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Original Article

Potential short-term neurobehavioral alterations in children associated with a peak pesticide spray season: The Mother's Day flower harvest in Ecuador

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ABSTRACT

Background: Exposures to cholinesterase inhibitor pesticides (e.g. organophosphates) have been associated with children's neurobehavioral alterations, including attention deficit and impulsivity. Animal studies have observed transient alterations in neurobehavioral performance in relation to cholinesterase inhibitor pesticide exposures; however, limited evidence exists regarding transient effects in humans.

Methods: We estimated the associations between neurobehavioral performance and time after Mother's Day flower harvest (the end of a heightened pesticide usage period) among 308 4-to 9-year-old children living in floricultural communities in Ecuador in 2008 who participated in the ESPINA study. Children's neurobehavior was examined once (NEPSY-II: 11 subtests covering 5 domains), between 63 and 100 days (SD: 10.8 days) after Mother's Day harvest (blood acetylcholinesterase activity levels can take 82 days to normalize after irreversible inhibition with organophosphates).

Results: The mean (SD) neurobehavioral scaled scores across domains ranged from 6.6 (2.4) to 9.9 (3.3); higher values reflect greater performance. Children examined sooner after Mother's Day had lower neurobehavioral scores than children examined later, in the domains of (score difference per 10.8 days, 95%CI): Attention/Inhibitory Control (0.38, 0.10–0.65), Visuospatial Processing (0.60, 0.25–0.95) and Sensorimotor (0.43, 0.10–0.77). Scores were higher with longer time post-harvest among girls (vs. boys) in Attention/Inhibitory Control.

Conclusions: Our findings, although cross-sectional, are among the first in non-worker children to suggest that a peak pesticide use period may transiently affect neurobehavioral performance, as children examined sooner after the flower harvest had lower neurobehavioral performance than children examined later. Studies assessing pre- and post-exposure measures are needed.

1. Introduction

Early life exposures to commonly applied agricultural pesticides have been associated with neurobehavioral delays in children. In particular, organophosphate exposures have been associated with attention deficit hyperactivity disorder symptoms, including decreased attention and inhibitory control (Bouchard et al., 2011; Eskenazi et al., 2007; Horton et al., 2012; Kofman et al., 2006; Marks et al., 2010; Rauh et al., 2011, 2006), and there is growing evidence in children and animals that males may be more susceptible to the harmful effects of pesticide exposures than

Abbreviations: AChE, acetylcholinesterase; BChE, butyrylcholinesterase; ESPINA study, The Secondary Exposure to Pesticides among Children and Adolescents Study.

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females (Dam et al., 2000; Horton et al., 2012; Johnson et al., 2009; Levin et al., 2001; Marks et al., 2010; Suarez-Lopez et al., 2013). Organophosphate insecticides exert their toxicity through inhibition of acetylcholinesterase (AChE) activity, which is an important regulator of the neurotransmitter acetylcholine, and likely through direct toxicity to neurons and glia (Abou-Donia, 2003; Aldridge et al., 2005; Qiao et al., 2003; Slotkin, 2004). We previously reported that lower AChE activity was associated with lower attention, inhibitory control and memory scores, among boys but not girls, within the Secondary Exposure to Pesticides among Children and Adolescents (ESPINA: Estudio de la Exposición Secundaria a Plaguicidas en Niños y Adolescentes) study, which examined children living in Ecuadorian floricultural communities (Suarez-Lopez et al., 2013).

A limited number of experimental studies indicate that pesticide exposures can also induce transient (subacute) decreases in neurobehavioral performance. In rats and zebrafish, single or recurrent exposures to organophosphates have been associated with initial decreases in neurobehavioral performance, followed by neurobehavioral improvement with greater time after removal of the exposure (Levin et al., 2003; Maurissen et al., 2000; Middlemore-Risher et al., 2010). Although limited information exists, human evidence appears to be congruent with experimental findings: seasonal use of pesticides has been found to increase pesticide exposures and to decrease neurobehavioral performance of agricultural workers (Khan et al., 2014; Rohlman et al., 2015). Furthermore, adults intoxicated with pesticides had lower neurobehavioral performance which improved over time (Delgado et al., 2004).

The objective of the present study was to estimate the associations between time after a peak pesticide spray season (Mother's Day flower harvest) and neurobehavioral performance among participants of the ESPINA study. This study examined children who lived in agricultural communities in Ecuador, but who did not work in agriculture. ESPINA study participants were examined during a low flower production season, but within approximately 100 days after Mother's Day (May). Mother's Day is one of the holidays with the most flower sales worldwide, and it is celebrated in May in 63% of countries in the world including the populous countries of China, India, USA, Brazil and Pakistan. Although the half-lives of organophosphates pesticides are short, normalization of erythrocytic AChE activity levels after irreversible inhibition (enzymatic aging) by organophosphates may take up to 3 months (Mason, 2000) and seasonal alterations of neurobehavioral performance may last for months after the end of pesticide applications (Rohlman et al., 2015). In the present study, we hypothesized that children assessed earlier in the examination period (closer to the end of the Mother's Day flower harvest) had lower neurobehavioral scores than children examined later.

2. Material and methods

In 2008, we examined 313 healthy 4- to 9-year-old children and surveyed their parents as part of the ESPINA study in Pedro Moncayo County, Pichincha, Ecuador. Most participants of the ESPINA study (73%) were recruited from their participation in the "2004 Survey of Access and Demand of Health Services in Pedro Moncayo County", collected by Fundacion Cimas del Ecuador in collaboration with the communities of Pedro Moncayo County. This was a representative survey of the county which obtained information of 71% of the population of Pedro Moncayo County, Ecuador and measured height and weight of 33% of children under the age of 5 years.

To supplement recruitment, new volunteers (27% of total sample) living in Pedro Moncayo County were also recruited through community announcements performed by leaders and governing councils, and by word of mouth. The ESPINA study aimed to have a balanced distribution of participants living with floricultural workers and non-agricultural workers. Participation of children was sought if they met the following criteria: cohabitation with a floricultural worker for at least one year for the group of children living with a floricultural worker; among children living with non-agricultural workers, they must have never cohabited with an agricultural worker, never inhabited a house where agricultural pesticides were stored and having no previous direct contact with pesticides. The ESPINA study comprises participants living in all 5 parishes of Pedro Moncayo county and has similar socio-economic and racial distributions as the general population of the county. Detailed participant recruitment information has been described elsewhere (Suarez-Lopez et al., 2012). Parents provided informed consent for themselves and for permission of participation of their children. Participants who were at least 7 years old provided assent for participation in the study. In total, 308 children had complete data for this study. This study was approved by the Institutional Review Boards of Fundación Cimas del Ecuador, the University of Minnesota and the University of California San Diego.

2.1. Floriculture in Pedro Moncayo County

The floriculture industry is central to the economy of Pedro Moncayo county using 5.3% of the geographic area (Gobierno Municipal del Canton Pedro Moncayo, 2011) (1800 ha) and employing 21% of all adults in the county (Suarez-Lopez et al., 2012). The Ecuadorian floriculture industry uses many different pesticides (mostly insecticides and fungicides), of which diethyldithiocarbamate fungicides and organophosphate insecticides are commonly used (Grandjean et al., 2006; Harari, 2004). There is tremendous worldwide demand for flowers for Christmas (December 25), Valentine's Day (February 14), Easter (March/April) and Mother's Day (2nd Sunday in May). Flower plantations, thus, increase their production and pesticide use around October and decrease production in May. After the Mother's Day harvest, the production slows substantially for the summer months. In response to countries' strict no-tolerance policies for the importation of crops with pests (U.S. Department of Agriculture, 2012), the usage of pesticides in floriculture increases as crops mature and continue until soon (days or hours) prior to the harvest (Harari, 2004; Narvaez et al., 2002).

2.2. Measures

Each child was examined once during the period of lowest flower production of the year, and within 100 days after the Mother's Day harvest (July 10 through August 15, 2008). During this 37-day period, examinations took place on 20 weekdays days, averaging 15 participants per day. Exams were conducted in 7 schools distributed across the 5 parishes that make-up Pedro Moncayo County during the summer months, when schools were not in session. We calculated the number of days between the approximate end of the Mother's Day harvest (5/08/2008, 00:00 a.m.) and the date and time of the beginning of the examination.

Five trained examiners applied the NEPSY-II test (Korkman et al., 2007a), a standardized test to assess neuropsychological development in children ages 3–16 years. Children were tested in 11 age-appropriate subtests in 5 domains: Attention and Inhibitory Control (also known as Attention and Executive Functioning; subtests: auditory attention and response set, inhibition, statue), Language (comprehension of instructions, speeded naming), Memory and Learning (memory-for-faces immediate and delayed, narrative memory), Sensorimotor (visuomotor precision) and Visuospatial Processing (design copying, geometric puzzles).