Estimation of the onset time of cerebral ischemia in rats using $T_{1\rho}$ MRI

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Introduction

The duration of ischemia is one of the most important factors determining the choice of patient management at hospital admission. Thrombolysis with rt-PA must be initiated within 3-6 hours of onset of symptoms to have beneficial effect on patient outcome. Hypothermia may be beneficial even if applied after 6 hours of the onset [1] and new treatment strategies may have other time limits. A confounding factor for assessment of the onset is due to occurrence of stroke while asleep and/or in the absence of observers. MRI provides a large repertoire of techniques to detect acute stroke, including diffusion and perfusion MRI, yet their value for determining the age of ischemia from one time point measurement is debated. It has been shown that ^{23}Na MRI signal intensity increases as a function of ischemia duration, thus ^{23}Na signal has been termed as the "ticking clock of stroke" [2-4]. However, only a few clinical centers have MR scanners capable of doing ^{23}Na MRI. There is a study showing the changes in absolute T_2 as a possible method for onset time estimation [5]. However, T_2 changes are ambiguous at the early stages of stroke. It is well established that $T_{1\rho}$ MRI is a sensitive and early index of irreversible ischemia as a result of either permanent or transient middle cerebral artery occlusion (MCAo) in rats. Furthermore, absolute $T_{1\rho}$ shows a constant linear increase as the ischemia evolves. In the present work we have examined the ability of absolute $T_{1\rho}$ to indicate the onset time from ischemia in rat models of stroke.

Methods

MRI data from male Wistar rats (n=29, weight ranging from 200-300 g), with either a transient middle cerebral artery occlusion (MCAo) [6] of 60 minutes (n=15) [7], 90-100 minutes (n=3) [8] and (n=8) [9] or permanent MCAo (n=3) [10] were retrospectively used for this study. MRI experiments were performed in a horizontal 4.7 T magnet interfaced to a Varian Inova console. MRI scans were acquired at multiple time points during ischemia and/or after reperfusion. Either a Litz-type volume coil (Doty Scientific, Columbia, SC, USA) and a dual-loop surface coil was used as transmitter and receiver respectively, or a quadrature half-volume coil as transmitter-receiver (HF Imaging LLC, Minneapolis, MN, USA), or a volume coil as transmitter and a quadrature half-volume coil as receiver (Rapid Biomedical GmbH, Rimpar, Germany). Fast spin-echo (FSE) readout (64 x 128 pixels, echo spacing 10 ms, FOV 2.56 x 2.56 cm^2, TR=2.5 s) or linescan method (1x128 pixels, line 3 mm x 3 mm x 35 mm, TE=15 ms) was used for $T_{1\rho}$ MRI. Absolute $T_{1\rho}$ data were acquired using conventional spin lock technique (AHP-SL-AHP) (B_1=0.4 G). Values were calculated as the mean from a small ROI positioned at the core of the ischemic lesion. The location for the ROI was decided visually based on the early changes in $T_{1\rho}$ and D_{av}. A corresponding homologic contralateral ROI was chosen accordingly.

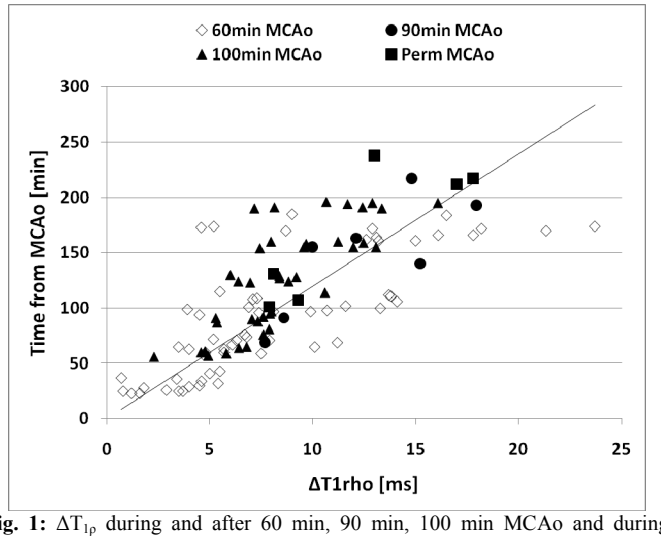

Fig. 1: $\Delta T_{1\rho}$ during and after 60 min, 90 min, 100 min MCAo and during permanent MCAo and the linear trendline of all the data. The trendline was forced through origo.

Table 1: Actual and estimated (from $\Delta T_{1\rho}$) mean ischemia times from MCAo and the differences between them for all MCAo data. Values are shown as mean ± S. D.

Time [min]	Mean measured time from MCAo [min]	Mean estimated time from MCAo [min]	Mean difference (estim-meas) [min]	Mean difference (estim-meas) [%]
20-40	29 ± 5	35 ± 19	6 ± 18	22 ± 60
40-80	64 ± 9	73 ± 23	9 ± 21	15 ± 33
80-120	99 ± 10	102 ± 18	3 ± 23	3 ± 30
120-180	154 ± 17	137 ± 55	-17 ± 49	-12 ± 30
180-240	199 ± 15	159 ± 42	-41 ± 39	-21 ± 20

Results

The time course for $\Delta T_{1\rho}$ (ipsi-contra) that follows either a long transient or permanent MCAo shows a correlation with time from MCAo (Fig. 1). A trendline taking into account the $\Delta T_{1\rho}$ data points from 90-100 min and permanent MCAo data showed a linear correlation of

$$\text{Time(from MCAo)} = 13.8 * \Delta T_{1\rho}$$

where R=0.77 ($p<0.001$). The $T_{1\rho}$ data from 60 min MCAo showed large variation and thus resulted in larger errors in onset time estimation. With the 60 min MCAo data the R was decreased to 0.70 ($p<0.001$). Values from animals exhibiting ΔCBF >100 ml/100g/min at between MCAo and reperfusion often showed high $\Delta T_{1\rho}$ values leading to overestimation of ischemia duration. Statistical data is given in Table 1.

Conclusions

The results indicate that $\Delta T_{1\rho}$ provides a good estimate for the duration (or onset) of ischemia in permanent MCAo rats, a model that is closest to the human non-reperfusing stroke. Using $\Delta T_{1\rho}$ as the sole measure with linear correlation, ischemia duration is obtained with ±20% accuracy during the first 4 hours of stroke. At around 1.5-2 h from the onset, when a patient may make it to hospital, the mean error was 3 ± 23 minutes suggesting a valuable estimate of the onset time. This prediction is somewhat compromised in transient MCAo. However, in animals with 90 - 100 min MCAo, prediction of onset from $\Delta T_{1\rho}$ data is close to that of permanent MCAo probably due to the fact that long MCAo will inevitably result in irreversible ischemia. We envisage that multiparametric MRI, incorporating diffusion, T_2 and CBF data, will improve accuracy of onset time determination also after transient brain ischemia. In this study a B_1 field of 0.4 G was used. Higher B_1 would also increase the contrast and thus potentially the accuracy of this estimation, but would hamper clinical feasibility due to higher SAR.

References:

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