Journal of Affective Disorders 236 (2018) 120–126

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

Do mothers who are anxious during pregnancy have inattentive children?

Blanca Bolea-Alamañac[a], Simon JC Davies[b,*], Jonathan Evans[c], Carol Joinson[d], Rebecca Pearson[e], Petros Skapinakis[f], Alan Emond[g]

[a] General Systems Division, Centre for Addiction and Mental Health, University of Toronto, 33 Russel St., room 1071, Toronto ON M5S 2S1, Canada
[b] Geriatric Psychiatry Division, Centre for Addiction and Mental Health, 80 Workman Way, 6th Floor, Toronto ON M6J 1H4, Canada
[c] Office Room BF12, Oakfield House, Oakfield Grove, Clifton BS8 2BN, Bristol, UK
[d] Developmental Psychology, School of Social and Community Medicine, University of Bristol, Oakfield House, Oakfield Grove, Clifton, Bristol BS8 2BN,UK
[e] Psychiatric Epidemiology, Office BF11, Oakfield House, Oakfield Grove, Clifton, Bristol BS8 2BN, UK
[f] Division of Psychiatry, University College London, London W1T 7NF, UK Department of Psychiatry, University of Ioannina School of Medicine, Ioannina 45110, Greece
[g] Centre for Child and Adolescent Health, School of Social and Community Medicine, University of Bristol, Office Room BG6a, Oakfield House, Oakfield Grove, Clifton, Bristol BS8 2BN, UK

ARTICLE INFO

Keywords:
Attention
Anxiety
Pregnancy
ADHD
Hyperactivity
ALSPAC

ABSTRACT

Background: Maternal somatic anxiety during pregnancy may affect neural foetal development via corticoid pathways. Using a large epidemiological cohort, this study explores the relationship between maternal somatic anxiety in pregnancy and child scores on the Test of Everyday Attention in Children (TEA-Ch).

Methods: Linear regression was used to analyse the association of maternal somatic anxiety during pregnancy and performance of children on three subtests of the TEA-Ch at age 8.5 years that assess selective attention (Sky Search), sustained attention (Sky Search Dual Test) and attentional control (Opposite Worlds).

Results: Children with complete data on each subtest were included in the analysis, comprising 4,198 children for the Sky Search subtest, 3,845 for the Sky Search Dual Test and 4,202 for the Opposite Worlds subtest. No association was found between exposure to maternal somatic anxiety and child's performance in any of the TEA-Ch subtests either before or after adjusting for confounders. The results did not change when stratifying by gender.

Limitations: Selective attrition, lack of sensitivity of tests and lack of adjustment for the postnatal environment are possible limitations to this study.

Conclusions: We found no evidence of an association between exposure to maternal somatic anxiety in pregnancy and TEA-Ch scores. These results suggest that anxiety during pregnancy does not affect the development of children's attentional skills measured by TEA-Ch.

1. Background

The "developmental origins of health and disease model" (also known as foetal programming) proposes that prenatal environmental conditions such as nutritional deficiencies or maternal stress can elicit a biological programming response in the foetus in order to adapt more readily to postnatal adversity (Barker, 1990). A classic example of this type of prenatal adaptation is the increased insulin resistance found in children of malnourished mothers (Swanson and Wadhwa, 2008). Since both the brain and the placenta have endocrine functions, the idea that programming can extend to the brain of the child while in utero has been proposed. Animal studies have suggested that the intrauterine environment may programme the foetal brain for certain behavioral traits (Schlotz and Phillips, 2009). Early evidence of a possible role for foetal brain programming in humans came from studies of the Dutch famine. Researchers in Holland traced children born to mothers who survived the "Winter of hunger" of 1944 and found increased prevalence of antisocial and schizoid personality disorders (Neugebauer et al., 1999). A possible explanation for this effect is interference from maternal stress hormones with neural migration and dendritic growth in key areas of the foetal brain (Power and Schulkin, 2005). Glucocorticoids are frequently suggested as metabolic targets for the transmission of stress from the mother to the child (Manojlović-Stojanoski et al., 2012). Different brain areas have been implicated in ADHD. Current research characterizes ADHD as a disorder of reduced connectivity of the default network, a set of brain regions in charge of wakeful rest, in other words of maintaining brain conscious activity when not engaged in an specific task (Callard and

* Corresponding authorat: Geriatric Psychiatry Division, Centre for Addiction and Mental Health, 80 Workman Way, 6th Floor, Toronto ON M6J 1H4, Canada.
E-mail address: simon.davies@camh.ca (S.J. Davies).

https://doi.org/10.1016/j.jad.2018.04.118
Received 1 June 2017; Received in revised form 3 March 2018; Accepted 8 April 2018
Available online 27 April 2018
0165-0327/

Margulies, 2014). This circuit encompasses the precuneus/posterior cingulate cortex, the medial prefrontal cortex and the medial, lateral, and inferior parietal cortex (Konrad and Eickhoff, 2010). This system receives information from the amygdala, thalamic and extra-thalamic structures. Decisions in the prefrontal cortex are made by a mechanism of "voting" from various independent nuclei, which appear to sub-specialize in specific tasks, such as motivation (ventral medial PFC), spatiotemporal coordination and direction of attention (dorso medial and anterior cingulate) (Faw, 2003). Glucocorticoid receptors, once thought to be limited to the thalamus, are abundant in extra-hypothalamic areas, including some regions of the prefrontal cortex, particularly the medial prefrontal cortex. Some studies have indicated that these neurodevelopmental abnormalities could alter the balance between inhibitory and excitatory circuits in the brain, increasing the severity of ADHD symptomatology in the child (Van den Bergh and Marcoen, 2004). Other pathways which may or may not be related to the Hypothalamic Pituitary Adrenal axis (HPA) and glucocorticoid metabolism have recently been discovered (Glover, 2014). High levels of stress during pregnancy have been associated with an increase in interleukins and other inflammatory markers— whether these could affect the child is unknown. Serotonin is a regulator of neuronal growth, favoring neural specialization and promoting generation of synapses. Exposure to serotonin dysregulation produces behavioral changes in animals. Moreover, a serotoninergic pathway has been discovered in the placenta which may be an interface between maternal HPA axis and serotonin regulation in the child (Glover, 2014). Genetic effects have also been discovered that could moderate the effect of maternal anxiety and child's behavior. Genetic variations in the coding of the enzyme catechol-O-methyltransferase (COMT), have been showed to influence the association between maternal prenatal anxiety, child ADHD symptoms and infant's working memory. COMT is involved in the breakdown of catecholamine neurotransmitters including dopamine, noradrenaline and adrenaline (O'Donnell et al., 2017).

Maternal depression during pregnancy and child rearing has been associated with increased risk of Attention Deficit and Hyperactivity Disorder (ADHD) in children (Foulon et al., 2015; Galera et al., 2011; Sagiv et al., 2013). Few studies have examined the effects of prenatal anxiety. Loomans and colleagues found increased rates of ADHD in boys but not in girls exposed to antenatal anxiety assessed at age 5 (Loomans et al., 2011). O'Connor and colleagues using data from the ALSPAC cohort found an association with hyperactivity in boys at age 4 and boys and girls at age 7 (O'Connor et al., 2002b; O'Connor et al., 2003), while Leis and colleagues did not find an effect at age 11 using the same database (Leis et al., 2014). Van Batenburg-Eddes and colleagues used data from two different cohorts (ALSPAC and Generation R) to examine the association between maternal anxiety in pregnancy and SDQ/CBCL scores in 4 and 3 year olds (Van Batenburg-Eddes et al., 2013). Prenatal maternal anxiety was associated with attentional symptoms. Most studies used symptom scales such as the Strengths and Difficulties Questionnaire (SDQ) and the Child Behaviour Checklist (CBCL) to evaluate outcomes but research where attentional skills have been measured with validated cognitive tasks is scarce. Van den Bergh and colleagues followed a group of children (aged 15) whose mothers have completed the State Trait Anxiety Inventory (STAI) at 12 and 22 weeks of pregnancy and evaluated them using an encoding task, a stop-go task and a Continuous Performance Test (CPT) (Van den Bergh et al., 2005,2006). They found slower reaction times for boys only on the CPT, more errors on the encoding task for both genders and no differences between exposed and non-exposed teenagers in the stop go task. However, the sample of the study was small (57 and 64 respectively), the findings may be due to chance and replication in larger samples is needed.

2. Aims of study

This study explores the association between exposure to maternal somatic symptoms of anxiety during pregnancy and attentional skills in school age children measured with a cognitive task, the Test of Everyday Attention in Children (TEA-Ch) performed at age 8.5 years. Somatic symptoms of anxiety were chosen because they are easy to detect by screening with validated anxiety scales, are relatively common and frequently improve with psychotropic treatment.

3. Methods

3.1. Participants

The Avon Longitudinal Study of Parents and Children (ALSPAC) is an on-going population based cohort in the former county of Avon (England, United Kingdom). 14,541 pregnant mothers with delivery dates between April 1991 and December 1992 were recruited, resulting in 14,775 live births, of these 13,988 children were alive at 1 year of age. Pregnant mothers and their children were followed for the subsequent 26 years. A complete description of the cohort is available elsewhere (Boyd et al., 2013). More detailed information on the ALSPAC study is available on the website: http://www.bristol.ac.uk/alspac which contains details of all the data available through a fully searchable data dictionary (http://www.bris.ac.uk/alspac/reserachers/data-access/data-dictionary/).

3.2. Ethics

Ethical approval for the study was obtained from the ALSPAC Law and Ethics committee and local research ethics committees. Details on ethical approval are available at: http://www.bristol.ac.uk/alspac/researchers/data-access/ethics/.

3.3. Measures

3.3.1. Exposure: maternal somatic anxiety

In the ALSPAC cohort, Information on mental health status during pregnancy was collected at around 18 and 32 weeks of pregnancy using a modified questionnaire based on the Crown Crisp Experiential Index (CCEI) (Crown and Crisp, 1966). This questionnaire had been reduced from the original 48 items to 23, with responses standardized to four distractors ("never", "sometimes", "often", "very often"). The CCEI was developed in the mid 1960s and was divided in a set of six subscales (somatization, depression, free floating anxiety, phobic anxiety, obsessive compulsive symptoms and hysteria). However, the items in these subscales do not correspond to the modern diagnostic definitions of the syndromes they are named after. Moreover, early factor analyses (Alderman et al., 1983) found a substantial overlap between subscales. A group of experts with extensive clinical and epidemiological experience selected five items: "troubled by dizziness or shortness of breath", "felt as though you may faint", "feel sick or have indigestion"," tingling or prickling sensations in body arms or legs" and "extra sweating" from the CCEI. These items were chosen because of their similarity with the ICD-10 and DSM-IV definitions of panic disorder and were judged representative of symptoms of somatic anxiety in mothers (American Psychiatric Association, 2000). Items were grouped and evaluated as a "somatic anxiety factor" using confirmatory factor analysis in two different populations (pregnant women and partners of these women (Bolea-Alamanac and Davies, 2016)). Analyses were performed using Mplus version 7.3 (Muthén, 2010). For the purposes of this study a composite measure of somatic anxiety at 18 and 32 weeks was used since the point of interest was somatic anxiety during pregnancy as exposure regardless of trimester of pregnancy (score range in the sample 10–35). This factor was dichotomized with the problem category being women with the top 20% scores during pregnancy for the main analysis, further analysis were performed with the anxiety factor considered as a continuous measure.