

Childcare outside the family for the under-threes: cause for concern?

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Changes in child-rearing and bonding

Child-rearing is culturally determined, varying between countries. For thousands of years in most cultures, it has been kinship groups and parents, especially mothers, who have been central.

Parenting changed in the mid-20th century, partly through better educational opportunities for women, partly through reliable birth control and partly through cultural agreement on female emancipation. Hence, many more women have entered work and universities.

Mothers of children aged under three years now increasingly go out to work. In England, 75% of women with dependent children work (Office of National Statistics, 2019), while their very young children are often placed in daycare with carers unknown to the child.¹

Governments encourage this, first, because work is an important counter to poverty. Second, a working mother contributes to the gross domestic product, as does her childminder, with UK estimates suggesting an average gain of £20,000 over four years. In the UK, a substantial bonus to reduce childcare costs is paid per child to working parents.

Humans, as mammals with relatively big brains, but comparatively narrow birth canals, ensured evolutionary survival by being born more immature than other mammals. Newborn lambs can walk at birth: human babies need about a year. Newborn human brains are exceptionally adaptable or 'plastic'.²

Mothers are primed by biological stimuli. Pregnancy for nine months, oxytocin release³ and breastfeeding combine to generate caring feelings. The remarkable power of human bonding is revealed when small babies shown a succession of female faces, demonstrate increased brain activity only with their mother's face. In reverse, mothers can detect their own baby's cry in a crowd of crying babies.

Small children become anxious when separated from their mothers. Attachment theory,⁴ based on maternal bonding, means a child acquires emotional security and learns self-regulation through loving

relationships at home. A child's hormonal bonding system is compromised by disrupted attachments, since reduced synthesis of oxytocin receptors follows frequent maternal separations. The possibility of forming strong bonds with a partner in adult life, as well as with future offspring, may be reduced.⁵ Also, the mother–infant bonding pathway in the brain is closely associated with the reward and addiction circuits. The stress of maternal separation can produce changes in the neural-circuit functions, which can appear as dependence or substance abuse in later life.⁶

Biological response to stress

How mammals respond to stress is well known as the limbic hypothalamic adreno-cortical response. Stimuli indicating danger generate changes in the hypothalamus near the pituitary gland in the brain. This produces adreno-corticotrophic hormone, which circulates in the blood stimulating the adrenal glands to produce cortisol.

The limbic hypothalamic pituitary adrenal axis (HPA axis) provides the fight/flight response, driving blood into the muscles, reducing digestion, protein synthesis (necessary for brain growth) and suppressing immune systems, enabling swift action.

Releasing cortisol is a valuable mammalian mechanism but is an emergency response. Quite different is long-term release of cortisol over hours or days. The question then is whether this is harmful?

In the 1980s, externalising, aggressive behaviour was noted more in children in nurseries compared to those at home, especially for children in nurseries more than 30 h per week.

However, it was difficult to test HPA activity in small children. Now it can be done non-invasively. Saliva gives a sample of cortisol which can be measured reliably in babies by touching the inside of their mouths with a cotton-wool swab. The effects of separating small children from their parents can therefore be studied by salivary cortisol, instead of blood.

Several studies are now available. There is substantial evidence that children in nurseries, particularly in poor-quality ones, have persistently higher levels of cortisol than children at home and that the normal circadian, 24-h pattern, of cortisol release is disrupted. Persistently raised cortisol levels have been found in children in nurseries even when carers considered that they had 'settled'.

US researchers found that cortisol levels were higher in children in daycare compared with children at home and that 63% (n = 151) in daycare had raised cortisol levels, of whom they considered 40% were stressed. A meta-analysis concluded that: 'children in daycare exhibit higher cortisol levels than children at home'.⁷

During the 1990s, experiments on other mammals investigated the effect of cortisone on developing brains and neuro-systems. Circulating cortisol was associated with delayed development or immature brains and nervous systems in at least four species of mammal: cattle, monkeys, rats and sheep.⁸

Evidence on the effect of cortisol on children's brains comes from three sources: stressed pregnant women secreting natural cortisol; cortisol treatment prescribed during pregnancy; and cortisol treatment prescribed for small children.

Women stressed in pregnancy have more cytokines, a chemical signaller, in their cord blood and steroids repeatedly administered during pregnancy were associated with abnormal behaviour in the children born subsequently.⁹ The children of mothers given steroid treatment had an increased incidence of delayed psychomotor development.¹⁰ Not all agree: some studies found no effect. Other evidence comes from brain scans which can now link specific brain functions to specific brain sites.

Raised blood cortisol levels in babies and small children are associated with changes in the temporal lobe, e.g. the hippocampus and the amygdala. These parts of the brain are where emotional stability is learned with the development of conscience. The amygdala is associated with the development of empathy.

More recent work has extended the key finding that raised cortisol in children in daycare is detrimental by showing that it also may be related to both lowered antibody levels and greater illness frequency.¹¹ The National Child Development Center at Harvard summarises it strikingly by reporting that raised stress levels distort the architecture of the child's brain.¹²

Long-term physical implications

Long-term research has now linked small children attending nurseries with subsequent physical and mental health in adolescence and adult life. Children

spending long hours in nurseries have an increased prevalence of later obesity.¹³ Also, there are reports of severe early-life stress being followed by increased incidence of basal cell carcinoma in adults.¹⁴

The nature/nurture debate has been clarified since genes and the environment are in continuous dialogue. Crucially, environmental stress can alter gene expression in the long term.

Normal DNA can be modified, for example by methylation of CpG sites by specific methylation enzymes, so-called epigenetic changes. The modification of the gene, or its promoter sequence, prevents its transcription or translation; the gene is then said to be silenced.

Prenatal exposure to famine in humans was associated with significantly less DNA methylation of the IGF2 (insulin-like growth factor 2) gene compared with the gene from unexposed same-sex siblings,¹⁵ which was detectable six decades later.

Large-scale genome-wide methylation studies have identified many genes involved with childhood adversity. DNA methylation in children from Russian orphanages was compared with the DNA methylation in children from their biological families of similar socioeconomic status. Differential methylation between the two groups was found at 914 DNA sites. The methylated genes include 28 of major importance for brain development. Different promoter methylation patterns occur in disadvantaged compared to affluent children.¹⁶

Methylation of the promoter of the human glucocorticoid receptor gene is associated differentially, with low levels of parental care, parental death or childhood maltreatment.¹⁷ These are the major effects occurring in the human genome.

Reduced plasma levels of a set of four interleukin biochemical predictors of chronic physical aggression (CPA) in infant boys persist into adult life. Differential DNA methylation regions in cytokine and transcription factor genomic loci are associated with physical aggression in these men compared with controls. CPA in boys involves hyperactivity, impulsive behaviour, failure at school and the likelihood of a criminal record.¹⁸

It is particularly important that genes changed through stress can pass on to future generations. The challenge now is to examine the links between these epigenetic changes introduced by childhood adversity or neglect to health outcomes.

Limitations

The evidence is not conclusive proof that all children under three in nurseries for long periods are always harmed, as the level of proof is mainly associations

and not based on randomised controlled trials. However, we cite one systematic review. Most children in nurseries are not affected but as many as 40% may be.

Strengths

Many small children in nurseries have persistently raised cortisol levels, indicating emotional stress. Raised cortisol levels can affect developing brain centres, which is potentially serious. Environmental factors interact with genes and can alter them. Once altered, such genes can pass to future generations.¹⁶

Declarations

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References

- Office of National Statistics. Families and the Labour Market, UK <https://www.ons.gov.uk/employmentandlabourmarket/peopleinwork/employmentandemployeetypes/articles/familiesandthelabourmarketengland/2019#employment-activity-of-mothers-and-fathers-in-a-family> (2019, accessed 15 January 2020).
- Narvaez D, Panksepp J, Schore AN and Gleason T (eds). *Evolution, Early Experience and Human Development: From Research to Practice and Policy*. USA: OUP, 2013.
- Uvnäs-Moberg K. Short-term and long-term effects of oxytocin released by suckling and skin-to-skin contact in mothers and infants. In: Narvaez D, Panksepp J, Schore A and Gleason T (eds). *Evolution, Early Experience and Human Development*. USA: OUP, 2013, pp.299.
- Bowlby J. *Attachment and Loss*. Vol. 1. 2nd ed. London: Hogarth Press, 1982 [1969].
- Wisner Fries AB, Ziegler TE, Kurian JR, Jacoris S and Pollak SD. Early experience in humans is associated with changes in neuropeptides critical for regulating social behavior. *PNAS* 2005; 102: 17237–17240.
- Maté G. Addiction: childhood trauma, stress and the biology of addiction. *J Restorative Med* 2012; 1: 56–63.
- Vermeer HJ, Marinus H and van IJzendoorn MH. Children's elevated cortisol levels at day-care: a review and meta-analysis. *Early Child Res Quart* 2006; 21: 390–401.
- Sapolsky RM, Uno H, Rebert CS, et al. Hippocampal damage associated with prolonged glucocorticoid exposure in primates. *J NeuroSci* 1990; 10: 2897–2902.
- Wright R, Visness C, Calatroni A, et al. Prenatal maternal stress and cord blood innate and adaptive cytokine responses in an inner city cohort. *Am J Resp Med Crit Care* 2010; 182: 25–33.
- Spinillo A, Viazzo E, Colleoni R, et al. Two-year infant neurodevelopment outcome after single or multiple antenatal courses of corticosteroids to prevent complications of prematurity. *Am J Obs Gynae* 2004; 191: 217–224.
- Watamura SE, Coe CL, Laudenslager ML and Robertson SS. Child care setting affects salivary cortisol and antibody secretion in young children. *Psychoneuroendocrinology* 2010; 35: 1156–1166.
- National Scientific Council on the Developing Child. (2005/2014). Excessive Stress Disrupts the Architecture of the Developing Brain: Working Paper 3. Updated Edition. See www.developingchild.harvard.edu (last accessed 5 January 2020).
- Geoffroy M-C, Power C, Touchette E, Dubois L, Bolvin M, Seguin JR, et al. Childcare and overweight or obesity over 10 years of follow up. *J Pediatrics* 2013; 162: 753–758.
- Fagundes CP, Glaser R, Johnson SL, Andridge RR, Yang EV, Di Gregorio MP, et al. Basal-cell carcinoma stressful life-events and the tumour environment. *Arch Gen Psych* 2012; 69: 618–626.
- Bowers ME and Yehuda R. Intergenerational transmission of stress in humans. *Neuropsychopharmacol Rev* 2016; 41: 232–244.
- Suderman M, Borghol N, Pappas JJ, Pinto Pereira SM, Pembrey M, Hertzman C, et al. Childhood abuse is associated with methylation of multiple loci in adult DNA. *BMC Med Genom* 2014; 7: 13.
- Tyrka AR, Price LH, Marsit C, et al. Childhood adversity and epigenetic modulation of the leukocyte glucocorticoid receptor: preliminary findings in healthy adults. *PLoS ONE* 2012; 7: e30148.
- Provençal N and Binder EB. The effects of early life stress on the epigenome: from the womb to adulthood and even before. *Exp Neurol* 2015; 268: 10–20.