



# Science versus society: is childcare for the under threes a taboo subject?

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First draft submitted: 9 April 2020; Accepted for publication: 7 May 2020; Published online: TBC

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For many years small children were reared within families, often by mothers. In recent decades, the custom developed for many of the under threes to be placed in day care with strangers, often for many hours a week. This is one of the biggest social revolutions in history as the result of the positive social movement to accept women across all areas of society.

During the first 3 years of life, synaptic pathways form which have a long-term influence on human development. Bowlby's attachment theory [1] was a classic insight and described mother-child bonding. It focused attention on the adverse effects for small children if separated from their mothers. This theory has been progressively supported by neurobiological research in animals and humans. From behavioral scientists came research showing less satisfactory behavior in children spending long times in day care. Studies followed showing increased cortisol levels in children when separated from their mothers, a sign of stress. Animal studies demonstrated that cortisol has adverse effects on the brain or nervous system in four species of mammal. Once adverse effects of cortisol were found on human brains, particularly the hippocampus and cortex, the stage was set for epigenomic research. However, discussion of small children in day care centres has become a fraught issue with social division, embarrassment and feelings of guilt; hence our use of the term a 'taboo subject'.

## Epigenetic changes to the mother-infant dyad

Early life stress (ELS) in infants (often categorized as adverse childhood experiences, ACEs) [2] is accompanied by clear epigenetic changes. The principal change at the molecular level is methylation of cytosine at CpG sites on DNA, either on the promoter region of a gene or on the gene itself. In extreme adversity, for example in institutionalized children from Russian orphanages, 914 DNA sites (compared with controls) were found to be methylated, out of which 28 genes were known to be involved in brain development [3]. This extreme example perhaps provides an upper limit on the number of DNA sites that can be methylated by childhood adversity.

Adversity, or ELS, is not precisely defined or quantified. A common ACE, like physical abuse, is often treated as a binary category as there is no easy way of grading the abuse for severity, or length of time that the child experienced the abuse. Similarly, in complex social situations, how is the mother's (or principal care giver's) emotional neglect of the developing child quantified? Is the neglect sporadic or persistent?

Adversity can be any event that stresses the infant; manifested through the release of cortisol [4]. Cortisol triggers DNA methylation (DNAm), in many cases at the promoter region [5]. ACEs give rise to poor health outcomes in affected children, both physically and emotionally. Over time, people with ACEs consume a disproportionately high level of resources in the healthcare system [6,7].

ACEs have a major effect on the child's future; however, so can aspects of maternal behavior, such as intrusiveness [8]. Intrusiveness is a mother's behavior that is characterized by over-control, in other words, interruption and subsequent neglect of an activity that has been initiated by the child, or excessive pressure on the child to do something different when the child's gaze indicates what its personal interest is. This intrusive activity by the mother interferes with the growing development of the child's autonomy. The mother's oxytocin (OT) encoded gene shows DNAm in the promoter region that changes throughout pregnancy. This dynamic trajectory of OT promoter DNAm correlates with the amount of later intrusiveness in maternal behavior 6 months after birth.

A big question in group childcare, where there is no equivalent to the mother-infant dyad, is how to handle the corresponding form of intrusiveness, namely the imposition of conformity by the carers who prioritize group needs over the needs of the individual child.

In early infancy, the behavior of the mother decisively affects her developing child. The oxytocin receptor gene (OXTR) can be methylated at conserved regulatory sites (OXTRm) in both the mother and her child [9]. In infancy, the child shows a wide variation in OXTRm; in the corresponding period the mother exhibits a relatively stable frequency distribution of OXTRm. Bonding in the mother-infant dyad through maternal behavior is largely controlled by the hormone OT interacting with its OXTR. This relational dyad begins *in utero* and epigenetic changes start during pregnancy.

Higher levels of OXTRm lead to fewer OXTR in the child at 5 and 18 months after the child's birth. In free-play, experiments between the mother and her child it is possible, using multigroup path analyses, to quantify the level of engagement within the mother-child dyad. Maternal engagement with the child at 5 months predicts the change in infant OXTRm; the infant's gender showed no statistically significant effect [9]. At 18 months the OXTRm levels start to reflect the infant's temperament for example fearfulness, sadness, shyness, frustration and soothability.

Evidence is accumulating for the involvement of OXTR DNAm in social and emotional behavior such as, callous emotional traits in youth, rigid thinking in anorexia nervosa and affect regulation problems [10].

These discoveries suggest that the mother's quality of engagement with her child significantly affects her child's epigenome; her engagement influences important qualities in the child's future social development. The natural engagement between the mother and her child is a constant and long-term occupation with epigenomic consequences. This raises the question of whether out-of-home childcare, by strangers in a child's first 3 years, can match the multiple epigenomic needs of developing children.

### Epigenomic associations for antisocial behavior

Conduct problems (CP) in childhood can lead to antisocial behavior and perhaps crime in later life. Do they arise from ELS of the child, or is the propensity passed to the child at birth epigenomically? Cecil *et al.* [11] used DNAm information from cord blood at birth and trajectory data from the Avon Longitudinal Study of Parents and Children database. Seven candidate methylated genes, found in cord blood, were associated with CP. Out of these, three were linked to early onset CP. The authors stress that their findings are correlational; causation is not yet proved.

### Intergenerational transmission

The lasting impact of these epigenomic changes may stretch beyond the child's lifetime. From the 1990s it has been suggested that epigenomic changes resulting from stressful events could be passed onto future offspring [12].

It has been hypothesized that this inheritance enables populations to adapt to changing environments. Recently, a study of newborns of mothers who had experienced childhood trauma found significantly less cortical grey matter than in children of mothers who reported no childhood trauma [13]. In humans, the research may be confounded by social and cultural inheritance but inheriting the epigenetic effects of ELS must be considered a possibility. Perhaps this is a warning of unforeseen changes in the well-being of one generation being passed on to the next.

### Possible impacts of the coronavirus pandemic

In the coronavirus pandemic, families in lockdown will reduce parent-child separation hopefully reducing stress for the child. Living together will probably magnify existing relationships. Strong parent-child bonding may improve, but poor relationships may deteriorate further.

### Conclusion

Record numbers of mothers are working and children under three are spending longer in day care than ever before. Research in both the behavioral and molecular sciences suggests that separation of children under three from their mothers may have important adverse effects for some children [14]. These effects are physical and psychological and may be long lasting. The biggest implication for society is that stressed children could pass on, epigenomically, their altered genes to future generations. Is science now in conflict with the childcare customs of modern society?

We have identified around 1000 research reports, in different sciences spread over 30 years, that separating small children from their mothers has a variety of adverse effects. However, we have not identified a systematic review in any leading general medical journal and as far as we know, this is the first editorial on this topic. In our judgment,

epigenomics can now shine significant light on childcare for children under three and may chart a way through the taboo on open debate.

#### Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

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