Imaging Brain Regions with Susceptibility-induced Signal Losses using Gradient and Spin Echo Techniques

Krishna P. Miyapuram (krishna.miyapuram@unilever.com)
Department of Physiology, Development and Neuroscience, University of Cambridge, CB2 3DY, U.K.
Unilever R & D, 120, Olivier van Noortlan, Vlaardingen, 3133 AT, The Netherlands

Philippe N. Tobler (pnt21@cam.ac.uk)
Department of Physiology, Development and Neuroscience, University of Cambridge, U.K.

Wolfram Schultz (ws234@cam.ac.uk)
Department of Physiology, Development and Neuroscience, University of Cambridge, U.K.

Robert Osterbauer (robert@fmrib.ox.ac.uk)
FMRIB Centre, John Radcliffe Hospital, Headington, Oxford, OX3 9DU, UK

Christian Schwarzbauer (christian.schwarzbauer@mrc-cbu.cam.ac.uk)
MRC Cognition and Brain Sciences Unit, 15 Chaucer Road, Cambridge, CB2 7EF, U.K.

Abstract

Most fMRI studies use gradient-echo (GE) echo planar imaging (EPI) technique for acquiring blood-oxygenation level-dependent signals. Signal losses occur in the GE-EPI due to macroscopic field gradients occurring at air-tissue boundaries such as the orbitofrontal cortex. The spin-echo (SE) EPI is preferentially sensitized to smaller vessels and is considerably more robust against signal dropouts at air-tissue interfaces. We used double echo EPI pulse sequence with simultaneous acquisition of gradient-echo (GE) and Spin-echo (SE) signal on a 3T Siemens Magnetom Trio Scanner. A custom-built fMRI compatible olfactometer was used to deliver two appetitive and two aversive odours. In an event-related experiment design, the colour of the fixation cue (red or green) prompted participants to breathe-out and breathe-in the odour delivered for 2sec followed by intensity or pleasantness ratings on a visual analog scale. Brain activation was assessed at the onset of breathe-in cue and thresholded maps ($p<0.005$) were combined for the four subjects and two odours within each valence to depict the number of comparisons (out of a total of 8) that survived the threshold criterion. The results suggest that SE acquisitions might particularly be suitable for studies that focus on frontal, temporal and striatal regions, while the GE acquisitions might be suitable for studies focussing on parietal and occipital regions.

Keywords: orbitofrontal cortex; olfactory; fMRI; Echo planar imaging; spin echo; dropouts; susceptibility.

Introduction

FMRI studies generally use the gradient-echo echo-planar imaging (EPI) technique, which is susceptible to artefacts near the air-tissue boundaries such as the orbitofrontal cortex (OFC) and medial temporal lobe. OFC and amygdala are among the key structures involved in reward processing. Optimisation of fMRI signal in these regions would be necessary in order to understand the neural systems involved in reward processing.

The human orbitofrontal cortex occupies the ventral surface of the frontal part of the brain. It receives inputs from the five classic sensory modalities: gustatory, olfactory, somatosensory, auditory and visual. It also has reciprocal connections with the amygdala, cingulate cortex, insula, hippocampus, and striatum. There is evidence of direct ascending and descending pathways to dopaminergic cell groups (see Kringelbach and Rolls, 2004). Hence, anatomically the OFC is uniquely placed to integrate sensory information to modulate behaviour and has been implicated in emotional processing. A meta-analysis of neuroimaging studies by Kringelbach and Rolls (2004) has revealed a medial-lateral distinction, which has been proposed in monitoring rewards and evaluating punishments, respectively (see also review by Elliot et al., 2000). Further, Kringelbach and Rolls (2004) found a posterior-anterior trend in activations by more primary and abstract rewards, respectively. The amygdala is found in the medial part of the anterior temporal lobe. Amygdala has long been known implicated to play a role in negative emotions, such as fear and aversive stimuli. However, more recent studies suggest that amygdala is involved in processing appetitive as well as aversive stimuli (see review by Murray, 2007). Using human neuroimaging, Gottfried et al., (2003) have demonstrated that the OFC and the amygdala are crucial for maintaining the current value of a reward. Schoenbaum et al. (2003) show that following lesions of the basolateral amygdala, the cue selective neurons in the orbitofrontal cortex were more sensory driven and less sensitive to the motivational value of the outcome. Using two patients with focal bilateral amygdala lesions, Hampton et al. (2007) demonstrate that in a reversal learning task, the activity in the ventromedial prefrontal

cortex was significantly reduced. This reduction could not be explained by behavioural differences as Hampton et al. compared the trials with correct choice in patients and controls. These previous studies indicate a critical role for the amygdala in establishing representations of reward expectation in the prefrontal cortex, which in turn may be used to guide behavioural choice.

Neuroimaging studies using BOLD fMRI pose a particular challenge in identifying activations, particularly in the regions nearby air-tissue interface such as the orbitofrontal cortex and the parts of the temporal lobe. Functional MRI techniques such as the echo-planar imaging allow measurement of activations using microscopic changes in magnetic susceptibility incurring from blood flow and oxygenation changes (blood oxygenation level-dependent BOLD signal) arising from neural activity. Static macroscopic susceptibility effects near air-tissue interfaces causes artefacts that attenuate the MRI signal causing dropout in these regions. Ojemann et al. (1997) quantified these signal losses, primarily localized in the medial orbitofrontal and the inferior lateral temporal lobe. Larger artefacts were produced by increased echo time (TE). Various methods have been suggested for optimising the signal in the orbitofrontal cortex (see review by Kringelbach and Rolls, 2004). Deichmann et al. (2003) have suggested reduction of in-plane susceptibility gradients by using a tilted slice orientation and through-plane susceptibility gradients would be partly compensated by using a preparation gradient pulse. This technique was applied by Gottfried et al. (2002) for fMRI study of olfaction. Application of a correction gradient would only be practically possible to optimise signal across a limited region. Using a coronal slicing direction aligns the slices perpendicular to the predominant direction of the susceptibility induced field gradients. Hence, coronal slicing direction is recommended rather than the more commonly used axial slicing direction. However, more number of slices would be required for whole brain coverage in the coronal direction, thus increasing the acquisition time (TR). Shimming is a technique to make the magnetic field more uniform. Active shimming uses shim coils, while passive shimming uses a small magnetic material to compensate for field inhomogeneity. Cusack et al. (2005) observed increased sensitivity in the OFC in a reward-punishment task. Osterbauer et al. (2006) observed significantly stronger activation in the OFC using a visual-olfactory fMRI paradigm. However, using a mouth-shim resulted in increased subject movements, frequent swallowing and tactile stimulation of the tongue. Hence, the passive shimming should be used only for studies targeting specifically the regions affected by susceptibility gradients.

For cognitive studies with focus on these regions, it is desirable that alternative fMRI techniques are used (such as those mentioned above) for compensating the susceptibility-induced dropouts. We used double echo EPI pulse sequence with simultaneous acquisition of gradient echo (GE) and Spin echo (SE) signal. The use of spin-echo sequences for reducing susceptibility-induced dropouts is discussed in the next section. This technique required twice the acquisition time (TR), but offered the flexibility to compare activations obtained by the more common GE with those by the SE EPI.

Spin-Echo Sequences for Reducing Susceptibility Artefacts

Most fMRI studies use gradient-echo (GE) echo planar imaging (EPI) technique for acquiring blood-oxygenation level-dependent (BOLD) signals. In general, this technique is more sensitive to changes in the BOLD contrast than the spin-echo (SE) EPI. Signal losses occur in the GE-EPI due to macroscopic field gradients occurring at air-tissue interfaces. The SE-EPI is preferentially sensitized to smaller vessels and is considerably more robust against signal dropouts at air-tissue interfaces. Bandettini et al. (1994) have compared motor cortex activation using GE and SE EPI at 1.5 Tesla. They found that the BOLD contrast ratio for GE sequence was about twice that of the SE sequence. However, the SE sequences may provide a good alternative to GE-EPI for functional activation studies due to the reduced susceptibility artefacts. The SE technique would provide a better spatial resolution due to its sensitivity to small vessels.

Norris et al. (2002) tested brain activations obtained using SE EPI at 3 Tesla during a stroop colour-word matching task. They found activations in all regions described previously using GE-EPI in the same task. Additionally, they found activation in the frontopolar and ventral frontomedian cortices. They conclude that SE-EPI is sufficient for studies that require higher degree of spatial localization (specificity) or able to detect activation in regions affected by susceptibility gradients (sensitivity).

Parkes et al. (2005) compared the point-spread function of the BOLD response for GE and SE acquisitions at 3 Tesla. They used rotating wind-mill stimuli and found that the contrast to noise ratio was reduced by a factor of 3 in the SE technique compared with the GE technique suggesting lower sensitivity to BOLD changes in the SE technique. However, they find 13% reduction in the spatial extent of the BOLD response. Thus, SE technique is less sensitive to the presence of deoxyhaemoglobin in the draining veins that may be distant from the actual site of the neuronal activity. This could implicate a greater spatial resolution for fMRI studies using SE technique.

Hulvershorn et al. (2005) investigated spatial and temporal variations in GE and SE fMRI at 3 Tesla to a brief visual stimulus. They found that SE BOLD contrast has a smaller peak haemodynamic activation time (i.e. reaches its maximum amplitude more quickly) than the GE acquisition. The BOLD changes in response to increased neuronal activity occur earlier in the microvasculature and then propagate in to the venous compartment. Their results suggest that the SE-EPI offers superior localization to the site of activation at 3 Tesla, signifying improved spatial sensitivity.

Schmidt et al. (2005) compared GE and SE-EPI using a double-echo sequence at 3 Tesla during visual perception of faces. They found similar activations using both SE and GE sequences with smaller spatial extent and significantly reduced activation in the SE sequences. While the SE sequence significantly restored the signal in orbitofrontal cortex, a susceptibility-prone region, there was no significant activation detected in this region. Schmidt et al. conclude that using optimised GE sequences that reduce susceptibility artefacts (e.g. low echo time, TE) are sufficient to detect activations in regions such as orbitofrontal cortex. Their conclusion is opposite to that by Norris et al. (2002) study in which only the SE sequence was acquired.

Recently, Schwarzbauer et al. (2005) have reported that the SE fMRI overcomes susceptibility-induced signal losses in the inferior temporal lobe that is particularly relevant for studies of semantic processing. Using transient hypercapnia (breathing carbogen – 5% CO2 95% O2) as a global stimulus, Schwarzbauer et al. (2006) have compared the GE and SE data. They calculated a differential activation index based on the number of subjects showing significant activation. They found that SE was superior to the GE acquisition in the orbitofrontal cortex, olfactory cortex, gyrus rectus and temporal poles. They suggest that SE-EPI as a choice for cognitive studies that involve regions affected by magnetic field inhomogeneities, albeit with a lower sensitivity in the SE data due to the lack of contribution from static dephasing effects.

Using olfactory stimuli

Previous neuroimaging studies have demonstrated robust activations of the amygdala and caudal OFC in olfactory processing. Gottfried et al. (2002a, b) tested the effects of odour valence by pairing neutral faces with pleasant, neutral, and unpleasant odours with 50% probability. While bilateral amygdala was activated by all odours regardless of valence, the activations in the posterior orbitofrontal cortex was segregated into medial and lateral segments for pleasant and unpleasant odours, respectively (Gottfried et al., 2002a). Further, neural responses common to both appetitive and aversive learning in rostral and caudal OFC and appetitive learning responses were observed in the nucleus accumbens and amygdala (Gottfried at al. 2002b). Anderson et al. (2003) dissociated intensity from valence of odours, demonstrating the role of amygdala in intensity and that of the OFC in valence of odours. Winston et al. (2005) have demonstrated that the amygdala exhibits an intensity x valence interaction in olfactory processing. These previous neuroimaging studies suggest that olfactory stimuli would be more appropriate for investigating the activation in susceptibility induced dropout regions.

Experimental procedures

The experiment used a hybrid blocked-event design. 4 trials constituted one mini-block in which two odours were delivered. A total of four odours were used with two odours for each valence (appetitive and aversive). The appetitive odours were geranium (250µl) and a fragrance (200 µl) (Unilever Research, Port Sunlight, UK) and the aversive odours were rubber (300 µl) and body odour (100 µl) (described in Dematte et al., 2007). All the odours were diluted in 40 ml dipropylene glycol solvent (Quest International, Ashford, England). The two odours within each valence category were matched for pleasantness and intensity ratings. Using two odours allowed us to overcome the habituation effects due to repeated presentation of odours over trials during the course of the experiment.

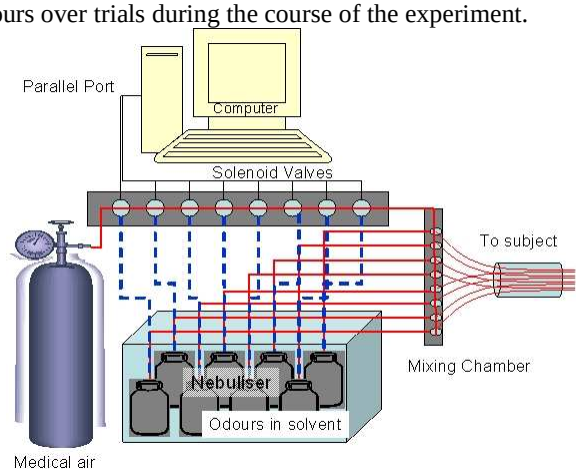

Figure – 1: Schematic diagram of olfactometer

The odours and a custom-built fMRI compatible olfactometer were provided by Robert Osterbauer, FMRIB centre, University of Oxford. The olfactometer consists of 8 computer-controlled valves that direct a stream of medical air (5 l/min) from a G-cylinder into one of the eight different lines of Teflon tubing. These lines are in turn connected to a nebuliser that uses the air stream to change the dissolved odorants into small particles. The outlets of each nebuliser are connected to a mixing chamber that combines the medical air stream with the odorised air. Participants held the tubes at a comfortable position away from their nose by their left hand with supporting cushion padding. A nasal mask was not used to avoid any odour left over from previous trials. A parallel port interface was used for computer controlled triggering of the eight solenoid valves to switch ON / OFF a particular odour.

A fixation '+' sign appeared at the centre of the screen for a Poisson distributed random inter-trial interval with mean 3 seconds. The fixation turned to red alerting the participants to breathe-out. After 1 second, the fixation turned green alerting the subjects to breathe-in. The red and green contingencies with breathe-out and breathe-in were counterbalanced across subjects. The odour was delivered to the subject for 2 seconds. The subjects then rated the odour for either pleasantness or intensity on a scale of -10 (very unpleasant / very weak) to +10 (very pleasant / very strong). The value of 0 was displayed at the middle of the scale as Neutral.

The data is presented from four participants who took part in the study. Participants had been pre-screened to exclude prior histories of neurological or psychiatric illness and gave informed consent. We conducted this pilot study on a 3 Tesla Siemens magnetom Trio Scanner. The research protocol was approved by the Cambridgeshire Local Research Ethics Committee, U.K.

Functional images using the double echo Gradient and spin echo acquisitions was performed on a 3 Tesla Siemens magnetom Trio Scanner. The imaging parameters were 22 slices of thickness 3 mm, slice gap 1mm, inter-scan interval of 3 sec and TE 30 ms. The in-plane resolution was 3.5 mm x 3.5 mm and the matrix size 64 x64. Images were analysed using SPM5 with the preprocessing steps of realignment, normalization to EPI template and smoothing with an isometric Gaussian filter with 8mm FWHM. Statistical analysis modelling the events at the onset of breathe-in cue convolved with the canonical HRF and its temporal and dispersion derivatives. The activation to appetitive and aversive odours was obtained using linear contrasts.

Results

The average pleasantness ratings (mean±SEM) on a scale of -10 to +10 for the two appetitive odours were 3.16±0.93 and 3.34±0.92 and for the two aversive odours were -2.31±1.11 and -2.75±1.31. The intensity ratings (mean±SEM) on a scale of -10 to +10 for the two appetitive odours were -0.77±0.71 and 0.39±1.35 and for the two aversive odours were 0.11±1.41 and -0.18±1.18. These ratings indicate that the valence of odours were distinguishable based on their pleasantness ratings but not by the intensity ratings. Further, there is less differentiation of ratings between the two odours for each valence.

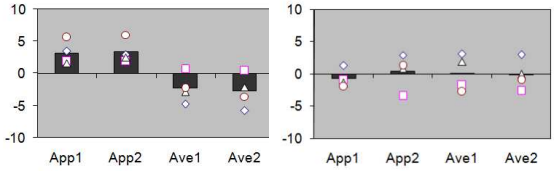

Figure - 2: Average pleasantness (top) and intensity (bottom) ratings for the odour stimuli

Brain activation was assessed at the onset of breathe-in cue for the four types of odours. Activation images were thresholded at $p<0.005$, uncorrected for multiple comparisons. These thresholded maps were combined for the four subjects and two odours within each valence to depict the number of comparisons (out of a total of 8) that survived the threshold criterion. A sensitivity measure was calculated as the average number of voxels activated for the appetitive and aversive odours. The number of voxels activated per brain area was calculated using the labels obtained from Talairach Daemon software (Lancaster et al., 2000) for all suprathreshold voxels. As the aim of this pilot study was to compare the Gradient-Echo (GE) and Spin-Echo (SE) acquisitions, the results are focussed on the sensitivity of these two acquisitions.

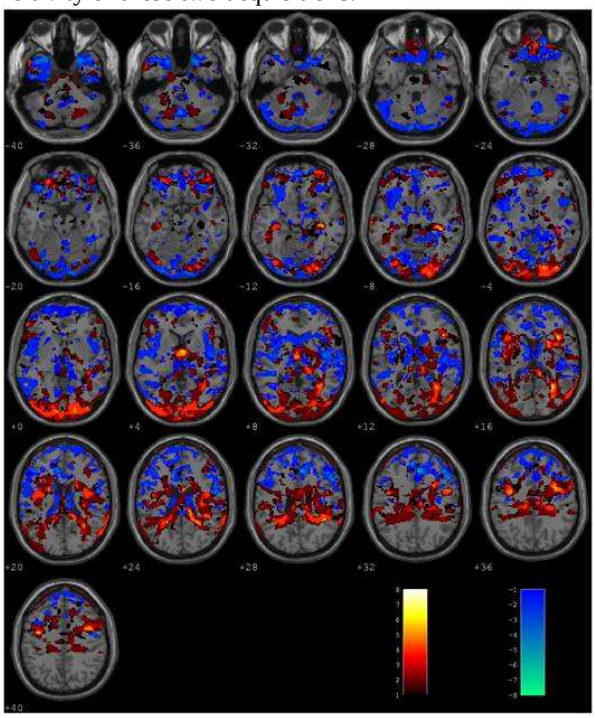

Figure – 3: Activations for appetitive odours for gradient echo (hot) and spin echo (cool) acquisitions. The colorscale indicates the number of subjects (4) x number of odours (2)

The GE acquisition had better sensitivity in the anterior cerebellum while the SE acquisition had better sensitivity in the posterior cerebellum (Figures 3 and 4 z = -40 to -16). The SE acquisition had better sensitivity in the anterior cingulate (z = 20 to 32, cool map), while the GE acquisition had better sensitivity in the cingulate gyrus and posterior cingulate (z = 24 to 36 hot map) and parahippocampal gyrus (z = -16 to -8 hot map). The SE acquisition particular seemed to have better sensitivity in the striatum (z = 8 to 12 cool map) and the inferior, medial frontal gyri (z > -12 cool map). The GE acquisition, on the other hand, had better sensitivity in the middle frontal and precentral gyri (z > 20 hot map). The SE sequence had greater sensitivity in the superior temporal gyrus (z = -28 to -24 cool map) , while GE detected sub-gyral activations in the frontal and temporal lobes (z = 16 to 24 hot map). The GE acquisition had a definite advantage in inferior parietal (z > 20 hot map) and middle occipital regions (z = -8 to 20 hot map). These results suggest that SE acquisitions might particularly be suitable for studies that focus on frontal, temporal and striatal regions, while the GE acquisitions might be suitable for studies focussing on parietal and occipital regions.

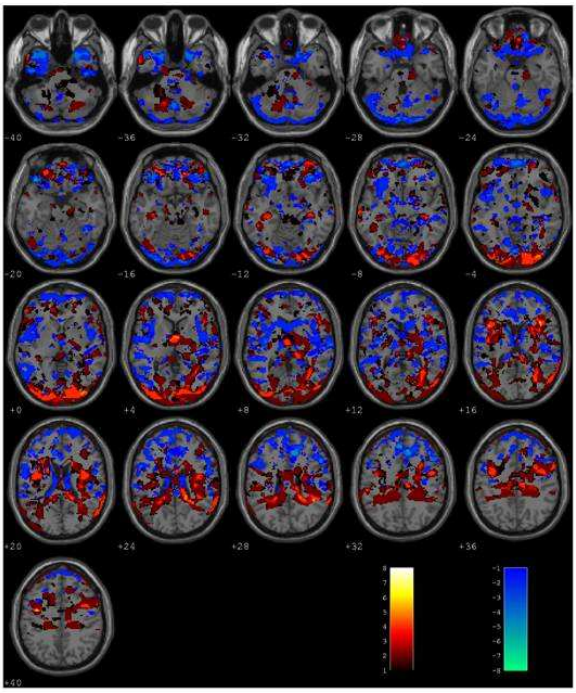

Figure – 4: Activations for aversive odours for gradient echo (hot) and spin echo (cool) acquisitions. The colorscale indicates the number of subjects (4) x number of odours (2)

This study attempted to resolve the apparent dilemma of the utility of SE sequences. In contrast to the usual group analysis (fixed or random effects), a completely different approach was used to measure the sensitivity of the different activations based on counting the number of suprathreshold activations to ensure that the differences between the two acquisitions can be clearly characterized. The SE acquisitions might particularly be suitable for studies that focus on frontal, temporal and striatal regions, while the GE acquisitions might be suitable for studies focussing on parietal and occipital regions.

Future directions

The advantage of using the double-echo acquisitions is that both the regularly acquired GE and the susceptibility insensitive SE are obtained with the compromise in temporal resolution requiring twice the repetition time (TR). The GE and SE acquisitions are pre-processed and analysed separately and the results are qualitatively compared. The difficulty with quantitatively comparing the two acquistions together is two-fold. Firstly, the comparison in drop out regions cannot be made as no signal is available in the GE sequences. This problem can be overcome by using an explicit mask obtained from the analysis of SE sequences to analyze the GE sequence data. Secondly, the sensitivity of the two sequences vastly differs depending on the brain region. Hence, a quantitative comparison between GE and SE sequences needs them to be weighted appropriately based on their sensitivity measures. One approach to combine the data from the two acquisitions would be to pick the maximum T-value of the two acquisitions. However, this can lead to inconsistencies in interpretation of linearly opposite T-contrasts (for example) in that a conclusion cannot be derived whether to declare a brain area as being activated or not. Establishment of validity of using the SE acquisitions and algorithms to integrate the results with GE acquisition needs to devised.

Acknowledgments

This research was funded by the Wellcome Trust and the MRC-Wellcome Behavioural and Clinical Neuroscience Institute (BCNI). KPM is supported by Cambridge Nehru Scholarship and Overseas Research Students Award Scheme, UK.

References

Anderson, A., Christoff, K., Stappen, I., Panitz, D., Ghahremani, D., Glover, G., Gabrieli, J., and Sobel, N. (2003). Dissociated neural representations of intensity and valence in human olfaction. Nat. Neurosci., 6:196–202.

Bandettini, P.A. (1994). Magnetic resonance imaging of human brain activation using endogenous susceptibility contrast, PhD Thesis, Medical College of Wisconsin.

Cusack, R., Russell, B., Cox, S., De Panfilis, C., Schwarzbauer, C., and Ansorge, R. (2005). An evaluation of the use of passive shimming to improve frontal sensitivity in fMRI. Neuroimage, 24:82–91.

Deichmann, R., Gottfried, J., Hutton, C., and Turner, R. (2003). Optimized EPI for fMRI studies of the orbitofrontal cortex. Neuroimage, 19:430–441.

Dematt`e, M., Osterbauer, R., and Spence, C. (2007). Olfactory cues modulate facial attractiveness. Chem. Senses, 32:603–610.

Elliott, R., Dolan, R., and Frith, C. (2000). Dissociable functions in the medial and lateral orbitofrontal cortex: evidence from human neuroimaging studies. Cereb. Cortex, 10:308–317.

Gottfried, J., Deichmann, R., Winston, J., and Dolan, R. (2002a). Functional heterogeneity in human olfactory cortex: an eventrelated functional magnetic resonance imaging study. J. Neurosci., 22:10819– 10828.

Gottfried, J., O'Doherty, J., and Dolan, R. (2002b). Appetitive and aversive olfactory learning in humans studied using eventrelated functional magnetic resonance imaging. J. Neurosci., 22:10829–10837.

Gottfried, J., O'Doherty, J., and Dolan, R. (2003). Encoding predictive reward value in human amygdala and orbitofrontal cortex. Science, 301:1104–1107.

Hampton, A., Adolphs, R., Tyszka, M., and O'Doherty, J. (2007). Contributions of the amygdala to reward expectancy and choice signals in human prefrontal cortex. Neuron, 55:545–555.

Hulvershorn, J., Bloy, L., Gualtieri, E., Leigh, J., and Elliott, M. (2005). Spatial sensitivity and temporal response of spin echo and gradient echo bold contrast at 3 T using peak hemodynamic activation time. Neuroimage, 24:216–223.

Kringelbach, M. and Rolls, E. (2004). The functional neuroanatomy of the human orbitofrontal cortex: evidence from neuroimaging and neuropsychology. Prog. Neurobiol., 72:341–372.

Murray, E. (2007). The amygdala, reward and emotion. Trends Cogn. Sci. (Regul. Ed.), 11:489–497.

Norris, D., Zysset, S., Mildner, T., and Wiggins, C. (2002). An investigation of the value of spin-echo-based fMRI using a Stroop colorword matching task and EPI at 3 T. Neuroimage, 15:719–726.

Ogawa, S., Lee, T., Kay, A., and Tank, D. (1990). Brain magnetic resonance imaging with contrast dependent on blood oxygenation. Proc. Natl. Acad. Sci. U.S.A., 87:9868–9872.

Ogawa, S., Tank, D., Menon, R., Ellermann, J., Kim, S., Merkle, H., and Ugurbil, K. (1992). Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging. Proc. Natl. Acad. Sci. U.S.A., 89:5951–5955.

Ojemann, J., Akbudak, E., Snyder, A., McKinstry, R., Raichle, M., and Conturo, T. (1997). Anatomic localization and quantitative analysis of gradient refocused echo-planar fMRI susceptibility artifacts. Neuroimage, 6:156–167.

Osterbauer, R., Matthews, P., Jenkinson, M., Beckmann, C., Hansen, P., and Calvert, G. (2005). Color of scents: chromatic stimuli modulate odor responses in the human brain. J. Neurophysiol., 93:3434–3441.

Osterbauer, R., Wilson, J., Calvert, G., and Jezzard, P. (2006). Physical and physiological consequences of passive intra-oral shimming. Neuroimage, 29:245–253.

Parkes, L., Schwarzbach, J., Bouts, A., Deckers, R., Pullens, P., Kerskens, C., and Norris, D. (2005). Quantifying the spatial resolution of the gradient echo and spin echo BOLD response at 3 Tesla. Magn Reson Med, 54:1465–1472.

Rorden, C, Brett, M (2000). Stereotaxic display of brain lesions. Behav Neurol, 12, 4:191-200.

Schmidt, C., Boesiger, P., and Ishai, A. (2005). Comparison of fMRI activation as measured with gradient- and spin-echo EPI during visual perception. Neuroimage, 26:852–859.

Schoenbaum, G, Setlow, B, Saddoris, MP, Gallagher, M (2003). Encoding predicted outcome and acquired value in orbitofrontal cortex during cue sampling depends upon input from basolateral amygdala. Neuron, 39:855-67.

Schwarzbauer, C., Raposo, A. & Tyler, L.K. (2005). Spin-echo fMRI overcomes susceptibility-induced signal losses in the inferior temporal lobes. NeuroImage, 26 (S1): 802.

Schwarzbauer C., Mildner T., Heinke W., Zysset S., Deichmann R., Brett M., Davis M.H. (2006). Spin-echo EPI – The method of choice for fMRI of brain regions affected by magnetic field inhomogeneities? Human Brain Mapping, Abstract No: 1049.

Tzourio-Mazoyer, N, Landeau, B, Papathanassiou, D, Crivello, F, Etard, O, Delcroix, N, Mazoyer, B, Joliot, M (2002). Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. Neuroimage, 15, 1:273-89.

Winston, J., Gottfried, J., Kilner, J., and Dolan, R. (2005). Integrated neural representations of odor intensity and affective valence in human amygdala. J. Neurosci., 25:8903–8907.