SN56 neuronal glutamate transmission dysfunction after 24 h and 14 days chlorpyrifos exposure.

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INTRODUCTION

Chlorpyrifos (CPF) is an insecticide described to induce cognitive disorders, both after acute and repeated administration. However, the mechanisms through which it induces these effects are unknown. CPF produces basal forebrain (BF) cholinergic neuronal cell death, involved on learning and memory regulation, which could be the cause of such cognitive disorders. Neuronal cell death was partially mediated by oxidative stress generation, P75NTR and α7-nAChRs gene expression alteration triggered through acetylcholinesterase (AChE) variants disruption, suggesting other mechanisms are involved. CPF alters glutamatergic transmission, which have been related with BF cholinergic neuronal cell death and development of cognitive disorders. According to these data, we hypothesized that CPF induces BF cholinergic neuronal disruption of glutamatergic transmission.

METHODS

We evaluated this hypothesis in septal SN56 basal forebrain cholinergic neurons, after 24 h and 14 days CPF exposure.

RESULTS

This study shows that CPF increases glutamate levels. CPF increases glutaminase activity and upregulates the VGLUT1 gene expression, which could mediate the disruption of glutamatergic transmission.

CONCLUSIONS

Our results provide new understanding of the mechanisms contributing to the harmful CPF effects, and its possible relevance in the pathogenesis of neurodegenerative diseases.