Using Short TE $^1$H MRS Methodology for the Reliable Detection of GABA in the Human Amygdala

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Introduction

Everyone has experienced fear and anxiety. Their expression is also known as conditioning, in which the amygdala is believed to play a central role (1). Such conditioned responses are modulated by inhibitory GABA ($\gamma$-aminobutyric acid)-ergic circuits (2). Deficiencies in these inhibitory processes within the amygdala have been suggested to produce pathological conditions (3). Hence, measurement of GABA levels in the amygdala would offer the unique opportunity to explore the neurochemical basis of fear, anxiety, and associated pathologies. However, performing MRS in this region is challenging due to its small size and location with strongly inhomogeneous B$_0$ and testing B$_1$ conditions. The aim of this study was to use short TE $^1$H MRS methodology to overcome such limitations and to reliably detect GABA in the human amygdala.

Methods

Scans were performed on a 3T Verio system (Siemens AG, Erlangen, Germany) using a Tx/Rx birdcage coil (RAPID Biomedical, Rimpar, Germany). First- and second-order shims were carefully adjusted using FAST(EST)MAP (4). Single volume data from the amygdala were acquired for N = 8 volunteers using the spin echo full intensity acquired localized (SPECIAL) MRS technique (5) with the following scan parameters: VOI = 15x15x15 mm$^3$, TR/TE = 3000/6.6, number of averages = 256, and $T\text{_{acq}}$ = 1024 ms. Metabolite quantification was performed using LCModel (6) with a simulated basis set.

Results

Localized shimming resulted in water linewidths of 7.4 ± 1.0 Hz, and metabolite linewidths were estimated as 5.6 ± 1.6 Hz. Resulting spectra showed no major artifacts (Fig. 1). Data quantification yielded Cramér-Rao lower bounds (CRLBs) for GABA in the range of 12-17% with a mean of 14% indicating reliable detection. In addition, eleven metabolites were quantified with CRLB < 20% (Table 1) including glutamate (Glu), glutamine (Gln), and glutathione (GSH). GABA levels were elevated relative to other brain regions, e.g. occipital cortex.

Discussion

Using the spin echo-based SPECIAL MRS technique at short TE allowed the reliable detection of GABA in the human amygdala as part of a neurochemical profile of in total twelve metabolites. Careful adjustment of the RF Tx and shim settings was found as a prerequisite for obtaining sufficiently high data quality. Elevated GABA levels in the amygdala are tentatively assigned to an increased number of GABA-ergic circuits according to functionality. However, a systematic overestimation in the measurement cannot be entirely ruled out pending further investigation. Comparison with literature values was difficult, since only few MRS studies in the amygdala have been conducted (7, 8), where to the best of our knowledge no quantification of GABA was reported. Nevertheless, the results of this study suggest the suitability of the proposed methodology to study anxiety disorders and other psychopathological conditions attributed to abnormal functions of the GABA system.

References