PBA and the Brain

On-screen text: PBA & the Brain

VO: For patients already struggling with a serious neurologic disorder or brain injury, living with Pseudobulbar Affect, or PBA, can feel like an additional burden.

VO: PBA is a separate condition that occurs secondary to other neurologic conditions or brain injuries, which may include but are not limited to:

- Stroke
- Dementia or Alzheimer’s disease
- Traumatic brain injury
- Amyotrophic lateral sclerosis
- Multiple sclerosis; and,
- Parkinson’s disease

On-screen text: Occurs secondary to an underlying neurologic condition or brain injury, such as:

- Stroke
- Dementia or Alzheimer’s disease
- Traumatic brain injury (TBI)
- Amyotrophic lateral sclerosis (ALS)
- Multiple sclerosis (MS)
- Parkinson’s disease

VO: Conditions and injuries like these can cause brain damage that disrupts the neural networks and neurotransmitter activities that regulate the way someone shows their emotions. This may contribute to the uncontrollable laughing and/or crying episodes typical of PBA symptoms.

VO and on-screen text: PBA symptoms are characterized by involuntary, sudden, and frequent episodes of laughing and/or crying that are exaggerated or incongruent with a patient’s underlying mood.

VO: Before we dive into the pathophysiology of PBA, it may help to review the processes involved in normal laughing and crying. In a healthy brain, when a stimulus is detected, the cerebellum modulates an appropriate emotional reaction, and the brain stem activates relevant somatic and visceral motor responses. Regions of the brain’s CPC network work together to produce this reaction.

On-screen text: CPC network = cortico-pontine-cerebellar network

VO: So, when someone experiences something sad, for example, their brain regulates an appropriate response, like becoming tearful.
On-screen text: Appropriate response

**VO:** When damage occurs to one or more parts of the brain’s CPC network, the areas of the brain may no longer communicate correctly. While the exact pathophysiology of PBA is not fully understood, evidence suggests that disruption to certain neurotransmitter activities along damaged CPC pathways contributes to inappropriate emotional responses.

**VO:** So, for example, when an individual with PBA experiences an event that is somewhat sad, they may begin sobbing uncontrollably — or they may cry without experiencing something sad at all. In short, their laughing and/or crying doesn’t match how they feel or feels exaggerated.

On-screen text: Inappropriate response

**VO:** One of the major neurotransmitters thought to be involved in these abnormal emotional reactions is glutamate.

On-screen text: Glutamate

**VO:** Glutamate receptors, including NMDA, exist throughout the brain as well as in the CPC network, where PBA is thought to arise. Normally, proper amounts of glutamate will bind to and activate these receptors to facilitate many neurologic functions, like laughing and crying.

On-screen text: NMDA = N-methyl-D-aspartate

**VO:** After the onset of a neurologic condition or brain injury, too much glutamate can be released in the brain. This can over activate the receptors and lead to abnormal signaling and cell dysfunction. Incorrect signaling could contribute to the uncontrollable laughing and/or crying seen in PBA.

On-screen text: Incorrect glutamate signaling could contribute to the uncontrollable laughing and/or crying seen in PBA.

**VO:** The good news is that PBA is treatable with medication. NUEDEXTA is the first and only FDA-approved treatment for PBA. The exact mechanism by which NUEDEXTA exerts its therapeutic effect in patients with PBA is unknown.

On-screen text: NUEDEXTA
The first and only FDA-approved treatment for PBA
*FDA = U.S. Food and Drug Administration
The exact mechanism by which dextromethorphan exerts its therapeutic effect in patients with PBA is unknown.
VO: NUEDEXTA contains quinidine, which inhibits CYP2D6 and may interact with other drugs metabolized by CYP2D6. Adjust the dose of CYP2D6 substrates as needed for patients also on NUEDEXTA. Please review the Important Safety Information at the end of the video.

On-screen text: NUEDEXTA inhibits CYP2D6. Adjust dose of substrates as needed. Refer to the Important Safety Information at the end of the video.

VO: Visit our website to watch part two of this series, the Science Behind NUEDEXTA.

On-screen text: Learn more at NUEDEXTAHCP.com

NUEDEXTA logo

INDICATION AND USAGE
NUEDEXTA® (dextromethorphan HBr and quinidine sulfate) is indicated for the treatment of pseudobulbar affect (PBA). PBA occurs secondary to a variety of otherwise unrelated neurological conditions, and is characterized by involuntary, sudden, and frequent episodes of laughing and/or crying. PBA episodes typically occur out of proportion or incongruent to the underlying emotional state. PBA is a specific condition, distinct from other types of emotional lability that may occur in patients with neurological disease or injury.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS
Quinidine and Related Drugs: NUEDEXTA contains quinidine and should not be used concomitantly with other drugs containing quinidine, quinine, or mefloquine.

Hypersensitivity: NUEDEXTA is contraindicated in patients with a history of NUEDEXTA-, quinine-, mefloquine-, or quinidine-induced thrombocytopenia, hepatitis, bone-marrow depression, lupus-like syndrome, or known hypersensitivity to dextromethorphan (e.g., rash, hives).

MAOIs: NUEDEXTA is contraindicated in patients taking monoamine oxidase inhibitors (MAOIs), or in patients who have taken MAOIs within the preceding 14 days, due to the risk of serious and possibly fatal drug interactions, including serotonin syndrome. Allow at least 14 days after stopping NUEDEXTA before starting an MAOI.

Cardiovascular: NUEDEXTA is contraindicated in patients with a prolonged QT interval, congenital long QT syndrome, history suggestive of torsades de pointes, heart failure, patients receiving drugs that both prolong QT interval and are metabolized by CYP2D6 (e.g., thioridazine and pimozide), patients with complete atrioventricular (AV) block without implanted pacemaker, or at high risk of complete AV block.
WARNINGS AND PRECAUTIONS

Thrombocytopenia and Other Hypersensitivity Reactions: Quinidine can cause immune-mediated thrombocytopenia that can be severe or fatal. Non-specific symptoms, such as lightheadedness, chills, fever, nausea, and vomiting, can precede or occur with thrombocytopenia. NUEDEXTA should be discontinued immediately if thrombocytopenia occurs.

Hepatotoxicity: Hepatitis, including granulomatous hepatitis, has been reported in patients receiving quinidine, generally during the first few weeks of therapy. Discontinue immediately if this occurs.

Cardiac Effects: NUEDEXTA causes dose-dependent QTc prolongation. QT prolongation can cause torsades de pointes-type ventricular tachycardia, with the risk increasing as the degree of prolongation increases. When initiating NUEDEXTA in patients at risk for QT prolongation and torsades de pointes, electrocardiographic (ECG) evaluation of QT interval should be conducted at baseline and 3 to 4 hours after the first dose. Some risk factors include use with CYP3A4 inhibitors or drugs that prolong QT interval, electrolyte abnormalities, bradycardia, or left ventricular hypertrophy or dysfunction. If patients taking NUEDEXTA experience symptoms that could indicate the occurrence of cardiac arrhythmias (eg, syncope or palpitations), NUEDEXTA should be discontinued, and the patient further evaluated.

Concomitant Use of CYP2D6 Substrates: NUEDEXTA inhibits CYP2D6 and may interact with other drugs metabolized by CYP2D6. Adjust dose of CYP2D6 substrates as needed.

Dizziness: NUEDEXTA may cause dizziness. Take precautions to reduce the risk of falls.

Serotonin Syndrome: Use of NUEDEXTA with selective serotonin reuptake inhibitors (SSRIs) or tricyclic antidepressants increases the risk of “serotonin syndrome.”

Anticholinergic Effects of Quinidine: Monitor for worsening in myasthenia gravis.

ADVERSE REACTIONS

The most common adverse reactions (incidence of ≥3% and two-fold greater than placebo) in patients taking NUEDEXTA are diarrhea, dizziness, cough, vomiting, asthenia, peripheral edema, urinary tract infection, influenza, increased gamma-glutamyltransferase, and flatulence. These are not all the risks for use of NUEDEXTA.
Please see Full Prescribing Information at https://www.nuedextahcp.com.


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