Beyond Sex Differences

Genes, Brains and Matrilineal Evolution

Recent developments in behavioural neuroscience and genomics are providing exciting new tools for understanding mammalian evolution. Drawing on a range of disciplines including genomic reprogramming, immunology, genomic imprinting, placentation and brain development, this book examines the leading role played by the mother's genome and epigenome in the successful evolutionary progression of humans from ancestral mammals.

Keverne begins by discussing the historic context of the perceived dominance of males and the patriline, before arguing that it is instead the matriline that exerts the dominant influence in shaping the evolution of our brain development and behaviour, especially the co-adaptive development of brain and placenta. Presenting a balanced outlook on the development of sex differences and an alternative to traditional views, *Beyond Sex Differences* will be of interest to anyone studying and researching mother and infant development.

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Preface

Understanding the Biology of Sex Differences: Mother Leads the Way

It is widely understood and well accepted that males and females differ biologically and in many ways. How our views of biological differences arose, and how these views have shaped our attitudes to the opposite sex has, however, been a long and ever-changing narrative in need of reconsideration. The ancient understandings of sex differences has, without doubt, nurtured some unrealistic malebiased opinions. Such male-biased evaluations of sex differences are nowhere more clearly illustrated than by the writings of men who have been considered eminent and respected in this field. In tracing this narrative historically, it appears that the early Athenian view of sex differences and human biology was that women were merely the incubators of the male seed. Greek philosophers advocated that 'mother is not the parent of that which is called the child, but it is mother that nurtures the seed of the child that grows. The parent is he that plants the seed' (Blundell, 1995). Aristotle, despite his infinite wisdom, claimed women merely supplied the material origins of humanity and males supplied the higher causes, thus making 'males superior to females' (Lange, 1983). It is by no means clear as to which, if any, biological knowledge of sex differences could have given rise to these opinions of women, other than the mothers' commitment to producing and caring for children. Of course, we rarely, if ever, hear the opinions or views of ancestral women on this subject, probably because women were seldom considered to be worthy writers or philosophers, and were primarily recognised by society through and for the man they married. Thucydides proclaimed that 'women's greatest joy is to be talked about among men, whether this be in praise or in blame'. Moving

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forward in time to the thirteenth century, but not progressing in ideology, St Thomas Aquinas, an Italian theologian, philosopher and the pre-eminent spokesman for Catholic reason and divine revelation, postulated that the production of women was a defect in the production of men.

In more recent times, the renowned psychiatrist, Sigmund Freud, theorised that femininity was an immature stage of masculine development. Freud, although a medical doctor, was primarily focused on the psyche in his work, but even those medics who worked on the physiology of reproduction were also inclined to consider female reproduction as the 'default' state. Alfred Jost, a receiver of many scientific awards for his work on the biology of sexual differentiation, and who subsequently became Secretary to the French Academy of Sciences 1991–2001, adopted this same viewpoint. He carried out animal experiments, which showed that male rats castrated before puberty developed a female phenotype (Josso, 2008); hence the conclusion that females represented a default state arising from males. This, to some extent, matched the human clinical findings where a biological insensitivity to male hormones also produces a 'female phenotype'. Even as recently as 1975, the concluding paragraph on sex determination in a medical text on reproduction stated that 'maleness means mastery of the Y chromosome over the X, the medulla over the cortex, androgen over oestrogen. So physiologically speaking, there is no justification for believing in the equality of the sexes; vive la difference'.

In the British Victorian era, sex and reproduction was a 'no-go area' for biological research. Biological research was primarily an all-male preserve with select women attending discussion meetings, but more as spectators than contributors. The Victorian convention was that science knowledge in women was not feminine, and certainly to be discouraged by the male scientists. Even the great libertarian, Thomas Huxley, noted that a minority of women, suitably educated, might become fit 'companions' of men, but not their 'competitors'. Their proper role was to be more concerned

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with the scientist than with his science (Richards, 1989). In 1864, Huxley claimed to have found anatomical evidence for female inferiority. In his Hunterian lectures, he described the structural differences in the brains of men and women, noting that 'the cerebral convolutions are simpler in women than men'. He went on to conclude that 'in every excellent character, whether mental or physical, the average woman is inferior to the average man in the sense of having that character less in quantity and lower in quality'. The great Charles Darwin followed Huxley's lead by arguing on evolutionary grounds 'that the higher education of women could have no long term impact on their social evolution and was, strictly speaking, a waste of resources'.

Paul Broca (1824–1880), an eminent anthropologist of his times, took a slightly different stance, stating that 'Although nature has not made men and women equal, these facts do not afford grounds for refusing to educate women or give them the same civil and political rights. In the name of Justice, law and custom should not add to the biological burdens that weigh women down. Women's subordination to man was natural and eternal and any attempt to revolutionise the education and status of women on the assumption of an imaginary sexual equality would induce a perturbation in their evolution' (Broca, 1868).

I have been somewhat surprised and dismayed to find these misogynous writings by such eminent philosophers and renowned scientists from the past, who were recognised for their rational thinking and wisdom. I would have liked to believe that such views were influenced and biased by opinions that were embedded in the culture of their times. However, many of these eminent male citizens helped to formulate this culture during their lifetime. Theirs was a weak and less-than-objective attempt to come to terms with what represents our current understanding of the biology and psychology of male/female differences today. My own view, after decades of studying the brain and behaviour, is that there are indeed biological sex differences but, importantly, these sex differences

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in humans are not purely driven by the male sex hormone testosterone, nor are they simply down to the genes on the Y chromosome. On the contrary, it is primarily the mother's genome and epigenome (the matrilineal genome) that has played the leading role in determining mammalian and, in turn, our own successful evolutionary progression. This matrilineal progression has finally resulted in the complex organisation of today's human societies. In understanding how this lead has been established by the matriline, I have focussed on genetics, epigenetics, brain development and behaviour. Each of these areas of study have further benefitted from their consideration within an evolutionary and genomic framework. In mammals, this has required taking account of the disproportionate biological role undertaken by the matriline in order to achieve reproductive success. Of course, males have benefitted equally, and share the advantages accruing from such progressive changes. However, for the most part, the patrilineal role has been mainly that of an essential but compliant passenger along our evolutionary road to biological success. Clearly, there is a mismatch between the historic social 'cognitive' view of the female and today's knowledge of the biological reality of gender differences.

What are the studies of the last 40 years that have challenged such biological delusions of male dominance and leadership, and provided a more informed and balanced view on the biology of male versus female sex differences? The two most important and informative areas of biological research to clarify our modern way of thinking have been in genetics and in neuroscience. My aim in this monograph is to draw upon this recent information in order to provide a more balanced overview of the role, indeed the leading role, which the matriline has contributed to our biological success, and how this has had impact on the evolutionary advancement of the human brain. I have spent my research career investigating the brain, its gross and functional anatomy, and the molecular genetics that regulate its development. It is clear to me that a comprehensive understanding of brain function requires that we take into account

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how the brain relates to the body, and equally important, how this relationship differs between males and females. Getting brain function into perspective further requires an understanding of its evolution. Evolutionary studies have provided a perspective that is relevant to all aspects of development and function of the brain, from genetics to physiology and anatomy, and provides a logical insight as to how brain structure and function have changed over the millennia.

The success of mammalian reproduction owes a great deal to maternal in-utero development (viviparity), as indeed does evolution of the brain (see Chapter 4). In the context of inutero viviparity, the female brain has developed mechanisms for regulation of post-partum care and mother-infant bonding. These same mechanisms have evolved to underpin social relationships and social living, as exemplified by the female bonded social groups of the large-brained monkeys and apes (Curley & Keverne, 2005). The extended period of care and commitment provided by social living has also provided a lengthy period for postnatal brain development and growth. Moreover, such brain development takes place within an environment dominated by complex social relationships. Social living thus heralded a massive evolutionary increase in those parts of the brain that take on social and executive functions. Importantly, human reproduction has witnessed a level of emancipation for maternal care and sexual behaviour from the determining action of the body's biological messengers, the hormones. So important has been the extended postnatal period of growth in the evolution of the human executive brain that the hormonal biology of reproduction has been succeeded by growth of the forebrain in guaranteeing reproductive success. From this pivotal stage forwards, the brain has been developing the capacity to shape the direction of its own evolutionary destiny. Only humans can override the basic instincts of hunger, sex and aggression. Only humans can undertake lifetime vows of chastity, or become committed mothers without undertaking pregnancy, as indeed can

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men, although the male social predisposition in this direction is rarely so devotional.

My aim in writing this book is to draw upon recent studies that inform and provide a balanced overview of the role, indeed the leading role, which the matrilineal genome has contributed to the evolutionary development of differences between males and females. The impact that the matriline has made on mammalian evolution is particularly reflected in the genetics and epigenetics of brain and placental development. The success of Motherhood, as exemplified by mammals, has been driven by in-utero placentation. This in turn has provided the coexistence of two genomes, those of mother and foetus, which have provided a platform for intergenerational genomic co-adaptation. It is motherhood, not sex, which has provided the selection pressures for achieving mammalian reproductive success. The mother-infant relationship has underpinned the evolutionary development of large brains, while the neural mechanisms for bonding and attachment have, in turn, provided the biological foundations for underpinning complex social organisations.

REFERENCES

- Blundell, S. (1995). *Women in Ancient Greece*. First (US) edn. Cambridge, MA: Harvard University Press.
- Broca, P. (1868). On anthology. Anthropol. Rev. 6: 35-52.
- Curley, J. P. & Keverne, E. B. (2005). Genes, brains and mammalian social bonds. *Trends Ecol. Evol.* 20: 561–67.
- Josso, N. (2008). Professor Alfred Jost: the builder of modern sex-differentiation. Sex. Dev. 1: 55–63.
- Lange, L. (1983). Woman is not a rational animal: on Aristotle's biology of reproduction. In: S. Harding & M. B. Hintikka (eds.), *Discovering Reality*. Dordrecht: D. Reidel Publishing Company, pp. 1–15.
- Richards, E. J. (1989). Huxley and woman's place in science: the 'woman question' and the control of Victorian anthropology. In: J. R. Moore (ed.), *History, Humanity and Evolution: Essays for John C. Greene.* New York, NY: Cambridge University Press.

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