Stress-mediated dopamine activity in the paraventricular nucleus of the thalamus drives feedforward disinhibition in the nucleus accumbens through amygdala-PVT interactions.

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Abstract

1. Intermittent hypoxia-induced noradrenergic hyperarousal is associated to increased disinhibitory dopamine activity in the paraventricular nucleus (PVN) of the midline thalamus. It also appears likely that chronic hypoxia increases tonic dopamine releases in the striatum through a disinhibitory reuptake mechanism associated with a Locus Coeruleus mediated rise in extracellular dopamine levels.

2. Chronic intermittent hypoxia (CIH) with a face mask enhances stress-dependent conditioned responses (c-Fos expression) in the paraventricular nucleus of the thalamus (PVN) and Locus Coeruleus.

3. Consequently, this hypoxic stress-induced persistent reuptake in extracellular dopamine (D2) in the paraventricular thalamus may creates a motivational conflict in decision-making associated to the brain circuits of addiction. In particular the nucleus accumbens (NA) is highly sensitive to dopaminergic dysregulation in the midline thalamus.

Mechanism

In summary, hypoxia-mediated noradrenergic dysregulation is caused by increased basolateral amygdala-striatum reactivity altering the dopamine-noradrenaline response (LC-NE) following chronic episodes of mild and intermittent hypoxia (IH), independently of pulse oxymetry status.

Hypoxia-mediated cerebral hypometabolism

1. Hypoxia-induced changes to noradrenergic signaling may activate the sympathetic nervous system thereby lowering cerebral blood glucose levels in the midbrain region (striatum and hippocampus) thus causing memory impairment in cognitive/verbal processing.

2. Secondly, the upregulation of cerebral blood flow (CBF) in the striatum caused by hypoxia-induced sympathetic activity (LC-NE) is influenced mostly by nitric oxide (NO)-mediated metabolic changes (ie: SpO2/FiO2) in tissues.

Hypoxia-induced aversive conditioning impair fear extinction learning

Human behavior is acutely more sensitive towards survival and more vulnerable to emotional eating overfeeding in hypoxic conditions. In specific, hypoxic stress-induced persistent reuptake in extracellular dopamine (D2) in the paraventricular thalamus (PVT) may creates a motivational conflict associated to the neurocircuitry of fear extinction learning and passive coping mecanism.

References

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