Simultaneous Observation of Lungs and Brain to enhance Versatility of 129Xe Washout Curve Analysis in Mouse Brain

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INTRODUCTION

Although hyperpolarized (HP) ^{129}Xe dynamic study is expected to offer important information on the brain function, much more elaborated studies are needed to enhance the reliability of the method in estimating parameters related to brain function. In the present study ^{129}Xe washout curve analysis is improved methodologically by simultaneously observing lungs and brain to remove the effect of lung parameters and by simplifying the formulation of data treatment to incorporate into a usual curve fitting algorithm readily. Thus, ^{129}Xe apparent relaxation time in mouse brain has become determined in each mouse without citation of standard values for lung parameters. This method will be useful for the detection of changes in the net (not apparent) relaxation time and cerebral blood flow when any stimulus affecting only one of these two is given.

METHODS

The Xe gas polarized to 3-5% in ^{129}Xe by a home-made apparatus(1) was supplied to ddY male mice (35 - 40 g) after pentobarbital (50 mg/kg) anesthesia under spontaneous respiration. MRS/MRI experiments were performed on Varian Unity INOVA 400WB equipped with 9.4 T vertical magnet and Litz coils tunable to ^{129}Xe, ^{3}He, ^{1}H and ^{19}F. ^{129}Xe spectrum was measured in every 0.7 or 1.4 sec in the washout process after changing the pass of HP gas to depolarizing pipe packed with steel wire to prevent any extra change in flow gas rate and composition. The position of mouse was changed by sliding the hausing tube for mouse, and lung and brain were measured repeatedly. Thus the washout data were ascertained to be reproducible and the resulting data were stored as the simultaneously observed data from lung and brain. In the washout curve simulation calculation a least squares program ORIGIN (LightStone Inc.) was utilized.

^{129}Xe washout formulation in lung and brain

From the basic model of ^{129}Xe uptake and washout phenomena (2,3) following equation was reached for the washout experiment for lung,

$$S_n = S_1 \exp[-\{\ln(\cos\theta)/T_R-(R_f/V_a) - (1/T_{1a}) - (\lambda\dot{Q}/V_a)\}\, t] \qquad [1]$$

where intensity of the gas signal S_n in the *n*th excitation is given as the function of washout time t under spontaneous respiration, and where θ, T_R, T_{1a}, R_f, V_a, λ, and $\dot{Q}$ are RF flip angle, repetition time, relaxation time in alveolar gas space, second ventilation volume, total volume of functional residual capacity and tidal volume, gas/blood partition coefficient, and pulmonary capillary blood flow, respectively. Also obtained was the equation for the washout process in brain,

$$S_n = S_1 \{U\exp(-Pt_w) + (1-U)\exp(-Rt_w)\} \quad \text{with } U= -W/\{(P-R)C_{i0}\},\ P= (R_f/V_a) + (1/T_{1a}) + (\lambda\dot{Q}/V_a),$$
$$R= F_i/\lambda_i+1/T_{1i}-\ln(\cos\theta)/T_R, \text{ and } W= (F_i\lambda/\cos\theta)C_{A0}\exp(-t_i/T_{1blood}) \qquad [2]$$

where t_w, F_i, λ_i, T_{1i}, t_i, and T_{1blood} are the washout time in brain, the perfusion rate, the partition coefficient between tissue i and blood, the ^{129}Xe relaxation time in tissue, the time the xenon spends in solution before reaching the capillaries of tissue i, and the ^{129}Xe relaxation time in blood, respectively, and C_{A0} and C_{i0} are the concentrations of HP Xe at the beginning of the decay in the washout curves in lung and brain, respectively.

RELUTS and DISCUSSION

The lung washout curve was analyzed first to give the P value in Eq. [2], and then the brain washout curve was analyzed using Eq.[2] fixing P at this value and R was determined. When the P value was obtained from the lung measurement just before the measurement of the brain washout curve, the data listed in Calculation 1 in Table 1 were obtained, and when the P value was obtained from the lung measurement just after the brain measurement, those listed in Calculation 2 were obtained. These two calculations has given consistent results with each other, supporting that the lung washout profile does not change throughout the measurement of lung, brain, and lung. When the two decay constants P and R in Eq.[2] were tried to determine in the same least squares fitting, successful convergence condition was not reached. This is probably because P and R are similar in magnitude, as may be seen from the estimation using reference values, and the two parameters interfere with each other over the whole range of washout time in the simulation calculation. It may worth noting that the estimated net relaxation time in brain tissue, T_{1i}= 15.9±1.0 (Table 1), is close to those estimated for human, 14 sec for gray matter and 8 sec for white matter[4].

Table.1 Parameters determined from the washout curve analysis with the simultaneous observation of lung and brain

Calculation	Decay constant in the washout curve [sec^{-1}]		Apparent relaxation time, T_{1i}^*	Net relaxation time, T_{1i}
	Lung, P	Brain, R		
1	0.180±0.028	0.122±0.032	10.3 sec	14.9 sec
2	0.204±0.044	0.114±0.026	11.3 sec	16.9 sec

The net relaxation time T_{1i} is calculated using a reference value of F_i/λ_i= 0.0295 from the relation: $1/T_{1i}^*= 1/T_{1i}+F_i/\lambda_i$.

CONCLUSION

The method proposed in the present study, simultaneous (or pseudo-simultaneous) observation of lungs and brain, would be useful for the reliable detection of changes in the net relaxation time and cerebral blood flow when any stimulus affecting only one of these two is given.

REFERENCE

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