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Prenatal p,p′-DDE exposure and establishment of lateralization and spatial orientation in Mexican preschooler

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ABSTRACT

Background: Prenatal exposure to p,p′-DDE is associated with impairments in motor development during the first year of life, with no related repercussions on mental or motor development at 12–30 months and with impairments in cognitive areas, but not in perceptual and motor areas at preschool age. However, its association with particular psychomotor factors, such as establishment of lateralization and spatial orientation, essential elements to the overall learning and specifically reading, writing and spelling in preschoolers, has not been independently evaluated, since cognitive and motor areas have only been explored globally.

Objective: To determine the association between prenatal exposure to p,p′-DDE and the establishment of lateralization and spatial orientation in children 5 years of age.

Materials and methods: Establishment of lateralization and spatial orientation was evaluated using the McCarthy Scale of Children's Abilities, with 167 children 5 years of age who participated in a birth cohort in the state of Morelos, Mexico. The information available for each child included: serum concentrations of p,p′-DDE of the mother during at least one trimester of pregnancy, mothers' intelligence quotients, stimulation at home and anthropometry. A logistic regression model was used to calculate the association between prenatal exposure to p,p′-DDE and lateralization and a multiple linear regression model was used for the association with spatial orientation.

Results: A two-fold increase in p,p′-DDE in lipid base during the second trimester of pregnancy was associated with a significant reduction, −0.18 points (95% CI −0.41; 0.04, in the spatial orientation index, with no impairment in the establishment of hemispheric dominance. Attending preschool and the maternal intelligence quotient were the main determinants of spatial orientation and the establishment of hemispheric dominance.

Conclusions: Prenatal exposure to p,p′-DDE may affect the 5 year old's ability to identify spatial orientation of oneself and surrounding objects. Given the observed role of attending preschool in the functions studied, early attendance in formal education might serve as a stimulation strategy for preschoolers. These preliminary results should be verified and expanded in further prospective studies with DDE.

1. Introduction

Dichlorodiphenyldichloroethylene (p,p′-DDE), the main metabolite of DDT, is a chemically stable compound which is highly persistent in the environment. It is found in the food chain, accumulates in the organism (Casarett & Doull's, 1986) and easily crosses the placental barrier (Dorea et al., 2001). DDT metabolites have neurotoxic capacity, they directly affect nerve cells (Casarett & Doull's, 1986) and have endocrine disruption effects in the hypothalamic-hypophysis-thyroid axis (Howdeshell, 2002; Takser et al., 2005).

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According to recent epidemiological studies, prenatal exposure to this compound is associated with diminished motor development during the first year of life (Eskenazi et al., 2006; Ribas-Fito et al., 2003; Torres-Sanchez et al., 2007). However, studies in preschool and school age children assessing DDE effect on subsequent development and other functions of the central nervous system are rare.

Only three studies have used the McCarthy Scale of Children's Abilities (MSCA) to evaluate the association between prenatal exposure to p,p′-DDE and the neurodevelopment of preschoolers (Gladen & Rogan, 1991; Ribas-Fito et al., 2006; Torres-Sanchez et al., 2013), none of which reported changes related to this test's motor index, but only an effect on cognitive performance (Torres-Sanchez et al., 2013).

Similar to other tests used before 3 years of age, the MSCA motor scale is primarily aimed at evaluating processes such as gross and fine motor coordination in children. Nevertheless, other complex components are included, such as lateralization, evaluating hemispheric dominance and spatial orientation, which determines knowledge of the left-right concept in relation to oneself and surrounding objects (McCarthy, 2004). These two components overlap with the general cognitive index and the perceptual index, since they are psychomotor aspects that are included in the motor area.

Establishment of lateralization, or hemispheric dominance, is one of the last stages in psychomotor development (Bottini, 2000), which together with visual-motor coordination, spatial organization, body schema and spatial perception are essential for proper learning process generally and specifically reading, writing and spelling for children (Cady, 2009; Ozbic & Filipcic, 2010). To-date, no study has separately evaluated the association between prenatal exposure to p,p′-DDE and the establishment of hemispheric dominance and spatial orientation.

In 2001, a cohort study was initiated in four municipalities in the state of Morelos, Mexico in a formerly malaria-endemic area, where DDT was used as part of anti-malaria campaign until 1998. The median values of maternal blood p,p′-DDE during pregnancy were 7.7 ng/ml (wet base) and 1020.4 ng/g (lipid base). In previous results with this cohort a two-fold increase in p,p′-DDE serum concentration during the first trimester of pregnancy was negatively associated ($\beta = -0.52$ points) with motor development only during the first year of life and, not with mental development (Torres-Sanchez et al., 2007).

In this same cohort no associations between maternal p,p′-DDE serum concentrations and mental and motor development of children were found between 12 and 30 months (Torres-Sanchez et al., 2009); at 3.5–5 years, two-fold increased concentrations of p,p′-DDE were associated with a significant reduction in the general cognitive index (−1.37 points), the quantitative index (−0.88 points), the verbal index (−0.84 points) and the memory index (−0.80 points), with no repercussions for motor and perceptual indexes, measured by the McCarthy Scale (Torres-Sanchez et al., 2013).

Preliminary results suggest that this metabolite has its main effect on later rather than earlier developmental ages. The effects measured to date were in the overall development of the child and not on particular aspects that may be masked by an overall assessment, such as the establishment of laterality and spatial orientation.

The objective of this study was to explore the association between prenatal exposure to p,p′-DDE and the establishment of lateralization, and the quality of spatial orientation at 60 months of age, during which laterality and spatial orientation are determined as development gains in the McCarthy Scales of Abilities (MSCA); this study was conducted in the same cohorts as those previously published and we re-analyzed the already published data, focusing on two specific subscales.

2. Materials and methods

A prospective cohort was created from January 2001 to June 2005 in order to evaluate the association between prenatal exposure to organochlorines compounds and neurodevelopment in children. The details about the creation of the cohort and the neurobehavioral evaluation were reported previously (Torres-Sanchez et al., 2007, 2013).

In summary, the participants included 990 women of reproductive age with no history of chronic diseases, who were not receiving treatment with anticonvulsants and who resided in one of four municipalities in the state of Morelos, Mexico. The women were identified during premarital talks that are required by law for civil marriages in the state. The objective of the study was explained to each person and written consent was requested to visit them before, during and after pregnancy. The study was approved by the ethics committee of the Mexico National Institute of Public Health and the National Institute of Perinatology of Mexico.

During the pre-pregnancy stage, a direct interview was held through which sociodemographic and reproductive information was obtained as well as information about work history, smoking, diet and alcohol use. This was followed by a phone call every 8 weeks for the early detection of pregnancy, and when confirmed a visit was scheduled for each trimester. During these visits the women were asked about the evolution of their pregnancy and diet, and a blood sample was requested to determine organochlorines compounds.

Visits after birth were scheduled at 1, 3 and 6 months of age and every 6 months thereafter until 60 months. The Bayley test was used for the neurobehavioral evaluation up to 30 months of age and the MSCA was used from 42 months to 60 months. During the first visit, women were asked about the conditions of the child's birth, including weight and size. The following postnatal evaluations also included anthropometric measurements (weight, height and cephalic perimeter) as well as a questionnaire about the child's diet, general health status, type of family and preschool attendance. The weight and height of the children were transformed into *z*-scores for analysis.

Of a total of 404 children from uncomplicated pregnancies, with birth weight >2 kg, no history of perinatal asphyxia or congenital defects, 30% were lost to follow-up between 1 and 42 months of age. Of the remaining children, 167 had information about lateralization and spatial orientation at 5 years of age and p,p′-DDE concentrations in mother's serum during at least one trimester of pregnancy.

2.1. McCarthy Scale of Children's Abilities

The MSCA (McCarthy, 2004) was used to evaluate establishment of lateralization and spatial orientation at 60 months of age. This test measures cognitive and motor abilities and is designed to evaluate children from 2 years and 6 months of age up to 8 years and 6 months. It consists of five sub-tests: verbal, quantitative, executive perceptual, memory and motor. The combination of the first three subtests make up the general cognitive index (GCI), which is considered equivalent to the intelligence quotient, measured by some intelligence tests (Goldstein & Hersen, 1984). The motor subtest evaluates legs, arms and hand movements according to 4 blocks of tasks: leg coordination, arm coordination, imitative action and drawing. While performing the tasks, the hand preference when hitting a ball, picking up and throwing an object, drawing and the preferred eye with which the child looked through a tube were observed and noted. When the tasks involved in the 4 blocks were performed with the same hand and eye, the child was considered to have an established hemispheric dominance (right- or left-handed). When some of the tasks were performed