Abstract
Therapeutic Strategies for Chromium-Induced Neurotoxicity: Exploiting NPTX2 and Autophagy Pathways in CNS Cells †
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Introduction: Chromium is the most prevalent metal present on earth in two valence states: hexavalent [Cr(VI)] and trivalent [Cr(III)]. Hexavalent chromium [Cr(VI)] is widely recognized as a teratogen, mutagen, and neurotoxin to humans. Chromium-induced autophagy is a novel avenue which involves a plethora of cellular and molecular intricacies, including the identification of the novel NPTX2 (neuronal pentraxin 2) as a critical mediator of chromium-induced autophagy dysregulation in CNS cells. NPTX2 has a broad expression pattern in the brain, with a principal role in synaptic plasticity and neuronal survival.

Material and Methods: This review compiles the most recent research on the molecular processes of chromium-induced autophagy, with a particular emphasis on NPTX2 as a mediator in the cells of the CNS. Research on NPTX2 expression patterns in different brain areas and its role in autophagy dysregulation in response to chromium exposure was compiled. In addition, we looked at the signaling pathways and processes that were involved in the dysregulation of autophagy caused by chromium, such as the inhibition of mTOR, the activation of ULK1, and the interaction of NPTX2 with Beclin-1.

Results: Abnormal autophagosome synthesis, lysosomal dysfunction, and improper autophagic substrate degradation are symptoms of disturbed autophagy, which is caused by an increase in NPTX2 expression in response to chromium exposure. The inhibition of mTOR, activation of ULK1, and interaction between NPTX2 and Beclin-1 are all components of the intricate signaling pathways that contribute to autophagy dysregulation. Furthermore, non-traditional pathways like peroxiphagy are involved; in this process, chromium-induced oxidative stress harms peroxisomes, which are then selectively engulfed by autophagosomes through PINK1/Parkin signaling, reducing cellular damage.

Conclusions: Targeting peroxiphagy and pharmacological interventions which restore autophagic flux offer the potential to reduce chromium-induced neurotoxicity.

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