



Samenvatting van het proefschrift

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"Pathophysiology of stress-induced visceral hypersensitivity"

Promotiedatum: 29 april 2014

Universiteit: Universiteit van Amsterdam

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Visceral hypersensitivity is observed in the majority of patients with IBS and considered a pathophysiological mechanism. The aim of the work described in this thesis was to obtain a better understanding of the stress related pathophysiology of visceral hypersensitivity. Investigations were carried out in the rat model of maternal separation. Because others already indicated that mast cells may be involved in post stress visceral hypersensitivity, we first set out to confirm these observations in our animal model in chapter 2. Next we investigated the role of nerve growth factor (NGF) because, in addition to histamine, it is one of the mast cell mediators known to modulate transient receptor ion channel 1 (TRPV1). We used two different TRPV1 antagonists to evaluate the functional role of TRPV1 in post stress visceral hypersensitivity.

In chapter 3 we focused on the possible role of corticotrophin releasing hormone (CRH). We evaluated whether there is such a thing as prolonged post-stress mast cell dependent visceral hypersensitivity in maternally separated rats using the antagonist α -helical CRF (9-41). In chapter 4, we tested two peripherally restricted H1R-antagonists for their capacity to reverse post-stress visceral hypersensitivity.

IBS transfer across generations may largely depend on environmental factors. Therefore, in chapter 5, we used our animal model to investigate whether susceptibility to stress induced visceral hypersensitivity in maternally separated Long Evans rats can be transferred across generations without further separation protocols and, if so, whether this depends on maternal care. Finally, the possible role of mast cells in the post stress phenotype of these second generation animals was investigated by the use of the mast cell stabilizer doxantrazole.

