Cerebellin1 is a novel orexigenic factor which potently increases food intake via hypothalamic neuropeptide Y release


**Background:** Cerebellin1 (Cbln1) is a highly conserved 16 amino acid neuropeptide. Cbln1 was originally identified in the cerebellum and has since been found to have widespread distribution in the CNS and periphery. High levels of Cbln1 mRNA expression are found in the hypothalamus, a critical area of the brain involved in appetite regulation. However, the role of Cbln1 in the regulation of food intake and body weight is not known.

**Aim:** To investigate the effects of Cbln1 on food intake in rodents.

**Methods:**

1. Ad libitum fed rats were injected intracerebroventricularly (ICV) with Cbln1 (1, 3, 10 and 30nmol) in the early light phase and food intake was measured for 24 hours post injection (n = 10 per group).

2. Behavioural analysis was carried out for 1 hour post ICV administration of Cbln1 (30nmol).

3. To investigate a possible mechanism of action, the effects of Cbln1 (10, 100 and 1000nM) on the release of orexigenic and anorexigenic neuropeptides from ex-vivo rat hypothalamic explants was determined using radioimmunoassay (n = 15 per group).

4. To determine whether Cbln1 has a physiological role in regulating food intake, hypothalamic Cbln1 mRNA and peptide levels were determined following 12 hour and 24 hour fasting in rats using quantitative PCR and radioimmunoassay, respectively (n = 15 per group).

**Results:**

1. ICV administration of Cbln1 to rats resulted in a significant increase in food intake 1 hour post-injection [0.34 ± 0.08g (saline); 0.72 ± 0.28g (3nmol); 1.68 ± 0.51g (10nmol); p < 0.01; 1.71 ± 0.53g (30nmol) p < 0.05].

2. ICV administration of Cbn1 did not cause any adverse behavioural effects.

3. Cbln1 (10, 100 and 1000nM) resulted in a significant increase in the release of the orexigenic factor, neuropeptide Y (NPY) [199%, 144% and 126% of basal release, respectively, p < 0.05]. Cbln1 had no effect on the release of the orexigenic neuropeptide, agouti related peptide or anorexigenic neuropeptides, cocaine and amphetamine regulated transcript or α-melanocyte stimulating hormone.

4. Hypothalamic Cbln1 mRNA and peptide levels were not significantly different in fed compared to fasted animals.

**Conclusions:** We have identified Cbln1 as a novel orexigenic factor and potential new therapeutic target for the development of anti-obesity agents.