



**Hyposerotonergic™ conditions** occur when serotonin concentrations are not enough, low, inadequate, depleted, deficient, or suboptimal on a modified normal diet.™

**Hypodopaminergic™ conditions** occur when dopamine concentrations are not enough, low, inadequate, depleted, deficient, or suboptimal on a modified normal diet.™

**Hypoglutathionemia™ conditions** occur when glutathione concentrations are not enough, low, inadequate, depleted, deficient, or suboptimal on a modified normal diet.™

- Giving only *serotonin precursors* can deplete dopamine and glutathione.™
- Giving only *dopamine precursors* can deplete dopamine and glutathione.™
- Giving only *glutathione or glutathione* precursors can deplete serotonin and dopamine.™

The centrally acting monoamines (monoamines) are serotonin, dopamine, norepinephrine, and epinephrine.

For the management of **hyposerotonergic conditions** or states that may accompany

## Fatigue

A **hyposerotonergic condition** or state often accompanies fatigue (see the right column).

After diagnosing fatigue, formulate a differential diagnosis to rule out accompanying issues, including a hyposerotonergic condition or state.

The presence of a hyposerotonergic condition or state may be identified with an empirical trial of the hyposerotonergic / hypodopaminergic condition protocol (see below).

Management of the hyposerotonergic condition or state which may accompany fatigue requires establishing serotonin concentrations higher than are possible with modification of the normal diet.

**Fatigue** may be accompanied by symptoms arising from a hyposerotonergic condition or a hypodopaminergic condition

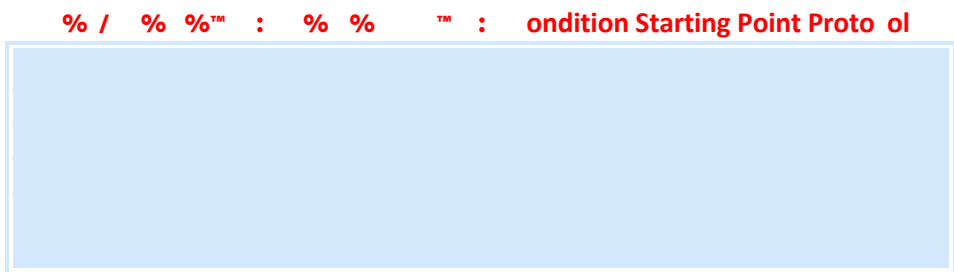
"To assess the involvement of serotonin in the symptoms of chronic fatigue syndrome, we investigated the serotonergic neurotransmitter system of chronic fatigue syndrome patients by the positron emission tomography (PET). Here we show that the density of serotonin transporters (5 HTTs) in the brain, as determined by using a radiotracer, [<sup>11</sup>C] (+)McN5652, was significantly reduced in the rostral subdivision of the anterior cingulate as compared with that in normal volunteers." (Note; compensation for reduced transporters may induce a hyposerotonergic condition that require an increase in serotonin concentrations.) Shigeyuki, Y. et al. Reduction of serotonin transporters of patients with chronic fatigue syndrome, NeuroReport December 3rd, 2004 - Volume 15 - Issue 17 - p 2571-2574

"Newsholme et al were the first to form the hypothesis that, because of its well-known effects on arousal, lethargy, sleepiness, and mood, 5-HT(serotonin) may have a role as a possible mediator of central fatigue." Davis, et al. Serotonin and central nervous system fatigue: nutritional considerations Davis, J. et al. Am J Clin Nutr 2000;72(suppl):573S-85.

"Among these factors, exercise-induced changes in the concentration of the monoamines 5-HT (serotonin), dopamine and noradrenaline have all been linked to central fatigue (Taylor et al. 2016)." Kavanagh, J. et al. Enhanced availability of serotonin increases activation of unfatigued muscle but exacerbates central fatigue during prolonged sustained contractions J Physiol 597.1 (2019) pp 319-332

"Serotonin has been linked to fatigue because of its well known effects on sleep, lethargy and drowsiness and loss of motivation." Meeusan, R. et al. Central fatigue: the serotonin hypothesis and beyond Review Sports Med Actions 2006; 36(10):881-909

"Indirect evidence indicates that central fatigue is caused by serotonin (5-HT), but the cellular mechanisms are unknown." Cotel, F. et al. Serotonin spillover onto the axon initial segment of motoneurons induces central fatigue by inhibiting action potential initiation PNAS March 19, 2013 vol. 110 no. 12, 4774-4779



**Figure 1:** If symptoms have resolved completely after seven days on any level, do not increase to the next level, do not order testing. Increase to the next level if symptoms are still present after seven days. **Order lab testing after seven days on level 3 if symptoms are still present. Lab testing determines if the serotonin or dopamine protocol is required** Dosing levels 1-3 do not require lab testing. Do not increase to level 4 through level 9 or switch to the dopamine protocol without first obtaining a serotonin and dopamine assay.