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

The Harvard community has made this article openly available. Please share how this access benefits you. Your story matters

<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Published Version</td>
<td>doi:10.1016/j.ebiom.2015.10.002</td>
</tr>
<tr>
<td>Citable link</td>
<td><a href="http://nrs.harvard.edu/urn-3:HUL.InstRepos:23993683">http://nrs.harvard.edu/urn-3:HUL.InstRepos:23993683</a></td>
</tr>
</tbody>
</table>
| Terms of Use     | This article was downloaded from Harvard University’s DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA
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 genomewide 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 that have limited our understanding of neuropsychiatric disorders in other populations.
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. African populations have 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 GWAS and has included South African samples in their analyses. To date, the PTC-PTSD group has access to approximately 20,000 samples from study sites. As depicted in Fig. 1b, the ancestry 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 aims to improve health in African populations by investigating genomic and environmental factors contributing to common disease. This initiative includes a study investigating the genetic basis of schizophrenia in the southern African Xhosa-speaking population group. Using exome-sequencing and by investigating genome-wide copy-number variation, this study aims to identify genes associated with schizophrenia. Similarly, an initiative tentatively called the Neuropsychiatric Genetics in African Populations (NeuroGAP), 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 genetic 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.

Funding Source

The authors are members of the Neuropsychiatric Genetics in African Populations (Neuro-GAP) consortium. Dan Stein is funded by the Medical Research Council of South Africa.

References


