Depression often accompanies involuntary emotional expression disorder; SSRIs can sometimes treat both.

BY KERRI WACHTER
Senior Writer

Baltimore — The lack of diagnostic criteria has hamstrung neurologists in their attempt to diagnose involuntary emotional expression disorder. Dr. Sharon Handel said at a meeting on Alzheimer’s disease and related disorders sponsored by Johns Hopkins University. Even when they make the diagnosis with certainty, neurologists have little to offer by way of Food and Drug Administration-approved therapy, said Dr. Handel, of the department of psychiatry at Johns Hopkins University, Baltimore.

Part of the problem with identifying this condition has been the numerous names under which it is known, she noted: Involuntary emotional expression disorder (IEED) is also known as pseudo-bulbar affect and pathologic laughing or crying.

It’s been estimated that more than 1 million people in the United States have IEED. The disorder has been associated with cerebrovascular accident, Alzheimer disease, multiple sclerosis, amyotrophic lateral sclerosis, and traumatic brain injury.

The hallmark of IEED is episodes of crying or laughing that are unrelated or out of proportion with the eliciting stimulus. There is a disconnection between emotional experience and expression. Emotional outbursts in IEED are involuntary, episodic, and incongruent with baseline mood. The outbursts are intense, but are followed by a return to baseline. Disorders of affect—which IEED appears to be—involves impairment of the moment-to-moment regulation of emotion. “There’s a disconnection of the neural networks in this condition from the experienced emotion to the display of emotion,” said Dr. Handel.

The neural networks of emotion involve the frontal lobes, the limbic system, the brainstem, the cerebellum, and white-matter tracts. In particular, the prefrontal cortex integrates complex sensory and limbic information that determines the emotional valence of a stimulus and modulates motor and autonomic responses involved in emotional expression. It’s not clear where the neural interruption occurs in IEED.

For now, the current diagnostic criteria include:
- Episodic of involuntary crying, laughing, or related displays.
- An origin in brain injury or disease.
- A change in the patient’s emotional behavior from that prior to the disease or injury.
- Incongruent or exaggerated mood.
- A response that is excessive or unrelated to the stimulus.
- Significant distress or impairment.

The differential diagnosis should include: epilepsy, facial dystonia or dyskinesias; vocal tics; axis I disorders (such as major depression or bipolar disorder); axis II disorders (such as borderline personality disorder); and substance abuse.

“These patients often have major depression, and while specific treatment is often the same, I think it’s important to differentiate the two conditions,” said Dr. Handel.

The differential diagnosis should also include affective liability, essential crying, and witzelsucht (a tendency to inappropriate jokes). With affective liability, the subjective and objective dimensions of affect are not dissociated. Essential crying is a hereditary and lifelong tendency to cry easily. Witzelsucht is an addiction to trivial joking, which can take the form of both an inappropriate giddy affect and irritability or aggressiveness.

In terms of clinical course, IEED frequently remits spontaneously within 6 months. Others may have remission with treatment within 3 months. Resolution of IEED can be independent of the resolution of depression. However, in some cases the disorder is chronic and persistent without treatment.

Treatment of IEED is still evolving. At present, there is no FDA-approved treatment for IEED. “What are typically used—at least up to this point—are SSRIs. They tend to work quite quickly,” said Dr. Handel.

In fact, response can be seen in just a few days in some patients.

Dextromethorphan, in combination with quinine, is being studied to treat patients with IEED. Dextromethorphan is a nonopioid antinocius, but it also has a number of other neuropharmacologic properties. It is a potent sigma, agonist (inhibiting the release of the excitatory neurotransmitter, glutamate) and is also an N-methyl-D-aspartic acid glutamate receptor antagonist.

Dextromethorphan undergoes significant first-pass metabolism by the cytochrome P450 isoenzyme CYP2D6. Quinidine is a potent inhibitor of this isoenzyme, thereby increasing and sustaining dextromethorphan levels.

Gene Mutations Linked to 5% Of Frontotemporal Dementia

BY JAMES BUTCHER
Contributing Writer

Salzburg, Austria — Mutations in the progranulin gene are found in approximately 5% of patients with frontotemporal dementia, according to research presented at the 88th International Conference on Alzheimer’s and Parkinson’s Diseases.

Frontotemporal dementia (FTD) is the second most common cause of dementia, after Alzheimer’s disease, in patients aged 65 years or less. Approximately 85%-90% of those patients with frontotemporal dementia have a family history of dementia, a statistic which suggests that there is a strong genetic component to the disease.

In 1998, investigators reported that they found mutations in the gene encoding the microtubule-associated protein tau (MAPT) caused familial FTD with parkinsonism linked to chromosome 17 (FTDP-17).

However, not all families who showed linkage to the same region on chromosome 17 mutations in MAPT, suggesting that mutations in at least one gene were responsible for the disease in these patients.

In addition, these patients had ubiquitin-immunoreactive neuronal cytoplasmic inclusions (FTD-U) but not tau-immunoreactive inclusion pathology.

In July 2006, two studies found that FTDU-17 is caused by mutations in progranulin, a polypeptide with growth-modulatory activity, leading to a loss of protein function (Nature 2006;442:916-9; Nature 2006;442:920-4).

Since then, researchers have been screening their patient populations for the mutations to determine their prevalence in the frontotemporal dementia community.

Stuart Pickering-Brown, Ph.D., who works at the University of Manchester (England), presented data from the Manchester cohort that currently includes 272 patients with FTD; some of the included patients have been followed for more than 20 years.

“We recently finished sequencing for progranulin mutations and found 14 cases,” commented Dr. Pickering-Brown.

He also noted that this frequency (5%) is about the same for tau gene mutations (6%) in his study cohort.

Alzheimer’s Mortality Increasing; Deaths From Stroke and Heart Disease Decreasing

The National Institute on Aging is offering a free book that is designed to help people who have limited reading skills learn about Alzheimer’s disease.”Understanding Alzheimer’s Disease” includes information about the signs of the disease, treatment options, and also offers help for caregivers. Visit www.nia.nih.gov/alzheimers/publications/understanding to download this book or order by calling 800-438-4380.