

## Different fMRI representations and brain connections for food odor stimuli depending on the BMI of infant volunteers

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**Introduction:** Obesity is a precursor of health problems (i.e. in cardiology, neurology, endocrinology, etc.). In Mexico this condition affects more than 70% of the population (2<sup>nd</sup> highest percentage of the world, 1) with a special prevalence in the infant bracket. It is known that odor/smell is one of the principal cues for the appearance and control of appetite (2). To fight obesity it is crucial to understand the brain mechanisms of this stimulus. Previous fMRI work has shown that adult obese and lean subjects interpret these types of stimuli differently (3). Nevertheless and surprisingly, no studies have been performed in infants who have different metabolism and brain development from adults. Furthermore, there is no information on the changes in connectivity between brain regions for this age group. In this work we studied the different brain fMRI activations and connections between normal weighted (NW) and obese (OB) infants for different types of food odors.

**Methods:** Experiment: 30 volunteers (infants 8.4±2 years) of both sexes (15 males and 15 females) were studied. Two cohorts of 15 subjects each were obtained from the sample, one with BMI between 19 and 24 kg/m<sup>2</sup> (NW) and the other with BMI over 30 kg/m<sup>2</sup> (OB). Protocol: Volunteers received three odor cues: One was pleasant and represented caloric foods (chocolate), the second was healthy and presented low calorie foods (onion); Finally the third was a neutral odor not associated with food (diluted acetone). Each stimulus was presented for 9 s. with a rest period of 18 s. and was repeated in random order 10 times per fMRI experiment. MRI Hardware: Experiments were performed in a 1.5 T Philips Intera-Achevia scanner using an 8 channel SENSE head-coil. fMRI: 278 brain volumes comprising 35 coronal slices covering the whole of the brain were acquired with a Fast-Echo-EPI sequence over a period of 13.9 minutes. TR=3 s., TE=50 ms., 64x64 matrix with a 3.6 x 3.6 mm *in-plane* resolution and 4 mm slice thickness (no gap between slices). Data was analyzed with SPM8 software in which standard analysis was performed (slice time correction, realignment, normalization (to EPI.nii) and smooth (6,6,6 mm kernel)). Correlation connectivity ROI to ROI analysis was performed with the conn toolbox v.1.3 from MIT. Results for both analysis were corrected for multiple comparisons (FWE p<0.05) and data was presented overlaid on template images.

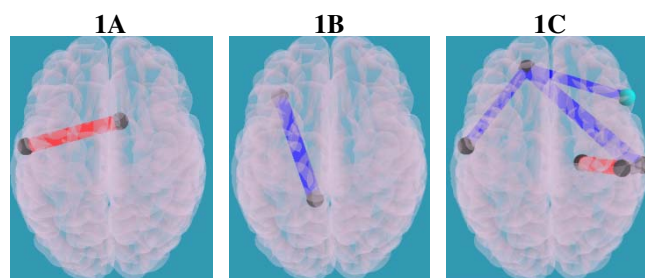
**Results:** Table 1 presents the main fMRI activations found when comparing NW vs. OB subjects for the three different odor cues. Figure 1 presents the different connections found for the NW vs. OB comparison depending on smell: Onion (1A), acetone (1B) and chocolate (1C). Red lines correspond to connections which were larger for NW subjects vs. OB. Blue lines correspond to stronger connections between OB vs. NW.

**Discussion:** fMRI results: All food smells presented larger activations in cerebellum for NW volunteers; this probably corresponded to the pleasure regulation function of this area (4). The cingulate gyrus was much more active for OB infants when presented with food smells. This response was possibly related to the emotional processing or the memory functions of this area. These two findings clearly indicated different mechanisms of interpretation of these stimuli between OB and LN volunteers. Connectivity results: For the onion smell (Figure 1A), a connection between ventral anterior cingulate cortex (reward anticipation) and the gustatory cortex was found. This pointed towards a brain process in which the value of a healthy food was being assessed against its taste in NW subjects (a mechanism which did not appear in OB infants). Figure 1B (acetone) showed a connection between dorsal cingulate cortex (memory retrieval) and the inferior prefrontal gyrus (risk assessment) for OB volunteers. This probably shows the brain processing of a smell which is not that usual, and it is being deciphered at a different level (Is this food safe?). In contrast NW volunteers seemed to be uninterested in this stimulus. Much larger numbers of significant connections were found for the chocolate smell (Figure 1C) for OB vs. NW. These connections related the orbitofrontal cortex (decision making) with several regions like: gustatory cortex, somatosensory and auditory cortex. These inputs indicated large somatosensory inputs which were not there in NW volunteers probably making it much more attractive smell to OB people. A connection between the perirhinal cortex (recognition and identification of environmental stimuli) and somatosensory cortex (identification of the smell) was found for NW volunteers.

**Conclusions:** Clear differences in fMRI and connectivity between the OB and NW groups were found, pointing at a very different processing of odor cues in infants.

**References:** (1) Encuesta Nacional de Salud y Nutrición 2006, www.insp.mx (2) *Physiol Behav.* 2006 Apr 15;87(4):800-4. Epub 2006 Mar 20. (3) *Obesity.* 2010 Aug; 18(8):1566-71. Epub 2010 Mar 25. (4) *J Neuropsychiatry Clin Neurosci.* 2009 Summer;21(3):245-53.

	Healthy>Obese			Obese>Healthy		
	Region	Position	Voxels	Region	Position	Voxels
Chocolate	Cerebellum Post. Lobe	8 -80 -28	8	Cingulate Gyrus	20 -22 34	9
	Cingulate Gyrus					
Acetone	Lingual Gyrus	-20 -68 -6	10	Temporal Gyrus	32 8 -26	12
	Temporal Gyrus	-54 -46 6	12	Med. Frontal Gyrus	20 24 28	10
	M. Occipital Gyrus	-20 -98 16	9	Pre-C- Gyrus	-24 -12 46	8
Onion	Cerebellum Inf. Semi-Lunar	-34 -72 -36	12	Cingulate gyrus	18 -28 34	14
	Cerebellum Cereb. Tonsil	-30 -40 -38	10			
	Cerebellum Vermis	0 -74 -24	11			



**Table 1, fMRI activations:** This table presents the main fMRI activations found when comparing NW vs. OB subjects for three different odor cues. **Figure 1 Brain connectivity.** This figure presents the different connections found for the NW vs. OB comparison depending on smell: Onion (1A), Acetone (1B) and Chocolate (1C). Red lines correspond to connections which were larger for NW subjects vs. OB. Blue lines correspond to stronger connections between OB vs. NW.