Inhibition of the enzyme 5'-deiodinase that catalyzes the conversion of T4 to T3 has been considered a possible mechanism responsible for the sick euthyroid syndrome. Additionally, many drugs that are commonly used in ICU, such as iodine, amiodarone and corticosteroids, also reduce the conversion of T4 to T3.

The majority of critically ill patients have low serum T3 concentrations, as do some outpatients during illness. Liver and skeletal muscle biopsies obtained within minutes after death from intensive care unit patients demonstrate reduced 5’-monodeiodinase activity and increased 5’-monodeiodinase activity (which converts T4 to rT3). Moreover, patients with fatal illness have low tissue T4 and T3 concentrations.

Several mechanisms can contribute to the inhibition of 5’-monodeiodination and therefore to the low serum T3 concentrations in critically ill patients with nonthyroidal illness: