Improving Mood, Sleep and Behaviour with Tryptophan, Ornithine, Serine, Glycine and Magnesium

Mood and sleep are intrinsically linked whereby biochemical or environmental disturbances can influence a cascade of dysregulation and disease manifestation. The ‘monoamine hypothesis’ suggests that the development of mood, sleep and behaviour disorders occurs when monoamines, such as the neurotransmitters serotonin and noradrenaline, are at insufficient levels in the synaptic cleft. Therefore, associated symptoms and conditions can be improved by increasing synaptic levels of monoamines (such as by supporting neurotransmitter synthesis, release or breakdown), and subsequent activation of serotoninergic and noradrenergic postsynaptic and autoreceptors. Whilst low serotonin can indeed contribute to lower mood, poor sleeping patterns and altered behaviour, this does not occur in isolation. Psychosocial and environmental factors, stress, nutritional status, inflammation and a range of other influences also contribute to the development of sleep and mood dysregulation and should be taken into consideration when implementing a nutritional intervention.

Synthesising Serotonin with Neurotransmitter Precursors

Serotonin (5-hydroxytryptamine, 5-HT) is a neurotransmitter that exerts its influence via the serotonergic system, a diffuse network within the central nervous system that plays a significant role in the regulation of mood, behaviour, cognition, sleep, learning and memory. The essential amino-acid L-tryptophan (tryptophan), is the sole precursor of peripherally- and centrally-produced serotonin. As a result, deficiency of tryptophan, and consequently serotonin in the brain can lead to dysfunction of the serotonergic system and has been associated not only with depression but a range of other disorders. (see Figure 1)

Tryptophan is also a precursor to melatonin, tryptamine, kynurenine, quinolinic acid and niacin. Nicotinic acid (vitamin B3) is synthesised from tryptophan through the kynurenic pathway. If nicotinic acid levels are low, tryptophan metabolism may favour this pathway and therefore the rate of serotonin synthesis may decline. (see Figure 2)

Tryptophan hydroxylase is the essential enzyme required for the conversion of tryptophan to 5-hydroxytryptophan (5-HTP). This enzyme is dependent on certain nutrients such as vitamin B6, zinc, magnesium, vitamin C and folate.

Improving Sleep and Stress Resilience with Amino Acids

Stress has been shown to induce a physiological response via the hypothalamic-pituitary-adrenal (HPA) axis, leading to the release of cortisol as well as altering the transmission and synthesis of a variety of neurotransmitters and catecholamines. It has been suggested that inflammation, stress and cortisol can activate the kynurenine pathway of tryptophan metabolism. As a result, there can be decreased availability of tryptophan and subsequent synthesis of serotonin and melatonin, contributing to poor mood and sleep.

Modulating the HPA-axis, down-regulating the stress response and promoting sleep quality requires a comprehensive and holistic approach to decrease allostatic load whilst improving stress resilience and adaptation. The effects of an increased allostatic load, sleep disturbance or deprivation from physical, psychological or environmental stressors on the brain, mind and body includes not only fatigue and depression, but also cognitive inefficiency, mood disruptions, sleepiness, impaired attention and memory deficits leading to impaired quality of life. New research highlights the novel, multi-target mechanisms that the amino acids L-ornithine, L-serine and L-glycine can exert as modulators of the HPA-axis, cortisol, mood and sleep.

**Figure 1: Serotonin’s involvement in mood and behaviour**

<table>
<thead>
<tr>
<th>Functions of Serotonin</th>
<th>Signs and Symptoms of Serotonin Deficiency</th>
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<tbody>
<tr>
<td>Mood</td>
<td>Anxiety</td>
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<tr>
<td>Memory recall</td>
<td>Depression</td>
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<tr>
<td>Sleep</td>
<td>Stress</td>
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<td>Behaviour</td>
<td>Inflammation</td>
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<tr>
<td>Regulation of Circadian Rhythms</td>
<td>Low Pain Tolerance</td>
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<td>Regulation of Pain</td>
<td>Impulse Tendencies</td>
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<tr>
<td>Control of Appetite</td>
<td>OCD</td>
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</tbody>
</table>

Factors that can contribute Serotonin deficiency:
- Anxiety
- Depressed Mood
- Aggression
- Insomnia
- Poor Memory
- Poor Attention Span
- Low Pain Tolerance
- Impulse Tendencies
- Carbohydrate Cravings
- OCD

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Figure 2: The fate of Tryptophan

**Tryptophan-niacin pathway**
- Stress, inflammation and B3 upregulates this pathway
  - L-tryptophan
  - Ornithine (Stress)
  - Kynurenine
  - Niacin

**Tryptophan-serotonin pathway**
- B3
  - 5-hydroxy-tryptophan
    - Mg, B6, Vit. C, Folate
  - Serotonin
    - Zinc
  - N-acetyl-serotonin
    - SAMe
  - Melatonin

References available upon request.
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