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# Neurodevelopment in offspring of hairdressers

Wendy M Kersemaekers\* MSc:

Nel Roeleveld PhD:

Gerhard A Zielhuis PhD: Department of Medical Informatics, Epidemiology and Statistics, University of Nijmegen, PO Box 9101, NL-6500 HB Nijmegen, The Netherlands.

Fons JM Gabreëls, PhD MD, Interdisciplinary Centre for Paediatric Neurology, University of Nijmegen, The Netherlands.

\*Correspondence to first author.

The hypothesis that intrauterine exposure to hairdressers' chemicals adversely affects neurodevelopment of the offspring was investigated. Neurodevelopmental characteristics were analysed using a historical cohort study of reproductive disorders among hairdressers in The Netherlands. Because exposure in hair salons to agents toxic to reproductive processes might have changed over time, two specific study periods were examined: from 1986 to 1988 and from 1991 to 1993. Nine thousand hairdressers and 9000 clothing sales clerks (referent group) who were in the reproductive age in the defined study periods were selected by the trade association for service jobs. Frequency matching assured comparability with regard to age. All women were invited by mail to complete a short self-administered questionnaire on their reproductive history, including questions on the ages of their child at the times of the first words, first sentences, and first steps, and the occurrence of seizures during fever. The results showed that in 1986 to 1988 more children of hairdressers started speaking their first words after 15 months and their first sentences after 24 months. For 1991 to 1993 no increased risks of these outcomes were found. Seizures during fever had occurred more often among children of hairdressers in 1986 to 1988, and in 1991 to 1993, especially when women had been working until maternity leave. Although the quality of the data in this explorative study requires careful interpretation, the consistent results seem to indicate adverse effects on neurodevelopment among offspring of hairdressers in the earlier years (1986 to 1988). In the later years the effect seemed to be disappearing. However, these findings should be confirmed in more detailed studies.

The causes of functional developmental disorders range from genetic to pre-, peri-, and postnatal factors (First and Palfrey 1994). In addition to influences from the psychosocial environment, occupational exposures should be considered as risk factors for functional developmental delay in offspring, as chemical agents are able to interfere with the development of the CNS (Roeleveld 1991, Decouffé et al. 1993). Although many studies have been performed on the associations between occupation and structural malformations of the CNS (Holmberg and Nurminen 1980, Shaw and Gold 1988, Blatter et al. 1996), few human data are available on possible influences on minor defects in brain architecture or functional disorders.

From 1979 to 1987 Roeleveld et al. (1991) conducted a case control study on mental retardation and parental occupation. An important finding was the increased risk of mental retardation among the offspring of hairdressers (odds ratio [OR]=4.1, 95% CI 1.1 to 15.8). In the same study, the use of several chemical products was associated with increased risks, such as hair cosmetics and dyes (OR=3.7, 95% CI 0.9 to 15.1), and alcohol (OR=1.9, 95% CI 1.0 to 3.5). The odds ratios increased with the number of months worked during pregnancy, suggesting that late pregnancy is the critical period for functional disturbances (Roeleveld 1991). This was also suggested by the finding that only offspring whose mothers were exposed to solvents throughout pregnancy walked later than children in the unexposed group (Eskenaazi et al. 1988). This was, however, not found for other neurodevelopmental outcomes. In another case control study on mental retardation and maternal employment, too few hairdressers were included to allow conclusions to be drawn (Decouffé et al. 1993).

Many hair products contain solvents (International Agency for Research on Cancer 1993, Kersemaekers et al. 1995b) and solvents are known to interfere with brain development. Intrauterine exposure to solvents has been associated with CNS malformations (Holmberg and Nurminen 1980). Ethanol has been associated with deficits in attention and mental and motor development at doses considerably lower than those associated with fetal alcohol syndrome (Streissguth et al. 1984, Barrison et al. 1985). Moreover, maternal alcohol consumption during pregnancy is reported to be a risk factor for mental retardation in offspring (Roeleveld et al. 1992).

Given the suggested increased risk of mental retardation in offspring of hairdressers, and the wide range of chemicals (including solvents) used in hairdressing salons, we hypothesized that exposure to hairdressers' chemicals during pregnancy might lead to functional developmental disorders in offspring. In a large study on reproductive disorders among hairdressers, information was gathered on three developmental milestones (age at first steps, first words, and first sentences) as proxy variables for child development (Neligan and Prudham 1969; Capute et al. 1986; Shapiro et al. 1987, 1990; Blasco 1991, First and Palfrey 1994). Also, the occurrence of seizures during a period of fever was investigated as a potential indicator for subnormal neurodevelopment (Smith 1994).

## Method

### STUDY PERIODS

Because the use of some hazardous chemicals (dichloromethane, some dye formulations) has recently (1990) been banned or limited in several countries (International Agency for Research on Cancer 1993), and increasing

attention has been paid to working conditions such as ventilation and the use of gloves, risks might be most likely in earlier years (Kersemaekers et al. 1995b). Therefore, we explored whether children of hairdressers had increased risks of delayed achievement of developmental milestones and of seizures during fever in two periods, 1986 to 1988 and 1991 to 1993. Based on the date of conception, pregnancies were included in the first study period when conceived between 1 January 1986 and 31 October 1988, and were included in the second study period when conceived between 1 January 1991 and 31 October 1993.

#### POPULATION

Hairdressers and clothing sales clerks (control group) were identified through the database of the trade association for service jobs (DETAM), which retains information about Dutch workers in this branch for a period of 5 years. At the start of the study, data as far back as 1989 were available. Women who were registered as a hairdresser ( $N=9000$ ) or a sales clerk in a clothing store ( $N=9000$ ) in 1989 or in 1991, and who were of reproductive age (22 to 35 years) in the two study periods (1986 to 1988 and 1991 to 1993), were selected. Sales clerks were chosen as controls because of comparability with regard to educational and socioeconomic level and working conditions (e.g. standing and stress) except for chemical exposure. Frequency matching in 5-year age groups assured comparability with regard to age.

#### DATA COLLECTION

All 18 000 women were sent a mailing consisting of an introductory letter and a short self-administered questionnaire. To increase the response rate, two reminders were sent after 2 and 6 weeks. In order to minimize selective non-response and information bias, the study was presented to the participants as a study on pregnancy and working conditions in general. In the questionnaire, women were asked whether they had ever been pregnant. If so they were asked questions about time to pregnancy and the outcome for each pregnancy. The functional developmental characteristics asked for were age at first words, age at first sentences, and age at first steps. Age at starting to speak the first sentences might be a better indicator of language development than age at first words. Because age at first sentences is more difficult to remember, we decided to ask for both language milestones. In addition, a question was asked as to whether the child had ever had seizures during a period of fever, including familial and atypical seizures, which might be an indicator of subnormal neurodevelopment. In addition, information was gathered on the month and year of conception, and gestational age at birth. The first day of the last menstrual period was considered to be the start of each pregnancy. As a check of the registered occupation, information was gathered on the actual occupation during pregnancy and the number of hours worked during three pregnancy periods: months 1 to 2, months 3 to 5, and month 6 until the beginning of maternity leave.

#### OUTCOME DEFINITIONS

The original outcome data were dichotomized in the analyses. For speaking the first words and making the first steps the cutoff point was 15 months; for using sentences the cutoff point was 24 months. These cutoff points were chosen based on the literature (Capute et al. 1986; Shapiro et al. 1987, 1990; First and Palfrey 1994). However, in the literature several cutoff

points were used. In choosing between these cutoff points we took into account that the number of children with 'delayed' milestone achievement would be sufficient, independently of occupational group. According to the literature, approximately 10% of the children studied achieve the milestones after these ages (Capute et al. 1986; Shapiro et al. 1990).

We considered age of the mother at conception, educational level, gravidity, birthweight, and gestational age and sex of the child as potential confounders. Based on the Dutch school system, women were divided into low and high educational levels, corresponding with 10 or fewer years and more than 10 years of education, respectively. Children with congenital malformations were excluded from the analyses in order to obtain a homogeneous study population.

Because the age of the children in the second study period ranged from 0 to 3 years with a median of 2 years in both occupational groups, many children were too young to have reached developmental milestones at the time of data collection. Therefore, only children older than 2 years at the start of data collection were included. As the cutoff point for speaking the first sentences was 24 months, this outcome was analysed among children older than 2.5 years.

#### ANALYSES

Separate analyses were performed for each study period. Relative risks and 95% confidence intervals were calculated. Only women who reportedly had worked at least 10 hours per week during the first 2 months of pregnancy were included in the analyses. To avoid problems with correlated outcomes, for each study period the first pregnancy of a woman that fulfilled the selection criteria was selected.

For each outcome additional analyses were performed for women who worked during months 1 and 2, months 1 to 5, and month 1 until maternity leave. To find out whether the number of hours worked affected the risks, separate analyses were performed for women who worked more than 25 hours per week.

The effect of confounding was investigated by stratification and comparison of the adjusted relative risk (Mantel Haenzel) with the crude relative risk.

#### Results

Response rates were 72 and 66% for hairdressers and sales clerks, respectively (Table 1). Approximately 4% of the questionnaires were returned because of incorrect addresses. Of the women who returned the questionnaire, 3358 (54%) hairdressers and 2796 (49%) sales clerks had been pregnant at least once, leading to 6012 and 5024 pregnancies, respectively. Most of the women registered as a hairdresser actually worked as a hairdresser during pregnancy (70%). However, only 58% of women registered as a sales clerk actually worked in this occupation while pregnant. The percentage of women who had not worked during pregnancy was 22 among hairdressers and 26 among sales clerks. The remaining women had worked in another occupation. The proportions of conceptions in the first and second study periods were comparable for hairdressers and sales clerks. After selecting one pregnancy per woman that had resulted in a liveborn child without malformations and in which the mother worked for more than 10 hours per week during the first 2 months, 539 women were included in the first study period and 1852 in the second study period. In the second study period 1044 children were older than 2 years.

**Table I: Response and number of pregnancies per occupational group and study period**

	Hairdressers (%)	Sales clerks (%)
Originally selected	9000	9000
Women who received the questionnaire	8668(96)	8629(96)
Respondents	6270(72)	5688(66)
Women with pregnancies	3358(54)	2796(49)
Pregnancies	6012	5024
Pregnancies worked as a hairdresser or sales clerk <sup>1</sup>	4236(70)	2932(58)
Pregnancies worked as a hairdresser or sales clerk conceived in 1986–1988	490(12)	304(10)
pregnancies of liveborn children	350	225
>10 worked hours per week		
children without malformations	340	217
one pregnancy per women	330	209
Pregnancies worked as a hairdresser or sales clerk conceived in 1991–1993	1606(38)	1181(40)
pregnancies of liveborn children	1175	881
>10 worked hours per week		
children without malformations	1132	859
one pregnancy per woman	1047	805

<sup>1</sup>In 89 pregnancies of registered hairdressers the women worked as sales clerks and in 12 pregnancies of registered sales clerks the women worked as hairdressers.

**Table II: Characteristics of the study population**

	1986–1988		1991–1993	
	Hairdresser N(%)	Control N(%)	Hairdresser <sup>1</sup> N(%)	Control <sup>1</sup> N(%)
Live births	330	209	611	433
Educational level				
low	199(61)	139(67)	374(62)	242(56)
high	125(39)	68(33)	230(38)	189(44)
Age at conception				
≤25	140(42)	97(46)	98(16)	66(15)
26–30	174(53)	101(48)	421(69)	296(68)
>30	16(5)	11(5)	92(15)	71(16)
Gravidity				
first	270(82)	165(79)	476(78)	324(75)
second	47(14)	37(18)	103(17)	81(19)
≥third	13(4)	7(3)	32(5)	28(6)
Sex				
boy	161(49)	107(52)	320(53)	221(51)
girl	168(51)	99(48)	287(47)	210(49)
Birthweight				
≤2500g	30(9)	15(8)	63(10)	33(8)
>2500g	287(91)	183(92)	539(90)	385(92)
Prematurity				
<37 weeks	26(8)	20(10)	74(12)	46(11)
≥37 weeks	304(92)	189(90)	537(88)	387(89)

<sup>1</sup>Distribution of background variables among children older than 2 years.

As can be seen in Table II, the distribution of background variables was comparable between the two occupational groups. Only educational level was slightly lower among hairdressers compared with sales clerks in the first study period, and slightly higher in the second study period. Because stratification by these variables did not show differences of more than 10% compared with crude relative risks, we present crude results (Thompson 1994).

In both periods and occupational groups, 32 was the median number of hours worked per week during the first 2 months and during months 3 to 5 of pregnancy. Between month 6 and maternity leave the median number of hours worked was 31 for hairdressers and 30 for sales clerks in the first study period, and 25 for hairdressers and 30 for sales clerks in the second study period.

The number of missing values among early developmental characteristics was considerable, especially for language milestones (14 to 30%), but comparable between hairdressers and sales clerks.

More children of sales clerks started walking after 15 months in the first study period ( $OR=0.8$ , 95%  $CI$  0.5 to 1.2). This was more pronounced in the second study period (Table III). No association with number of months worked and number of hours worked was found. In the first study period children of hairdressers more often started speaking after 15 months ( $OR=2.4$ , 95%  $CI$  1.1 to 5.1). This risk was 8.4 (95%  $CI$  1.1 to 62.8) among women who worked more than 25 hours per week, but the numbers were small. Also, children of hairdressers started using sentences more often after 24 months ( $OR=4.1$ , 95%  $CI$  1.2 to 13.6). For this parameter, we found no association with number of months worked during pregnancy and number of hours worked per week. In the second study period, no increased risks were found for delayed speaking. Seizures during fever occurred more often among children of hairdressers in both study periods. In the first study period, this risk increased with the number of months worked during pregnancy (Table III). These risks were higher among women who worked more than 25 hours per week:  $OR_{months\ 1-2}=4.1$ , 95%  $CI$  0.9 to 17.7,  $RR_{months\ 1-5}=4.2$ , 95%  $CI$  1.0 to 18.2,  $OR_{month\ 1\ leave}=6.4$ , 95%  $CI$  0.8 to 49.4). In the second study period, confidence intervals excluded unity only when the mother worked until maternity leave ( $OR_{month\ 1\ leave}=1.8$ , 95%  $CI$  1.1 to 3.2). However, among women who had worked more than 25 hours per week the relative risk was 1.9 for all women irrespective of the number of months worked.

## Discussion

Based on literature and personal communication with manufacturers, we hypothesized that the risk of developmental delay among children of hairdressers was greatest in earlier years (1986 to 1988). The results tentatively confirm this hypothesis, showing increased risks of delayed speaking and seizures during fever, especially in the first study period. In evaluating the associations presented, however, the limitations of the study should be considered.

Concern among hairdressers about their occupational risks could have led to higher response rates among hairdressers, especially among those who have had poor reproductive outcomes. This would artificially inflate the risk estimates of a study. We attempted to prevent this by presenting this study as a study on pregnancy and working conditions in general, including physical workload and stress at the workplace.

However, the higher response rate of 72% among hairdressers compared with 66% among sales clerks makes our study vulnerable to selection bias. On the other hand, it should be noted that the outcomes studied are less known to be associated with occupational exposure than, for example, spontaneous abortions and congenital malformations.

Early developmental characteristics are sensitive to problems with recall: recall of early language acquisition may be imprecise in particular (Majnemer and Rosenblatt 1994). We attempted to reduce recall problems by advising the women to use the reports on growth of the infant from their pediatric center to answer the questions, but large variation in reporting these variables might still have occurred. This is evident from the considerable number of missing values on language milestones in our data. However, the similar proportions of missing values for hairdressers and sales clerks suggests random errors. It is also unlikely that information or selection bias accounted for increased risks in the first study period only. On the other hand, it should be noted that prevalences of delayed speaking and seizures during fever among children of sales clerks are low in the first period. Because these outcomes are not known to be related to occupational exposures, it is suggested to be unlikely that only sales clerks underreported in the first study period, but rather that both hairdressers and sales clerks underreported. The actual occurrence of delayed milestones would then be higher for both hairdressers and sales clerks, leading to similar relative risks. Because we do not have hard data on this, it cannot be ruled out that recall problems and selection bias have partly accounted for the associations found.

Seizures that occurred during a period of fever included both familial and atypical seizures. Because it is most likely that familiar seizures are equally distributed among children of sales clerks and hairdressers, atypical febrile seizures are expected to account for the differences found between hairdressers and sales clerks.

Self-reported job title was used as a proxy for exposure. No information was available on specific tasks performed or on actual exposure to hairdressers' products. In the analyses, only women who reported that they had worked more than 10 hours per week as a hairdresser or a sales clerk were included. We did not restrict the analyses to full-time workers, as a recent exposure assessment study has shown higher exposure levels of solvents during weekends and shopping nights, when most part-timers work (Kersemaekers et al. 1995a). If we restricted the analyses to women who worked more than 25 hours per week, only the risks of delayed speaking of the first words and of seizures during fever increased considerably.

Limited information was available on potential confounders. The control group was chosen because of assumed comparability concerning educational level, socioeconomic status, and physical workload. Although the available background variables were comparable between hairdressers and sales clerks, confounding by family history or other factors such as use of medication, alcohol consumption, and paternal exposure cannot be ruled out.

To our knowledge, no other studies have described early developmental characteristics in relation to exposure to hairdressers' chemicals. Eskenazi et al. (1988) did not find increased risks of adverse neurodevelopmental outcome due to

**Table III: Crude relative risks of delayed language and motor development and seizures that occur during fever per study period**

	1986-1988			1991-1993		
	Hairdresser <i>N</i> (%) <sup>1</sup>	Control <i>N</i> (%) <sup>1</sup>	RR (95% CI)	Hairdresser <i>N</i> (%) <sup>1,2</sup>	Control <i>N</i> (%) <sup>1,2</sup>	RR (95% CI)
Liveborn children	330	209		611	433	
1st steps						
>15 months	45(14)	36(18)	0.8(0.5-1.2)	66(11)	72(11)	0.6(0.5-0.9)
≤15 months	275(86)	169(82)		538(89)	353(83)	
1st words						
>15 months	30(12)	8(5)	2.4(1.1-5.1)	51(10)	34(10)	1.0(0.7-1.5)
≤15 months	225(88)	154(95)		477(90)	318(90)	
1st sentences						
>24 months	20(8)	3(2)	4.1(1.2-13.6)	22(6) <sup>3</sup>	19(9) <sup>3</sup>	0.7(0.4-1.3)
≤24 months	219(92)	144(98)		333(94)	203(91)	
Ever had seizures during a period of fever						
yes	21(6)	5(2)	2.6(1.0-6.9)	48(8)	24(6)	1.4(0.9-2.3)
no	306(94)	200(98)		558(92)	405(94)	
yes <sup>4</sup>	21(7)	3(2)	4.4(1.3-14.7)	46(8)	23(6)	1.4(0.9-2.3)
no <sup>4</sup>	287(93)	192(98)		526(92)	378(94)	
yes <sup>5</sup>	17(6)	2(1)	5.2(1.2-22.4)	42(9)	16(5)	1.8(1.1-3.2)
no <sup>5</sup>	251(94)	163(99)		431(91)	315(95)	

<sup>1</sup>Percentage of the known values of a specific outcome.

<sup>2</sup>Only children older than 2 years in May 1995 (start data collection) were included.

<sup>3</sup>Only children older than 2.5 years in May 1995 (start data collection) were included (hairdressers *N*=429, sales clerks *N*=284).

<sup>4</sup>Analyses among offspring of women who worked in pregnancy months 1-5.

<sup>5</sup>Analyses among offspring of women who worked until maternity leave.

in utero exposure to solvents, except for the age at first walking among offspring of mothers who had worked throughout pregnancy. However, the authors argue that this might have been due to insensitive outcome measures, low exposure levels, or diversity of solvents (Eskenazi et al. 1988). Mental retardation was related to exposure to hairdressers' chemicals in the study of Roeleveld et al. (1991), who described increased risks of mental retardation among offspring of hairdressers and of mothers who worked with solvents and hair dyes, especially during late pregnancy (Roeleveld 1991). In our data, only the more pronounced relative risks of seizures among offspring of women who worked in late pregnancy support the latter finding. Among the other outcomes, we did not find increasing risks with number of months of pregnancy worked. This might be due to the little contrast between women in the number of months worked in our study population.

Early developmental characteristics are suggested to be early indicators of later functional development. Language development is the best predictor of intelligence (Blasco 1991) and mental retardation (Shapiro et al. 1987). Motor milestones are known to be an excellent indicator of motor competence but not of cognition (Capute et al. 1985, Blasco 1991) or mental retardation, except for profoundly retarded children (Kaminer and Jedrysek 1996). With regard to this literature, and assuming that our results are due to chemical exposure, the results indicate that cognitive development in particular may be vulnerable to prenatal chemical exposure. The finding that children of sales clerks more often start walking later than 15 months of age is difficult to interpret.

Given the quality of the data in this explorative study, careful interpretation is needed. The data are consistent, however, with regard to speech development and seizures that occurred during fever, suggesting adverse effects on speech development among offspring of hairdressers between 1986 and 1988 and on the occurrence of these seizures among children of hairdressers in both periods, with most pronounced risks between 1986 and 1988. These findings should be confirmed in more detailed studies with emphasis on the measurement of confounding variables and functional development, and detailed exposure assessment in the hairdressing salon.

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