B-value dependence of DTI quantitation and sensitivity in detecting neural tissue changes

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A B S T R A C T
Recently, remarkable success has been demonstrated in using MR diffusion tensor imaging (DTI) to characterize white matter. Water diffusion in complex biological tissue microstructure is not a free or Gaussian process but is hindered and restricted, thus contradicting the basic assumption in conventional DTI that diffusion weighted signal decays with b-value in a monoexponential manner. Nevertheless, DTI by far is still the fastest and most robust protocol in routine research and clinical settings. To assess the b-value dependence of DTI indices and evaluate their sensitivities in detecting neural tissues changes, in vivo DTI data acquired from rat brains at postnatal day 13, 21 and 120 with different b-values (0.5–2.5 ms/μm²) and 30 gradient directions were analyzed. Results showed that the mean and directional diffusivities consistently decreased with b-value in both white and gray matters. The sensitivity of axial diffusivity (λ⊥) in monitoring brain maturation generally decreased with b-value whereas that of radial diffusivity (λ∥) increased. FA generally varied less with b-value but in a manner dependent of the age and tissue type. Analysis also revealed that the FA sensitivity in detecting specific tissue changes was affected by b-value. These experimental findings confirmed the crucial effect of b-value on quantitative DTI in monitoring neural tissue alterations. They suggested that the choice of b-value in conventional DTI acquisition can be optimized for detecting neural tissue changes but shall depend on the specific tissue type and its changes or pathologies targeted, and caution must be taken in interpreting DTI indices.

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Introduction

MR diffusion tensor imaging (DTI) has been shown to provide microstructural information in characterizing tissue microanatomy (Basser, 1995; Basser and Pierpaoli, 1996) that other non-invasive modalities cannot offer. Typical DTI indices, derived from the diffusion tensor as rotationally-invariant parameters, include fractional anisotropy (FA), mean (MD), axial (λ⊥) and radial (λ∥) diffusivities. As water diffusion in nerve fibers is anisotropic due to myelination and other inherent axonal structures (Beaulieu, 2002), DTI has demonstrated remarkable success in probing the white matter (WM) integrity, and in describing the orientational neuroarchitecture and connectivity in the central nervous system (CNS). In recent years, DTI has been employed extensively to study the WM associated with both normal physiological and pathophysiological changes, including brain development and aging (Rockhorst et al., 2008; Qiu et al., 2008; Sullivan and Pfefferbaum, 2006; Verma et al., 2005), neurological and psychiatric disorders (Damoiseaux et al., 2008; Kolbe et al., 2009; Roosendaal et al., 2009; Rusch et al., 2007; Song et al., 2004; Sun et al., 2005), brain injuries and tumor (Chan et al., 2009a,b; Kidwell and Wintermark, 2008; Schonberg et al., 2006; Wang et al., 2008, 2009), and cognitive functions (Bucur et al., 2008; Qiu et al., 2008; Teipel et al., 2009).

The 2nd-order three-dimensional diffusion tensor (DT) model assumes that diffusion weighted (DW) signal has a monoexponential dependence on the diffusion-weighting factor (i.e., b-value). In other words, it assumes that water diffusion occurs in a free and unrestricted environment, yielding a Gaussian distribution of water diffusion displacement. However, the complex cellular or axonal microstructures in biological tissues hinder and restrict water molecule diffusion, and lead to restricted or non-Gaussian diffusion. DW signal from biological tissues is thus non-monoexponential with respect to b-value. In addition, because of the anisotropic nature of WM such as the corpus callosum, the extent of diffusion restriction is direction-dependent. Therefore, both directional diffusivities and FA can be b-value dependent, complicating the quantitative and comparative DTI studies.

Despite these fundamental limitations, conventional DTI is still the fastest, relatively robust and accessible protocol for investigation of water diffusion characteristics in neural tissues under routine clinical and research settings. Thus one key question is whether b-
value in DTI can be optimized for characterizing the diffusion behaviors and/or their changes associated with specific cellular microstructure or pathology. A number of studies have been reported to optimize b-value for improving the detection of changes involved in brain development (Dudink et al., 2008; Jones et al., 2003), infarction (Meyer et al., 2000; Toyoda et al., 2007) and glioma (Alvarez-Linera et al., 2008; Seo et al., 2008). Several studies also investigated the effect of b-values on MD and FA derived in DTI (Jones and Basser, 2004; Melhem et al., 2000). However, the majority of these studies focused on MD and FA only. It is important to note that FA often cannot distinguish one pathologic condition from another because most pathologies, such as demyelination and axonal damage (Sun et al., 2006), would simply result in FA loss or reduction. Similarly, MD cannot provide the direction along which a specific pathology occurs. Given that the DTI directional analysis has been successfully demonstrated in previous studies for elucidating specific neural tissue pathologies in both humans and animal models (Ewing-Cobbs et al., 2008; Sizonenko et al., 2007; Song et al., 2002, 2003; Sun et al., 2006; Trip et al., 2006), it is imperative to investigate the b-value dependence of both FA and directional diffusivities, and its effect on DTI sensitivity in probing neural tissue alterations.

This study aimed to examine the quantitative effect of b-value on DTI indices, and to study the optimal b-value for detecting subtle changes in tissue microstructures. As brain development is accompanied by gradual and local morphological changes in both WM and gray matter (GM) (Bockhorst et al., 2008; Dubois et al., 2006; Huppi and Dubois, 2006), subtle changes in water diffusion characteristics are expected to occur during brain development. Therefore, the postnatal brain maturation in the well-controlled rat model was analyzed in the present study with in vivo DTI that employed various b-values.

Materials and methods

DWIs acquired from the postnatal developing rat brains in a recent study by our group (Cheung et al., 2009) were employed to derive DTI indices for various b-values. These DWIs were originally collected to evaluate the efficacy of diffusion kurtosis imaging. In brief, three groups of normal Sprague–Dawley (SD) rats were scanned. They were postnatal day 13 (P13), 31 (P31) and 120 (P120). Sample size was six for each age group. All experiments were conducted using a Bruker PharmaScan 7T scanner. DWIs were acquired with a respiration-gated 4-shot SE-EPI sequence with six different b-values (0.0, 0.5, 1.0, 1.5, 2.0, and 2.5 ms/m²) along 30 gradient encoding directions. For P13, a 23 mm birdcage quadrature RF coil was used for both transmission and receive. The imaging parameters were TR/TE = 3000/33.3 ms, ∆/Δ = 5/20 ms, slice thickness = 0.7 mm, FOV = 25 mm, data matrix = 128 × 128 (zero-filled to 256 × 256) and NEX = 4 for P13 rats. For P31 and P120 rats, a birdcage transmit-only coil with a 72 mm inner diameter in combination with an actively decoupled receive-only quadrature surface coil was used. The imaging parameters were TR/TE = 3000/30.3 ms, ∆/Δ = 5/17 ms, slice thickness = 1 mm, FOV = 30 mm × 30 mm, data matrix = 128 × 128 (zero-filled to 256 × 256) and NEX = 4. For each rat, DWIs were first co-registered before computing DT matrix using AIR5.2.5 (Woods et al., 1998a,b). All DTI index map computation was performed by a home-written MATLAB program. MD, FA, λ// and λ⊥ maps were calculated from DWIs with two b-values, 0.0 versus 0.5, 1.0, 1.5, 2.0 or 2.5 ms/m², respectively. These DTI index maps were also computed by fitting all DWIs with all six b-values to the monoexponential model DW(b)/DW(0) = exp(− bΔ).

Multi-slice region-of-interests (ROIs) were first defined in the FA maps as previously described (Cheung et al., 2009; Hui et al., 2008). They included four WM structures, including corpus callosum (CC), external capsule (EC), cerebral peduncle (CP) and anterior commissure (AC), and three GM structures, namely cortex (CT), hippocampus (HP) and caudate putamen (CU) as shown in Fig. 1. They were used to measure the average MD, FA, λ// and λ⊥ values computed by DTI using various b-values (as well as all six b-values) in these tissue structures. These quantitative DTI indices were analyzed for their b-value dependence. To evaluate their sensitivity in detecting brain maturational changes, analysis of variance (ANOVA) was performed on these b-value specific measurements, followed by Tukey’s test to examine their differences among three age groups. +p<0.05 and #p<0.01 were considered as statistically significant. The sensitivities associated with different b-values were compared. For each specific b-value, the overall sensitivity was assessed by the number of statistical

Fig. 1. Typical ROI definitions overlaid on the fractional anisotropy (FA) maps in a postnatal day 120 (P120) rat brain. ROIs were used to measure the DTI indices associated with various b-values used by DTI. Four WM structures, corpus callosum (CC), external capsule (EC), cerebral peduncle (CP), and anterior commissure (AC), and three GM structures, cerebral cortex (CT), hippocampus (HP), and caudate putamen (CU), were identified in the FA maps.
significances found in all three inter-group comparisons for four WM and three GM structures.

**Results**

*DTI index maps computed by DTI using different b-values*

Fig. 2 illustrates the typical FA, MD, $\lambda_{//}$ and $\lambda_{\perp}$ maps for each age group as computed by DTI model using different two b-value sets (0.0 versus a non-zero b-value) as well as using all six b-values via monoexponential fitting (Monoexp). Note that each type of DTI index maps is displayed in the same grayscale for all three age groups. It can be easily observed that the mean and directional diffusivities generally decreased with b-value. The structural contrasts between WM, GM and cerebrospinal fluid (CSF) in MD, $\lambda_{//}$, $\lambda_{\perp}$ and FA maps are also seen to vary with b-value.

Fig. 3 illustrates the typical non-monoexponential b-value dependence of DW signals observed in both WM and GM structures.
also given in Table 1. As shown in Fig. 4 and Table 1, MD, FA was also observed to vary with b-value, smallest decreases. FA was also observed to vary with b-value, generally decreased with b-value (one-way ANOVA, p<0.001) in all seven structures in each age group, with P13 group generally exhibiting the smallest decreases. FA was also observed to vary with b-value, however, without a general trend for all structures in all age groups. For example, as shown in Table 1 and Fig. 4b, GM FA in P120 group increased slightly with b-value whereas WM FA generally increased and then decreased slightly. P13 and P31 groups showed largely similar but not identical FA variations with b-value.

Discussions

In our previous study, the diffusion kurtosis imaging model that requires DWIs with multiple b-values was shown to offer more sensitive and directionally specific detection of the brain developmental changes in both WM and GM than conventional DTI, including the DTI based on the monoexponential fitting of DWIs with all b-values (Cheung et al., 2009). Despite the inadequacy of DTI model to comprehensively characterize the neural tissue as compared to diffusion kurtosis imaging and other high-order diffusion models (Bennett et al., 2003; Callaghan, 1991; Jensen et al., 2005; Liu et al., 2004; Lu et al., 2006; Maier et al., 2004; Mulkern et al., 1999; Niendorf et al., 1996; Ozarslan and Mareci, 2003; Tuch et al., 1999; Wedeen et al., 2004; Lu et al., 2005), DTI remains to be the most efficient and robust protocol. The current study systematically examined the critical role of b-value in DTI quantitation. More importantly, it demonstrated that b-value in conventional DTI acquisition can be optimized for improved sensitivity in detecting neural tissue alterations, depending on the specific tissue type and its physiological or pathological alterations to be examined.

B-value dependence of DTI quantitation

The current study demonstrated that b-value strongly influences the quantitation of various DTI indices when applied to developmental rat brains. As shown in Fig. 4, the directional and mean diffusivities decreased substantially with the b-value used in the current DTI protocol. Moreover, FA quantitation was also influenced by b-value to various extents, depending on the brain structure and maturation. Note that earlier studies have shown that inadequate SNR can affect the DTI quantitation. However, such SNR related variation can be substantially reduced when the SNR in raw DWIs is higher than 20 (Bastin et al., 1998; Farrell et al., 2007). Given the large SNRs (>20 for all b-values and age groups) and that 30 diffusion directions were used to derive diffusion tensor in the current study, the quantitation of various DTI indices and their sensitivities in detecting group differences should not be affected substantially by the SNR variations between different b-values.

The decrease of apparent diffusivity with b-value has been previously accounted for by the non-monoexponentiality of DW

DTI sensitivity in detecting brain maturational changes versus b-values

The results in Fig. 4 are re-plotted in Fig. 5. The sensitivity of various DTI indices associated with specific b-value and those computed from all six b-values was examined for their ability to detect brain maturational changes in different tissue structures. The numbers of statistically significant differences detected for four WM and three GM structures are indicated in upper right corner of each plot. Fig. 5 clearly demonstrates that the b-value used in DTI affected the ability of MD, \( \lambda_{//} \) and \( \lambda_{\perp} \) to monitor tissue changes. For example, the number of statistical significances detected by \( \lambda_{//} \) generally decreased with b-value in each WM structure (excluding CC), with total number decreasing from eight to four in all four WM structures. However, the opposite trend existed for \( \lambda_{\perp} \), with the number of statistical significances observed in 4 WM structures increasing from 3 to 10. For GM structures, \( \lambda_{//} \) and \( \lambda_{\perp} \) again exhibited b-value dependent sensitivity (generally higher at either lower or high b-values) in detecting maturational changes while MD sensitivity generally decreased with b-value. As for FA, the number of statistical significances decreased slightly at the highest b-value for CC and EC, and remained the same at all b-values for CP and AC. For GM structures, it decreased at both low and high b-values for CT, generally decreased with b-value for HP and increased for CU. Note that the sensitivity of the indices computed from all six b-values via monoexponential DTI model generally falls within those at the lowest and highest b-values.

Normalized DW signal averaged along 30 diffusion gradient directions versus b-value is plotted for CP and CU in P13, P31 and P120 rats. Error bars represent the DW signal variations among all gradient directions. These normalized decay curves for P13, P31 and P120 brains sometimes cross each other within the b-value range studied, particularly for the WM CP, indicating the change in non-monoexponential behavior during brain maturation. Such observation confirms that the non-monoexponential behavior, i.e., nature of non-free or restricted diffusion, is dependent of the neural tissue microstructural characteristics that, in this case, accompany the brain maturation. The signal-to-noise ratio (SNR) in typical DWIs was assessed and computed as the average SNR of whole brain among 30 diffusion gradient directions (as measured as the ratio of whole brain signal to the standard deviation of background noise). It was sufficiently high for all b-values and age groups, typically above 25 for the largest b-value of 2.5 ms/\( \mu \text{m}^2 \) and 120 for the smallest b-value of 0.5 ms/\( \mu \text{m}^2 \).

DTI index quantitation versus b-values

Fig. 4 shows the ROI measurements of various DTI indices that were computed by DTI using different b-values in various WM and GM structures in three age groups. The trends of these measurements generally reflect those shown in Fig. 2. The P120 measurements are also given in Table 1. As shown in Fig. 4 and Table 1, MD, \( \lambda_{//} \) and \( \lambda_{\perp} \) decreased with b-value (one-way ANOVA, p<0.001) in all seven structures in each age group, with P13 group generally exhibiting the smallest decreases. FA was also observed to vary with b-value, however, without a general trend for all structures in all age groups. For example, as shown in Table 1 and Fig. 4b, GM FA in P120 group increased slightly with b-value whereas WM FA generally increased and then decreased slightly. P13 and P31 groups showed largely similar but not identical FA variations with b-value.
signal using a two-compartment model (Clark and Le Bihan, 2000; Mulkern et al., 1999; Niendorf et al., 1996). The tortuous and hindered extracellular space and restricted intracellular space can be generally considered as fast and slow compartments, respectively, though the water exchange across cellular membrane is viewed as another key factor. In the presence of these compartments, DW

Fig. 4. $\lambda_{//}$ and $\lambda_{\perp}$ (a) and FA and MD (b) in different WM and GM structures in three age groups ($n=6$ per group) that were computed by DTI using different b-values (in ms/$\mu$m$^2$) and all b-values via monoexponential fitting (Monoexp). Error bar indicates the standard deviation of ROI measurements within each age group. One-way ANOVA confirmed the $\lambda_{//}$, $\lambda_{\perp}$, and MD decreases with respect to b-value ($p<0.0001$) for each tissue structure in each age group.
signal arises as the weighted sum of these compartments. The signals from the fast compartment decay much faster with b-value than those from the slow compartment. Consequently, all apparent diffusivities that are quantified by fitting the monoexponential DT model with 2 DW measurements (using the zero b-value and one non-zero b-value as in conventional DTI) will gradually decrease with the non-zero b-value used. As the non-monoexponential decay behavior is dictated by the complex underlying cellular microstructures that are not necessarily isotropic, it can vary with the microstructural orientation. In other words, the b-value dependence of apparent diffusivity can be direction dependent. Therefore, FA quantitation can also be influenced by b-value as observed in the current study.

It is noteworthy that the diffusion time used in DTI protocol can potentially affect the non-monoexponential decay behavior because the exact effect of the restrictive diffusion environment on DW signals depends on not only the tissue microstructures and their dimensions, but also the probing distance or diffusion distance within diffusion time. Although an earlier study indicated that WM DTI indices were largely unchanged for diffusion time ranging from 8 to 80 ms at $b=0.7$ ms/$\mu$m² in human CC (Clark et al., 2001), more comprehensive study is needed to characterize the effect of diffusion time on DTI quantitation of both WM and GM structures.

**Effect of b-value on the sensitivity of DTI indices in detecting brain maturation**

In general, the sensitivity of $\lambda_i$ in detecting rat brain WM maturation was observed to be the highest at low b-value (0.5 ms/$\mu$m²) as judged by the total number of statistical significances shown in Fig. 5a whereas that of $\lambda_c$ was the highest at high b-value (2.5 ms/$\mu$m²). At relatively low b-value, apparent diffusivity is primarily contributed from the fast water diffusion activities along extracellular space that depend on both cellular microstructure and membrane permeability (Clark and Le Bihan, 2000; Ford et al., 1998; Niendorf et al., 1996; Pfeuffer et al., 1999; Ronen et al., 2005). Thus their changes can be best detected using low b-value. The high $\lambda_i$ sensitivity at low b-value observed in the current study suggested the alterations of these fast water diffusion activities along axonal direction during brain maturation. Such alterations may result from the increase in packing density of fiber bundles and axons, axonal diameter increase, changes in neuroblobs, and increased complexity of extracellular matrix (Dubois et al., 2006; Huppi and Dubois, 2006). On the other hand, the diffusion changes probed in WM using high b-value are ascribed more to the slow water molecule diffusion particularly along the direction perpendicular to axonal direction, i.e., when traversing the membranes and myelin sheaths (Cheung et al., 2009; Hui et al., 2008; Ronen et al., 2005). The high sensitivity of $\lambda_c$ at high b-value in detecting brain maturation shown in Fig. 5a likely reflects these WM microstructural changes, including myelination and axonal density and diameter changes during postnatal brain development.

The current study also demonstrated that b-value does affect the FA quantitation and its ability in detecting brain maturational changes as shown in Figs. 4b and 5b though its exact effect can vary among different structures. These findings implied that the WM connectivity or tractography (Mori et al., 1999) that is typically derived from the preferential diffusion direction and FA magnitude computed in conventional DTI should be assessed with caution because FA quantitation can be influenced by b-value differently for different WM structures and under different developmental or pathological conditions.

**Other issues concerning optimal b-value in DTI for detecting tissue changes**

Several DTI studies (using b-value ranging from 0.8 to 1.0 ms/$\mu$m²) by others showed that axonal damage leads to $\lambda_i$ decrease whereas demyelination causes $\lambda_c$ increase (Kolbe et al., 2009; Roosendaal et al., 2009; Song et al., 2003, 2002; Sun et al., 2006). Our current study suggested that $\lambda_i$ at lower b-value and $\lambda_c$ at higher b-value may be more sensitive in detecting such axonal damage and demyelination, respectively. However, the current results also indicated that, in general, whether $\lambda_i$ or $\lambda_c$ is capable of detecting any such changes critically depends on the specific b-value used, underscoring a fundamental limitation of DTI when analyzing the directional diffusivities. This highlights the need for careful validation before associating any directional diffusivity changes with specific normal or pathological conditions. Furthermore, though numerous studies have demonstrated the FA quantitation...
a

\[ \lambda_2 \] (\mu m^2/ms)

\begin{align*}
\text{P13} & \quad \text{P31} & \quad \text{P120} \\
8(7^2+1^2) \div 6(3^2+3^2) & \quad \text{b=0.5} & \quad \text{b=0.5} \\
9(7^2+2^2) \div 2(2^2) & \quad \text{b=1.0} & \quad \text{b=1.0} \\
7(4^2+3^2) \div 2(2^2) & \quad \text{b=1.5} & \quad \text{b=1.5} \\
4(3^2+1^2) \div 3(3^2) & \quad \text{b=2.0} & \quad \text{b=2.0} \\
4(2^2+2^2) \div 4(4^2) & \quad \text{b=2.5} & \quad \text{b=2.5} \\
6(3^2+3^2) \div 2(2^2) & \quad \text{Monoexp} & \quad \text{Monoexp} \\
\end{align*}

b

\[ \text{FA} \]

\begin{align*}
\text{P13} & \quad \text{P31} & \quad \text{P120} \\
11(10^2+1^2) \div 6(4^2+2^2) & \quad \text{b=0.5} & \quad \text{b=0.5} \\
11(11^2) \div 6(5^2+1^2) & \quad \text{b=1.0} & \quad \text{b=1.0} \\
11(11^2) \div 5(5^2) & \quad \text{b=1.5} & \quad \text{b=1.5} \\
11(10^2+1^2) \div 5(5^2) & \quad \text{b=2.0} & \quad \text{b=2.0} \\
9(8^2+1^2) \div 5(5^2) & \quad \text{b=2.5} & \quad \text{b=2.5} \\
10(10^2) \div 6(5^2+1^2) & \quad \text{Monoexp} & \quad \text{Monoexp} \\
\end{align*}

\[ \text{MD} \] (\mu m^2/ms)

\begin{align*}
\text{P13} & \quad \text{P31} & \quad \text{P120} \\
7(4^2+3^2) \div 5(3^2+2^2) & \quad \text{b=0.5} & \quad \text{b=0.5} \\
2(1^2+1^2) \div 3(3^2) & \quad \text{b=1.0} & \quad \text{b=1.0} \\
3(1^2+2^2) \div 3(1^2+2^2) & \quad \text{b=1.5} & \quad \text{b=1.5} \\
5(4^2+1^2) \div 2(1^2+1^2) & \quad \text{b=2.0} & \quad \text{b=2.0} \\
9(7^2+2^2) \div 3(2^2+1^2) & \quad \text{b=2.5} & \quad \text{b=2.5} \\
4(1^2+3^2) \div 3(1^2+2^2) & \quad \text{Monoexp} & \quad \text{Monoexp} \\
\end{align*}
dosages can induce apoptotic neurodegeneration and subsequent 

λ showed that the mean and directional diffusivities consistently 

changes during rat brain development was investigated. The results 

probed by DTI using very high b-values (Meier et al., 2003; Pfeuffer et 

exact effect of b-value in quantitation of various DTI indices. Previous 

addition, the neonatal rats were not longitudinally studied because of 

numerous and complex determinants, including cellular microstruc-


tions. FA generally changed less with b-

value but in a manner dependent of the age and tissue type. The FA 

sensitivity in detecting specific tissue changes was also affected by 

value. These experimental findings confirmed the crucial effect of b-

value on quantitative DTI in monitoring neural tissue alterations. They 

suggested that the choice of b-value in conventional DTI acquisition 

can be optimized for detecting neural tissue changes, depending on the 

specific tissue type and its changes or pathologies targeted, and 

caution be taken in interpreting DTI indices.

**Limitations of current study**

In this study, the direct histological correlation between DTI indices and specific tissue morphological characteristics was not attempted because water diffusion process in vivo is affected by numerous and complex determinants, including cellular microstructures, membrane permeability or water exchange, and possibly other biophysical properties associated with different water populations. In addition, the neonatal rats were not longitudinally studied because of the likely adverse effects of repetitive anesthesia during MRI scans on early postnatal brain development. Studies have shown that exposure to common anesthetic drugs including isoflurane at clinically relevant dosages can induce apoptotic neurodegeneration and subsequent cognitive deficits in neonatal rodents (Ikonomidou et al., 1999; Jevtovic-Todorovic et al., 2003; Loepeke et al., 2006). Another limitation of the current study was the b-value range studied. Ideally, a larger range with smaller intervals would be desired to examine the exact effect of b-value in quantitation of various DTI indices. Previous studies have shown that extra microstructural information can be probed by DTI using very high b-values (Meier et al., 2003; Pfeuffer et al., 1999). Nevertheless, the main focus of the current study was to investigate the effect of b-value on various conventional DTI indices and their sensitivities in detecting tissue changes. The b-value range used in the current study covered those from typical DTI protocols and human DTI studies. Moreover, though technical challenging, more isotropic voxel, true 3D acquisition and voxel-based analysis would strengthen the current study and may potentially lead to more findings.

**Conclusions**

The effect of b-value on the absolute quantitation of various DTI indices and their sensitivity in detecting tissue microstructural changes during rat brain development was investigated. The results showed that the mean and directional diffusivities consistently decreased with b-value in both white and gray matter. The sensitivity of λ⊥ in monitoring brain maturation generally decreased with b-value whereas that of λ∥ increased. FA generally changed less with b-value but in a manner dependent of the age and tissue type. The FA sensitivity in detecting specific tissue changes was also affected by b-value. These experimental findings confirmed the crucial effect of b-value on quantitative DTI in monitoring neural tissue alterations. They suggested that the choice of b-value in conventional DTI acquisition can be optimized for detecting neural tissue changes, depending on the specific tissue type and its changes or pathologies targeted, and caution be taken in interpreting DTI indices.

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