During the last decade, the idea of major depression as a condition characterized by impaired neuronal plasticity has been developed, suggesting that psychopathology may be associated with reduced expression and function of proteins that are important for cellular resilience, leading to enhanced vulnerability under “challenging situations” (Pittenger and Duman, 2008). Hence, it is feasible to hypothesize that conditions, such as those determined by a genetic impairment of serotonin transporter (SERT), that are associated with increased risk for depression, can lead to an impairment of the mechanisms that are important for neuronal plasticity and that may contribute to disease vulnerability. On this basis, we investigated if genetic abnormalities of the SERT can lead to alterations in the expression of brain-derived neurotrophic factor (BDNF), a neurotrophin that, because of the activity-dependent regulation of its expression and secretion (Bramham and Messaoudi, 2005), has emerged as crucial mediator of neuronal plasticity. BDNF is involved in the etiopathology of mood disorders as well as in the mechanism of action of antidepressant drugs (Berton and Nestler, 2006; Calabrese et al., 2007; Groves, 2007; Martinowich et al., 2007; Molteni et al., 2009), and a close link between serotonin and the neurotrophin has been suggested. In my presentation, we investigated the expression of BDNF in different brain regions from SERT mutant rats (+/− and −/−). Moreover, given the complex genomic structure of the neurotrophin (Aid et al., 2007), we have investigated the influence of SERT deletion on its different transcripts and evaluated the involvement of epigenetic mechanisms in their modulation.

Finally, we have examined if alterations on BDNF expression were also present in human leukocytes from healthy individuals with different 5-HTTLPR genotypes.

References: