Dynamic dephasing contrast in developing cerebral ischaemic infarction in rat

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Introduction

Acute cerebral ischaemia is associated with compensatory haemodynamic and metabolic changes including increased oxygen extraction ratio and redistribution of cerebral blood flow through collateral vasculature. As a result of these adaptive processes deoxyHb builds up in ischaemic tissue leading to expression of negative BOLD in MRI [1, 2]. DeoxyHb induced susceptibility changes have recently been studied by Carr-Purcell T_2 (CP-T_2) MRI [3] owing to an inherent property of CP sequence to weight the echo signal to dynamic susceptibility effects by varying the echo spacing [4].

Previous evidence shows that the negative BOLD, as revealed by Hahn echo T_2, is detectable in focal cerebral ischaemia only for the first hour or so [2], possibly due to decreased oxygen consumption ($CMRO_2$) and oedema formation. To further examine the time-dependent transverse relaxation and tissue susceptibility changes in the developing infarction, we have quantified CP-T_2 with short and long interpulse delay (τ_{CP}) together with diffusion in the rat brain after exposure to middle cerebral artery occlusion (MCAo).

Methods

Wistar rats were anesthetized with 0.8-1.5% halothane in N_2O/O_2 (70%/30%). The gas composition and the core temperature were monitored on-line and normothermia was maintained either by an electrical heating element during surgical procedures or circulating warm water in a heating pad in the magnet bore.

Focal cerebral ischaemia was induced (day 0) by transient middle cerebral artery occlusion (MCAo) using the intraluminal thread method [5]. Animals (n = 3) were transferred into the magnet after complete insertion of occluder. MRI variables were quantified 60 minutes after MCAo following in-bore retraction of the occluder thread. The animals were reanesthetised with halothane for further MRI examinations on day 1, 2, 3, 5 and 7 after MCAo.

The MRI experiments were carried out in a 4.7 T horizontal magnet interfaced to a Varian ^{UNITY}INOVA spectrometer console (Varian Associates, Palo Alto, CA, USA), using a quadrature surface coil as a transmitter/receiver. The transverse images covering MCA territory were positioned according to T_1-weighted coronal pilot images. D_{av} was quantified using Hahn echo sequence with four bipolar gradients along each gradient axis [6] with b values of 0-1000 s/mm^2 (TR = 1.5 s, TE = 56 ms, 2 averages, voxel size 0.11x0.47x2 mm^3). CP-T_2 was acquired with fully adiabatic multi-echo spin-echo sequence using hyperbolic secant (HS1) pulses in CP train, an adiabatic half passage pulse for spin excitation and a pair of HS1 pulses for slice selection and spin refocusing (TR = 2.5 s, 2 averages, voxel size 0.11x0.31x2 mm^3). Different TEs (15, 55, 95 ms) were obtained either by increasing the inter-pulse delay between the centres of HS1 pulses (τ_{CP} = 2.5-20 ms; referred to as long τ_{CP}) or increasing the number of HS1 pulses (0, 16, 32) and keeping τ_{CP} constant (τ_{CP} = 2.5 ms; referred to as short τ_{CP}).

Absolute D_{av}, CP-T_2 and relative susceptibility were analysed in the regions-of-interest (ROI) centred to ipsilateral striatum. Relative susceptibilities [%] were determined from long and short τ_{CP} CP-T_2-weigted images at TE = 55 or 95 ms as $(SI_{short\ \tau CP} - SI_{long\ \tau CP})/SI_{long\ \tau CP}$ [4]. The absolute MR parameters were fitted by least square fitting to a single exponential function of b-values and TEs, respectively. Data are presented as mean ± SEM and Student's t-test was used for statistical analysis.

Results

Low D_{av} (Fig. 1D) confirmed the presence of ischaemia in striatum after 60 min MCAo. A strong hyperintensity was evident in CP-T_2-weighted images (TE = 95 ms) one day after MCAo and beyond as MRI sign of infarction (Fig. 2; upper and middle rows). Analyses of relative susceptibility in developing infarct showed decreased values calculated from signal intensities at both echo times in ROI (Fig. 1C) as well as in subtracted CP-T_2-weighted images (Fig. 2; bottom row). Decreased signal in relative susceptibility images was evident until day 3 after MCAo followed by slow return towards value detected in non-ischaemic tissue. D_{av} recovered to control level by day 3 after MCAo (Fig. 1D).

Conclusions

The CP-T_2 method used reveals altered dynamic dephasing effects caused by diffusion through field gradients and exchange [4]. We show decreased signal intensity in relative susceptibility images in developing infarction during the first three days. The time course of susceptibility contrast detected in developing infarction closely follows oedema formation [7, 8] and it is likely that cell swelling and cell morphological changes [8] reduce endogenous microscopic susceptibility gradients in the tissue. In the ischaemic tissue, D_{av} was low on a day 0, while relative susceptibility was still normal (Fig. C, D). Therefore, reduced diffusion as such would not explain the observation. The exchange contributions would involve chemical exchange between water and macromolecular protons and molecular exchange of hydration water. The fact that the former exchange pathway is pH sensitive, yet the signal change in susceptibility images observed is not present in the acidotic tissue within the first hour of ischaemia indicates that chemical exchange is not predominant mechanism in contrast generation. It is interesting to note that time course of the altered susceptibility contrast closely resembles that of MT contrast [7, 9], suggesting that also dipolar effects involving exchange of magnetisation between bulk and macromolecular pools may contribute to our observation in association with altered tissue microenvironment.

Acknowledgements

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References

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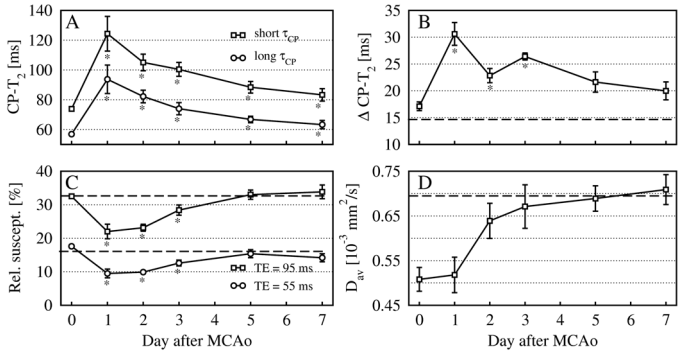

Fig. 1. CP-T_2 (**A**), difference of short and long τ_{CP} CP-T_2 (**B**), relative susceptibility (**C**) and D_{av} (**D**) in ipsilateral striatum. * denotes $P < 0.05$ relative to day 0 value. Dashed line represents the respective value in non-ischaemic tissue.

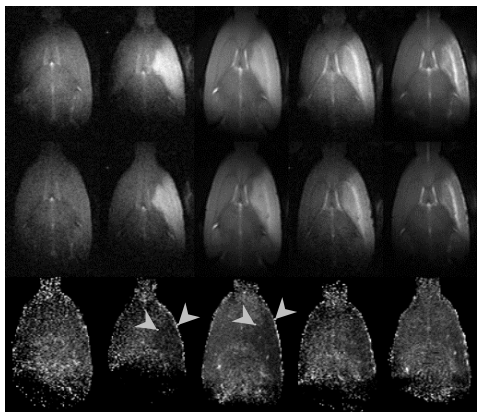

Fig. 2. Short (upper row) and long (middle row) τ_{CP} CP-T_2-weighted images (TE = 95) and images of relative susceptibility (bottom row) acquired, from left to right, on a day 0, 1, 2, 3 and 7, after right MCA occlusion. Note reduced dynamic dephasing (arrow heads) in the area of infarction on a day 1 and 2 post ischaemia.