fMRI of the human amygdala using ultra-high field MRI. Parcellation of emotional human non-linguistic sounds

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Introduction: The amygdala has been related to a variety of emotional processes which can be identified in different parts of its structure [1-3]. However, the relationship between specific emotions and amygdala anatomy has not been entirely clarified. First, susceptibility artifacts have confounded MR imaging due to the proximity of the amygdala to the sphenoid sinus. The standard spatial resolution commonly used at a 3T MRI (3 mm)³ exacerbates susceptibility artifact, and has insufficient spatial precision to distinguish activations within the amygdala. To distinguish the anatomical substrate of various emotions, we performed an fMRI study at high field strength (7T MRI) and high spatial resolution with a 24-channel RF coil. We used auditory emotional human vocalization stimuli. In addition, *in vivo* derived probabilistic maps were used to further improve the precise localization of emotions within the amygdala. Here we demonstrate that using 7T MRI and *in vivo* probabilistic maps, we can establish correspondence between the functional organization of emotions and its anatomical location within the amygdala.

Methods: Eleven healthy volunteers, with no known history of any neurological or pathological condition, were scanned using a 7T whole body MR scanner (Siemens, Erlangen, Germany) with a 24-element phased array head coil (Nova Medical, Wilmington, MA, USA). Written informed consent was obtained. A whole-brain T1-weighted data set was first acquired for anatomical localization using an MP2-RAGE sequence [4]. Subsequently, 46 coronal slices were scanned for functional imaging covering the amygdala region with an interleaved silent steady state (ISSS) sequence [5] (TR/TE = 2500/25 ms; isotropic voxels of (1.5 mm)³; iPAT = 3; partial Fourier transform of 6/8). An improved auditory system was employed for clear audition (Sensimetrics Corporation, Malden, MA, USA). The experimental conditions consisted of 4 emotional non-linguistic human acoustic stimuli: laughter, crying, surprise and disgust. Block length was 30 s [3]. Functional data were linearly registered to the anatomical image for each subject. FMRI analysis were performed analyzed using FEAT (FSL, FMRIB, Oxford) at a single subject level, to ensure congruence between the activation maps and structural images. Data were spatially smoothed to 3 mm. Next, the *in vivo* probabilistic maps obtained from high field structural imaging and DTI [6,7] were linearly co-registered to the individual brains with FSL. The centroid of all subjects' activations to different emotional categories (z>2.7 and p<0.05 (corrected)) were plotted and 3D rendered together with the probabilistic maps (70 % threshold). This systematically classifies the position of the response associated with amygdala regions. Statistical comparisons contrasted the different experimental conditions: (laughter vs. crying; laughter vs. disgust; laughter vs. surprise; crying vs. surprise; crying vs. laughter; crying vs. disgust; disgust vs. surprise; disgust vs. laughter; surprise vs. disgust; surprise vs. crying). Participants were asked mentally to evoke personal emotional situations related to the acoustic stimuli.

Results: After scanning, participants reported personal involvement in the stimuli used. They rated contagiousness and naturalness, and all categories combined yielded an average rating of 62 %. The results revealed small but significant amygdala responses to the different emotional categories (Fig. 1. colour-coded). This figure also shows the 3D rendered centroids of emotional activations when data from all subjects were combined. The *in vivo* probabilistic maps helped to localize the emotional conditions within the amygdala and enabled the clustering of positive (laughter, surprise) and negative (crying, disgust) pathways.

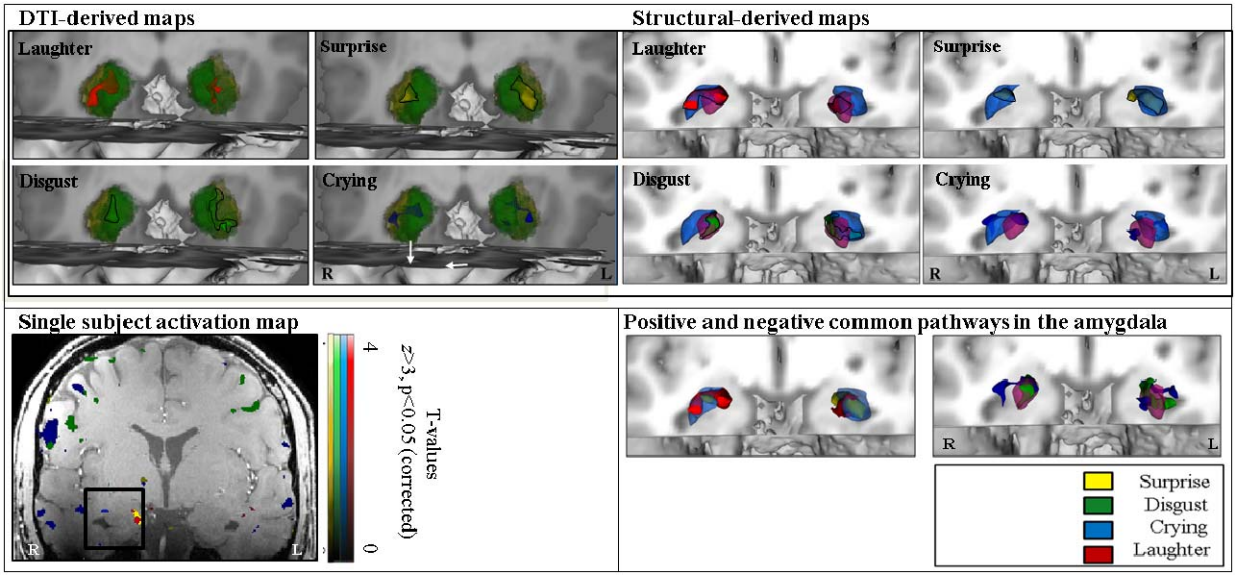

Figure 1. (upper row) DTI-derived and structural-derived maps of the amygdala and functional maps 3D rendered. Laughter and disgust tend to be located towards the medial clusters and surprise and crying towards the lateral clusters. (bottom row, left) Single subject activation map of positive and negative emotions (colour-coded). (bottom row, right) When common positive valence pathways (laughter, surprise) and negative (crying, disgust) were checked, positive emotions had an overlap in the lateral cluster while the medial segment covered the negative emotions.

Conclusions: These findings support previous hypotheses relating the amygdala to different emotions. Furthermore, using higher resolution at 7T and *in vivo* probabilistic maps of the amygdala, this study provided in one study the clearest account so far of the location of these emotions. The interpolation of postmortem maps to MR resolution may affect the localization of the significant small activations shown here. The techniques shown in this study will play an important role in the functional examination of emotional specificity within the amygdala and similar structures.

References: [1] Ball T et al. J Neurosci Methods 2009;180(1):57-70. [2] Phelps EA et al. Neuron 2005;48(2):175-187. [3] Sander K et al. Brain Res Brain Res Protoc 2003;11(2):81-91. [4] Marques JP et al. 2010;49(2):1271-1281. [5] Schwarzbauer C et al. Neuroimage 2006;29(3):774-782. [6] Solano-Castiella E et al. Neuroimage 2010;49(4):2958-2965. [7] Solano-Castiella E et al. Neuroimage 2009;47 (Supplement 1):S72.