

Action of the ciliary neurotrophic factor in mouse brainstem

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Systemic administration of ciliary neurotrophic factor (CNTF) determines sustained weight loss in rodents and humans. The anorectic effect of CNTF is due, at least in part, to activation of the signal transducer and activator of transcription (STAT) 3, STAT1 and STAT5 in neuronal and glial cells of the tuberal hypothalamus (Severi et al., 2012, 2013 and unpublished data). To assess whether CNTF also exerts an action on the brainstem feeding centres, male Swiss CD-1 mice were intraperitoneally treated with rat recombinant CNTF (0.3 mg/kg of body weight; CNTF-treated mice) or with saline (control mice) for 45 minutes (min) to perform P-STAT3, P-STAT1 and P-STAT5 immunohistochemistry, and for 120 min to detect c-Fos expression. Double staining experiments with neuronal and glial markers and confocal microscopy analyses were performed to assess the phenotype of the CNTF-responsive cells. P-STAT3-, P-STAT1- or P-STAT5-positive cells were not detected in brainstem coronal sections from control mice. In contrast, CNTF administration led to a strong activation of the transcription factors STAT3, STAT1 and STAT5 in CNTF receptor α -bearing glial cells of the area postrema, a circumventricular organ devoid of blood-brain barrier, that allows circulating molecules to gain access to the adjacent brain parenchyma. In 120 min CNTF-treated mice specific nuclear staining for c-Fos was detected not only in cells of the area postrema but also in numerous neurons widely distributed in the nucleus of the solitary tract (Sol), the dorsal motor nucleus of vagus (DMV) and parabrachial nuclei. Ongoing experiments on capsaicin-treated (deafferented) mice will disclose a possible vagal contribution to the Sol and DMV neuronal activation due to a peripheral action of CNTF in the gastro-intestinal tract. Collectively, these data show for the first time that CNTF similarly to other satiety factor, like leptin, has redundant actions on both hypothalamic and brainstem energy balance neuronal networks. Unravelling the phenotype of brainstem neurons responsive to CNTF will clarify its role in distinctive aspects of feeding behaviour.

References

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Keywords

Obesity; neuropeptides; growth factors; hindbrain.