The effects of alcohol on CSF flow and the glymphatic system

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The glymphatic system is a solute clearing system in the brain that uses the perivascular space as a site of exchange between CSF and brain parenchyma[1]. It is believed that glymphatic function is necessary for maintaining a healthy environment in the brain. Dysfuntion of the glymphatic system exacerbates plaque pathology and worsens cognitive scores in animal models of Alzheimer's disease. Alcohol is a widely consumed substance and it is known that excessive consumption of alcohol leads to dementia. We investigated the effects of alcohol on the glymphatic system in mice.

Methods: 6 months old C57bl6 mice received intraperitoneal injections the following doses of ethanol: 0.5 mg/kg (low), 1.5 mg/kg (medium) or saline as control, corresponding to 2 and 6 units of alcohol for a 70kg person. We performed cisterna magna injections of BSA-AlexaFlour647 through an implanted cannula in the awake state to avoid interactions between ethanol an anesthetics. Tracer influx was assessed after 30 mins and efflux was assessed after 180 mins using fluorescence microscopy of slices. Immunohistochemistry of GFAP and AQP4 was performed to assess gliosis after 30 days of ethanol treatment.

Results: Acute exposure to low dose ethanol increased tracer influx in perivascular pathways, whereas tracer influx was impaired by acute exposure to the medium dose of ethanol. Long term effects after 30 days exposure showed similar effects. Efflux at 180 mins was greater in mice that received low-dose ethanol compared to control. 30 days treatment of the medium dose of alcohol conferred gliosis measured by GFAP and AQP4 immunofluorescence signal.

Discussion: Low dose of ethanol (0.5 mg/kg) increases glymphatic influx after acute exposure and increases both influx and efflux after 30 days exposure, suggesting that this dose of alcohol enhances glymphatic function in 6 months old mice. The medium dose of ethanol (1.5 mg/kg) showed detrimental effects on glymphatic function both after the acute and chronic exposure, possibly mediated by network level activity after the acute exposure and gliosis after long-term exposure.

References: 1 Iliff JJ, Wang M, Liao Y, Plogg BA, Peng W, Gundersen GA, Benveniste H, Vates GE, Deane R, Goldman SA, Nagelhus EA, Nedergaard M. A paravascular pathway facilitates CSF flow through the brain parenchyma and the clearance of interstitial solutes, including amyloid β. Sci Transl Med. 2012 Aug 15;4(147):147ra111.

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