

Evolutionary Origins of Autism and Psychosis?

Christopher Badcock writes about a new theory that suggests that two apparently unrelated psychiatric disorders share a common genetic origin in conflict between the mother's and the father's genes.

Although a child inherits half its DNA from each parent, we now know that certain genes are only expressed if they come from one rather than the other parent. IGF2 codes for a growth hormone (insulin-like growth factor 2), and is only normally expressed from the father's gene. If the mother's IGF2 gene is also expressed Beckwith-Wiedemann syndrome results. Beckwith-Wiedemann babies are one-and-a-half times normal birth-weight and show excessive growth during adolescence along with other over-growth symptoms, such as tumours. In the past, many mothers must have been killed trying to give birth to such enormous babies, and so it is not surprising that normally the mother's copy of the IGF2 gene is silenced, or imprinted. But if both copies of this gene are silenced, the result is the opposite: a pre- and post-natal growth retardation syndrome.

The underlying logic of this reflects the contrasting costs and benefits of growth to the mother as opposed to the father. Although the mother's genes in her children benefit from their growth to exactly the same extent as the father's, only the mother pays the cost. In the tangible terms of a child's birth-weight, the mother's contribution is hundreds of billions of times greater than the father's, which is only a single sperm! As a result, paternally-active imprinted genes favour growth much more than maternally-active ones, and are particularly strongly expressed in the placenta – an organ primarily designed to extract resources from the mother. Indeed, an abnormal conceptus with a double set of paternal genes without any genes whatsoever from the mother results in a massive proliferation of the placenta without any associated foetus!

The imprinted brain

The other organ in which imprinted genes are mainly expressed is the brain. Experimental studies on chimeric mice who have larger than normal genetic contributions from one or the other parent show that maternal genes are preferentially expressed in the parts of the brain that correspond to the human neo-cortex, and that paternal genes are predominantly expressed in parts corresponding to the limbic system in human beings. To see what this means in practice, imagine that you are on a diet. The part of your brain that is making you hungry was built by your father's genes: appetite, along with other emotional and instinctual drives, originates in parts of the limbic system like the hypothalamus. But the part of your brain that makes you worry about getting fat and want to resist was made from your mother's genes – especially the pre-frontal cortex, which plays a major role in inhibition and control of outputs from the limbic system – for example, countering feelings of hunger.

Evidence that imprinted genes play a conflicting role in behaviour is suggested by two other paediatric syndromes: Angelman and Prader-Willi. In both cases there is abnormal expression of imprinted genes in a region of chromosome 15. In Angelman there is more paternal and/or less maternal gene expression, but in Prader-Willi the opposite: more maternal and/or less paternal genes are expressed. Angelman is also called Happy Puppet syndrome because jerky and poorly-co-ordinated movements are listed as symptoms along with 'paroxysms of laughter'. You could see the latter as a very low pleasure threshold which contrasts with the high pain threshold seen in Prader-Willi children (who often cause serious lesions by picking at wounds which normal children would find too painful to touch). And whereas Angelman children feature prolonged suckling, frequent crying, hyper-activity and sleeplessness – every mother's worst fear – Prader-Willi cases are characterized by poor suckling, weak crying, inactivity and sleepiness – much more like the ideal baby!

Because the mother's genes are equally present in all her offspring, her genetic self-interest is best served by co-operation and family unity. Any net benefit from social behaviour among her offspring is also a benefit to the ultimate reproductive success of her genes invested in them. Thanks to gestation and lactation, the mother is the prime nurturer, and so it serves her interests to be able to nurture, educate, and instruct her children – for example to teach them their 'mother-tongue' and then use it to program their thinking in ways she approves. By these means the mother can indoctrinate, condition, and socialize her offspring in behaviour that is likely to benefit her equitable genetic investment in all of them. The father, on the other hand, need make no obligatory biological contribution to his offspring beyond a single sperm, and other children of the same mother need not share his genes: Mother's baby – father's? Maybe! As a result, the father's genes build parts of the brain that tend to motivate self-interested, instinctual, and non-social behaviour, and his genetic self-interest is not necessarily served by his child seeing things its mother's way – for example, in making sacrifices for siblings to which its paternal genes may not be related in any way whatsoever. The striking social deficits seen in autism would certainly fit the idea that paternal genetic self-interest underlies the disorder because autistic children seem perversely committed to doing things their own way and in their own time. If they can learn at all, they usually refuse to do so in the way adults think they should, and certainly pose a severe challenge to any care-giver (who in our evolutionary past would predominantly have been the mother and her relatives).

Autism and psychosis

Angelman children show severe retardation, little or no language, and tend to be diagnosed as autistic. Prader-Willi cases with two copies of chromosome 15 from their mother (and none from the father) are always diagnosed psychotic in adulthood and show less severe retardation. Further hints that imprinted genes may have something to do with autism and psychosis come from the finding that autistics have heavier birth-weight (especially males) while schizophrenics are lighter – just as you would expect if paternal genes were more prominent in autism. Again, more paternal and/or less maternal genetic influence is sometimes implicated in cancer (another form of over-growth) and here the striking finding is that schizophrenics have less cancer than autistics despite the fact that the former smoke much more. Again, there is evidence that autistics by contrast to psychotics show early brain growth at the expense of the mother.

Although both autism and schizophrenia appear to have a predominantly genetic basis, the exact genes concerned have so far defied definition. But if both disorders were linked to the imprinting mechanism, much might be readily explained. This is because imprints are re-set each generation, and as the cases of Angelman, Prader-Willi, and Beckwith-Wiedemann syndromes show, can have genetic causes which are not necessarily heritable in the classical Mendelian manner. Again, autism can be caused by tuberous sclerosis and environmentally induced by prenatal valproic acid, thalidomide, or viral infection. Such factors could easily affect the expression of imprinted genes, and certainly could directly affect the relative development of the different parts of the brain where they are preferentially expressed. Many symptoms of autism have been interpreted in terms of deficits in what you might call mentalism defined as our evolved ability to understand our own behaviour and that of others in purely mental terms such as intention, feeling, or belief. Certainly, mentalistic cognition appears to be the prime adaptation that humans have acquired for social behaviour because essentially it enables you to see things from other people's point of view, understand their motives and feelings, and predict their behaviour. Research into autism has now become the main source of our scientific insights into mentalism because autistics characteristically lack mentalistic skills, such as monitoring gaze and correctly interpreting intention. However, it's a striking fact that you find the exact opposite in paranoid schizophrenia. For example, paranoiacs notoriously over-interpret direct of gaze to the extent that they think they are being watched or spied on. Indeed, recent laboratory experiments have proved that schizophrenics are abnormally responsive to the direction of others' gaze, whereas autistics notoriously are not.

When you say someone is 'being paranoid': you mean that they are over-interpreting someone else's behaviour, words, or expressions. But paranoid psychotics take such hyper-mentalism to bizarre and pathological lengths. They also over-interpret intention, but do so in two completely different ways. Other people's intentions towards you can be positive or negative, and it is interesting that although most paranoiacs over-interpret negative intention in the characteristic symptoms of delusions of persecution, others (particularly women) over-interpret positive intentions to the extent of believing that others are in love or are infatuated with them (so-called erotomania).

Again, autistics' typical failure to understand shared attention in groups is countered by paranoid delusions of conspiracy, which vastly exaggerate it. And where many autistics have a diminished sense of personal agency and identity, psychotics often become megalomanic and subject to delusions of grandeur. Whereas autistics are often mistakenly thought to be deaf thanks to their mentalistic deficits, one of the most common features of paranoid schizophrenia is hearing voices. While autistics tend to be literal and to find deception difficult, psychotics characteristically suffer from severe delusional thinking and bizarre self-deception. Indeed, schizophrenics show measurable deficits in the more mechanistic aspects of cognition at which autistics savants typically excel. Finally, autism is a disorder with an early onset because the affected child never matures mentalistically. Psychosis, on the other hand, is an adult-onset disorder because you can't become hyper-mentalistic before acquiring normal mentalism In other words, the symptoms of both autism and paranoid psychosis resemble the pattern seen in Angelman and Prader-Willi, suggesting that both the hypo-mentalism of autism and hyper-mentalism of paranoia can be traced to a common genetic origin lying in genomic imprinting and the contradictory effects it tends to produce. But clearly, normality must represent a balanced expression of both, and could be understood as enough mentalistic ability to understand other people's minds, but not so little as to be autistic, or so much as to be paranoid. What passes for sanity, in other words, begins to look like a mid-point on a mentalistic continuum stretching from autism to psychosis and ultimately reflecting the balance of forces between the father and mother in the individual's genome.

Christopher Badcock

Medicine in South-East Asia – conference report

Ayo Wahlberg reports on the first-ever International Conference on the Thistory of Medicine in South-East Asia

In early January, a group of about thirty or so researchers from around the world gathered in Siem Reap, Cambodia for the first-ever International Conference on the History of Medicine in South-East Asia. Sponsored by the Wellcome Centre for the History of Medicine and hosted by the Centre for Khmer Studies in Siem Reap, the conference took place a few kilometres from the spectacular Angkor ruins which date back to the 8th century when the first temples were built to mark the Khmer capital. Since the return of relative political stability to Cambodia in the 1990s, Siem Reap has burgeoned into quite a thriving tourist town in recent years with planeloads of passengers shuffling between airport-hotel-Angkor ruins-hotel-airport.

Conference participants spent two days listening to presentations covering aspects of ancient, colonial and postcolonial medicine in Malaysia, Cambodia, Vietnam, Indonesia, the Philippines and Thailand. Professor Warwick Andersen previewed the central arguments of his forthcoming book on *Colonial Pathologies in the Philippines* which investigates some of the disciplining hygiene practices that colonial bodies were subject to as well as the ways in which colonial medical experiences could also feedback into American medical settings as colonial doctors returned to their home towns. Dr. Hans Pols showed how contested views of the 'native mind' had influenced the ways in which colonial psychiatry in the former Dutch East Indies was organised and practiced. And Ooi Keat Gin provided a fascinating account of how economic, public health and nationalist rationalities competed in the implementation of anti-opium campaigns in early 20th century Malaya.

Thanks to financial assistance from the LSE Department of Sociology and the Danish Research Agency I was able to attend the conference to present a paper on my ongoing comparative research into the traditional indigenous herbal medicine of Vietnam and the United Kingdom respectively. My paper, titled 'A revolutionary movement to bring traditional medicine back to the grassroots level' – on the bio-politicisation of herbal medicine in Vietnam', described how a national programme to revive the practice of traditional herbal medicine had been made possible in the past fifty years. With most international conferences covering science and medicine in the East Asian region often dominated by researchers working with China, Japan and Korea, the occasion for researchers working in the smaller nations of South-East Asia to get together was particularly welcomed by participants. Indeed plans have been made to hold a second conference in Penang, Malaysia in 2007.

Ayo Wahlberg, PhD student