

DANDRITE LECTURE

Choroid plexus paracrine signaling regulates nicotine craving.

Abstract: Cellular mechanisms that govern the risk of relapse to tobacco use in abstinent smokers are poorly understood. Using unbiased whole-brain cFos mapping and functional magnetic resonance imaging in rodents, we identified brain regions in which neural activity was by nicotine. This revealed that the activity of neurons in the triangular septal nucleus (TSn), a largely unexplored component of the limbic system, was persistently inhibited during nicotine abstinence. Connectomic profiling showed that TSn neurons innervate brain regions that regulate mood, memory, and motivation, including the medial habenula (mHb). Disruption of TSn-mHb signaling by nicotine triggered intense craving-like behavior during abstinence, while stimulating TSn-mHb signaling attenuated nicotine craving. Spatial and single-cell transcriptional profiling showed that nicotine remodels choroid plexus epithelia surrounding the TSn to reduce the secretion of insulin-like growth factor-2 (IGF2) and other regulatory proteins into ventricular cerebrospinal fluid (CSF). IGF2 treatment rescued nicotine-induced deficits in TSn activity and abolished nicotine craving. These findings suggest that choroid plexus-derived factors in the CSF regulate the fidelity of septo-habenula communication and that perturbations in this paracrine network drive nicotine craving and relapse.

Host: Anna Klawonn



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Date: **Tuesday 29 October 2024**
Time: **10.00 - 11.00**
Venue: **1170 - 347**
Address: **Ole Worms Allé 3**
8000 Aarhus C

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