Dynamic in Vivo T1 Relaxation Measurements of Mouse Spinal Cord for Manganese-Enhanced MRI at 9.4 T

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Introduction:

Mouse spinal cord has proved to be a focus of interest due to its capability to model both injury and neural degenerative diseases of the spinal cord. Manganese-enhanced MRI (MEMRI), highly spatially resolved and independent to hemodynamic response, not only can delineate many fine structures but also is able to trace neural tracts and detect neuronal activity, which seems to be a promising way to study the spinal cord function in vivo[1-2]. The T1-weighted manganese-enhancement effect is generally found to reach its peak within first 24 h after systemic administration of $MnCl_2$[3]. We were the first to take dynamic T1 relaxation measurements of mouse spinal cord with MEMRI within the initial 32 h to optimize future protocols. Dynamic R1 relaxivity was also analyzed to determine the fastest manganese uptake and best stimulation interval for neural activity detection.

Materials and Methods:

Sixteen male ICR mice (28-32g) received three bolus intraperitoneal (IP) injections of 50mM $MnCl_2$/saline solution within 50 min, reaching final dose of 126 mg/kg and followed by 0.5 ml saline injection to minimize dehydration effect. With Biospec 9.4T/31 cm scanner and mouse gradient and birdcage RF coils (Bruker, Germany), animals underwent MRI scans under IP 60mg/kg pentobarbital anesthesia. Baseline spinal cord T1 measurements were acquired from eight mice. The following measurements were taken at 4h, 8h, 12h, 16h, 20h, 24h, 28h, and 32h post $MnCl_2$ injection. Data of every two time points, with interval of 16 h, were obtained from the same four mice. For anatomy imaging, we used multi-slice spin-echo sequence TR/ TE= 400/ 8 ms; FOV=2x2 cm^2; matrix size= 256x 256; slice thickness= 0.5 mm, 30 continuous slices, NEX=4 (Fig 1). For T1 measurement, we applied standard spin-echo inversion recovery sequence, TR/ TE= 9000/8 ms; same geometry as the anatomy, but lower matrix size of 128x128 and NEX=1; Inversion time was 50, 100, 200, 500, 1000, and 1500 ms, respectively. Animal ECG, respiratory, and anal temperature were monitored and respiratory gating was performed during every scan. A water bath warming pad was applied to maintain core temperature within 36±1℃. AFNI software was used for image processing. ROIs were drawn in 5 slices for both white matter (WM) and gray matter (GM). Normalized T1 relaxation time and R1 relaxivity were measured and compared over time with student t-test.

Results and Discussion:

At 9.4 T baseline T1 time of WM and GM of mouse spinal cord was 1624±32 ms and 1758±43 ms. No statistically significant difference was found in either WM or GM when comparing the corresponding values of cervical and lumbar level (P> 0.05). With axon transportation and passing through calcium channels, manganese was actively transported into spinal cord tissue to increase its T1 relaxivity. T1 of both WM and GM experienced a steady decrease within 28 h and 24 h after $MnCl_2$ administration (Table 1). Within 24 h post $MnCl_2$ injection, spinal cord GM showed 72% T1 shortening, while it was only 54% for the WM, which indicated higher Manganese deposition. This may be a result from the fact that GM is denser in neurons and microvessels than WM. Computed dynamic WM and GM R1 curves (Fig 2) showed continuous increase within 24 h. Since R1 is approximately linearly related to local tissue concentration of manganese, the slope of R1 curve should be a proper index of manganese uptake speed. For simplicity, if imaging acquisition is performed at maximum-enhanced 24-h post $MnCl_2$ administration, the slopes of every segment connecting two neighboring time points become the best parameters to find the fastest manganese uptake, and therefore, the best neural stimulation period. For WM it is best to perform stimulation from 8-12h, while for GM the optimum choice would be 4-8h, the physiological mechanism of which has yet to be determined.

Table 1. Dynamic T1 Values (msec) in Mouse Spinal Cord after $MnCl_2$ Administration

Spinal Cord	Post- $MnCl_2$ Administration Time (h)								
Region	0	4	8	12	16	20	24	28	32
White Matter	1624±32	1550±21	1333±17	943±19	901±24	840±15	762±34	752±28	813±45
Gray Matter	1758±43	1408±36	794±25	680±27	571±19	532±20	492±35	526±22	591±37

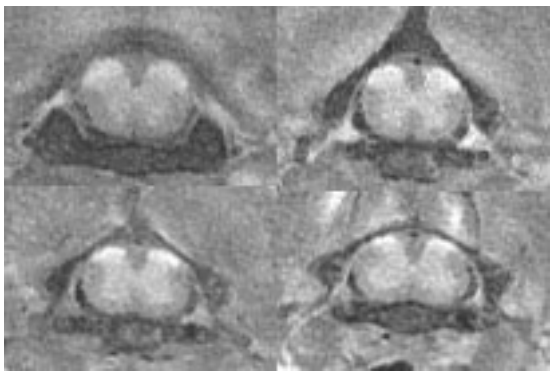

Fig 1 T1-weighted anatomy images to draw ROI for WM and GM

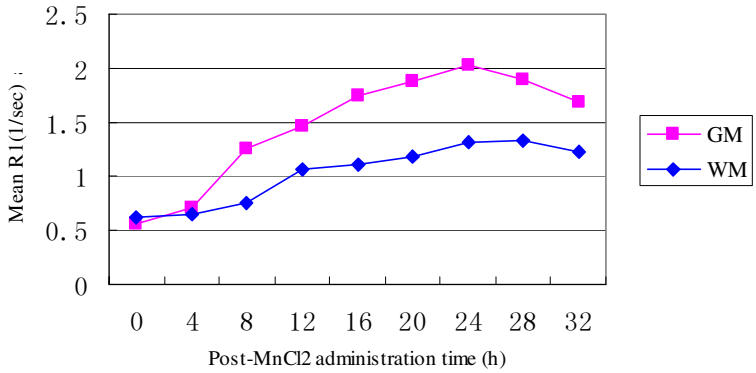

Fig 2 Dynamic R1 changes after $MnCl_2$ administration

References:

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