UIC UNIVERSITY OF ILLINOIS AT CHICAGO

Office for the Protection of Research Subjects (MC 672)
Office of the Vice Chancellor for Research
203 Administrative Office Building
1737 West Polk Street
Chicago, Illinois 60612

June 30, 2014

Dear Parent or Guardian or Adult Subject,

We are contacting you because you or your child has been identified as a participant in one or more of the following research studies, "Affective Neuroscience of Pediatric Bipolar Disorder" "Developing Brain Function in Adolescent Bipolar Disorder" or "Brain Networks Modulating Affect Self-Regulation in Pediatric Mania", conducted by Dr. Mani Pavuluri with the Department of Psychiatry, College of Medicine at the University of Illinois at Chicago.

The University of Illinois at Chicago (UIC) Institutional Review Board (IRB) has examined the conduct of these research studies. The IRB is an independent oversight committee at UIC that reviews and approves research studies involving human subjects. This evaluation identified several problems with the conduct of these studies. These problems seen are listed below. If you or your child participated in these studies as a "control" or did not have an existing psychiatric condition or did not receive lithium, it is unlikely these problems affected you or your child.

1). Failure of Dr. Pavuluri to clearly separate her roles as a psychiatric care provider versus medical researcher. When the investigator conducting a research study is the subject's medical care provider, a conflict may arise between the physician's desire to successfully complete the study with that of providing medical care to the individual. To minimize potential harm to the participant, the research plan reviewed and approved by the IRB describes how this conflict will be avoided. While the plans for Dr. Pavuluri's research studies stated that she would have no involvement in making medical care decisions for the research subjects, this plan did not appear to have been consistently followed.

2). Failure to prevent individuals who did not meet the requirements from participating in the study. An important component of every research plan is describing factors that allow (for example, age range, specific medical condition) or not allow (for example, heart condition, allergic reaction to medication) an individual to qualify for the study. The purpose of these eligibility factors is to ensure the findings of the study are valid and to exclude participants at risk for serious untoward effects from the study tests. In the studies referred to above, Dr. Pavuluri enrolled subjects who did not qualify for the studies for one or more of the following reasons: age, prior medication exposure, psychiatric diagnosis, other medical conditions, or use of illicit drugs or alcohol.

3). Failure to describe key research activities, alternatives to participating in the research, and the risks associated with the activities in the informed consent document. A physician in the course of providing care to a patient may use a medication outside the indications approved by the U.S. Food and Drug Administration (FDA), referred to as off-label use, or change the treatment when the physician feels it is in the patient's best interest. However, these actions during a research study require a greater level of scrutiny. Specifically, the IRB must approve the procedures associated with these actions and the procedures and risks described in the informed consent and parental permission forms.

In the research study, "Affective Neuroscience of Pediatric Bipolar Disorder", the participants or their parents were not informed that administration of lithium in children less than 12 years of age was off-label or that withdrawal of other psychotropic medications may occur and the risks associated with the withdrawal.

4). Failure to perform tests described in the IRB-approved research plan. One purpose of the testing performed during research studies is to prevent or identify the occurrence of any untoward effects. In the studies referred to above, Dr. Pavuluri failed to perform tests in several subjects intended to minimize the risks of lithium use.

These errors may have placed you or your child at a greater risk of harm than explained in the informed consent or parental permission documents signed by you. Although we currently are not aware that study participants have been harmed as a result of the problems described above, a child who was undergoing a withdrawal of their psychiatric medications that began before they entered one of the studies experienced a worsening of their mental health condition requiring hospitalization after lithium was started. If we do become aware of any untoward effects, we will notify you promptly. If you feel you or your child may have experienced harm as a result of their participation in these research studies or you have any questions about your rights as a research subject, please contact the Office for the Protection of Research Subjects (OPRS) at 312-996-1711 (local) or 1-866-789-6215 (toll-free) or email OPRS at uicirb@uic.edu. If you have any questions about the study, please contact: Ms. Darcel Brothers at 312-996-6243 in the Department of Psychiatry, College of Medicine.

The Department of Psychiatry and the IRB have put policies and procedures in place to assure that similar problems with the conduct of research do not occur in the future.

Further, as a consequence of the discovery of these findings, [redacted] The University of Illinois at Chicago realizes that an important benefit to you for participating in research is to contribute to the advancement of medical knowledge in this area, and thus believes it is important that you be informed of this decision.

We appreciate your or your child's participation in research at UIC. Please accept our sincere apologies for the occurrence of these issues in these studies, and our assurance that we are working to prevent similar problems from occurring in the future.

Sincerely,

Dimitri Azar, M.D., Ph.D.
Dean, College of Medicine

James Fischer, PharmD
Human Protections Administrator
Executive Chair, UIC Institutional Review Board

UIC

UIC Department of Psychiatry
UNIVERSITY OF ILLINOIS AT CHICAGO
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October 7 2015

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Dear Dr. Brambilla and Dr. Soares,

As the senior author and PI of the federally funded grants that supported this research, I am writing to inform you of the request by the University of Illinois at Chicago that **two** articles published in the Journal of Affective Disorders be retracted. This request follows the conclusion of a formal institutional investigation that was prompted by allegations of research misconduct against me, and that was conducted in accordance with the Public Health Service Policies on Research Misconduct (CFR 42 Part 93).

*Where, when and how high, and how long? The hemodynamics of emotional response in psychotropic-naíve patients with adolescent bipolar disorder*, Journal of Affective Disorders, 147:304-311, 2013.

With regard to the above published article, the Investigation Panel concluded that the allegations of research misconduct were supported by a preponderance of evidence. The Investigation Panel concluded that I intentionally and knowingly made two false statements in the Methods section of the article whereby the medication status of the subjects recruited to participate in the research study and whose data were included in the analyses was represented as “psychotropic-naïve” and “never having taken psychotropic medications”. Further, the Investigation Panel found by a preponderance of evidence that I intentionally and knowingly made a false statement in the Methods section whereby

"…Each child and their parent were interviewed by doctoral-level clinicians…" The Investigation Panel concluded that the accuracy and quality of the published results and conclusions were seriously compromised by these false statements.

*Deficits in emotion recognition in pediatric bipolar disorder: the mediating effects of irritability*, Journal of Affective Disorders, 144:134-140, 2013.

With regard to the above published article, the Investigation Panel concluded that the allegations of research misconduct were supported by a preponderance of evidence. The Investigation Panel concluded that I intentionally and knowingly made one false statements in the Abstract and four false statements in the Methods section of the article. Specifically, these statements misrepresented the medication status of the research participants as "medication-naïve" and "unmedicated". In addition, false statements were made regarding the use of the "…Washington University Kiddie Schedule for Affective Disorders and Schizophrenia…to determine placement into diagnostic group" and that "All clinical interviews and rating scales were completed by a master's or doctoral level rater…" The Investigation Panel concluded that the false statements seriously compromised "the quality of the results and conclusions in the manuscript."

My coauthors, who have been notified of the request for retraction, were not implicated in the research misconduct.

Sincerely,

Mani Pavuluri, MD, PhD

cc: Mark D. Grabiner, PhD
Associate Vice Chancellor for Research and Research Integrity Officer

Cc CO AUTHORS:

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Dear Dr. Boksa and Dr. Joober,

As the senior author and PI of the federally funded grants that supported this research, I am writing to inform you of the request by the University of Illinois at Chicago that an article published in the Journal of Psychiatry and Neuroscience be retracted. This request follows the conclusion of a formal institutional investigation that was prompted by allegations of research misconduct against me, and that was conducted in accordance with the Public Health Service Policies on Research Misconduct (CFR 42 Part 93).

*Altered affective, executive and sensorimotor resting state networks in patients with pediatric mania*, Journal of Psychiatry and Neuroscience, 38:232-240, 2013.

With regard to the above published article, the Investigation Panel concluded that the allegations of research misconduct were supported by a preponderance of evidence. The Investigation Panel concluded that I intentionally, knowingly and recklessly made two false statements in the Results section of the article whereby the medication status of research participants whose data were included in the analyses was misrepresented. Based upon the results of an IRB-directed audit, he Investigation Panel concluded that the false statements seriously compromised the results and conclusions of the article.

My coauthors, who have been notified of the request for retraction, were not implicated in the research misconduct.

Sincerely,

Mani Pavuluri, MD, PhD

cc: Mark D. Grabiner, PhD
Associate Vice Chancellor for Research and Research Integrity Officer

Cc CO AUTHORS:

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