The administration of sertraline plus naltrexone reduces ethanol consumption and motivation in a long-lasting animal model of post-traumatic stress disorder

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This study was aimed to evaluate the effects of sertraline (STR) and/or naltrexone (NTX) on ethanol consumption and motivation in an animal model of post-traumatic stress disorder (PTSD) and alcohol use disorder (AUD). Male C57BL/6J mice were submitted to an intermittent and progressively increasing stressful stimuli simulating PTSD behavioural features. Behavioural alterations were explored by the fear conditioning (FC), novelty suppressed feeding test (NSFT) and acoustic startle response (ASR) paradigms. Afterwards, mice were evaluated in the voluntary ethanol consumption (VC) and the oral ethanol self-administration (OEA) paradigms. The effects of STR (10 mg/kg) and/or NTX (0.7 mg/kg) on ethanol consumption and motivation were analysed in the OEA. Furthermore, relative gene expression analyses of tyrosine hydroxylase (Th), mu-opioid receptor (Oprm1) and 5-hydroxitryptamine transporter (Slc6a4) were performed in the ventral tegmental area (VTA), nucleus accumbens (NAcc) and dorsal raphe nucleus (DR), respectively. PTSD-like mice presented increased fear-related memory, anxiety-like behaviours, and startle response, as well as enhanced ethanol consumption and motivation in the VC and OEA paradigms. Interestingly, STR plus NTX combination significantly reduced ethanol intake and motivation in the OEA. Gene expression analyses revealed reduced Th and Oprm1 whereas Slc6a4 gene expression increased in PTSD-like mice. STR and/or NTX modulated Th and Slc6a4 gene expression changes in PTSD-like mice. Furthermore, NTX increased Oprm1 gene expression revealing a synergistic action when combined with STR. These results provide evidence about the efficacy of the STR plus NTX to attenuate ethanol reinforcement and motivation in an animal model of PTSD and AUD dual pathology.

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