# Roles of amygdala and insula during brain activation with dynamic gastric distention

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**INTRODUCTION:** Recent studies that used a balloon placed in the stomach showed that gastric distension, one of the mechanisms modulating food intake, activates the amygdala and the insula[1]. However, the specific effects of gastric volume (GV) and rate of gastric volume changes (RGVC) on brain activation in these regions are still unclear. Here we used a gastric distension paradigm[1] with larger distention volume and a different statistical analysis method to study the effects of GV and RGVC on brain activation during gastric distention. We hypothesized that GV would activate the amygdala, consistently with its role in the perception of fullness, and RGVC would activate the insula, consistently with its role in visceral sensation.

**METHODS:** Twenty-two healthy non-smoking and right-handed subjects (19 males; age: 31.6 ± 5.5 years, education: 14.5 ± 2.3 years; body mass index = 27.2 ± 6.2; 5 subjects were in the class I obesity range; fasting time = 16−18 hours) participated in the study. A customized balloon was placed in the stomach as shown in Fig 1 (see Ref 1 for detailed procedures). The balloon was cyclically filled with water ($37^{o}$ Celsius temperature) by using an electric pump (Fig 2). Thus, balloon volume (blue line; Fig 2) was varied from 0 ml to a maximum volume = 700 ml with constant water flow (red line) = ± 5.56 ml/s during the inflow (+; orange) and outflow (−; cyan) epochs; subjects rated their fullness, discomfort, hunger, and desire for food during the last 15 s of the null-flow epochs (light gray shading; Fig 2) by pressing buttons in response to visually presented questions. BOLD-fMRI signals were measured in a 4-Tesla MRI scanner using a single-shot gradient-echo EPI sequence (TE/TR = 20/2000 ms, 4 mm slice thickness, 35 coronal slices, 64 × 64 matrix size, 355 time points). The fMRI time series were motion corrected, normalized, and smoothed. Activation maps were calculated for each subject using the general lineal model in SPM2 with a box-car design modeling the visual stimulation and respond epochs (ratings; Fig 2 shaded) and 2 regressors: GV (Fig 2 blue line), modeling the volume of the balloon, and RGVC (Fig 2 red line), modeling the water in/out flow. These BOLD maps were entered into t-tests and simple regression (random-effect) analyses in SPM2; complementary ROI analyses were carried out to validate the SPM results using a customized IDL code.

**RESULTS:** Subjects rated higher fullness for the 700 ml gastric distention condition than for the 0 ml condition (p = 0.001; paired t-test). Reading and responding questions during rating epochs strongly activated occipital and prefrontal (PFC) cortices across subjects ($p_{corr} < 0.001$, cluster-level corrected for multiple comparisons; Fig 3 Ratings). The left parietal cortex, left superior PFC, bilateral cerebellum and the left amygdala were strongly activated by the volume (not by flow) of the balloon ($p_{corr} < 0.001$; Fig 3 GV). The posterior insula and the posterior parietal cortex were activated by the water flow (not by volume; $p_{corr}<0.01$; Fig 4). BMI and GV-activation were linearly correlated in the cerebellum ($p_{corr}<0.001$; Fig 4).

**CONCLUSIONS:** These results are consistent with those of previous studies that used the gastric distention paradigms with lower maximum distention (500 ml) in non-obese healthy subjects[1]. However, here we show that during balloon distention the amygdala senses the volume of the balloon while the posterior insula senses balloon volume changes as a function of time. Furthermore, GV activated the cerebellum proportionally to BMI. This study highlights the important role of the amygdala, posterior insula, and cerebellum for the processing of vagal signals from the stomach in lean and obese subjects, and identifies the cerebellum as a region involved in the obese phenotype that merits further investigation.

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Fig 1: Placement of the balloon in the stomach

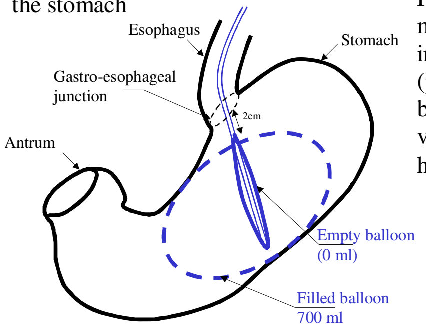


Fig 2: Time course of the balloon distention paradigm. Constant water flow (red line) is used to filled up the balloon to a volume (blue line) 700ml (orange) or emptied (cyan) in 140 s.

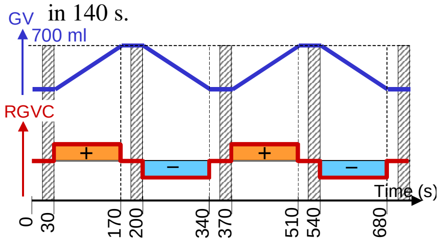
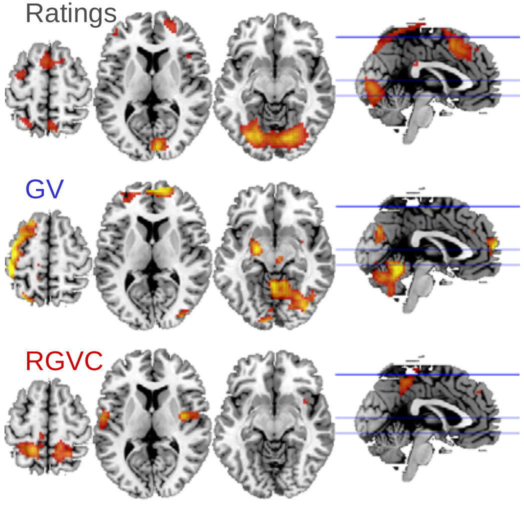


Fig 3: Statistical maps of brain activation components for the 700-ml balloon distention paradigm. Ratings: highlights brain regions involved in reading questions (MRI goggles) and responding them (pressing buttons); GV: highlights brain regions that are activated by increased balloon volume; RGVC: shows brain regions sensing volume changes caused by water inflow or outflow. Sample = 22 healthy subjects.



**REFERENCES**: 1-Wang GJ (2008) Neuroimage **39**: 1824-1831.

Fig 4: GV-fMRI activation as a function of body mass index (BMI) Note that 5 subjects are in the Class I obesity range (BMI > 30).