Alcohol corrupts body movements by inhibiting sodium-potassium pumps in the cerebellum

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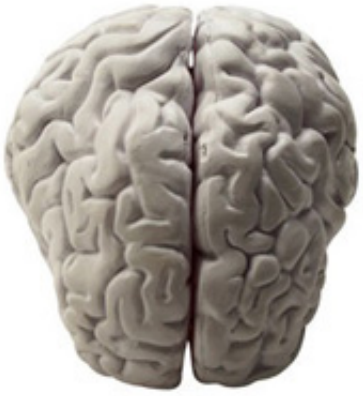

Alcohol is used, and in some cases abused, by millions of people worldwide. How it acutely changes brain function to cause inebriation, and chronically changes brain function to cause dependency, is largely unknown. The latter especially can destroy lives and families. Understanding the mechanisms of action is the foundation to countering them. A "sobriety pill" would have immense medical, sociological and commercial potential.

It is likely that the different aspects of the alcohol response are mediated by alcohol's action upon different molecular targets in different brain

regions.

The cerebellum is responsible for the control of body movements. Purkinje neurons in the cerebellum have a disproportionately pivotal role in cerebellar computation, being the final integrator in the canonical connectivity motif of the cerebellar cortex. Prior work has described alcohol's effect upon the firing pattern of cerebellar Purkinje neurons. However, these results are hard to understand with different Purkinje neurons showing different activity patterns before alcohol administration, and alcohol shifting different Purkinje neurons into different activity states. In this new paper, Dr. Forrest has used a novel mathematical model of a Purkinje neuron to show that all this diversity and complexity can be understood if alcohol modifies Purkinje neuron firing by inhibiting its sodium-potassium pumps. Indeed, Dr. Forrest and co-workers have previously shown that the sodium-potassium pump controls the intrinsic firing mode of Purkinje neurons and that the sodium-potassium pump is a computational element in the cerebellum and the brain. This is a significant reappraisal of the role of these pumps, which previously were thought to have no direct role in brain computations.

Alcohol consumption corrupts body movements, and this is a significant factor in a large number of accidental injuries and deaths every year. This corruptive effect to the motor system is widely considered an unwanted side effect of alcohol's coveted effects on mood and sociability. An alcoholic beverage ingredient that could counteract/block alcohol's effect upon the motor system and leave its other physiological effects intact would likely have commercial potential. However, this aim may be complicated because the cerebellum may control some higher-order cognitive and emotional functions in addition to its motor role, and may confer additional aspects to the alcohol response. Furthermore, alcohol may act upon other brain cells/regions by sodium-potassium pump inhibition. Further study is needed. But what is more clear is that a

"sobriety pill" would have to confront alcohol's detriment to sodium-potassium pump function. It could block alcohol's binding to, and/or alcohol's negative modulation of, sodium-potassium pump activity. Alternatively, it could stimulate sodium-potassium pumping. Alcohol may inhibit a proportion of sodium-potassium pumps, but if the activity of the remaining, uninhibited cohort can be increased, this may compensate.

More information: Forrest MD (2015) Simulation of alcohol action upon a detailed Purkinje neuron model and a simpler surrogate model that runs >400 times faster. *BMC Neuroscience* 16(1):27. , www.biomedcentral.com/1471-2202/16/27

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