What role does the LPA_1 receptor play in regulating emotional-like behaviours?

LPA_1 receptor is one of the six characterized G protein-coupled receptors (LPA1–6) through which lysophosphatidic acid acts as an intercellular signalling molecule. It has been proposed that this receptor has a role in controlling anxiety-like behaviours and in the detrimental consequences of stress. In general, the neurobiological mechanism of fear extinction is strikingly similar to that of the adaptative stress response (distress regulation), sharing similar neuroanatomical, neuroendocrine, and neurochemical basis. Inadequate control of the stress response could precipitate or provoke anxiety disorders. In this context, we tried to elucidate the LPA_1 receptor involvement in emotional regulation. For this purpose, we first examined fear extinction in normal wild-type (wt) and maLPA_1-null mice. Additionally, to study the role of the LPA_1 receptor in the absence of developmental abnormalities induced by its permanent loss, the effect of LPA_1 antagonist Ki16425 administration was examined in contextual fear extinction on wild-type mice. Next, we studied the consequences of the absence of the LPA_1 receptor in two key areas involved in emotional regulation, characterizing the structure and GABAergic composition of the medial prefrontal cortex (mPFC) and the amygdala. Lastly, we examined the corticosterone response and the expression of a marker of neuronal activity, c-Fos protein, in the amygdala and the mPFC after acute stress. Our results revealed that lack of LPA_1 induces exaggerated amygdala reactivity and endocrine responses to emotional stimuli (e.g., an acute episode of stress), revealing a role of LPA_1 receptor in regulating emotional-like behaviours.

Taking together, LPA_1 receptor is involved in emotional behaviours and in the anatomical integrity of the corticolimbic circuit, the deregulation of which may be a susceptibility factor for anxiety disorders and a potential therapeutic target for the treatment of these diseases.