

## 2022 VNS Study Participation Guidelines

### Ages

- Participants need to be between the ages of 6 - 22 years old.

### Sleep

- Participants must be able to sleep independently in a bed alone.
  - Body heat generated by another person, and their weight in the bed, will disrupt data collection.
- If the participant can not sleep independently in a bed alone another person can be *nearby* provided they maintain:
  - A minimum of 1.5 feet distance from the subject at all times;
  - Completely separate sheets, blankets, or other covers.

### Mood Stable\*

- Participants must be mood stable and taking a proven mood stabilizer:
  - *Ideally the participant will be stable on lithium carbonate.*
  - Alternative acceptable mood stabilizers:
    - Trileptal - Oxcarbazepine
    - Tegretol - Carbamazepine
    - Depakote - Sodium divalproex
    - Lamictal - Lamotrigine

### Thermoregulatory and Thermosensory Disturbances\*

- Participants must be experiencing associated symptoms.

### Diagnosis

There are no specific diagnoses that are required or prohibited for the screening process.

Participants can not currently be taking ketamine.

\*For questions regarding how to determine mood stability please see the supplemental information on distinguishing mood instability from thermoregulatory disturbance induced symptoms.

## Mood Instability vs. Thermoregulatory Symptoms

While often difficult to distinguish between, there are some distinct differences between mood and thermoregulatory symptoms.

### Mood Disruptions

All people experience mood fluctuations throughout the day. However, with clinically significant mood disruptions those changes in mood occur rapidly, unexpectedly, and without a clear cause. They include symptoms of depression and mania (or hypomania).

Depressive symptoms include feelings of sadness, irritability, loss of interest in pleasurable activities, and feelings of worthlessness and helplessness.

Symptoms of mania include racing thoughts, irritability, distractibility, goal directed fixations known as “Mission Mode”, and grandiosity. (Hypomania looks similar, with reduced intensity.)

In children, symptoms of depression, mania, and hypomania can also present as chronic irritability, crankiness, a quick temper, as well as rigidity and refusal to try new things.

Mood swings happen quickly, sometimes without any warning or outside stimulus, and can change multiple times throughout a single day. Often, but not always, manic and hypomanic symptoms occur in the late afternoon or early evening.

### Thermoregulatory Disturbances

Put simply, thermodyregulation is the body’s inability to correctly regulate its temperature. This is a physical phenomena that may be independent from the mood disruptions explained above.

The ratio between proximal and distal body temperature is a measure of how well the body is shifting core heat to the skin so that it will be dissipated. Clinical signs of a disturbance in this system may sometimes manifest in the following ways:

Often, the child feels hot and sweaty in normal room temperatures. These neutral ambient temperatures don’t feel so neutral to the child and they feel excessively hot in the evening and cold in the morning.

Other telltale signs of temperature dysregulation are bright red ears that are often warm or hot to the touch. Another is a refusal to wear weather appropriate clothes, for example wearing shorts or *not* wearing a coat in cold winter temperatures and experiencing little to no discomfort when exposed to the cold.

This disruption in body temperature regulation leads to several other symptoms.

#### 1. Sleep/Wake Disturbances

Sleep/wake disturbances are categorized in three different ways:

A. Issues such as sleepwalking, sleep talking, night sweats, bedwetting, and teeth grinding, which demonstrate problems with the proper execution of sleep cycles.

B. Frequent and recurrent nightmares and night terrors themed with pursuit and/or abandonment with violent and often gory imagery involving scenarios where they or someone they love is being hurt, maimed, or killed. These images may linger with the patient long after they awaken and may plague them throughout the day as repetitive intrusive thoughts.

C. Alterations in circadian rhythms, including difficulty falling asleep, difficulty staying asleep, and difficulty waking.

Falling asleep: it's very difficult for the child to "wind down" in the evenings and prepare for bed as they experience rising energy levels, anticipatory dread about being unable to fall asleep, and anticipatory fear of nightmares.

Staying asleep: restlessness includes frequent middle of the night awakenings, trips to the bathroom, and bedsheets, pillows, and pajamas in wild disarray.

Waking: they often do not appear to have the energy to move in the morning when awakened.

## 2. Fear/Anxiety

The part of the brain that controls temperature regulation is the same part of the brain that controls the activation of the fight or flight instinct. As a result, children with thermoregulatory disturbances experience a triggering of their fight or flight response when it's not needed, causing them to feel intense anxiety and fear. The child is on constant alert, looking for threats and dangers, causing separation anxiety, fear of germs, fear of intruders, or of the dark to be pushed to debilitating degrees. They create elaborate rituals at bedtime, mealtime, or bathtime to help them feel safe.

Functioning in a near constant state of fight or flight also results in distorted reactions to normal stimuli. They experience threats that don't exist, either by misperceiving something neutral in their environment as threatening, or by feeling excessively defensive from feeling embarrassed, misunderstood, unheard, dismissed, or rejected.

## 3. Aggression

All children can be aggressive at times and it can be difficult to differentiate clinically significant aggression from either normal childhood behaviors, or from

other diagnoses.

It's developmentally normal for young children to have tantrums. However, in a child triggered by thermodyregulation their tantrums continue for many years past what is considered developmentally normal. The tantrums also can last for several hours and are accompanied by physical and verbal aggression, such as screaming, throwing things, slamming doors, putting holes in walls, kicking, hitting, biting, and scratching. These behaviors escalate with the child's age to include cursing and verbal threats.

Parents know when their child's tantrums are unusual and deviate from the developmentally normal outbursts that occur in early childhood.

Aggression is also shown in other ways such as defiant and oppositional behavior and refusals to follow simple instructions, complete expected tasks, and do basic chores such as teeth brushing, showering, homework, and getting dressed. Requests can be met with verbal abuse which can quickly escalate into tantrums, leaving parents, siblings, and caregivers feeling as though they are walking on eggshells all of the time.

### **Mood Stability**

For the purposes of this study, ideal participants will have achieved relative mood stability while still experiencing thermoregulatory disturbances and accompanying symptoms. This would be seen as:

- Fewer mood swings throughout the day;
- Fewer episodes of sadness, general irritability, and feelings of worthlessness;
- Increased participation in pleasurable activities and in trying new things;
- Fewer episodes of racing thoughts, distractibility, and grandiosity; and
- An increase in flexibility and adaptability.