

## Nicotine Gum in Psychiatry Investigation: A Promising Tool for Brain Plasticity and Rehabilitation in Some Disorders

Thiago P. Fernandes<sup>1,2</sup>, Natanael A. Santos<sup>1,2</sup>, Givago S. Souza<sup>3</sup>

<sup>1</sup>Federal University of Paraiba, Joao Pessoa, Brazil

<sup>2</sup>Perception, Neuroscience and Behavior Laboratory, Federal University of Paraiba, Joao Pessoa, Brazil

<sup>3</sup>Federal University of Para, Belem, Brazil

Dear Editor,

In our brain, more specifically, the expression of nicotine acetylcholine receptors (nAChRs) is selective and is still unclear, which justifies further studies. However, to this date, there is more knowledge on the nicotine effects than was before and hence this is the purpose of this prelude. What are the benefits of nicotine use for psychiatric investigation? Is this feasible or just a myth?

Here, we report that nicotine gum (an easy, low-cost, and reliable form of nicotine administration) can be used as a tool for recovery, protection, and improvement of neuronal and sensory processes.<sup>1-7</sup> We are not postulating that one form of nicotine administration is better than another, but it is essential to bear that the choice to use nicotine gum over other forms of nicotine administration is mainly due to its low cost, rapid absorption (compared to transdermal patches, for example), high bioavailability, easy consumption, availability in low doses (e.g., 2-mg or 4-mg), and fewer side effects than the other forms.<sup>8</sup>

Recently, interesting debates on how desensitization of nAChRs can occur in particular conditions were observed and reported. Briefly, desensitization is something to be careful of in clinical practice<sup>9</sup> since it can affect the reward system. Although the action of nicotine on the cholinergic system has some positive aspects, in certain sensory and cognitive domains such as working memory and executive functions,<sup>4,10</sup> and is also considered as a neuroprotective agent for conditions such as Parkinson's Disease and Alzheimer's Disease,<sup>1,11</sup> these are aspects that should be considered before the use of nicotine gum—since not all psychiatric conditions, necessarily, would need or be aided by this pharmacological tool.

Nicotinic receptors are found throughout the nervous system, having a very complex expression throughout the nervous system. Due to this variety, nAChRs can represent pleiotropy, that is have different expressions in the organism. These effects, which have behavioral and brain implication, sometimes make long-term study in humans difficult.<sup>3</sup> However, the findings so far are relevant and provide evidence of its use. The effects of nicotine on the dopaminergic system, for example, are described as an important element in the reward system in animals and humans.<sup>12</sup> The presence of nAChRs in the cell bodies of dopaminergic neurons in the ventral tegmental area and in their endings in the nucleus accumbens may contribute to the reinforcement of the reward system.<sup>12,13</sup> That is, nicotine-induced modulations of dopamine release led to the maintenance of cigarette self-administration,

**Corresponding author:**

Thiago P. Fernandes

**E-mail:**

thiagompfernandes@gmail.com

**Received:** October 4, 2022

**Accepted:** December 9, 2022

**Publication Date:** January 26, 2023

Cite this article as: Fernandes TP, Santos NA, Souza GS. Nicotine gum in psychiatry investigation: A promising tool for brain plasticity and rehabilitation in some disorders. *Neuropsychiatr Invest.* 2023;61(1):40-41.



Content of this journal is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

contributing both to strengthening and avoiding the negative strengthening (anhedonia or dysphoria) induced by withdrawal.<sup>13</sup>

Nicotine administration has been used not only as an important tool in smoking cessation<sup>14</sup> but also as a neuroprotective agent against neurodegenerative diseases. Since nicotine modulates acetylcholine and, consequently, dopamine in neurotransmission pathways such as the nigrostriatal pathway, which is impaired in Parkinson's Disease, its use can cause an improvement or cause protection before further damage occurs. Still, studies indicate that the cortex is selective for processing visual information, where the right hemisphere responds better to the processing of low spatial frequencies and the left hemisphere responds better to high spatial frequencies.<sup>15</sup> This type of processing can serve as a basis for future studies that are interested in using nicotine gum in conditions where there is damage in one of the hemispheres, such as stroke.

Finally, we are not pointing out or mentioning the use of nicotine gum as the sole or gold standard tool for possible neuronal remediation, but it brings up discussions of the possibility of its use under controlled research and its possible application for some diseases, as already observed. All these results need to be interpreted with caution. Some questions still need to be answered, but this prelude proposes to contribute in different areas of knowledge aiming at inspiring other researchers and understanding.

---

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - T.P.F., N.A.S., G.S.S.; Design - T.P.F., N.A.S., G.S.S.; Supervision - T.P.F., N.A.S., G.S.S.; Resources - T.P.F., N.A.S., G.S.S.; Literature Search - T.P.F., N.A.S., G.S.S.; Writing Manuscript - T.P.F., N.A.S., G.S.S.

**Declaration of Interests:** The authors have no conflicts of interest to declare.

**Funding:** Support for this work was provided by a grant from the National Council for Scientific and Technological Development (CNPq), to T.P. Fernandes (163780/2020-0).

## REFERENCES

1. Quik M, O'Leary K, Tanner CM. Nicotine and Parkinson's disease; implications for therapy. *Mov Disord.* 2008;23(12):1641-1652. [\[CrossRef\]](#)
2. Fernandes TP, Hovis JK, Almeida N, et al. Effects of Nicotine Gum Administration on Vision (ENIGMA-Vis): study protocol of a double-blind, randomized, and controlled clinical trial. *Front Hum Neurosci.* 2020;14:314. [\[CrossRef\]](#)
3. Fernandes TP, Butler PD, Rodrigues SJ, et al. Short-term effects of nicotine gum on facial detection in healthy nonsmokers: a pilot randomized controlled trial. *J Addict Dis.* 2021;39(1):15-25. [\[CrossRef\]](#)
4. Almeida NL, Rodrigues SJ, Gonçalves LM, et al. Opposite effects of smoking and nicotine intake on cognition. *Psychiatry Res.* 2020;293:113357. [\[CrossRef\]](#)
5. Fernandes TP, Oliveira MEC, Silva GM, Santos NA. Improvement in visual performance after nicotine gum administration in tobacco use disorder: a case report. *J Addict Dis.* 2022;40(4):568-576. [\[CrossRef\]](#)
6. D'Mello DA, Bandlamudi GR, Colenda CC. Nicotine replacement methods on a psychiatric unit. *Am J Drug Alcohol Abuse.* 2001;27(3):525-529. [\[CrossRef\]](#)
7. Gross J, Stitzer ML. Nicotine replacement: ten-week effects on tobacco withdrawal symptoms. *Psychopharmacol (Berl).* 1989;98(3):334-341. [\[CrossRef\]](#)
8. Aslani A, Rafiei S. Design, formulation and evaluation of nicotine chewing gum. *Adv Biomed Res.* 2012;1(1):57. [\[CrossRef\]](#)
9. Picciotto MR, Addy NA, Mineur YS, Brunzell DH. It is not "either/or": activation and desensitization of nicotinic acetylcholine receptors both contribute to behaviors related to nicotine addiction and mood. *Prog Neurobiol.* 2008;84(4):329-342. [\[CrossRef\]](#)
10. Silva GM, Almeida NL, Souto JJS, Rodrigues SJ, Fernandes TP, Santos NA. Does chronic smoking affect performance on a go/no-go task?. *Curr Psychol.* 2022;41(11):7636-7644. [\[CrossRef\]](#)
11. Akaïke A, Takada-Takatori Y, Kume T, Izumi Y. Mechanisms of neuroprotective effects of nicotine and acetylcholinesterase inhibitors: role of alpha4 and alpha7 receptors in neuroprotection. *J Mol Neurosci.* 2010;40(1-2):211-216. [\[CrossRef\]](#)
12. Damsma G, Day J, Fibiger HC. Lack of tolerance to nicotine-induced dopamine release in the nucleus accumbens. *Eur J Pharmacol.* 1989;168(3):363-368. [\[CrossRef\]](#)
13. Balfour DJK, Munafò MR. *The Neuropharmacology of Nicotine Dependence.* Berlin: Springer; 2015.
14. Hartmann-Boyce J, Chepkin SC, Ye W, Bullen C, Lancaster T. Nicotine replacement therapy versus control for smoking cessation. *Cochrane Database Syst Rev.* 2018;5(5):CD000146. [\[CrossRef\]](#)
15. Kauffmann L, Ramanoël S, Peyrin C. The neural bases of spatial frequency processing during scene perception. *Front Integr Neurosci.* 2014;8:37. [\[CrossRef\]](#)