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BRIEF REPORT

Development of children born to mothers with mental health problems: subcortical volumes and cognitive performance at 4½ years

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Abstract In a prospective longitudinal study, we investigated the outcomes of children born to mothers clinically referred for mental health problems during pregnancy (risk group, $n = 17$) relative to a control group ($n = 31$). Child cognitive functioning, and for subgroups ($n = 10 + 17$), brain morphometry as derived from Magnetic resonance imaging (MRI), was measured at 4½ years. Cognitive data included abstract visuospatial reasoning/problem solving and verbal scores. Subcortical regions of interest included the amygdala, accumbens area, hippocampus, caudate and putamen, chosen because their development seems potentially sensitive to an adverse intrauterine milieu and environmental experiences, and also due to their implication in cognitive and emotional processes. The risk group exhibited poorer abstract reasoning scores than the control group. No differences were found for verbal scores. MRI revealed smaller putamen volume in children in the risk group. Irrespective of group, putamen volume was positively related to visuospatial reasoning performance. Our results suggest that maternal psychopathology may be associated with child putamen development, nonverbal reasoning and problem solving skills.

Keywords Maternal psychopathology · Neuroimaging · Cognitive development · Brain morphology · Abstract reasoning · Putamen

Introduction

The importance of maternal mental health for childreńs neurocognitive development is increasingly recognized [1, 2]. An early indicative that antenatal stress might affect brain development in humans was the finding that stressful life events during mid-gestation were associated with smaller newborn head circumferences [3]. A recent prospective study with Magnetic resonance imaging (MRI) found that pregnancy-specific anxiety was associated with decreased gray matter density in multiple regions [4]. Most studies investigating prenatal or postnatal effects of stress on brain morphology have focused on the amygdala and the hippocampus [5, 6]. In contrast, evidence point to basal ganglia structures as among those particularly vulnerable to intrauterine drug exposure [7]. It is uncertain whether the development of these brain structures is especially vulnerable to substances, or may more generally differ in biomedical risk groups. As these structures are involved in cognitive and emotional

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processes [8–13], alterations in their development might have long term consequences for cognitive and emotional functioning of the child.

In the current prospective longitudinal study, we investigated the outcomes of children born to mothers with mental health problems (risk group) relative to a comparison group. Brain morphology and aspects of cognitive functioning of the children were measured at 4½ years. We chose, based on the above and due to a small sample, to focus on medial temporal and basal ganglia neuroanatomical volumes. Recent findings show that prenatal maternal depression symptoms are associated with lowered cognitive functioning of the child [1, 2], and we tentatively hypothesized that the risk group could show lower neurocognitive scores. As for neuroanatomical volumes findings have been mixed for child effects of maternal cortisol levels, depression and anxiety, with indications of larger amygdala volumes, yet no hippocampal difference [5, 6], or temporal reductions [4]. However, based on reductions in other at-risk groups [7], we tentatively hypothesized smaller basal ganglia.

Methods

Mothers were recruited during pregnancy as part of a prospective longitudinal project on the development of children born to mothers with substance abuse and/or mental health problems [14]. We here focus on the children born to mothers with mental health problems. They were recruited from an outpatient clinic where pregnant women were offered treatment for mental health problems. The comparison group did not have known prenatal risk factors and was mostly recruited through local official well-baby clinics. This article comprises cognitive and MRI data collected at 4½ years of age. Birth and cognitive data were available from 48 participants (risk group: 17 mother–child dyads (11 girls); comparison group: 31 dyads (15 girls)). MRI data were available from a subset of 27 (15 girls), thereof (risk group: 10 children (7 girls); comparison group: 17 children (8 girls)). For a flow chart of the study see Supplementary Fig. 1.

MRI data were collected using a 1.5 T Siemens Avanto scanner and neuroanatomical volumes were estimated using Free Surfer 5.1.0. (http://surfer.nmr.mgh.harvard.edu). The matrix reasoning, a measure of nonverbal abstract problem solving (or inductive reasoning) and the picture naming subtests from the Wechsler Preschool and Primary Scale of Intelligence, third edition [15] were used to measure aspects of cognitive performance. Further information about samples, maternal antenatal psychopathology, MRI acquisitions, image analysis, cognitive measures and maternal cognition is presented in supplementary materials.

Groups were compared using general linear models (GLMs) with the characteristic of interest as dependent variable and group as fixed factor. For the MRI segmentations, ICV was used as a continuous covariate. For the analyses of cognitive scores, sex and group were used as fixed factors. For details of analyses and additional analyses, see Supplementary Material.

Results

Although within the normal range on birth parameters, children in the risk group had lower weight [F (1,45) = 9.67, 3,319 ± 629, range 1,740–4,132, vs. 3,791 ± 403, range 3,060–4,715, $p < 0.01$, partial $\eta^2 = 0.18$] and shorter gestational age [F (1, 40) = 9.28, 38.9 ± 1.3, range 36–41, vs. 39.7 ± 1.4, range 37–42, $p < 0.01$, partial $\eta^2 = 0.19$]. Head circumference did not differ between the two groups (See Supplementary Table ST 1).

There was a main effect of group on putamen volume [F (1, 24) = 6.59, $p < 0.02$, partial $\eta^2 = 0.22$], with smaller putamen in the risk group ($M = 11332$, SD = 1261) compared to the comparison group ($M = 12375$, SD = 1090). No group differences were found for other structures (Table 1).

The risk group had a lower matrix reasoning score (raw scores) ($M = 11.29$, SD = 4.2) than the comparison group ($M = 13.48$, SD 3.0) [F (1, 45) = 5.00, $p < 0.05$, partial $\eta^2 = 0.10$]. There was no difference between the groups on verbal ability performance.

Gestational age and putamen volume correlated with matrix reasoning performance ($r = 0.37$, $p < 0.01$, $df = 43$ and $r = 0.44$, $p < 0.05$, $df = 23$), as plotted in Fig. 1.

Table 1 Neuroanatomical volumes (mm^3) of the two groups

Subcortical volume	Risk group $n = 10$		Comparison group $n = 17$			
	Mean	SD	Mean	SD	F	Sig.
Caudate	7667	1079	7739	677	0.06	0.811
Putamen	11332	1261	12375	1090	6.59	**0.017**
Accumbens	1398	199	1562	226	2.97	0.098
Hippocampus	7671	624	7553	759	0.93	0.344
Amygdala	2581	271	2650	265	0.09	0.774

Differences in volume of selected subcortical structures were tested with general linear model, with neuroanatomical volumes as dependent variables, group as fixed factor and intracranial volume as covariate

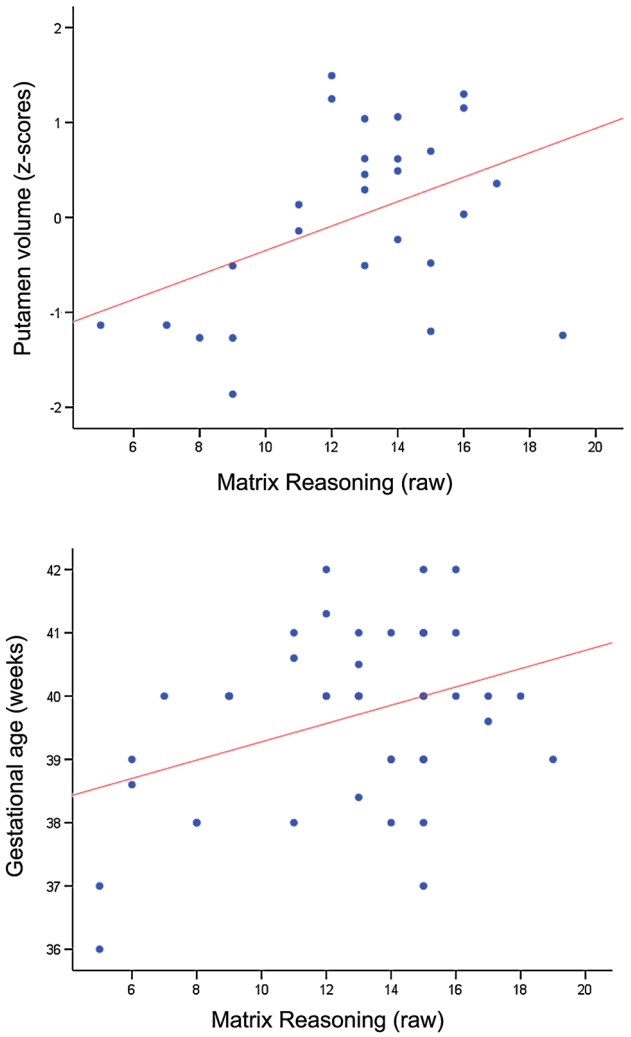

Fig. 1 Matrix reasoning. The *plots* illustrate the relation between matrix reasoning scores at 4½ year and putamen volume and gestational age (weeks) at birth. In the *upper plot,* variability associated with sex and intra cranial volume is removed and putamen values are plotted as *z*-transformed residuals.

Discussion

The present results are indicative that maternal mental health problems are associated with brain development and cognitive functioning of the child. In line with population-based data, children born to mothers with psychiatric problems had shorter gestational age [16] and also lower birth weight. In our small at-risk population we demonstrated, albeit normal, lower abstract reasoning performance and smaller putamen volume in the children at 4½ years compared to the comparison group. Length of gestation correlated with reasoning performance, supporting a possible link between subtle variations in fetal maturity and neurocognitive development. Abnormalities of the HPA axis and disruption of the circadian rhythm of cortisol secretion may occur in depression and anxiety [17]. Stress hormones may be a common candidate mechanism affecting putamen development and the length of gestation. Child putamen segmentations have, to our knowledge, not specifically been investigated in relation to maternal mental health. Our findings are suggestive that maternal mental health might influence child development of inductive reasoning, and the association between putamen volume and reasoning performance points to a possible neural foundation.

The implication of the putamen in inductive reasoning is supported by fMRI studies [18, 19] and studies of patients with putamen/basal ganglia lesions showing impaired abstract reasoning performance [11, 20]. Also in line with our findings, recent studies are pointing to associations between striatal and putamen morphology and different aspects of intelligence [13, 21–23]. In a large sample of children positive intelligence-striatal size (not separating caudate and putamen) relations were reported, but only in males [22]. In preadolescent children, a complex relation between putamen shape and intelligence was reported, where for the matrix reasoning both compression and expansion of the putamen were related to improved performance [23]. Also, studies of young adults have found positive correlations between putamen volume and figural crystallized [13], spatial and fluid intelligence [21]. However, for this age group knowledge of how structural maturation of the putamen and other brain regions enables development of intelligence is not well established. The putamen has been found to increase by more than 100 % in the first year of life, with continued, yet markedly lower (7.5–8.6 %) growth in the second year [24]. We know less of the developmental changes ongoing at the exact age of the children in the present study. However, at some point, there is likely a shift from putamen gray matter growth to reductions in development. Large-scale brain development studies starting at age 4.5 or 8 are suggestive that the putamen is moderately and linearly (negatively) related to age [25, 26], although inverted U-shaped developmental trajectory, peaking at 7.5 years in girls and 10.0 years in boys also has been reported (only caudate volume reported) [27]. Regardless of the exact maturational trajectory, however, the smaller putamen volumes in the present risk group may potentially be associated with their lower birth weight. Birth weight has been found to be positively related to striatal volumes, including putamen, throughout development independently of age [28], possibly indicating a stable effect. Further investigations and larger sample sizes are, however, needed to determine if this may be the case.

A major concern of the study is the small sample size. Conclusions cannot be drawn with certainty. Maternal mental health problems may relate to multiple factors that influence fetal and postnatal environment that might affect both brain and cognitive development.

There is a growing recognition that maternal mental health is an important factor contributing to the neurocognitive development of the child. Our results suggest that maternal antenatal psychopathology is associated with putamen volume and inductive reasoning performance in children. Better understanding of these relations is important for the development of appropriate prevention as well as treatment and follow-up strategies of high-risk mothers and children.

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Conflict of interest None of the authors have competing financial interests regarding this work.

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