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AUTISM AND ANOREXIA NERVOSA

TWO FACETS OF THE SAME DISEASE?

The recent emergence in the scientific literature of 'gene expression' as a frequent keyword has suddenly assigned an unexpected new function to our database.

Apart from purely genetic diseases such as Down syndrome, cystic fibrosis, colour blindness, haemophilia, phenylketonuria, Huntington's chorea, sickle-cell disease, or Turner syndrome, it is now well-accepted that both genetic and environmental factors are at the origin of most pathological conditions and personality traits.

Until recently, it was commonplace to contrast genetic and environmental factors. There have been endless discussions about the relative contributions of these two factors. Such discussions led in particular to twin and adoption studies, in order to disentangle the effects of genes versus environment. Today many geneticists aim to identify genes involved in the predisposition towards specific diseases while e pidemiologists look for environmental risk factors. The dialogue has always been difficult between those who tend to exaggerate the genetic factors and those who tend to minimize them. We are still under the indirect influence of the obsolete Nature versus Culture debates based on narrow preconceived ideas. The view that humans acquire all, or almost all, their traits from "nurture" was known as *tabula rasa.* The opposite view was the basis for philosophical movements such as 'Nativism' and 'Innatism'.

Today the concept of 'gene expression' is a turning point regarding our understanding of the origin of pathological conditions and personality traits. We are now in a position to explain that some of our genes express themselves, while others

become extinct; of course they still exist and they will reappear within the next generation. Gene expression is the process by which inheritable information from a gene, such as a DNA sequence, is made into a functional gene product, such as=2 0a protein or RNA. It has been demonstrated that methylation of DNA is a common method of gene silencing.

Toward a new classification of diseases

Gene expression is to a great extent dependent on environmental factors during the primal period. We must constantly keep this important point in mind. That is why, in the current scientific context, the first questions related to disease causation are not about the identification of the genes involved or the relative roles of genetic and environmental factors. The questions are about the timing. They concern the critical periods for genes-environment interaction. This is why the Primal Health Research Database is suddenly assigned an unexpected new function. The database has become a unique tool to provide some clues about the critical period for the genesis of states of health, pathological conditions, and personality traits. It can even contribute to an unprecedented classification of health conditions according to their critical period for genes-environment interaction.

An example

In order to illustrate this new role of the primal health research database, we'll explore the possible links between *autism* and *anorexia nervosa*, two conditions that, according to the data we have at our disposal, are to a great extent determined during the perinatal period. The mysterious increased prevalence of both diseases, concomitantly, is one of the reasons why we choose this example. It is well-accepted today that the increased prevalence in these two conditions is not simply resulting from improved diagnostic and greater public awareness.

Among the three recent large and authoritative studies of autism from a Primal Health Research perspective, the Australian study will convince anyone that the main risk factors occur in the perinatal period.[1] The 465 subjects born in Western Australia between 1980 and 1995 and diagnosed with an autism spectrum disorder by 1999 were compared with the birth records of 481 siblings of the cases, and with1313 controls. No differences in gestational age at birth (including premature infants), weight for gestational age, head circumference, or length were observed between cases and control subjects. Pre-eclampsia did not appear as a risk factor. These negative findings lend

more credence to perinatal factors. Compared with their siblings, *autism* cases were more likely to have been induced, to have experienced fetal distress, and to be born with a low Apgar score. Compared with control subjects, they were more likely to be born after induction and to be born by elective or emergency c-section.

Similar conclusions can be drawn from a study involving all Swedish children20born from 1974 to 1993. No association was found between *autism* and head circumference, maternal diabetes, being a twin, or season of birth, while c-section appeared to be a risk factor.[2] This study could not consider labour induction as a possible risk factor, since this term did not appear in the Swedish birth registers until 1991. A recent report from Israel also found no prenatal differences between autistic children and controls, but the rates of birth complications were higher among the autistic population.[3]

We must add to these negative findings a series of studies exploring the possible links with different types of vaccinations in infancy. These, too, indirectly give weight to the perinatal factors. All epidemiological studies included in our database confirm that the risks of *autism* seem to be the same among children who did or did not receive MMR.[4,5,6,7] They also seem to be the same among children who had or had not received a vaccine containing a mercury derivative.[8] If we take into account that the risk of *autism* is not related to the mode of infant feeding (breast or bottle) we must conclude that the significant risk factors precede=2 0infancy.

We can draw similar conclusions from a large and authoritative Swedish study of risk factors for anorexia nervosa. The researchers had access to the birth records of all girls born in Sweden from 1973 to 1984,[9] and of the 781 girls who had stayed in a Swedish hospital due to *anorexia nervosa* between age 10 and age 21. For each anorexic girl there were five controls (non-anorexic girls born in the same hospital during the same year). Apart from being born before 32 weeks gestation, the most significant risk factor for *anorexia nervosa* was a *cephalohematoma* at birth. Forceps and ventouse deliveries were also risk factors. An Italian retrospective study of subjects with eating disorders found that the risk of developing *anorexia nervosa* increased with the total number of obstetric complications. In addition, an increasing number of complications significantly anticipated the age of onset of *anorexia nervosa.*[10]

It appears from this Italian study that being shorter for gestational age significantly differentiates subjects with *bulimia nervosa* from those with *anorexia nervosa.* A study of smoking in pregnancy as a risk factor for *bulimia nervosa* also

suggests that the concept of 'eating disorder' should be dismantled. *Anorexia nervosa* and *bulimia nervosa* should be studied separately. Not only can Primal Health Research establish links between pathological entities, but it can also dismantle of pre-existing entities.

The contribution of other perspectives

The links suggested by the primal health research perspective between *anorexia* and *bulimia* prompt us to wonder what we can learn from other perspectives. This question inevitably leads to refer to clinical considerations mentioned by several teams of psychiatrists. Janet Treasure *et al* of the Institute of Psychiatry of King's College hospital, in London, have emphasized the importance of autistic traits in *anorexia nervosa*.[11] People with *anorexia nervosa* find it difficult to change self-set rules; they see the world in close-up detail, as if they were looking through a zoom lens, and risk getting constantly lost in the details.[12] Christopher Gillbert and the team of the Department of Child and Adolescent Psychiatry at Goteborg University in Sweden, found that 23% of female patients with severe eating disorders had symptoms of the autism spectrum.[13]

The oxytocin system in both conditions offers another promising avenue of research. The first clues came20from a study of midday blood samples from 29 autistic and 30 age-matched normal children.[14] The autistic group had significantly lower blood oxytocin levels than the normal group. Oxytocin increased with age in the normal but not the autistic children. These results inspired an in-depth inquiry into the oxytocin system of autistic children. In recent years it has become clear that oxytocin can appear in the brain in several forms. There is the nonapeptide oxytocin (OT) and the 'C-terminal extended peptides', which are described together as OT-X. The OT-X represent intermediates of oxytocin synthesis that accumulate due to incomplete processing. Twenty-eight male children diagnosed with autistic disorder were compared with 31 age-matched non-psychiatric control children: there was a decrease in blood OT, an increase in OT-X and an increase in the ratio of OT-X/OT in the autistic sample, compared with control subjects.[15] In other words, autistic children show deficits in the processing of oxytocin.

There have not been such in-depth inquiries into the oxytocin system of anorexic patients. However, it has been reported that the level of oxytocin in the cerebrospinal fluid of women with E2restricting anorexia' is significantly lower than the level of oxytocin in bulimic and control subjects.[16] Such studies of the oxytocin system provide new reasons to dismantle the framework of 'eating disorders' while reinforcing the links between *anorexia* and *autism*. They offer interpretations of the perinatal period as critical in the origin of both conditions, since it is a time when the oxytocin system is highly-challenged, with a deep redistribution of the specific neuroreceptors. These are important considerations when the physiological processes in the perinatal period are routinely disturbed as happens these days.

Towards a new phase in the history of nosology?

Until now nosology – the naming and classification of diseases – was mostly based on descriptions of symptoms (e.g. scarlet fever), on altered functions (e.g., hyperthyroidism) or on altered organs (e.g., myocardial infarction). Today, the Primal Health Research Database makes possible a classification according to critical periods for genes-environment interaction. After studying in parallel *anorexia nervosa* and *autism*, one can reinforce the suggestions expressed by some psychiatrists that *anorexia nervosa* might be considered a female variant of the autistic spectrum. A plausible interpretation of why it is undoubtedly more female is that prenatal exposure to male hormones might protect against the expression of *anorexia nervosa*. Such an interpretation is suggested by a study of twins.[17] Girls who have a twin brother were at low risk of anorexia nervosa, compared with girls who had a twin sister and with controls. This interpretation is reinforced by the negative results of genetic linkage analyses that could not detect any change on the X chromosome.[18]

With the fast development of primal health research we can anticipate that new nosological entities will appear while others will more or less fall away.

Michel Odent

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