



Original contribution

Choroid plexus cysts analyzed using diffusion-weighted imaging with short diffusion-time

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ABSTRACT

Introduction: Oscillating gradient spin-echo (OGSE) sequences can shorten diffusion times by replacing the long-lasting diffusion-sensitizing gradients used in pulsed gradient spin-echo (PGSE) methods with rapidly oscillating gradients. To obtain information regarding the internal structure of choroid plexus cysts that appear hyperintense on diffusion-weighted imaging (DWI), we investigated the apparent diffusion coefficient (ADC) values acquired with a shorter diffusion time using an OGSE sequence.

Material and methods: Twenty-seven patients with choroid plexus cysts were scanned using a 3 T magnetic resonance scanner. DWI was performed with both OGSE and PGSE, with effective diffusion times (Δ_{eff}) of 6.5 and 35.2 ms, respectively. ADC values for choroid plexus cysts, white matter (WM), and cerebrospinal fluid (CSF) were measured. The ADC values obtained with the shorter and longer diffusion times were compared using the Wilcoxon signed-rank test. $P < .05$ was considered significant.

Results: The ADC values of choroid plexus cysts and WM were significantly higher at the Δ_{eff} of 6.5 ms on OGSE than with the Δ_{eff} of 35.2 ms on PGSE. The ADC values of CSF were significantly lower at the Δ_{eff} of 6.5 ms on OGSE than with the Δ_{eff} of 35.2 ms on PGSE. The ADC values of choroid plexus cysts were lower than the ADC values of CSF with Δ_{eff} of 35.2 and 6.5 ms.

Conclusions: The dependence of ADC values on the diffusion time in choroid plexus cysts suggested spatially restricted diffusion. In measurements obtained with short diffusion times, the lower ADC values for choroid plexus cysts in comparison with the CSF indicated the presence of spatially restricted diffusion and increased cyst viscosity.

1. Introduction

Choroid plexus cysts are common, incidental, and almost invariably asymptomatic lesions. A total of 124 autopsy cases have reported choroid plexus cysts in 38% of the telencephalic choroid plexuses [1]. In most cases, they are below 1 cm in diameter and are usually located in the trigones of the lateral ventricles. They are bilateral in two-thirds of the cases. In general, a helpful feature is that they usually have an extremely high signal on diffusion-weighted imaging (DWI) [2]. There

is an overlap in the magnetic resonance (MR) appearance of choroid plexus cysts and choroid plexus xanthogranulomas. Pathologically, choroid plexus xanthogranulomas show peripheral clusters of calcium, which are not a frequent feature of choroid plexus cysts [3]. As their clinical history is the same, there is no clear distinction between choroid plexus cysts and choroid plexus xanthogranulomas in MR images. In surgically proven cases, choroid plexus cysts usually contain clear serous fluid resembling cerebrospinal fluid (CSF), and the protein concentration of the cyst fluid is mildly higher than that of CSF [4,5]. A

Abbreviations: ADC, apparent diffusion coefficient; CSF, cerebrospinal fluid; DWI, diffusion-weighted imaging; MR, magnetic resonance; MRI, magnetic resonance imaging; OGSE, oscillating gradient spin-echo; PGSE, pulsed gradient spin-echo; ROI, regions of interest; SSIFT, selective size imaging filters via diffusion times; WM, white matter

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previous study reported that choroid plexus cysts usually show quite high signals on DWI because of the restricted motion of the water molecules due to the slightly higher protein content [2]. However, the actual influence of the protein content or the size of the cyst wall on the high DWI signal is unknown.

DWI can be used to infer information about the sizes of cells and viscosities of substrates, and these estimations are based on calculations of the apparent diffusion coefficient (ADC) [6]. The measurements rely on the ADC changing with the diffusion time as measurements move from the restricted to the free diffusion compartment. Clinically, conventional DWI is performed mainly using a pulsed gradient spin-echo (PGSE) sequence, which utilizes relatively long diffusion times [7]. Hence, the spatial sizes that can be probed on DWI with a conventional PGSE sequence are limited. Recently, the oscillating gradient spin-echo (OGSE) sequence has become available on clinical magnetic resonance imaging (MRI) scanners. The OGSE sequence has been used in animal studies since the late 1990s [8–10]. OGSE sequences can shorten the diffusion times by replacing the long-lasting diffusion-sensitizing gradients in PGSE methods with rapidly oscillating gradients. If most molecules do not move far enough to interact with any obstacle during the preset diffusion time, the observed ADC is the intrinsic diffusion coefficient of cellular water [11]. As the diffusion time increases, molecules interact with more barriers and the observed ADC will decrease asymptotically [12,13]. Therefore, it is expected that DWI with the OGSE sequence can estimate the substrate's viscosity and spatially restricted diffusion on the basis of the internal structures of pathologic lesions from changes in the ADC values with differing diffusion times [6,10,14]. Recently, the OGSE sequence has been used in clinical studies covering cerebral infarctions and intracranial epidermoid cysts [15–18].

There has been no study that evaluated choroid plexus cysts using DWI with short diffusion times to assess their hyperintense signals on DWI. Evaluation of choroid plexus cysts on DWI with a short diffusion time may be helpful to differentiate ADC contributions from substrate viscosity and spatially restricted diffusion due to complex internal structures. Clinically, this may be useful for differential diagnosis of lesions appearing as hyperintense lesions on DWI by adding the OGSE sequence and evaluating contributions to ADC values from substrate viscosity and spatially restricted diffusion. To estimate the internal structures of choroid plexus cysts, we investigated the ADC values of choroid plexus cysts scanned with shorter diffusion times on DWI with an OGSE sequence.

2. Material and methods

2.1. Subjects

MRI data from 27 patients (16 men, 11 women; age range 22–89 years, mean age 63.1 ± 16.7 years) who were referred for various clinical reasons between July 2017 and April 2018 were retrospectively analyzed. The study was approved by the relevant institutional review board, and the requirement for written informed consent was waived due to its retrospective nature.

2.2. MRI data acquisition and processing

All subjects underwent scanning on a 3 T MR scanner (MAGNETOM Prisma, Siemens Healthcare, Erlangen, Germany) with a 20-channel head coil. DWI was performed with prototype sequences using b-values of 0 and 1000 s/mm^2 (number of excitations, 1 for each sequence) and six uniformly distributed directions for both OGSE and PGSE acquisitions. OGSE using a trapezoid-cosine waveform [19] was performed with an effective diffusion time (Δ_{eff}) of 6.5 ms (frequency = 30 Hz; diffusion gradient pulse duration [δ] = 7.6 ms). For OGSE sequences, the b-value was obtained as $b = N\gamma^2 M_{\text{enc}}^2 \Delta_{\text{eff}}$, where N denotes the total number of oscillation cycles, γ represents the hydrogen nuclear

gyromagnetic ratio, and M_{enc} denotes the 0th moment of the first lobe of the oscillating diffusion-encoding gradients ($M_{\text{enc}} = G \delta$, where G denotes the diffusion gradient magnitude). PGSE sequences were performed with an Δ_{eff} of 35.2 ms and δ of 36.3 ms. On PGSE sequences, the b-value was obtained as $b = \gamma^2 M_{\text{enc}}^2 \Delta_{\text{eff}}$. Other parameters for the OGSE and PGSE sequences were as follows: repetition time, 4800 ms; echo time, 101 ms; field of view, $200 \times 200 \text{ mm}^2$; matrix size, 82×82 ; slice thickness, 5 mm; and acquisition time, approximately 2 min.

Circular regions of interest (ROIs) were placed within the choroid plexus cysts on ADC maps. ROIs were placed carefully to avoid partial-volume effects from adjacent CSF, and to fit within the choroid plexus cysts. ROIs were also placed in the white matter of the frontal lobe and lateral ventricle to determine the ADC values of white matter (WM) and CSF, respectively. For WM and CSF, three circular ROIs of 40 mm^2 were placed, and the averages of the ADC values were calculated.

2.3. Statistical analysis

The Shapiro-Wilk test was used to assess normality. Since all the data were not normally distributed, we used the Wilcoxon signed-rank test to compare the ADC values of choroid plexus cysts, WM, and CSF with Δ_{eff} values of 6.5 and 35.2 ms. $P < .05$ was considered significant. All statistical analyses were performed using SPSS v.25 (v25, IBM SPSS Statistics, IBM CM, Corporation, Chicago, IL).

3. Results

A representative case of choroid plexus cysts from a 64-year-old female is shown in Fig. 1. The choroid plexus cysts showed high intensity in the lateral ventricles on DWI using PGSE with an Δ_{eff} of 35.2 ms (Fig. 1A). Meanwhile, the choroid plexus cysts showed decreased visualization on DWI using OGSE with an Δ_{eff} value of 6.5 ms (Fig. 1B). The ADC values of the choroid plexus cysts appear higher at short Δ_{eff} values, in comparison with those at long Δ_{eff} values (Fig. 1C, D).

The ROIs of choroid plexus cysts (size range, 4–25 mm^2 ; mean size, $10.5 \pm 4.9 \text{ mm}^2$) were analyzed. The mean ADC values and the rate of change of choroid plexus cysts, WM, and CSF by ROI analysis are shown in Table 1. The ADC values of choroid plexus cysts and WM were significantly higher at the Δ_{eff} of 6.5 ms on OGSE, compared with those at the Δ_{eff} of 35.2 ms on PGSE. The ADC values of CSF were significantly lower at the Δ_{eff} of 6.5 ms on OGSE, compared with those at the Δ_{eff} of 35.2 ms on PGSE. The ADC values of choroid plexus cysts were lower than the ADC values of CSF at Δ_{eff} values of 35.2 and 6.5 ms.

4. Discussion

Histologically, choroid plexus cysts consist of a fibrous outer membrane and an inner layer of cuboidal choroid plexus epithelium [20,21]. The formation of choroid plexus cysts is related to the histogenesis of the choroid plexus. Most authors attribute the origin of these lesions to the primitive neuroepithelium that lines the neural tube. The most unifying theory about their pathogenesis suggests that a neuroepithelial tube or a small cyst is formed by a folding of the neuroepithelium into the choroid's matrix and of the stroma into the ventricle. This forms finger-like projections to create choroidal villi. The neck of the folded epithelial sacs occasionally may be pinched off and become separated from the ventricle. The accumulation of secretions from the secretory activity of these epithelial cells in the congenitally formed cyst and the fluid activity transported from the exterior will produce a clear CSF-like substance.

The ADC values of choroid plexus cysts were higher at the shorter Δ_{eff} of 6.5 ms. This diffusion time-dependence suggests spatially restricted diffusion, consistent with pathological findings. Choroid plexus cyst is a fluid-filled structure and the cyst wall consists of columnar epithelium. Previous pathological reports have shown that the diameter

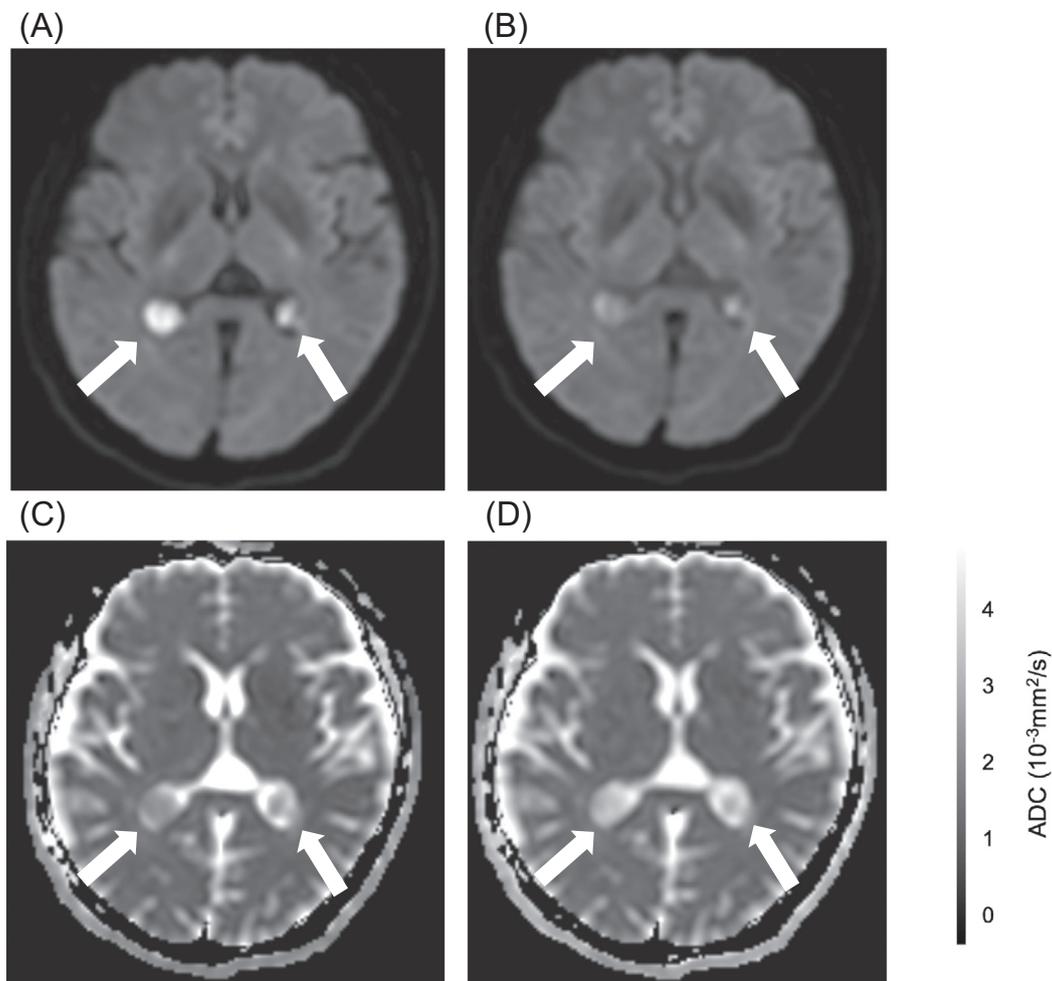


Fig. 1. Diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) map of choroid plexus cysts. The choroid plexus cysts show high intensity in the lateral ventricles on PGSE with long Δ_{eff} values (Fig. 1A). On the other hand, the choroid plexus cysts showed decreased visualization on OGSE with short Δ_{eff} (Fig. 1B). The ADC values of choroid plexus cysts appear higher at short Δ_{eff} , compared with those at the long Δ_{eff} (Fig. 1C, D).

of the cyst wall consisted of columnar epithelium is $50 \times 75 \mu\text{m}$ [1]. Mean square distances (r) of water molecule movement for isotropic diffusion in three dimensions are defined by the Einstein-Smoluchowski equation [22]:

$$\langle r^2 \rangle = 6Dt$$

where D is the diffusion coefficient and t is diffusion time. The D value for water molecules is $3 \times 10^{-3} \text{mm}^2/\text{s}$ at human body temperature, which is 37°C . Mean square distances (r) of water molecule movement for diffusion times of $\Delta_{\text{eff}} = 6.5 \text{ms}$ and 35.2ms are thus $10.8 \mu\text{m}$ and $25.1 \mu\text{m}$, respectively, at body temperature. Both were smaller than $50 \mu\text{m}$, and the influence of spatially restricted diffusion of the wall could be small. However, our results showed that the ADC values of CPCs were higher at the shorter Δ_{eff} of 6.5ms . The influence of spatially restricted diffusion of the wall is larger at the longer Δ_{eff} of

35.2ms and smaller at the shorter Δ_{eff} of 6.5ms . Furthermore, it is also presumed the presence of cyst walls with distances smaller than $50 \mu\text{m}$ as well as the influence of interstitial tissues and cystic components. In addition, the ADC values of choroid plexus cysts were lower than those of CSF at Δ_{eff} values of 35.2ms and 6.5ms , and the difference in ADC values between choroid plexus cysts and CSF was smaller at the shorter Δ_{eff} . This suggests that the influence of the spatially restricted diffusion becomes more important with longer Δ_{eff} values. If we can perform investigations with Δ_{eff} values smaller than 6.5ms and eliminate the influence of spatially restricted diffusion, we can confirm the ADC values due to the viscosity of choroid plexus cysts.

Moreover, the ADC values of CSF were higher at the Δ_{eff} of 35.2ms on PGSE even though the liquids exhibit isotropic diffusion. This may be due to the effect of flow in the lateral ventricles. The OGSE sequence with a trapezoid-cosine waveform has an intrinsic flow compensation

Table 1

The mean ADC values of choroid plexus cysts, white matter (WM), and cerebrospinal fluid (CSF).

Sequence	Δ_{eff} (ms)	Frequency (Hz)	Apparent diffusion coefficient ($10^{-3} \text{mm}^2/\text{s}$)		
			Choroid plexus cysts	WM	CSF
PGSE	35.2	0	1.61 ± 0.23	0.75 ± 0.05	3.29 ± 0.14
OGSE	6.5	30	2.22 ± 0.19	0.83 ± 0.05	2.99 ± 0.12
<i>P</i> value			$P < .001$	$P < .001$	$P < .001$
Rate of change (%)			+37.5	+10.6	-9.12

feature [23]. On the other hand, as PGSE does not have such a feature, it is sensitive to flow. It is desirable to add the multiple diffusion times and measure the ADC values of CSF in several different areas in order to clarify how much the difference in CSF speed affects the ADC values of CSF. It is expected that the ADC values are constant even if the diffusion time is changed on OGSE with flow compensation, and the ADC values increase as the diffusion time become longer on PGSE without flow compensation. It is also expected that the ADC values of CSF increase on PGSE without flow compensation when the CSF flow is faster. However, we investigated the ADC values of CSF only in the lateral ventricles with one diffusion time on PGSE and OGSE, respectively. In the future, we will analysis on PGSE and OGSE with multiple diffusion times and measure the ADC values of CSF in several different areas in order to clarify the correlation between the CSF flow and the ADC values.

In addition, the ADC values of WM were lower at the Δ_{eff} of 35.2 ms on PGSE. A previous study reported a time-dependence of diffusion coefficients in the WM of healthy volunteers [24], with decreasing ADC for increasing diffusion times between 45 and 600 ms. Although we used diffusion times of 6.5 ms and 35.2 ms, our results agree with their study. Besides, it has been reported that the rise in ADC in response to a decrease in the diffusion time is a key feature to extract the cell size for the diffusion spectra of restricted water diffusion inside impermeable spheres [25]. The range of axon sizes in WM is 1–6 μm [26], which is smaller than the columnar microstructure in choroid plexus cysts. Therefore, the spatial restriction of diffusion in WM is stronger than that in choroid plexus cysts, and the ADC values and expected changes are lower in WM than in choroid plexus cysts.

Our study has several technical limitations. To estimate the true diameter of the cyst wall consisted of columnar epithelium by the OGSE method, it would be necessary to acquire data with Δ_{eff} values shorter than 6.5 ms. Technical and physiological limitations (due to peripheral nerve stimulations) pose a limit to Δ_{eff} reduction in clinical use. We used an Δ_{eff} value that was as minimal as technically feasible in this study. In our previous study, we have clarified that the ADC values does not depend on the diffusion time in free diffusion using isotropic alkane phantoms [27]. If we are able to exclude spatially restricted diffusion of cyst walls with a shorter Δ_{eff} than our study in the future, the actual viscosity in the choroid plexus cysts may be measured by comparing with the ADC values of the isotropic alkane phantoms [27,28]. The viscosity inside the lesions cannot be evaluated *ex vivo* because liquid components leak when histopathological specimens are created in clinical practice. Clinically, evaluating the viscosity of lesions would be helpful in differentiating tumors and distinguishing them from abscesses. It is important to note that DWI with short Δ_{eff} allows clinicians to obtain information that is inaccessible by histopathology.

An OGSE study on intracranial epidermoid cysts was published recently [18]. The ADC values of the intracranial epidermoid cysts measured using the OGSE sequence were higher than that measured using the PGSE sequence, indicating that water diffusion was spatially restricted in the laminated keratin layers within the cyst, which was also demonstrated by histopathology. The following exemplary masses show high signal intensity on DWI: lymphoma, glioblastoma, meningioma, and abscess. Application of the OGSE diffusion technique to these masses has not been reported yet in human studies. In addition, the detailed mechanism by which these masses exhibit high signal intensity on DWI is still unknown. Clinically, it may be useful in the differential diagnosis of lesions appearing as high signal intensity lesions on DWI by adding the OGSE sequence and evaluating contributions to ADC values from substrate viscosity and spatially restricted diffusion with shorter Δ_{eff} . Analyzing other intracranial masses on DWI with short diffusion-time is expected to show different results from choroid plexus cysts which have relatively simple structures. In the future, we intend to compare the differences between the choroid plexus cysts and other brain tumors on DWI with short diffusion-time. Recently, a new technique called selective size imaging filters via diffusion times (SSIFT) for estimating the cell size has been developed [29]. SSIFT is a

new technique based on OGSE. When the diffusion time is varied, the change rate of the signal intensity on DWI depends on the size of the object. SSIFT is a method for imaging this rate of change. In the future, we would like to examine the cell sizes of tumors by performing DWI with different diffusion times and SSIFT for other tumors that show high intensity on DWI.

5. Conclusions

The observed diffusion time-dependence of ADC values in the choroid plexus cysts suggests spatially restricted diffusion. The lower ADC values of the choroid plexus cysts measured with short diffusion times in comparison with CSF suggest the presence of spatially restricted diffusion and increased viscosity of the cysts. To separate ADC contributions from substrate viscosity and spatially restricted diffusion in choroid plexus cysts, it is necessary to investigate diffusion properties with a shorter Δ_{eff} than 6.5 ms.

Disclosure statement

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