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ORIGINAL ARTICLE

Foetal origins theory: Links with adult depression and general self-efficacy

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Abstract

OBJECTIVE. Foetal origins theory has suggested that early environment can affect vulnerability to major diseases in later life. Recent research also suggests that foetal hormonal programming may influence neurotransmitter and hormone levels affecting adult psychological states (i.e. depression and general self-efficacy). However, investigations into early environment and depression have focused on hospitalised or elderly participants, using non-standard measures. This study investigates links between birthweight and depression in a non clinical adult population, as well as links with general self-efficacy and depression.
METHODS. This is a retrospective design. 100 participants mean age 25.9 self reported birthweight, current height and weight to allow computation of BMI. A General Self-Efficacy Scale and the Hospital Anxiety and Depression Scale were also completed. The official classification of low birthweight (2.5 kg) and the median weight for the group (3.26 kg) were used to identify three groups.
FINDINGS. One way ANOVA showed that variance in depression [$F = 5.31$, (2,97) $p = .006$] and lower general self-efficacy [$F = 4.04$, (2,96) $p = .021$] is explained by membership of birthweight group. There was no variance between depression and age, although general self-efficacy did increase with age [$F = 6.13$, (2,95) $p = .003$). There was no significant variance between BMI and birthweight or depression.
DISCUSSION. Findings add to the growing body of research suggesting that foetal environment influences later life, particularly that early programming may affect hormone and neurotransmitter secretions which may influence later life psychological as well as physical health.

Introduction

There is now substantial evidence that small size at birth is linked to higher prevalence of coronary heart disease hypertension, type 2 diabetes, and osteoporosis, independent of adult lifestyle such as smoking, exercise and alcohol consumption [1]. The Barker Hypothesis [2] also known as the Foetal Origins theory, has suggested that an unfavourable foetal environment causes nutrients to be diverted. This can lead to foetal programming of a number of systems that impact upon later life health. It is also beginning to appear that programming not only influences physical disease but also psychological outcomes such as depression.

Depression is extremely common, with an estimated 20% of women and 10% men suffering symptoms at some time, impacting not only emotional or social functioning, but also physical functioning, pain and general health [3]. The co-morbidity of depression and chronic disease is not fully understood, hence understanding the origins of depression merits investigation. Because depression and general self-efficacy have been linked with similar biochemical changes, this report investigates relationships between birthweight, depression and general self-efficacy.

Feotal programming

Growth of the foetus is largely determined by the amount of oxygen and nutrients it receives. Animal and human studies, suggest that for a variety of reasons an imbalance between foetal demand and supply can lead to metabolic and endocrine adaptations [1] a process referred to as foetal compensation [4]. The human foetus has a large brain to body mass ratio and slow somatic growth rate [5]. This means that as the foetus develops, metabolic demands increases, with the total metabolic demand being kept within viable limits. If these viable limits are compromised, (e.g. limited supply of nutrients and or oxygen) body growth slows leaving brain growth relatively spared. The result is a baby that is small for gestation age. These adaptations are beneficial in the short term, in the longer term however or at times of rapid growth, the adaptations are maladaptive leading to increased risk of disease.

An adverse environment during early development can also influence the set point of the hypothalamic-pituitary-adrenal (HPA) axis [6]. This leads to a long lasting effect known as hormonal programming, in which the plasma levels of hormones (e.g.serotonin, norepinephrine & dopamine) or the set points of neuroendocrine systems are altered permanently [7]. Animal models [e.g. 8, 9, 10] show that environmental factors such as undernutrition, maternal stress or exposure to synthetic glucocorticoids result in the offspring having elevated basal or stress induced glucocorticoid secretions. Pregnant ewes treated with glucocorticoid, and rats with corticosteroids results in offspring with hyptertension [9, 11].

Feotal programming and psychological outcomes

General Self-Efficacy

Self-efficacy is a cognitive behavioural construct, which makes the difference on how people think, feel and act. Proposed initially by Bandura [12] as domain specific efficacy, Schwarzer [13] argues that self-efficacy can also apply to general situations. Until recently, it was believed that both general and domain specific self-efficacy was socially learned. However a recent study reported that low general self-efficacy was associated with lower birthweight [14]. The authors suggested this might be due to reduced levels of serotonin, which as stated earlier, is believed to be linked with foetal hormonal programming. An interaction between biological factors and social learning mechanisms is likely to explain these results.

Mechanisms that may affect psychological cognition prior to birth are not clear, although both depression and self-efficacy have been shown to be associated with biochemical changes. For example, experimental work has indicated that in stressful situations low self-efficacy is associated with plasma catacholamines; low levels of norepinphrine and high levels of dopac were observed [15]. Levels of plasma catacholamines were measured over a period of time as participants underwent mastery training to increase their self-efficacy in carrying out tasks associated with a phobia. Where self-efficacy was low, participants withdrew from the task. Measures were taken at baseline, withdrawal, medium and strong self-efficacy. While performing the task with medium self-efficacy, epinephrine and norepinephrine levels were higher than when self-efficacy was strong or where they had withdrawn from the task. Levels dropped sharply when participants withdrew from the task and self-efficacy was weak.

The dopac levels however were different. In participants with extreme perceived inefficacy, levels of dopac rose to the highest point even though there was no contact with the phobic object. When training was completed, during controlled handling of the phobic object, dopac levels mirrored those of norepinephrine and epinephrine. Bandura et al., [15]suggest that low self-efficacy increases stress levels during phobic contact, with even the thought of the phobic object being sufficient to raise dopac levels. Where levels of perceived self-efficacy are strong, levels of all three catacholamines follow a similar pattern during controlled handling of a phobic object. Dopac is a metabolite of dopamine [16], and an indicator of brain dopamine neurone activity [15].

Evidence that dopamine may be prone to foetal programming comes from the Dutch Hunger Winter. People exposed to foetal under-nutrition during the first two months of gestation are twice as likely to suffer schizophrenia [17–19]. Dopamine is the most complex of neurotransmitters, associated with a number of functions including learning, memory and reinforcement. As dopamine can both inhibit and stimulate postsynaptic potentials depending on the postsynaptic receptor [20], the influence on psychological outcomes is not as simple as over or under production, an abnormality of one neurotransmitter is likely to affect others. However, because of its involvement with learning and reinforcement, it is possible that disrupted levels of dopamine may affect socially learned cognitions such as general self-efficacy.

Depression

The causes of depression are also not entirely understood. Genetic predisposition is often postulated, especially in more sever forms of depression. However no individual genes have been identified, and whilst familial associations can be made in around 36–44% of

cases [21] there are doubts as to the reliability and consistency of a genetic hypothesis [7]. It is therefore necessary to consider alternative origins of depression.

A precursor to Barker's Hypothesis [e.g. 2, 22], is Gupta's [23, 24] suggestion that foetal humor-humour interaction alters tuning of the brain affecting later life, and may be responsible for the Endocrine Personality. He argued that exposure of the foetus to higher or lower than normal maternal hormonal secretions such as norepinephrine and serotonin can alter brain development, leading to significant changes in adulthood.

It is widely believed that norepinephrinergic and seratoninergic pathways are strongly implicated in the chemical pathology of depression and depressive disorders. As with the dopamine, it is not a simple case of too much or too little [25]. As norepinephrine is synthesised by dopamine and the enzyme dopamine β-hydroxylase [20] it is likely however, that dopamine is also involved in depression. Evidence of links between early life and depression comes from a longitudinal study in Herefordshire UK which identified that men and women who committed suicide (which is commonly linked with depression) had low birthweight and weight gain in infancy [26]. It was originally thought the suicides were due to adverse psychosocial influences, however there is no evidence to support this, and it is now thought to be due to other reasons [22]. Patients with depression are found to have abnormal secretions of growth hormone and abnormalities in the HPA and hypo-thalamic-thyroid axes [27]. Because of the mounting evidence that these may be programmed in-utero, it leads to the suggestion of foetal origins of depression.

Studies of the Dutch Hunger Winter indicate that people exposed to foetal under-nutrition during the second-trimester are more likely to be hospitalised for depression [19]. These studies give some information regarding foetal origins of depression but are limited as they rely on an assumption of depression or hospital admissions.

General psychological distress has been linked to birthweight at age 23 [28] and age 42 [29], with the authors suggesting that foetal programming of the HPA axis may be a contributory factor. These studies used the Malaise Inventory, consisting of a 15-item psychological system scale and 9-item somatic scale. Psychological distress is indicated where there is a score of at least 5 on the psychological scale and 3 on the somatic scale. These findings also have limitations; the term psychological distress is a broad one, the inclusion of somatic symptoms can be misleading, and this particular measure has been closely related to stress responses [e.g. 30, 31].

In another study, Thompson, et al. [7] report a link between birthweight and depression in an elderly population (mean age 68 years) placing risk of later life depression in the same category as coronary heart disease, suggesting that vulnerability begins in foetal life. Limitations of this study are stated as the use of a hybrid scale for depression, the possibility that later life depression may differ from depression in earlier life, and that certain illness variables such as dementia may have remained uncontrolled.

The studies cited add to the growing body of evidence that links early environment with depression. However they relied on hospital admissions, assumptions that suicides were depressed, hybrid measures, or an elderly population. This study aims to address some of these limitations by investigating non-elderly adults from a non clinical population, and utilising a scale designed specifically to measure depression. Additionally, because depression and general self-efficacy are linked to similar biochemical changes, the study investigates links between depression and general self-efficacy. It is hypothesised that both depression and general self-efficacy will be linked with birthweight, and that lower general self-efficacy will be associated with higher depression.

Table 1. Range mean and standard deviation of age, birthweight and BMI of participants.

	range	mean	STD
age	19–62	25.9	8.63
birthweight	1.93–4.88	3.34	.54
BMI	14–44	22.11	4.34

Method

Data were collected as part of a larger study. This is a cross sectional retrospective design with participants reporting on the previous month.

Measures

The Hospital Anxiety and Depression Scale [32] was completed. This scale is designed for use in a non-clinical population, distinguishing between anxiety and depression, and eliminating somatic symptoms. The General Self-Efficacy Scale [33] measures self-efficacy as a general psychological construct and has been shown to be stable over time, age and culture. Birthweight was self-reported which is considered to be a reliable measure [e.g. 34, 35, 36]. Current height and weight were give to allow the computation of BMI (body mass index).

Paticipants

An opportunity sample of 100 student participants (81 female, 19 male) range, mean and standard deviation are shown in Table 1.

Three birthweight groups were identified, those below the official low birthweight threshold of 2.5.kg (n = 4). As there is no official classification for normal birthweight , a median split for the group identified mid range birthweights (range = 2.5–3.26 kg, n = 44) and normal birthweights (range –3.27–4.88 kg n = 52).

BMI was calculated as height mm/weight kg^2. Three groups were identified based on Centre for Disease Control [37] classifications, underweight (below 18.5,

n = 19) normal weight (18.6–24, n = 58) and overweight (25–44, n = 18). There were three age groups, up to 30 (n = 70), 31–40, (n = 19) over 40 (n = 10).

Results

79% of participants had depression scores within the normal range, 21% report mild (n = 15) or moderate to severe (n = 6) depression which is within normal perimeters, Zeigmond & Snaith [32] report observing 20% using this scale [see also 3]. Mean scores for depression and general self-efficacy can be seen in figure 1.

One-way ANOVA (1x3) was carried out to test whether or not membership of birthweight group explains levels of depression and general self-efficacy. Results revealed that variance in depression [F = 5.31, (2,97) p = .006] and general self-efficacy efficacy [F = 4.04, (2,96) p = .021] can be explained by membership of birthweight group. Post hoc testing revealed a significant difference for depression between low birthweight group and the midzone and normal groups (p = .047 and .010 respectively). There was no difference between the mid zone and normal birthweight groups, although this may be partly explained by the small number in the low birthweight group. For general self-efficacy, there was significant variance between the midzone and normal birthweight groups (p = 022).

It is possible that the effect of birthweight on depression is due to psychological issues surrounding poor body image, a one-way ANOVA (1x3) was carried out with no significant results. There was also no significant effect of birthweight on BMI.

As depression may increase with age, a one-way ANOVA was carried out (1x3). Age did not explain the variance in depression scores, but it did explain general self-efficacy [F = 6.13, (2,95) p = .003]. Post hoc testing revealed that there was no difference between age group 1 and 2, but there were differences between group 1 and 3 (p = .003) and 2 and 3 (p = .016) with the higher age group reporting higher general self-efficacy.

Discussion

This study has identified a link between birthweight, depression and general self-efficacy in an adult population below retirement age. The smaller the baby, the higher the rate of depression and lower the level of general self-efficacy. A link with birthweight and depression due to BMI and psychological factors such as poor body image, could be possible. However, there was no significant relationship between birthweight and current BMI; there is no evidence that smaller babies lead to smaller underweight people or visa versa. There was also no relationship between BMI or BMI group and depression.

The mechanism by which foetal programming could affect depression and general self-efficacy is unclear, and it was not the intention of this study to investigate that. However it is possible to speculate it is due to foetal programming of neurotransmitters. A number of animal studies have linked foetal under-nutrition with disruption of the endocrine system, hormones and neurotransmitters including seratonin and norepinephrine [23, 24], disruption of which is strongly associated with depression [25]. The neurotransmitter dopamine is linked with learning, memory and reinforcement. As stated earlier a disruption between dopamine and glutamate is linked with schizophrenia a disease that may have a foetal under nutrition connection. As both glutamate and dopamine are associated with learning, memory and reinforcement, it is possible that the socially learned reinforced beliefs of general self-efficacy are associated with disruption in these chemicals. The foetally programmed set points of these chemicals could leave the individual with a reduced propensity to acquire positive self-beliefs, and vulnerability for depression.

The link with depression and general self-efficacy is as expected. Psychologically, self-efficacy buffers against depression [15]. As these cognitions appear to have similar biochemical associations, the findings that they are both linked with birthweight adds to the growing body of evidence that psychological outcomes may be influenced by foetal programming.

It has been suggested that levels of depression increase with age [7]. These data do not support this, although this study uses a non-elderly population. General self-efficacy however is shown to increase with age, which may be expected given that self-efficacy is a socially learned phenomenon. However it is contrary to Schwarzer's [38] findings where in a population aged from 15 to 50 no correlation was found. The population age in the present study range from 19–62, with a differences in variance being found between the young and older groups. The difference in size of the group could be a confounding variable, but it is also indicative of social learning aspect of the construct.

The foetal origin of disease hypothesis has been criticised for not considering the effect of early postnatal influences on physical health. Early life data

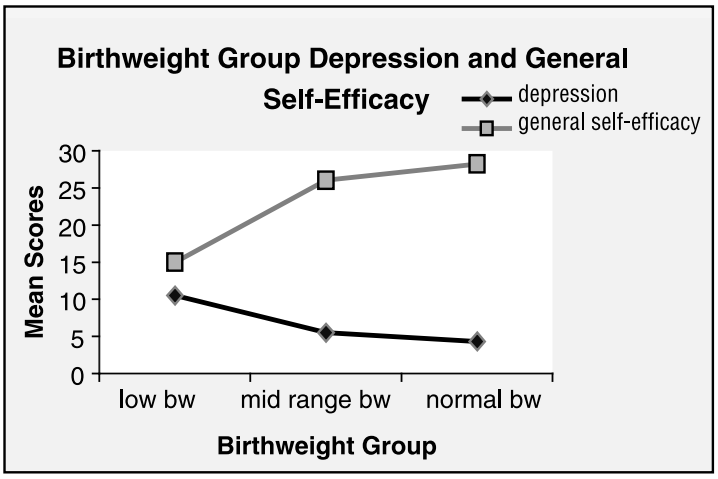

Figure 1. Mean Scores for depression and general self-efficacy for birthweight groups.

were not available for this study population, however, the chemicals associated with these psychological outcomes have been shown in animal studies to be disrupted by foetal under-nutrition. Birthweight was self-reported, and whilst it may be preferable to use data collected at time of birth a number of studies have been cited where self-reported birthweight is shown to be reliable, particularly in populations with a similar age to this.

Conclusions

Results indicate that depression and general self-efficacy are linked with birthweight, and as expected, depression and general self-efficacy are also linked. Both of these are associated with biochemical disruption which animal studies show can result from foetal under nutrition. This study has added to the growing body of evidence contributing to "foetal origins" theory. Whilst the majority of work in this area studies foetal origins of disease, this study suggests that psychological variables may also have origins in foetal life.

REFERENCES

1 Phillips DI. Fetal growth and programming of the hypothalamic-pituitary-adrenal axis. Clin Exp Pharmacol Physiol 2001; **28**(11): 967–70.
2 Barker DJ. Mothers, Babies and Health in Later Life. 1998, Edinburg, London: Churchill Livingstone.
3 Irwin M. Psychoneuroimmunology of depression: clinical implications. Brain Behav Immun 2002; **16**(1):1–16.
4 Nathanielsz PW. Life in the womb, the origin of health and disease. 1999, Ithaca New York: Promethean Press.
5 Lumbers ER, Yu ZY, and Gibson KJ. The selfish brain and the barker hypothesis. Clin Exp Pharmacol Physiol 2001;**28**(11): 942–7.
6 Matthews SG, Challis JRG, Cox DB, and Sloboda DM. The Hypothalamic-Pituitary-Adrenal and Hypothalamic-Pituitary-Gonadal Axes in Early Life: Problems and Perspectives, in Fetal Origins of Cardiovascular and Lung Disease, Barker DJ , Editor. 2001, Marcel Dekker: USA.
7 Thompson C, Syddall H, Rodin I, Osmond C, and Barker DJ. Birth weight and the risk of depressive disorder in late life. Br J Psychiatry, 2001; **179**:450–5.
8 Barbazanges A, Piazza PV, Le Moal M, and Marccari S. Maternal glucocorticoid secretion mediates long-term effects of prenatal stress. Journal Neuroscience, 1996; **16**:3943–3949.
9 Langley-Evans SC. Intrauterine programming of hypertension by glucocorticoids. Life Sci, 1997; **60**(15):1213–21.
10 Lesage J, Grino M, Bernet F, Dutriez-Casteloot I, Montel V and Dupouy JP. Consequences of prenatal morphine exposure on the hypothalamo-pituitary-adrenal axis in the newborn rat: effect of maternal adrenalectomy. J Neuroendocrinol, 1998; **10**(5): 331–42.
11 Dodic M, May CN, Wintour EM, and Coghlan JP. An early prenatal exposure to excess glucocorticoid leads to hypertensive offspring in sheep. Clin Sci (Lond), 1998; **94**(2):149–55.
12 Bandura A. Self-efficacy: Toward a unifying theory of behavioural change. Psychological review, 1977. **84**:191–215.
13 Schwarzer R. Optimism, vulnerability, and self-beliefs as health-related cognitions: A systematic overview. Psychology and Health: an International Journal, 1994. **9**:161–180.
14 Bellingham-Young DA, and Adamson-Macedo EN. Early prediction and psycho-immunologic mediation of minor illness in adulthood. Neuroendocrinol Letters, 2002; **23**(3):219–25.
15 Bandura A, Taylor CB, Williams SL, Mefford IN, and Barchas JD. Catecholamine secretion as a function of perceived coping self-efficacy. J Consult Clin Psychol, 1985; **53**(3):406–14.
16 Stein TD, and DeJesus OT. Effect of 6-fluoro-m-tyrosine on dopamine release and metabolism in rat striatum using in vivo microdialysis. Brain Res, 2000; **884**(1–2):192–5.
17 Susser E, Neugebauer R, Hoek HW, Brown AS, Lin S, Labovitz D, and Gorman JM. Schizophrenia after prenatal famine. Further evidence. Arch Gen Psychiatry, 1996; **53**(1):25–31.
18 Brown AS, Susser ES, Lin SP, Neugebauer R, and Gorman JM. Increased risk of affective disorders in males after second trimester prenatal exposure to the Dutch hunger winter of 1944–45. Br J Psychiatry, 1995; **166**(5):601–6.
19 Brown AS, J van Os, Driessens C, Hoek HW, and Susser ES. Further evidence of relation between prenatal famine and major affective disorder. Am J Psychiatry, 2000; **157**(2):190–5.
20 Carlson NR. Physiology of Behaviour. Boston, London: Allyn & Bacon. 1998.
21 Bierut LJ, Heath AC, Bucholz KK, Dinwiddie SH, Madden PA, Statham DJ, Dunne MP, and Martin NG. Major depressive disorder in a community-based twin sample: are there different genetic and environmental contributions for men and women? Arch Gen Psychiatry, 1999; **56**(6):557–63.
22 Barker DJ. Fetal origins of cardiovascular and lung disease. 2001, USA: Marcel Dekker.
23 Gupta D. Humors and Hormones in Pregnancy: Determinants of Personality Development in the Child. International Journal of Prenatal and Perinatal Studies, 1992; **4**(1/2):1–15.
24 Gupta D. Prenatal Exposure to hormones and drugs: consequences for postnatal development of body and mind. International Journal of Prenatal and Perinatal Studies, 1989; **1**(2): 151–165.
25 Kolb B, and Whishaw IQ. Funadmentals of Human Neuropyschology. 1996, New York: W. H. Freeman & Co.
26 Barker DJ, Osmond C, Rodin I, Fall CH, and Winter PD. Low weight gain in infancy and suicide in adult life. Bmj 1995; **311**(7014):1203.
27 Checkley, S. and E.S. Paykel, Handbook of Affective Disorders. 1992, Edinburg: Churchill Livingstone.
28 Cheung YB. Early origins and adult correlates of psychosomatic distress. Soc Sci Med, 2002; **55**(6):937–48.
29 Cheung YB, Khoo KS, Karlberg J, and Machin D. Association between psychological symptoms in adults and growth in early life: longitudinal follow up study. Bmj, 2002; **325**(7367):749.
30 Hirst MA. Evaluating the Malaise Inventory. An item analysis. Soc Psychiatry, 1983; **18**(4):181–4.
31 Rodgers B, Pickles A, Power C, Collishaw S, and Maughan B. Validity of the Malaise Inventory in general population samples. Soc Psychiatry Psychiatr Epidemiol 1999; **34**(6):333–41.
32 Zeigmond AS, and Snaith RP. The Hospital Anxiety and Depression Scale. Acta psychiatr.scand, 1983; **67**:361–370.
33 Jerusalem, M. and R. Schwarzer, Selbstwirksamkeit [Self-Efficacy Scale], in Skalen zur Befindlichkeit und Personlichkeit, R. Schwarzer, Editor. 1986, Freire Universitat, Instuitut fur Psychologie (Cited by Jerusalem & Mittag): Berlin.
34 Troy LM, Michels KB, Hunter DJ, Spiegelman D, Manson JE, Colditz GA, Stampfer MJ, and Willett WC. Self-reported birthweight and history of having been breastfed among younger women: an assessment of validity. Int J Epidemiol, 1996; **25**(1):122–7.
35 Sandhu MS, Luben R, Day NE, and Khaw KT. Self-reported birth weight and subsequent risk of colorectal cancer. Cancer Epidemiol Biomarkers Prev, 2002. **11**(9):935–8.
36 Allen DS, Ellison GT, I dos Santos Silva, De Stavola BL, and Fentiman IS. Determinants of the availability and accuracy of self-reported birth weight in middle-aged and elderly women. Am J Epidemiol 2002; **155**(4):379–84.
37 Control CfD. Body Mass Index for Adults. www.cdc.gov/nccdphp/dnpa/bmi/bmi-adult.htm, 2000.
38 Schwarzer R, Meuller J, and Greenglass E. Assessment of optimistic self-beliefs on the Internet: Data collection in cyberspace. Anxiety, Stress and Coping, 1999; **12**(145–161).