

Interactions between biology and the social environment in relation to early intervention and prevention.

Paul Haggarty, Deputy Director for Research, Rowett Institute of Nutrition and Health, University of Aberdeen, Aberdeen, UK.

Inequality and the persistence of disadvantage across the generations is becoming increasingly entrenched in UK society [1]. People living in the poorest neighbourhoods in England die on average seven years earlier than people living in the richest neighbourhoods [1]. They also spend more of their shorter lives with a disability; the average difference in disability free life expectancy between the richest and poorest neighbourhoods is 17 years [1]. Inequality is not good for the individuals who are directly affected but it also impacts negatively on the whole of society [2]. Inequalities in health arise because of inequalities in the conditions in which people are born, grow, live, work, and age and a growing body of evidence indicates that early life (childhood and even before birth) is a particularly important time for interventions designed to improve health and wellbeing across the life-course [1, 3]. Examples include a series of UK health policies aimed at the improvement of the diet in poorer socio-economic groups. These range from the Welfare Food Scheme, designed to protect children's health during rationing, to the Healthy Start programme through which pregnant women from low income families receive free fruit and vegetables and vitamin supplements. However, the pathways and mechanisms by which early experiences become embedded in an individual's life-course, and how they influence behaviour, life choices, and health, are not fully understood. There is a need to understand these processes in order to develop effective strategies to improve social mobility and reduce inequality.

There are many examples of socioeconomic status influencing biological factors relevant to the persistence of disadvantage. Cortisol is a glucocorticoid hormone, released in response to stress, that influences the brain (e.g. memory formation and retrieval) and numerous organ systems within the body. In animals, maternal stress during pregnancy and increased glucocorticoid exposure are associated with reduced birth weight, a higher risk of hypertension and hyperglycemia, and altered brain HPA activity and behaviour in the offspring after birth [4, 5]. In humans psychosocial stress and the physiological responses to stress are patterned by social class [6] and high levels of maternal stress are associated with low birth weight [7, 8]. Cortisol levels of low-birth-weight babies are higher throughout life and neuropsychiatric disorders in later life have been linked to maternal stress in pregnancy, with some of these behavioural effects apparently being passed to subsequent generations [4]. The effects on the human brain of early socioeconomic status can also be observed by magnetic resonance imaging. Childhood socioeconomic status predicts hippocampal volumes [9] and the burden of brain white matter hyperintensities – associated with vascular risk factors, cognitive decline, dementia and death – more than 50 years later [10].

The environment can influence biology but biology can also influence the social and environmental exposures experienced across the life-course. Human intelligence is partly determined by innate factors such as genetics [11, 12] and intelligence is an important determinant of educational and occupational success, social mobility, health, and longevity [13] though it is not clear whether higher intelligence leads to better health and longevity through improved lifestyle choices and life opportunities or whether there is a common biological basis to a well-functioning brain and body. Intelligence is related to diet quality in adult life [14, 15] and children whose parents have lower intelligence scores also have poorer selected health and health behaviours independent of socioeconomic status and the child's own intelligence [16]. Intelligence is also related to birth weight [17, 18] and low birth weight is more common in deprived areas of Britain [19-23].

Poor social and economic status is characterised by a nexus of disadvantage in both the social and biological realms that appear to be self-perpetuating and self-reinforcing within and across the generations. In order to develop effective strategies to break this cycle it is necessary to understand the nature of the feedback loops between biology and the social environment and this is an important aim of the emerging field of 'biosocial' research. The epigenetic paradigm allows for such cross talk and is particularly relevant to biosocial research. Epigenetics refers to the information in the genome over and above the purely genetic information contained in the DNA base sequence and there is a growing body of evidence base demonstrating effects of the environment on epigenetic states and the importance of epigenetics to brain function, cognition, behaviour, and health [24]. Epigenetic states can be heritable in the sense that they may be passed from one generation to another during reproduction or they may persist within a lifetime in tissues and organs, even as the constituent cells are replenished. The former is relevant to the transgenerational transmission of health and the latter to the time delay between exposure and later health within a lifetime. The field of epigenetics is of increasing interest to policy makers searching for explanations for complex epidemiological observations and conceptual models on which to base interventions and it has been proposed that "the persistence of health inequalities across the social spectrum, particularly in West Central Scotland, may be associated with such (epigenetic) effects" [25]. The hope is that biosocial research will contribute to the development of effective intervention strategies to lessen intergenerational inequalities and child poverty, and improve social mobility.

References

1. Marmot M. Fair Society, Healthy Lives. London: 2010 2010. Report No.
2. Wilkinson R, Pickett K. The Spirit Level: Why Equality is Better for Everyone. London: Penguin; 2010.
3. Acheson D. Report of the independent inquiry into inequalities in health. London: 1998 1998. Report No.
4. Seckl JR, Meaney MJ. Glucocorticoid "programming" and PTSD risk. *Ann N Y Acad Sci.* 2006;1071:351-78. doi: 1071/1/351 [pii];10.1196/annals.1364.027 [doi].
5. Meaney MJ, Szyf M, Seckl JR. Epigenetic mechanisms of perinatal programming of hypothalamic-pituitary-adrenal function and health. *Trends Mol Med.* 2007;13(7):269-77.
6. Muennig P, Sohler N, Mahato B. Socioeconomic status as an independent predictor of physiological biomarkers of cardiovascular disease: evidence from NHANES. *Prev Med.* 2007;45(1):35-40.
7. Borders AE, Grobman WA, Amsden LB, Holl JL. Chronic stress and low birth weight neonates in a low-income population of women. *Obstet Gynecol.* 2007;109(2 Pt 1):331-8.
8. Paarlberg KM, Vingerhoets AJ, Passchier J, Dekker GA, Heinen AG, van Geijn HP. Psychosocial predictors of low birthweight: a prospective study. *Br J Obstet Gynaecol.* 1999;106(8):834-41.
9. Staff RT, Murray AD, Ahearn TS, Mustafa N, Fox HC, Whalley LJ. Childhood socioeconomic status and adult brain size: childhood socioeconomic status influences adult hippocampal size. *Ann Neurol.* 2012;71(5):653-60. doi: 10.1002/ana.22631 [doi].
10. Murray AD, McNeil CJ, Salarirad S, Whalley LJ, Staff RT. Early life socioeconomic circumstance and late life brain hyperintensities--a population based cohort study. *PLoS One.* 2014;9(2):e88969. doi: 10.1371/journal.pone.0088969 [doi];PONE-D-13-38919 [pii].
11. Davies G, Tenesa A, Payton A, Yang J, Harris SE, Liewald D, et al. Genome-wide association studies establish that human intelligence is highly heritable and polygenic. *Mol Psychiatry.* 2011. doi: mp201185 [pii];10.1038/mp.2011.85 [doi].
12. Deary IJ, Yang J, Davies G, Harris SE, Tenesa A, Liewald D, et al. Genetic contributions to stability and change in intelligence from childhood to old age. *Nature.* 2012. doi: nature10781 [pii];10.1038/nature10781 [doi].
13. Deary IJ. Intelligence. *Annu Rev Psychol.* 2012;63:453-82. doi: 10.1146/annurev-psych-120710-100353 [doi].
14. McNeill G, Jia X, Whalley LJ, Fox HC, Corley J, Gow AJ, et al. Antioxidant and B vitamin intake in relation to cognitive function in later life in the Lothian Birth Cohort 1936.

European journal of clinical nutrition. 2011;65(5):619-26. Epub 2011/02/25. doi: 10.1038/ejcn.2011.2. PubMed PMID: 21346712.

15. Whalley LJ, Duthie SJ, Collins AR, Starr JM, Deary IJ, Lemmon H, et al. Homocysteine, antioxidant micronutrients and late onset dementia. *Eur J Nutr*. 2013. doi: 10.1007/s00394-013-0526-6 [doi].

16. Whitley E, Gale CR, Deary IJ, Kivimaki M, Singh-Manoux A, Batty GD. Influence of maternal and paternal IQ on offspring health and health behaviours: evidence for some trans-generational associations using the 1958 British birth cohort study. *European psychiatry : the journal of the Association of European Psychiatrists*. 2013;28(4):219-24. Epub 2012/05/01. doi: 10.1016/j.eurpsy.2012.01.005. PubMed PMID: 22541368; PubMed Central PMCID: PMC3696866.

17. Richards M, Hardy R, Kuh D, Wadsworth ME. Birth weight and cognitive function in the British 1946 birth cohort: longitudinal population based study. *BMJ*. 2001;322(7280):199-203.

18. Shenkin SD, Starr JM, Deary IJ. Birth weight and cognitive ability in childhood: a systematic review. *Psychol Bull*. 2004;130(6):989-1013.

19. Dibben C, Sigala M, Macfarlane A. Area deprivation, individual factors and low birth weight in England: is there evidence of an "area effect"? *J Epidemiol Community Health*. 2006;60(12):1053-9.

20. Spencer N, Bambang S, Logan S, Gill L. Socioeconomic status and birth weight: comparison of an area-based measure with the Registrar General's social class. *J Epidemiol Community Health*. 1999;53(8):495-8.

21. Fairley L. Changing patterns of inequality in birthweight and its determinants: a population-based study, Scotland 1980-2000. *Paediatr Perinat Epidemiol*. 2005;19(5):342-51.

22. Gisselmann MD. The influence of maternal childhood and adulthood social class on the health of the infant. *Soc Sci Med*. 2006;63(4):1023-33.

23. Moser K, Li L, Power C. Social inequalities in low birth weight in England and Wales: trends and implications for future population health. *J Epidemiol Community Health*. 2003;57(9):687-91.

24. Haggarty P, Ferguson-Smith A, C. Life course epigenetics and healthy ageing. In: Kuh D, Cooper R, Hardy R, Richards M, Ben-Shlomo Y, editors. *A Life Course Approach to Healthy Ageing. A Life Course Approach to Adult Health*. 1st ed. London: Oxford University Press; 2014. p. 198-212.

25. C.M.O.Scotland. Health in Scotland 2011, Transforming Scotland's Health. Edinburgh: 2012 2012. Report No.