BRAIN METABOLITES AND NEUROCOGNITION DURING RECOVERY FROM ALCOHOLISM: A SHORT-TE MULTI-SLICE 1H MRSI STUDY

T. C. Durazzo[1], S. Gazdzinski[1], D. J. Meyerhoff[1,2]

[1]DVA Medical Center, San Francisco, California, United States, [2]Radiology, University of California, San Francisco, California, United States

Introduction

A potential mechanism underlying alcohol-induced neurocognitive deficits is alcohol's effect on biochemical constituents of neural and glial tissues. Short-TE proton magnetic resonance spectroscopic imaging (1H MRSI) measures in multiple brain regions metabolites that are putative markers of neuronal and glial cell integrity. Previous single-volume MRS studies in alcoholics showed changes in the concentrations of N-acetylaspartate (NAA), choline (Cho), and myo-inositol (mI) and recovery of metabolite abnormalities with abstinence, primarily in frontal lobe and cerebellum. It is unclear, however, if these metabolite changes are localized to those brain regions examined by single-volume MRS, and if they are related to neurocognitive changes during short- and long-term abstinence.

Methods

We studied 25 alcoholics enrolled in substance abuse treatment (recovering alcoholics, RA; 49±9 years; 260±140 standard alcoholic drinks/mo over lifetime) at 6±3 days (TP1), 32±9 days (TP2) and 6-9 months of abstinence (TP3). Twenty light social drinkers served as controls (LD, 46±7; 14±15 dri/mo). At TP3, RAs were grouped into relapsers (n = 9) if they consumed 6 or more alcoholic drinks over 3 consecutive days at any time between TP2 and TP3, or abstainers (n = 11) if they remained abstinent or consumed less than 6 alcoholic drinks over 3 consecutive days. 3D MRI (MPRAGE, TR/TE/TI=10/4/300 ms), DSE (TR/TE = 5000/20/80 ms), and multislice ^{1}H MRSI (TR/TE/TI=1800/25/170 ms) was performed at all time points. Regional white matter (WM), gray matter (GM) and CSF volumetry used automated probabilistic segmentation and automated atlas-based region labeling of major lobes, cerebellum, brainstem and subcortical structures. Concentrations of brain metabolites N-acetylaspartate (NAA), choline (Cho), and myoinositol (mI), were measured in 3 parallel planes through the centrum semiovale, nuclei of the basal ganglia, and cerebellar vermis. Regional atrophy-corrected metabolite concentrations were calculated by combining SI and segmented MRI data. A brief neurocognitive battery was administered at TP1, and a comprehensive battery at TP2 and TP3.

Results

At TP1, RA showed lower NAA compared to LD in all regions measured except the cerebellar vermis (all $p < .03$). Relative to LD, RA also had lower Cho in the frontal WM, parietal GM and WM, thalamus and caudate (all $p < .02$). Between TP1 and TP2 (approx. 3 weeks), frontal WM NAA, Cho and mI, parietal GM Cho, and cerebellar mI increased in abstinent RA ($p < .03$). At TP3, after 6-9 months of abstinence, NAA in abstainers remained depressed in the frontal and temporal GM, frontal, temporal, parietal, and occipital WM as well as thalami relative to LD (all $p < .05$). Cho in abstainers at TP3 returned to levels in LD.

RA improved between TP1 and TP2 on measures of visuospatial learning, aural attention/concentration, and visuomotor scanning speed and incidental learning (all $p < .001$). From TP2 to TP3, abstainers showed improvements in executive skills, processing speed, auditory-verbal learning, and general intelligence (all $p < .04$), while relapsers showed no cognitive improvements. At TP3, abstainers performed better than relapsers in most cognitive domains (all $p < .04$).

At TP1, RA visuomotor scanning speed and visuospatial memory correlated with cerebellar Cho ($r > .48$) and NAA ($r >. 62$, all $p <.02$). Incidental learning correlated with frontal GM NAA ($r = .62$) and cerebellar Cho ($r = .48$, all $p < .02$). Improvements of visuospatial learning and memory between TP1 and TP2 correlated with increases of cerebellar NAA ($r = 0.73$, $p = .04$).

At TP2, parietal and temporal WM NAA correlated positively with auditory-verbal memory and fine motor skills ($r > 0.57$; $p < .03$). By contrast, Cho and mI in multiple brain regions correlated inversely with auditory-verbal learning, visuospatial abilities, and general intelligence ($r < -0.42$, $p < .04$).

Conclusions

This is one of the first clinical multislice short-TE 1H MRSI studies suggesting widespread neuronal damage (i.e., decreased NAA) and membrane dysfunction (i.e., decreased Cho) in recently detoxified alcoholics. Recovery of Cho after 6-9 months of sobriety and persistently low levels of NAA after 6 to 9 months of sobriety suggest that membrane repair precedes neuronal recovery. Although NAA levels remained depressed during this time even in abstainers, their neurocognitive performance improved. Increasing cerebellar NAA during short-term recovery is associated with improving learning and memory functions, while high mI and Cho at TP2 are associated with poorer cognitive performance. Astrocytes are known to be involved in the mediation of neurotrophic factors, extracellular ions, and amino acid neuromodulators/neurotransmitters. Therefore, their proliferation during recovery from alcoholism, as suggested by longitudinal mI and Cho increases, may also be involved in the short and long-term recovery of cerebral neural tissue and cognitive function from chronic alcohol-induced brain damage. Longitudinal short-TE 1H MRSI allows monitoring metabolite changes throughout the brain and illuminates mechanisms potentially involved in recovery from alcoholism.