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Short Report

Subsequent Effects of Glyphosate and the Neuropeptide PACAP on Neurobehavioral Functions in Mice

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Abstract

Glyphosate (GLY), the most widely used herbicide worldwide, has been linked to neurological dysfunctions, while Pituitary adenylate cyclase-activating polypeptide (PACAP) exhibits neuroprotective properties. This short report investigates the effects of GLY exposure and PACAP treatment on neurobehavioral functions in Swiss albino mice. Behavioral assessments including Tail Suspension Test, Dark/Light Box, Elevated-Plus-Maze, and Open Field Test revealed that repeated GLY exposure induces anxiety- and depression-like behaviors, whereas co-treatment with PACAP alleviates these effects. Our findings highlight PACAP as a potential therapeutic candidate against glyphosate-induced neurobehavioral impairments.

Keywords: Traumatic, Stroke, Pneumocephalus

Introduction

Organophosphate compounds, widely applied in agriculture, are known to affect neurological function and neurobehavioral performance [2,5]. Glyphosate (GLY) is the active ingredient in the most widely used herbicide worldwide [1]. Pituitary adenylate cyclase-activating polypeptide (PACAP) is a 38-amino-acid neuropeptide of the secretin/glucagon/vasoactive intestinal peptide (VIP) family with neuroprotective properties [3,4]. This study evaluates the behavioral consequences of GLY exposure and the neuroprotective role of PACAP in mice.

Materials and Methods

Sexually mature male Swiss albino mice were treated with GLY and/or PACAP for 15 days. Behavioral tests performed after 48 hours included: Tail Suspension Test (TST) for depressive-like behavior, Dark/Light Box test for anxiety, Elevated-Plus-Maze for open space-induced anxiety, and Open Field Test for locomotor and anxiety behavior. Behavioral parameters were recorded via Ethovision XT Noldus 8.5 and analyzed using GraphPad Prism 8.0. Data are mean ± SD. Statistical significance was assessed with one-way ANOVA and Tukey's post hoc test (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).

Results

GLY exposure increased immobility in TST, indicating heightened depressive-like behavior (**). Co-treatment with PACAP reduced immobility time compared to GLY alone,

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demonstrating antidepressant-like effects. In the Dark/Light Box test, GLY-treated mice displayed more crossings and increased time in the bright compartment (****), whereas PACAP reduced these behaviors (@@@@). In the Elevated-Plus-Maze, GLY mice spent less time in open arms; co-treatment with PACAP moderated this effect, suggesting anxiolytic properties. Open Field Test confirmed increased anxiety-like thigmotaxis and defecation in GLY-treated mice; PACAP ameliorated these behaviors.

Conclusion

GLY exposure induces anxiety- and depression-like behaviors in mice, while PACAP co-treatment mitigates these effects. These findings support PACAP as a potential neuroprotective agent against glyphosate-induced neurobehavioral impairments and provide insights into mechanisms underlying pesticide-related mood disorders.

Author Contributions

Conceptualization: B.E., E.H.; Methodology: B.E., A.C.; Investigation: B.E., E.H., A.C.; Data curation: B.E.; Writing – original draft: B.E.; Writing – review & editing: E.H., M.M.K.; Supervision: M.M.K. All authors have read and approved the final manuscript.

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Institutional Review Board Statement

Not applicable.

Conflicts of Interest

The authors declare no conflict of interest.

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