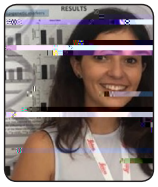

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With the increase in life expectancy, the study of age-related diseases and the development of different strategies to deal with them become mandatory. Cognitive and behavioural disturbances are growing public healthcare issue for the modern society, which is experiencing an increasingly common stressful lifestyle. Taking into consideration the convergence of aging, stress and neurodegenerative diseases, such as AD, there is impaired glucocorticoid (GC) signalling. Therefore, the study of GC-mediated stress response to chronic moderate stressful situations, as account in the daily life, becomes of huge interest in order to design harmacological strategies to prevent neurodegeneration. To address this issue, we determined the target engagement between RL-118 and 11 -HSD1 and afterwards SAMP8 were exposed for 4 weeks to CMS paradigm and treated with RL-118, an 11 -HSD1 inhibitor. In fact, several pieces of evidence link the inhibition of this enzyme with reduction of GC levels and cognitive improvement and CMS exposure has been associated with reduced cognitive performance. The aim of this project was to assess whether RL-118 treatment could restore the deleterious effects of CMS on cognition and

: Dolors Puigoriol-Illamola Determination of target engagement through TAPS assay: behaviour and molecular analysis after RL-118 treatment, a potent 11 -HSD1 inhibitor; Pharmacology 2020; July 17, 2020; Paris, France