Taurine and dopamine-related effects of ethanol

- an experimental study in rodents

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i hörsal Arvid Carlsson, Medicinaregatan 3, Göteborg, den 12 december 2019, klockan 09.00

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Avhandlingen baseras på följande delarbeten

I. Ericson M, **Ulenius L**, Andrén A, Jonsson S, Adermark L, Söderpalm B. (2019). Different dopamine tone in ethanol high- and low-consuming Wistar rats. *Addiction Biology* 2019; doi: 10.1111/adb.12761

II. **Ulenius L**, Andrén A, Adermark L, Söderpalm B, Ericson M. The influence of sub-chronic taurine administration on locomotor activity and nucleus accumbens dopamine following ethanol. Submitted 2019

III. **Ulenius L**, Adermark L, Andrén A, Ademar K, Söderpalm B, Ericson M. The role of astrocytes in regulating taurine and dopamine interactions during ethanol exposure. Manuscript

IV. **Ulenius L**, Adermark L, Söderpalm B, Ericson M. (2019). Energy drink constituents (caffeine and taurine) selectively potentiate ethanol-induced locomotion in mice. *Journal of Pharmacology, Biochemistry and Behavior* 2019; doi: 10.1016/j.pbb.2019.172795

SAHLGRENSKA AKADEMIN
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Taurine and dopamine-related effects of ethanol

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Abstract

The reinforcing properties of alcohol (ethanol) are associated with activation of the mesolimbic dopamine system and the concomitant increase in dopamine in the nucleus accumbens (nAc). Changes in this system are thought to be a predominant underlying factor in promoting excessive alcohol intake and alcohol use disorder. We have previously shown that a simultaneous increase in endogenous taurine is required in order for ethanol to increase nAc dopamine levels, and hypothesize that taurine, which acts as an osmoregulator, is released in order to re-equilibrate the osmotic pressure. The intake of taurine has escalated over the last decade due to consumption of taurine-containing energy drinks, but whether a long-term intake of taurine induces adaptations influencing ethanol-induced dopamine elevation is not clear. Thus, the overall aim of this thesis was to investigate correlations between taurine and dopamine during ethanol exposure, with special focus on the nAc. To this end, behavioral tests were combined with neurochemical measurements and gene expression analysis performed in rodents. Our data show that systemically administrated taurine enters the CNS, a process that is not influenced by sub-chronic taurine treatment. Even though acute exposure does not increase locomotion, repeated exposure leads to behavioral sensitization to the drug, and taurine combined with caffeine potentiates ethanol-induced locomotion, a phenomenon previously linked to the reinforcing properties of the drug. By means of *in vivo* microdialysis we show that rats consuming high levels of ethanol respond with a blunted taurine elevation in response to acute ethanol treatment, and exhibit a lower dopamine tone compared to rats consuming low amounts of ethanol. At the same time, repeated taurine exposure does not influence the dopamine elevating properties of ethanol. By combining microdialysis with pharmacological and chemogenetic manipulations, we found that ethanol-induced taurine release is not action potential dependent and may involve astrocytes and volume regulated anion channels (VRACs). In conclusion, we suggest that increased nAc taurine levels following ethanol exposure mainly derives from astrocytes and involves VRACs, supporting an osmoregulatory role of taurine. Even though ethanol-induced dopamine release is not influenced by sub-chronic taurine exposure, taurine could contribute to the increase in alcohol consumption seen in humans drinking alcohol mixed with energy drinks.

Keywords: Addiction, alcohol, caffeine, nucleus accumbens, microdialysis

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