Discrepancy in \( T_1 \) and \( T_2 \) Shortening of the Globus Pallidus in Hepatic Insufficiency: Evaluation by Susceptibility-weighted Imaging

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Purpose: We assessed the signal of the globus pallidus (GP) in cases of hepatic insufficiency, especially to evaluate the degree of discrepancy in paramagnetic effects on shortening of \( T_1 \) and \( T_2^* \) using susceptibility-weighted images (SWI).

Materials and Methods: Seven patients with hepatic insufficiency underwent magnetic resonance (MR) examinations that included \( T_1 \)-weighted images (\( T_1 \)WI), \( T_2 \)-weighted images (\( T_2 \)WI), and SWI on a 1.5-tesla MR imager, and we compared their results to those of controls. On \( T_1 \)WI and \( T_2 \)WI, we measured signal intensity in the GP and posterior segment of the putamen (Put) to obtain a signal ratio (GP/Put ratio), and on SWI, we classified signal intensity into 4 grades: A, higher than the cortex; B, lower than the cortex and higher than the cerebrospinal fluid (CSF); C, lower than the CSF and higher than the red nucleus; and D, lower than the red nucleus.

Results: In the 7 patients with hepatic insufficiency, the mean GP/Put ratio was significantly higher on \( T_1 \)WI and \( T_2 \)WI than those values in controls. On SWI, we classified 2 cases each as Grade A, Grade B, and Grade C, and one as Grade D. Although the signal of the GP was elevated on \( T_1 \)WI, there was no decrease in signal on \( T_2 \)WI. On SWI, we obtained no low signal intensity.

Conclusion: In patients with hepatic insufficiency, the globus pallidus did not show low signal intensity on \( T_2 \)WI or SWI. Hyperintensity of the GP on \( T_1 \)WI without hypointensity on \( T_2 \)WI, or even SWI, suggests a discrepancy between paramagnetic effect on \( T_1 \) and \( T_2 \) shortening that reflects the accumulation of manganese and the presence of hepatic insufficiency.

Keywords: globus pallidus, hepatic encephalopathy, SWI

Introduction

The high signal intensity of the globus pallidus (GP) on \( T_1 \)-weighted images (\( T_1 \)WI) in cases of hepatic insufficiency is well known (Fig. 1)\(^1,2\) and hypothesized to result from the paramagnetic effect from deposition of manganese within the GP.\(^3\) However, it is also known that even in cases of hepatic insufficiency, the GP does not show low signal on \( T_2 \)-weighted images (\( T_2 \)WI), which indicates a discrepancy in paramagnetic effects on shortening of \( T_1 \) and \( T_2 ^* \).\(^2\) The very high sensitivity of susceptibility-weighted images (SWI) to paramagnetic effect\(^4\) supports their use to detect paramagnetic effect within the GP in cases of hepatic insufficiency. Using SWI to detect paramagnetic effect, we assessed the signal of the GP in cases of hepatic insufficiency to evaluate the degree of discrepancy in paramagnetic effects on \( T_1 \) and \( T_2 ^* \) shortening.

Materials and Methods

Subjects

We evaluated 7 subjects with hepatic insufficiency (5 male, 2 female; aged 16 to 82 years, mean age, 62 years); two each with Inose disease or chronic hepatitis C and one each with idiopathic portal hypertension, antiphospholipid antibody syndrome, or alcoholic hepatic cirrhosis. According to...
Fig. 1. Signal intensity of the globus pallidus (GP) on magnetic resonance imaging in a case of hepatic insufficiency (75-year-old man). (a) The GP shows apparent high signal intensity on T1-weighted imaging. (b) The GP shows isointensity compared to the putamen and almost the same signal intensity as the gray matter on the T2-weighted image. (c) On susceptibility-weighted imaging (SWI), the GP does not show lower signal intensity. It shows a relatively high signal compared to the white matter and cortex.

Child-Pugh classification, 2 cases were Class A, and 5 cases were Class B. We also evaluated 14 control subjects (7 younger subjects aged 13 to 28 years and 7 older subjects aged 54 to 66 years) who underwent MR examination that included SWI to assess head trauma and showed no pathological changes in the basal ganglia nor evidence of liver dysfunction.

Imaging
MR examinations were carried out on a 1.5-tesla clinical MR system (Magnetom Avanto, Siemens, Erlangen, Germany) and included spin-echo T1-weighted, turbo spin-echo T2-weighted, and SWI sequences. The parameters for the 3 sequences were: for spin-echo T1-weighted sequence: repetition time (TR), 500 ms; echo time (TE), 12 ms; 6-mm thickness; 256×256 matrices; and 230-mm field of view (FOV); for turbo spin-echo T2-weighted sequence: TR, 4000 ms; TE, 120 ms; 6-mm thickness; 256×256 matrix; and 230-mm FOV; and for SWI: velocity-compensated 3-dimensional (3D) gradient echo sequence, magnitude plus image (3D fast low angle shot [FLASH]); TR, 49; TE, 40; FA, 15; bandwidth, 80 Hz/Px; FOV, 230; matrix, 320×272; 1.6-mm slice thickness; and 72 slices per slab.

Analysis
We quantitatively assessed the signal intensity of the bilateral GP on T1WI and T2WI. We measured signal intensities in the GP and posterior segment of the putamen (Put) to establish a signal ratio (GP/Put ratio) of the regions of interest (ROIs). We classified signal intensity on SWI into 4 grades: Grade A, higher than the cortex; B, lower than the cortex and higher than the cerebrospinal fluid (CSF); C, lower than the CSF and higher than the red nucleus; and D, lower than the red nucleus (Fig. 2).

Results
The mean GP/Put ratios on T1WI were 1.28 for both the right (SD = 0.08; range, 1.16 to 1.35) and left (SD = 0.12; range, 1.18 to 1.52) sides. In the normal controls, the ratios were 1.07 for the right (SD = 0.06) and left (SD = 0.04) sides in younger subjects and 1.11 (SD = 0.04) for the right side and 1.08 (SD = 0.05) for the left side in the older subjects. Statistically significant differences in the mean GP/Put ratio between cases with hepatic insufficiency and normal controls indicated higher signal intensity of the GP on T1WI in the cases with hepatic insufficiency (P < 0.01, P < 0.001) (Fig. 3a). The mean GP/Put ratios on T2WI were 0.82 for both the right (SD = 0.12; range, 0.67 to 0.97) and left (SD = 0.14; range, 0.67 to 1.04) sides. In the normal controls, the ratios were 0.64 (SD = 0.08) for the right side and 0.61 (SD = 0.06) for the left in younger subjects and 0.68 (SD = 0.06) for the right and 0.69 (SD = 0.09) for the left in older subjects. Statistically significant differences between the cases with hepatic insufficiency and normal controls
Fig. 2. Grading of the signal intensity of the globus pallidus (GP) on susceptibility-weighted imaging (SWI). Signal intensity was classified into 4 grades: Grade A, higher than the cortex (a); B, lower than the cortex and higher than the cerebrospinal fluid (CSF) (b); C, lower than the CSF and higher than the red nucleus (c, d); and D, lower than the red nucleus (e, f).

indicated higher signal intensity of the GP on T2WI in the cases with hepatic insufficiency ($P<0.05$, $P<0.01$) (Fig. 3b).

On SWI, classification of one case as Grade A, two as Grade B, three as Grade C, and one as Grade D indicated that six (85.7%) of 7 cases showed higher signal intensities than that of the red nucleus. In the normal controls, among the younger subjects, no case was classified as Grade A, two were B, four were C, and one was D, and in the older subjects, one case was classified as Grade A, two were B, three were C, and one was D (Fig. 3c).

Discussion

We aimed to evaluate further the signal intensity on SWI of the GP in cases with hepatic insufficiency in which the GP shows high signal intensity on T1WI, a well known phenomenon. Zeneroli's group reported bilateral and symmetrical hyperintensity of the GP in T1WI of patients with liver cirrhosis and hepatic encephalopathy and suggested the cause as accumulated paramagnetic compound, especially manganese, that escaped hepatic clearance because of a portal-systemic shunt or liver dysfunction. Inoue observed hyperintensity in the basal ganglia on T1WI in patients with large portal-systemic collateral vessels that received blood from the superior mesenteric vein. In 4 autopsy cases of hepatic cirrhosis, Maeda and colleagues measured mean manganese concentrations in the GP approximately 4.5 to 9.5 times the normal values. Their histopathological findings showed remarkable atrophy, necrosis, and decidualation of nerve cells and proliferation of glial cells and microglia in the GP that were similar to those findings in chronic manganese poisoning. Our study showed discrepancy between $T_1$ and $T_2^*$ shortening effect in the GP in cases with hepatic insufficiency even when SWI was used for imaging. This discrepancy could be explained by the accumulation of a nonparamagnetic substance, such as a protein or phospholipid, which can cause a $T_1$ shortening effect. The ratio of $T_1/T_2$ alteration in the GP of patients with hepatic encephalopathy differed little from that in suspensions of phospholipid vesicles. Our findings of high signal intensity on T2WI in the GP in cases with hepatic insufficiency compared to controls seems to support this hypothesis. However, though phospholipid lev-
Fig. 3. Signal intensity of the globus pallidus (GP) on T1-(T1WI), T2-(T2WI), and susceptibility-(SWI) weighted imaging. (a) Signal intensity of the GP (GP/putamen [Put] ratio) was higher on T1WI in cases with hepatic insufficiency than in controls. (b) The GP also showed higher signal intensity (GP/Put ratio) on T2WI in cases with hepatic insufficiency than in controls. (c) The GP of the cases with hepatic insufficiency on SWI did not show a lower signal intensity than that in controls.

els within the cortex have been reported to be depressed in cases of hepatic insufficiency, we found no report of altered phospholipid levels in the GP in such cases. Gliosis in the GP may provide some explanation for this phenomenon. It is known that microgliosis is observed in the GP in cases with hemichorea-hemiballism, which shows similar hypointensity on T1WI. However, none of these explanations can fully resolve the discrepancies between T1WI and T2WI or SWI. In addition, as we mentioned, several reports demonstrate the accumulation of manganese within the GP.

Zeneroli and colleagues reported no abnormal signal intensities of the GP on T2WI in patients with liver cirrhosis and hepatic encephalopathy, although they observed bilateral and symmetrical hyperintensity of the GP. If pallidal hyperintensity on T1WI in cases with hepatic insufficiency is due to a substance with strong T2* as well as T1 shortening effect, such as iron, the GP is expected to show hypointensity on T2WI. However, our current data and previous data examining signal intensity of the GP in T2WI show no hypointensity. Moreover, T2WI from patients with hepatic insufficiency showed higher signal intensity than that in controls. To clarify the reported data, we used SWI to test whether hypointensity was observed in the GP; we believe no report has examined SWI of the GP in cases of hepatic insufficiency. However, none of our cases demonstrated hypointensity in the GP on SWI. If the lack of hypointensity or existence of hyperintensity in the GP on T2WI in cases with hepatic insufficiency is attributable to sensitivity to paramagnetic effect, the very high sensitivity of SWI to this effect might enable observation of the hypointensity in the GP. Our results suggest that the T2* shortening effect cannot be observed in the GP of patients with hepatic insufficiency, even when SWI is applied.

This discrepancy may be attributable to too little
manganese accumulation in the GP to permit its observation as a paramagnetic effect on SWI. However, several reports of autopsy cases have shown concentrations of manganese 4.5- to 9.5-fold higher in patients with hepatic insufficiency than in normal controls. Another possibility for the discrepancy might be the difference in the longitudinal relaxivity ratio \( R_1 \) effect and transverse relaxivity ratio \( R_2 \) effect of manganese \textit{in vivo}. Several reports have measured relaxivity of manganese \textit{in vivo}. Southon's group measured the relaxation ratio of mangafodipir trisodium (MnDPDP) in rat livers and found the \( R_2 \) of MnDPDP to be too small to affect T2WI.\(^{10}\) From relaxography analyses of isolated rat cardiac tissue excised after manganese enrichment, Nordhøy and associates reported weaker response of \( R_2 \) than \( R_1 \) to tissue signal enhancement.\(^{11}\) A weak relaxivity ratio for T2 compared to T1 by manganese may be one cause for the discrepancy in our present findings for T1WI and T2WI or SWI.

The current study has some limitations. It is retrospective and evaluates only a few cases; a larger sample size might clarify the results. However, despite our small sample size, a striking feature of this study is the very high percentage of cases in which the GP did not show hypointensity on SWI. Second, we did not quantitatively analyze our signal intensity measures from SWI because the signal intensity on SWI is subject to alteration by the angle of the slice, low pass filtering, or slice thickness. Finally, we could not definitively explain the discrepancy between T1 and T2WI or SWI for the GP in hepatic insufficiency.

**Conclusion**

We demonstrated that manganese deposition produced hyperintensity of the GP on T1WI, but there was no hypointensity on T2WI or SWI in patients with hepatic insufficiency. Such hyperintensity of the GP on T1WI without hypointensity on T2WI, or even SWI, is highly suggestive of the discrepancy between paramagnetic effect on T1 and T2 produced by manganese accumulation, which reflects the presence of hepatic insufficiency.

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