Large Scale Genetic Research on Neuropsychiatric Disorders in African Populations is Needed

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Accessibility
In recent years there have been significant insights into the complex aetiologies of neurodevelopmental brain disorders. For example, neuropsychiatric genetics has achieved success with the identification of 108 loci for schizophrenia (Schizophrenia Working Group of the Psychiatric Genomics Consortium, 2014). Furthermore, meta-analyses of genome-wide association study (GWAS) results encompassing thousands of samples have been completed for other psychiatric disorders including attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorders, bipolar disorder, and major depressive disorder. However, published results on neuropsychiatric disorders have – thus far – predominantly included samples of European ancestry. In Fig. 1a, we compare world ancestry to the ancestry of individuals in the largest psychiatric GWAS meta-analyses published prior to 2015 (Total N = 121,985). The lack of African samples in the meta-analyses so clearly depicted here, raises concern that Africa will be left behind in terms of neuropsychiatric genetic research and subsequent treatment innovation.

There is biological rationale for conducting genetic research in African populations. It has been shown that modern humans originated in Africa and subsequently migrated to other parts of the world (Campbell and Tishkoff, 2008). As the cradle of humanity, Africa and its indigenous populations are a valuable resource when it comes to genetic research. Modern African genomes are characterised by a unique pattern of variation as a result of migration and admixture in earlier generations as well as recombination, natural selection and mutation. With an increase in allelic diversity and shorter segments of linkage disequilibrium, African genomes hold informative alleles which are useful for fine mapping of disease causing alleles (Campbell and Tishkoff, 2008). However, there is limited knowledge on African-specific functional variants highlighting the need to investigate African population groups, particularly for neuropsychiatric disorders.

As genetic findings are translated into intervention, genetic research focused solely on European populations threatens to widen the existing gaps of knowledge and understanding. The African continent has diverse genetic landscapes and different patterns of migration and admixture, which add to the complexity of the disorders. With an estimated 1.28 billion people across 54 countries, Africa is the second most diverse continent in terms of genetic diversity (Genomes Africa Project, 2013). As such, the study of African populations is crucial for a comprehensive understanding of neuropsychiatric disorders.

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Researchers in Africa are faced with a number of unique challenges. Research funding is scarce, and African scientists are often not eligible for training mechanisms offered by the National Institutes of Health (NIH). Much of the funding that is available focuses on neuroscience rather than on public mental health issues. African scientists are often not eligible for training mechanisms offered by the NIH.

In conclusion, while there is a clear need for further work in elucidating the genetics of neuropsychiatric disorders in African populations, the integration of neuroscience with public mental health is essential. Also, many African countries lack the infrastructure required to conduct large-scale neuropsychiatric genetics research, e.g., for brain imaging and genomics, has also included samples from South Africa. This consortium comprises 70 institutions world-wide and consists of different disease working groups including those for schizophrenia, bipolar disorder, and PTSD, respectively. The cohort consists of 1200 mother–child pairs and a subset of these individuals has already been genotyped with a genome-wide panel of markers shown to be relevant to psychiatric disorders. The post-traumatic stress disorder (PTSD) subgroup of the multi-national Psychiatric Genomics Consortium (PGC) aims to carry out large-scale GWASs and has included South African samples in their analyses. To date, the PGC-PTSD group has access to approximately 20,000 samples from study sites. As depicted by Fig. 1b, the anomaly of individuals in the PGC-PTSD studies is more diverse than large psychiatric GWAS in general. The Enhancing Neuro Imaging Genetics through Meta-Analysis (ENIGMA) Network initiative seeks to improve health in African populations by investigating genetic and environmental risk factors for common mental disorders. The cohort consists of 1200 mother–child pairs and a subset of these individuals has already been genotyped with a genome-wide panel of markers shown to be relevant to psychiatric disorders. The post-traumatic stress disorder (PTSD) subgroup of the multi-national Psychiatric Genomics Consortium (PGC) aims to carry out large-scale GWASs and has included South African samples in their analyses. To date, the PGC-PTSD group has access to approximately 20,000 samples from study sites. As depicted by Fig. 1b, the anomaly of individuals in the PGC-PTSD studies is more diverse than large psychiatric GWAS in general. The Enhancing Neuro Imaging Genetics through Meta-Analysis (ENIGMA) Network initiative seeks to improve health in African populations by investigating genetic and environmental risk factors for common mental disorders. The cohort consists of 1200 mother–child pairs and a subset of these individuals has already been genotyped with a genome-wide panel of markers shown to be relevant to psychiatric disorders. The post-traumatic stress disorder (PTSD) subgroup of the multi-national Psychiatric Genomics Consortium (PGC) aims to carry out large-scale GWASs and has included South African samples in their analyses. To date, the PGC-PTSD group has access to approximately 20,000 samples from study sites. As depicted by Fig. 1b, the anomaly of individuals in the PGC-PTSD studies is more diverse than large psychiatric GWAS in general. The Enhancing Neuro Imaging Genetics through Meta-Analysis (ENIGMA) Network initiative seeks to improve health in African populations by investigating genetic and environmental risk factors for common mental disorders. The cohort consists of 1200 mother–child pairs and a subset of these individuals has already been genotyped with a genome-wide panel of markers shown to be relevant to psychiatric disorders. The post-traumatic stress disorder (PTSD) subgroup of the multi-national Psychiatric Genomics Consortium (PGC) aims to carry out large-scale GWASs and has included South African samples in their analyses. To date, the PGC-PTSD group has access to approximately 20,000 samples from study sites. As depicted by Fig. 1b, the anomaly of individuals in the PGC-PTSD studies is more diverse than large psychiatric GWAS in general.

Fig. 1. Proportion of world population groups in psychiatric GWAS. (a) Proportion investigated in the largest meta-analyses published prior to 2015 for four leading psychiatric disorders (PGP) (http://www.med.unc.edu/pgc), by the Stanley Center for Psychiatric Research of the Broad Institute of MIT and Harvard University, in collaboration with the University of Cape Town and a number of other African institutions, aims to improve and achieve equity in mental health by expanding the infrastructure and research findings from large-scale psychiatric genetic epidemiology to Africa. This will be achieved by enhancing neuropsychiatric genetics research capacity in Africa through the training of scientists, conducting very large-scale sample collection and analysis through supporting the development of locally led research programmes in neuropsychiatric genetics and leveraging unique opportunities in population genetics. In conclusion, while there is a clear need for further work in elucidating the genetics of neuropsychiatric disorders in African populations,
several challenges will first need to be tackled. An effective local network of neurogenetic researchers needs to be established in order to discover genetic variation predisposing to neuropsychiatric disorders. This research needs to avoid prior pitfalls of “safari research” by engaging and training African scientists and physicians to improve phenotyping and perform studies of African populations to ensure long-term capacity to translate genetic findings in a way that will benefit African peoples.

Conflicts of Interest

Dan Stein has received research grants and/or consultancy honoraria from AMBRF, Biocodex, Cipla, Lundbeck, National Responsible Gambling Foundation, Novartis, Servier, and Sun.

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