant. Correspondingly, the monthly rates of volume change in WM and subcortical regions were greater within the first month of abstinence than in the following months of sobriety (all p≤0.03). Rates of GM volume changes were not significantly different between the first month and the following months of sobriety. After 6 to 9 months of sobriety lobar WM had recovered to light-drinking values, whereas total GM (p=0.06), in particular in frontal lobe (p=0.03), remained significantly reduced. Regional volumes in relapsers did not change significantly between TP2 and TP3.

Discussion

WM volume recovery in alcoholics is faster in the first month of sobriety than in the following months, whereas GM volume is recovering at a similar rate through 6-9 months of abstinence. Thus, our findings suggest that WM recovers faster than GM during prolonged abstinence from alcohol and that re-myelination in WM precedes neuronal cell body volume increases, dendritic re-arborization or increases in synaptic density in GM. Our findings were obtained with mostly automated methods, provide information on anatomically defined brain regions, and are in general concordance with earlier neuroimaging results.