

Solution structure of a new hypothalamic neuropeptide, human hypocretin-1/orexin-A

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Orexin-A and orexin-B (also called hypocretin-1 and hypocretin-2, respectively) are novel hypothalamic neuropeptides encoded by a single mRNA transcript; they stimulate food intake and regulate sleep cycle. We have determined the three-dimensional solution structure of human hypocretin-1/orexin-A, which has two intra-molecular disulfide bonds in N-terminus. On the basis of NOEs, $^3J_{\text{HN}\alpha}$ coupling constants and hydrogen deuterium exchange rates data, human orexin-A was determined as having a short α -helix and two turns in H₂O solution. The structural comparison among diet related hormones, orexin-A, orexin-B and neuropeptide Y would be also discussed.