Altering serotonin synthesis by the acute tryptophan depletion method: a model for irritable bowel syndrome?

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Background: Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder. The pathophysiology of IBS is not fully understood. A multi-component conceptual model of IBS has been postulated, involving physiological, affective, cognitive and behavioural factors. The 'brain-gut axis' is a theoretical model describing the bi-directional neural pathways linking cognitive and emotional centres in the brain to neuroendocrine centres, the enteric nervous system and the immune system and plays a major role in the concept of IBS. IBS is associated with visceral hypersensitivity and with a high co-occurrence of psychiatric symptoms, in particular affective dysregulation. Serotonin, a key denominator of the 'brain-gut axis' is involved in the regulation of gastrointestinal motility, secretion and perception as well as cognition and mood.
Aim: To assess the effects of an acutely lowered serotonin synthesis, using the acute tryptophan depletion (ATD) method, on visceral perception, affective memory performance and mood in diarrhoea-predominant irritable bowel syndrome patients (d-IBS) and healthy matched controls.
Methods: In a randomised, double blind crossover design, fourteen d-IBS patients and fourteen matched controls were studied in an ATD and placebo condition, respectively. Visceral perception of urge and pain was scored during rectal distensions. Affective memory performance, mood and biochemical parameters of serotonergic metabolism were simultaneously assessed.
Results: ATD significantly decreased plasma tryptophan and 5-hydroxyindole acetic acid concentrations ($p<0.0001$), relative to placebo. ATD was associated with significantly increased urge scores specifically in the lower pressure range ($p<0.0001$) and overall increased pain scores ($p<0.05$). ATD significantly lowered the perceptual threshold for first perception ($p<0.006$), but not for maximal tolerable discomfort. ATD induced a significant shift in affective memory bias towards a preferential loss of positive material ($p<0.005$), but no significant changes in mood. ATD did not differentially affect the patient or control group.
Conclusions: We provide evidence that serotonergic modulation by ATD affects both visceral perception as well as cognition in d-IBS and controls. Simultaneous measurement of brain and gut function and the application of ATD contribute to the elucidation of the complex pathophysiology of IBS.

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