

OLFACTORY RECEPTOR CELLS MAY PROVIDE CLUES TO PSYCHIATRIC DISEASE

Nose cells provide a window into the brain

Philadelphia, PA (March 1, 2005) – In the first study to examine living nerve cells from patients with psychiatric disease, scientists from the Monell Chemical Senses Center, the University of Pennsylvania, and collaborating institutions report altered nerve cell function in olfactory receptor neurons from patients with bipolar disorder.

Like other psychiatric and neurodegenerative disorders, bipolar disorder affects nerve cells in the brain, making it difficult to study underlying neurobiological causes of the disease during its actual course.

According to senior author Nancy Rawson, PhD, a Monell cellular biologist, “Previous studies have used non-nerve cells, such as fibroblasts or red blood cells, to examine how cells function in patients with bipolar disorder. But since this is a psychiatric disorder, we need to understand what’s going on in nerve cells.”

Olfactory receptor neurons (ORNs), located in a small patch of epithelium inside the nose, are nerve cells that contain receptors for the thousands of odorant molecules detected by humans. Easily obtained using a simple 5-minute biopsy procedure, ORNs share many characteristics with nerve cells in the brain. These features make ORNs a useful model to study the neural effects of psychiatric disease.

Calcium is integral to properly-functioning nerves, and previous studies have implicated dysfunctions of cellular calcium metabolism as a contributing factor to bipolar disorder. Changes in how much calcium is inside ORNs and other nerve cells tell researchers how the nerves respond to stimulation.

In the study, researchers used a fluorescence imaging technique to measure basal and stimulated calcium levels in ORNs from 17 patients with bipolar disorder and age- and sex-matched healthy controls. Seven patients were medication free and 10 were being treated with mood-stabilizing drugs.

Calcium responses were predominantly decreased in nerves from patients with bipolar disease. Rawson comments, “The decreased calcium responses point to a specific set of pathways that will allow us to narrow the target for identifying the defect of calcium regulation associated with bipolar disorder. Once identified, these pathways will provide new targets for drug development.”

The researchers regard the ORNs as a valuable model which will provide needed insight into the neurobiological factors underlying psychiatric disease.

Rawson notes, “The calcium dysregulation that we see in ORNs of bipolar patients is different from what has previously been reported in studies using non-neuronal cells. This suggests that nerve cells might behave differently from other cell types.”

Lead author Chang-Gyu Hahn, MD, PhD, a psychiatrist at the University of Pennsylvania School of Medicine, observes, “A major issue in treating bipolar disorder – or psychiatric disorders in general – is that it is hard to predict which medication a patient will respond to. So, clinicians go through a series of trials and errors and the patient suffers until the right medication is found. It is possible that ORNs might be developed as a ‘medication responsiveness test’ to indicate which medication a patient should be on.”

Hahn continues, “Another strength of this approach is that we can sample neurons from patients during specific stages of the illness and therefore we will be able to distinguish trait from state dependent characteristics of the disorder, which is particularly important in understanding mood disorders. ”

Co-lead author was Monell neurobiologist George Gomez, PhD, currently at the University of Scranton. Also contributing to the studies were Diego Restrepo, PhD, University of Colorado; Eitan Friedman, PhD, MCP Hahnemann University; Richard Josiassen, PhD, Arthur P. Noyes Research Foundation and University of Pennsylvania; Edmund A. Pribitkin, MD and Louis Lowry MD, Thomas Jefferson University; and Robert J. Gallop, West Chester University.

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The Monell Chemical Senses Center is a nonprofit basic research institute based in Philadelphia, PA. Scientists at the Monell Center conduct research devoted to understanding the senses of taste, smell, and chemical irritation: how they function and how they affect our lives, from before birth through old age. The Center’s approach is multidisciplinary. Scientists from a variety of backgrounds collaborate to address topic areas in sensation and perception, neuroscience and molecular biology, environmental and occupational health, nutrition and appetite, health and well being, and chemical ecology and communication. For more information about Monell, visit the Center’s web site at www.monell.org or email inquiries to media@monell.org.

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