Why is the emperor naked? Researching causes of schizophrenia: methodological madness

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Incompetence by medical researchers investigating causes for the debilitating condition called "schizophrenia" is endemic, even though different approaches have been taken to investigate the issue from several perspectives[1]. Moreover, a myth has developed that claims that schizophrenia rates are similar across all countries, while WHO data suggests that national schizophrenia rates are varied.

In terms of background to the situation, we know that the concept of what we call "schizophrenia" today has been round for a long time and indeed was known to the ancient Greeks.

In 1859 Darwin published his monograph "On the origin of the species", and later, in 1865, Gregor Mendel discovered the gene, although the actual label "gene" was not used for some time. He later stated words to the effect that finding a cause for this problem that we now call "schizophrenia" was now possible.

The idea that genes present from birth cause schizophrenia became fashionable and the quest began to find the gene responsible, without success. There have been many studies that claim to have shown a genetic basis as cause of schizophrenia. There are 3 main types of such research (twin studies, family studies and meta-analysis) , but in the interests of parsimony, only one example of each research method will be discussed here.

1 Similar opinions have been expressed in Jay, Joseph, 2004, The gene illusion: genetic research in psychiatry and psychology under the microscope. Algora publishing, USA

The first research method is twin studies. An early example was that of Göttesman and Shields[2] study of MZ twins and has been included due to its serious methodological flaws. They did not ask whether genes caused schizophrenia, so convinced were they that genes were responsible that, by their own admission, they set out to demonstrate that genes **did** cause schizophrenia. In order to achieve their aim, they decided to examine schizophrenia concordance rates in MZ twins. Over 16 years they found 24 hospitalised males each of whom was one half of a pair of MZ twins. The matching non hospitalised 24 male twins were interviewed but only 4 of the matching twins were diagnosed as also having schizophrenia. That is, the concordance rate was 16%, thereby clearly demonstrating that it is impossible for genes to cause schizophrenia. For genes to be responsible, concordance rates should approximate to 100% due to MZ twins sharing close to 100% of genes.

They refused to accept the null hypothesis. Instead, they changed the definition of schizophrenia and re – interviewed the remaining 20 males, and only the remaining males. In spite of this methodological cheating, the concordance rate was still only raised to 10/24, that is, 42%. This still provided clear evidence that genes cannot be responsible for schizophrenia because MZ twins share 99.9% of genes, yet they accepted the experimental hypothesis, with a rider that environment plays some part. This was a type 1 error, that is, they accepted the experimental hypothesis instead of the null hypothesis. Their approach was highly subjective, and therefore unscientific.

This was only one of many such twin and adoption studies. Not one of any such study has shown genuine evidence of gene involvement through obtaining concordance rates of close to 100%, although most claim that there is evidence of gene involvement[3].

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2 Göttesman, I. I., and Shields, J. 1966, "Schizophrenia in twins: 16 years' consecutive admissions to a psychiatric clinic", British Journal of Psychiatry, 112:809-818

3 I am reminded of the children's story by Hans Christian Anderson (1837) about the emperor's new clothes. They did not exist. Two conmen got lots of money from the emperor by falsely claiming they were sewing wonderful garments of fine silks. He was made to look a fool by walking around naked while asking people to admire his fine new clothes. Even worse, other adult citizens no doubt influenced by social desirability issues and having entered an agentic state, also claimed he looked wonderful in his new clothes. It was a small boy who eventually disabused everyone by calling out "the emperor is naked".

A second type of research into causes of schizophrenia is the family study. For example, Millar et al, 2000[4], reported on a Scottish family that had six family members who had mental health problems of varying types, including schizophrenia. After the onset of psychosis in this family, biological samples were taken and DNA analysed. At the epigenetic level, abnormalities on two alleles were found, which they named "DISC-1" and "DISC-2". The researchers stated that these abnormalities caused schizophrenia.

However, there were many methodological problems with the study. They did not take samples before the onset of psychosis for comparison purposes. Nor did they consider other explanations for the finding. It is also unclear whose DNA was taken or from how many family members. There is much missing information in the article. As such the findings are unreliable, and there are serious questions about the study's validity. They stated: "This family may be atypical due to the wide spectrum of disorders present (schizophrenia, schizoaffective disorder, bipolar affective disorder, unipolar affective disorder and adolescent conduct disorder)." Yet they seemed to claim that only 2 genes were responsible for all these problems. Their research methods were inadequate, the evidence was partial, their arguments lacked rigor, and yet again conclusions drawn were not supported by the evidence provided because co-occurrence does not prove cause and effect. More new clothes for the emperor.

A further type of study involves meta-analysis. For example, results of a Swedish study were published[5] by Lichtenstein et al. The study used medical data for the whole of Sweden. The researchers undertook a multivariate GLM analysis of family structure and schizophrenia prevalence. They concluded that "we showed evidence that schizophrenia and bipolar disorder partly share a common genetic cause". They did no such thing. The type of data involved concerned family structure only. In essence it was a correlation study, and simply showed greater likelihood of these two disorders in certain family structures. But because no data about psychosocial environment was included, it was impossible for this study to reach any genuine conclusion about relative likelihood of biological or environmental (that is, psychosocial) factors as being more important.

The existence of schizophrenia, or bi-polar disorder, for that matter, in both parent and child does not demonstrate genetic cause and effect,

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4 http://hmg.oxfordjournals.org/content/9/9/1415.full

5 (Lichtenstein, et al. 2009): www.thelancet.com/journals/lancet/article/PIIS0140-6736(09)60072-6/abstract

merely co-occurrence. It is impossible to determine environmental variable impact from statistically analysing family structure alone, by definition. Such data says nothing about the nature of parent-child relations and therefore psycho-social environment. However these obvious limitations were ignored by the researchers. They appeared to want to demonstrate that genes are mostly responsible, and wilfully ignored other possibilities. Yet again, the conclusions were not supported by the evidence. How well dressed the emperor is!

Researchers undertaking all such studies are badly informed about the nature of genes themselves. There are two important issues that are relevant. They are the belief that genes are fixed and immutable at birth and that genes are capable of causing problems such as psychoses among other. I will return to the issue of the nature of genes themselves, later.

Not one of these studies gave serious consideration to environment as possible cause. Moreover, any allusions to "environment", were vague ideas, yet there is considerable evidence that points to specific environmental factors as being responsible. Various professionals such as Laing and Esterson[6] (1964/1970), among others, for example, cited evidence of certain interaction patterns that Berne (1964)[7] describes as "game playing"among family members as being present in all diagnosed cases of schizophrenia. In spite of discussing many case studies that supported their views, reactions to Laing and Esterson were varied, and their findings were largely ignored by medical researchers who continued to search for this elusive gene as was demonstrated above.

In order to provide circumstantial support for environment as being important, I examined national schizophrenia rates to determine if there was any evidence at the societal level to support a hypothesis of environmental association of any type, by examining co-variance with various factors which might or might not be important when considering issues from a sociological perspective.

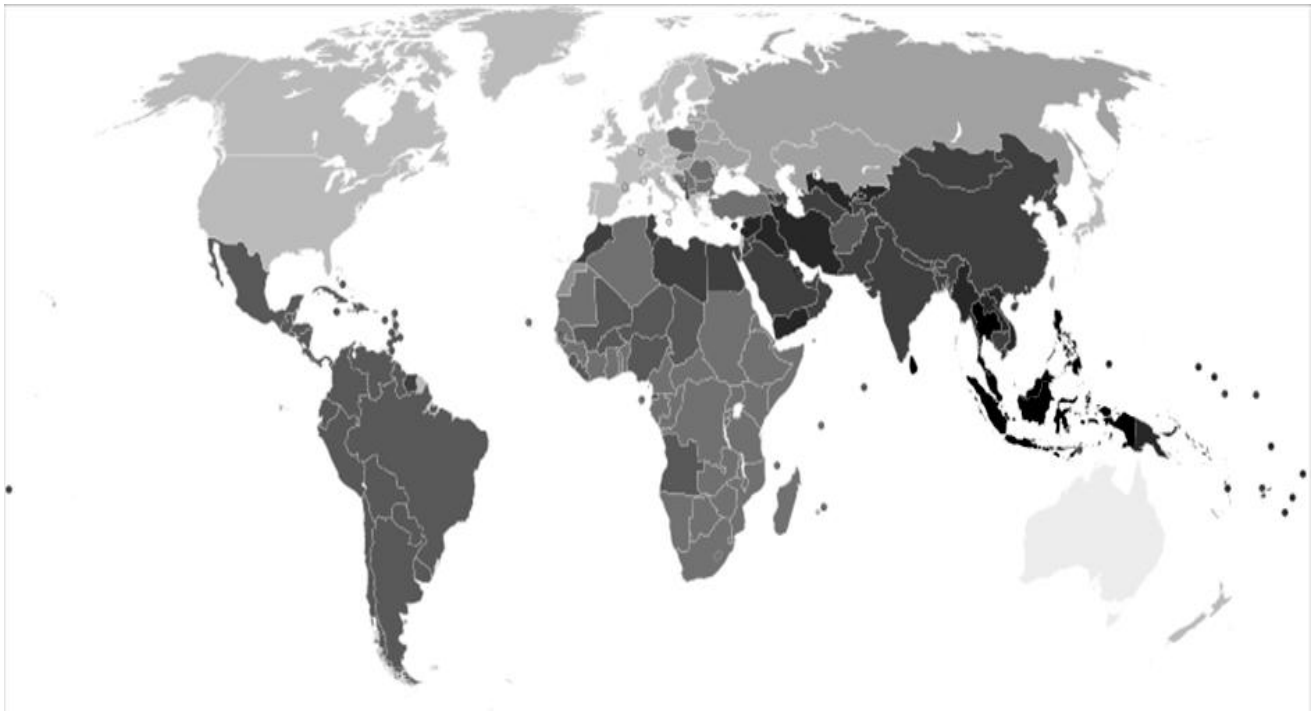
Data for 192 member countries were downloaded from the WHO website. National schizophrenia rates were rank ordered on the basis

6Laing, R.D. and Esterson, A. (1964, 1970) Sanity, Madness and the Family. London: Pelican Books.

7 Berne, E., (1964) The Games People Play, Harmondsworth: Penguin.

of age standardised DALY rates from highest to lowest rate[8]. This was used as the dependent variable. It can be seen from Figure 1 below that there is considerable variation in national schizophrenia rates, with Indonesia having the greatest rate while Australia has the lowest rate. It is colour coded so that severity of disease has darkest colouring while countries with low rates have lighter shading. There are clear regional variations also with most of Europe having low rates while many south-east Asian countries and Pacific islands have high rates.

Figure 1 National Schizophrenia Rates



Source: WHO Age-standardized DALYs per 100,000 by cause, and Member State, 2004 [cited 2011-04-01].

From a sociological perspective, potential causative issues were considered as independent variables and a list drawn up. The internet websites of the UN and other organisations were searched for available data. As a result of these investigations, choice of variables was modified due to what was and was not available from various UN websites such as UNDP and OECD, on the internet. After considerable research, the following variables were used: 3 on education, religiosity

8 Murray CJL, Salomon JA, Mathers CD, Lopez AD (eds.) (2002). Summary measures of population health: concepts, ethics, measurement and applications. WHO, Geneva. Available at: www.who.int/pub/smph/en/index.html

rates[9], religion, climate, HDI, population density, type of government, ethnicity, per capita income, region, intentional homicide rates, capital punishment, torture, and internal warfare. Data for the latter three were obtained from the Human Rights Watch, Amnesty International and Uppsala University's Department of Peace and Conflict Studies websites. These variables were then correlated with the dependent variable using Excel.

Because it could be seen that patterns at extremes were marked when looking at the raw data, the top and bottom 12 ranked countries were analysed separately with results set out below. Table 1 lists the 12 highest and 12 lowest ranked countries including DALY scores, while Table 2 shows the results of correlating the variables.

These rankings are influenced by data reliability. The WHO has acknowledged that data for many countries are unreliable and colour coded all data. Many African countries are in the middle ranks, yet provide highly unreliable data. The top and bottom ranked countries are more reliable due to source. Some countries are so poor that they have GDP of less than $500 AD per person per annum. Areas of such countries have non monetary economies. When income is so low, governments do not have income to spend on data collection.

When the dependent and independent variables were correlated, It could be seen that high national schizophrenia rates are associated with:

a) Low levels of human development, that is, health, income and education factors;

b) High internal levels of conflict such as war, torture, murder and capital punishment.

9 Data obtained from Gallop: www.gallup.com/poll/114211/Alabamians-Iranians-Common.aspx, www.gallup.com/poll/142727/Religiosity-Highest-World-Poorest-Nations.aspx

Table 1: 12 highest and 12 lowest ranked countries

1	Indonesia	321.87	181	U S A	185.629
2	Philippine	317.079	182	Ireland Re	185.626
3	Thailand	315.533	183	Italy	185.589
4	Malaysia	314.199	184	Luxembou	185.307
5	Sri lanka	312.278	185	United Kir	185.182
6	Brunei	312.101	186	Austria	185.116
7	Singapore	311.872	187	Greece	185.063
8	Tuvalu	287.66	188	Malta	184.87
9	Laos	287.175	189	San Marin	184.854
10	Uzbekista	286.942	190	Monaco	184.831
11	Marshall i	284.733	191	Iceland	184.83
12	Myanmar	281.795	192	Australia	164.255

Table 2: Results of Data Correlation for 12 top and bottom ranked countries

Order	***Variable***	***R***
1	Climate	0.81
2	HDI	0.799
3	Internal armed conflict (war)	0.782
4	Torture	0.763
5	Religiosity rates	0.71
6	Capital punishment	0.61
7	Per capita income	0.594
8	Intentional homicide rates	-0.53
9	PISA country educational ranks	-0.37
10	Adult literacy rates	0.31
11	Population density /km2	0.12
12	Educational inequalities	-0.083

Moreover, descriptive data analysis of these 24 countries revealed the following:

For the 12 Lowest ranked countries:

Parliamentary democracy as govt.	92%
Ethnically homogeneous	92%
Culturally European	100%

For the 12 Highest ranked countries:

Military dictatorship/ coercive govt.	75%
Ethnically heterogeneous	75%
Culturally East Asian/ Pacific	100%

These statistics provide strong circumstantial evidence at the national level that schizophrenia rates are associated with conflict, coercion, level of control and value systems. That is, environment is extremely important. Because correlation rates were so high, it is clear that environment in general must affect psychosis levels, and it is therefore likely that environment is also extremely important at the individual level. It is possible that forms of conflict within the home are also associated with raised schizophrenia levels.

However, in order to further the debate about the role of genes, properly conducted gene studies elsewhere were considered which revealed interesting information about the nature of genes themselves. For example, Idaghdour et al, 2008[10], conducted a study on Moroccan Amazighs (Berbers). They demonstrated that genetic change was caused by environment. They concluded that as many as one third of genes are affected by lifestyle and geography.

Idaghdour stated: "The most important implication of this study is that people with the same genetic makeup can be in different environments and have different expression profiles. The same gene can be expressed in the city but not in a rural place because of the environment. So you must look at the environment when studying associations between genes and disease."

10 www.plosgenetics.org/article/info:doi/10.1371/journal.pgen.1000052

Hence, gene expression is not fixed and immutable at birth. It changes during a person's life time in response to environment[11], while genes themselves are blunt tools – they do not have the capacity to cause problems such as psychoses, autism and other similar problems as others too have noted[12],[13]. According to Ridley (2003), when the structure of chromosomes and genes are examined, it can be seen that there is not sufficient variance in the biochemistry for the possibility of genes causing schizophrenia to exist. Ridley further asserts:

"Genes themselves are implacable little determinists, churning out utterly predictable messages. But because of the way their promoters switch on and off in response to external instructions, genes are very far from being fixed in their actions. Instead they are devices for extracting information from the environment. Every minute, every second, the pattern of genes being expressed in your brain changes, often in direct or indirect response to events outside the body. Genes are the mechanisms of experience."

This finding has serious implications for the nature – nurture debate. In the case of approximately one third of our genes, it is nature through nurture. The interesting question now addresses the issue of which genes are affected by environment and which are not.

In further conclusion, and taking into consideration the work of Laing and Esterson (ibid), among others, as well as the findings from the above analysis of WHO data, it is likely that schizophrenia itself is caused by environmental factors such as types of family interaction and resulting levels of family conflict that in turn cause change in gene expression.

That is, it is likely that the onset of problems such as schizophrenia and possibly bi polar disorder cause change at the epigenetic level, which may well explain the findings of Millar et al (ibid). That is, Millar et al found change after the onset of psychosis. Had they examined family members before onset, then the genetic profile probably would not have shown these patterns.

This also has implications for evolutionary theory. Change may not be quite as random as Darwin envisaged.

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11 I am indebted to Alan Poots, who clarified issues and improved my use of terminology here.

12 Ridley, M., 2003, Nature via Nurture: Genes, Experience and What makes us Human, Harper Collins, New York and London.

13 Slatkin, M., 2009, "Epigenetic Inheritance and the Missing Heritability Problem Genetics", Genetics, July 2009; 182: 845.

Moreover, for around 150 years, medical researchers have been metaphorically burying their heads in the sand by denying that schizophrenia is environmentally caused. Yet the lives of affected people continue to be damaged and many sufferers commit suicide, while the NHS continues to fund treatment using expensive drugs, costly infrastructure and employing many staff. Research money is also wasted on futile attempts to find the elusive gene. This is shameful and irresponsible.

Because of attitudes and values within the medical research profession, as demonstrated above, it is not likely that anyone from a medical background will identify genuine causes of schizophrenia and other forms of psychosis. Such progress is more likely to come from within the social sciences[14].

This "naked emperor syndrome" is a serious problem, whereby one researcher makes a claim, and successive others continue to make the claim in spite of no genuine evidence to support the experimental hypothesis. All research cited above was published in peer reviewed journals. It therefore reveals a further problem - that the peer review method for journal publication lacks rigor and is in need of reform.

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14 See Saunders, V., "Principles of Socialisation; and consequences of psychosocial privation", unpublished monograph. Chapter 10, "A Theory of Psychosocial Privation as Cause of all forms of Psychosis", sets out necessary and sufficient conditions for onset of all forms of psychosis in physiologically normal humans.