Available online at www.sciencedirect.com
ScienceDirect
Magnetic Resonance Imaging 26 (2008) 45–53
MAGNETIC RESONANCE IMAGING

Improved functional mapping of the human amygdala using a standard functional magnetic resonance imaging sequence with simple modifications

Carmen Morawetz[a], Petra Holz[a], Claudia Lange[b], Jürgen Baudewig[a], Godehard Weniger[b], Eva Irle[b], Peter Dechent[a,*]

[a]MR Research in Neurology and Psychiatry, Medical Faculty, Georg-August-University Göttingen, 37099 Göttingen, Germany
[b]Department of Psychiatry and Psychotherapy, Medical Faculty, Georg-August-University Göttingen, 37099 Göttingen, Germany

Received 20 March 2007; revised 13 April 2007; accepted 14 April 2007

Abstract

As the amygdala is involved in various aspects of emotional processing, its characterization using neuroimaging modalities, such as functional magnetic resonance imaging (fMRI), is of great interest. However, in fMRI, the amygdala region suffers from susceptibility artifacts that are composed of signal dropouts and image distortions. Various technically demanding approaches to reduce these artifacts have been proposed, and most require alterations beyond a mere change of the acquisition parameters and cannot be easily implemented by the user without changing the MR sequence code. In the present study, we therefore evaluated the impact of simple alterations of the acquisition parameters of a standard gradient-echo echo-planar imaging technique at 3 T composed of echo times (TEs) of 27 and 36 ms as well as section thicknesses of 2 and 4 mm while retaining a section orientation parallel to the intercommissural plane and an in-plane resolution of 2×2 mm^2. In contrast to previous studies, we based our evaluation on the resulting activation maps using an emotional stimulation paradigm rather than on MR raw image quality only. Furthermore, we tested the effects of spatial smoothing of the functional raw data in the course of postprocessing using spatial filters of 4 and 8 mm. Regarding MR raw image quality, a TE of 27 ms and 2-mm sections resulted in the least susceptibility artifacts in the anteromedial aspect of the temporal lobe. The emotional stimulation paradigm resulted in robust bilateral amygdala activation for the approaches with 2-mm sections only — but with larger activation volumes for a TE of 36 ms as compared with that of 27 ms. Moderate smoothing with a 4-mm spatial filter represented a good compromise between increased sensitivity and preserved specificity. In summary, we showed that rather than applying advanced modifications of the MR sequence, a simple increase in spatial resolution (i.e., the reduction of section thickness) is sufficient to improve the detectability of amygdala activation.

Keywords: fMRI; Gradient echo; Susceptibility artifacts; Medial temporal lobe; Emotion; Ekman faces; Spatial filter

1. Introduction

The amygdala is an important structure of the limbic system located in the anteromedial aspect of the temporal lobe. It is a core region in fear-related and many other emotional processes, such as emotional learning and memory, emotional modulation of memory as well as emotional influences on attention and perception [1–7]. Therefore, its functional characterization using modern neuroimaging modalities is of great interest, especially in the fields of psychiatry and psychology.

Functional magnetic resonance imaging (fMRI) using the blood oxygenation level-dependent (BOLD) effect described by Ogawa et al. [8,9] offers the possibility of monitoring brain function noninvasively. Since its first application in humans in 1992 [10–13], the focus has extended from the characterization of simple motor or sensory systems to higher cognitive processes. Consequently, the number of fMRI studies of the human amygdala published has steadily increased over the past 10 years, from less than 10 to about 100 per year (relying on a PubMed search for "fMRI" AND "amygdala", http://www.ncbi.nlm.nih.gov).

* Corresponding author. Tel.: +49 551 39 13141; fax: +49 551 39 13243.
E-mail address: pdechen@gwdg.de (P. Dechent).

0730-725X/$ – see front matter © 2008 Elsevier Inc. All rights reserved.
doi:10.1016/j.mri.2007.04.014

The standard method used in the vast majority of fMRI experiments is the gradient-echo (GE) echo-planar imaging (EPI) technique. The necessary T_2* weighting is achieved by image acquisitions with a sufficiently long effective echo time (TE). This provides the sensitivity to local magnetic field inhomogeneities caused by the intrinsic contrast agent deoxyhemoglobin and thereby enables indirect monitoring of brain function via the BOLD contrast. The optimal BOLD contrast is achieved with a TE close to the T_2* value of gray matter, which is dependent on the strength of the static magnetic field [10,14–16]. A TE longer than this T_2* value results in a reduced signal-to-noise ratio (SNR) without any further gain in BOLD sensitivity, whereas a shorter TE leads to an increased SNR but less BOLD sensitivity. GE-EPI is a fast method that allows for whole-brain imaging at an acceptable spatial resolution within a few seconds. However, because of its desired sensitivity to BOLD-related susceptibility effects, the standard T_2*-weighted GE-EPI technique is also sensitive to unwanted susceptibility effects caused by macroscopic field inhomogeneities. These occur at the borders of compartments with large differences in magnetic susceptibility, such as tissue and air-filled spaces, and are composed of signal dropouts and spatial distortions [17]. An area especially vulnerable to such susceptibility artifacts is the amygdala region.

Recently, the problems in imaging the orbitofrontal cortex as well as the medial and inferior temporal lobes when using the standard GE-EPI technique have been evaluated [18–20]; in addition, it has been questioned whether this technique is suitable for reliably characterizing amygdala function [21–23]. However, most of the recent studies relied on the standard technique with rather large voxel sizes (usually, in-plane dimensions of 3–4 mm and section thicknesses of 4–8 mm) and only sometimes moderately reduced TE (in some cases still up to 60 ms at a field strength of 1.5 T and 50 ms at 3 T) — two factors that are critical regarding the impact of susceptibility variations. Unfortunately, only a few of these studies documented sufficient data quality by presenting functional raw images (e.g., [21,24,25]). Furthermore, the artifact load may not have been well defined as common fMRI images display overlay color-coded functional activation maps onto standard anatomical images that do not have corresponding susceptibility artifacts.

Several methodological approaches have been implemented to address the issue of reliable mapping of the amygdala without, or at least with an acceptable amount of, artifacts in the target region. Those approaches include, for example, the use of tailored radiofrequency pulses [20,26,27], two-dimensional and three-dimensional z-shimming [28–32], slice-dependent TE variation [33] and spiral trajectories [34,35]. However, these methods are technically demanding, require alterations beyond a mere change of the acquisition parameter settings, and cannot be easily implemented by the user without changing the MR sequence code.

In contrast to these approaches, rather simple modifications at the acquisition parameter level, which are beneficial for the reduction of susceptibility artifacts, include the reduction of TE and the increase of spatial resolution (i.e., reduction of voxel size) [17,18,22,23,32,36,37]. As stated above, the chosen TE represents a tradeoff between BOLD sensitivity on the one hand and SNR as well as vulnerability to susceptibility variations on the other. Regarding spatial resolution, one has to take several factors into account. A rather low spatial resolution has the advantage of a higher SNR, which is particularly important when the expected changes of the MR signal are rather low. However, this principal increase in sensitivity is at the expense of specificity as a large amount of brain tissue is averaged into a single image voxel. This so-called partial volume effect might leave brain activation undetected, which is cancelled out by the averaging with nonactivated tissue in the same voxel. Furthermore, the vulnerability of the GE-EPI technique to susceptibility artifacts increases with decreasing spatial resolution, whereas the voxel dimension in the section direction is more critical than the in-plane dimensions [22]. As susceptibility gradients are not equally distributed in the brain, the orientation of the acquired sections is also critical regarding areas close to susceptibility borders, and there are conflicting suggestions concerning the optimal orientation [18,22,23,33,38,39]. However, section orientation has an immediate impact on the number of sections necessary to cover the whole brain. As a consequence of these partly counteracting mechanisms, the measurement parameters of the GE-EPI sequence chosen always represent a certain tradeoff, especially when whole-brain coverage within a few seconds is an important issue.

In the present study, we sought to find fMRI parameter settings that represent a good compromise to reliably image the amygdala region on the one hand and enable functional imaging of other brain areas with good functional sensitivity on the other. Furthermore, this technique ought to be available on standard MR systems and the necessary modifications should be easy to implement. According to the literature, we chose a section orientation parallel to the intercommissural (AC–PC) plane and a high in-plane resolution of 2×2 mm^2. Given these prerequisites, we performed simple modifications on a standard GE-EPI sequence regarding TE and section thickness, resulting in four GE-EPI versions for fMRI. BOLD sensitivity is more affected by susceptibility artifacts than image intensity [28]. Therefore, in contrast to previous reports, the main focus of our study was to evaluate the reliability with which activation of the amygdala can be detected using a standard emotional paradigm. Furthermore, we assessed the effect of spatial filtering in the course of data processing on the resulting activation maps.

2. Materials and methods

Eleven healthy subjects (age range, 20–30 years; mean±S.D., 25.2±2.7 years; five males) with normal or