Medicinal Chemistry of Drugs Acting on CRH Receptors

https://neurodegenerationresearch.eu/survey/medicinal-chemistry-of-drugs-acting-on-crh-receptors/

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USA

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Medicinal Chemistry of Drugs Acting on CRH Receptors

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Research Abstract
The stress system is well known to play an important role in relapse to drug abuse and excessive eating and is largely controlled by corticotropin releasing hormone receptors (CRHR) and their endogenous ligands. Recent work has shown that stress and corticotropin-releasing hormone (CRH) are involved in the pathogenesis of Alzheimer’s disease (AD), but agents that impact CRF signaling have not been carefully tested for therapeutic efficacy or long-term safety in animal models. We have examined the question of whether antagonism of the type-1

corticotropin-releasing hormone receptor (CRHR1) could be used as a disease-modifying treatment for AD, we used a preclinical prevention paradigm and treated 30-day-old AD transgenic mice with the small-molecule, CRHR1-selective antagonist, R121919, (2,5-dimethyl-3-(6-dimethyl-4-methylpyridin-3-yl)-7 dipropylaminopyrazolo1,5-apyrimidine) for 5 months, and examined AD pathologic and behavioral end points. We found that R121919 significantly prevented the onset of cognitive impairment in female mice and reduced cellular and synaptic deficits and beta amyloid and C-terminal fragment- levels in both genders. We observed no tolerability or toxicity issues in mice treated with R121919. We conclude that CRHR1 antagonism may present a viable disease-modifying therapy for AD, and that appropriate CRHR1 antagonists should be considered for human studies.

Further information available at:

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Investments < €500k

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