Fact Sheet 4: Nicotine and the Brain

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Abstract

People with mental illness (MI), alcohol use disorder, and other substance use disorders (SUDs) have higher tobacco smoking and e-cigarette use rates than the general population. Mood and anxiety disorders, suicidal ideation, depressive symptoms, and negatively perceived mental health are all associated with smoking AND e-cigarette use. There is evidence that early smoking is a risk factor for developing a mental illness and difficulty quitting as an adult. Notwithstanding, there are myths that nicotine is benign in the brain and may have little impact on mental health or other substance use and abuse, their progress and clinical treatment. This Fact Sheet describes *some* of nicotine's structural and functional effects on the brain, which is detrimental to brain development and growth.

Individuals with MI and SUDs are motivated to quit smoking. Smoking cessation improves symptoms and quality of life in those with mental illness to the same degree as SSRIs improve mood or anxiety disorders. There is no evidence that nicotine abstinence interventions negatively affect abstinence from alcohol and other substances. Furthermore, the same interventions that are effective for the general public also work for those with MI and SUDs. Strategies include pharmacotherapies, education around smoking, and smoking cessation counselling.

1. Nicotine is a highly addictive alkaloid in tobacco products and acts as a nicotinic acetylcholine receptor agonist (Benowitz, 2009).

2. Nicotine exposure during brain development can lead to lasting changes in the brain's number and function of nicotinic acetylcholine receptors (Dwyer et al., 2009).

3. Nicotine exposure during adolescence can lead to alterations in the structure and function of the prefrontal cortex, a brain region involved in executive functions such as planning and decision-making (Goriounova & Mansvelder, 2012).

4. Nicotine disrupts the microarchitecture of the corpus callosum and other white matter tracts (Kangiser et al., 2019; Umene-Nakano et al., 2014).

5. In the perinatal period & adolescence, nicotine exposure disrupts hippocampus structure, functioning, and related learning and memory (Zeid et al., 2018).

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6. Nicotine exposure can lead to changes in the structure and function of the anterior cingulate cortex, a brain region involved in emotional regulation and impulsivity control (Chen et al., 2022).

7. Nicotine exposure can lead to changes in the function of the amygdala, a brain region involved in emotional processing and the hypothalamic-pituitary-adrenal axis (Shen et al., 2017).

8. Nicotine exposure reduces monoamine oxidase (MAO) A and B activity in the basal ganglia and reduces alpha4beta2 nicotinic acetylcholine receptor (nAChR) availability in the thalamus and putamen (Sharma & Brody, 2009; Yu et al., 2018).

9. Nicotine exposure can lead to changes in the levels of neurotransmitters, such as dopamine and serotonin, which can affect brain function and behaviour (Alasmari et al., 2019; Benowitz, 2009).

10. Nicotine exposure can lead to changes in the expression of genes involved in brain development and function, particularly those related to neuroplasticity and neurogenesis (Goriounova & Mansvelder, 2012).

11. Nicotine exposure can lead to increased oxidative stress and inflammation in the brain, contributing to neuronal damage and dysfunction (Mishra et al., 2015).

12. Nicotine impairs the action of endothelial nitric oxide in the brain, reducing cerebral blood flow (Toda & Okamura, 2016).

13. Nicotine, by reducing cerebral blood flow, promotes the deposition of B-amyloid plaques, the hallmark of Alzheimer's Disease (Toda & Okamura, 2016).

14. Nicotine exposure decreases neuronal GLUT1 expression and glycolysis whilst up-regulating α7 nAChR expression (Sifat et al., 2018).

15. Nicotine exposure promotes hypothalamic secretion of corticotropin-releasing hormone, disrupting the HPA axis & potentially disinhibiting pro-inflammatory cascades (Rohleder & Kirschbaum, 2006).

16. Nicotine exposure can lead to changes in the brain's response to drugs of abuse, as it can potentiate the reinforcing effects of other psychoactive substances (DiFranza, 2016).

17. Nicotine exposure increases the dopaminergic response to alcohol consumption in the nucleus accumbens, a brain region that links motivation and action (Tolu et al., 2017).

18. Nicotine exposure can lead to changes in the brain's response to aging, affecting the integrity of the blood-brain barrier, inflammation and oxidative stress, and the brain's regenerative capacity (Heldt et al., 2020).

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19. Nicotine exposure can lead to changes in the brain's response to neurodegenerative diseases, such as Parkinson's and Alzheimer's, as it can affect the integrity of the blood-brain barrier, inflammation and oxidative stress, and the brain's regenerative capacity (Mazzone et al., 2010).

20. Nicotine exposure can lead to changes in the brain's response to neurodevelopmental disorders, such as ADHD, as it can affect the integrity of the blood-brain barrier, inflammation and oxidative stress, and the brain's regenerative capacity (Lee & Lee, 2023; Poirier et al., 2017).

21. Nicotine appears to alter the brain's response to pain by altering the expression of endorphins and GABA (Zhang et al., 2020).

22. Finally, many chemicals may interact with nicotine in the brain, enhancing nicotine uptake. Importantly today, electronic cigarettes or vapes may contain menthol to enhance usage, but exposure in conjunction with nicotine can enhance dopamine neuron excitability to nicotine, increasing use and dependence and making it harder to quit nicotine (Alsharari et al., 2015; Wickham, 2015, 2020).

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