

Neuropsychiatric genetics in developing countries: Current challenges

Diego A Forero, Alberto Vélez-van-Meerbeke, Smita N Deshpande, Humberto Nicolini, George Perry

Diego A Forero, Laboratory of NeuroPsychiatric Genetics, Biomedical Sciences Research Group, School of Medicine, Universidad Antonio Nariño, Bogotá 110231, Colombia

Alberto Vélez-van-Meerbeke, Neuroscience Research Group (NeURos), School of Medicine and Health Sciences, Universidad del Rosario, Bogotá 110231, Colombia

Smita N Deshpande, Department of Psychiatry, De-addiction Services and Resource Center for Tobacco Control, PGIMER-Dr. Ram Manohar Lohia Hospital, New Delhi 110001, India

Humberto Nicolini, Laboratory of Psychiatric and Neurodegenerative Diseases, Instituto Nacional de Medicina Genómica, 14610 Ciudad de México, México

George Perry, College of Sciences, University of Texas at San Antonio, San Antonio, TX 78229, United States

Author contributions: All authors contributed to the writing and revision of the manuscript.

Supported by Research grants from VCTI-UAN and Colciencias, and research grants from Universidad del Rosario

Conflict-of-interest: None reported.

Open-Access: This article is an open-access article which selected by an in-house editor and fully peer-reviewed by external reviewers. It distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Dr. Diego A Forero, MD, PhD, Professor, Laboratory of NeuroPsychiatric Genetics, Biomedical Sciences Research Group, School of Medicine, Universidad Antonio Nariño, Bogotá 110231, Colombia. diego.forero@uan.edu.co

Telephone: +57-313-2610427

Fax: +57-1-3405871

Received: November 3, 2014

Peer-review started: November 3, 2014

First decision: November 21, 2014

Revised: November 27, 2014

Accepted: December 3, 2014

Article in press: December 10, 2014

Published online: December 22, 2014

Abstract

Neuropsychiatric disorders (NPDs) constitute a heavy

burden on public health systems around the world and studies have demonstrated that the negative impact of NPDs is larger in Low and Middle Income Countries (LMICs). In recent decades, several studies have come to the understanding that genetic factors play a major role in the risk for a large number of NPDs. However, few neuropsychiatric genetics studies have been published from LMICs. In this Editorial, we discuss important issues impinging on advances in neuropsychiatric genetics research in LMICs. It is essential that scientists educate policymakers and officials of funding agencies on the importance of providing adequate funding for research in these areas. Development of local well-supported research programs focused on NPD genetics should be an important asset to develop; it would facilitate the establishment of sustainable research efforts that could lead to appropriate diagnosis and specific, affordable and feasible interventions in LMICs. It is important to point out that research into the biological basis of human NPDs is not only an academic effort reserved for a few elite institutions in economically developed countries, but it is vitally important for the mental health of people around the world.

© 2014 Baishideng Publishing Group Inc. All rights reserved.

Key words: Neurogenetics; Psychiatric genetics; Mental health; Neurosciences; Public health

Core tip: Neuropsychiatric Disorders (NPDs) constitute a heavy burden on public health systems around the world. Studies have demonstrated that the negative impact of NPDs is larger in Low and Middle Income Countries (LMICs). However, few neuropsychiatric genetics studies have been published from LMICs. In this Editorial, we discuss important issues impinging on advances in neuropsychiatric genetics research in LMICs. It is essential that scientists educate policymakers and officials of funding agencies on the importance of providing adequate funding for research in these areas. Development of local research programs focused on

NPD genetics should be an important asset to develop in LMICs.

Forero DA, Vélez-van-Meerbeke A, Deshpande SN, Nicolini H, Perry G. Neuropsychiatric genetics in developing countries: Current challenges. *World J Psychiatr* 2014; 4(4): 69-71 Available from: URL: <http://www.wjgnet.com/2220-3206/full/v4/i4/69.htm> DOI: <http://dx.doi.org/10.5498/wjpv4.i4.69>

IMPORTANCE OF NEUROPSYCHIATRIC GENETICS IN DEVELOPING COUNTRIES

Neuropsychiatric Disorders (NPDs) constitute a heavy burden on public health systems around the world, as they represent around 30% of the disability-adjusted life-years associated to non-communicable diseases^[1]. Considering the severity and chronicity of some of these disorders, such as major depression or substance abuse, the annual costs of NPDs can be estimated at several trillion dollars around the world^[2,3]. Furthermore, studies have demonstrated that the negative impact of NPDs is substantially greater in Low and Middle Income Countries (LMICs), also called developing countries, given their particular demographic, cultural and economic conditions^[1,4]. Until recently, the negative effect of some NPDs on LMICs was underestimated due to a historical emphasis on the study of infectious diseases.

In recent decades, the understanding that genetic factors play a major role in the risk for a large number of NPDs has increased^[5]. Heritability ranges from 40% to 80% for several major NPDs and hundreds of studies have been published exploring genetic factors for NPDs, mainly in populations of European descent^[5,6]. However, few neuropsychiatric genetics studies have been published from LMICs^[7]. In this Editorial, we discuss important issues impinging on advances in neuropsychiatric genetics research in LMICs.

Why is basic genetic research necessary in LMICs? Why not extrapolate findings from existing studies from the rest of the world? Populations differ in their susceptibility to diseases while disease prevalence differs across populations. Replicability of genetic findings is notoriously difficult and replicability across populations is needed to identify “genuine” genetic associations^[7]. Few examples of genetic studies of NPDs and related endophenotypes in LMICs are found, in a global perspective; some led by local scientists and others led by researchers from developed countries^[8-16].

Research in mental health is a challenging task in LMICs^[17] due to lack of resources and trained personnel. The relative lack of local research infrastructure in many LMICs arises due to cultural and economic factors (poor funding sources, internal conflicts, general poverty or massive external debt) and political aspects (lack of vision about the importance of public funding of

research and innovation, for example). There is also a scarcity of local human resources, which is more evident in neuropsychiatric genetics: in addition to the need for personnel with adequate formal clinical training and experience, there is an urgent need for scientific personnel with adequate research training and experience.

Research into biological basis of mental disorders is a relatively recent scientific effort, in comparison to other biomedical areas^[18]. Lack of awareness about its importance is exacerbated in LMICs because of specific cultural and educational factors, especially stigma^[19]. So, it is important that laboratory-based researchers educate health professionals, and the general public, on the relevance of basic biomedical research into NPDs and the underlying basic concepts^[20]. Clinicians should understand that basic research is a crucial way to understand mechanisms of NPDs that could lead to discoveries for better treatments and diagnosis strategies in the future. Well-planned and organized collaborations between geneticists, psychiatrists, neurologists and psychologists are vital^[21], to select those pathologies to be studied, based on criteria such as prevalence, severity and heredability. This is more important in LMICs because the knowledge gained through genetic research may help health professionals provide better care, given the difficulty of patient access to advanced healthcare facilities. It is also essential that scientists educate policymakers, officials of funding agencies and advocacy groups, on the importance of providing adequate funding for research on these areas^[20]. When results from research are available, policymakers should create the mechanisms to improve the identification of patients at genetic risk for suffering NPDs and establish the means for consultation and management once the symptoms appear.

It must be kept in mind that genetic epidemiology of NPDs is not equal in all regions of the world, so scientists should insist on having their own data. Development of local well-supported research programs focused on NPD genetics should be an important asset to develop; it would facilitate the establishment of sustainable research efforts that could lead to appropriate diagnosis and specific, affordable and feasible interventions in LMICs. Given that there is an international bias toward research into genetics of specific disorders^[7], researchers from LMICs should be able to study those NPDs of high importance in their regions^[22]. In addition to the participation of scientists from LMICs in research networks led by institutions in developed countries, a consolidation of the collaborations between groups from different LMICs would lead to additional advantages^[23], such as establishment of international research consortia that could lead to studies with larger samples sizes. Advances in genomics of NPDs will benefit the entire humanity rather than one or other population group.

Finally, we suggest that scientists in developed countries, especially those acting as peer reviewers of grant applications and journals, should try to understand the constant challenges that scientists in LMICs face to carry

out their research. It is important to point out that research into the biological basis of human NPDs^[1,18,24] is not only an academic effort reserved for a few elite institutions in economically developed countries, but it is vitally important for the mental health of people around the world.

REFERENCES

- 1 **Prince M**, Patel V, Saxena S, Maj M, Maselko J, Phillips MR, Rahman A. No health without mental health. *Lancet* 2007; **370**: 859-877 [PMID: 17804063 DOI: 10.1016/S0140-6736(07)61238-0]
- 2 **Uhl GR**, Grow RW. The burden of complex genetics in brain disorders. *Arch Gen Psychiatry* 2004; **61**: 223-229 [PMID: 14993109 DOI: 10.1001/archpsyc.61.3.223]
- 3 **DiLuca M**, Olesen J. The cost of brain diseases: a burden or a challenge? *Neuron* 2014; **82**: 1205-1208 [PMID: 24945765 DOI: 10.1016/j.neuron.2014.05.044]
- 4 **Demyttenaere K**, Bruffaerts R, Posada-Villa J, Gasquet I, Kovess V, Lepine JP, Angermeyer MC, Bernert S, de Girolamo G, Morosini P, Polidori G, Kikkawa T, Kawakami N, Ono Y, Takeshima T, Uda H, Karam EG, Fayyad JA, Karam AN, Mneimneh ZN, Medina-Mora ME, Borges G, Lara C, de Graaf R, Ormel J, Gureje O, Shen Y, Huang Y, Zhang M, Alonso J, Haro JM, Vilagut G, Bromet EJ, Gluzman S, Webb C, Kessler RC, Merikangas KR, Anthony JC, Von Korff MR, Wang PS, Brugha TS, Aguilar-Gaxiola S, Lee S, Heeringa S, Pennell BE, Zaslavsky AM, Ustun TB, Chatterji S. Prevalence, severity, and unmet need for treatment of mental disorders in the World Health Organization World Mental Health Surveys. *JAMA* 2004; **291**: 2581-2590 [PMID: 15173149 DOI: 10.1001/jama.291.21.2581]
- 5 **Burmeister M**, McInnis MG, Zöllner S. Psychiatric genetics: progress amid controversy. *Nat Rev Genet* 2008; **9**: 527-540 [PMID: 18560438 DOI: 10.1038/nrg2381]
- 6 **Sullivan PF**, Daly MJ, O'Donovan M. Genetic architectures of psychiatric disorders: the emerging picture and its implications. *Nat Rev Genet* 2012; **13**: 537-551 [PMID: 22777127 DOI: 10.1038/nrg3240]
- 7 **Gatt JM**, Burton KL, Williams LM, Schofield PR. Specific and common genes implicated across major mental disorders: A review of meta-analysis studies. *J Psychiatr Res* 2015; **60C**: 1-13 [PMID: 25287955 DOI: 10.1016/j.jpsychires.2014.09.014]
- 8 **Forero DA**, Benítez B, Arboleda G, Yunis JJ, Pardo R, Arboleda H. Analysis of functional polymorphisms in three synaptic plasticity-related genes (BDNF, COMT AND UCHL1) in Alzheimer's disease in Colombia. *Neurosci Res* 2006; **55**: 334-341 [PMID: 16698101 DOI: 10.1016/j.neures.2006.04.006]
- 9 **Benítez BA**, Forero DA, Arboleda GH, Granados LA, Yunis JJ, Fernandez W, Arboleda H. Exploration of genetic susceptibility factors for Parkinson's disease in a South American sample. *J Genet* 2010; **89**: 229-232 [PMID: 20861575 DOI: 10.1007/s12041-010-0030-1]
- 10 **Ojeda DA**, Niño CL, López-León S, Camargo A, Adan A, Forero DA. A functional polymorphism in the promoter region of MAOA gene is associated with daytime sleepiness in healthy subjects. *J Neurol Sci* 2014; **337**: 176-179 [PMID: 24360188 DOI: 10.1016/j.jns.2013.12.005]
- 11 **Hernández HG**, Mahecha MF, Mejía A, Arboleda H, Forero DA. Global long interspersed nuclear element 1 DNA methylation in a Colombian sample of patients with late-onset Alzheimer's disease. *Am J Alzheimers Dis Other Dement* 2014; **29**: 50-53 [PMID: 24164934 DOI: 10.1177/1533317513505132]
- 12 **Castro T**, Mateus HE, Fonseca DJ, Forero D, Restrepo CM, Talero C, Vélez A, Laissue P. Sequence analysis of the ADRA2A coding region in children affected by attention deficit hyperactivity disorder. *Neurol Sci* 2013; **34**: 2219-2222 [PMID: 24178896 DOI: 10.1007/s10072-013-1569-4]
- 13 **Márquez L**, Camarena B, Hernández S, Lóyzaga C, Vargas L, Nicolini H. Association study between BDNF gene variants and Mexican patients with obsessive-compulsive disorder. *Eur Neuropsychopharmacol* 2013; **23**: 1600-1605 [PMID: 23999029 DOI: 10.1016/j.euroneuro.2013.08.001]
- 14 **Kukshal P**, Kodavali VC, Srivastava V, Wood J, McClain L, Bhatia T, Bhagwat AM, Deshpande SN, Nimgaonkar VL, Thelma BK. Dopaminergic gene polymorphisms and cognitive function in a north Indian schizophrenia cohort. *J Psychiatr Res* 2013; **47**: 1615-1622 [PMID: 23932573 DOI: 10.1016/j.jpsychires.2013.07.007]
- 15 **Fears SC**, Service SK, Kremeyer B, Araya C, Araya X, Bejarano J, Ramirez M, Castrillón G, Gomez-Franco J, Lopez MC, Montoya G, Montoya P, Aldana I, Teshiba TM, Abaryan Z, Al-Sharif NB, Ericson M, Jalbrzikowski M, Luyckx JJ, Navarro L, Tishler TA, Altshuler L, Bartzokis G, Escobar J, Glahn DC, Ospina-Duque J, Risch N, Ruiz-Linares A, Thompson PM, Cantor RM, Lopez-Jaramillo C, Macaya G, Molina J, Reus VI, Sabatti C, Freimer NB, Bearden CE. Multisystem component phenotypes of bipolar disorder for genetic investigations of extended pedigrees. *JAMA Psychiatry* 2014; **71**: 375-387 [PMID: 24522887 DOI: 10.1001/jamapsychiatry.2013.4100]
- 16 **Gonzalez S**, Camarillo C, Rodriguez M, Ramirez M, Zavala J, Armas R, Contreras SA, Contreras J, Dassori A, Almasy L, Flores D, Jerez A, Raventós H, Ontiveros A, Nicolini H, Escamilla M. A genome-wide linkage scan of bipolar disorder in Latino families identifies susceptibility loci at 8q24 and 14q32. *Am J Med Genet B Neuropsychiatr Genet* 2014; **165B**: 479-491 [PMID: 25044503 DOI: 10.1002/ajmg.b.32251]
- 17 **Alem A**, Kebede D. Conducting psychiatric research in the developing world: challenges and rewards. *Br J Psychiatry* 2003; **182**: 185-187 [PMID: 12611776 DOI: 10.1192/bjp.182.3.185-b]
- 18 **Price BH**, Adams RD, Coyle JT. Neurology and psychiatry: closing the great divide. *Neurology* 2000; **54**: 8-14 [PMID: 10636118 DOI: 10.1212/WNL.54.1.8]
- 19 **Sewilam AM**, Watson AM, Kassem AM, Clifton S, McDonald MC, Lipski R, Deshpande S, Mansour H, Nimgaonkar VL. Suggested avenues to reduce the stigma of mental illness in the Middle East. *Int J Soc Psychiatry* 2014; Epub ahead of print [PMID: 24957595 DOI: 10.1177/0020764014537234]
- 20 **García PJ**, Curioso WH. Strategies for aspiring biomedical researchers in resource-limited environments. *PLoS Negl Trop Dis* 2008; **2**: e274 [PMID: 18852845 DOI: 10.1371/journal.pntd.0000274]
- 21 **Vicens Q**, Bourne PE. Ten simple rules for a successful collaboration. *PLoS Comput Biol* 2007; **3**: e44 [PMID: 17397252 DOI: 10.1371/journal.pcbi.0030044]
- 22 **Maestre GE**. Dementia in Latin America and the Caribbean: an overlooked epidemic. *Neuroepidemiology* 2008; **31**: 252-253 [PMID: 18931520 DOI: 10.1159/000165363]
- 23 **Maestre GE**. Strategic alliances in neuroscience. *Int J Neurosci* 1999; **99**: 91 [PMID: 10495200]
- 24 **Patel V**, Kim YR. Contribution of low- and middle-income countries to research published in leading general psychiatry journals, 2002-2004. *Br J Psychiatry* 2007; **190**: 77-78 [PMID: 17197661 DOI: 10.1192/bjp.bp.106.025692]

P- Reviewer: Hosak L, Ponizovsky AM **S- Editor:** Tian YL **L- Editor:** A **E- Editor:** Liu SQ





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>

