Over-expression of cortico-limbic 5-HT1A receptors leads to enhanced stress-induced anxiety and LPS-induced depression /

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Rationale. Dysfunction of 5-HT1A receptors, especially those located in the cortico-limbic circuitry, has been linked to depression and stress-related disorders. We hypothesised that overexpression of 5-HT1A heteroreceptors (TG mice) in the frontal cortex and hippocampus could influence innate anxiety- and depression-like responses. In addition, we assessed their phenotype under environmental challenges known to induce pathological anxiety- and depression-like behaviours. Objectives. We have compared the behavioural responses of male and female TG mice in ethological and conflict-based anxiety paradigms, and also evaluated the impact of the pre-exposition to a stressful event on these behavioural responses. In addition, we evaluated the manifestations in mice subjected to an animal model of inflammation-induced depression (lipopolysaccharide administration) using anxiety and depression tests. Results. TG mice, especially female subjects, exhibited a basal (non stressed condition) behaviour characterized by hypocolomotion and anxiety. When they were pre-exposed to a stressful event, an enhanced anxiogenic and depressive-like responses were clearly observed. Interestingly, TG mice subjected to the LPS model exhibited higher hypolocomotion, freezing (panic-like) response and increased immobility.Conclusions. The over-expression of cortical-hippocampal 5-HT1A receptors increases the susceptibility of mice, especially in female subjects, to develop maladaptive and enhanced anxiety-like responses when they have experienced a previous stressful event. In addition, TG mice are particularly more vulnerable to suffer the manifestations associated to the LPS-induced model of depression.

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