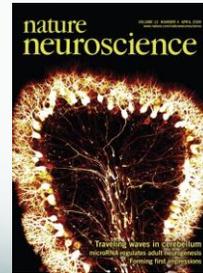


Chronic alcohol remodels prefrontal neurons and disrupts NMDAR-mediated fear extinction encoding

Presented by Rachel Au and Jacqui Mulholland
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- Monthly scientific journal published by the Nature Publishing Group
- Impact factor of 15.531
- Focuses on original research papers related to neuroscience

Authors

- Andrew Holmes
 - Faculty of 1000 Faculty Member
 - Chief Laboratory of Behavioral and Genomic Neuroscience, National Institute of Alcohol Abuse and Alcoholism, National Institutes of Health
- University of North Carolina Department of Pharmacology members Kristen E Pleil, Chia Li, Catherine A Marcinkiewicz, Thomas L Kash also worked closely with Holmes
- Also involved were Paul J Fitzgerald, Kathryn P MacPherson, Lauren DeBrouse, Giovanni Colacicco, Shaun M Flynn, Sophie Masneuf, Ozge Gunduz-Cinar & Marguerite Camp



Alcohol and Anxiety

- Commonly associated
- Anxiety symptoms are commonly attributed to a history of heavy drinking
- Not prevalent research to the effects of alcohol abuse on the risk for anxiety disorders



Previous Findings

- Fear extinction heavily recruits analogous regions across species
- Alcoholics exhibit deficits in PFC-mediated cognitive functions
- Medial prefrontal cortex is known to be integral in the development and extinction of fear association and the expression of emotional behavior



Hypothesis

Chronic alcohol impairs fear extinction by disrupting mPFC function



<http://www.addiction11.com/blog/wp-content/uploads/communication-skills-and-an-alcoholic-brain.jpg>

Groups

- Control group, received only air
- CIE group received enough vaporized ethanol to achieve ~175 mg dl⁻¹
- Exposure lasted 16 hours with an 8 hour break for 4 consecutive days, followed by a 3 day withdrawal
- This week long cycle was repeated four times
- Repeated exposure was chosen over acute exposure to mimic the effects of long term alcohol abuse

Test

- Exposed mice to a regimen of chronic induced ethanol (CIE) to mimic heavy alcohol abuse
- Trained to fear an auditory conditioned stimulus by pairing it with a foot shock
- Tested mice's fear extinction the next day by presenting the conditioned stimulus (sound) without the shock
- Measured fear by conditioned stimulus related freezing

Results

- Researchers found that both groups of mice had the same reactions during fear conditioning and the first extinction trial
- After the first trial however, there was a distinct difference between the CIE mice and those just given air
- Both groups showed extinction, but CIE mice had higher freezing rates



Figure 1a

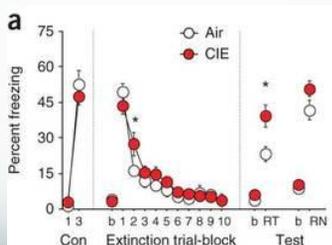
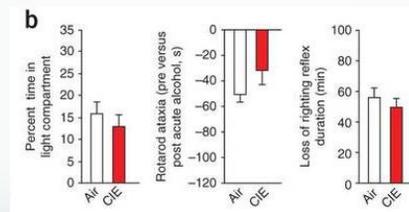
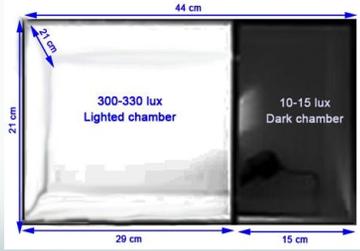


Figure 1b



Light Compartment test



Rotarod Ataxia test



Righting Reflex



Figure 2abc

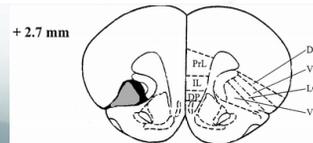
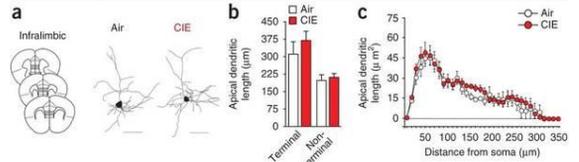
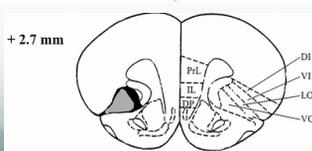
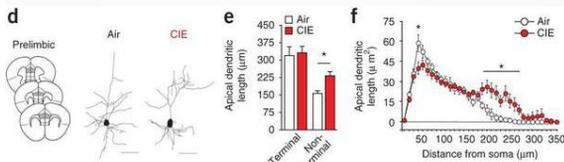


Figure 2def



Comparing infralimbic to prelimbic

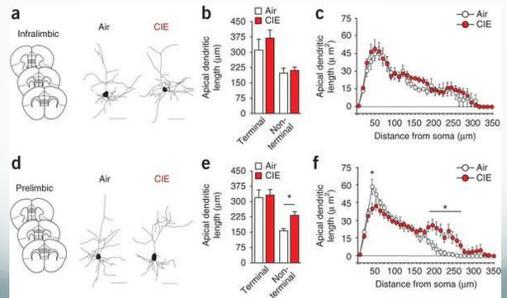


Figure 3a

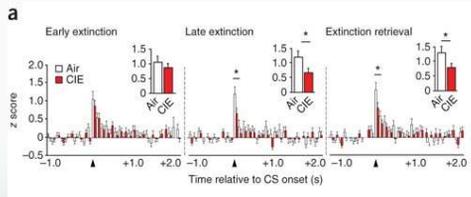


Figure 3bcd

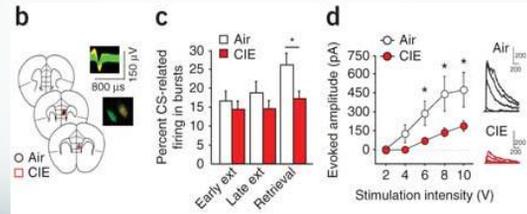
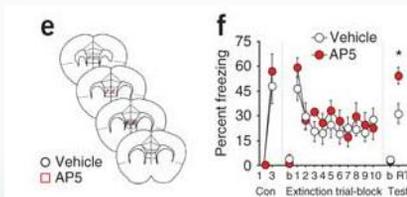


Figure 3ef

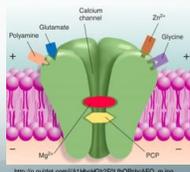


Summary

- Results indicate that CIE impairs fear extinction retention but does not disrupt memory formation or expression
- CIE does not appear to affect righting reflex, performance
- Dendritic morphology of the CIE and air mice is different

So what?

- Shows increased length of non-terminal infralimbic apical and terminal prelimbic dendrites in mPFC and decreased neural activity in response to stimuli
- mPFC is largely involved in the fear response pathway, specifically the NMDA receptors
- Glutamate receptor activation is necessary for NMDA activation
- Alcohol is shown to be a glutamate receptor blocker



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