Subjective Memory Impairment and Subjective Cognitive Improvement: Role for D-C2H5OH (Deuterated Ethyl Alcohol)? Results of a Double-Blind, Crossover Trial

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ABSTRACT

Subjective memory impairment (SMI) is a common complaint among older people. We performed a double-blind, placebo-controlled study[1] which showed that deuterated two carbon fragments ameliorated the condition but at the expense of objective memory function. Future studies are needed to confirm the results before endorsing the treatment of SMI with deuterated ethyl alcohol.

INTRODUCTION

Subjective memory impairment (SMI) is an increasingly prevalent problem as the population ages. It is defined by the self-perception of memory impairment that has not been recognized by others, and has not led to an objective decline in intellectual and social function. For research purposes, it is confirmed by normal objective memory testing. It is also an increasingly popular focus of clinical research. Using the PubMed search engine, the first paper published on this subject dates from 1975, with 158 listed in PubMed as of this writing, with more than half indexed since 2015. While some people with SMI go on to develop dementia, whether the risk is increased compared to age-matched controls remains unknown. On the opposite end of the subjective cognition spectrum, subjective cognitive improvement (SCI) is defined by the self-perception that one's memory or cognitive capabilities are stronger than they had been self-perceived at some well-defined baseline.

Preliminary experiments (unpublished) have shown that ethyl alcohol (ethanol) in small amounts (60–120 ml), given in a non-blinded fashion, produces a profound benefit both on SMI and SCI. Because elimination half-life of ethanol depends on serum levels, the effect of the drug is variable and unpredictable. And, although a large variety of over-the-counter formulations of ethanol are available, their bioavailability and concentrations are not subject to the same quality controls as FDA-approved medications. Using a patented deuteration technology used in FDA-approved formulations of tetrabenazine and amantadine, in which a neutron added to one carbon atom of this 2-carbon compound, the half-life and side-effect profile of ethanol was significantly altered to improve compliance and reliability. D-ethyl alcohol, the deuterated form, has been found to be tasteless.

METHODS

After approval by an Institutional Review Board (IRB),[3] 50 subjects over the age of 70 with no history of medical, psychiatric problems or substance abuse, were recruited from a convenience population of attendees at a Patriots' football game in December 2017. After obtaining signed informed consent, volunteers were enrolled if they met inclusion criteria of baseline blood alcohol level of 0, scores on The Montreal Cognitive Assessment (MoCA) >28, Ten Item Memory Recall Test (TIMER)>6, with complaints of SMI and a score>21 on the Subjective Memory Impairment Inventory Test (SMIT), indicative of moderate to severe SMI. All subjects rated themselves on the Clinical Global Impression Scale, a 0-7 scale rating their SMI from 0, not present, to 7, extremely severe. All subjects were then invited to begin the protocol within 2-4 weeks of screening. They were asked to refrain from alcohol intake for the week before the baseline visit and during the 6 weeks of the study. Blood alcohol level (BAL) was measured, and if 0, subjects were tested on the SMIT and Subjective Cognitive Assessment Battery (SCAB). Subjects were then given 60 ml of study drug or placebo at noon of the test day, and re-tested at hours 2, 4 and 8 for blood levels of study drug, SMIT, SCAB, TIMER and CGIS. This was repeated daily for 2 weeks, followed by a washout period of 2 weeks. Subjects were then crossed over to the other treatment arm. At the end of the trial subjects were asked to choose which treatment arm

they thought they had been assigned to for each part of the study. Next generation statistical metrics using Bonferoni-Friedman-Fake Data imputations for non-reliable data, artificially contracted Student-t tests, and the standard Stata programs were used to smooth outcome results.

RESULTS

Forty-eight (48) subjects completed the protocol. One withdrew due to problems related to liver function and the other to a subdural hematoma sustained in a fall. None were thought to be study-drug related. On the first day, subjects showed a mean improvement of 5.3 points on the SMIT at 2 hours ($p<0.01$), 4.8 at 4 hours ($p<0.02$) and 5.0 at 8 hours ($p<0.01$). The CGIS also showed similar improvement with 3 at 2 hours, 3.4 at 4 hours, 3.4 at 8 hours (all $p<0.04$). Interestingly, the TIMER revealed worsened memory, with declines of 1.2, 1.1, 1.2 at hours 2, 4 and 8 (all $p<0.2$). The SCAB scores improved by 2.1, 2.2 and 2.3 at hours 2, 4 and 8 (all p values <.03). However, over the course of the 13 subsequent days, the changes associated with the study drug waned mildly so that, although statistically significant benefits in SMIT, SCAB and CGIS were sustained through day 8, no results were statistically significant by day 14. There were no statistically significant changes in the placebo arms. SCAB scores, indicative of subjective improvement, were inversely correlated with TIMER, objective memory changes ($p<0.5$).

CONCLUSION

D-ethyl alcohol was found to improve subjective memory impairment, subjective cognitive capabilities, and the clinical global impression of memory function. However, objective measure of memory function worsened, revealing that objective measures had an inverse correlation with subjective benefit. We believe that these results suggest a role for D-C2H5OH in the treatment of subjective memory impairment, and good tolerance. Future research will be needed to confirm our results and determine if higher doses or doses given 12 hours apart will produce longer lasting benefits. (April Fool. This is an entirely fictional study. Deuterated ethanol does not exist, so far as we are aware.) ❖

[*Editor's note: This commentary continues a decades-old tradition of Dr. Friedman's 'April Fools' Day' commentaries. In this dire time, RIMJ hopes it provides a moment or two of levity to RIMJ's readers.*]

Disclosures

Conflict of interest:
Consultation fees from Neutronix Pharmaceuticals[2]

References

1. Journal of Meaningless Research (Friedmania publications, Inc.). 2019,16(7):187-88.
2. A subsidiary of VampireSquid Investments. Motto: "Life is healthier when wealthier."
3. Friendly IRB of America, mail order division, #31X526L.2019.

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