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Nicotine Addiction Functional Networks: A Whole-Brain Connectome Analysis in 24,000 Individuals

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Nicotine addiction is a complex neuropsychiatric disorder that profoundly impacts brain function through interactions with neural pathways. Despite its significance, the impact of nicotine addiction on the whole-brain functional connectome remains largely unexplored. To address this gap, we conducted a whole-brain analysis using resting-state functional magnetic resonance imaging (rs-fMRI) scans from a large sample of 31,934 adults aged 40+ participating in the UK Biobank study. We employed a data-driven network analysis to 1) compare the resting-state functional connectivity (rsFC) between smokers (n=1392) who consistently reported as current smokers at baseline and imaging visits and non-smokers (n=30,542) included subjects who were either never exposed to smoking or have smoked but less than 100 cigarettes in life; 2) identify functional connectome subnetworks specifically related to nicotine addiction. The results revealed two nicotine-addiction-related subnetworks with organized topological patterns (permutation p-values <0.001). The first nicotine-addiction-related subnetwork exhibits a *rich-club* structure that consists of basal ganglia regions (e.g., nucleus accumbens) as *hubs* and 181 regions as peripheral nodes based on The Human Brainnetome Atlas[1]. Reduced rsFC within the first subnetwork among smokers suggest a dominant role of basal ganglia in nicotine addiction. The second subnetwork, consisting of ventral/dorsal attention, visual, and frontalparietal regions, also demonstrate decreased rsFC in smokers. These results suggest significant alterations associated with nicotine addiction in the communication and coordination among the basal ganglia and the broader brain-wide networks, as well as a nicotine-addiction-related disruption in the connectivity patterns.

1. Fan L, Li H, Zhuo J, et al. The Human Brainnetome Atlas: A New Brain Atlas Based on Connectional Architecture. Cereb Cortex N Y NY. 2016;26(8):3508-3526. doi:10.1093/cercor/bhw157