

Link between anxiety and alcohol abuse identified

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New research from the University of Aberdeen and the University of Edinburgh has identified how sections of DNA might contribute to the risk of alcohol abuse in men.



Published in *Molecular Psychiatry*, the study found a section of DNA that switches on key genes in parts of the brain that control <u>alcohol</u> intake and mood.

Identified for the first time, these sections of DNA may act as future drug targets for the development of precision medicines to treat <u>alcohol</u> <u>abuse</u> and <u>anxiety</u> in men.

Dr. Alasdair MacKenzie who led the study at the University of Aberdeen explains: "Alcohol abuse kills millions of people around the world each year and can account for up to 8% of all male deaths. On top of this, there is evidence that the lockdown has contributed to increased anxiety and alcohol intake.

"Given the link between anxiety and alcohol abuse this increase is not really surprising. However, the questions remain; does anxiety lead to increased alcohol intake or does alcohol induce anxiety? Or, could there be a common mechanism driving both anxiety and alcohol intake?"

The team from both universities attempted to answer these questions by exploring human DNA to find genetic mechanisms that could contribute to the relationship between anxiety and alcohol.

Dr. MacKenzie explains "We know that the <u>human genome</u> contains gene sequences which encode the proteins that make up our cells. However, what we don't know is how these genes are turned on in the correct cells at the correct times to produce a healthy human body.

"The most up-to date research shows that the majority of changes in our DNA associated with disease might occur within enigmatic "enhancers" or "<u>switch</u>" areas that control where and when these genes should be switched on and off and this is where we have focused our efforts to answer these questions"



Once Aberdeen had identified this 'switch' section of DNA, Prof Andrew McIntosh and Dr. Toni-Kim Clarke from Edinburgh University, found that changes within the switch were linked to alcohol abuse in men who also suffered anxiety.

Dr. MacKenzie continued "This exciting and unexpected link prompted us to use CRISPR genome editing in mice to delete this switch from the mouse DNA.

"We then allowed the mice access to a choice of water or an alcohol mix. Ordinary mice drunk mostly from the bottle with alcohol. Surprisingly, the mice without the switch largely avoided the alcohol."

Dr. Andrew McEwan who also worked on the project in Aberdeen added: "What was particularly interesting was that, the male mice without the switch showed less signs of anxiety compared to the normal male <u>mice</u> who tended to hide." So the results of our mouse tests mirrored the results found in humans.

Dr. MacKenzie added: "This is the first time that a switch has been identified that has been linked to behaviors with such a major impact on human health. We believe that our unique approach provides a template for understanding the role of genetic switches in the development of other complex psychiatric diseases whose causes have so far evaded scrutiny."

More information: Andrew R. McEwan et al. CRISPR disruption and UK Biobank analysis of a highly conserved polymorphic enhancer suggests a role in male anxiety and ethanol intake, *Molecular Psychiatry* (2020). DOI: 10.1038/s41380-020-0707-7



Provided by University of Aberdeen

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