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Consumption of a High-Fat Diet in Adulthood Ameliorates the Effects of Neonatal Parathion Exposure on Acetylcholine Systems in Rat Brain Regions

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Running title: High-Fat Diet Ameliorates Parathion Developmental Effects

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Key words: Acetylcholine
Brain development
High-fat diet
Organophosphate insecticides
Parathion

Abbreviations: ACh, acetylcholine
ANOVA, analysis of variance
ChAT, choline acetyltransferase
HC3, hemicholinium-3
nAChR, nicotinic acetylcholine receptor

Descriptors: Neurodevelopment, Developmental Biology

Outline of Section Headers

Abstract

Introduction

Materials and Methods
- Animal treatments and diet
- Assays
- Data analysis

Results

Discussion

References

Figure Legends

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ABSTRACT

Background: Developmental exposure to a wide variety of developmental neurotoxicants, including organophosphate pesticides, evokes late-emerging and persistent abnormalities in acetylcholine (ACh) systems. We are seeking interventions that can ameliorate or reverse the effects later in life.

Objectives: We administered parathion to neonatal rats and then evaluated whether a high-fat diet begun in adulthood could reverse the effects on ACh systems in adulthood.

Methods: Neonatal rats received parathion on postnatal days 1-4 at 0.1 or 0.2 mg/kg/day, straddling the cholinesterase inhibition threshold. In adulthood, half the animals were switched to a high-fat diet for 8 weeks. We assessed three indices of ACh synaptic function: nicotinic ACh receptor binding, choline acetyltransferase activity and hemicholinium-3 binding. Determinations were performed in brain regions comprising all the major ACh projections and cell bodies.

Results: Neonatal parathion exposure evoked widespread abnormalities in ACh synaptic markers, encompassing effects in brain regions possessing ACh projections as well as ACh cell bodies. In general, males were affected more than females. Of 17 regional ACh marker abnormalities (10 male, 7 female), 15 were reversed by the high-fat diet.

Conclusions: A high-fat diet reverses neurodevelopmental effects of neonatal parathion exposure on ACh systems. This points to the potential for nonpharmacologic interventions to offset the effects of developmental neurotoxicants. Further, cryptic neurodevelopmental deficits evoked by environmental exposures may thus engender a later preference for a high-fat diet to maintain normal ACh function, ultimately contributing to obesity.