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Dynamic state of water molecular displacement of the brain during the cardiac cycle in idiopathic normal pressure hydrocephalus

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ABSTRACT

The predictive accuracy of iNPH diagnoses could be increased using a combination of supplemental tests for iNPH. To evaluate the dynamic state of water displacement during the cardiac cycle in idiopathic normal pressure hydrocephalus (iNPH), we determined the change in water displacement using q-space analysis of diffusion magnetic resonance image. ECG-triggered single-shot diffusion echo planar imaging was used. Water displacement was obtained from the displacement probability profile calculated by Fourier transform of the signal decay fitted as a function of the reciprocal spatial vector q. Then maximum minus minimum displacement (delta-displacement), of all cardiac phase images was calculated. We assessed the delta-displacement in white matter in patients with iNPH and atrophic ventricular dilation (atrophic VD), and in healthy volunteers (control group). Delta-displacement in iNPH was significantly higher than those in the atrophic VD and control. This shows that water molecules of the white matter in iNPH are easily fluctuated by volume loading of the cranium during the cardiac cycle, due to the decrease in intracranial compliance. There was no significant correlation between delta-displacement and displacement. The delta-displacement and the displacement do not necessarily yield the same kind of information. Delta-displacement demonstrated to obtain biophysical information about fluctuation. This analysis may be helpful in the understanding physiology and pathological condition in iNPH and the assisting in the diagnosis.

1. Introduction

Normal pressure hydrocephalus (NPH) has been characterized as a chronic communicating hydrocephalus in elderly patients with the clinical triad gait disturbance, dementia, and incontinence [1–3]. The clinical symptoms of both secondary and idiopathic NPH (iNPH) can be reversed by the removal of the accumulated cerebrospinal fluid (CSF) [3]. Secondary NPH can result in subarachnoid hemorrhage, trauma, and stroke. Although numerous investigations have attempted to clarify the underlying mechanism of and to diagnose iNPH, its exact causes remain poorly understood. The CSF tap test is one of the major supplemental tests for the diagnosis of iNPH; this test has a high positive predictive value of successful shunting, but is not sufficient to diagnose iNPH because of its low sensitivity in predicting surgical outcomes [4]. Other supplemental tests are used to diagnose iNPH, including external lumbar CSF drainage, the lumber infusion test, intracranial pressure monitoring, the aqueductal CSF stroke volume, and intracranial compliance measurements using a phase-contrast cine magnetic resonance imaging (MRI) [5–11]. However, several problems remain in terms of the iNPH diagnostic criteria and the selection of appropriate patients for shunt surgery [13]. Marmarou et al. suggested that the predictive accuracy of iNPH diagnoses could be increased using a combination of supplemental tests for iNPH besides conventional X-ray computed tomography and MRI [3].

In contrast, Alperin et al. developed a hemodynamic-independent analysis to evaluate the mechanical coupling of

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vascular pulsations to spinal CSF, i.e., intracranial compliance analysis [12]. Arterial flow into the cranium induces venous CSF movement and spinal cord displacement during the cardiac cycle. Subsequently, the intracranial volume loading during the cardiac cycle is derived from the differences between the cranial inflow and outflow at each time point during the cardiac cycle. The intracranial compliance expresses the ability to buffer the rising intracranial pressure with an increase in intracranial volume loading. Miyati et al. reported that in iNPH, the intracranial compliance was low [11].

In a previous study, the apparent diffusion coefficient (ADC) changes during the cardiac cycle (delta-ADC) were observed to synchronize with the volume loading [14]. This change in ADC during the cardiac cycle explained that the water molecules in intracranial tissues were moved by the systolic volume loading force. Moreover, in iNPH, the delta-ADC of the cerebral white matter increased in association with the decrease in intracranial compliance [15]. However, compared with ADC (mm^2/s), a more appropriate dimension for analyzing the change in water diffusion is displacement (μm). The diffusion distance of water molecules was acquired by q-space imaging [16]. This measurement enabled researchers to noninvasively provide information about intracranial tissue geometry [17]. The aim of the present study was to evaluate the dynamic changes in regional water molecule displacement in the brain during the cardiac cycle (delta-displacement) in iNPH, using q-space analysis. These findings may improve our understanding of the physiology and pathological conditions of iNPH and help to diagnose in iNPH as a supplemental tool.

2. Methods

2.1. Subjects

Delta-displacement analysis was performed in patients with iNPH (12 men and 4 women; 77.6 ± 4.15 years), atrophic ventricular dilation (VD) with an Evans index value greater than 0.3 (atrophic VD; 7 men and 4 women; 72.9 ± 9.29 years), and in healthy volunteers (control; 4 men and 6 women; 71.9 ± 6.98 years), using a 1.5-T MRI system (Gyroscan Intera; Philips Medical Systems International, Best, The Netherlands). The criteria for iNPH selection were based on clinical evidence from clinical examinations, brain imaging, and CSF tap tests, according to the Japanese guidelines [18]. All patients with iNPH showed improvement after CSF tap tests, according to symptom analyses after lumbar punctures and CSF removal. All patients with iNPH had the clinical symptoms, and positive CSF tap test result, while the atrophic VDs did not have any clinical symptoms and underlying diseases. The all images in the patients with iNPH were acquired before CSF tap tests. The purpose and procedures associated with our investigations were fully explained to all patients, and the studies were performed only after obtaining informed consent from each patient. This study was approved by the institutional review board of our institution.

2.2. Delta-displacement measurements

Electrocardiogram (ECG)-triggered single-shot diffusion echo planar imaging (EPI) was performed to obtain diffusion-weighted images (DWI) for each b-value during the cardiac cycle. The signal decay was fitted using the exponential curve as a function of the b-value. Subsequently, we converted data from the fitted exponential curve into the reciprocal spatial vector q, defined as Eq. (1)-based curve:

$$q = \frac{\gamma G \delta}{2\pi} \quad (1)$$

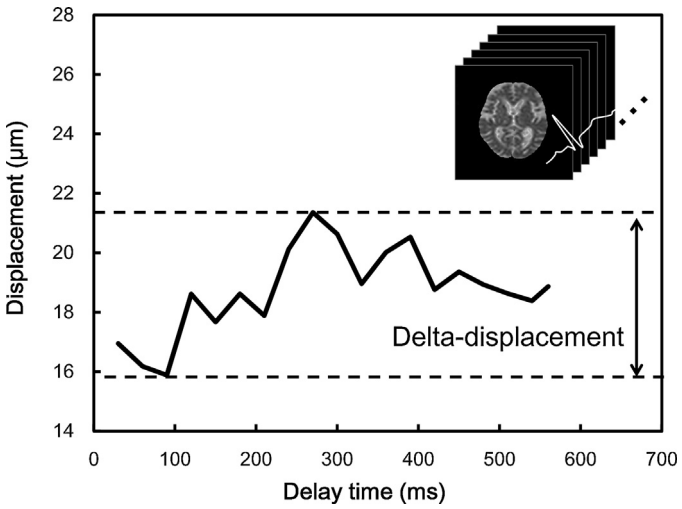

Fig. 1. Overview of the delta-displacement analysis. Displacement and intracranial volume changes during the cardiac cycle. The displacement synchronized with the volume loading during the cardiac cycle.

where γ is the gyromagnetic ratio, δ is the duration of the pulsed gradients, and G is the amplitude of the diffusion gradients.

We increased the data points as a function of the reciprocal spatial vector q, using interpolation and extrapolation processes to reduce the truncation artifacts in the subsequent Fourier transform and improve the resolution. Hence, the extrapolated maximum q value was 7941 mm^{-1}. The displacement probability profiles were obtained by performing a Fourier transform on the resulting curve with regard to the q for each pixel. The full width at half-height was used to calculate the mean water molecule displacement from these profiles on a pixel-by-pixel basis. The delta-displacement was calculated from the entire cardiac phase on a pixel-by-pixel basis, using the following equation:

$$\text{Delta-displacement} = \text{displacement}_{max} - \text{displacement}_{min} \quad (2)$$

In this equation, $\text{displacement}_{max}$ and $\text{displacement}_{min}$ represents the maximum and minimum displacement values during the cardiac cycle, respectively (Fig. 1). Moreover, the delay time of peak displacement during the cardiac cycle was also calculated on a pixel-by-pixel basis. We assessed delta-displacement, displacement, and the delay time of peak displacement value in frontal white matter. To obtain the inherent water diffusion data in the intracranial tissues, the diastolic phase displacement value was measured [19]. The region of interest (ROI) was manually defined only in the frontal white matter and excluded the periventricular high intensity area in b0 image, since the white matter areas excepting the frontal lobe were extremely small in the iNPH and atrophic VD cases. Therefore, we evaluated only the frontal white matter to avoid a partial volume effect. Moreover, Nakamura et al. reported that only ADC in the white matter was changed by volume loading [14]. Each value represented the estimated average of both deep white matter areas greater than 50 mm^2 (Fig. 2).

2.3. Imaging conditions

The DWIs for each b-value at the basal ganglia level were obtained using ECG-triggered multi-phase single-shot diffusion EPI, which is largely insensitive to motion. However, single-shot EPI alone cannot completely eliminate the bulk motion effect of the brain parenchyma because of the long data-sampling window. These artifacts may still be visible, even in a single-shot EPI image [20]. Therefore, single-shot EPI was combined with the parallel imaging, half-scan, and rectangular field-of-view (FOV) techniques