

# Early-life origins of schizotypal traits in adulthood

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## Background

Although schizotypal traits, such as anhedonia and aberrant perceptions, may increase the risk for schizophrenia-spectrum disorders, little is known about early-life characteristics that predict more pronounced schizotypal traits.

## Aims

To examine whether birth size or several other early-life factors that have been previously linked with schizophrenia predict schizotypal traits in adulthood.

## Method

Participants of the Northern Finland 1966 Birth Cohort Study ( $n=4976$ ) completed a questionnaire on positive and negative schizotypal traits at the age of 31 years.

## Results

Lower placental weight, lower birth weight and smaller head circumference at 12 months predicted elevated positive schizotypal traits in women after adjusting for several confounders ( $P<0.02$ ). Moreover, higher gestational age, lower childhood family socioeconomic status, undesirability of pregnancy, winter/autumn birth, higher birth order and maternal smoking during pregnancy predicted some augmented schizotypal traits in women, some in men and some in both genders.

## Conclusions

The results point to similarities in the aetiology of schizotypal traits and schizophrenia-spectrum disorders.

## Declaration of interest

None.

Schizotypy refers to latent liability to schizophrenia on the level of personality organisation. Several lines of evidence link schizotypy with schizophrenia. Schizotypy consists of positive and negative schizotypal traits, which closely resemble symptoms characterising schizophrenia.<sup>1</sup> In addition, prospective studies have shown increased risk for developing schizophrenia-spectrum disorder among those with more pronounced schizotypal traits,<sup>2,3</sup> and relatives of people with schizophrenia have been shown to exhibit clinical schizotypy (schizotypal personality disorder), suggesting a genetic link between these disorders.<sup>4</sup> Moreover, recent studies of brain structure and function have shown comparable brain abnormalities and cognitive deficits between individuals with schizotypal personality disorder and schizophrenia.<sup>5</sup> Although epidemiological studies addressing risk factors for schizotypy remain sparse, those increasing the risk of schizophrenia have been intensively studied. These factors include small placental weight and body size at birth,<sup>6,7</sup> short gestational age,<sup>8</sup> maternal antenatal depression,<sup>6</sup> winter birth,<sup>9</sup> perinatal brain damage,<sup>6</sup> undesirability of pregnancy,<sup>10</sup> late birth order,<sup>9</sup> twin birth,<sup>11</sup> central nervous system (CNS) viral infections in childhood,<sup>12</sup> urban early childhood environment,<sup>13</sup> and high<sup>14</sup> or low<sup>15</sup> childhood socioeconomic status. Moreover, in several neurodevelopmental models of schizophrenia (e.g. Murray<sup>16</sup>), prodrome to schizophrenia<sup>17</sup> and schizotypal personality<sup>18</sup> have been suggested. The models underline the interplay of early and late environmental influences and genes in the development of the disorder. We aimed to study whether placental weight, body size at birth or at 12 months, or other above-mentioned early-life factors that have been linked with schizophrenia in previous research also predict schizotypal traits in adulthood.

## Method

### Participants

Births in 1966 in Northern Finland (96.3% of all births) were eligible ( $n=12\,058$  live births).<sup>19</sup> Women were recruited through

maternity health centres, approximately 80% visited these centres for the first time by the sixteenth gestational week. In 1997, individuals in the original cohort who were living in the original target or Helsinki area were invited for clinical examination ( $n=8463$  eligible; 72.7% of those alive). Questionnaires concerning behavioural tendencies, opinions and experiences were given to those participating in the study ( $n=6033$ ). Of those participating in the clinical examination, 84.7% ( $n=5112$ ) returned the questionnaire on schizotypal traits. The analytical sample for this study comprises 4976 (58.8% of those eligible: 2233 males and 2743 females; mean age: 31.2 years (s.d.=0.36)) participants who provided adequate data on schizotypal traits (<50% missing data; 79 participants were excluded), who were not diagnosed with schizophrenia according to DSM-III-R<sup>20</sup> criteria after re-checking all psychiatric diagnoses appearing in the National Finnish Hospital Discharge Register (32 participants were excluded),<sup>21</sup> and scored below four on the validity scale (25 participants were excluded), which was incorporated into the questionnaire (the Infrequency Scale).<sup>22</sup> We used the validity scale, as recommended by Chapman *et al*,<sup>22</sup> to ensure that participants were not responding in a highly idiosyncratic or random fashion (sample item: 'I cannot remember a time when I talked with someone who wore glasses.'). Compared with the initial cohort, the participants in this study were more often women, had higher family socioeconomic status in early life and the pregnancy was more often desired; their mothers were less likely to smoke during pregnancy and were less depressed during pregnancy (data not shown). Even after adjusting for these factors, the participants were born at higher gestational age, were longer and heavier at birth and had longer head circumference at 12 months (data not shown). According to the validated data from the National Finnish Hospital Discharge Register,<sup>21</sup> 6 participants were diagnosed with an organic psychotic condition, 15 with other psychoses, 5 with psychotic or non-psychotic bipolar disorder, 23 with psychotic or non-psychotic unipolar depression, 14 with anxiety disorder, 34 with substance dependence, 31 with other Axis I mental disorders and 17 with personality disorder, in

1997. All the participants provided their written informed consent and the University of Oulu ethics committee approved the study.

## Measures

### Early-life characteristics

The course of pregnancy was prospectively recorded in maternity records and transferred by midwives onto the study forms (for a detailed description of the procedures see Rantakallio<sup>19</sup>). Mothers reported their smoking during pregnancy (yes/no), mood (normal/depressed), place of residence (urban/rural), birth order and desirability of pregnancy (yes/no/pregnancy wanted later) by answering a questionnaire during their 24–28th gestational week at the maternity health centres. Moreover, childhood family socioeconomic status was defined as mother-reported spouse's occupation, which was classified into five groups:<sup>14</sup> upper-level professionals/employers (highest prestige and usually requiring academic education, e.g. dentists, teachers; socioeconomic status class I); lower-level professionals (professionals with lower valuation and shorter education than in class I, e.g. office managers and ship's engineers; socioeconomic status class II); skilled workers (e.g. clerks and stewards; socioeconomic status class III); unskilled workers (e.g. night watchmen and office boys; socioeconomic status class IV); and farmers (socioeconomic status class V). Data were missing in 3.0% of the participants ( $n = 150$ ), so the mother's occupation was used instead.

Data on birth (99% occurred in hospitals) and on the newborn at the time of delivery was obtained from the hospital records. Gestational age was determined based on the mother's last menstrual period. Placental weight (g) and infant weight (kg) and length (cm) were measured immediately after birth. Children were considered to have incurred perinatal brain damage if they had an Apgar score of zero at 1 min or of less than five at 15 min after birth, convulsions during the neonatal period or a diagnosis of asphyxia, brain injury or intraventricular haemorrhage, but showed no CNS malformation, chromosomal aberrations or hereditary CNS degeneration (for more details, see Jones *et al.*)<sup>6</sup>. The season of birth was classified into four groups: Summer birth (June to August), Autumn birth (September to November), Winter birth (December to February), and Spring birth (March to May). Head circumference (cm) was measured at the welfare centres at 1 year of age, and data on CNS viral infections up to the age of 14 were collected mainly from the admissions records of four children's hospitals, the National Finnish Hospital Discharge Register, and the records of neurological out-patient clinics (for more details, see Rantakallio *et al.*)<sup>12</sup>.

### Adulthood characteristics

Adulthood data from the 31-year follow-up were collected with a questionnaire in 1997. Each participant's socioeconomic status was based on occupation and occupational status in 1997 with the following categorisation:<sup>23</sup> upper white collar employees with administrative, managerial, professional and related occupations (e.g. senior official, upper management); lower white collar employees with administrative and clerical occupations (e.g. clerical and sales worker); entrepreneurs; manual labourers; farmers; students/pensioners/ungrouped socioeconomic status; and the long-term unemployed. Adulthood body mass index (BMI) ( $\text{kg/m}^2$ ) was calculated and categorised (< 18.5 low weight; 18.5–25: normal weight; > 25: overweight).

## Schizotypal traits

In conjunction with the 31-year follow-up examination, a questionnaire on positive and negative schizotypal traits was given

to the participants. Positive schizotypal traits were measured with the Perceptual Aberration Scale (PAS)<sup>24</sup> as suggested in the literature.<sup>1</sup> The PAS explores the distorted perception of one's body or of other objects with 35 items such as 'I have sometimes felt that some parts of my body no longer belong to me' and 'Sometimes when I look at things like tables and chairs, they seem strange'. The PAS has successfully identified individuals who report psychotic-like experiences, schizotypal symptoms and social withdrawal during structured diagnostic interviews,<sup>25</sup> and, together with the Magical Ideation scale, predicted increased risk for DSM-III-R psychoses, schizotypal symptoms, and psychotic-like experiences in a 10-year follow-up,<sup>2</sup> as well as diagnoses of depression in a 5-year follow-up.<sup>3</sup> The internal consistency of the PAS was good (Cronbach's  $\alpha = 0.83$ ).

As suggested by Vollema & Van den Bosch,<sup>1</sup> negative schizotypal traits were measured with scales tapping on anhedonia, a decreased capacity to experience pleasure, with the following questionnaires: (a) revised version of the 61-item Physical Anhedonia Scale (PhAS); and (b) 40-item revised version of the Social Anhedonia Scale (SAS) (the original PhAS and SAS were published,<sup>22</sup> but the revised versions of 1978 and 1982 respectively were not: further details available from the author). These true-false self-reporting measures provide indices of the pleasure derived from physical (sample item of the PhAS: 'One food tastes as good as another to me') and social-interpersonal sources (sample item of the SAS: 'I attach very little importance to having close friends') respectively. Previous studies have shown that individuals with schizophrenia score higher on the PhAS and SAS scales than do control groups.<sup>22</sup> Furthermore, participants scoring exceedingly high on the PhAS exhibit more schizotypal symptoms, greater social isolation and lower heterosexual interest and activity than do controls.<sup>25</sup> Moreover, longitudinal studies have shown that higher SAS scores among college students have been associated with increased risk for psychosis, more pronounced schizotypal personality, or diagnoses of schizophrenia-spectrum disorder or any combination of these.<sup>2,3</sup> The internal consistency of the PhAS and the SAS were good (Cronbach's  $\alpha = 0.84$  and  $0.82$  respectively).

## Statistical analyses

We used multiple linear regression analyses to test the study hypothesis that small placental weight, small body size at birth or at 12 months or both predict more pronounced schizotypal traits at the age of 31. We re-ran the analyses and controlled for the other early-life factors and adulthood socioeconomic status and BMI. Moreover, we used multiple linear regression analyses to test whether other early-life factors (i.e. gestational age, birth order, twin birth, season of birth, perinatal brain damage, maternal smoking during pregnancy, maternal antenatal depression, desirability of pregnancy, place of residence and the family socioeconomic status in early childhood and CNS viral infections in childhood) predict schizotypal traits in adulthood. We tested in separate multivariate models whether each early life factor was associated with schizotypal traits after controlling for the other life factors: birth weight, adulthood socioeconomic status and BMI. Furthermore, multiple regression analyses were performed for a substratum of those born full term.

We conducted all analyses separately for both genders due to gender differences in schizotypal traits and gender-specific findings in the epidemiology of schizophrenia. The PAS was inversely transformed and the PhAS and the SAS were log-transformed to attain normality and all the dependent variables were standardised separately by gender (mean = 0, s.d. = 1). Independent categorical variables were dummy coded before

entering them into the regression analyses. In all reported multivariate analyses, multicollinearity indices remained at an acceptable level.

## Results

Women had a lighter placenta, were lighter and shorter at birth, had a smaller head circumference at 12 months of age, higher gestational age, and experienced fewer viral CNS infections in childhood than did men (online Table DS1). Compared with men, women also had a lower BMI in adulthood, more often belonged to lower white collar occupations, were less often manual labourers and scored higher on the PAS, and lower on the PhAS and the SAS.

### Placental weight, body size at birth and at 12 months and schizotypal traits in adulthood

Table 1 shows that in women, lower placental weight, lower birth weight and smaller head circumference at 12 months of age predicted higher scores on the PAS after adjusting for gestational age ( $P < 0.04$ ). Thus, for every 100 g increase in placental weight, 1 kg increase in birth weight and 1 cm increase in head circumference at 12 months, the PAS decreased by 0.04, 0.09 and 0.04 standard deviations respectively. Placental weight, birth weight and head circumference at 12 months remained significant predictors of the PAS in women after further adjusting for maternal smoking during pregnancy, maternal antenatal depression, season of birth, perinatal brain damage, desirability of pregnancy, birth order, twin birth, place of residence and the family socioeconomic status in early childhood, and CNS viral infections in childhood as well as socioeconomic status and BMI in adulthood. In men, placental weight, or body size at birth or at 12 months were not significantly associated with schizotypal traits at the age of 31 years ( $P > 0.28$ ).

### Other early-life factors and schizotypal traits in adulthood

The univariate and multivariate effects of other early-life factors on positive schizotypal traits appear in the online Table DS2,

and on negative schizotypal traits in the online Table DS3. In women, multivariate analyses showed that higher birth order predicted elevated scores in the PAS after controlling for the other early-life factors, birth weight, adulthood socioeconomic status and BMI ( $P = 0.01$ ). In addition, the family socioeconomic status in early childhood contributed to higher scores in the PAS and the SAS independently such that the offspring of unskilled workers (Class IV) scored higher on the PAS, whereas offspring of farmers (Class V) scored higher on the SAS ( $P < 0.04$ ). Furthermore, those women with a higher gestational age ( $P = 0.01$ ) and who were born in the winter or autumn compared with the summer ( $P = 0.04$ ), scored higher on the PhAS after controlling for the other early-life factors, birth weight, adulthood socioeconomic status and BMI. In addition, we tested whether prematurity (gestational age  $< 37$  weeks) predicted schizotypal traits, but failed to find any significant associations (in women  $P > 0.22$  and in men  $P > 0.44$ ).

In men, multivariate analyses showed that the desirability of the pregnancy predicted the PAS and the SAS after controlling for the other early-life factors (birth weight, adulthood socioeconomic status and BMI) such that undesired pregnancies yielded higher scores than did desired pregnancies in both questionnaires ( $P < 0.01$ ); pregnancies desired at a later time also yielded higher scores in the SAS ( $P = 0.02$ ). Furthermore, maternal smoking during pregnancy independently predicted elevated scores in the PhAS ( $P < 0.01$ ), and offspring of farmers reported higher scores on the PhAS and the SAS than did the offspring of socioeconomic status class III after controlling for the other early-life factors (birth weight, adulthood socioeconomic status and BMI ( $P < 0.007$ )).

### Early-life characteristics and schizotypal traits in adulthood in full-term infants

By excluding 114 participants who were born preterm (4.4% of the study population) and by conducting the analyses in a substratum of participants who were born full term (37+0 to 42+0 weeks of gestation), all significant inverse associations between placental weight, birth weight and head circumference at 12 months with the PAS remained so. Furthermore, shorter

**Table 1** Linear regression analyses showing one standard deviation difference in schizotypal traits at the age of 31 years according to one unit difference in placental weight and body size at birth or at 12 months in women

	Gestational age adjusted model ( $n = 2232$ to 2594)		Fully adjusted model <sup>a</sup> ( $n = 2107$ to 2446)	
	$B^b$ (95% CI)	$P$	$B^b$ (95% CI)	$P$
Perceptual Aberration Scale (PAS) <sup>c</sup>				
Placental weight (100 g)	-0.04 (-0.07 to -0.01)	0.01	-0.04 (-0.07 to 0.01)	0.02
Birth weight (1000 g)	-0.09 (-0.17 to -0.00)	0.04	-0.12 (-0.21 to -0.03)	0.01
Birth length (1 cm)	-0.02 (-0.04 to 0.00)	0.05	-0.02 (-0.04 to 0.00)	0.07
Head circumference at 12 months (1 cm)	-0.04 (-0.07 to -0.01)	0.004	-0.05 (-0.08 to -0.02)	0.002
Physical Anhedonia Scale (PhAS) <sup>c</sup>				
Placental weight (100 g)	-0.01 (-0.04 to 0.02)	0.50	-0.02 (-0.05 to 0.02)	0.29
Birth weight (1000 g)	-0.05 (-0.13 to 0.04)	0.29	-0.03 (-0.07 to 0.02)	0.26
Birth length (1 cm)	-0.02 (-0.04 to 0.00)	0.08	-0.01 (-0.03 to 0.01)	0.19
Head circumference at 12 months (1 cm)	0.02 (-0.01 to 0.05)	0.23	0.02 (-0.01 to 0.05)	0.25
Social Anhedonia Scale (SAS) <sup>c</sup>				
Placental weight (100 g)	0.01 (-0.02 to 0.04)	0.64	0.00 (-0.03 to 0.04)	0.79
Birth weight (1000 g)	0.03 (-0.06 to 0.12)	0.49	0.01 (-0.04 to 0.06)	0.64
Birth length (1 cm)	-0.01 (-0.03 to 0.01)	0.46	-0.00 (-0.02 to 0.02)	0.66
Head circumference at 12 months (1 cm)	0.00 (-0.03 to 0.03)	0.91	0.00 (-0.03 to 0.03)	0.97

a. Models adjusted for gestational age, birth order, twin birth, season of birth, perinatal brain damage, maternal smoking during pregnancy, maternal antenatal depression, desirability of pregnancy, place of residence and the family socioeconomic status (SES) in early childhood, and central nervous system viral infections in childhood, as well as SES and body mass index in adulthood.

b.  $B$  refers to unstandardised regression coefficient derived from linear regression analyses.

c. Scale scores were transformed to attain normality and standardised separately by gender.

birth length in women predicted higher scores on the PAS after adjusting for gestational age (unstandardised  $B = -0.02$ , 95% CI  $-0.04$  to  $-0.00$ ,  $P = 0.02$ ) and for all other early-life factors (unstandardised  $B = -0.02$ , 95% CI  $-0.04$  to  $-0.00$ ,  $P = 0.04$ ). With regard to other early-life factors, all the previously mentioned significant associations with schizotypal traits remained so, except for one: in women, the effects of gestational age on the PhAS were rendered non-significant ( $P = 0.08$ ).

## Discussion

We found that in women at the age of 31 years, small placental weight, low birth weight and small head circumference at the age of 12 months predicted more pronounced positive schizotypal traits. These associations were not explained by other early-life factors that previous research has linked with increased risk for schizophrenia or with small body size at birth; i.e. gestational age, birth order, twin birth, season of birth, perinatal brain damage, maternal smoking during pregnancy, maternal antenatal depression, desirability of pregnancy, place of residence and the family socioeconomic status in early childhood, and CNS viral infections in childhood, as well as socioeconomic status and BMI in adulthood.<sup>6–15</sup> It is highly unlikely that these results reflect diagnosed schizophrenia since we excluded all individuals with hospital treatment for schizophrenia or that they reflect immaturity-related illness since the results remained after excluding those born prematurely. Placental weight and body size at birth or at 12 months, failed to predict negative schizotypal traits in either men or in women.

To our knowledge, this study is the first to report associations between placental weight or body size at birth and at 12 months and schizotypal traits. Our findings are in line with those of previous studies showing that small placental weight, small body size at birth or both predict schizophrenia<sup>6,7</sup> and personality traits in adulthood,<sup>26</sup> as well as with studies showing that maternal–fetal undernutrition, one of the underlying causes of small body size at birth, affect adulthood personality disorders.<sup>27</sup> Moreover, our results are concordant with a study of individuals with schizophrenia or affective psychosis that showed an inverse association between birth weight and retrospectively reported schizoid and schizotypal traits in childhood and adolescence.<sup>28</sup>

In addition to placental weight and body size at birth and at 12 months we also tested whether several other early-life factors that previous research has linked with increased risk for schizophrenia or small body size at birth<sup>6–15</sup> predicted more pronounced schizotypal traits in adulthood independently of each other, birth weight and of adulthood socioeconomic status and BMI. We found that in both women and men, negative schizotypal traits were more pronounced in the offspring of farmers and in women, and that positive schizotypal traits were more characteristic if the childhood family socioeconomic status was low. Although an association between childhood socioeconomic status and subsequent schizophrenia is uncertain, our findings are in line with those of previous studies showing increased risk for schizophrenia in those with low childhood socioeconomic status.<sup>15</sup> In line with some epidemiological studies of schizophrenia,<sup>9</sup> later birth order and winter/autumn birth predicted respectively augmented positive and negative schizotypal traits in women. Contrary to expectations, we found that a higher gestational age predicted elevated physical anhedonia in women. This finding may reflect neurodevelopmental alterations found in postmaturely born infants, and interestingly, a recent study found that postmaturity (gestational age  $>41$  weeks) was more prevalent in a small subtype of schizophrenia.<sup>29</sup> Moreover, those men whose

mother's smoked during pregnancy were characterised by elevated physical anhedonia. Smoking during pregnancy has been associated with low birth weight, may lead to dysregulation in neurodevelopment and can indicate a higher risk for psychiatric problems.<sup>30</sup> However, to the best of our knowledge, no previous study has examined associations between prenatal nicotine exposure and schizophrenia or schizotypal traits. Furthermore, we found that in men, positive and negative schizotypal traits were more pronounced if the mother considered the pregnancy undesired or desired it later. This finding is concordant with those of previous studies linking the undesirability of a pregnancy, possibly reflecting prenatal and postnatal psychosocial stress with increased risk for schizophrenia in the offspring.<sup>10</sup>

## Possible explanations

Obviously, we can only speculate about the mechanisms by which small placental weight or body size at birth and other early-life factors associate with schizotypal traits in adulthood. According to the developmental origins of health and disease hypotheses, a suboptimal early-life environment may induce changes in fetal physiology and set the stage for less optimal life-course development.<sup>31</sup> Fetal growth is regulated by the complex interplay of genetic and environmental factors, the latter of which include for instance the quantity or quality of maternal macronutrient intake or both, the maternal–fetal hormonal milieu and maternal psychosocial stress. Furthermore, hypoxia, placental insufficiency and the restriction of placental blood flow may limit the growth of the fetus. Due to a large genetic component in the vulnerability to schizophrenia-spectrum disorders<sup>16–18</sup> it is also possible, although empirical evidence is lacking, that some of the associations we found are explained by gene–environment interactions or by pleiotropic genetic effects.

Empirical evidence shows that small body size at birth along with other pre- and perinatal factors associate with alterations in brain structure and function resembling those found in schizophrenia-spectrum disorders. Recent studies link low birth weight with increased lateral ventricular volume in adulthood,<sup>32</sup> and preterm birth with a smaller hippocampus.<sup>33</sup> Concurrent with these findings, enlarged ventricular volume and decreased hippocampal size are among the most consistent structural brain abnormalities found in people with schizophrenia, and interestingly, some studies have recently found women with schizotypal personality disorder to have smaller hippocampal size.<sup>34</sup> Moreover, fetal hypoxia has been associated with enlarged ventricular volume in people with schizophrenia<sup>35</sup> and small hippocampal volume in those with schizophrenia in first-degree relatives.<sup>36</sup>

Schizotypal personality disorder has been associated with alterations in several physiological systems, such as increased hypothalamic–pituitary–adrenal (HPA) axis activity,<sup>37</sup> and psychotic-like symptoms of schizotypal personality disorder have been linked with increased dopamine function, as measured with the dopamine metabolite homovanillic acid in cerebrospinal fluid (CSF) or plasma, whereas deficit-like symptoms were related to reduced dopamine function.<sup>5</sup> Interestingly, evidence suggests that altered HPA activity is associated with small body size at birth,<sup>38</sup> prenatal stress,<sup>39</sup> parental low socioeconomic status<sup>40</sup> and prenatal nicotine exposure<sup>41</sup> in humans. Although direct evidence of associations between small body size at birth and dopamine neurotransmission is lacking, research in animals shows that prenatal stress, which has been shown to decrease birth size, results in gender-specific alterations in the dopamine neurotransmission of the offspring.<sup>42</sup> Consistently, low social status associated with lower homovanillic acid concentrations in the

CSF of non-human primates,<sup>43</sup> and prenatal nicotine exposure significantly reduced serotonin and dopamine turnover in the rat forebrain.<sup>44</sup> However, the extent to which these findings explain our results remain unclear.

### Gender differences

In accordance with the neurodevelopmental model of schizophrenia,<sup>16</sup> we found gender differences in the associations between early factors and schizotypal traits. Previous studies have shown clear differences in the epidemiology and course of schizophrenia between women and men; for example the association between lower prenatal and postnatal growth with schizophrenia may be confined to women<sup>45</sup> and age at onset of this disorder tends to be 3–4 years later in women. Although the neurobiology underlying these findings is unclear, it has been hypothesised to result, in part, from differences in the growth hormone–insulin-like growth factor axis,<sup>45</sup> and neuroprotective and neuromodulatory effects of oestrogens.<sup>46</sup> Interestingly, evidence exists that lower exposure to maternal insulin-like growth factor-I and oestrogens *in utero* is associated for example with lower birth weight,<sup>47,48</sup> higher parity<sup>49</sup> and maternal smoking during pregnancy.<sup>47,48</sup> Although speculative, gender dimorphism in the growth hormone–insulin-like growth factor axis and protective effects of oestrogens may partly explain gender differences in our study and some of the associations between early-life factors and schizotypal traits.

### Strengths and limitations

The obvious strengths of our study include a large sample of ethnically homogenous participants derived from a general population, the prospective study design, the wide variety of early factors that could contribute to augmented schizotypal traits and the use of well-validated scales to measure schizotypal traits. This study also has its limitations. Compared with the original cohort, our sample more often comprises women from more affluent families and with larger body size at birth. However, these differences should only diminish the associations between early-life factors and schizotypal traits in adulthood. It is also notable that participants of the study have passed through the high-risk period for schizophrenia, and although some may exhibit late-onset disorder, others exhibit enduring behavioural dispositions rather than an escalating disorder. The use of self-report questionnaires to measure sensitive topics, such as aberrant experiences, may infuse the responses with bias. Furthermore, in addition to the prenatal and early-life factors that predicted schizotypal traits in our study, subsequent studies should take into account other factors that may be relevant to the epidemiology of schizotypy, such as breastfeeding, maternal influenza during pregnancy, and traumas/maltreatment or low parental affection or nurturing and aversive parenting behaviour during childhood. Moreover, as suggested by Cannon *et al*,<sup>17</sup> it will also be important to examine more complex interplay of prenatal and early postnatal factors on schizophrenia-spectrum disorders in the future studies.

As hypothesised based on epidemiological studies of schizophrenia, we found that lower placental weight and birth weight and smaller head circumference at 12 months predicted more pronounced positive schizotypal traits in women at the age of 31 years. Moreover, several other early-life factors, such as lower childhood family socioeconomic status, the undesirability of a pregnancy, winter/autumn birth, higher birth order and maternal smoking during pregnancy predicted augmented schizotypal traits in women, in men or in both genders.

As with the studies associating the origins of schizophrenia with prenatal life, our findings show that vulnerability factors may have their origins in the suboptimal early environment. Thus, our findings shed light on the early-life origins of schizophrenia-spectrum disorders through the aetiology of the vulnerability characteristics. Since several early-life factors that have been shown to increase the risk for schizophrenia also predict schizotypal traits, our results may lend indirect support to the shared genetic vulnerability to schizophrenia-spectrum disorders. Furthermore, from the perspective of public health, our findings provide important clues for identifying the early signs of vulnerability to schizophrenia-spectrum disorders, which may help in future preventive action.

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First received 5 May 2008, final revision 5 Dec 2008, accepted 30 Jan 2009

### Funding

This study was financially supported by the Academy of Finland (grants 104769, 106424, 212848), the Emil Aaltonen Foundation and the Finnish Graduate School in Psychology.

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