Tactile Stimulation Activates the BDNF Signaling Cascade in the *Substantia nigra* of Rats Previously treated with Haloperidol

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INTRODUCTION: Tactile stimulation (TS) is a sensory intervention commonly used to investigate animal behavioral mechanisms and neurobiological changes. TS has shown beneficial effects across various neuropsychiatric conditions, from the neonatal period to adulthood. It has been demonstrated to enhance neurogenesis and neuroplasticity, prevent depressive-like behaviors and the adverse effects of stress, and reduce anxiety-like responses. However, the underlying mechanisms of TS in the brain remain unclear. First-generation antipsychotics, such as haloperidol, are associated with severe side effects, including extrapyramidal syndrome (e.g., parkinsonism, akathisia, and tardive dyskinesia), which significantly impair patients' quality of life. OBJECTIVE: This study aimed to evaluate the effects of TS in rats previously treated with haloperidol and to investigate the molecular changes in the *Substantia nigra*. MATERIALS AND METHODS: Twenty-four male rats received haloperidol for twenty-one days. During the final fourteen days of treatment, rats underwent TS three times a day for 15 min per session. At the end of the experimental protocol, animals were anesthetized and euthanized. The *Substantia nigra* was dissected following the Paxinos and Watson atlas for subsequent molecular analyses. RESULTS: TS restored *Grβ* mRNA levels after haloperidol treatment, activating the glucocorticoid response element *Rack1*, which promotes BDNF transcription. This effect was evidenced by increased expression of the *Bdnf long* isoform and mBDNF, along with activation of its signaling cascade, as shown by elevated levels of AKT and S6 proteins. CONCLUSION: These findings suggest that TS may induce beneficial neurobiological effects in the brain, enhancing neurogenesis and neuroplasticity.

Keywords: Typical antipsychotic; Handling; Neuroplasticity;

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