

# **Brain iron accumulation as a potential mechanism for alcohol-related cognitive deficits: results from a recent large observational study using a UK biobank**

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## Introduction

While it is acknowledged that alcohol consumption in large/moderate amounts has negative effects on cognition, the exact pathogenesis, despite different hypotheses, has not been fully clarified. It has been postulated that a possible pathway to alcohol-related cognitive dysfunction could involve iron accumulation. The implication-of-iron hypothesis, which has been investigated in the pathophysiology of neurodegenerative disorders, such as Alzheimer's and Parkinson's diseases, was also recently investigated in the UK by researcher Dr Anya Topiwala in observational studies suggesting a possible association between iron accumulation and alcohol-related negative effects on cognition.

## The observational biobank study in the UK and possible involvement of iron accumulation in alcohol-related brain pathology

In particular the results of a large observational study recently published by Dr. Topiwala tried to explain how moderate drinking might be linked to negative effects on cognitive function. The means by which alcohol consumption affects cognitive decline, as suggested by the observational study, may be through iron accumulation in the brain, as shown using brain MRI. The study included 20,729 UK Biobank participants recruited from 2006 to 2010. Participants were equally distributed by gender with a mean age of 54.8 years, and were divided into different categories according to self-declared alcohol consumption (i.e., current use, previous use or never used). The total weekly number of units of alcohol consumed for current drinkers was calculated, taking into account that one UK unit corresponds to 8 grams of alcohol. The weekly consumption was calculated and divided into quintiles, which used the lowest quintile as the reference category.

Brain iron levels were estimated in the study participants using MRI. Moderate drinkers, that is those drinking between 7–14 units (56–112 g) weekly showed lower total grey matter volumes. Moreover, brain MRI showed that the regions most affected by iron accumulation were deep brain structures of the basal ganglia, and putamen, caudate, hippocampi, thalami, and substantia nigra. Participants were also scanned using hepatic MRI as a marker of iron levels in the liver and indicator of systemic iron. Participants who drank at least 56 grams of alcohol a week or more showed higher susceptibility for iron accumulation in all brain regions. Nonetheless significant interactions in the association between alcohol and iron accumulation were proven with age but not with sex, smoking, or social conditions. As well as other factors such as blood pressure, cholesterol and menopause did not seem to alter the association between alcohol and iron accumulation in the brain in the analysis.

A cognitive battery, exploring different cognitive domains, in different subsets of patients was administered. Results of the study showed that poorer cognitive performance in certain tests **was** associated with increased iron in certain brain regions for those with moderate drinking. In particular alcohol consumption of more than 7 units (56 g) weekly was associated with iron accumulation in the basal ganglia as **evidenced** by neuroimaging in those **whose** with the poorest cognitive performance.

## Conclusions

While previous researches have investigated the negative effects of alcohol dependence/consumption on cognition, and other studies have investigated the possible correlation **between** iron levels and cognitive deficits, the potential link between iron accumulation and alcohol-related cognitive dysfunction was not established. This large observational study may indeed suggest that higher systemic iron levels may be partially mediated by alcohol consumption. Moreover, even moderate alcohol consumption is suggested to be responsible **for** iron accumulation in the brain. Although other additional mechanisms might be involved, and further studies will be needed, brain iron accumulation could be a possible mechanism for alcohol-related cognitive decline in moderate/high drinking.

## **References:**

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## **HIGHLIGHT BOX**

- Alcohol dependence has been linked to several neurodegenerative conditions and to negative effect on cognition
- A possible pathway to alcohol-related cognitive damage could be iron accumulation in the brain
- A possible role of iron in brain neurotoxicity is also supported by the demonstration of its accumulation in numerous neurodegenerative conditions including Alzheimer's and Parkinson's disease
- As investigated in a recent large observational study in UK biobank, using brain MRI and complete cognitive batteries, brain iron accumulation is a possible mechanism for alcohol-related cognitive deficits



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