Supplemental Figure Legends

Supplemental Figure 1: Effect of different forms of neuronostatin on heart rate.
Rats bearing i.c.v. and carotid cannulae were injected with either saline vehicle or vehicle containing 300 pmole neuronostatin-13, neuronostatin-19, scrambled neuronostatin (Neuronostatin-Scr), or non-amidated neuronostatin-13 (NA-Neuronostatin-13), and heart rate was recorded for 45 minutes. Neuronostatin-19 induced significant alteration in HR during Phase 2. Data represent change from pre-injection baseline (average of MAP for 5 minutes before injection). Data were analyzed using a Mann-Whitney U test (*p<0.05, **p<0.01, versus Saline-injected controls).

Supplemental Figure 2: Heart rate changes during phentolamine treatment.
Rats were pretreated intra-arterially with either saline vehicle or 10 mg/kg phentolamine. After a 15 minute stabilization period, rats were injected with saline vehicle or vehicle containing 300 pmole neuronostatin i.c.v. No significant trends in HR were observed. Data were analyzed using a Mann-Whitney U test (*p<0.05, **p<0.01. Comparisons were made as follows: Saline/Saline versus Saline/Neuronostatin; Phentolamine/Saline versus Phentolamine/Neuronostatin).

Supplemental Figure 3: Heart rate changes during V1 antagonist treatment.
rats were pretreated with saline or V1 antagonist i.v. prior to i.c.v. injection of either saline 300 pmole neuronostatin. No significant alterations in HR trend were observed. Data were analyzed using a Mann-Whitney U test (*p<0.05. Comparisons were made as follows: Saline/Saline versus Saline/Neuronostatin; V1 antagonist/Saline versus V1 antagonist/Neuronostatin).

Supplemental Figure 4: Heart rate changes during SHU9119 treatment.
We pretreated animals i.c.v. with the melanocortin 3/4 receptor antagonist, SHU9119 (300 pmole) prior to i.c.v. injection of either saline or 300 pmole neuronostatin. No significant changes in trend of HR were observed. Data were analyzed using a Mann-Whitney U test (*p<0.05. Comparisons were made as follows: Saline/Saline versus Saline/Neuronostatin; SHU9119/Saline versus SHU9119/Neuronostatin).