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the newsletter of

Research into the Causes of Schizophrenia and Bipolar Disorder

Western Psychiatric Institute & Clinic - University of Pittsburgh

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The Family Study of Schizophrenia at the University of Pittsburgh

Dr. Vishwajit Nimgaonkar, an Associate Professor of Psychiatry and Human Genetics at the University of Pittsburgh, is inviting volunteers to participate in a research study of schizophrenia. Funded by the National Institute of Mental Health, this study extends Dr. Nimgaonkar's efforts to identify the genetic and environmental causes of this severe brain disorder. It is being conducted in cooperation with researchers at the University of Pennsylvania and the Southwest Foundation for Biomedical Research, San Antonio, Texas.

Who may participate in the study?

The study is seeking participation from extended families with two first-degree relatives (i.e., two siblings, or parent/child pairs) who are both diagnosed with Schizophrenia or Schizoaffective Disorder. Additional relatives of the diagnosed individuals are also eligible to participate (e.g., other siblings, parents, grandparents, aunts and uncles, nieces and nephews, and cousins). These other relatives do *not* need to be affected to take part.

What are participants asked to do?

Participants are not required to change treatment or to travel. Each family member meets individually with a research staff person to complete a one-time interview, provide a small blood sample, and do a series of exercises examining attention, memory, and coordination. Our staff meets participants in their homes or other convenient locations. It takes about 4 – 8 hours for one person to complete the study procedures. Participants are paid \$100 for their help.

An Exciting New Contribution to the Study (by Laurie Brar)

We are currently planning to begin a new phase of our bipolar research. In conjunction with the *Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD), we are preparing to assist in the collection of blood samples for those STEP-BD patients who are interested in genetics research. This project differs from our family studies in that the blood samples will be sent to the National Institute of Mental Health where they will be stored with samples from up to 19 other sites. **These samples will eventually be made available to qualified scientists around the world to help determine both the causes of bipolar disorder, and how individual genetic differences may play a role in treatment response.** Hopefully, this collective effort will provide a larger (and more powerful) sample than can be obtained from individual investigators.

*The **STEP-BD** is a national, multi-site program sponsored by the National Institute of Mental Health for people who are diagnosed with any form of bipolar disorder (i.e. Bipolar I, Bipolar II, Bipolar NOS). This project is evaluating both standard and novel approaches and prevention of mania, depression, mixed states, and rapid cycling episodes of bipolar disorder. Those who participate receive their care within the STEP-BD program. Pittsburgh is one of the lead sites of the project. Those who participate in Pittsburgh must live within a reasonable driving distance to attend regular treatment appointments. Anyone interested in receiving additional information, may call 412-624-STEP (7837) or 1-888-427-1532.

Recent Study Results: (by Laurie Brar)

Swati Ranade, M.S. presented the results of her sample analyses at the Fourth International Conference on Bipolar Disorder in June, 2001. The association studies using candidate gene polymorphisms that she employed supported an association of Bipolar Disorder I with 5-HT_{2A} (serotonin receptor). Future analyses with larger samples are needed to support or refute this finding. The cause(s) of bipolar disorder is very complex and there are multitudes of factors that remain unknown. That's why each family who participates, by contributing to our analyses, plays a big part in the research effort.

Study Vocabulary

What is **polymorphism**? It's the presence of two or more distinct phenotypes in a population due to the expression of different alleles of a given gene, such as human blood groups O, A, B, and AB.

What is a **candidate gene**? Certain genes, because of their association with or involvement in chemical pathways in our bodies, are chosen by scientists as more likely to be involved in the expression of a condition and are therefore candidates for research.

Join the growing number of families who have helped worldwide!

	Type of Family			TOTAL
	2+ Affected Siblings	1 Affected Person & 2 Parents	1 Affected Person & 1 Parent	
Schizophrenia—USA	70	127	200	397
Schizophrenia—India	78	210	35	323
Bipolar Disorder—USA	7	47	67	121
TOTAL	155	384	302	841

As the above table shows, our combined research staff in the United States and New Delhi, India, has completed work with a total of 841 families who have generously volunteered their time to promote our understanding of schizophrenia & bipolar disorder. Worldwide, schizophrenia and bipolar disorder each affect an average of 1% of the population of any given country or culture. Appropriately, the effort to defeat these illnesses has become international in scope. **If you can count yourself among the families who have volunteered, we cannot thank you enough!** To provide even greater power to our laboratory work, we are striving to include several hundred more families into our study. We are always happy to hear from new families interested in participating. If you would like to participate, or learn more about our study, please call us toll free at 1 - 877 - 363 - 5895.

The Schizophrenia Research Memorial Fund (by Mary K. Miller)

Since we have been conducting our research studies, a few families have approached us regarding memorial gifts or honorariums. We have deeply appreciated these acts of support. We regard them as a great tribute to the members of the families who have suffered from serious mental illnesses. Therefore, we would like to inform you that in order to combine and acknowledge these gifts we have created a Memorial Fund. If you have any questions about the fund, please contact our project director, Patrick Reitz at 1-877-363-5895.

If you would like to send a tax-deductible gift in memory of or to honor a loved one, please make the check payable to Western Psychiatric Institute and Clinic. With your gift, please enclose the name of the person to be remembered, your address, and the address of the person who should receive an acknowledgment. Send it to:

**Western Psychiatric Institute and Clinic / Attention: Patrick Reitz
3811 O'Hara Street #444 / Pittsburgh, PA 15213**

A summary of our recent lab work and other studies

By Vishwajit L. Nimgaonkar, MD, PhD

We have spent the past 18 months working with colleagues in our Neuroscience and Neurobiology Departments. They include several well-known scientists, such as Drs. David Lewis, Pat Levitt and Karoly Mirnics. Our colleagues have been studying post-mortem brain samples for many years. They have noted several abnormalities in the cortex, a specialized region of the brain. In order to pinpoint these abnormalities, they compared the gene expression profiles of over 3,000 genes among post-mortem brain samples from patients and unaffected individuals. They found significant differences with respect to a large number of genes. Unfortunately, it was difficult to know if these changes were the causes or the effects of the illness.

We offered to examine variations in the sequences of these genes among the families who have been helping with our research. We felt that significant results from our studies would only occur if the genes played a causative

role. To our delight, we found that some variants of a gene called 'Regulator of G protein Synthesis - 4' (RGS4) were more common among patients with schizophrenia living in the USA as well as those in India. Similar trends were also present among patients with schizophrenia who had participated in a study organized by the National Institute of Mental Health. Suggestive results were also present among US patients with bipolar disorder.

In other words, we found similar trends in four different groups composed of over 1,800 participants. It was also interesting to see similar trends among patients with both schizophrenia and bipolar disorder. Before we suggest that RGS4 plays a role in the causation of either disorder, we would like to see if other scientists find similar evidence. Therefore, we have sent all our results to researchers in the USA, Canada, UK and Finland. We are waiting for their analyses with baited breath.

CONTACT US !

Toll free: **1-877-363-5895** (Schizophrenia) / **1-800-994-8182** (Bipolar Disorder).

www.pitt.edu/~nimga/ (schizophrenia) / **www.wpic.pitt.edu/research/neurogen/** (bipolar disorder)

Contact Dr. Nimgaonkar directly at (412) 624-0823 or email nimga+@pitt.edu

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