## Population-based neurobiological studies of psychiatric disorders in developing countries are feasible and relevant

É possível e relevante realizar pesquisas neurobiológicas de base populacional sobre os transtornos psiquiátricos em países em desenvolvimento

Traditionally, epidemiological studies investigating frequency rates, levels of social adjustment and needs for care related to psychiatric disorders in developing countries have been seen as serving primarily to organize local mental health services. However, it has recently been recognized that such investigations can also serve broader purposes of global significance, such as providing clues to the identification of modifiable environmental or genetic factors that could influence the incidence and course of neuropsychiatric disorders.

In contrast, the question of whether it is also valid to carry out clinical neuroscientific studies of psychiatric conditions in developing nations has very rarely been addressed.

Clinical neuroscience studies from less favored countries have been quite scarce, and this has been attributed to the limited access to technological resources and lack of local expertise. However, a closer look at the current neuroscientific scenario in some emerging countries suggests that the productivity gap relative to high-income countries is narrowing. In Brazil, for instance, a variety of diagnostic medical equipment, employed for both clinical and research purposes, is now readily available in urban centers. Many psychiatrists and neurocientists returning from postgraduate research training courses abroad have dedicated themselves to improving the expertise of the mental health research staff at our local universities. In addition, web resources now ensure regular communication between Brazilian neuroscientists and their foreign collaborators, as well as swifter access to recently published information, together with e-mail broadcast systems for research discussions. As a result, the number of scientific papers published by Brazilian authors in leading psychiatric periodicals has progressively increased, 1 clinical neuroscience studies accounting for a significant portion of that number.

However, if clinical neuroscience research is viable in some developing countries, can we say that the data generated in such studies is relevant to increasing the worldwide knowledge regarding mental illnesses? We argue that the answer to this question is affirmative, and, to exemplify our point, we take the case of neuroimaging studies of schizophrenia. Magnetic resonance imaging (MRI) studies have consistently demonstrated that anatomical abnormalities in specific brain portions (involving most notably the frontal cortex, temporal cortex, insula and thalamus) are detectable in schizophrenia patients at the early stages of illness, whereas no such abnormalities are detected in healthy controls.<sup>2</sup> Nevertheless, epidemiological studies have suggested an intriguing differential advantage in terms of course and outcome for individuals with schizophrenia living in developing countries.3 One important question that stems from such evidence is whether there would be differences between developing and developed countries in terms of the brain pathology underlying the symptoms of schizophrenia. Identifying similar brain imaging abnormalities in such contrasting nations would be relevant, suggesting that despite environmental differences, the final brain pathway underlying schizophrenia remains the same.

Recently, brain volumetric abnormalities compatible with those reported in high-income countries were documented using sophisticated MRI methods in a small sample of antipsychotic-

naïve individuals with schizophrenia recruited in India.<sup>4</sup> However. larger studies are needed to confirm whether the pattern of brain abnormalities detected in psychosis samples recruited in developing countries are comparable to those found in high-income nations, using epidemiological designs to guarantee that the samples investigated are truly representative of the population from which they are recruited. We recently conducted such a morphometric MRI investigation in a sample of approximately 120 subjects with first-onset psychosis living in a circumscribed geographical region of the city of Sao Paulo, comparing their mean regional brain volumes to those of 100 asymptomatic subjects randomly selected from the same geographical area. Preliminary analyses revealed foci of significantly decreased gray matter in schizophrenia patients relative to controls in the same frontotemporal regions as those seen in MRI studies conducted in high-income nations.5

Although the abovementioned neuroimaging data suggest that the supposedly distinct outcomes of schizophrenia between developing and high-income countries are not related to differences in the patterns of brain abnormalities at the first episode of the disorder, it is possible to speculate that such brain differences could become evident later during the course of the illness.4 In high-income countries, longitudinal MRI studies have shown increases in the degree of brain abnormalities associated with schizophrenia over the course of the illness, despite appropriate treatment.<sup>6</sup> This indicates that a next logical step would be to conduct studies investigating the longitudinal course of brain abnormalities in patients with schizophrenia under regular treatment in developing countries in order to ascertain whether there is less progressive worsening of brain abnormalities in such environments than in developed countries. If such studies indicate that the long-term course of brain abnormalities associated with schizophrenia is more benign in developing countries, this will increase interest in the identification of environmental variables that might act as protective factors against the worsening of brain changes over the course of the disorder.

Finally, neuroscientific studies of psychiatric disorders might also have a beneficial effect on public health policies in developing countries. In the current population-based investigation of individuals with psychosis in Sao Paulo, we are carrying out a follow-up MRI evaluation of cases one year after their first contact with mental health services. We have found that a proportion of these subjects either have had only intermittent pharmacological treatment for their condition or have completely abandoned treatment soon after their initial diagnosis, thereby leading to extended periods of psychosis without appropriate treatment interventions. We will therefore be able to investigate whether the brain abnormalities in subjects who remain poorly treated for long periods of time are greater in comparison to those found in subjects who have remained under regular treatment. If such a possibility is confirmed, this will lend support to the concept that proper maintenance treatment is highly relevant for psychotic disorders and can encourage authorities to allocate additional funds to increase access to adequate long-term treatment for patients suffering from severe mental disorders in Brazil.

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## References

- Bressan RA, Gerolin J, Mari JJ. The modest but growing Brazilian presence in psychiatric, psychobiological and mental health research: assessment of the 1998-2002 period. Braz J Med Biol Res. 2005;38(5):649-59.
- Job DE, Whalley HC, McConnell S, Glabus M, Johnstone EC, Lawrie SM. Structural gray matter differences between first-episode schizophrenics and normal controls using voxel-based morphometry. Neuroimage. 2002;17(2):880-9.
- Hopper K, Wanderling J. Revisiting the developed versus developing country distinction in course and outcome in schizophrenia: results from ISoS, the WHO collaborative follow up project. International Study of Schizophrenia. Schizophr Bull. 2000;26(4):835-46.
- Jayakumar PN, Venkatasubramanian G, Gangadhar BN, Janakiramaiah N, Keshavan MS. Optimized voxel-based morphometry of gray matter volume in first-episode, antipsychoticnaïve schizophrenia. Prog Neuropsychopharmacol Biol Psychiatry. 2005;29(4):587-91.
- Schaufelberger MS, Duran FL, Menezes PR, Scazufca M, Castro CC, Leite C. Brain abnormalities associated with schizophreniform and affective first-contact psychosis. Schizophr Res. 2006;81(Suppl):164.
- Lieberman J, Chakos M, Wu H, Alvir J, Hoffman E, Robinson D, Bilder R. Longitudinal study of brain morphology in first episode schizophrenia. Biol Psychiatry. 2001;49(6):487-99.