Evolutionary psychiatry and the schizophrenia paradox: a critique

PIETER R. ADRIAENS

*Institute of Philosophy, University of Leuven, Parijsstraat 72b, 03.04, B-3000, Leuven, Belgium
(e-mail: pieter.adriaens@hiw.kuleuven.be)*

Received 12 April 2006; accepted in revised form 4 August 2006

Key words: Balancing selection, Evolutionary psychiatry, Heterogeneity, Natural kinds, Schizophrenia

Abstract. Evolutionary psychiatrists invariably consider schizophrenia to be a paradox: how come natural selection has not yet eliminated the infamous ‘genes for schizophrenia’ if the disorder simply crushes the reproductive success of its carriers, if it has been around for thousands of years already, and if it has a uniform prevalence throughout the world? Usually, the answer is that the schizophrenic genotype is subject to some kind of balancing selection: the benefits it confers would then outbalance the obvious damage it does. In this paper, however, I will show that the assumptions underlying such evolutionary accounts of schizophrenia are at least implausible, and sometimes even erroneous. First of all, I will examine some *factual* assumptions, in particular about schizophrenia’s impact on reproductive success, its genetics, its history, and its epidemiology. Secondly, I will take a critical look at a major *philosophical* assumption in evolutionary psychiatric explanations of schizophrenia. Indeed, evolutionary psychiatrists take it for granted that schizophrenia is a natural kind, i.e. a bounded and objectively real entity with discrete biological causes. My refutation of this natural kind view suggests that schizophrenia is in fact a reified umbrella concept, covering a heterogeneous group of disorders. Therefore, schizophrenia, as we now know it, simply doesn’t have an evolutionary history.

Introduction: meet the schizophrenia paradox

Evolutionary psychiatric hypotheses about schizophrenia have always appealed to the imagination. Some evolutionary psychiatrists claim that schizophrenia may well be the price that some of us pay for mankind’s possession of some valuable adaptive asset. Thus schizophrenia would be intimately related to our very humanity. Others have alleged that some schizophrenics may have been charismatic leaders or visionary artists, that held high positions in the social world of our ancestors. As such, evolutionary psychiatry has certainly made a positive contribution to our incessant attempts at making sense of such a devastating disorder, and to get rid of the stigma that still surrounds it.

The starting point of every single evolutionary psychiatric account of schizophrenia is amazement about its paradoxical nature. How come natural selection has not yet eliminated the infamous ‘genes for schizophrenia’ if the disorder has been around for thousands of years already, if it has a fairly

uniform prevalence throughout the world, and if it simply crushes the reproductive success of those suffering from it? The solutions to this paradox have been manifold. In the first section of this paper, I will briefly discuss one of the most popular evolutionary psychiatric accounts, which invokes some kind of balancing selection. In the next section, I move backwards and take a close look at some four *factual* assumptions underlying this account. While hurrying to resolve the paradox, evolutionary psychiatrists have failed to check the truth of its assumptions about schizophrenia's impact on reproductive success, its genetics, its history, and its epidemiology. Finally, in a third section, I will critique a major *philosophical* assumption adhered to by most evolutionary psychiatrists, by showing that schizophrenia is not a natural kind, but rather a peculiar psychiatric reification behind which a heterogeneous group of disorders is hiding.

A paradox and its resolutions

Darwinians are mad about paradoxes. For there are so many traits that, for some reason, have not been purged by selection even though they do not help our reproductive success. Mental disorders, such as schizophrenia, are excellent examples of such traits. Hence the question with which nearly any natural history of schizophrenia begins: 'Why has natural selection allowed genes to persist in the human genome that increase the likelihood of suffering from these devastating disorders, despite the reproductive disadvantage of schizophrenia?' (Brüne 2004, p. 41).

In the past five decades, many solutions of this paradox have been suggested. Most evolutionary psychiatrists assume that the 'genes for schizophrenia' have been maintained in the human gene pool by some kind of *balancing selection* (e.g. Huxley et al. 1964; Allen and Sarich 1988; Sullivan and Allen 2004). In such scenario, the genes that are conducive to schizophrenia are being kept in the human genome because of the unusual advantages they (or their allelic variants) may offer in a different genetic or environmental configuration. Such advantages are enjoyed mostly by the schizophrenic patients' closest relatives, with whom they share a large part of their DNA.

The classic example of balancing selection is sickle cell anaemia – a disease that is commonly observed in people from African and Mediterranean heritage. Geneticists have shown that anaemic patients are (recessively) homozygotic (*ss*) for the β -haemoglobin locus in their DNA. Dominantly homozygotic (*SS*) individuals do not develop anaemia, but they are susceptible to malaria, which is very common in some parts of Africa and the Mediterranean. Heterozygotics (*Ss*), however, do not produce anaemia and they appear to be resistant to malaria. Thus the net fitness effects of these allelic variants (*ss*, *SS*, *Ss*) balance each other out.

Similar suggestions have been made about schizophrenia. The advantages of the (fictitious) schizophrenic genome are sometimes supposed to be of a

physiological nature: schizophrenic patients and their relatives would better withstand all sorts of infections and allergies (Carter and Watts 1971; Brown 2003). Also, (female) relatives of patients would be more fertile than average, thus providing at least *some* compensation for the reduced reproductive fitness of their mentally ill relatives (Srinivasan and Padmavati 1997; Avila et al. 2001; although see Haukka et al. 2003).

Schizophrenogenic families have also been said to enjoy benefits of a *social* nature. Many psychiatrists have argued that the incidence of schizophrenia may have been sustained throughout our evolutionary history because the illness is in some way associated with creativity (Karlsson 2001; Nettle 2001; O'Reilly et al. 2001). Anecdotes are legion. Newton would have been psychotic, just like John Nash, the 1994 Nobel Prize winner in economics. Albert Einstein's son, James Joyce's daughter, and Carl Gustav Jung's mother were all schizophrenics. Especially *artistic* creativity would be a good candidate to counterbalance the detrimental effects of schizophrenia, because the display of such creativity seems to correlate with enhanced mating success (Nettle and Clegg 2005). Indeed, artists appear to score high on some components of a minor variant of schizophrenia, i.e. schizotypy. And schizotypy has also been shown to affect many close relatives of schizophrenic patients (Fanous and Kendler 2005).

Many theories have been designed to account for the peculiar association between schizophrenia and creativity. My focus will be mostly on David Horrobin's account. Horrobin suggested that minor mutations in the genetic code of the fat metabolism of our early ancestors, and the associated exponential increase of our cerebral capacities, have heralded the beginning of our species, while at the same time making us vulnerable for schizophrenia. Such disadvantage, however, is nullified by the benefits of our amazing creativity (Horrobin 2001)¹.

Thus Horrobin clearly appeals to some kind of balancing selection to account for the persistence of schizophrenia, though his theory is a little more complicated than that. Indeed, he also believes in a rather straightforward adaptationist scenario, in which schizophrenia 'may have been a somewhat, or even much, milder illness than we have recognized in the past 150 years. Schizotypy, rather than schizophrenia, may be a better description' (Horrobin 2001, p. 239). As such, the 'first schizophrenics' may have been shamans or priests of some sort – a position that certainly did not block their reproductive success. It is only with the advent of the agricultural and industrial revolution, and their baleful impacts on the intake of essential fatty acids, that schizotypy turned into schizophrenia as we now know it. Then balancing selection set in,

¹ A highly similar theory about the evolution of schizophrenia has been proposed by Tim Crow. According to Crow, schizophrenia is the price we pay for the advantages related to the asymmetrical construction of our brains (cerebral asymmetry). Crow claims that this asymmetry, and particularly the specialisation of our left hemisphere, plays a major part in the development of our capacity for language. Many schizophrenics seem to lack such asymmetry (Crow 2000).

and ever since, the detrimental effects of full-blown schizophrenia have been balanced by the unquestionable profits of human creativity.

Unfortunately, as Keller and Miller (2006) have shown, balancing selection is probably not the most likely resolution to the paradox of common and harmful mental disorders. First of all, trade-offs like sickle cell anaemia appear to be rare in nature. Also, they are highly provisional because they are so costly. As Keller and Miller note: '[S]election would strongly favour genetic events that positions both *S* and *s* on the same chromosomal arm, so they can be passed on together without disruption, or mutations that reduce the fitness costs of either homozygote' (Keller and Miller 2006, p. 19). Finally, and more specifically about schizophrenia, most scenarios involving balancing selection are the subject of fierce discussion. Studies demonstrating physiological advantages have not been replicated (Allen and Sarich 1988), while those in favour of the connection with creativity suffer from either methodological errors or definitional deficits (Waddell 1998).

More importantly, however, few evolutionary psychiatrists have actually dwelled upon the assumptions underlying the paradox they were trying to resolve. In the next section, I will touch on some *factual* assumptions, while the final section contains a thorough critique of one of the major *philosophical* assumptions underlying the schizophrenia paradox.

A paradox and its assumptions

All evolutionary explanations of schizophrenia are grounded on a number of assumptions that are not obviously true and perhaps are even wrong. In this section, I will hold four major assumptions up to the light. All too often, evolutionary psychiatrists assume (1) that schizophrenia indiscriminately crushes the reproductive success of those suffering from it, (2) that there are 'genes for schizophrenia', (3) that the illness has been around for a very long time (probably even since the very beginning of our species), and (4) that the prevalence of schizophrenia has been stable throughout all times and places.

Does schizophrenia reduce reproductive success?

The first assumption underlying the schizophrenia paradox is that the illness sharply reduces the reproductive success of its carriers (e.g. Huxley et al. 1964; Brüne 2004). It is telling, for example, that Burns, in his 2004 *BBS* target article, refers to a 1973 study to prove that 'schizophrenia is associated with lower fecundity' (Burns 2004, p. 832). For that matter, evolutionary hypotheses about male homosexuality are often grounded on a similar presupposition: how can a 'gay gene' spread through a population if its carriers do not reproduce? The answer to this question, however, is fairly simple: human history and cross-cultural anthropology teach us that most men engaging in

same-sex sexual practices were simultaneously married; thus they had sexual relationships with men (mostly boys or adolescents) *and* women. Homosexuality as we now know it, i.e. an *exclusive* sexual bond between two partners of the same sex that, necessarily, forecloses the biological possibility of having children, is an eighteenth century social construction (Adriaens and De Block 2006).

Similarly, some evolutionary psychiatrists (e.g. Stevens and Price 2000; Horrobin 2001) have argued that schizophrenia as we now know it is a relatively recent phenomenon, and that its impact on reproductive success used to be less sweeping than it is now. However, most of them simply assume that data about the reproduction of contemporary North American and European schizophrenics are representative of the entire evolutionary history of schizophrenia.

What is clear is that *male* schizophrenics are definitely at a high reproductive disadvantage when compared to female schizophrenics, as well as to the general male population (Nanko and Moridaira 1993). Yet according to Huxley and his colleagues, this need not necessarily be the case for *female* schizophrenics. On the contrary: 'Female schizophrenics (...) not infrequently marry, and seem to seek for affectional satisfaction through children: so their fertility may possibly be above average' (Huxley et al. 1964, p. 221). Recent data from Palau (Micronesia) partly substantiate Huxley's hypothesis: the average fertility in a group of 49 males and 21 females with chronic schizophrenia was respectively 0.5 and 2.3 offspring, compared to the 1990 total Palauan fertility of 2.8 offspring (Sullivan and Allen 2004). The fertility of Micronesian women suffering from schizophrenia was only slightly lower than the average female fertility in Palau, thus providing some sort of compensation for the drastically reduced fertility of local male schizophrenics.

Secondly, Bhatia and his colleagues have found that male Indian schizophrenics were much more likely to marry than male American schizophrenics (29% vs. 4%, respectively): 'Thus, the severe procreational deficit noted previously among male patients may not be an invariable feature of the disorder' (Bhatia et al. 2003). The high marriage rate of male Indian schizophrenics is probably due to the tradition of arranged marriages in India, but in ancient times such marriages were in fact common ground all over the world. Therefore, historical marriage rates of schizophrenics probably approximated to the contemporary Indian rates, rather than the American rates.

Finally, one Irish study found that male schizophrenics had indeed low marriages rates, but those who *did* marry produced more children than married female schizophrenics, whose marital fertility is close to the 'normal' number of children. The authors conclude that 'men might represent a more fertile group of schizophrenic patients with some biological advantage of increased fecundity, which may help to compensate for negative selection pressures' (Lane et al. 1995). Unfortunately, the results of this study have not been replicated.

In short, many evolutionary psychiatrists take it for granted that schizophrenia is always pernicious for the reproductive success of those suffering

from it. But such an assumption is at least over-simplified. Besides the obvious intersex variability in reproductive success of schizophrenics, evolutionary psychiatrists should also be able to reckon with important geographical and even ethnic differences (Hutchinson et al. 1999).

Are there such things as ‘genes for schizophrenia’?

A second assumption that underlies evolutionary psychiatric thinking about schizophrenia is that somewhere in our DNA, there is an orderly and limited number of major impact genes that code for the susceptibility to this disorder: ‘[S]everal major genes must be simultaneously present in the same individual if that person is to be schizophrenic. We don’t know how many “several” is, but three or four would not be an unreasonable guess’ (Horrobin 2001, p. 170; see also Meehl 1990; Crow 2000). In fact this assumption is one of the main dogmas of twentieth-century psychiatry in general. Blom, for example, has pointed out that psychiatrists like Kraepelin and Bleuler simply took it for granted that schizophrenia was a fairly simple hereditary disorder (Blom 2003; see also Joseph 2003). It is only later that family studies, twin studies and adoption studies were set up to confirm this assumption. The first molecular-psychiatric papers about schizophrenia appeared around 1950; these papers gave the starting shot for a tide of claims about the discovery of ‘genes for schizophrenia’.

Molecular psychiatrists have always been quite optimistic. A single dominant gene, though perhaps with low penetrance, would be responsible for the bulk of the cases of schizophrenia (Böök 1953). In 1964, Huxley and his colleagues even made mention of a simple chromatographic urine analysis for schizophrenia: ‘Chromatographic tests are beginning to provide evidence of detectable “mauve” and “pink” chemical factors in the urine of a large majority of schizophrenics’ (Huxley et al. 1964, p. 221). However, it became clear soon that the development of the disorder would involve more than one gene, if any. So one started to talk about genetic susceptibility, polygenetic thresholds, epistasis, pleiotropy, imprinting, genetic heterogeneity, etcetera (Fanous and Kendler 2005). Yet such complexifications cannot conceal that half a century of thorough genetic research has brought conspicuously few results. As Holden said in a remarkably honest paper in *Science*: ‘[S]chizophrenia is still a disease whose mechanism is totally unknown (...). Dozens of genetic studies have failed to reveal more than a tiny contribution from any single gene’ (Holden 2003, p. 333; see also Gottesman and Gould 2003 and Keller and Miller 2006).

Obviously, it is impossible to maintain that genes play no role in schizophrenia. Heritability studies have consistently shown that a major part (about 80%) of the variation in the susceptibility to schizophrenia is due to *genetic* variation between schizophrenic individuals. The question is, however, how many genes are involved, and what their effect size is. As Keller and Miller

note, 'one of the strongest predictions from practically every model of balancing selection is that it will lead to relatively few polymorphic loci, each harbouring just a few (usually two) different alleles (...) that account for most of the genetic variation of the trait' (Keller and Miller 2006, p. 31). Such prediction is indeed compatible with the current trend of gene mapping in psychiatric genetics. Oddly enough, while gene-mapping studies have failed to yield any consistent results, many researchers, including evolutionary psychiatrists, have held on to their belief that there is such thing as an orderly number of high-impact schizophrenia susceptibility genes ('the true schizophrenia susceptibility genes', as Thaker and Carpenter 2001 say).

Those who do acknowledge the discrepancy between their credo and the actual evidence are quick to point their finger at psychiatric diagnostics. Genotyping the disorder, they argue, is obviously impossible for as long as the concept of schizophrenia remains unclear. Recently, there have been some efforts to deconstruct the notion of schizophrenia by focusing on so-called 'endophenotypes', i.e. separable and heritable components of the schizophrenic phenotype (Gottesman and Gould 2003). However, one of the basic criteria an endophenotype should meet is that it is already associated with a candidate gene or gene region. As such, the discussion about endophenotypes is not very likely to open up new vistas for psychiatric diagnostics (nor for psychiatric genetics), because there is simply no consensus about the putative 'genes for schizophrenia'.

But perhaps defective diagnostics and floundering genetics are both symptoms of a more basic problem in schizophrenia research. According to Keller and Miller (2006), mental disorders reflect the immense mutational target size of the human brain. According to them, the average human brain is affected by at least 500 mutations in both coding and non-coding regions of our DNA. Like many other traits, mutation load is continuously distributed across the population, so some individuals probably carry a few thousand brain-related genetic mutations. And it is expected that 'individuals with an especially high load in mutations that disrupt a particular configuration of brain systems will tend to act in aberrant, harmful ways that provoke social comment and psychiatric categorization' (Keller and Miller 2006, p. 33). The authors note that only those mutations that have detrimental phenotypic effects will be eliminated immediately. However, most mutations have very little effect on reproductive fitness, so it may take hundreds of generations before natural selection removes them from the human gene pool.

Are there such things as 'genes for schizophrenia', then? The provisional answer is: yes, but mapping those genes will be wildly more complicated than psychiatric geneticists think. Mutations contributing to the development of schizophrenia are probably scattered across a myriad of locations in our genome, while their effect size will be very small. Now, whatever the number of genes involved in the aetiology of schizophrenia, the fact that there are indeed such genes seems to imply that the illness already existed before Bleuler gave it its name. And that is exactly the third assumption of the schizophrenia paradox.

How long has the illness been around?

One of the central assumptions of the schizophrenia paradox is that the illness has existed long enough already to be amenable to the process of natural selection. Horrobin, for example, believes that 'an origin of schizophrenia less than 80,000 years ago is unlikely, and one of 140,000 years ago is perfectly reasonable' (Horrobin 2001, p. 219). This assumption is in marked contrast with the fact that there are hardly any descriptions of schizophrenia in written history, at least no descriptions of the illness as we now know it. Yet there are plenty of descriptions of other mental illnesses, including those illnesses whose current prevalence is much lower than the (current) prevalence of schizophrenia. The first descriptions of bipolar disorder, for example, date from the sixth century (Jeste et al. 1985; Ellard 1987; Hare 1988). Most descriptions of schizophrenia, by contrast, date from the beginning of the nineteenth century.

The literature about the history of schizophrenia can be divided roughly in two camps. Evolutionary psychiatrists are convinced that schizophrenia, or at least one of its subtypes or subclinical forms, has probably been around for (hundreds of) thousands of years already. Their argumentation is twofold. For one thing, they say, there actually do exist a number of historical descriptions of schizophrenia (Jeste et al. 1985; Heinrichs 2003). At the same time, they admit that, for various reasons, these descriptions are rare. Secondly, they claim that a limited number of such descriptions is not conclusive evidence that schizophrenia is a recent illness. Indeed, the identification of chronic mental illnesses, such as schizophrenia, requires a costly long-term observation. In its turn, such observation requires an extensive health care. And health care, Jeste concludes, is a fairly recent invention. Jeste's argumentation, however, fails, for there are other chronic mental illnesses that *have* in fact been known for ages.

Another argument in the debate is the idea that, during our evolutionary history, schizophrenics have probably populated alternative niches, such as religion or shamanism, which allowed them to transform their illness into something socially acceptable (Jeste et al. 1985; Polimeni and Reiss 2002). Unfortunately, this argument is too romantic, as Linton already noted in 1956: 'In order to exploit the advantages of abnormal behavior one must be capable of appraising situations in realistic terms and of devising behavior which would be advantageous to one. The inability to do this, to my mind, is the real test of psychosis.' (quoted in Torrey 1980, p. 48). Of course one might argue, as Horrobin (2001; see also Stevens and Price 2000) did, that the symptoms of schizophrenia used to be less drastic than they are now, and that the historical symptoms would now be typified as *schizotypal*, rather than schizophrenic. But then schizotypics, too, have a fairly distorted relationship with reality, and it is unclear how they would be able to use that relationship to their advantage.

Researchers from the other camp believe that there are no historical descriptions of schizophrenia before 1800 because the illness is barely 200 years old. Edward Torrey, for example, has always contended that schizophrenia is a disease of civilisation, with a viral aetiology. The illness would have its origins

in the urbanization and industrialization at the beginning of the nineteenth century. Recently, Ledgerwood, Ewald and Cochran have even put forward a candidate pathogen: *Toxoplasma gondii* (Ledgerwood et al. 2003).

The idea that schizophrenia is a recent viral disorder (the 'viral hypothesis') has a number of theoretical advantages. Firstly, it simply invalidates evolutionary psychiatry's problems with schizophrenia: the illness has not been weeded out yet because it is too recent to be amenable to any kind of selection (Hare 1988). Also, the viral hypothesis outbalances the 'genetic hypothesis' in explanatory power. Thus it is able to explain why there is still a significant difference between dizygotic twin concordance (for schizophrenia) and full sibling concordance. Indeed, though full siblings and dizygotic twins have the same genetic relatedness, the twins display much higher concordance values. This difference may be accounted for by the fact that 'the mother's state of [viral] infection during pregnancy will be identical for dizygotic twins but not for non-twin full siblings' (Ledgerwood et al. 2003, p. 322).

Finally, the viral hypothesis can also account for the peculiar increase in the incidence of schizophrenia during the second half of the nineteenth century. Indeed, almost immediately after the appearance of the first descriptions of schizophrenia, there was a real influx of new cases. Now Hare (1988) claims that the latter increase in incidence matches the rise of the industrial revolution, for which there is a good explanation: if schizophrenia is indeed a viral disease, then it has surely taken advantage of the expansion of urban areas associated with the industrial revolution.

A final advantage of the viral hypothesis is its ability to explain why the prevalence of schizophrenia is not uniform throughout the world. So the viral hypothesis can help us to emasculate the fourth assumption of the schizophrenia paradox.

Does schizophrenia have a uniform prevalence?

Grounding just about every evolutionary psychiatric account of schizophrenia, this supposition runs that the prevalence of schizophrenia is, and has always been, uniform throughout all parts of the world: 'In all populations of the world, from the Canadian Arctic to Patagonia, from Lapland to the Cape of Good Hope, from Siberia to the world of the Australian Aborigines, the picture is the same' (Horrobin 2001, p. 152; see also Crow 2000; Stevens and Price 2000; Burns 2004). In other words: evolutionary psychiatrists claim that the proportion of people suffering from schizophrenia has always been stable, at any moment in time. This claim is almost as persistent as the conviction that schizophrenia is at least a few thousand years old. The two assumptions are indeed connected: if it is true that schizophrenia can be found all over the world, then the illness probably already existed before our early ancestors left the African continent to conquer the world. As Burns says: 'The fact that this disorder is found universally implies that the schizophrenic genotype dates to

at least 150–100,000 years ago when the migration of *Homo erectus* out of Africa occurred' (Burns 2004, p. 832).

However, it is at least unclear whether schizophrenia can in fact be found all over the world, let alone in a uniform fashion, as many (evolutionary) psychiatrists have claimed. They often quote the WHO 10 nation study (Jablensky et al. 1992) to 'prove' that the incidence and prevalence of schizophrenia is invariant worldwide. However, McGrath (2005) has shown that the data in this study did not warrant its conclusions. Prevalence studies have in fact yielded a diversity of results. High prevalence rates have been found in the North of Sweden, Western Ireland, and the Northwest of Croatia. Very low prevalences, on the other hand, have been found among the Amish in America, among Taiwanese aboriginals, and in Ghana (Torrey 1987). These remarkable epidemiological patterns ask for a decent explanation which, to date, no one has been able to give. Even evolutionary psychiatrists, who have always prided themselves in the integrative power of their accounts (Nesse 1984), have failed to provide an answer, if they have seen the problem at all.

In short, evolutionary psychiatrists have consistently disregarded (or at least failed to account for) some remarkable findings about the aetiology, history and epidemiology of schizophrenia, as well as its impact on reproductive success. These findings surely seem to enfeeble the schizophrenia paradox. Just now it seems that the viral hypothesis is most apt to explain them, e.g. because it implies that schizophrenia is a recent illness, and that the illness will be found to have higher prevalence rates when the conditions for its dispersal are best fulfilled.

And yet the viral hypothesis shares another, very important assumption with the prevailing evolutionary psychiatric hypotheses about schizophrenia. As it happens, proponents of both hypotheses take it for granted that schizophrenia is a natural kind, i.e. something that exists 'out there', independently of our theories and observations. In the next section I will take a critical look at this natural kind view of schizophrenia.

What, if anything, is schizophrenia?

The claim that mental disorders are natural kinds is indeed one of the core assumptions of evolutionary psychiatry, and biomedical psychiatry in general. By definition, a natural kind is a bounded entity with fixed internal properties. These properties enable us, with perfect reliability, to identify the entity in question and to distinguish it from other, related entities. The natural kind view of mental disorders has three important implications (Haslam 2000): (1) it implies that mental disorders are indifferent to changing conventions in psychiatric diagnostics, (2) that mental disorders are bounded categories, i.e. that they differ categorically from each other, as well as from normality, and (3) that mental disorders are grounded in discrete biological causes. However,

in this section I will show that none of these claims can reasonably be said to be self-evident, at least in the case of schizophrenia.

Is schizophrenia objectively real?

Claiming that schizophrenia is objectively real, and that it is therefore indifferent to changing diagnostics, is a little hasty, since none of the existing schizophrenia concepts has been empirically validated yet (Blom 2003). The only indications we have of the supposed reality of schizophrenia are the number of patients suffering from the disorder, and their actual symptoms. Unfortunately, epidemiology figures and symptom lists have always been anything but constant. Boyle (1990) has demonstrated, for example, that the prevalence of dementia praecox in Kraepelin's clinic needed less than ten years to rise from a mere 5% (in 1892) to a solid 50% (in 1900). Of course, this may reflect a genuine increase in the number of people suffering from schizophrenia, as proponents of the natural kind view would claim, but fact remains that there is a remarkable coincidence between changes in the epidemiology of schizophrenia and conceptual alterations in psychiatry. In the case of Kraepelin's clinic, for example, the increase in prevalence was most probably due to the increasing looseness of Kraepelin's diagnostic criteria, as Boyle (1990) has argued.

Also, the fact that different psychiatrists have adhered to wildly different schizophrenia concepts *at the same time*, does not plead for the natural kind view either. Indeed, an ambitious international investigation, the *US/UK Diagnostic Project* (Cooper et al. 1972), revealed that American psychiatrists made the schizophrenia diagnosis *twice* as much as their colleagues from Britain, even though both teams made use of identical diagnostic criteria. And as late as 1993, it turned out that French and English psychiatrists were still using substantially different concepts of schizophrenia (Van Os et al. 1993).

Is schizophrenia a bounded category?

The natural kind view of schizophrenia also assumes that the disorder is categorically different from other disorders, as well as from normality. If this claim were true, one should be able to group schizophrenic patients on the basis of some unique and observable set of features ('markers'), such as neuropsychological or neurophysiological abnormalities, which sets these patients apart from 'normal' people, as well as from patients suffering from other mental disorders. Failing this, it should at least be possible to detect statistically significant differences between these three groups (patients with schizophrenia, 'healthy' individuals, and non-schizophrenic mentally ill people).

However, except for some triumphant neuroscientists, who recently claimed to be able to diagnose schizophrenia even before its first symptoms appear (Davatzikos 2005), no one has found a unique marker for schizophrenia,

and all hopes of finding such marker have been abandoned. Moreover, Heinrichs (2001) has shown that statistically significant differences are pretty scarce, especially between ill and 'healthy' individuals. According to his review of a great number of research literatures in schizophrenia, 'close to 40% of the biological findings are so weak and variable that they may represent minor, unimportant, or chance abnormalities with no intrinsic link to schizophrenia. Clearly, the cognitive evidence wins the neuroscience sweepstakes. Yet even the cognitive findings do not characterize *all* patients with the illness' (Heinrichs 2001, p. 259). In short, nearly all supposedly unique schizophrenia markers also appear in the 'normal' population, or in other mental disorders.

Such overlaps are not the only factors that invalidate the natural kind view of schizophrenia. There is also the fact that some schizophrenic patients have no symptoms in common at all: 'Indeed, experienced clinicians often remark that it is quite possible to encounter patients with no features in common' (Fanous and Kendler 2005). Some thinkers even say that in fact each case of schizophrenia is different, not only regarding the onset of the illness, but also regarding its course or its reaction to psychopharmacological substances – thus making the concept of schizophrenia rather superfluous (Bentall et al. 1988; Sarbin 1990).

Is schizophrenia grounded in discrete biological causes?

Yet proponents of the natural kind view have always claimed that schizophrenia *does* in fact have discrete biological origins. However, as Keller and Miller (2006) have argued, schizophrenia's phenotypic heterogeneity probably points towards a fairly complicated genetic heterogeneity. In other words: what we now know as 'schizophrenia' may in fact be 'a heterogeneous group of dysfunctions in different mechanisms whose final common pathways lead to [more or less] similar symptoms' (Keller and Miller 2006, p. 27).

Criticism of the unitary concept of schizophrenia has been going on since the very beginning of the twentieth century. Even Bleuler realized that his concept probably covered a group of different disorders (*Gruppe der Schizophrenien*; Bleuler 1911). In a recent reference book on the neurobiology of mental disorders, William Byne and his colleagues suggest that schizophrenia may indeed be a catchall for a jumble of disorders: 'Given the heterogeneity of schizophrenia, it is (...) likely that impairments resulting from a variety of different neurological insults are collectively classified as schizophrenia in our current nosology' (Byne et al. 1999, p. 236). Others have made similar suggestions (e.g. Meehl 1990; Bentall 1993; Keen 1999; Charlton 2000; Blom 2003; Keller and Miller 2006).

In short, biomedically oriented psychiatrists, including evolutionary psychiatrists, have always considered schizophrenia to be a natural kind, yet such view is hardly tenable. Rather, 'schizophrenia' seems to be an umbrella term

for a heterogeneous group of disorders – a view that may be called the ‘heterogeneity hypothesis’. The major theoretical advantage of the heterogeneity hypothesis is that it is able to explain why, at any level (neuroanatomic, genetic, symptomatologic,...), researchers find it so hard to detect any consistent common denominator in any given group of schizophrenic patients. In other words, the heterogeneity hypothesis explains why an empirical validation of the current schizophrenia concept is simply impossible. And as Blom observes, ‘There is little to be gained by pursuing these [evolutionary psychiatric] theses as long as the validity of the concept [of schizophrenia] has not been secured’ (Blom 2003, p. 212).

Conclusion

Evolutionary psychiatric accounts of schizophrenia invariably consider the illness to be a paradox: how come natural selection has not yet eliminated the infamous ‘genes for schizophrenia’ if the disorder has been around for thousands of years, and if it simply crushes the reproductive success of those suffering from it? In this paper I have indicated that most of the assumptions underlying this paradox are at least doubtful, and perhaps even incorrect.

First of all, it is mostly male schizophrenics that are at a high reproductive disadvantage, and even this is not true for all cultures. Female patients approach the average fertility rate of the ‘normal’ female population, while the marital fertility (i.e. number of children) of some male patients may actually be higher than the marital fertility of female patients. Secondly, evolutionary psychiatrists take it for granted that there is such thing as an orderly and limited number of ‘genes for schizophrenia’. Obviously, there *are* ‘genes for schizophrenia’, but finding them may turn out to be wildly more complicated than current methods of gene mapping presume, while their effect size will probably be much smaller than expected. A third assumption underlying the paradox is that schizophrenia has existed long enough to be amenable to the process of natural selection. Unfortunately, however, the illness as we now know it is barely mentioned in written history. Fourthly, evolutionary psychiatrists claim that schizophrenia displays a uniform prevalence throughout the world, while recent reports at least tend to modify this claim.

Fifthly and finally, evolutionary psychiatry considers schizophrenia to be a natural kind, by analogy with Mendelian disorders such as Huntington’s disease. However, since one can hardly contend that schizophrenia is objectively real, neither that it is a bounded category, nor that it is grounded in discrete biological causes, schizophrenia is not very likely to be a natural kind. On the contrary, my critique of evolutionary psychiatry’s view on schizophrenia supports the heterogeneity hypothesis. This hypothesis states that ‘schizophrenia’ is in fact a reified umbrella concept constructed by psychiatry to cover a

heterogeneous group of disorders. Some of these disorders may indeed turn out to be genuine natural kinds, and thus have their own evolutionary history. Yet schizophrenia as we now know it simply doesn't have such history.

Acknowledgements

I would like to thank all members of the *Interdisciplinary Center for Evolution and Behaviour* (ICEG), Jan Dirk Blom, Vishwajit Nimgaonkar, William Byne, and an anonymous referee for their thoughtful comments.

References

- Adriaens P. and De Block A. 2006. The evolution of a social construction: the case of male homosexuality. *Perspect. Biol. Med.* 49(4) (in press).
- Allen J. and Sarich V. 1988. Schizophrenia in an evolutionary perspective. *Perspect. Biol. Med.* 32: 132–153.
- Avila M., Thaker G. and Adami H. 2001. Genetic epidemiology and schizophrenia: a study of reproductive fitness. *Schizophr. Res.* 47: 233–241.
- Bentall R. et al. 1988. Abandoning the concept of 'schizophrenia': some implications of validity arguments for psychological research into psychotic phenomena. *Br. J. Clin. Psychol.* 27: 303–324.
- Bentall R. 1993. Deconstructing the concept of 'schizophrenia'. *J. Ment. Health* 2: 223–228.
- Bhatia T. et al. 2003. Gender and procreation among patients with schizophrenia. *Schizophr. Res.* 68: 387–394.
- Blom J. 2003. Deconstructing Schizophrenia. An Analysis of the Epistemic and Nonepistemic Values that Govern the Biomedical Schizophrenia Concept. Boom, Amsterdam.
- Böök J. 1953. Schizophrenia as a gene mutation. *Acta Genet.* 4: 133–139.
- Boyle M. 1990. Schizophrenia: A Scientific Delusion? Routledge, New York.
- Brown J. 2003. Identification of candidate genes for schizophrenia based on natural resistance to infectious diseases. *Acta Neuropsychiatr.* 15(3): 108–114.
- Brüne M. 2004. Schizophrenia – an evolutionary enigma? *Neurosci. Biobehav. Rev.* 28: 41–53.
- Burns J. 2004. An evolutionary theory of schizophrenia: cortical connectivity, metarepresentation, and the social brain. *Behav. Brain Sci.* 27(6): 831–885.
- Byne W. et al. 1999. The neurochemistry of schizophrenia. In: Charney D., Nestler E. and Bunney B. (eds.), *Neurobiology of Mental Illness*, Oxford University Press, Oxford.
- Carter M. and Watts C. 1971. Possible biological advantages among schizophrenics' relatives. *Br. J. Psychiatry* 118: 453–460.
- Charlton B. 2000. *Psychiatry and the Human Condition*. Radcliffe Medical Press, Oxford.
- Cooper J. et al. 1972. *Psychiatric Diagnosis in New York and London*. Oxford University Press, Oxford.
- Crow T. 2000. Schizophrenia as the price that Homo sapiens pay for language: a resolution of the central paradox in the origin of the species. *Brain Res. Rev.* 31: 118–129.
- Davatzikos C. et al. 2005. Whole-brain morphometric study of schizophrenia revealing a spatially complex set of focal abnormalities. *Arch. Gen. Psychiatry* 62: 1218–1227.
- Ellard J. 1987. Did schizophrenia exist before the eighteenth century? *Aust. N. Z. J. Psychiatry* 21(3): 306–318.
- Fanous A. and Kendler K. 2005. Genetic heterogeneity, modifier genes, and quantitative phenotypes in psychiatric illness: searching for a framework. *Mol. Psychiatry* 10(1): 6–13.

- Gottesman I. and Gould T. 2003. The endophenotype concept in psychiatry: etymology and strategic intentions. *Am. J. Psychiatry* 160: 636–645.
- Hare E. 1988. Schizophrenia as a recent disease. *Br. J. Psychiatry* 153: 521–531.
- Haslam N. 2000. Psychiatric categories as natural kinds: essentialist thinking about mental disorders. *Soc. Res.* 67: 1031–1058.
- Haukka J. et al. 2003. Fertility of patients with schizophrenia, their siblings, and the general population. *Am. J. Psychiatry* 160(3): 460–463.
- Heinrichs R. 2001. In search of madness. *Schizophrenia and neuroscience*. Oxford University Press, Oxford.
- Heinrichs R. 2003. Historical origins of schizophrenia: two early madmen and their illness. *J. Hist. Behav. Sci.* 39(4): 349–363.
- Holden C. 2003. Deconstructing schizophrenia. *Science* 299: 333–335.
- Horrobin D. 2001. *The Madness of Adam and Eve. How Schizophrenia Shaped Humanity*. Bantam Press, London.
- Hutchinson G. et al. 1999. Fertility and marital rates in first-onset schizophrenia. *Soc. Psychiatry Psychiatr. Epidemiol.* 34: 617–621.
- Huxley J. et al. 1964. Schizophrenia as a genetic morphism. *Nature* 204: 220–221.
- Jablensky A. et al. 1992. Schizophrenia: manifestations, incidence and course in different cultures. A World Health Organization ten-country study. *Psychol. Med. – Monogr. Suppl.* 20: 1–97.
- Jeste D. et al. 1985. Did schizophrenia exist before the eighteenth century? *Compr. Psychiatry* 26(6): 493–503.
- Joseph J. 2003. *The Gene Illusion. Genetic Research in Psychiatry and Psychology Under the Microscope*. PCCS Books, Ross-on-Wye.
- Karlsson J. 2001. Mental abilities of male relatives of psychotic patients. *Acta Psychiatr. Scand.* 104: 466–468.
- Keen T. 1999. Schizophrenia: orthodoxy and heresies. A review of alternative possibilities. *J. Psychiatr. Ment. Health Nurs.* 6: 415–424.
- Keller M. and Miller G. 2006. Resolving the paradox of common, harmful, heritable mental disorders: which evolutionary genetic models work best? *Behav. Brain. Sci.* (in press).
- Lane A. et al. 1995. Reproductive behaviour in schizophrenia relative to other mental disorders: evidence for increased fertility in men despite decreased marital rate. *Acta Psychiatr. Scand.* 91(4): 222–228.
- Ledgerwood L. et al. 2003. Genes, germs and schizophrenia. An evolutionary perspective. *Perspect. Biol. Med.* 46(3): 317–348.
- McGrath J. 2005. Myths and plain truths about schizophrenia epidemiology. *Acta Psychiatr. Scand.* 111(1): 4–11.
- Meehl P. 1990. Toward an integrated theory of schizotaxia, schizotypy, and schizophrenia. *J. Personal. Disord.* 4: 1–99.
- Nanko S. and Moridaira J. 1993. Reproductive rates in schizophrenic outpatients. *Acta Psychiatr. Scand.* 87: 400–404.
- Nesse R. 1984. An evolutionary perspective on psychiatry. *Comp. Psychiatry* 25: 575–580.
- Nettle D. 2001. *Strong Imagination: Madness, Creativity and Human Nature*. Oxford University Press, Oxford.
- Nettle D. and Clegg H. 2005. Schizotypy, creativity and mating success in humans. *Proc. R. Soc. B* 273: 611–615.
- O'Reilly. et al. 2001. Schizotypy and creativity: an evolutionary connection? *Pers. Individ. Differ.* 31:1067–1078.
- Polimeni J. and Reiss J. 2002. How shamanism and group selection may reveal the origins of schizophrenia. *Med. Hypotheses* 58: 244–248.
- Sarbin T. 1990. Toward the obsolescence of the schizophrenia hypothesis. *J. Mind Behav.* 11(3): 259–284.
- Srinivasan T. and Padmavati R. 1997. Fertility and schizophrenia: evidence for increased fertility in the relatives of schizophrenic patients. *Acta Psychiatr. Scand.* 95: 260–264.

- Stevens A. and Price J. 2000. *Prophets, Cults and Madness*. Duckworth, London.
- Sullivan R. and Allen J. 2004. Commentary: Natural selection and schizophrenia. *Brain Behav. Sci.* 27(6): 865–866.
- Thaker G. and Carpenter W. 2001. Advances in schizophrenia. *Nat. Med.* 7(6): 667–671.
- Torrey E. 1980. *Schizophrenia and Civilization*. Jason Aronson, New York.
- Torrey E. 1987. Prevalence Studies in Schizophrenia. *Br. J. Psychiatry* 150: 598–608.
- Van Os J. et al. 1993. Schizophrenia sans frontières: concepts of schizophrenia among French and British psychiatrists. *Br. Med. J.* 307: 489–492.
- Waddell C. 1998. Creativity and mental illness: is there a link? *Can. J. Psychiatry* 43: 166–172.