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Kisspeptin – a possible drug-candidate for mental and cognitive disorders

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Kisspeptins are a family of proteins that are known as regulators of sex hormones. Recently, we found that abnormal sensorimotor gating (measured in paradigms of prepulse inhibition; PPI) in immune deficient mice (SCID) and the poly I:C model for developmental schizophrenia is correlated to irregular expression of Kisspeptin. Systemic IP injection of the Kisspeptin-derived peptide, Kp-10, enhanced PPI in a dose-dependent manner, while a Kisspeptin receptor antagonist reduced PPI. Furthermore, Kisspeptin can improve performance in several models of behavioral disorders including reduced PPI induced by poly I:C or MK-801, disturbed learning and memory in SCID mice or induced by MK-801, and behavioral despair. The effect of Kisspeptin on PPI was found to be mediated via neurotensin, a neuropeptide known to be related to several CNS disorders.

Kp-10, the peptide used in our studies, is a 10 amino acid peptide and may not be stable enough to use in mental and cognitive disorders in humans. Therefore, we produced several Kp-10 derivatives with improved pharmaceutical properties; two of these analogs exhibit antipsychotic activity in vivo in the MK-801 mouse model for schizophrenia. The performance of one of these peptides, a 6 amino acid cyclic peptide, was better in this model than that of the original Kp-10.

Our results indicate that this cyclic peptide might be a suitable drug candidate for disorders involving PPI, learning and memory or behavioral despair such as schizophrenia, depression, Alzheimer's disease and other age-related dementias.

Biography

Michal Cardon completed her PhD, and started her postdoctoral studies in 2010 at the Weizmann Institute of Science. She has published more than 9 papers in reputed journals.

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