Available Online at http://www.bjbmr.org

BRITISH JOURNAL OF BIO-MEDICAL RESEARCH

Cross Ref DOI: https://doi.org/10.24942/bjbmr.2017.06 Volume 01, Issue 01, March-April 2017

Review Article

Solving the Central Paradox of Schizophrenia Using Migration-Urbanization Balanced Model

Mutaz Amin[1], Sara Omer[1], Azza Elshafiea[2]

[1]Faculty of Medicine, University of Khartoum
[2]Institute of Endemic Diseases, University of Khartoum

ARTICLE INFO

Article History:
Received on 05th March, 2017
Peer Reviewed on 19th March 2016
Revised on 16th April, 2017
Published on 25th April, 2017

Keywords:
Schizophrenia, Central paradox, Migration, Urbanization

ABSTRACT

Schizophrenia is a debilitating chronic mental disorder that disturbs person's ability to think, feel, behave and interact with the surrounding society. It is caused by interplay of multiple genetic and various environmental factors that render the disease very complex in terms of inheritance, susceptibility and presentation. Schizophrenia is associated with low fecundity and low fertility rate as schizophrenic patients are less likely to find a mate and the disease is associated with lower fitness. However the disease is not rare (1% of worldwide populations). So a question arises in respect to evolutionary terms how did schizophrenia persist in human lineage? Many researchers have tried to solve this paradox by invoking different hypotheses but none of them is satisfactory. In this article we present a new theory that can solve the schizophrenia paradox depending on the balance between migration and urbanization. Our theory, the balance between selective migration and settlement with sexual selection can explain the worldwide invariant prevalence of schizophrenia. And it is supported by a study which found that the greatest environmental risk factor for schizophrenia is migration followed by urbanization. This clearly indicates that different factors played different roles in different populations with different circumstances but all summed up with a unified prevalence of schizophrenia among populations.

INTRODUCTION:

Schizophrenia is a debilitating chronic mental disorder that disturbs person's ability to think, feel, behave and interact with the surrounding society (1). It is caused by interplay of multiple genetic and various environmental factors that render the disease very complex in terms of inheritance, susceptibility and presentation. Patients usually present with a combination of positive symptoms (delusions and hallucinations) and negative symptoms (apathy, blunted mood and lack of motivation) (2).

Schizophrenia significantly impairs the social life of affected individuals (3). With an average suicide rate of 10%, and a global economic burden of 1% of domestic products, schizophrenia is one of the top 25 causes of disability in the world (4). The global prevalence of schizophrenia is 0.6-1% with around 21 million affected cases worldwide. The onset of the disease is usually adolescence in both males and females but with a slight male predominance (5). This explains the debilitating nature of the disease through impairment of the productive life of individuals. Moreover, individuals with schizophrenia are more likely to suffer from co-morbid conditions than the general population (6). These include HIV infection, respiratory illnesses and metabolic disorders like obesity and diabetes (7). In addition to that, side effects of anti-psychotic medications also contribute to the reduction in quality of life noted in patients with schizophrenia (8). Despite these maladies, relatives of schizophrenic patients (and sometimes schizophrenic patients themselves) have a higher average IQ level than the general population (9,10). Schizophrenic patients make use of their intelligence in order to explain the un-believed delusions and hallucinations they personally encounter to the surrounding individuals.

Schizophrenia is associated with low fecundity and low fertility rate (11) as schizophrenic patients are less likely to find a mate and the disease is associated with lower fitness (12). However the disease is not rare (1% of worldwide populations). So a question arises in respect to evolutionary terms how did schizophrenia persist in human lineage? Genes with low fecundity and low fitness (as supposedly for those of schizophrenia) should have been negatively selected; and with time the disease should either disappear or become rarer unless of course other factors played a role in their favor. This is known as the central paradox of schizophrenia and poses a challenge to evolutionary scientists. Furthermore, the prevalence of schizophrenia is uniform across cultures (13). Many studies found an average prevalence of 0.5-1% with altered frequencies depending on the sampled study and the methods of diagnosis (14,15). This is another added mystery because it is well known that schizophrenia is a multifactorial disorder caused by both genetic and environmental factors and the complex interaction between these two. Different populations from different geographical locations surely have different allele frequencies, and even if they don't, they certainly don't face the same environmental pressures. Many researchers have tried to solve this paradox by invoking different hypotheses but none of them is satisfactory. In this article we present a new theory that can solve the schizophrenia paradox depending on the balance between migration and urbanization.

DISCUSSION

As we have mentioned above, schizophrenia is a multifactorial disorder with both genetic and environmental factors contributing to the risk of the illness. The near Constance in the worldwide prevalence of schizophrenia may be caused by balanced genetic-environmental risks in which genes contribute to the risk of schizophrenia in one place and the environment plays in another. However this hypothesis is refuted when heritability of schizophrenia is taken into consideration. Heritability is a measurement of how much of variation in a trait is attributed to genetic factors. If this was the case then we would find differences in heritability measures in different reports, however, despite differences between studies, most reported twin concordance of about 45% and heritability of at least 80% (16,17). This indicates that genetics play an important role in the etiology of schizophrenia but does not explain why schizophrenia is found in all cultures with uniform prevalence.

What about environmental factors? Many studies have linked several environmental factors with the etiology of schizophrenia. These include but not limited to obstetric complications, influenza virus infection, migration, famines and urban residence (18). These factors even pose a greater challenge towards the schizophrenia paradox because the burden of no one of the above mentioned factors is distributed evenly between countries or populations. This leaves us solely with the genetics of the disease but it's well known among scientists that whenever a trait is found to be universal and shared by all humans (like religion and romantic love) (19,20) then we have to invoke an evolutionary explanation showing a survival advantage for current traits in pre-historic cultures. This approach is acceptable and used for many of the currently prevalent

diseases in humans, including diabetes (21), hypertension (22), depression (23)and schizophrenia is not an exception (24).

Trials to explain the universality of schizophrenia were previously made using the sexual selection theory (25). It is well known in both current (and perhaps ancestral) human populations that intelligence is a desirable trait in a mate for both males and females. Selection for intelligence related genetic loci will lead to their increase over the time, and since intelligence is a quantitative trait, accumulation of too many loci in a single individual is perhaps what causes schizophrenia (although there is difficulty in estimating what too many means). Studies have indeed found a higher than average increase in the IQ level in relatives of schizophrenia including Albert Einstein himself (and many others) whose son suffered from the terrible disease (26,27). The sexual selection theory is satisfactory in explaining the persistence of schizophrenia in populations (whether ancestral or modern) and its transmission from generation to another but it does not solely solve the problem of uniform prevalence.

In this article we present a new hypothesis that can solve this central paradox based on the balance between selective migration and urbanization (sedentism). Let's go back to the Eastern parts of Africa 80.000 years ago where all current humans originated (28). A small group of humans decided to migrate outside the African continent in what's currently known as the "Out of Africa theory". This group (and with others who migrated later) ultimately populated all continents of earth (perhaps except Antarctica). Now the question is was there any physical or mental traits that favored those who migrated over the non-migrants? In other words, were there any advantageous traits in favor of migration? Many researchers believe there are (29). It is logic to think that the first migrants and those who followed had mental traits that enable them to be more exploratory, more risk takers and perhaps more imaginative, all traits that are found in schizophrenics and their relatives (30). The increased prevalence of schizophrenia worldwide may be caused by serial founders who acquired (or rather inherited) some alleles that make them more likely to try new options and settle new habitats. Indeed we have conducted a preliminary analysis of all SNPs in the Exac database that has a difference in allele frequency of at least 0.1 in populations from South America, Eastern Asia and Africa. We filtered the SNPs which are highest in South America, followed by Asia and then Africa following the predicted path of early migrants and corresponding to a serial founder effect. We found that a significant proportion of these SNPs were associated with schizophrenia and/or other psychotic disorders. This is confirmed by many other previous studies which showed that the incidence of schizophrenia is significantly higher in migrants compared to resident groups (31–33). However the latter results could be easily explained by the increased stress associated with migration itself and its altered environment, but we showed that genetic factors could also play a role.

What about non-migrant populations? Following this model alone we should predict a prevalence of schizophrenia that is lowest in Africa and highest elsewhere. Despite migrations in and out of Africa didn't end with the "out of Africa" theory and continue to this day which makes no currently living population as either purely migrant or purely resident, the prevalence of schizophrenia in Africa is not lower than other places (13), and this poses a challenge for our hypothesis not only for African populations but also for populations which endured little migrations in their history. However we hypothesized that settlement in itself is a risk for schizophrenia because when people settle down (which is known as sedentism) their numbers start to increase and sexual selection becomes more intense. Sedentism is a known pre-requisite for invention of agriculture, which brings too many people in one place and sets the race of sexual selection into motion. The increased social interaction between human beings in aggregated society plays a role in cognitive development, language and intelligence (34), factors which underpin many theories of the emergence of schizophrenia. This hypothesis is supported by studies which found that aggregated societies and urbanization significantly the risk of schizophrenia (35–37).

The self-domestication that occurred in the human's line since the discovery of agriculture about 10.000 years ago contradictory led to an increase in the average intelligence of humans despite in animals it seems to do the reverse. Some researchers suggested that failure of neoteny which is the retain of juvenile traits in humans in a self-domesticated population is responsible for the emergence of psychiatric disorders (38). (If you want to see neoteny in humans just look at chimpanzees and notice that humans look much like young chimpanzees than

adult ones). Whether it was sexual selection or failure of neoteny, it is evident that settlement and urbanization lead to increase in the average intelligence and this may explain high prevalence of schizophrenia in some areas.

For the non-migrant groups which tend to settle in social groups, the relatively high prevalence of schizophrenia despite its low fertility can be explained by many social theories. Although genes of schizophrenia are capable of making the individuals maladaptive to their society in serious cases but in less severely affected patients or their relatives it can be a way for producing creative ideas that help solving social group problem in unique ways to face new challenges, also creative individuals are sexually attractive to opposites sex this will expand matting opportunities.

Another theory related to the ancient creation of society and it`s relation to migration, refer to the role of schizoid personalities in group splitting, how these people become leaders with their delusion of grandeur and bizarre thought and fixed ideas and have the ability to recognize the needs for group splitting and migration in order to find new resources to cover group needs for better life. To achieve this dissociation or splitting as a whole group successfully they should rely on those creative charismatic mentors who are most probably suffering of some degree of schizophrenia.

Our theory, the balance between selective migration and settlement with sexual selection can explain the worldwide invariant prevalence of schizophrenia. And it is supported by a study which found that the greatest environmental risk factor for schizophrenia is migration followed by urbanization (39). This clearly indicates that different factors played different roles in different populations with different circumstances but all summed up with a unified prevalence of schizophrenia among populations.

REFERENCES

1. NIMH » Schizophrenia [Internet]. [cited 2017 Mar 26]. Available from: https://www.nimh.nih.gov/health/topics/schizophrenia/index.shtml
2. Schizophrenia Symptoms and causes - Mayo Clinic [Internet]. [cited 2017 Mar 26]. Available from: http://www.mayoclinic.org/diseases-conditions/schizophrenia/symptoms-causes/dxc-20253198
3. Moll MF, Saeki T. Social life of people with diagnosis of schizophrenia, attended at a psychosocial care center. Rev Lat Am Enfermagem [Internet]. 2009 Dec [cited 2017 Mar 26];17(6):995–1000. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0104-11692009000600011&lng=en&nrm=iso&tlng=en
4. Chaiyakunapruk N, Chong HY, Teoh SL, Wu DB-C, Kotirum S, Chiou C-F. Global economic burden of schizophrenia: a systematic review. Neuropsychiatr Dis Treat [Internet]. 2016 Feb [cited 2017 Mar 26];12:357. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26937191
5. Ochoa S, Usall J, Cobo J, Labad X, Kulkarni J, Kulkarni J. Gender Differences in Schizophrenia and First-Episode Psychosis: A Comprehensive Literature Review. Schizophr Res Treatment [Internet]. 2012 [cited 2017 Mar 26];2012:1–9. Available from: http://www.hindawi.com/journals/schizort/2012/916198/
6. Buckley PF, Miller BJ, Lehrer DS, Castle DJ. Psychiatric Comorbidities and Schizophrenia.
7. Salokangas RK. Medical problems in schizophrenia patients living in the community (alternative facilities). Curr Opin Psychiatry [Internet]. 2007 Jul [cited 2017 Mar 26];20(4):402–5. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17551357
8. de Araújo AA, de Araújo Dantas D, do Nascimento GG, Ribeiro SB, Chaves KM, de Lima Silva V, et al. Quality of Life in Patients with Schizophrenia: The Impact of Socio-economic Factors and Adverse Effects of Atypical Antipsychotics Drugs. Psychiatr Q [Internet]. 2014 Sep 1 [cited 2017 Mar 26];85(3):357–67. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24789610
9. Černis E, Vassos E, Brébion G, McKenna PJ, Murray RM, David AS, et al. Schizophrenia patients with high intelligence: A clinically distinct sub-type of schizophrenia? Eur Psychiatry [Internet]. 2015 Jul [cited 2017 Mar 26];30(5):628–32. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25752725
10. Verweij KHW, Derks EM, Hendriks E, Cahn W, Vu T. The Association between Intelligence Scores and Family History of Psychiatric Disorder in Schizophrenia Patients, Their Siblings and Healthy Controls. Lu L, editor. PLoS One [Internet]. 2013 Oct 9 [cited 2017 Mar 26];8(10):e77215. Available from:

http://dx.plos.org/10.1371/journal.pone.0077215

11. Del Giudice M, Thaker G, Adami H, Mushtaq Y, Hikida T. Reduced Fertility in Patients' Families Is Consistent with the Sexual Selection Model of Schizophrenia and Schizotypy. Gilbert MTP, editor. PLoS One [Internet]. 2010 Dec 29 [cited 2017 Mar 26];5(12):e16040. Available from: http://dx.plos.org/10.1371/journal.pone.0016040
12. Thara R, Srinivasan TN. Outcome of marriage in schizophrenia. Soc Psychiatry Psychiatr Epidemiol [Internet]. 1997 Oct [cited 2017 Mar 26];32(7):416–20. Available from: http://www.ncbi.nlm.nih.gov/pubmed/9383973
13. Jablensky A, Sartorius N, Ernberg G, Anker M, Korten A, Cooper JE, et al. Schizophrenia: manifestations, incidence and course in different cultures. A World Health Organization ten-country study. Psychol Med Monogr Suppl [Internet]. 1992 [cited 2017 Mar 27];20:1–97. Available from: http://www.ncbi.nlm.nih.gov/pubmed/1565705
14. Bhugra D. The Global Prevalence of Schizophrenia. 2005;2(5):372–3.
15. Ayuso-mateos JL. Global burden of schizophrenia in the year 2000 : Version 1 estimates. World Heal Organ Glob Progr Evid Heal Policy Draft. 2001;1–11.
16. Gejman P V, Sanders AR, Duan J. The role of genetics in the etiology of schizophrenia. Psychiatr Clin North Am [Internet]. 2010 Mar [cited 2017 Mar 27];33(1):35–66. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20159339
17. Light G, Greenwood TA, Swerdlow NR, Calkins ME, Freedman R, Green MF, et al. Comparison of the Heritability of Schizophrenia and Endophenotypes in the COGS-1 Family Study. Schizophr Bull [Internet]. 2014 Nov 1 [cited 2017 Mar 27];40(6):1404–11. Available from: https://academic.oup.com/schizophreniabulletin/article-lookup/doi/10.1093/schbul/sbu064
18. Opler M, Charap J, Greig A, Stein V, Polito S, Malaspina D. Environmental Risk Factors and Schizophrenia. Int J Ment Health [Internet]. 2013 Apr 1 [cited 2017 Mar 27];42(1):23–32. Available from: http://www.tandfonline.com/doi/full/10.2753/IMH0020-7411420102
19. Karandashev V. A Cultural Perspective on Romantic Love. Online Readings Psychol Cult [Internet]. 2015 [cited 2017 Mar 27];5(4). Available from: http://dx.doi.org/10.9707/2307-0919.1135
20. Musacchio JM. The universality of religious beliefs. In: Contradictions [Internet]. Berlin, Heidelberg: Springer Berlin Heidelberg; 2012 [cited 2017 Mar 27]. p. 1–12. Available from: http://link.springer.com/10.1007/978-3-642-27198-4_1
21. Moalem S, Storey KB, Percy ME, Peros MC, Perl DP. The sweet thing about Type 1 diabetes: A cryoprotective evolutionary adaptation. Med Hypotheses [Internet]. 2005 Jan [cited 2017 Mar 27];65(1):8–16. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15893109
22. Rossier BC, Bochud M, Devuyst O. The Hypertension Pandemic: An Evolutionary Perspective. Physiology [Internet]. 2017 Mar 15 [cited 2017 Mar 27];32(2):112–25. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28202622
23. Wolpert L. Depression in an evolutionary context. Philos Ethics Humanit Med [Internet]. 2008 Feb 29 [cited 2017 Mar 27];3:8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18312654
24. Polimeni J, Reiss JP. Evolutionary perspectives on schizophrenia. Can J Psychiatry [Internet]. 2003 Feb [cited 2017 Mar 27];48(1):34–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12635562
25. Shaner A, Miller G, Mintz J. Schizophrenia as one extreme of a sexually selected fitness indicator. Schizophr Res [Internet]. 2004 Sep 1 [cited 2017 Mar 27];70(1):101–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15246469
26. Janet E. Pletson. Progress in Schizophrenia Research [Internet]. Nova publisher; 2005 [cited 2017 Mar 27]. 9 p. Available from: https://books.google.com/books?id=Woe0zYjPjb4C&pg=PA9&lpg=PA9&dq=psychosis+einstein+son+evolution&source=bl&ots=sXkOG6rnPm&sig=aOu61ywuAfGZT5aA-PaHtHyoz0A&hl=en&sa=X&ved=0ahUKEwjhp9LlnvbSAhWII8AKHakFAyAQ6AEIKTAC#v=onepage&q=psychosis einstein son ev

27. Jeste, D V. Chronic Late-Onset Schizophrenia-Like Psychosis That Remitted: Revisiting Newtons Psychosis? Am J Psychiatry [Internet]. 2000 Mar 1 [cited 2017 Mar 27];157(3):444–9. Available from: http://ajp.psychiatryonline.org/article.aspx?articleID=174014
28. Shriner D, Tekola-Ayele F, Adeyemo A, Rotimi CN, Cabrera VM. Ancient Human Migration after Out-of-Africa. Sci Rep [Internet]. 2016 Jul 23 [cited 2017 Mar 27];6(1):26565. Available from: http://www.nature.com/articles/srep26565
29. Moreno E. The society of our "out of Africa" ancestors (I): The migrant warriors that colonized the world. Commun Integr Biol [Internet]. 2011 Mar [cited 2017 Mar 27];4(2):163–70. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21655430
30. Sass LA. Schizophrenia, Modernism, and the "Creative Imagination": On Creativity and Psychopathology. Creat Res J [Internet]. 2001 Jan [cited 2017 Mar 27];13(1):55–74. Available from: http://www.tandfonline.com/doi/abs/10.1207/S15326934CRJ1301_7
31. Cantor-graae E, Ae CA, Pedersen CB, Neil TFMC, Mortensen PBO. Migration as a risk factor for schizophrenia : a Danish population-based cohort study. 1999;1.
32. Cantor-graae E, Ph D, Selten J, Ph D. Reviews and Overviews Schizophrenia and Migration : A Meta-Analysis and Review. 2005;(January):12–24.
33. Cooper B. Immigration and schizophrenia : the social causation hypothesis revisited *. 2001;
34. Heyes C. New thinking: the evolution of human cognition. Philos Trans R Soc Lond B Biol Sci [Internet]. 2012 Aug 5 [cited 2017 Mar 27];367(1599):2091–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22734052
35. Krabbendam L, van Os J. Schizophrenia and Urbanicity: A Major Environmental Influence--Conditional on Genetic Risk. Schizophr Bull [Internet]. 2005 Sep 15 [cited 2017 Mar 27];31(4):795–9. Available from: https://academic.oup.com/schizophreniabulletin/article-lookup/doi/10.1093/schbul/sbi060
36. Marcelis M, Takei N, van Os J. Urbanization and risk for schizophrenia: does the effect operate before or around the time of illness onset? Psychol Med [Internet]. 1999 Sep [cited 2017 Mar 27];29(5):1197–203. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10576311
37. Chan KY, Zhao F-F, Meng S, Demaio AR, Reed C, Theodoratou E, et al. Urbanization and the prevalence of schizophrenia in China between 1990 and 2010. World Psychiatry [Internet]. 2015 Jun [cited 2017 Mar 27];14(2):251–2. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26043349
38. Brüne M. Philosophy , Ethics , and Humanities On human self-domestication , psychiatry , and eugenics. Biomed Cent. 2007;9(2):1–9.
39. Cantor-Graae E, Selten J-P. Schizophrenia and Migration: A Meta-Analysis and Review. Am J Psychiatry [Internet]. 2005 Jan [cited 2017 Mar 27];162(1):12–24. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15625195

How to cite this article:

Mutaz Amin, Sara Omer, Azza Elshafiea *Solving the Central Paradox of Schizophrenia Using Migration-Urbanization Balanced Model*. Br J Bio Med Res , Vol.01, Issue 01, Pg.50-55, March-April 2017.

Source of Support: Nil **Conflict of Interest:** None declared.