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Neuropsychological sequelae from acute poisoning and long-term exposure to carbamate and organophosphate pesticides

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Abstract

This research examines the effects of different degrees of pesticide exposure on neuropsychological performance. Exposures varied from acute poisoning coupled with chronic exposure to low or high levels of chronic exposure (defined by years of exposure). A cross-sectional neuropsychological and biochemical study was conducted in greenhouse farmers from southern Spain: data from 24 acutely poisoned workers and 40 non-poisoned but chronically (low or high) exposed sprayers were compared to 26 controls. We examined performance on 21 neuropsychological tests that assessed attention, memory, praxis, gnosis, motor coordination, naming and reasoning and also examined values of plasmatic cholinesterase. Results indicated statistically significant neuropsychological deficits in the acute poisoning and high chronic exposure groups after controlling for confounds, whereas similar performance was seen in the low chronic exposed subjects and controls. Subjects who were acutely poisoned performed worse than the other groups on perceptual, visuomotor, visual memory and mood state domains. Both the acutely poisoned and the chronically high exposed subjects obtained significantly lower scores in the perceptual, verbal memory and visuomotor domains. Levels of butyrylcholinesterase were related to the seasonal sprayer activity except in the case of acutely poisoned subjects. Conclusions: Both acutely poisoned long-term workers and chronically high (>10 years) exposed workers exhibited similar disturbances in perception and visuo-motor processing, in the absence of any related acute effect of butyrylcholinesterase inhibition. In the case of acutely poisoned subjects, verbal and perceptive learning and recall and constructive abilities were also impaired. These results point to the need for follow-up studies to assess the possible sequelae of chronic and acute exposure to pesticides and their interactions.

Keywords: Chronic exposure; Long-term sequelae; Neuropsychological profile; Pesticide poisoning

1. Introduction

Organophosphates (OP) and carbamates are widely used as pesticides in industry, farming and chemical warfare. These toxic compounds can be absorbed through the skin, mucous membranes, gastrointestinal and the respiratory tracts, and produce their toxic effects by the inhibition of acetylcholinesterase (AChE) and the subsequent accumulation of synaptic acetylcholine (ACh) in peripheral and central nervous systems [8,20,40]. Acute effects from pesticide poisoning include nicotinic and muscarinic symptoms [24]. Furthermore, exposure to high concentrations of these cholinesterase inhibitors (CIs) may have chronic or long-term effects that have been linked to delayed-onset peripheral neuropathies and neuropsychological changes [17]. In the latter case, the delayed effect may result from the permanent inhibition of different serine hydrolases such as the neuropathy target esterase (NTE), which yields a covalent modification of an active serine residue site, producing a permanent inhibition of the enzyme. Nevertheless, this irreversible inhibition may not be the direct cause of the neuropathy, but the results of a new function of the modified enzyme, which would be toxic [18].

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A number of studies have reported psychological and neuropsychological effects, together with motor impairments after acute poisoning episodes [9,17,33,35,38,43,45]. Although the dysfunctions vary according to the task, the type of pesticide and the severity of poisoning, the above studies all describe a common profile of impaired cognitive functions and altered mood states: decreased academic abilities, motor skills, increased psychological distress, post-traumatic stress disorder, as well as self-reported symptoms of depression, irritability and confusion.

Nevertheless, in most of these studies there has not been adequate control of the time elapsed between the poisoning event and the subsequent evaluation, making it difficult to distinguish between acute alterations after poisoning and long-term sequelae. A number of epidemiological studies suggest neurobehavioural and/or neurocognitive effects after long-term exposure to pesticides [3,10,11]. Especially remarkable in this context are the studies which reveal a linear relationship between degree of exposure, in terms of years working with pesticides, and neuropsychological impairment [19].

The purpose of our work was to evaluate the possible long-term neurocognitive sequelae produced by acute intoxication with OP and carbamates (acute poisoning group) in comparison with non-acutely poisoned, but nevertheless chronically exposed individuals with exposures for a number of years to these same compounds (chronic exposure groups). With the exception of only one case, all the subjects diagnosed with acute hypercholinergic syndrome due to pesticide exposure were greenhouse workers who had been exposed to pesticides for a variable number of years, who all returned to the same job immediately after recovery. We decided to compare their neuropsychological performance with that of subjects from a previous study in which we evaluated the effects of chronic subacute exposure. In this previous study [32], we demonstrated a significant relationship between long-term exposure (more than 10 years working with pesticides) and impaired neuropsychological performance (perceptual functioning, visuomotor praxis and integrative task performance time).

2. Materials and methods

2.1. Participants

In southeastern Spain, a large part of employment and income is concentrated in intensive agriculture in greenhouses. These are crops grown under plastic of 70×15 km, corresponding to almost 30,000 ha of greenhouses.

We recruited by phone 24 poisoned farmers (acutely *poisoned group*) who received treatment in the Internal Medicine Department of the Hospital de Poniente (Almeria, Spain) and who had suffered accidental poisoning with OP and/or carbamates within the past 3 months (between September and November, 1997). The farmers were all Spanish men, aged 16–66 years at the time of testing, literate and with a score of at least 28 on the MSE [22], a mini-mental status exam. Participants did not have a history of any disease or condition that could induce nervous system damage (except previous intoxication) or interfere with testing. Subjects who had suffered intentional poisoning (volitional suicide) were excluded. Twenty-two subjects were poisoned while carrying out agricultural work: spraying, blending pesticides or handling them without using the protective equipment. One subject was poisoned while harvesting the crop and another suffered a massive accidental ingestion (by mistakenly drinking a glass of methomyl). All the acutely poisoned subjects required medical assistance in the Emergency Unit: shower and atropine in almost all the cases, and antiemetics in two cases (activated charcoal and gastric wash). On arrival at the hospital, the Glasgow Coma Scale was completed for all the patients (average 15 points, S.D.=0) and the cholinesterase levels and symptoms and substances that caused the intoxication were recorded. The mean cholinesterase level was significantly lower than the normal range (between 4.900 and 12.200 units; see Fig. 1a). The most frequently reported symptoms of poisoning included nausea, abdominal pain, excessive sweating, general weakness, salivation, headache, vomiting, blurred vision, muscle cramps and breathing difficulties. No

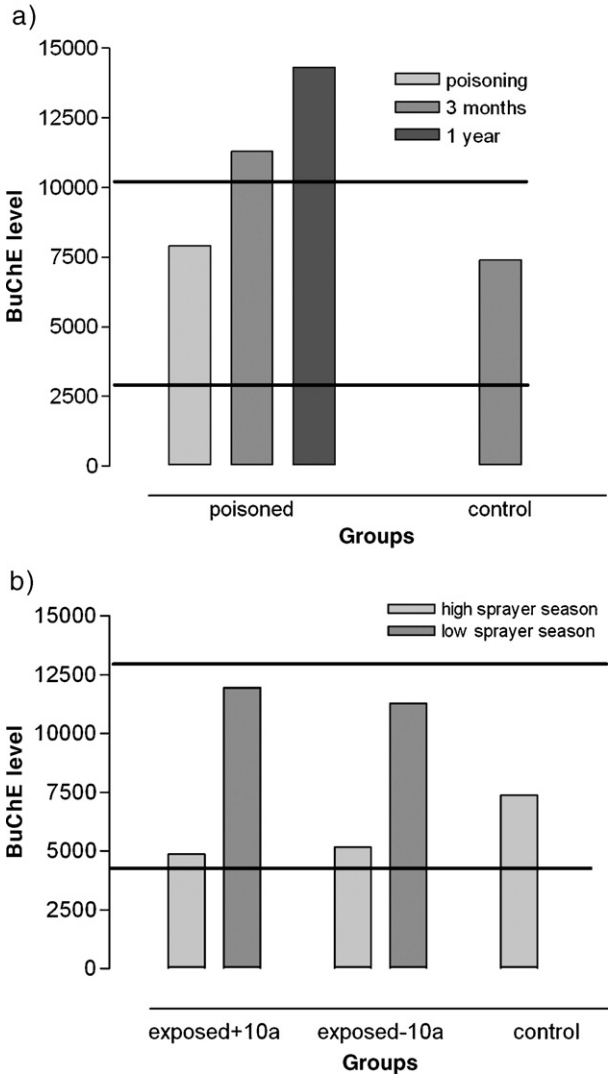

Fig. 1. (a) Cholinesterase level in poisoned and control groups. (b) Cholinesterase level in exposed and control groups.