

# Acute Ethanol Alters GABA and MyoInositol in Human Brain

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## Background

Ethanol facilitation of  $\gamma$ -aminobutyric acid-A (GABA<sub>A</sub>) receptor function is responsible for a component of ethanol intoxication [1], and GABAergic adaptations contribute to ethanol tolerance, dependence, and withdrawal. During withdrawal, reduced GABAergic function is implicated in the adverse effects of early sobriety, including seizures and neurotoxicity, but little is known about the acute effects of ethanol on the GABAergic system in humans.

## Methods

Eight non-dependent drinkers enrolled and completed the study. Subjects were first scanned to ensure ability tolerance for the MR environment. Then in the Hospital Research Unit subjects were administered ethanol intravenously (IV) with a computer-driven protocol that is fine-tuned for each subject [2]. The protocol raised breath ethanol levels to 60 mg% (similar to 2-3 drinks) in 20-30 minutes obtaining breath samples every 1-2 minutes and venous blood samples every 10 minutes. The final session consisted of the same IV infusion in a 4 Tesla magnet (Bruker Instruments, Billerica, MA, USA) while performing J-difference editing of GABA. In the magnet, breath samples could not be obtained, but venous blood samples were measured every 10 minutes to verify reproduction of the original breath ethanol profile. Metabolites were quantified as percentages of their initial values, except ethanol, normalized to its final value.

## Results

Brain ethanol rose with plasma ethanol (Fig. 1) but venous ethanol lagged (Fig. 1). GABA fell an average of 17% by 10 minutes of infusion and remained there throughout the study ( $p = 0.033$ ; Fig. 2). Glutamate rose 5-14% over the time course and returned to normal by one hour ( $p = 0.05$ ). MyoInositol dropped steadily to 16% below normal ( $p = 0.007$ ) by one hour. Tissue water did not change.

## Conclusions

Brain ethanol kinetics appear to follow breath alcohol kinetics closely, although % visibility is not addressed here. Brain GABA levels is rapidly reduced by ethanol. Further studies are required to assess the impact on GABAergic activity.

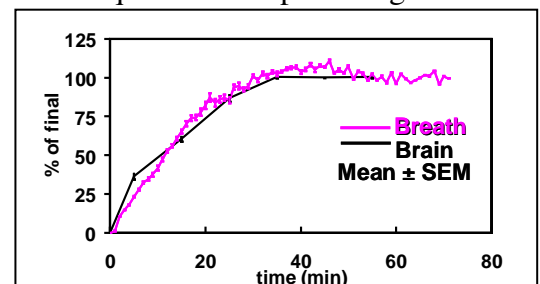


Fig. 1. Average alcohol profiles of breath and brain with IV ethanol.

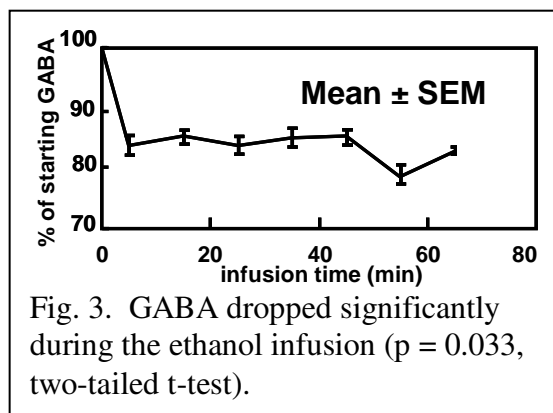


Fig. 3. GABA dropped significantly during the ethanol infusion ( $p = 0.033$ , two-tailed t-test).

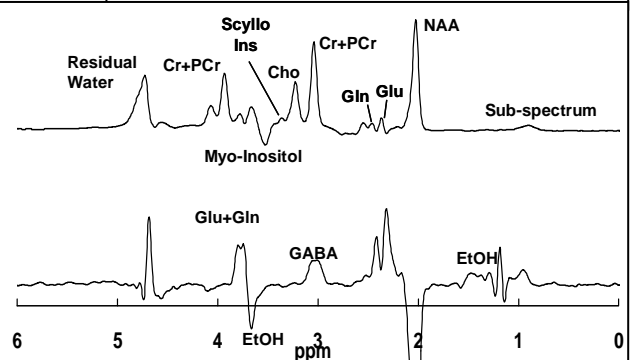


Fig. 2. Subspectrum and edited difference spectrum during ethanol administration.

## References

1. Buck, K.J., Behavior Genetics, 1996. **26**: p. 313-323.
2. Ramchandani, V.A., S. O'Connor, T. Blekher, D. Kareken, S. Morzorati, J. Nurnberger, Jr., and T.K. Li, Alcoholism: Clinical & Experimental Research., 1999. **23**: p. 1320-30.