Sickness behavior in Juvenile Idiopathic Arthritis (JIA) - from understanding to nutritional interventions.

Mechiel Korte en Bas Vastert (Sciences/UMC Utrecht).

According to the WHO, noncommunicable diseases (NCDs) produce a large burden on individuals and society. Chronic inflammation is a common risk factor in many NCDs. For example, Juvenile Idiopathic Arthritis (JIA) is a painful, debilitating disease characterized by inflammation of the joints, which begin before 16 years of age. JIA patients are characterized by high blood levels of proinflammatory cytokines, such as TNF-α, IL-1, IL-6. These cytokines have been suggested to alter both tryptophan and tyrosine metabolism via stimulating neopterin instead of co-factor tetrahydrobiopterin (BH4) synthesis and kynurenine instead of serotonin synthesis, thereby reducing the neurotransmitter concentrations of dopamine, noradrenaline, serotonin and melatonin in the brain. Here it is hypothesized that monoamine levels may be associated with sickness behavior, e.g., malaise, nausea, less appetite, fatigue, poor sleep, no interest in pleasurable activities (i.e. anhedonia), and pain. Remarkably, the folate antagonist methotrexate (MTX), the cornerstone in the management of arthritis, is also thought to alter tryptophan and tyrosine metabolism, also by reducing BH4 activity. Thus, altered amino acid metabolism in JIA patients may be, at least partly, responsible for MTX-intolerance (abdomal pain, nausea, vomiting, behavioral symptoms, such as restlessness, crying, irritability). To proof that tryptophan and tyrosine metabolism is altered in JIA, the biological markers (Tryptophan, Kynurenine, Neopterin, Phenylalanine, Tyrosine) will be measured in JIA patients with active arthritis and during remission. By connecting our knowledge, we aim to develop and understand new concepts for specialized nutrition to reduce sickness behavior in inflammatory disorders.