Gender differences in the alcohol-related alterations P.6.b.008 in cortical activity – a combined TMS-EEG study

Outi Kaarre^{1,2}, Elisa Kallioniemi³, Mervi Könönen^{4,5}, Tommi Tolmunen^{1,6}, Virve Kekkonen¹, Petri Kivimäki², Noora Heikkinen², Florinda Ferreri⁷, Eila Laukkanen^{1,6}, Sara Määttä^{4,8}

> ¹Department of Adolescent Psychiatry, Kuopio University Hospital ²Doctoral Programme of Clinical Research, School of Medicine, University of Eastern Finland ³Brain Stimulation Laboratory, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine ⁴Department of Clinical Neurophysiology, Kuopio University Hospital ⁵Department of Clinical Radiology, Kuopio University Hospital **UNIVERSITY OF** ⁶Department of Psychiatry, School of Medicine, University of Eastern Finland EASTERN FINLAND ⁷ Department of Neurology, Universita Campus Bio-Medico di Roma ⁸Department of Clinical Neurophysiology, Institute of Clinical Medicine, Faculty of Health Sciences, University of Eastern Finland



Kuopio

University

Hospital

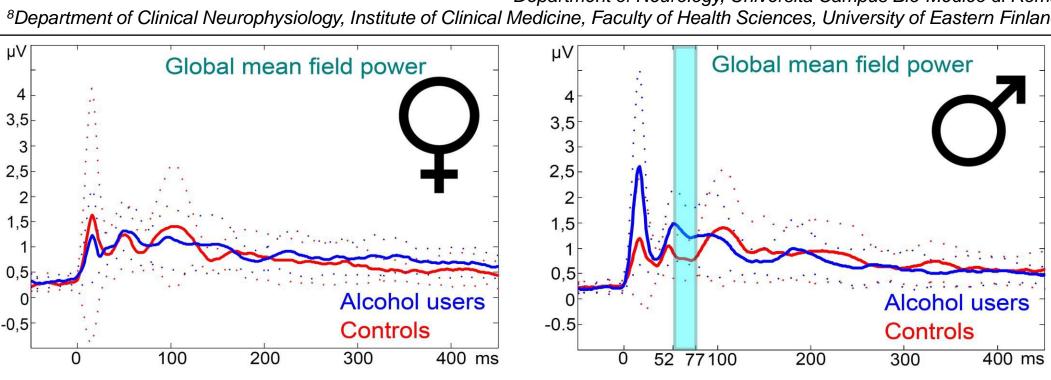


Figure 1. TMS-EEG.

Figure 2. GMFP in females (left) and males (right). Standard deviation presented with dotted lines. Significant difference marked with a blue box.

BACKGROUND

- Long-term alcohol use harms brain functioning in adolescence. The effects of alcohol are particularly mediated by alterations in GABAergic neurotransmission (1).
- Neuroimaging: simultaneous electroencephalogram (EEG) recording with transcranial magnetic stimulation (TMS) enables direct, in vivo exploration of cortical excitability and assessment of effective and functional connectivity (Figure 1).
- After motor cortex stimulation, the TMS-evoked EEG potentials (TEPs) N45 and N100 are known to reflect GABA-A- and GABA-B-ergic functioning, respectively (2).

RESULTS

- Global-mean field power (GMFP): The total activity of EEG was significantly increased in the male alcohol users' group between 52 – 77 ms (p<0.05) (Figure 2).
- Females and males tested separately with Linear mixed model
 - TEP N45 amplitude: In both genders, a significant group*AP interaction was found (females: p=0.003, males: p<0.001). The significant difference was located frontally in both genders, the N45 amplitude being larger in alcohol users (left panel in Figure 3).
 - TEP N100 amplitude: In males, a group*AP difference was encountered (p < 0.001), which can be seen in dissimilar topographic distribution (upper right panel in Figure 3).

AIMS

- The aim of the current study was to explore whether long-term alcohol use in adolescence affects the cortical activity of the male and female brain differently.
- Previously, we have demonstrated that alcohol use in adolescence is associated with altered cortical activity (3).

METHODS

- ✤ 27 (11 males) young adults with heavy 10-year alcohol use in adolescence and 25 (12 males) controls with little or no alcohol use participated in TMS-EEG measurements.
- 61-channel EEG was registered
 - TMS targeted to the motor cortex (M1); 150 stimuli
 - Intensity of TMS was 90% of the resting motor threshold of the abductor pollicis brevis muscle
- Data analysis: MATLAB with the EEGLAB toolbox
- Statistical analyses: IBM SPSS Statistics, version 22
 - Linear mixed model with 2 groups (users vs. controls) and
 - anterior-posterior regions (frontal, central, parieto-3 occipital) was used for statistical analyses.

References

1 Hillmer, A. T., Mason, G. F., Fucito, L. M., O'Malley, S. S., & Cosgrove, K. P. (2015). How imaging glutamate, gamma-aminobutyric acid, and dopamine can inform the clinical treatment of alcohol dependence and withdrawal. Alcoholism: Clinical and Experimental Research, 39(12), 2268-2282.

2 Premoli, I., Castellanos, N., Rivolta, D., Belardinelli, P., Bajo, R., Zipser, C. et al. (2014). TMS-EEG signatures of GABAergic neurotransmission in the human cortex. Journal of Neuroscience, 34(16):5603-5612.

3 Kaarre, O., Kallioniemi, E., Könönen, M., Tolmunen, T., Kekkonen, V., Kivimäki, P., Heikkinen, N., Ferreri, F., Laukkanen, E., and Määttä, S. (2016) Heavy alcohol use in adolescence is associated with altered cortical activity: a combined TMS-EEG study. Addiction Biology, doi: 10.1111/adb.12486.

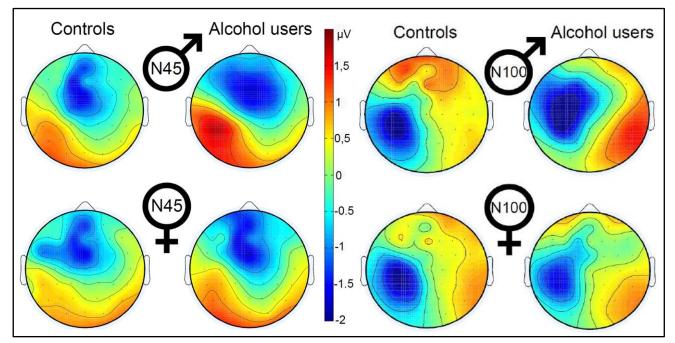


Figure 3. The N45 and N100 components at the time of group specific mean latencies.

CONCLUSIONS

Our results support the hypothesis that alcohol use affects the developing brain differently in males and females.

Interestingly, in males, alcohol use was associated with more pronounced findings: altered GMFP and GABA-A- and GABA-B-ergic cortical functioning, whereas in females the alterations were found only in the GABA-A-ergic activity. The relationship between sex hormones and neurotransmission should be further studied.

Disclosure: There are no potential conflicts of interest.

Copyright ©2017 Outi Kaarre et al. Correspondence to: outi.kaarre@kuh.fi

Outi Kaarre

Outi Kaarre combines clinical work with research and Ph.D. studies. She graduated from the University of Kuopio, Finland with a MD degree in 2005. She has over ten years' clinical work experience in the field of psychiatry and adolescent psychiatry. Having finished her specialist's degree in adolescent psychiatry in the University of Eastern Finland in 2014, she works in outpatient care at the Kuopio University Hospital.

Being interested in neuroscience and especially developing brain, she started her Ph.D. studies in the spring 2015 at the University of Eastern Finland, in the Doctoral Programme of Clinical Research. She is a doctoral student in the *Adolescents and Alcohol* research group in the Kuopio University Hospital and focuses on examining how long-term alcohol use affects the young developing brain, especially neurophysiological functioning. Of particular interest are alcohol use related changes in the brain electrical activity, measured using transcranial magnetic stimulation combined with electroencephalography (TMS-EEG). So far, she has published two articles as the first author.

In her spare time she is the head of the Doctors' Association of Pohjois-Savo. In the 30th ECNP Congress, she is a winner of the ECNP Travel Award. Kaarre can be reached by email at outi.kaarre@kuh.fi.



