

SHORT REPORT

Measurement of amygdala T2 relaxation time in temporal lobe epilepsy

P A Bartlett, M P Richardson, J S Duncan

J Neurol Neurosurg Psychiatry 2002;**73**:753–755

Objectives: To implement and validate the use of coronal dual echo T2 maps for the measurement of T2 relaxation time of the amygdala (AT2) as a rapid and reproducible method for identifying amygdala abnormality.

Methods: 20 healthy subjects and 25 patients with known hippocampal sclerosis (HS) were studied using a dual echo CSE sequence on a 1.5T MRI GE scanner. The T2 relaxation time of the amygdala was calculated and measured using a previously validated method.

Results: The mean control AT2 was 88.1 ms (SD 2 ms). The coefficient of reliability was good at 6.3% test-retest and 7.4% inter-rater. The upper limit of normal AT2 was 92 ms. AT2 was abnormal ipsilaterally in six, and bilaterally in three, of 20 patients with unilateral HS. Two of five patients with bilateral HS had unilateral abnormal AT2.

Conclusion: Reliable T2 measurements can be obtained in the amygdala, and may be useful in the detection of amygdala abnormality.

Hippocampal sclerosis (HS) is the most common abnormality underlying intractable temporal lobe epilepsy (TLE), with 60% to 70% of these patients becoming seizure free after surgery.¹

There is also electro-clinical evidence of seizure onset in the amygdala in 10% and simultaneous onset in the amygdala and hippocampus in 50% of patients with TLE.²

Although amygdala lesions may be seen in pathological specimens, the detection rate by visual assessment on magnetic resonance imaging (MRI) is very low.^{3,4}

The identification of an abnormality in the amygdala with non-invasive imaging is important as it could affect the extent of the surgical procedure performed in a patient with HS and also the post-surgical outcome in these patients. Furthermore, the identification of an abnormal amygdala in a patient with no overt abnormality would be very important in the consideration of possible surgical treatment.^{2,5}

Increased signal within the hippocampus on T2 weighted magnetic resonance scans is a well known feature of HS.⁶ In about 20% of patients with HS, there is also evidence of amygdala disease.⁷ Previously described techniques for measuring amygdala T2 relaxation times have involved the use of a 16 echo technique in an axial oblique plane parallel to and above the long axis of the hippocampus.² This technique prolongs the total examination time as it requires a separate data acquisition.

The aim of this study was first to implement and evaluate AT2 mapping using sequences that are used for clinical imaging and T2 measurements of the hippocampus⁸ and secondly, to examine whether a randomly selected subgroup of patients with HS have abnormally increased amygdala T2 measurements, and whether this subgroup had specific clinical characteristics.⁵

METHODS

Twenty healthy subjects and 25 patients with MRI evidence of HS according to qualitative and quantitative criteria⁹ were scanned using a dual echo conventional spin echo sequence. All scans were obtained on a 1.5T IGE Signa Echospeed MRI scanner (Milwaukee, WI). Twenty eight contiguous 5 mm thick sections were obtained with the sections orientated in the coronal oblique plane, in the same axis as the brain stem, orthogonal to the hippocampus. The parameters were TR=2000/TE1=30, TE2=120/Inex with a 192×256 matrix and a 18×24 cm field of view. Amygdala T2 relaxation times were obtained from a 5 mm section in the plane of the anterior brain stem and anterior to the head of hippocampus.

Image data were transferred to a Sun Microsystems (Mountain View, CA) workstation and converted to a variant of the University of Carolina's "/usr/image" format. Pixel by pixel T2 maps were calculated from the images by using the expression $T2 = (TE2 - TE1) [\ln(S1/S2)]$, where S1 and S2 are the signal intensity in the early echo and late echo images, with echo times TE1 and TE2 respectively. T2 maps were presented and regions of interest drawn using the Dispimage (University of London, London, UK) image display program.¹³ The section anterior to the head of the hippocampus was used for the amygdala T2 measurements. Elliptical regions of interest were placed within the amygdala and were as large as they could be, typically 20 mm², avoiding boundaries that would give rise to partial volume effects (fig 1).

The T2 maps of the healthy subjects were measured twice with an interval of two weeks by one rater and measured once by another rater. Subsequently, the T2 maps of the healthy subjects and the patients were blinded and again measured twice by one rater and once by the second rater to establish test-retest and inter-rater reliability.

Statistics

Amygdala T2 (AT2) data were analysed using SPSS 9.0 (SPSS, Chicago, IL) on a Dell PC. Test-retest reliability and inter-rater reliability were assessed on 40 amygdalae from the healthy subjects and 50 amygdalae from the HS patient group by calculating the coefficient of reliability,¹⁴ which is a stringent test of repeatability and is calculated as $2 \times$ standard deviation of the mean difference between two measures divided by the mean of both measures. The normal range of AT2 was defined as the control mean (2 SD).

Fisher's exact and Mann-Whitney tests were used to evaluate the association between categorical and continuous variables and abnormal AT2 times.

Abbreviations: HS, hippocampal sclerosis; TLE, temporal lobe epilepsy; MRI, magnetic resonance imaging

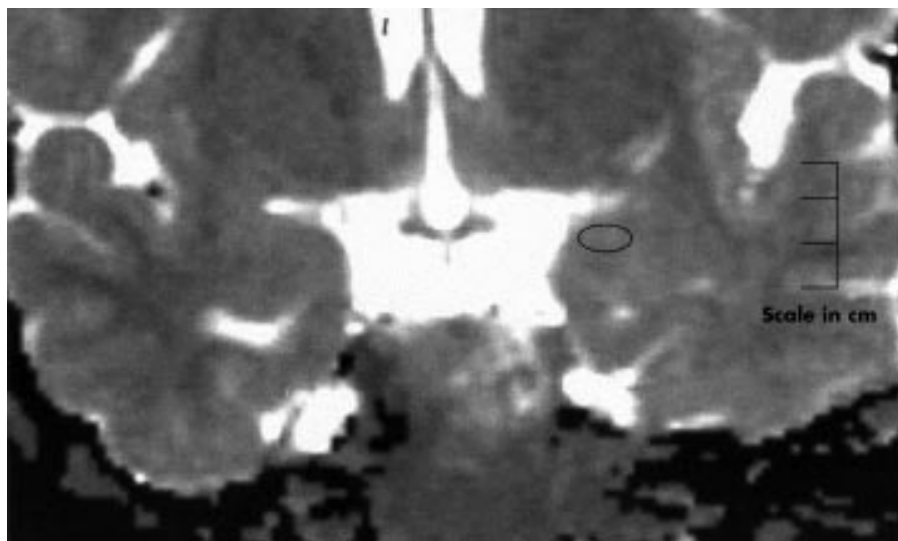


Figure 1 Placement of region of interest on T2 calculated image.

RESULTS

Evaluation of measures of amygdala T2 relaxation times in a control population

Data were available from 40 amygdalae in 20 healthy subjects. There was no difference in AT2 between the left and the right side in healthy controls. Mean AT2 in the control group was 88.1 ms with a standard deviation of 2 ms. The upper limit of normality of AT2 was defined as the control mean (2 SD), thus an AT2 value of greater than 92 ms was considered abnormal.

Reliability of measures

The test-retest repeatability in the total of 20 controls and 25 patients was -0.4 (2.7) ms and the inter-rater repeatability was 0.5 (3.2) ms, which gives a coefficient of repeatability of 6.3% and 7.4% respectively.

Evaluation of measures of amygdala T2 relaxation times in a patient population

Data were available from 50 amygdalae in 25 patients with well documented TLE on clinical and EEG grounds—10 with MRI evidence of right HS, with MRI evidence of left HS and five with bilateral HS on quantitative grounds (fig 2).⁹

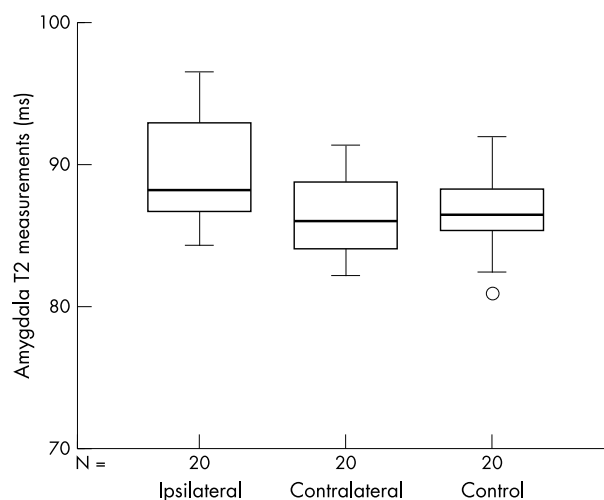


Figure 2 Boxplot (showing median, quartiles, smallest and largest values, and outlier) of the T2 measurements of the ipsilateral amygdala in patient group with unilateral hippocampal sclerosis in comparison with the contralateral amygdala of same group and the control group.

Amygdala T2 mapping in patients with right HS

Six of the 10 patients measured had normal T2 measurements—that is, each amygdala measured less than 92 ms.

Three patients had a unilateral raised measurement on the right side—that is, greater than 92 ms.

One patient had bilaterally increased T2 measurements. The left measuring 92 ms and the right measuring 94.1 ms.

Amygdala T2 mapping in patients with left HS

Five of the 10 patients measured had normal T2 measurements—that is, each amygdala measured less than 92 ms.

Three patients had a unilaterally raised measurement on the left side—that is, greater than 92 ms.

Two patients had bilaterally increased T2 measurements but with the left measurement greater than the right.

Amygdala T2 mapping in patients with bilateral HS

Three of the five patients had normal T2 measurements—that is, each amygdala measured less than 92 ms.

Two patients had increased T2 measurements on the right only. The hippocampal T2 measurements were equally increased bilaterally.

Clinical correlates

Age of onset of seizures, history of prolonged early childhood convulsion, duration of epilepsy, frequency of seizures, frequency of secondarily generalised seizures, and complex partial seizures were not significantly related to AT2 being normal or abnormal.

DISCUSSION

AT2 mapping using the coronal dual echo conventional spin echo technique that was used for producing proton density and T2 weighted images and to calculate HT2, was straightforward to implement. The excellent inter-rater and intra-rater repeatability indicated the method was reliable.

It was an easy and reliable technique to perform and can be added to the current routine measurement protocol, with a processing and measurement time of five minutes per case.

In accordance with other studies of AT2 measurements,² 44% of patients with HS also had an increased AT2 ipsilateral to increased HT2 and bilateral raised AT2 in 3 of 20 (15%), with the higher AT2 value ipsilateral to the HS.

The placement of the region of interest requires care and as the slice thickness of the imaging sequence is 5 mm, there may be some partial volume effect with tissue other than amygdala being included in the measurement. It is possible that there could be some residual high signal tissue from the hippocampus present in the region, and great care was taken to guard against this.

The spatial resolution of the T2 maps does not permit reliable measurements of individual amygdala subnuclei.

As already discussed, the dual echo method is easy and reliable to acquire but although it gives a reproducible result, the values given are not the true T2 values compared with the 16 echo technique.⁸ In a clinical setting however, in which the important issue is whether the value is normal or not, this is not a concern.

As with studies of amygdala volumetrics,¹⁰⁻¹² there were no evident clinical correlations to the coexistence of high AT2 with HS.

The pathological basis of increased AT2 has included amygdala sclerosis and micro dysgenesis.² As the patients were randomly selected for this study, only three have proceeded to surgery and the pathological material is not available as piecemeal removal of the amygdala is used in anterior temporal lobe resection at our hospital.

Post-surgical follow up studies will determine whether raised AT2 affects outcome after anterior temporal lobe resection and may lead to different surgical approaches for patients with high or low AT2. The further application of this technique will permit routine measurement of the AT2 and permit exploration of the relevance of raised AT2 values in patients with no visually evident abnormality and normal hippocampal quantification. These studies are now underway.

ACKNOWLEDGEMENTS

We are grateful to the National Society for Epilepsy for their support and to Drs B E Kendall and JM Stevens for their expert neuroradiological evaluation of the images.

Authors' affiliations

P A Bartlett, M P Richardson, J S Duncan, MRI Unit, National Society for Epilepsy, Chalfont St Peter, Buckinghamshire, UK, and Department of Clinical and Experimental Epilepsy, Institute of Neurology, London, UK

Correspondence to: Professor J S Duncan, National Society for Epilepsy, Chalfont St Peter, Buckinghamshire SL9 0RJ, UK; j.duncan@ion.ucl.ac.uk

Received 17 May 2002

In revised form 12 August 2002

Accepted 21 August 2002

REFERENCES

- 1 **Berkovic SF**, McIntosh AM, Kalnins RM, *et al.* Preoperative MRI predicts outcome of temporal lobectomy: an actuarial analysis. *Neurology* 1995;**45**:1248-50.
- 2 **Van Paesschen W**, Connelly A, Johnson C, *et al.* The amygdala and intractable temporal lobe epilepsy: A quantitative magnetic resonance study. *Neurology* 1996;**47**:1021-31.
- 3 **Hudson LP**, Munoz DG, Miller L, *et al.* Amygdaloid sclerosis in temporal lobe epilepsy. *Ann Neurol* 1993;**33**:622-31.
- 4 **Miller LA**, McLachlan RS, Bouwer MS, *et al.* Amygdalar sclerosis: preoperative indicators and outcome after temporal lobectomy. *J Neurol Neurosurg Psychiatry* 1994;**57**:1099-105.
- 5 **Van Paesschen W**, King MD, Duncan JS, *et al.* The amygdala and temporal lobe simple partial seizures: a prospective and quantitative MRI study. *Epilepsia* 2001;**47**:857-862.
- 6 **Grunewald RA**, Jackson GD, Connelly A, *et al.* MR detection of hippocampal disease in epilepsy: factors influencing T2 relaxation time. *AJNR* 1994;**15**:1149-56.
- 7 **Kalviainen R**, Salmenpera T, Partanen K, *et al.* MRI volumetry and T2 relaxometry of the amygdala in newly diagnosed and chronic temporal lobe epilepsy. *Epilepsy Res* 1997;**28**:39-50.
- 8 **Duncan JS**, Bartlett PA, Barker GJ. Technique for measuring hippocampal T2 relaxation time *AJNR* 1996;**17**:1805-10.
- 9 **Woermann FG**, Barker GJ, Birnie KD, *et al.* Regional changes in hippocampal T2 relaxation and volume: a quantitative magnetic resonance imaging study of hippocampal sclerosis. *J Neurol Neurosurg Psychiatry* 1998;**65**:656-64.
- 10 **Salmempera T**, Kalviainen R, Partanen K, *et al.* Hippocampal and amygdaloid damage in partial epilepsy: a cross-sectional MRI study of 241 patients. *Epilepsy Res* 2001;**46**:69-82.
- 11 **Cendes F**, Andermann F, Gloor P, *et al.* MRI volumetric measurement of amygdala and hippocampus in temporal lobe epilepsy. *Neurology* 1993;**43**:719-25.
- 12 **Guerreiro C**, Cendes F, Li LM, *et al.* Clinical patterns of patients with temporal lobe epilepsy and pure amygdala atrophy. *Epilepsia* 1999;**40**:453-61.
- 13 **Plummer DL**. Dispimage, a display and analysis tool for medical images. *Rev Neuroradiol* 1992;**5**:489-95.
- 14 **Bland JM**, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986;**8**:307-10.