MRI findings in children with school problems who had been exposed prenatally to alcohol

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This study examined 17 children (nine males, eight females; mean age 13 years) with prenatal alcohol exposure of various durations. The aim of the study was to detect specific brain morphological alterations by means of MRI and to see if findings correlated with particular cognitive deficits. Of the 17 children, five had been exposed to heavy maternal consumption of alcohol (over 10 drinks/week) during the first trimester only; four had been exposed during the first and second trimester; and eight had been exposed throughout pregnancy. Five children had alcohol related neurobehavioural disorder, seven were diagnosed as having foetal alcohol effects and five were diagnosed as having foetal alcohol syndrome. Hypoplasia of the vermis was observed in 10 children and malformed posterior vermis in one additional child. Five children had hypoplastic cerebellar hemispheres. Hypoplasia of the corpus callosum was observed in two children. Small hippocampi were observed in three children and wide cortical sulci in six. No specific structural anomaly correlated with a particular neuropsychological deficit. In this study, deviations in the development of the vermis was the most sensitive morphological indicator of the effects of prenatal alcohol exposure. It was seen in every diagnostic group including children who had been exposed during only the first trimester of pregnancy.

The pattern of anomalies following exposure to heavy amounts of alcohol in utero were first reported by Lemoine and colleagues in France in 1968 and then independently by Jones and coworkers in the United States in 1973 (Jones et al. 1973). In 1980, Rosett established criteria, still widely used, for foetal alcohol syndrome (FAS): (1) pre- and/or postnatal growth retardation, (2) dysfunction of the CNS, and (3) a particular pattern of craniofacial characteristics. During the 1980s, it became evident that FAS represented only one end of a continuum of disturbed foetal development following prenatal exposure to heavy amounts of alcohol. Many children are born with only some of the characteristics of classic FAS. Such children have been described as exhibiting foetal alcohol effects (FAE; Rosett 1980, Robinson 1987, Conry 1990, Nanson and Hiscock 1990), partial FAS, or alcohol-related neurobehavioural disorder (ARND; Stratton 1996).

Children with FAS can be identified by experienced physicians. However, diagnosing FAE and ARND is difficult, especially if the information relating to prenatal alcohol exposure is lacking. Although similar neuropsychological deficits (attention disorders, school problems – especially in relation to mathematics) and poorer verbal than non-verbal performance have been reported in many prospective studies of children exposed to heavy amounts of alcohol in utero (Nanson and Hiscock 1990; Coles et al. 1991; Streissguth et al. 1991; Korkman et al. 1994,1998a; Streissguth et al. 1996), such deficits can be caused by prenatal factors other than prenatal alcohol exposure.

While neuropathological studies have revealed no consistent alcohol-induced morphological alterations in the developing nervous system of infants with FAS, various midline anomalies are markedly overrepresented. The first neuropathological study revealed severe dysmorphogenesis of the brain: aberration of neuronal migration resulting in multiple heterotopias, leptomeningeal hamartoma of glial and neuronal cells, incomplete development of the cerebral cortex, and agenesis of the corpus callosum (Jones and Smith 1973). In subsequent neuropathological studies, the most common anomalies reported have been leptomeningeal glioneuronal heterotopias, agenesis of the corpus callosum, and dysgenesis of the cerebellum and/or brainstem (Clarren et al. 1978, Pfeiffer et al. 1979, Wiesniewski 1983, Ferrer and Galofre 1987). Cases of anomalies in the holoprosencephaly–arhinencephaly spectrum have been reported (Pfeiffer et al. 1979, Jellinger et al. 1981, Ronen and Andrews 1991, Schaefer et al. 1991).

No consistent findings have been reported concerning brain-imaging studies of children with FAS or FAE. In the few CT studies reported, cortical or subcortical dysplasia has been recorded only in some patients and most CT findings were normal (Cremin and Jaffer 1981, Schaywitz et al. 1981, Neri et al. 1988, Riikonen et al. 1993). Reports of MRI studies on children with FAS or histories of heavy exposure to prenatal alcohol have been few, so far. A hypoplastic or agenetic corpus callosum was reported in a few patients by Matsson and colleagues (1992), Riley and coworkers (1995), and Swayze and coworkers (1997). Sowell and colleagues (1995) found the anterior cerebellar vermis to be significantly smaller in children who had been exposed to large amounts of alcohol than in control children. Mattson and coworkers (1994) demonstrated, using detailed volumetric analyses in six children and adolescents with FAS, that volumes of basal ganglia

were lower than normal, especially of the caudate nucleus, even when allowing for overall reductions in brain sizes. In a positron emission tomography study of four children with FAS, three children exhibited lower levels of glucose metabolism in the cerebellum than control individuals (Hannigan et al. 1995). Riikonen and colleagues (1999) found brain perfusion SPECT showed mild hypoperfusion of the left hemisphere in all 10 children with FAS studied.

The study reported here is a part of a prospective follow-up study involving a group of 82 children. The mothers of these children had been enrolled for study early in pregnancy because they were drinking large amounts of alcohol (Halmesmäki 1988). MRI of the brain was offered to those children experiencing learning difficulties at school and who had undergone detailed neuropsychological testing between 12 and 14 years of age. The aim was to determine whether there were specific structural findings that might help to identify causes of specific learning difficulties in children suspected of having been exposed to heavy maternal alcohol consumption during pregnancy.

Method

PARTICIPANTS

Early in their second trimester of pregnancy 82 mothers visited a special outpatient clinic at the University Central Hospital, Helsinki, for women who were consuming alcohol during pregnancy (Halmesmäki 1988). They were subsequently seen at intervals of 2 to 4 weeks by an obstetrician and social worker and their alcohol, nicotine, and drug consumption were registered. Alcohol concentration in blood and urine (Halmesmäki et al. 1988), mean cellular volume, and gammaglutamyltransferase were measured (Ylikorkala et al. 1987). Intraindividual daily consumption varied between 1 to 20 drinks. Efforts by the women to reduce alcohol consumption or abstain from drinking were supported. Foetal alcohol exposure was categorized as heavy if consumption exceeded 140 g per week or 630 g per month (Rosett et al. 1983). It was assumed that one drink of more than 33 cL strong beer (mean concentration of alcohol 5%), 12 cL light wine (<15% alcohol), 8 cL strong wine (15 to 21% alcohol), 4 cL spirits (>30 cL alcohol) contained about 14 g of alcohol.

Children who had been exposed in utero to heavy maternal consumption of alcohol were divided into three groups according to registered duration of exposure (self-reported exposure at control visits and results of blood and urine analysis). Group 1 children (n=29) had been exposed to heavy maternal consumption of alcohol during the first trimester of pregnancy only; group 2 children (n=27) had been exposed to heavy maternal consumption of alcohol during the first and second trimesters; and group 3 children (n=26) had been exposed to heavy maternal consumption of alcohol throughout pregnancy.

The study was approved by the ethics committee of the Hospital for Children and Adolescents and the Department of Radiology, University of Helsinki.

The children had undergone regular follow-up (Autti-Rämö et al. 1991a, b,1992a, b; Autti-Rämö 1993, 2000; Korkman et al. 1994, 1998a). One of the diagnoses listed below had been reached during long-term follow-up.

Foetal Alcohol Syndrome (FAS)
All of the three criteria listed below were met in this diagnosis: (1) Prenatal growth retardation in relation to length, weight, and/or head circumference (≤ 2SD according to Finnish normative material; Pihkala et al. 1989) and/or postnatal growth retardation in relation to length, head circumference (≤ 2SD) or relative weight (≤ 10%; Sorva et al. 1990a,b). (2) Dysfunction of the CNS indicated by difficulties in relation to cognitive ability, ranging from learning disability to specific learning difficulties. (3) Fulfilment of at least two of the following craniofacial criteria: (a) head circumference ≤ 2SD; (b) short palpebral fissure; (c) thin upper lip and hypoplastic philtrum.

Foetal Alcohol Effects (FAE)
Only two of the three FAS criteria listed above met. (In this study all children diagnosed as having FAE did not meet the craniofacial criteria.

Alcohol-related Neurobehavioural Disorder (ARND)
Cognitive difficulties (e.g. attention deficit, verbal and/or perceptual difficulties) consistently exhibited during follow-up without pre- or postnatal growth retardation or typical facies.

NEUROPSYCHOLOGICAL ASSESSMENTS

Detailed neuropsychological study was offered to all of the children in the study when they were between 12 and 14 years of age. The offer was accepted by 27 children experiencing learning difficulties at school. Two other children who had recently been clients of local psychologists expressed willingness to participate in the MRI study only.

Mean age of the children at the time of neuropsychological assessment was 12.9 years (SD 9.4); range 12–14.1 years. Neuropsychological assessment was performed using the Wechsler Intelligence Scale for Children – III; Finnish version (Wechsler 1991) and a developmental NEuroPSYchological assessment (NEPSY; Korkman et al. 1997). The latter involves detailed evaluation of performance in 27 neuropsychological subtests covering the domains of attention and executive functions, language, sensorimotor function, visuomotor function, and memory and learning. The tests have been standardized in the USA (Korkman et al. 1998b) and Finland (Korkman et al. 1998a) for children of 3 to 12 years of age. In this study, the children underwent 15 of the subtests. In this case, the Finnish version was used. Normative values for 13- and 14-year-old children were obtained by studying a group of 39 children recruited from two schools in Southern Finland. The schools were selected as being comparable to the sample of the Finnish NEPSY (Korkman 1997) with respect to social structure. Children were randomly selected from appropriate age groups. NEPSY results are expressed on a scale on which the normal mean is 10 and the standard deviation is 3.

MRI was offered to all children who were in special classes or exhibited neuropsychological deficits according to neuropsychological testing: 17 children agreed to participate in this part of the study. Five of these 17 children were from group 1, four children from group 2, and eight from group 3.

IMAGING PROTOCOL

MRI was performed using a Siemens Vision imager (Siemens, Erlangen, Germany) operating at 1.5T. Axial T_2 turbo spin echo (TSE) sequence 3500/90/2 (TR/TE/excitations) and FLAIR (fluid attenuation inversion recovery) 9999/105/1 (TR/TE excitations) scans were obtained. Both T_2 and FLAIR were 5 mm

thick with a 1 mm interslice gap. The field of view was 240 and matrix size was 196×256 on T_2 SE. The corresponding values were 280 and 182×256 respectively in the case of FLAIR images.

T_2 coronal slices were also obtained, using TSE sequence 4000/99/3 (TR/TE/excitations) with matrix size 330×512 and FOV 230. Images were 4 mm thick with a 0.8 mm interslice gap. A 3-dimensional (3D) magnetization-prepared rapid gradient echo (MPRAGE) sequence was also obtained, using the following parameters: 9.7/4.0/1 (TR/TE/ excitations), 10° flip angle, 256×256 matrix and FOV 250 yielding an in-plane pixel size of 1.0×1.0. Sagittal 3D slabs, 186 mm thick with 158 partitions and resulting section thickness, 1.18 were used. 3D data sets acquired were processed into 3D images. Axial and coronal reconstructions were undertaken for all patients.

VISUAL IMAGE ANALYSIS

Images were evaluated independently by two experienced neuroradiologists. Consensus was reached through discussion. The neuroradiologists were unaware of the length of time for which each child had been exposed to alcohol in utero and of diagnoses of the children.

Supratentorial and infratentorial atrophy was specifically sought. Hypoplasia of cerebellar hemispheres was recorded if sulci were clearly visible in any plane or sequence. Hypoplasia of the vermis was graded as described below (Fig. 1): grade I, slight widening of the anterior vermian sulci in the midsagittal T_1-weighted image; grade II, moderate widening of the anterior vermian sulci in midsagittal T_1-weighted and axial and/or coronal T_2-weighted images with mild thinning of the foliae; grade III, heavy widening of the vermian sulci in all planes with severe thinning of the foliae. Midline structures were

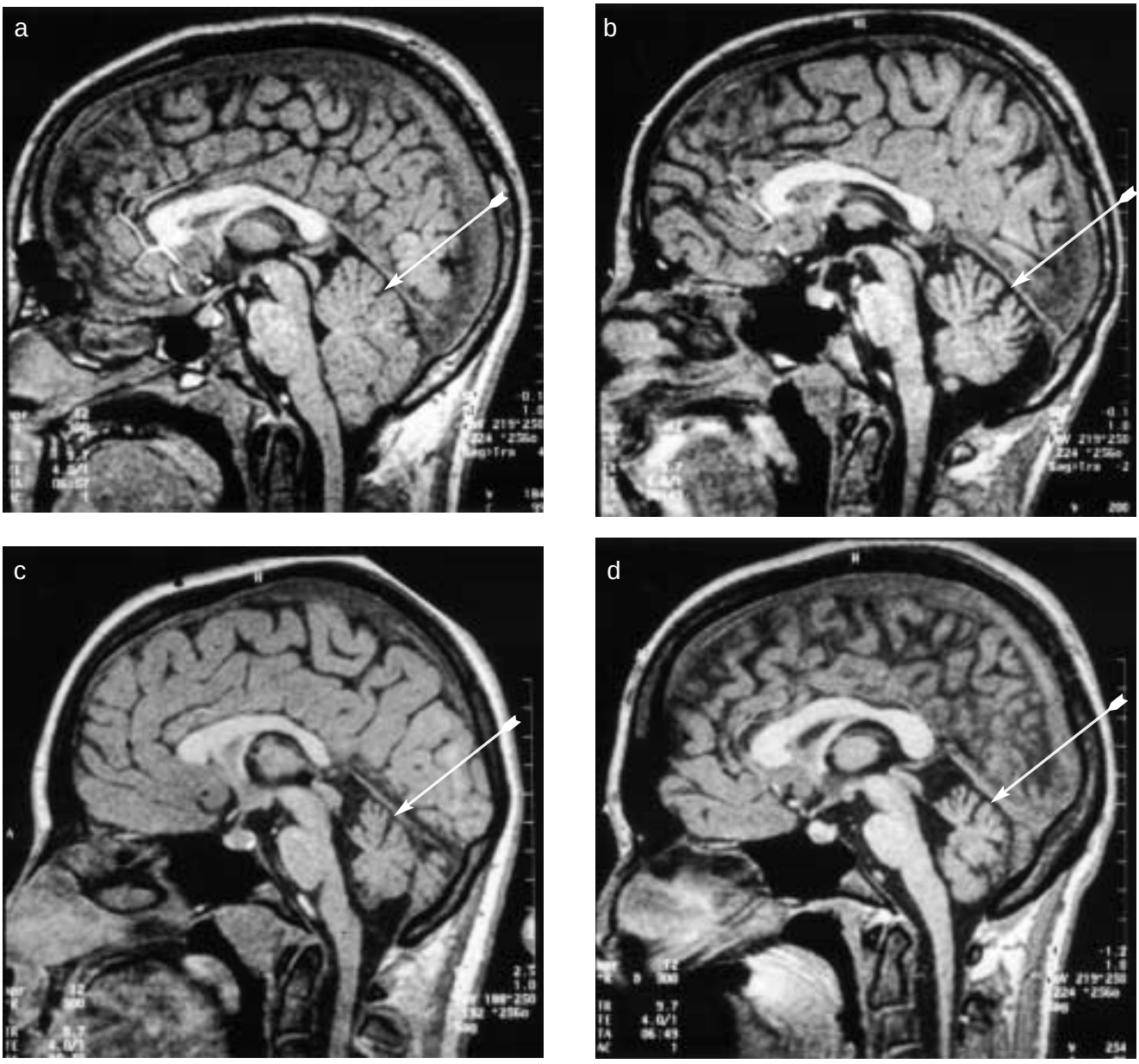

Figure 1: *Classification of degree of vermis hypoplasia (indicated by arrows): (a) normal, (b) grade I, (c) grade II, (d) grade III.*

evaluated for abnormalities. Focal parenchymal lesions and white-matter changes were recorded separately.

STRUCTURAL MEASUREMENTS

Structural measurements were made by a third experienced radiologist unaware of the diagnoses relating to the child and of the duration of exposure in utero to heavy maternal alcohol consumption. Midsagittal diameters of the brain stem were measured from T_1-weighted images in the mesencephalon, pons, and medulla oblongata (Raininko et al. 1994). Lengths and surface area of the corpus callosum, midsagittal diameters of the genu, body, and splenium and the midline internal skull-face area were measured as described by Laissy and colleagues (1993). Cerebral surface area was also measured. Areas of the mesencephalon, pons, medulla oblongata, posterior fossa, and vermis were measured from midsagittal images as described by Hashimoto and coworkers (1993). The bicaudate ratio (BCR) was obtained from T_2-weighted axial images in which the frontal horns were clearly visible and the septum was thinnest. The BCR was obtained from the width along the same line (Aylward et al. 1991). Ratios were calculated of areas measured from midsagittal images of posterior fossa:vermis, cerebrum:vermis, and cerebrum:corpus callosum. For each exposed child a control child of the same age and sex was chosen who was retrospectively verified not to have been prenatally exposed to heavy alcohol, had normal growth measurements, normal facial appearance, and no difficulties at school. As the study involved a small number of children, statistical analysis of the measurements was made between all exposed children and the controls, not between subgroups (e.g. according to the length of exposure.

STATISTICS

Significances of differences in results of measurements made on MRI images between patients and age- and sex-matched control individuals were tested using the Mann–Whitney *U* test. Relations between morphological abnormalities and neuropsychological findings were first assessed using correlational analyses (Pearson's product–moment correlation). Significances of relations were then assessed using contingency tables and kappa analyses. For the NEPSY subtests values more than 1SD below the normal mean (i.e. of 6 or less) were considered poor.

Results

Sex, age, diagnosis, results of growth measurements, types of schooling education, and type of carer are shown in Table I.

VISUAL FINDINGS ON MRI

These results are to be found in Table II. Hypoplasia of the vermis of varying severity was observed in two of the five children in group 1, in three of the four children in group 2, and in five of the eight children in group 3. One additional child in group 3 had an abnormal lower part of the vermis suggesting a migration disorder. Five children had mild hypoplasia of their cerebellar hemispheres. In four of the children this was combined with vermian hypoplasia.

A thin, hypoplastic corpus callosum was observed in only two children in group 3 – in one of them the rostrum was absent. One child in group 2 had small, thin hippocampi, and the normal serrated upper surface of the hippocampal head was lacking. Two additional children (one in group 1, one in group 3) exhibited left-sided hippocampal thinning. There were no signal increases in the affected hippocampi in the T_2-weighted images. Six children had wide cortical sulci. The parietal region was affected in all of these children. In one child, lesions consistent with periventricular leukomalacia were noted. One child exhibited a small focal lesion in the lentiform nucleus, most probably an old ischemic lesion.

MEASUREMENTS ON MRI

Measurements are shown in Table III. Internal surface areas of the skull, posterior fossa, and cerebrum were significantly

Table I: Details of children exposed prenatally to alcohol

Group	*Participant nr*	*Sex*	*Age (y)*	*Diagnosis*	*HC SD*	*Length SD*	*Weight %*	*Carer(s)*	*Schooling*
I	1	M	14.02	ARND	0.5	0.7	10	Biological mother	PS
I	2	M	13.17	ARND	–0.3	0.35	4	Biological father	LI
I	3	F	13.28	ARND	0.2	1.7	–6	Foster parents	SLD
I	4	M	13.71	FAE	–0.7	–0.1	–14	Biological parents	SLD
I	5	M	13.3	FAE	–1	–1	–11	Orphanage	LI
II	6	F	13.4	ARND	0.5	–0.5	–5	Biological mother	M
II	7	F	14.54	ARND	–1	–1.6	–9	Adoptive parents	M
II	8	M	13.19	FAE	–2.1	0.4	–1	Foster parents	M
II	9	F	14.82	FAE	–0.2	–1.2	19	Biological parents	SLD
III	10	M	14.49	FAE	–1.5	0.3	–18	Foster parents	M
III	11	M	13.49	FAE	1.7	2.5	–16	Foster parents	SLD
III	12	F	15.14	FAE	–2.6	–0.3	–16	Adoptive parents	LI
III	13	F	14.72	FAS	–3.4	–2.4	0	Orphanage	M
III	14	F	13.57	FAS	–4	–1.3	–3	Foster parents	M
III	15	M	13.65	FAS	–2	1.2	–21	Biological father	SLD
III	16	F	14.59	FAS	–3.3	0	–16	Foster parents	LI
III	17	M	14.85	FAS	–3.7	–1.7	–30	Grandmother	LI

ARND, alcohol-related neurobehavioural disorder; FAE, foetal alcohol effects; FAS, foetal alcohol syndrome; PS, class for children with psychosocial difficulties; LI, class for children with low IQ (65–85); SLD, class for children with school problems; M, mainstream class.

smaller in all three exposed groups ($p=0.0175$, $p=0.03$, and $p=0.0103$ respectively). Area of vermis did not differ significantly between groups. The two children exhibiting grade II and grade III vermis atrophy had significantly smaller vermis areas (5.5 and 6.1 cm^2) than the mean vermis area of the control group (12.43, SD 1.23 cm^2). The corpus callosum was significantly smaller in area ($p=0.0103$), length ($p=0.001$), and diameter of splenium ($p=0.152$) in children who had been exposed in utero to heavy maternal consumption of alcohol. As regards midbrain structures, only the diameter of the mesencephalon was significantly smaller in the exposed group ($p=0.0252$). There was no significant difference in bicaudate ratio. Calculated ratios of areas of posterior fossa:vermis, cerebrum:vermis, and cerebrum:corpus callosum did not differ between the exposed children and control participants.

NEUROPSYCHOLOGICAL FINDINGS

Findings relating to the children following neurocognitive tests are summarized in Table IV.

NEUROPSYCHOLOGICAL FINDINGS IN RELATION TO MRI FINDINGS

When correlation coefficients between neuropsychological and neuroanatomical parameters were 0.40 or greater the relations were given further consideration. Head circumference had a positive correlation of 0.465 (*ns*) with Performance IQ. In a contingency table defining head circumference of 2 SDs or more below the normal mean as a pathological sign, the kappa value was 0.595 ($p=0.020$). Head circumference also had a correlation of 0.4 (*ns*) with the Tower subtest result, of 0.695 ($p=0.012$) with the Speeded Naming subtest result, and of 0.597 ($p=0.019$) with the results of the Manual Motor Series subtest. When applied to contingency table analyses, however, these correlations were not significant.

Table II: Visual MRI findings in individual patients

Participant nr	*Diagnosis*	*Corpus callosum*	*Cerebellar vermis*	*Cerebellar hemispheres*	*Liquor space*	*Other specific findings*
1	ARND					
2	ARND					
3	ARND		Gr I atrophy	Gr I atrophy		
4	FAE		Gr I atrophy		Wide parieto-occipitally	Left hippocampus small Small foci in left lentiform nucleus Arachnoidal cyst in cisterna magna
5	FAE			Gr I atrophy		
6	ARND					
7	ARND		Gr I atrophy		Wide parietally	
8	FAE		Gr I atrophy	Gr I atrophy	IV ventricle enlarged	
9	FAE		Gr I atrophy	Gr I atrophy		
10	FAE		Gr I atrophy		Wide parietally	
11	FAE		Gr I atrophy			Both hippocampi small, Gr I PVL
12	FAE					
13	FAS		Gr III atrophy	Gr I atrophy	Wide fronto-parietally	
14	FAS	Hypoplastic, absent rostrum	Gr II vermis atrophy		Wide parietally	
15	FAS		Malformed lower part of vermis			
16	FAS					Left hippocampus small
17	FAS	Thin	Gr I atrophy		Wide fronto-parieto-occipitally	

ARND, alcohol-related neurobehavioural disorder; FAE, foetal alcohol effects; FAS, foetal alcohol syndrome; PVL, periventricular leukomalacia.

Table III: Results of structural measurements that showed significant difference between exposed and non-exposed groups

Structure	*Exposed mean*	*Group SEM (n=17)*	*Control mean*	*Group SEM (n=17)*	*p*
Skull surface area	117.12	3.6	188.54	2.9	0.0175
Cerebral area	114.68	2.6	123.54	2	0.0103
Corpus callosum area	5.63	0.22	6.53	0.22	0.0103
Length of corpus callosum	66.47	1.24	71.82	0.82	0.001
Width of splenium	9.06	0.28	10.29	0.35	0.0132
Posterior fossa area	34.69	1.05	37.73	0.67	0.03
Mesencephalon area	2.36	0.06	2.55	0.05	0.0313
Mesencephalon width	16.71	0.27	17.53	0.23	0.0252

There was a tendency to a significant correlation between abnormality of vermis and poor results in the Visual Attention subtest (correlation coefficient 0.404). A significant correlation was found between abnormality of the cerebellar hemispheres and poor results on the Repetition of Nonsense Words subtest (correlation coefficient 0.548, p=0.034). Enlarged liquor spaces also had a correlation of 0.448 (*ns*) with poor results on the Repetition of Nonsense Words. In a contingency table and kappa analysis significant correlations were not found.

Three children exhibited hippocampal abnormality. Results of tests were examined only at individual level. There were no findings common to the three children. The results achieved in the three NEPSY memory subtests were similar to those of the total exposed group.

There were marked individual variations in the test results. No individual pattern of impairment seemed to be characteristic of specific MRI findings.

Discussion

Participation in this prospective follow-up study was voluntary, which inevitably led to bias. Children exhibiting severe psychiatric symptoms in addition to school problems and children with general severe learning disorder did not participate in the study. Such children might have exhibited more marked abnormalities of brain morphology. However, all of the children who participated in the study reported here exhibited cognitive deficits on detailed neuropsychological analysis. As all participants had been exposed to alcohol in utero for known periods of time. Therefore, the aetiology may be assumed to be the heavy consumption of alcohol for known periods of time by the mothers of the children during pregnancy. In five children impairment was fairly generalized. In the other children the pattern of deficits varied, affecting one domain or several domains. Thus, this study provides evidence that MRI might be used as a means to evaluate whether the specific cognitive difficulties of a child are related to prenatal alcohol exposure.

The results of this study further increase the number of morphological abnormalities reported following MRI of the brains of children exposed to heavy maternal alcohol consumption. In contrast with earlier reports, abnormalities of the cerebellum, especially hypoplasia of the vermis, were the most common visual findings. Sowell and colleagues (1996) reported smaller anterior vermis sizes, measured using MRI, in the brains of children who had been exposed in utero to heavy maternal alcohol consumption as compared with control children. In the present study, vermis areas were measured along the surface of the vermis. They did not reflect widening of the anterior sulci (grade I vermis hypoplasia). In grade II and grade III vermis hypoplasia, mean vermis surface was less than half of the mean for the control group. Malformations in the structure of the cerebellum (Clarren et al.1978, Wiesniewski 1983) and complete agenesis of the vermis (Pfeiffer et al. 1979) have been observed on autopsies of children with FAS but Riikonen and colleagues (1999) were the first to report cerebellar atrophy in two of 11 children with FAS. The cerebellar vermis is formed by fusion of the developing hemispheres. The vermis is fully formed by the end of the 15th gestational week (Volpe 1995). This finding corresponds to our results suggesting that development of the cerebellar vermis is sensitive to exposure of the foetus to heavy maternal alcohol consumption early in pregnancy. The finding also corresponds to results of a recent animal study (Maier et al. 1999) showing loss of cerebellar Purkinje cells following exposure of foetuses to heavy amounts of alcohol.

Hypoplasia of the vermis has, to our knowledge, not been reported in any study on children with school problems, but several investigators have suggested that cerebellar functions affect cognitive functions (Schmahmann 1990, Botez 1992, Nicolson et al. 1995, Fiez 1996, Bloedel et al. 1997, Berquin et al. 1998, Rae et al. 1998). In the study reported here, cerebellar abnormality (of the hemispheres) correlated significantly only with results on a task of repetition of nonsense words. This task requires oromotor skills in articulating complex, unfamiliar words and auditory, phonological perception of their speech sounds. In a study by Paradiso and coworkers (1997) of normal volunteers, vermis abnormality was found to be related to IQ, verbal memory, and motor dexterity. Ciesielski and colleagues (1997) studied brain sequelae of childhood radiation and chemotherapy in normally developing control individuals and individuals with autism. In all groups, vermis abnormality correlated with results of neuropsychological measurements. Vermis hypoplasia may, however, be unrelated to any specific cognitive function, but may indicate a more global brain and cognitive impairment. This would seem to be the case in the present study in which all of the children with widened cortical sulci also exhibited hypoplasia of the vermis. In children, anatomical and functional deviance may be relatively diffusely and globally related, due to many mechanisms of neural plasticity and adjustment during development.

A thin, hypoplastic corpus callosum was observed in two

Table IV: Mean performance of children exposed to alcohol in utero on WISC III and NEPSY (n=15)

Assessment	*Mean*	*SD*
WISC		
Full-Scale IQ	84	15.52
Verbal IQ	87.9	14.6
Performance IQ	88.7	19.4
NEPSY		
Attention and executive functions	7.25	5.13
Tower	7.24	5.13
Auditory attention and response set	7.24	5.18
Visual attention	9.65	4.09
Language		
Phonological processing	5.85	4.45
Speeded naming	7.51	2.89
Repetition of nonsense words	6.77	2.95
Sensorimotor functions		
Visuomotor precision	9.58	3.68
Manual motor series	6.33	4.95
Visuospatial functions		
Design copying	8.93	3.39
Arrows	7.89	4.29
Memory and learning		
Memory for faces	9.53	3.79
Name learning	7.51	3.9
Narrative memory	7.90	3.98

NEPSY results are expressed on a scale on which the normal mean is 10, (SD 3) and values below 7 are considered poor.

children with FAS. In one of them the rostrum was also absent. Areas and lengths of the corpus callosum and the diameter of the splenium were significantly smaller in the group of children who had been exposed in utero to heavy maternal alcohol consumption. The ratio between the midsagittal areas of the corpus callosum and cerebrum was not statistically smaller in the exposed children compared with the control children. This explains the visual image of a normal-sized corpus callosum. The significance of a small corpus callosum is not clear (Schaefer et al. 1991). Njiokiktjien and coworkers (1994) found smaller corpus callosum surface areas in children with school problems following perinatal adverse events than in children with school problems attributable to genetic factors. These findings suggest that impaired growth of the corpus callosum may be a factor involved in the occurrence of school problems. Development of the corpus callosum is associated temporally with migrational events in the cerebrum, particularly between the third and fifth months of pregnancy (Volpe 1995). However, thickening of the corpus callosum in the occipital and temporal regions becomes complete only after birth. This corresponds to our finding of hypoplasia of the corpus callosum only in children who had been exposed in utero to heavy maternal alcohol consumption throughout pregnancy. In several studies, (Mattson et al. 1992, Riley et al. 1995, Swayze et al. 1997, Riikonen et al. 1999) all children reported to exhibit hypoplasia or agenesis of the corpus callosum were children affected by FAS. Previous findings of our group (Autti-Rämö 1993) suggests that children with FAS are exposed to heavy amounts of alcohol beyond mid-pregnancy.

Small hippocampi were observed in three children, one in group 1 and two in group 3. The small sizes could have reflected loss of pyramidal cells in CA1 (Barnes and Walker 1981, Bonthius and West 1990) as the structure of the hippocampus was otherwise normal; no mesial sclerosis was observed, nor did any of these individuals have a history of prolonged febrile convulsions or epilepsy. None of the three children exhibited specific memory deficits, contrary to what might have been expected on the basis of the results of the study by Uecker and Nadel (1996). No abnormalities of the basal ganglia were observed on MRI. No differences were found between children who had been exposed in utero to heavy maternal alcohol consumption and control children when bicaudate measurements were used to assess the size of basal ganglia. Our findings in this connection, therefore, differ from those of Mattson and coworkers (1994).

In the study reported here, enlarged liquor spaces were observed in four children with FAE and two children with FAS. The parietal region was affected in all of these children. Cortical atrophy was significantly related to Performance IQ. This finding corresponds to prevailing conceptions of the posterior cortex being important for visuospatial and visuoconstructional functions. Cortical atrophy was also reported by Riikonen and colleagues (1999) in two of 11 children with FAS but it was not confined to the parietal region.

Measurements made using MRI images suggest that brain growth overall is affected as the relations of different brain regions did not differ significantly between groups, although the midsagittal area of the cerebrum, corpus callosum, posterior fossa, and the BCR were smaller in those children who had been exposed in utero to heavy maternal alcohol consumption. This could partly explain why individual patterns and degrees of impairment showed no clear relation to MRI findings, and why significant relations were found only between head circumference and neurocognitive functions, in particular non-verbal intelligence (Performance IQ). This variable also tended to affect the results of the Tower subtest (considered to be an executive functions subtest), the Speeded Naming subtest, and the Manual Motor Series subtest. Relationships between head circumference and neurocognitive performance anticipated on the basis of the reports of Nelson and Deutschberger (1970), Sells (1977), and Dolk (1991) were seen in spite of the small group size.

The number of children studied was relatively small. When the children were divided into subgroups by morphological abnormality the numbers were, obviously, even smaller. Exposure in utero to heavy maternal alcohol consumption varied between individuals, with respect to amounts of alcohol consumed, and with respect to timing and duration. Time-specific morphological and functional deficits obviously vary greatly between individuals (Stratton et al. 1996). In a larger group of exposed children additional correlations between structural and functional deviations might have been shown. In this study, development of the vermis was particularly affected by exposure in utero to heavy maternal alcohol consumption. It was seen in every diagnostic group, including the children exposed to heavy maternal alcohol consumption only during the first trimester of pregnancy, even in the presence of normal head circumferences. Widening of the cerebral sulci was the second most common abnormality but was seen only in children with FAS or FAE. Our results suggest that when hypoplasia of the vermis – alone or in combination with other structural abnormalities – is noted in a child with a school problem, exposure in utero to heavy maternal alcohol consumption should be considered as a possible cause. However, further studies may indicate that the same type of findings may occur following other risk factors operating during early gestation.

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Notices

9th International Child Neurology Congress and 7th Asian and Oceanian Congress of Child Neurology
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