Volumetric Pseudo-Continuous Arterial Spin Label (PCASL) Imaging in Chronic Alcoholism: Return to Default Mode Network Activity Levels after a Spatial Working Memory Task

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Background. Current concepts of activity in neural networks differentiate activation in response to a task from activation while in a resting state, the latter activations occurring in the "default mode network (DMN)" (*1*). Given that selective functioning depends on local cerebral perfusion, disease-related disturbance of perfusion can have a profound influence on brain function. We examined recovering alcohol dependents and low-drinking controls with volumetric arterial spin labeling (ASL) measurements of regional cerebral blood flow (rCBF) under rest and task conditions. We expected that regions in the DMN would have higher CBF during rest than task conditions and thus be differentiated from task-activated regions; we also asked whether alcoholism would modify these patterns and further questioned whether DMN-related activation would return to pre-task levels in alcoholics as previously observed in healthy adults (*2*).

Subjects. The groups comprised 12 men with chronic alcoholism and 12 control men matched in age (mean of each group=46 years, range=38-54 years), education, and handedness. The alcoholics drank 36 times more alcohol in their lifetime than the controls; all but 1 alcoholic had refrained from drinking for at least 31 days. None of the controls were ever cigarette smokers, but 9 alcoholics were current or past smokers. All subjects gave written informed consent for study participation.

Methods. The protocol included 3 runs of a whole-brain pseudo-continuous ASL 3D perfusion sequence (PCASL) (*3, 4*) (TR=1381ms, TE=5.2ms, thick=5mm, skip=0mm, xy matrix=518x8; flip angle=155°, locations=36) and accompanying structural data (SPGR 1.3 mm thick and FSE 2.5mm thick) used for anatomical location of perfusion. The 3 PCASL acquisitions permitted quantification of rCBF during rest, a spatial working memory task (*5*), and a second rest, run in that order; subjects had eyes open in all 3 conditions.

The FSE and SPGR were used for skull stripping, image registration, and region identification. Bias-corrected FSE images were aligned with bias-corrected SPGR images via nonrigid registration (*6*). Skull-stripped images were generated by running FSL BET on the SPGR, early-echo, and late-echo FSE images separately, reformatting the two FSE masks into SPGR space, and combining the resulting brain masks by voting. The SPGR images were then segmented into three tissue classes (CSF, gray and white matter) using FSL FAST. For each subject and each PCASL, CBF data were aligned with the gray matter probability map because the CBF signal is predominantly in gray matter. Anatomical locations were identified with 18 parcellations (*2*) from the SRI24 atlas (*6*). Data were analyzed as raw CBF in ml/100cc of gray matter/min for each region for each condition. To account for subject differences in global CBF and to express the data in terms of effect size, each individual's data were normalized by dividing the CBF value of each voxel minus the mean of the whole brain CBF by the standard deviation of the whole brain CBF. All CBF images were reformatted into the coordinate space of the SRI24 atlas for group-average displays.

Results. The two groups achieved similar performance levels for accuracy and reaction time in the spatial working memory test. Despite higher incidence of smokers in alcoholics than controls, alcoholics had higher (albeit not significantly) average native, non-normalized, whole-brain cortical gray matter CBF values than controls in all PCASL conditions. Analyses (2-group by 3-condition ANOVAs; FDR p=.0028) performed on bilateral, normalized rCBF revealed 4 patterns: 1) DMN pattern (high activation for rest, low for task) was present in medial frontal (Fig. 1), temporal, calcarine, anterior and posterior cingulate, insular, and posterior precuneus cortices and the hippocampus-amygdala (p=.0001 for all but posterior cingulate p=.0357); 2) task-activated pattern (high activation for task, low for rest) occurred in parietal (p=.0285), occipital (p=.0334), and middle precuneus (p=.0014) cortices and inferior and superior cerebellum (p=.0001) (Fig. 2); 3) interaction pattern of anterior precuneus CBF (p=.0029) indicated opposing activation patterns in the groups, with controls showing the task-activation pattern and alcoholics showing the DMN pattern (Fig. 3); 4) modest group effects indicated lower CBF in alcoholics than controls in the insula (p=.0031), caudate/putamen (p=.026), and globus pallidus (p=.036). Neither group nor condition effects were significant in CBF in lateral frontal cortex, or thalamus.

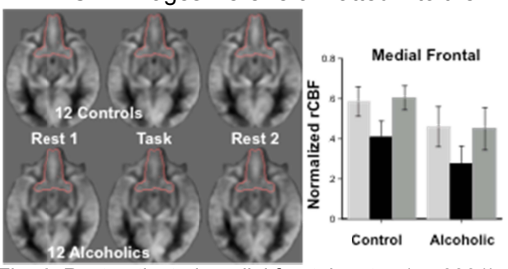

Fig. 1. Rest-activated medial frontal cortex (p=.0001). Rest 1=light gray, Task=black, Rest 2=dark gray.

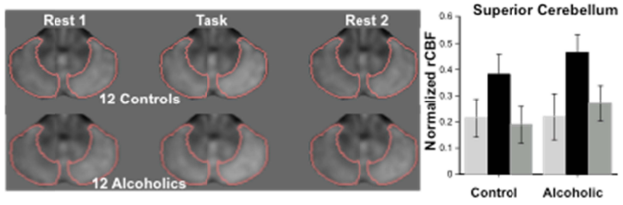

Fig. 2. Task-activated superior cerebellum (p=.0001). Rest 1=light gray, Task=black, Rest 2=dark gray.

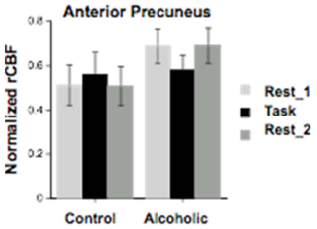

Fig. 3. Interaction pattern (p=.0029).

Discussion. Both groups exhibited the high-low-high pattern of regional perfusion levels in DMN regions during the rest-task-rest runs and the opposite pattern in posterior and cerebellar regions known to be associated with the spatial working memory task employed. The alcoholics showed selective differences from controls, however, in the rest-task-rest pattern of CBF activation in the anterior precuneus and of the CBF level in the insula, brain regions involved in addiction circuitry.

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References

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