

Visuoperceptual functioning differs in 9- to 12-year olds prenatally exposed to cigarettes and marihuana

Peter A. Fried*, Barbara Watkinson

Department of Psychology, Carleton University, Ottawa, Ontario, Canada K1S 5B6

Received 10 March 1999; accepted 21 June 1999

Abstract

Visuoperceptual performance was examined in 146 9- to 12-year old children for whom prenatal exposure to marihuana and cigarettes had been ascertained. The subjects, participants in an ongoing longitudinal study, were from a low-risk, predominantly middle class sample. The tasks ranged in complexity from those that required basic visuoperceptual skills to those that required considerable integration and cognitive manipulation of such skills. Trend analysis revealed a dose dependent negative association between prenatal cigarette exposure and an overall score reflecting basic visuoperceptual functioning. This association remained after consideration of potential prenatal confounds, pre- and postnatal secondhand smoke exposure, and the nonperceptual demands of the tasks. This poorer performance in the basic visuoperceptual domain underlay a poorer performance in more complex visuoperceptual tasks among the offspring of cigarette smokers. In contrast, prenatal marihuana exposure was not associated with basic visuoperceptual functioning but was negatively associated with performance in visual problem solving situations. The interpretation of the marihuana findings is discussed in relation to a “top-down” integrative ability associated with executive function, the extant prefrontal literature, and earlier observations of this sample. © 1999 Elsevier Science Inc. All rights reserved.

Keywords: Marihuana; Cigarettes; Prenatal; Children; Visuoperceptual function; Executive function

1. Introduction

The Ottawa Prenatal Prospective Study (OPPS), an ongoing longitudinal project initiated in 1978, has examined the neurobehavioral and developmental effects of prenatal exposure to cigarettes and marihuana in offspring from birth until early adolescence. Recently we have published a number of articles describing outcomes in the 9- to 12-year-old children from this study in the domains of reading and language [21], cognition and executive functioning [19], and growth [20]. The present report is an examination, in this age group, of neurobehavioral tasks that focus on visuoperceptual abilities.

The literature has been relatively inconsistent with respect to an association between prenatal exposure to cigarettes and performance on visuoperceptual tasks. Studies carried out in the seventies failed to find a significant relationship between maternal smoking and the performance of 6 and 7-year-old offspring on tests of visual-motor integration that required copying geometric figures [8,24]. However, a recent investigation did find a negative association in such a task in 5-year-old children [29]. No negative effect of prenatal smoking was noted in a study assessing the ability

of 5-year-old children to form comparisons and organize spatial perceptions by identifying the missing section of a patterned matrix from a group of symbols [9].

No consistent pattern of association with prenatal cigarette smoking has emerged from a number of reports describing visuoperceptual subscales that are part of standardized cognitive tests. In the OPPS sample, at 12 and 24 months of age, using measures derived from the Infant Behavior Record of the Bayley Scales of Infant Development [2], maternal cigarette use was not associated with visuoperceptual behavior although it was with auditory-perceptual behavior [15]. In the same sample using discriminant function analysis (DFA), at both 3 and 4 years of age, the Perceptual Performance scale (consisting of visual motor coordination tasks and nonverbal reasoning through manipulation of objects) of the McCarthy Scales of Children's Abilities [28] was an important predictor in distinguishing across heavy, light, and nonsmoking groups with better performance in the nonsmoking group [16]. In another sample assessing 3-year olds, the Perceptual Performance scale of the McCarthy test was lower ($p = 0.06$) among those children whose mothers smoked ten or more cigarettes per day compared with children of mothers who quit during pregnancy [36].

Within the OPPS at 5 and 6 years of age, using DFA, the Perceptual Performance scale of the McCarthy test was

* Corresponding author. Tel.: 613-520-2676; Fax: 613-520-3667.
E-mail address: peter_fried@carleton.ca (P.A. Fried)

again an important predictor in distinguishing across the smoking groups in the direction of better performance in the nonsmoking group [14]. Dunn et al. [8], in a work that did not control for other drug use, observed, in 6 1/2-year-old children of normal birth weight, impairments associated with prenatal smoking on the composite Performance Scale of the Wechsler Intelligence Scale for Children (WISC-III) [43] with the largest contributor appearing to be the Block Design subtest. This subtest, which requires subjects to assemble blocks to form a design identical to one presented in a picture, includes demands on basic visuoperceptual skills as well as analytical and integrative abilities. In the OPPS sample [19], using DFA for the data of children between the ages of 9- to 12 years, the composite Performance Scale of the WISC-III was an important predictor in distinguishing across smoking groups in the direction of better performance among the nonsmokers.

Relatively few studies have examined the possible relationship between prenatal marihuana exposure and the visuoperceptual abilities of offspring. With the OPPS sample, Fried and Makin [13] reported a significant relationship at birth between poorer habituation to visual stimuli and maternal marihuana use. Other studies, however, did not find a similar relationship [34,41]. Prenatal marihuana exposure was not associated with the visual cluster derived from the Infant Behavioral Record of the Bayley test when the OPPS sample was assessed at 12 and 24 months [15] nor was there an association with this sample on the Perceptual Performance scale of the McCarthy test between the ages of 3 to 6 years [14,16]. In this sample, between 6 and 9 years of age, children of marihuana users scored more poorly on visuoperceptual tasks but this association did not remain significant after controlling for postnatal environmental factors [30].

Two reports have noted an association between marihuana exposure during pregnancy and poorer performance on the abstract/visual reasoning score of the Stanford-Binet Intelligence Scale [42] in 3-year-old children [6,23]. At this age, this score is derived from a formboard puzzle task and the ability to replicate different block designs. At approximately 10 years of age prenatal marihuana use continued to be a significant predictor of poorer abstract/visual reasoning [33] with, at this age, the score being derived from performance on a block design-type task, a progressive design matrices task and the ability to copy geometric shapes. In the OPPS sample at approximately the same age [19], using stepwise DFA, maternal marihuana use was noted to negatively impact upon tasks requiring visuoperceptual abilities applied to visually based problems that included the Block Design and Picture Completion subtests of the WISC. The Picture Completion subtest requires the subject to identify a missing portion of an incompletely drawn picture. Thus overall, although far from being entirely consistent, there is a suggestion from the extant literature that prenatal marihuana exposure may impact in a negative fashion upon perceptual tasks that require visuoperceptual integration and analysis.

In considering visuoperceptual functioning, it is necessary to ascertain that the nonvisual demands of this type of task which may include attention, memory, and motor components are not the facets of behavior that underly the negative performance observed in the perceptual tasks. This is particularly relevant when considering the role of prenatal cigarette and marihuana use because both of these substances have been implicated with poorer performance in the offspring in nonperceptual behaviors that are, nevertheless, required to carry out many visual spatial tasks.

2. Methods

2.1. *Ottawa Prenatal Prospective Study cohort*

The OPPS was designed to explore the effects, on children, of maternal soft drug use during pregnancy in a predominantly low-risk, middle-class sample. Marihuana and cigarettes have been the primary drugs of interest in recent reports. A total of 698 women volunteered after learning of the Study through the media or through notices in obstetricians' offices. Interviews were conducted, usually in the mother-to-be's home, during each trimester remaining in the pregnancy at the time of entrance into the study. For subjects included in the present study, 21% entered the study during their first trimester and 36% during their second trimester. The same interviewer was used throughout the pregnancy with the repetition of interviews enhancing the rapport between the subject and the interviewer and providing an opportunity to assess the consistency of the self-report [17]. Data were collected on the amounts and patterns of maternal drug use, maternal caffeine use, maternal age, height, prepregnancy weight, weight gained during pregnancy, regular maternal exposure to the cigarette smoke of others, general health (both present and prior to pregnancy), and history of previous pregnancies. At each interview, a 24-h dietary recall was requested of the mother and was evaluated in reference to a recommended standard. The father's medical history, parents' level of education, and the family's socioeconomic level were also recorded.

For cigarette use, a nicotine score was derived by multiplying the daily average of the number of cigarettes smoked by the nicotine content of the brand specified. Marihuana use was recorded in terms of number of joints smoked per week. Measurement of alcohol consumption included beer, wine, and liquor use. Both the quantity and pattern of consumption were recorded and converted to ounces of absolute alcohol (AA) per day.

From the original sample, a cohort of children was selected for follow-up beyond birth. Among this cohort were children of women who reported any use of marihuana during pregnancy, children of women who drank alcohol beyond a daily average of 0.85 ounces AA, and children whose mothers smoked an average of at least 16 mg of nicotine per day during pregnancy. This resulted in a cohort of 140 subjects. In addition to these children, children of 50

women who were nonusers of marihuana, who abstained or drank little alcohol, and who were nonsmokers were randomly selected to be included in the follow-up study.

Of these 190 subjects, 146 children ranging in age from 9 to 12 years inclusive were tested. Of the remaining 44 not tested, most involved families who had moved out of the Ottawa area. In addition, two families withdrew from the study and a few children were unavailable for the testing. No differential loss of subjects with respect to drug variables occurred. The final sample of 146 9- to 12-year-old children included 82 boys and 64 girls with four 9-year-olds, 79 10-year-olds, 37 11-year-olds, and 26 12-year-olds.

2.2. Instruments and procedure

As part of an overall neuropsychological assessment, an extensive battery of tests was administered to the 9- to 12-year-old children. Those measures within that battery that assessed aspects of visual functioning form the basis of the present report and are described in Table 1. Briefly, these included the Test of Visual-Perceptual Skills (TVPS) [22], a nonmotor task with an overall derived summary score (Perceptual Quotient) and seven subscales that assess basic visuoperceptual skills; the Trail Making Test [31] requiring visual scanning, visuospatial sequencing, attention, mental flexibility, and motor function; the Knox Cube [38] requiring visual attention, visual memory and visual sequencing; and the Wechsler Intelligence Scale for Children-III (WISC-III) Perceptual Organization Index, its four subscales each of which require problem solving abilities (Block Design, Object Assembly, Picture Completion, Picture Arrangement), and the subscales of Symbol Search, Mazes, and Coding [43], all requiring various aspects of visuoperceptual functioning.

Abilities that might influence performance on visual tasks were also assessed and used in the present report. The WISC Full Scale was used as a measure of general intelligence, the WISC Digit Span as a test of memory, the WISC

Freedom of Distractibility as a measure of attention, and the Developmental Test of Visual-Motor Integration [3] as a measure of visuomotor coordination.

All tests had norms available for the age range tested and these standardized scores were used in the tables and the analyses. The tests were administered in a blind fashion with respect to prenatal drug exposure.

2.3. Statistical procedures

2.3.1. Group categorization

For analytic purposes, maternal cigarette smoking (average use across pregnancy) was categorized into three groups: nonsmoking, light, and heavy (≥ 16 mg nicotine/day, which approximates a minimum of one package of average strength). Maternal average marihuana use across pregnancy was categorized into three groups: no use, infrequent or moderate use (>0 and <6 joints/week), and heavy use (≥ 6 joints/week). Using three categories for both the nicotine and marihuana analyses, a sample of 146 allowed the detection of a medium effect size ($f = 0.30$ standard deviation of the weighted standardized means) with 90% power [4].

2.3.2. Analysis

In order to examine relationships of the outcome variables and maternal drug use, analyses of variance (ANOVA) were conducted. Trend analysis was employed to study the shape of the relationships between maternal drug use and both the unadjusted and adjusted outcome variables [40]. Trend analysis requires equal spacing across levels of maternal drug use or a selection of coefficients that takes into account the unequal spacing [10]. Ordinal categorization (e.g., 0,1,2) assumes equal spacing between the three levels of cigarette smoking or marihuana use. Because this is not representative of the data (Table 2), the means of nicotine in milligrams per day for each level of smoking and marihuana in joints per day for each level of marihuana use were substituted as coefficients in the polynomial analysis for linear trends.

Table 1
Visuoperceptual test battery

Test of Visual-Perceptual Skills (TVPS) [22]

A nonmotor task with an overall summary score (Perceptual Quotient) and seven subscales measuring Visual Discrimination (finding an exact match among similar forms), Visual Memory (memory of all characteristics of a given form), Visual-Spatial relationships (finding a form identical to others but with a different orientation), Visual Form Constancy (ability to find a stimulus form that may vary in size, shading, or orientation), Visual Sequential Memory (memory of a series of forms), Visual Figure-Ground (ability to find a stimulus hidden in a conglomerated background), and Visual Closure (ability to identify stimulus form among incomplete forms), was used to assess basic visuoperceptual functioning.

Trail Making Test [31]

Part A (connecting by pencil lines randomly placed numbers in order) and Part B (connecting by pencil lines randomly placed letters and numbers in alternating order) were used to assess visual scanning and visuospatial sequencing.

Knox Cube [38]

Blocks are tapped in prearranged sequences and the subject is required to imitate the tapping patterns to assess visual attention, span, visual memory, and visual sequencing.

Wechsler Intelligence Scale for Children, 3rd ed. (WISC-III) [43]

The Perceptual Organization Index (derived from the sum of the Picture Completion, Picture Arrangement, Block Design, and Object Assembly subscales and reflecting the ability to interpret and organize visually presented material) and the subscales of Symbol Search (a visual scanning task), Mazes (a task requiring rudimentary planning), and Coding (involving discrimination and memory of visual symbols), were considered to reflect various aspect of visual functioning.

Table 2

Characteristics that differ across prenatal maternal drug groups

	Cigarettes (nicotine mg/day)			Marihuana (joints/week)		
	None (0) group 1	Light (>0 and <16) group 2	Heavy (≥16) group 3	None (0) group 1	Infrequent/moderate (>0 and <6) group 2	Heavy (≥6) group 3
<i>N</i>	61	55	30	102	23	21
Nicotine (mg/day)	0.0	6.7	27.0***,b	8.2	7.9	7.5
Marihuana (joints/week)	2.9	2.5	2.1	0.0	1.8	16.0***,d
Alcohol (oz. AA/day)	0.19	0.18	0.19	0.18	0.24	0.12
Average parent education	3.0	2.5	2.0***,b	2.8	2.5	1.9***,d
Prenatal secondhand cigarette smoke exposure (% responding yes)	0.30	0.69	1.0***,b	0.55	0.52	0.86*,c
Child's postnatal passive exposure (number of years exposed as a proportion of age)	0.23	0.56	0.82***,b	0.41	0.48	0.76*,c
Home Environment Questionnaire (HEQ)						
Supervision	50.9	47.1	43.4***,c	48.0	47.9	48.4
Affiliation	54.4	52.0	48.8*	54.1	48.3	49.2*,c
Socioeconomic status	60.8	56.6	52.0***,c	57.7	58.2	56.0

Note: Statistical tests were one-way between-subjects ANOVAs with the Scheffé test ($\alpha = 0.05$) [35] used for post hoc comparisons.

^a Education coded as: 1, did not finish high school; 2, graduated from high school; 3, graduated from college or university; 4, obtained a postgraduate degree.

^b All pairwise comparisons differ.

^c Group 1 differs from group 3.

^d Groups 1 and 2 differ from group 3.

^e Group 1 differs from group 2.

* $p \leq 0.05$.

** $p \leq 0.01$.

*** $p \leq 0.001$.

2.3.3. Confounding variables

Potentially confounding prenatal variables that were considered were the average level of parental education, other maternal drug use, prenatal passive smoke exposure, and sex of the baby. Postnatal variables considered as potentially affecting the relationship between maternal drug use and the visuoperceptual outcomes were the home environment, current socioeconomic status (SES), the child's gender, and the environmental tobacco smoke (ETS) exposure of the child. To assess the home environment and current SES, the Home Environment Questionnaire (HEQ) [37], which was administered at the time of subject testing, was used. Ten scales were derived from the HEQ: Achievement, Aggression-External, Aggression-Home, Aggression-Total, Supervision, Change, Affiliation, Separation, Sociability, and Socioeconomic Status. The child's postnatal smoke exposure, which included sources both within and outside the home, was determined for each year of the child's life up to the date of testing by asking the mother if her child, during each year, had been exposed to cigarette smoke on a regular basis of at least 2 h a day. Any of these variables related to the drug of interest at an alpha level of 0.10 or less were selected as potential confounds and then examined for association with individual outcomes using analyses of covariance (ANCOVA). Prenatal potentially confounding variables that were related ($p \leq 0.05$) to outcomes in the ANCOVAs were retained as covariates in the first level of the control analysis. In the second stage of this analysis, postnatal variables that were related ($p \leq 0.05$) to the individual out-

comes were added as covariates in the ANCOVA containing the prenatal potentially confounding covariates. When satisfying the above criteria for selection of potentially confounding variables, the covariates may differ for separate analyses. Alcohol and the drug that was not of primary interest (marihuana or cigarettes) were always included as covariates.

2.3.4. Interactions of maternal cigarette and marihuana use

To explore interactions of maternal cigarette and marihuana use with the outcome variables, factorial ANOVAs were conducted. Categorization of both marihuana and cigarette use into three levels of drug use was not feasible for these analyses because of inadequate cell size in the combination of heavy cigarette and heavy marihuana use. Therefore, cigarette use was delineated into smoking and non-smoking groups and marihuana use into heavy use and infrequent or moderate or no use. These categories were based on the previously published neurobehavioral OPPS research in which negative effects of maternal cigarette smoking were found with both light and heavy use and negative effects of maternal marihuana use were found with heavy use but not with infrequent or moderate use (e.g., 16,19).

3. Results

The family income, age, and parity of the present sample are similar to those of women who gave birth at the partici-

pating hospitals in the same years that the women were recruited. Of the demographic and other potentially confounding characteristics that were described in the Methods section, only those that differed across levels of maternal cigarette or marihuana use are presented in Table 2.

In the examination of outcomes with the univariate analyses, assumptions regarding lack of factor by covariate interactions and homogeneity of variance-covariance matrices were met. One nicotine and two marihuana and alcohol values were extreme univariate outliers with respect to their distributions (z score >4). To retain the cases for analysis but to reduce their influence, each score was adjusted to one unit greater than the next heaviest user in the distribution, while maintaining their rank order [40]. Drug values were used as continuous variables when used as covariates in ANCOVA procedures and were log transformed to reduce positive skewness.

3.1. Prenatal cigarette smoking

The means of the outcome variables across levels of maternal smoking are presented in Table 3. Unadjusted means and standard deviations as well as the means and standard errors adjusted for prenatal potential confounds are included. Using 95% confidence intervals as reported in Table

3, most of the visuoperceptual outcomes were negatively and linearly associated with maternal smoking before adjusting for potential confounders. The Knox Cube, WISC Symbol Search, and WISC Mazes showed a similar negative trend ($p < 0.10$).

In considering confounds, ETS exposure was problematic as both the mother's prenatal ETS exposure and the postnatal ETS exposure of the child were significantly associated with prenatal active maternal smoking (Pearson product-moment correlation coefficients 0.55 and 0.51 respectively, both $p < 0.001$). Therefore, in order to examine the effects of ETS exposure independent of the influence of active maternal smoking, the sample was restricted to the children of nonsmokers. The potential impact of both prenatal and postnatal measures of ETS exposure was investigated with all of the visuoperceptual variables. In this nonsmoking group, prenatal ETS exposure was associated only with Block Design [$F(1, 59) = 5.4, p < 0.05$] and therefore was retained as a covariate in the univariate analysis of Block Design with prenatal maternal smoking in the overall sample.

The postnatal ETS exposure among the children born to nonsmokers was associated with the TVPS Perceptual Quotient and the TVPS Visual Discrimination subscale (Pearson product-moment correlation coefficients -0.31 and -0.34 respectively, both $p < 0.05$) and was therefore retained as a

Table 3
Unadjusted and adjusted outcome variables across cigarette groups

	Prenatal maternal use of cigarettes (nicotine mg/day)					
	Unadjusted (mean[SD])			Adjusted for prenatal covariates (adj. mean[SE])		
	None (0)	Light (>0 and <16)	Heavy (≥ 16)	None (0)	Light (>0 and <16)	Heavy (≥ 16)
N	61	55	30	61	55	30
TVPS						
Perceptual quotient (summary score)	129.3 [13.9]	122.7 [12.3]	115.2 [15.8] ^{a,***}	126.8 [1.8]	122.6 [1.8]	117.8 [2.7] ^{a,*}
Visual discrimination	15.8 [3.3]	15.4 [3.1]	14.1 [3.8] ^{a,*}	15.8 [0.43]	15.4 [0.45]	14.1 [0.61] ^{a,*}
Visual memory	12.8 [2.8]	11.9 [2.5]	11.0 [2.4] ^{a,***}	12.5 [0.35]	11.9 [0.35]	11.4 [0.52]
Visual-spatial relations	13.7 [2.9]	13.3 [2.7]	11.9 [2.9] ^{a,**}	13.6 [0.39]	13.3 [0.38]	12.0 [0.56] ^{a,*}
Visual form constancy	13.0 [3.1]	11.9 [3.0]	10.6 [3.0] ^{a,***}	12.8 [0.42]	11.8 [0.41]	10.8 [0.61] ^{a,*}
Visual sequential memory	11.8 [3.1]	11.6 [3.1]	9.3 [2.3] ^{a,***}	11.3 [0.40]	11.6 [0.39]	9.8 [0.58] ^{a,*}
Visual figure-ground	15.7 [3.2]	14.2 [3.8]	14.0 [4.0]			
Visual closure	15.4 [3.3]	14.1 [3.1]	13.7 [3.5] ^{a,*}	15.0 [0.45]	14.0 [0.44]	14.1 [0.65]
WISC-III						
Perceptual organization index	116.4 [12.1]	109.6 [13.8]	106.1 [12.6] ^{a,**}	116.1 [1.8]	109.7 [1.7]	106.4 [2.6] ^{a,*}
Picture completion	12.3 [2.3]	11.2 [2.8]	11.2 [2.9]			
Picture arrangement	12.3 [3.2]	11.3 [3.4]	10.4 [4.3] ^{a,*}	12.3 [0.45]	11.3 [0.47]	10.4 [0.64] ^{a,*}
Block design	13.6 [3.4]	12.1 [3.5]	11.5 [2.6] ^{a,*}	12.9 [0.45]	12.2 [0.43]	12.0 [0.65]
Object assembly	12.3 [2.7]	11.3 [2.6]	10.5 [2.5] ^{a,**}	12.1 [0.36]	11.3 [0.36]	10.7 [0.53]
Coding	11.4 [2.3]	10.3 [3.0]	9.5 [3.1] ^{a,***}	11.1 [0.38]	10.3 [0.37]	9.9 [0.55]
Symbol search	12.7 [3.2]	12.5 [3.7]	11.3 [4.3]			
Mazes	11.7 [2.8]	10.7 [3.3]	10.3 [3.4]			
Trail Making						
Time A	0.41 [1.2]	0.50 [1.0]	0.71 [1.2]			
Time B	0.08 [0.91]	0.16 [0.94]	0.15 [0.92]			
Knox cube	0.01 [1.2]	-0.22 [0.94]	-0.45 [1.1]			

^a Linear trend.

* $p \leq 0.05$.

** $p \leq 0.01$.

*** $p \leq 0.001$.

covariate in the univariate analyses of these two outcomes with prenatal maternal smoking in the overall sample.

Following adjustment for other drug use and parental education, the two variables that met the confound inclusion criteria described in the Methods section, the TVPS visuo-perceptual outcomes most strongly related to maternal smoking were Visual Form Constancy (linear trend $t = -2.4$, $p < 0.05$), Visual Sequential Memory (linear trend $t = -2.3$, $p < 0.05$) and Visual-Spatial relationships (linear trend $t = -2.2$, $p < 0.05$). The overall Perceptual Organization Index remained associated with prenatal cigarette use after adjusting for other drug use, parental education, and the SES scale derived from the HEQ (linear trend $t = -2.3$, $p < 0.05$). Picture Arrangement, one of the subscales of the Perceptual Organization Index, also remained associated with prenatal cigarette use after controlling for other drug use (linear trend $t = -2.2$, $p < 0.05$).

The TVPS Perceptual Quotient and the Visual Discrimination subscale were both associated with prenatal maternal smoking after controlling for prenatal covariates (linear trends $t = -2.4$ and $t = -2.3$ respectively, both $p < 0.05$). Prenatal covariates used were parental education and other drug use in the analysis of the Perceptual Quotient and other drug use in the analysis of the Visual Discrimination subscale. After adjusting for the child's ETS exposure, prenatal smoking did not retain its statistical association with either of these two outcome variables. However, because of the high correlation between maternal smoking during pregnancy and the ETS exposure of the child, the interpretation of the results of this adjustment is problematic.

In an effort to disentangle this confounding relationship between prenatal active smoking and the child's ETS exposure, children who had never been exposed regularly to ETS were selected. In this way, the impact of prenatal smoking on these two outcome variables could be examined independently of the influence of the child's ETS exposure. Fifty children met the criterion of no regular ETS exposure. Only one child in the prenatal maternal heavy smoking group was not exposed postnatally and therefore to investigate this issue, prenatal smoking was used as a continuous rather than categorical variable. Using this subsample of children and hypothesizing the same negative effect of maternal smoking as seen in the overall sample, the Pearson product-moment correlation between prenatal cigarette use and the Perceptual Quotient was statistically significant ($r = -0.25$, $p = 0.04$, one-tailed) and no prenatal confounding variables were identified. In the same subsample, no statistically significant relationship was found between prenatal smoking and the Visual Discrimination subscale.

3.1.1. Influence of basic visuoperceptual abilities

The Perceptual Quotient of the TVPS, the summary score derived from the seven subscales of that subtest, was used to represent the latent variable, fundamental visuoperceptual skills. With the Perceptual Quotient as a covariate, an ANCOVA was used to determine whether this summary

score accounted for the significant relationship between prenatal maternal smoking and the WISC Perceptual Organization Index and its subscales, Block Design, Object Assembly, and Picture Arrangement. In all cases, after controlling for the TVPS, the relationships between prenatal cigarette use and the four variables were no longer statistically significant.

3.1.2. Influence of intelligence

Previous reports emanating from this study have suggested that maternal smoking adversely affects areas of cognition in the offspring [14,16,19]. Because of the potentially positive association of intelligence and visuoperceptive abilities [22] and because of the actual significant correlation found in the present report between the WISC Full Scale and the TVPS Perceptual Quotient (Pearson product-moment correlation coefficient 0.61, $p < 0.001$), the data were examined to determine if the association between maternal smoking and the TVPS was mediated by the child's intelligence. Using trend analysis with the three levels of maternal smoking as the independent variable, the Perceptual Quotient as the dependent variable, and the WISC-Full Scale as a covariate, the association between the Perceptual Quotient and maternal smoking remained after removing any mediating influence of the child's intelligence (linear trend $t = -2.3$, $p < 0.05$). The adjusted means for the control, light, and heavy smoking groups were 125.4, 122.7, and 118.5 respectively.

3.1.3. Influence of visual-motor integration

Prenatal maternal smoking was not statistically associated with the Beery test of visual-motor integration and therefore effects of prenatal cigarette smoking could not be attributed to visual-motor integration.

3.1.4. Influence of memory

The WISC-Digit Span, used as a test of memory, was negatively associated with prenatal maternal smoking [$F(2, 143) = 6.9$, $p < 0.01$]. After adjustment for the influence of memory, the TVPS Perceptual Quotient remained associated with maternal smoking (linear trend $t = -3.3$, $p < 0.01$) and the adjusted means for the control, light, and heavy smoking groups were 127.6, 122.7, and 116.9, respectively.

3.1.5. Influence of attention

The WISC Freedom from Distractibility, used as a measure of attention, was negatively related to prenatal cigarette use [$F(2, 143) = 8.5$, $p < 0.001$]. After its control, prenatal smoking and the TVPS Perceptual Quotient remained significantly related (linear trend $t = -2.7$, $p < 0.01$) with adjusted means for the control, light, and heavy smoking groups of 126.6, 122.4, and 118.2, respectively.

The influence of intelligence, memory, and attention were used together to examine their combined influence on the relationship between maternal cigarette use and the TVPS Perceptual Quotient. Using the WISC-Digit Span (memory), WISC-Freedom from Distractibility (attention), and the WISC-Full Scale (intelligence) as covariates, the

prenatal smoking/Perceptual Quotient relationship remained significant (linear trend $t = -1.99$, $p < 0.05$). Adjusted means for the control, light, and heavy smoking groups were 125.0, 122.5, and 119.1 respectively.

3.2. Prenatal marihuana use

The unadjusted and adjusted means, with standard deviations and standard errors respectively, for the outcome variables across levels of maternal marihuana use are presented in Table 4. The strongest negative associations with maternal marihuana use were found with the Perceptual Organization Index of the WISC-III (linear trend $t = -2.2$, $p < 0.05$) and one of its subscales, Object Assembly (linear trend $t = -2.2$, $p < 0.05$), after adjusting for other maternal drug use (the only variables that met the criteria for inclusion as prenatal or postnatal covariates). None of the TVPS variables was associated with maternal marihuana use.

3.2.1. Influence of basic visuo perceptual abilities

As with the smoking data, the Perceptual Quotient of the TVPS was used as a covariate in three separate ANCOVAs. In these analyses, maternal marihuana use was the independent variable and the three variables associated with mater-

nal marihuana use (the Perceptual Organization Index and its two subscales, Block Design and Object Assembly) were the dependent variables. After controlling for the Perceptual Quotient, maternal marihuana use remained negatively associated with the Perceptual Organization Index, Block Design, and Object Assembly (linear trend $t = -2.3$, $t = -2.4$, and $t = -2.0$, respectively, all $p < 0.05$).

3.2.2. Influence of intelligence, memory, attention, and visual-motor integration

The WISC Full Scale assessing intelligence, the WISC Digit Span used as a test of memory, the WISC Freedom from Distractibility used as a measure of attention, and the Developmental Test of Visual-Motor Integration were not associated with prenatal marihuana use and thus were not considered as potential confounds with the marihuana findings.

3.3. Interactions of maternal cigarette and marihuana use

As described in the Method section, maternal smoking was dichotomized into smoking and nonsmoking groups and maternal marihuana use into heavy and less than heavy use. Examining the visuo perceptual outcome variables using factorial ANOVAs with maternal marihuana and ciga-

Table 4
Unadjusted and adjusted outcome variables across marihuana groups

	Prenatal maternal use of marihuana (joints/week)					
	Unadjusted (mean[SD])			Adjusted for prenatal covariates (adj.mean[SE])		
	None (0)	Infrequent/ moderate (>0 and <16)	Heavy (≥ 16)	None (0)	Infrequent/ moderate (>0 and <16)	Heavy (≥ 16)
N	102	23	21	102	23	21
TVPS						
Perceptual quotient (summary score)	124.6 [14.8]	122.6 [13.9]	122.2 [15.1]			
Visual discrimination	15.5 [3.4]	15.4 [3.5]	14.4 [3.2]			
Visual memory	12.1 [2.6]	12.3 [2.7]	11.9 [2.9]			
Visual-spatial relations	13.4 [2.8]	12.6 [3.2]	12.8 [2.9]			
Visual form constancy	12.1 [3.3]	12.2 [2.7]	12.0 [3.3]			
Visual sequential memory	11.2 [3.1]	11.2 [3.1]	10.9 [2.7]			
Visual figure-ground	14.9 [3.8]	14.3 [3.4]	14.5 [3.6]			
Visual closure	14.7 [3.4]	13.8 [3.1]	14.9 [3.4]			
WISC-III						
Perceptual organization index	111.8 [13.9]	116.0 [9.8]	106.7 [13.2] ^{a,*}	111.9 [1.2]	115.8 [2.6]	106.9 [2.7] ^{a,*}
Picture completion	11.8 [2.8]	11.4 [2.3]	11.2 [2.5]			
Picture arrangement	11.3 [3.7]	12.9 [3.0]	11.1 [3.5]			
Block design	12.7 [3.3]	13.3 [2.9]	11.1 [4.0] ^{a,*}	12.6 [0.32]	13.0 [0.67]	11.6 [0.72]
Object assembly	11.5 [2.7]	12.6 [2.4]	10.6 [2.8] ^{a,*}	11.5 [0.25]	12.6 [0.53]	10.6 [0.55] ^{a,*}
Coding	10.6 [3.0]	10.6 [2.9]	10.7 [2.0]			
Symbol search	12.2 [3.8]	13.0 [3.5]	12.3 [3.0]			
Mazes	11.1 [3.4]	10.8 [2.4]	10.9 [3.0]			
Trail making						
Time A	0.60 [1.2]	0.21 [0.97]	0.36 [1.0]			
Time B	0.27 [0.94]	-0.15 [0.63]	-0.28 [0.87]			
Knox cube	-0.17 [1.1]	-0.32 [1.0]	0.01 [0.93]			

^a Linear trend.

* $p \leq 0.05$.

** $p \leq 0.01$.

*** $p \leq 0.001$.

rette use as independent variables, no potentiating effect of cigarette and marihuana use was noted.

4. Discussion

The results in this report continue the presentation of findings arising from the OPPS. The protocol described here focuses upon various forms of visuoperceptual functioning in 9- to 12-year-old children. The visuoperceptual tasks that were used in the present study ranged from those that required basic capabilities to those that required considerable integration and cognitive manipulation of this domain. The findings extend earlier reports in nonperceptual domains of the differential consequences of prenatal exposure to cigarettes and marihuana.

Among the 9- to 12-year-old children born to women who smoked cigarettes during pregnancy, the principle area of vulnerability appeared to be within the sphere of fundamental visuoperceptual skills. These skills, which include various elemental aspects of visual discrimination, visual memory, and visual-spatial relationships, were assessed using the TVPS [22]. This test assesses basic visuoperceptual functions without demanding, to any great degree, integrative, analytical skills. After controlling for prenatal covariates, four of the subtests in addition to the Perceptual Quotient (the summary score of the TVPS), were significantly negatively associated, in a linear fashion, with maternal smoking.

The negative linear association between smoking groups and the Knox Cube, WISC-Symbol Search, and WISC Mazes was weaker ($p < 0.10$), which suggests that these visuoperceptual tasks may not have the test specificity of other discriminating visuoperceptual tasks. However, overall there is a general concordance among visuoperceptual outcomes in their association with maternal prenatal cigarette use. The lack of association between maternal smoking and the time taken to perform the Trail Making Tests suggests that speed of performance is not a factor in the negative relationship between prenatal cigarette use and the children's ability to perform visuoperceptual tasks.

In interpreting these observations, one issue is whether deficits observed in visuoperceptual tasks are due to the perceptual demands of these tests or due to one or more nonperceptual requirements that are necessary for their successful performance. Included among these latter requirements may be competency in domains such as memory, attention, intelligence, visual scanning, and visuomotor integration. In order to separate the perceptual component from the nonperceptual demands, tests that measure nonperceptual facets of behavior were used as covariates in the analysis of the Perceptual Quotient of the TVPS. The outcome of these analyses did not result in a loss of a predictive association between in utero exposure to cigarettes and the visuoperceptual measure suggesting that the significant component of this negative association is not mediated by the influence of these underlying, nonperceptual domains.

The Perceptual Organization Index of the WISC-III [43] and the four subtests comprising this Index were used to examine visuoperceptual tasks that require a combination of basic visuoperceptual skills and analytical abilities in order to solve different types of visuoperceptual problems. After controlling for appropriate confounding variables, the Perceptual Organization Index and the Picture Arrangement subtest were negatively associated in a linear fashion with prenatal cigarette smoking.

However, when the Perceptual Quotient summary score of the TVPS, a surrogate for basic visuoperceptual abilities was used as a covariate, the Perceptual Organization Index and the WISC subtest were no longer statistically associated with prenatal cigarette use. Thus, the relationship between prenatal cigarette use and these WISC tests appears to be mediated [1] by basic visuoperceptual skills as represented by the TVPS Perceptual Quotient.

Although not a major focus in this study, ETS exposure both during pregnancy (i.e., prenatal passive exposure) and postnatally (i.e., child's postnatal smoke exposure) was examined for its possible influence on the visuoperceptual findings in this report. The results of several analyses revealed that the TVPS Perceptual Quotient was associated with the child's ETS and that this association reduced the significant relationship between maternal smoking during pregnancy and the Perceptual Quotient. However, using a subsample of children having no ETS, thereby isolating the effect of in utero exposure from postnatal ETS exposure, prenatal active smoking retained its significant association with the Perceptual Quotient. It would therefore appear that a prenatal maternal smoking effect exists with the Perceptual Quotient independent of the influence of the child's ETS. Because there is shared variance among prenatal smoking, the child's ETS and the Perceptual Quotient makes the assignment of this shared explanatory variance solely to the child's postnatal smoke exposure problematic. Such an assignment is a conservative statistical approach [15] that does not reflect the true state of affairs. Some of the shared variance attributed to the child's ETS exposure should be, as outlined above, ascribed to prenatal smoking. Thus prenatal smoking likely has a stronger impact on the TVPS Perceptual Quotient than appears after the conservative use of the child's ETS as a covariate. Caution must be exercised in interpreting the ETS data. As detailed in the Method section, ETS exposure was defined in a dichotomous fashion: regular exposure to tobacco smoke of at least 2 hours a day with anything less being considered no exposure. However, the degree of such exposure beyond 2 hours a day was not ascertained thereby limiting the interpretation of the influence of ETS.

As noted in the Introduction, earlier investigations that have examined the association between maternal smoking and performance on visuoperceptual tasks by their children have been inconsistent in their findings. In none of these studies was the child's exposure to ETS reported. The results described in the present work suggest that this variable may be of considerable importance (both as a statistical control and an independent factor) in attempting to ascertain the association between prenatal cigarette exposure and visuoperceptual performance.

The consequences of prenatal marihuana use appear to differ considerably from prenatal cigarette use on the offsprings' performance on visuoperceptual tasks with the effect of maternal marihuana use varying depending upon the nature of the visuoperceptual task. In contrast to the results associated with prenatal cigarette exposure described above, no association was noted between prenatal marihuana exposure and any of the TVPS subtests or the overall Perceptual Quotient summary score of that test. Thus, in tasks that demanded little or no analytical or integrative skills but did require basic fixed, functional visuoperceptual abilities, children exposed to marihuana in utero were not impacted. However, a contrasting picture emerged with prenatal marihuana exposure and the Perceptual Organization Index. This score, derived from subtests that require skill in planning, integration, analysis, and synthesis in addition to basic visuoperceptual abilities was negatively associated with maternal use of this drug.

It is interesting to note that abstract/visual reasoning subscale scores, derived from the Stanford-Binet Intelligence Test and based on problem-solving tasks requiring visuoperceptual skills, are negatively associated with prenatal marihuana exposure among 3-year-old [6,23] and 10-year-old [33] children in samples other than from the OPPS. These results parallel the observations described in the present report of the impact of prenatal marihuana use on complex visuoperceptual tasks. In these studies, however, the possible underlying mechanisms contributing to these findings were not examined.

The finding suggesting an association between prenatal marihuana exposure and the Perceptual Organization Index of the WISC is consistent with and extends earlier observations with respect to cognitive functioning in children participating in the OPPS. Previously, on the basis of data collected from this sample at 4, 6, and 9–12 years of age [16,18,19], it has been proposed that in utero exposure to marihuana may be negatively associated with behaviors or cognitive abilities that fall under the construct of executive function [5,11,19]. The types of behaviors associated with this nonunitary function include those necessary for effortful, nonroutine, problem solving situations [12]. The present findings suggest that prenatal marihuana use is negatively associated with performance in situations which demand "top-down", integrative [7] visuoperceptual processing—the type of neurocognitive requirement underlying executive function. Further, this negative outcome was apparently not mediated by a dysfunction in basic perceptual competencies but rather was due to marihuana's impact upon the analytical and integrative demands of the tasks making up this composite Perceptual Organization Index. This conclusion is derived from the observation that, after using the TVPS Perceptual Quotient Index as a covariate representing basic visuoperceptual capabilities, the significant negative association between prenatal marihuana exposure and the Perceptual Organization Index remained.

The clinical literature provides additional, indirect support for associating prenatal marihuana exposure with visuoperceptual tasks that involve aspects of executive func-

tioning. The frontal cortical region plays a major role in mediating cognitive behaviors subsumed under the term executive function [12]. Although patients with damage to the frontal region are not impaired on basic visuoperceptual tasks, one of the most striking negative consequences noted among such subjects is in the performance of tests requiring visuoperceptual planning and integration [27,39]. These observations which parallel those of the present study and which link the frontal cortical area and these types of visuoperceptual tasks, are consistent with the hypothesis that prenatal marihuana exposure may impact upon aspects of executive function.

As described elsewhere [19], with prenatal marihuana use, the main discriminating measure in a series of cognitive and executive function tasks, was the number of errors in the Category Test [32]. In this concept formation task, visual stimuli are presented sequentially and the child is required to identify abstract categories and then shift cognitive sets as response criteria change. Successful performance in this task requires nonverbal abstract reasoning and mental flexibility. A factor analysis of the Wechsler Adult Intelligence Scale (WAIS) and Category Test has shown that the Category Test shares a high loading with two of the subtests comprising the Perceptual Organization Index: Block Design and Object Assembly [25,26]. In the present study, it is these two subtests within the Perceptual Organization Index that had the highest association with prenatal marihuana use and thus the outcomes on the visuoperceptual tasks are quite consistent with the earlier published observations of prenatal marihuana's influence on cognitive performance.

In summary, the present findings indicate that, in the 9- to 12-year-old offspring, maternal cigarette use has markedly different associations with visuoperceptual functioning compared with maternal marihuana use. The data extend earlier reports in which prenatal cigarette exposure was associated with cognitive performance in a relatively ubiquitous fashion whereas the consequences of prenatal marihuana use were limited to cognitive tests that involved on-line integrative visual analysis and hypothesis testing. In the present report, maternal cigarette smoking appears to have its major impact upon fundamental aspects of visuoperceptual functioning compared with a lack of effect for prenatal marihuana use within this sphere. Rather, prenatal marihuana use is associated with the application of these fundamental abilities to problem-solving situations requiring integration, analysis and synthesis. The marihuana findings are consistent with the hypothesis that prenatal exposure to this drug impacts upon aspects of executive functioning.

Acknowledgments

The authors thank H. Lintell for her continuing invaluable assistance in data collection and R. Gray for his data management skills. This research was supported by a grant to the first author from the National Institute on Drug Abuse.

References

- [1] R.M. Baron, D.A. Kenny, The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations, *J Person Soc Psychol* 6 (1986) 1173–1182.
- [2] N. Bayley, Bayley Scales of Infant Development, Psychological Corporation, New York, 1969.
- [3] K. Beery, Developmental Test of Visual-Motor Integration, Modern Curriculum Press, Cleveland, OH, 1982.
- [4] J. Cohen, Statistical power analysis for the behavioral sciences, Academic Press, New York, 1977.
- [5] L.I. Cripe, The ecological validity of executive function testing, in: R.J. Sbordone, C.J. Long (Eds.), *Ecological Validity of Neuropsychological Testing*, St. Lucie Press, Boca Raton, FL, 1996, pp. 171–202.
- [6] N.L. Day, G.A. Richardson, L. Goldschmidt, N. Robles, P.M. Taylor, D.S. Stoffer, M.D. Cornelius, D. Geva, Effect of prenatal marijuana exposure on the cognitive development of offspring at age three, *Neurotoxicol Teratol* 16 (1994) 169–175.
- [7] M.B. Denckla, A theory and model of executive function, in: G.R. Lyon, N.A. Krasnegor (Eds.), *Attention, Memory and Executive Function*, Paul H. Brookes, Baltimore, 1996, pp. 263–278.
- [8] H.G. Dunn, A.K. McBurney, S. Ingram, C.M. Hunter, Maternal cigarette smoking during pregnancy and the child's subsequent development: II. Neurological and intellectual maturation to the age of 6–1/2 years, *Can J Public Health* 68 (1977) 43–50.
- [9] B. Eskenazi, L.S. Trupin, Passive and active maternal smoking during pregnancy, as measured by serum cotinine, and postnatal smoke exposure. II. Effects on neurodevelopment at age 5 years, *Am J Epidemiol* 142 (1995) S19–S29.
- [10] G.A. Ferguson, Y. Takane, Statistical analysis in psychology and education (6th ed.), McGraw-Hill, New York, 1989.
- [11] P.A. Fried, The Ottawa Prenatal Prospective Study (OPPS): Methodological issues and findings—it's easy to throw the baby out with the bathwater, *Life Sci* 56 (1995) 2159–2168.
- [12] P.A. Fried, Behavioral evaluation of the older infant and child, in: W. Slikker, Jr., L.W. Chang (Eds.), *Handbook of Developmental Neurotoxicology*, Academic Press, San Diego, 1998, pp. 469–486.
- [13] P.A. Fried, J.E. Makin, Neonatal behavioral correlates of prenatal exposure to marihuana, cigarettes and alcohol in a low risk population, *Neurotoxicol Teratol* 9 (1987) 1–7.
- [14] P.A. Fried, C.M. O'Connell, B. Watkinson, 60- and 72-month follow-up of children prenatally exposed to marijuana, cigarettes, and alcohol: cognitive and language assessment, *J Dev Behav Pediatr* 13 (1992) 383–391.
- [15] P.A. Fried, B. Watkinson, 12- and 24-month neurobehavioral follow-up of children prenatally exposed to marihuana, cigarettes and alcohol, *Neurotoxicol Teratol* 10 (1988) 305–313.
- [16] P.A. Fried, B. Watkinson, 36- and 48-month neurobehavioral follow-up of children prenatally exposed to marijuana, cigarettes, and alcohol, *J Dev Behav Pediatr* 11 (1990) 49–58.
- [17] P.A. Fried, B. Watkinson, A. Grant, R.M. Knights, Changing patterns of soft drug use prior to and during pregnancy: a prospective study, *Drug Alcohol Depend* 6 (1980) 323–343.
- [18] P.A. Fried, B. Watkinson, R. Gray, A follow-up study of attentional behavior in 6-year-old children exposed prenatally to marihuana, cigarettes, and alcohol, *Neurotoxicol Teratol* 14 (1992) 299–311.
- [19] P.A. Fried, B. Watkinson, R. Gray, Differential effects on cognitive functioning in 9- to 12-year olds prenatally exposed to cigarettes and marihuana, *Neurotoxicol Teratol* 20 (1998) 293–306.
- [20] P.A. Fried, B. Watkinson, R. Gray, Growth from birth to early adolescence in offspring prenatally exposed to cigarettes and marihuana, *Neurotoxicol Teratol* 21 (1999) 513–525.
- [21] P.A. Fried, B. Watkinson, L. S. Siegel, Reading and language in 9- to 12-year olds prenatally exposed to cigarettes and marijuana, *Neurotoxicol Teratol* 19 (1997) 171–183.
- [22] D.R. Griffith, S.D. Azuma, I.J. Chasnoff, Three-year outcome of children exposed prenatally to drugs, *J Am Acad Child Adolesc Psychiatry* 33 (1994) 20–27.
- [23] M. Gardner, Test of Visual-Perceptual Skills (Nonmotor). Special Child Publications, Seattle, WA, 1982.
- [24] J.B. Hardy, E.D. Mellits, Does maternal smoking during pregnancy have a long-term effect on the child? *Lancet* II (1972) 1332–1336.
- [25] H. Klonoff, Factor analysis of a neuropsychological battery for children aged 9 to 15, *Percept Mot Skills* 32 (1971) 603–616.
- [26] H. Lansdell, E.F. Donnelly, Factor analysis of the Wechsler adult intelligence scale subtests and the Halstead-Reitan category and tapping tests, *J Consult Clin Psychol* 45 (1977) 412–416.
- [27] A.R. Luria, *The Working Brain. An Introduction to Neuropsychology*, Allen Lane The Penguin Press, London, 1973.
- [28] P. McCarthy, McCarthy Scales of Children's Abilities, The Psychological Corporation, New York, 1972.
- [29] A. Niemelä, A.-L. Järvenpää, Is breastfeeding beneficial and maternal smoking harmful to the cognitive development of children? *Acta Paediatr*, 85 (1996) 1202–1206.
- [30] C.M. O'Connell, P.A. Fried, Prenatal exposure to cannabis: a preliminary report of postnatal consequences in school-age children, *Neurotoxicol Teratol* 13 (1991) 631–639.
- [31] R. Reitan, Trail making results for normal and brain-damaged children, *Percept Motor Skills* 33 (1971) 575–581.
- [32] R. Reitan, L. Davison, *Clinical Neuropsychology*, John Wiley & Sons, New York, 1974.
- [33] G.A. Richardson, N.L. Day, A comparison of the effect of prenatal marijuana, alcohol, and cocaine use on 10-year child outcome, *Neurotoxicol Teratol* 19 (1997) 256.
- [34] G.A. Richardson, N.L. Day, P.M. Taylor, The effect of prenatal alcohol, marijuana and tobacco exposure on neonatal behavior, *Inf Behav Dev* (1989) 12 (1989) 199–209.
- [35] H.A. Scheffé, A method of judging all contrasts in the analysis of variance, *Biometrika* 40 (1953) 87–104.
- [36] M. Sexton, N.L. Fox, J.R. Hebel, Prenatal exposure to tobacco: II. Effects on cognitive functioning at age three, *Int J Epidemiol* 19 (1990) 72–77.
- [37] J. Sines, The Home Environment Questionnaire, Psychological Assessment and Services, Iowa City, IA, 1983.
- [38] M. Stone, B. Wright, Measuring attending behavior and short-term memory with Knox's cube test, *Educational Psychol Measurement* 43 (1983) 803–814.
- [39] D.T. Stuss, G.A. Eskes, J.K. Foster, Experimental neuropsychological studies of frontal lobe functions, in: F. Boller, J. Grafman (Eds.), *Handbook of Neuropsychology*, Vol. 9, Elsevier Science, Amsterdam, 1994, pp. 149–185.
- [40] B.G. Tabachnik, L. S. Fidell, *Using Multivariate Statistics* (2nd ed.), Harper & Row, New York, 1989.
- [41] K. Tennes, N. Avitable, C. Blackard, C. Boyles, B. Hassoun, L. Holmes, M. Kreye, Marijuana: Prenatal and Postnatal Exposure in the Human, in: T.M. Pinkert (Ed.), *Consequences of Maternal Drug Abuse*, NIDA Res Monogr 59 (1985) 48–60.
- [42] R.L. Thorndike, E. Hagen, J. Sattler, *The Stanford-Binet Intelligence Scale: 4th Edition*, Riverside Publishing, Chicago, 1986.
- [43] D. Wechsler, *Wechsler Intelligence Scale for Children* (3rd Edition), The Psychological Corporation, New York, 1991.