

Title: Morphine and gluten/casein derived opiate peptides inhibit cysteine uptake and decrease glutathione: Implications for autism and other inflammatory disorders

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Parents of autistic kids observe improvement upon removal of casein and gluten (GF/CF) from their child's diet. Peptides β -casomorphin-7 (β CM7) and α -gliadin-7 (α G7) are formed after ingestion of milk and wheat/rye, respectively, and activate opiate receptors. Blood and urine samples from autistic and schizophrenic patients contain higher amounts of these peptides. A SNP in casein results in higher amounts of β CM7 produced from the milk of certain cows (A1 vs. A2). Several studies show a correlation between A1 milk consumption and inflammatory disorders.

Systemic oxidative stress and brain neuroinflammation have been described in autistic subjects, in association with significantly lower plasma levels of the antioxidant glutathione (GSH). Cysteine availability is rate-limiting for GSH synthesis and the excitatory amino acid transporter-3 (EAAT3) provides a major source of cysteine uptake in both neurons and intestinal epithelial cells.

Here we demonstrate the ability of α G7, as well as human and bovine forms of β CM-7 to inhibit cysteine uptake in human cultured cells, in similar but less extensive manner to the effect of morphine. This was also associated with significant changes in intracellular thiol levels, including a decrease in the level of GSH. Time-course studies revealed a complex pattern of inhibition and recovery of cysteine uptake, eventually leading to sustained inhibition. The bovine form of β CM-7 was more effective than the human form in inhibiting cysteine uptake and altering thiol metabolite levels.

The current study provides a novel mechanistic explanation for the benefit of GF/CF dietary intervention for the treatment of autism and other inflammatory disorders.