Correlation of oxygenation and perfusion sensitive MRI with invasive micro probe measurements in healthy mice brain☆,☆

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Abstract

The non-invasive assessment of (patho-)physiological parameters such as, perfusion and oxygenation, is of great importance for the characterization of pathologies e.g., tumors, which may be helpful to better predict treatment response and potential outcome. To better understand the influence of physiological parameters on the investigated oxygenation and perfusion sensitive MRI methods, MRI measurements were correlated with subsequent invasive micro probe measurements during free breathing conditions of air, air+10% CO2 and 100% O2 in healthy mice brain.

MRI parameters were the irreversible (R2), reversible (R2') and effective (R2) transverse relaxation rates, venous blood oxygenation level assessed by quantitative blood oxygenation level dependent (qBOLD) method and cerebral blood flow (CBF) assessed by arterial spin labeling (ASL) using a 7T small animal MRI scanner. One to two days after MRI, tissue perfusion and pO2 were measured by Laser-Doppler flowmetry and fluorescence quenching micro probes, respectively. The tissue pO2 values were converted to blood oxygen saturation by using the Hill equation. The animals were anesthetized by intra peritoneal injection of ketamine-xylazine-acepromazine (10-2-0.3 mg/ml·kg).*

Results for normal/hypercapnia/hyperoxia conditions were: R2[s^-1] = 20.7/20.4/20.1, R2[s^-1] = 31.6/*

Korrelation oxygenierungs- und perfusionssensitiver MRT mit invasiven Mikrosondenmessungen im gesunden Mäusehirn

Zusammenfassung

Die nicht-invasive Erfassung (patho-)physiologischer Parameter, wie Perfusion und Oxygenierung, ist von wichtiger Bedeutung für die Charakterisierung von Pathologien wie Tumoren und erlaubt eine Prognose über den möglichen Erfolg einer Behandlung. Für ein besseres Verständnis des physiologischen Einflusses auf die oxygenierungs- und perfusionssensitiven MRT-Methoden wurden die MRT-Messungen mit invasiver Mikrosondenmessung im gesunden Mäusehirn während freier Atmung von Luft, Luft+10%CO2 und 100%O2 miteinander korreliert.

Die am 7T-Kleintierscanner untersuchten MRT-Parameter waren die irreversible (R2), reversible (R2') und effektive (R2) transverse Relaxationsrate, die mittels Quantitative Blood Oxygenation Level Dependent (qBOLD) erfasste venöse Sauerstoffsättigung und der mittels Arterial Spin Labeling (ASL) erfasste zerebrale Blutfluss (CBF). Die Mikrosonden erfassten die Gewebeperfusion mit Hilfe der Laser-Doppler-Flussmessung und die Gewebe-pO2 mit Hilfe der Fluoreszenzlöschung. Die Gewebe-pO2 wurde*

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29.6/25.9, R2'[s-^1] = 10.9/9.2/5.7, qBOLD venous blood oxygenation level = 0.43/0.51/0.56, CBF[ml·min^-1·100g^-1] = 70.6/105.5/81.8, Laser-Doppler flowmetry[a.u.] = 89.2/120.2/90.6 and pO2[mmHg] = 6.3/32.3/46.7. All parameters were statistically significantly different with P < 0.001 between all breathing conditions. All MRI and the corresponding micro probe measurements were also statistically significantly (P ≤ 0.03) correlated with each other. However, converting the tissue pO2 to blood oxygen saturation = 0.02/0.34/0.63, showed only very limited agreement with the qBOLD venous blood oxygenation level.

We found good correlation between MRI and micro probe measurements. However, direct conversion of tissue pO2 to blood oxygen saturation by using the Hill equation is very limited. Furthermore, adverse effects of anesthesia and trauma due to micro probe insertion are strong confounding factors and need close attention for study planning and conduction of experiments. Investigation of the correlation of perfusion and oxygenation sensitive MRI methods with micro probe measurements in pathologic tissue such as tumors is now of compelling interest.

Keywords: qBOLD, ASL, hypercapnia, hyperoxia

mittels der Hill-Gleichung in die Blutsauerstoffsättigung umgerechnet. Die Tiere wurden mit einer intraperitonealen Injektion von Ketamine-Xylazine-Acepromazine (10-2-0.3 mg/ml·kg) anästhesiert.

Die Ergebnisse unter Normal/Hyperkapnie/Hyperoxie-Bedingung waren: R2[s-^1] = 20.7/20.4/20.1, R2[s-^1] = 31.6/29.6/25.9, R2'[s-^1] = 10.9/9.2/5.7, qBOLD venöse Sauerstoffsättigung = 0.43/0.51/0.56, CBF[ml·min^-1·100g^-1] = 70.6/105.5/81.8, Laser-Doppler Flussmessung[a.u.] = 89.2/120.2/90.6 und pO2[mmHg] = 6.3/32.3/46.7. Alle Parameter waren statistisch signifikant (P<0.001) unterschiedlich zwischen den verschiedenen Atmungsbedingungen. Weiterhin korrelierten die MRT- mit den korrespondierenden Mikrosondenmessungen statistisch signifikant (P≤ 0.03). Die aus der Gewebe-pO2 umgerechnete Blutsauerstoffsättigung = 0.02/0.34/0.63, zeigte nur eine geringe Übereinstimmung mit der qBOLD-venösen Sauerstoffsättigung.*

Es wurde eine gute Korrelation zwischen den MRT- und Mikrosondenmessungen festgestellt. Allerdings ist die Umrechung der Gewebe-pO2 zur Blutsauerstoffsättigung mit Hilfe der Hill-Gleichung sehr limitiert. Weiterhin können Nebenwirkungen der Anästhesie und der durch die Mikrosonden verursachten Verletzung nicht ausgeschlossen werden und müssen als potentielle Störgrößen in zukünftigen Studien berücksichtigt werden. Weitere Untersuchungen der Korrelation von perfusions- und oxygenierungssensitiven MRT-Methoden mit Mikrosondenmessungen in pathologischem Gewebe wie Tumoren sind nun von großem Interesse.

Schlüsselwörter: qBOLD, ASL, Hyperkapnie, Hyperoxie

Introduction

The tomographic assessment of (patho-)physiological parameters, such as perfusion and oxygenation, has great potential for improved characterization of heterogeneous pathologies e.g., tumors, which may be helpful to better predict treatment response and potential outcome. It is known that the histopathological classification and treatment response of tumors are related to the metabolic and vascular properties of the tumor tissue [1–3]. Current techniques, like near infrared spectroscopy or 15O positron emission tomography (PET), suffer from insufficient spatial resolution or are not widely available [4,5]. On the other hand, magnetic resonance imaging (MRI) is much more available than 15O-PET and offers exquisite soft tissue contrast without the use of radioactive tracers. However, it is challenging to measure absolute quantitative values by MRI and it is not clear if and how oxygenation or perfusion sensitive MRI measurements reflect the true physiological state of the tissue. Therefore, continuous efforts are requisite to further develop and improve these MRI techniques.

Validation of quantitative Blood Oxygenation Level Dependent (qBOLD) MRI in rat showed good agreement with blood gas analysis of the jugular vein [6]. Also, blood T2 Relaxation Under Spin Tagging (TRUST) MRI was validated by pulse oximetry under mild hypoxia in human [7]. Furthermore, the blood oxygenation level of single veins in humans during normal physiological condition, breathing Carbogen (5% CO2, 95% O2) and after intake of caffeine was measured by analyzing the effective transverse magnetization decay of single voxels including single veins as well as their surrounding tissue [8]. However, oxygenation sensitive MRI methods are sensitive to the oxygenation level of the blood which may only indirectly reflect the oxygenation of the tissue. Thus, investigating the correlation of the oxygenation and perfusion sensitive MRI methods with subsequent micro probe measurements, which directly measure tissue oxygenation, is necessary and was the purpose of this study.