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Review article

Diffusion MRI abnormalities in pediatric neurological disorders

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Abstract

Diffusion-weighted imaging (DWI) makes it possible to measure early changes in cellular function in the central nervous system. The purpose of this article is to discuss the diagnostic value of diffusion-weighted and diffusion tensor imaging (DTI) in different pediatric cerebral disorders. First, the principles of DWI and DTI are briefly reviewed. The clinical usefulness of these imaging techniques is then discussed using cases with pediatric neurological disorders, such as hypoxic–ischemic encephalopathy in neonates, trauma (shaken baby syndrome), encephalopathy or encephalitis in infants, posterior reversible encephalopathy syndrome and congenital brain anomaly (callosal dysgenesis). In addition, using DTI, we evaluate normal brain development, particularly in the corpus callosum and cortico-spinal tract, and discuss the application of DTI to the study of white matter in the developing brain.

Keywords: Diffusion-weighted imaging; Diffusion tensor imaging; Brain edema; Pediatric neurological disorders; Developing brain; Neuroplasticity

1. Introduction

The development of diffusion-weighted imaging (DWI) has facilitated the imaging of acute physiological function of the brain in children [1]. The first studies with DWI in children with cerebral infarction and hypoxic–ischemic encephalopathy (HIE) were published in the late 1990s [2,3]. These studies found that DWI could detect the early presence and extent of parenchymal injury and differentiate between hypoxic–ischemic injury and focal infarction. Lately, DWI has also been recommended for neuroimaging in the neonate, and has been used as a tool for assessing the outcome and the effects of neuroprotective agents [4,5]. MRI with DWI is now not only the most important diagnostic tool for evaluating children when stroke is part of the differential diagnosis but has also become an essential part of the evaluation of nearly all pediatric central nervous system disorders. Furthermore, the novel techniques of diffusion tensor imaging (DTI) and tractography (DTT) may also lead to new avenues of research for the clinical evaluation of brain development, including neuroplasticity [6–9].

2. Principle

2.1. Diffusion properties

Diffusion occurs as a result of the constant movement of water molecules, which is called "Brownian motion" after the scientist who first described it. This phenomenon (i.e. diffusion) can be demonstrated by adding a few drops of ink to a still bucket of water. Initially, the ink will be concentrated in a very small volume, but it will quickly spread out and mix with the rest of the water. This process can be detected by DWI, which adds specific field gradients (motion-probing gradient; MPG) to conventional MRI (usually T2-WI) [10]. The brain is a complex of fibrous, globular and other structures and membranes, which may or may not allow water to move freely. Since water molecules run into the components of cells at different concentrations in

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different cellular compartments, they spread at different rates. In addition, they do not behave in the same way when moving in different directions. The former phenomenon is reflected by the apparent diffusion coefficient (ADC) and the latter, called diffusion anisotropy, is measured as fractional anisotropy (FA).

2.2. Signal intensity of DWI and ADC map

According to the Einstein equation, the degree of diffusion is determined by the value of the diffusion coefficient in the diffusion system. On DWI, the diffusion coefficient is called the apparent diffusion coefficient and the signal intensity of DWI depends on the value of the ADC. For instance, if the ADC is high, the intensity of DWI is decreased. Thus, the diffusion process can be detected by DWI, which adds a motion-probing gradient (MPG) to conventional T2-weighted MR imaging. MPG reduces the MR signal intensity when the degree of diffusion is increased. Thus, if the ADC value is high, the intensity of DWI is reduced and usually appears dark. Despite the high ADC value, a high intensity on DWI is occasionally seen, as a result of T2 prolongation. This well-known phenomenon is called T2 shine-through [11]. On the other hand, if the ADC value is low, the signal intensity of DWI is increased and appears bright.

Based on the percentage decrease in signal intensity on DWI, the computer calculates an ADC value in each part of the brain. An ADC map shows the ADC value, where a high ADC value is represented by a bright display. Thus, in contrast to DWI, an ADC map shows an area of increased diffusion with a bright signal and an area of decreased diffusion with a dark signal.

2.3. Brain edema

Brain edema is defined as the accumulation of excess fluid in cells or in the extracellular space, and can be classified as cytotoxic, vasogenic or interstitial edema. Cytotoxic edema, which is mainly caused by an energy failure in neuronal and/or glial cells, may accompany infarction, HIE, traumatic brain injury, such as in shaken baby syndrome, status epilepticus, encephalitis/encephalopathy, and the early phase of neuro-glial degeneration. Cytotoxic edema characteristically shows hyperintensity on DWI associated with decreased ADC [12,13]. Generally, the affected area of cytotoxic edema on DWI seems to be irreversibly damaged tissue, resulting in coagulative or liquefactive necrosis. However, some cytotoxic edema, such as intramyelinic edema, may reflect a reversible disorder. On the other hand, vasogenic edema, which is characterized by dysfunction of the blood–brain barrier, allows for the abnormal passage of proteins, electrolytes and water into extracellular compartments. Osmotic and hydrostatic gradients can also cause interstitial edema, by increasing the extracellular space as water moves from vessels and/or ventricles. These kinds of edema (vasogenic and interstitial edema) show an increase in interstitial space in white matter and result in a decreased signal on DWI with increased ADC [13,14]. The affected area of vasogenic and/or interstitial edema on DWI is usually reversible. Thus, DWI can differentiate cytotoxic edema, which usually is not reversible, from vasogenic and interstitial edema, which usually are reversible.

3. Cases (diseases)

3.1. Normal brains of neonates and infants

The water content of the pediatric brain is higher than that of the adult brain. Therefore, the normal brains of neonates and infants have significantly higher ADC values than adult brains. Since the ADC values in both gray and white matter of newborns are considerably higher than those in adults, and since ADC in white matter is higher than that in gray matter, the deep white matter in newborns normally shows hypointensity on DWI in association with increased ADC [15–17]. ADC at birth is also higher in subcortical white matter than in both the anterior and posterior limbs of the internal capsule (Fig. 1)[18]. In addition, it is higher in the cortex and caudate nucleus than in the thalamus and lentiform nucleus. With maturation, ADC values tend to be decreased in most areas of the pediatric brain [19].

3.2. Hypoxic–ischemic encephalopathy (HIE)

HIE is the result of decreased global perfusion or oxygenation, generally due to neonatal asphyxia, hypoglycemia, cardiac arrest or child abuse. Since the water content of the pediatric brain is significantly high, it is more difficult to diagnose HIE in neonates and infants

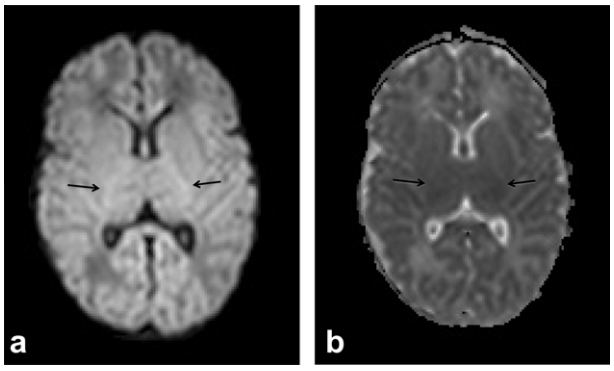

Fig. 1. DWI (a) and ADC map (b) in a 20-day-old neonate. The frontal and temporo-occipital white matters show a much lower intensity with increased ADC compared to that of the cerebral cortex. Note that the posterior limb of the internal capsule (arrows) shows a slightly high intensity with decreased ADC compared to the surrounding basal gray matter.