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Review

Diffusion tensor imaging in hemorrhagic stroke

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ABSTRACT

Diffusion tensor imaging (DTI) has evolved considerably over the last decade to now be knocking on the doors of wider clinical applications. There have been several efforts over the last decade to seek valuable and reliable application of DTI in different neurological disorders. The role of DTI in predicting outcomes in patients with brain tumors has been extensively studied and has become a fairly established clinical tool in this scenario. More recently DTI has been applied in mild traumatic brain injury to predict clinical outcomes based on DTI of the white matter tracts. The resolution of white matter fiber tractography based on DTI has improved over the years with increased magnet strength and better tractography post-processing. The role of DTI in hemorrhagic stroke has been studied preliminarily in the scientific literature. There is some evidence that DTI may be efficacious in predicting outcomes of motor function in animal models of intracranial hemorrhage. Only a handful of studies of DTI have been performed in subarachnoid hemorrhage or intraventricular hemorrhage scenarios. In this manuscript we will review the evolution of DTI, the existing evidence for its role in hemorrhagic stroke and discuss possible application of this non-invasive evaluation technique of human cerebral white matter tracts in the future.

Contents

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Introduction

Stroke is one of the most common causes of morbidity and mortality in the developed and the developing world (Pendlebury, 2007; Leak et al., 2014). There are two major stroke subtypes, ischemic stroke and hemorrhagic stroke. The commonest of them is ischemic stroke (IS) followed by subarachnoid hemorrhage (SAH), intraventricular hemorrhage (IVH) and then intracerebral hemorrhage (ICH) in the hemorrhagic subtype (Xi et al., 2014; Chen et al., 2014; Pandey and Xi, 2014; Zhang, 2014). Amongst the different types of stroke the incidence of ICH is approximately 13% and SAH is 25–30%. In the SAH group of patients, surgical treatment in the form of clipping or endovascular coil embolization is performed to preclude the risk of a subsequent fatal hemorrhage. Similarly in the ICH patients surgical evacuation is performed in large hemorrhages with mass effect. However, currently there are very few effective therapeutic options available to reduce the neurological dysfunction caused by the hemorrhagic insult. The understanding of the mechanisms of neuronal injury in these clinical settings continues to evolve. Several therapeutic options in the form of neuroprotective agents have been shown to hold promise in the animal population but have not yet translated to show benefit in human subjects.

While better and more non-human primate models are being devised to improve the understanding of the underlying pathophysiology of hemorrhagic stroke (Tso and Macdonald, 2014; Wagner, 2007), non-invasive imaging with MRI and CT of the brain is being utilized with a view to develop biomarkers to visualize these mechanisms of neuronal injury. Standard MRI of the brain delineates superficial and deeper brain parenchymal structures in great detail. Then there are other specialized sequences that have been developed that have not yet entered the routine clinical domain. These specialized sequences are able to shed light on the normal physiology of neuronal and axonal function. Diffusion tensor imaging or "tractography" is one such sequence that specifically looks at directionality and integrity of the axonal fibers of the brain and how they change in the event of neuronal injury due to various etiologies one of them being hemorrhagic stroke.

Conventional MRI techniques are based on registering signal from a volume of tissue by repeated rephasing and dephasing of precessing protons in the particular volume imaged. Diffusion tensor imaging relies on slightly different properties of the tissues. Water molecules in most tissues diffuse equally in all directions (isotropic diffusion) but in white matter tracts the diffusion is along the direction of the tract (anisotropic). Essentially the main parameter that is measured in DTI is the degree of fractional anisotropy (FA) in a given voxel of the precessing proton and its Eigen vector in an ellipsoid domain. In each voxel imaged by DTI the Eigen vector direction in 3 dimensions has to be acquired in at least nine elements of the matrix to portray the directionality of the elaborate dataset or "tensor". At the minimum 6 directions of DTI datasets are needed to create color maps of white fiber tracts. Mathematical calculations and data processing are then utilized to show color coded maps of different white matter fiber tracts in the brain called fiber tractography (Filler, 2009). In the current manuscript we will concentrate on reviewing the role of diffusion tensor imaging (DTI) in hemorrhagic stroke i.e., SAH, IVH and ICH.

Diffusion tensor imaging — history and development

Work on the tractographic sequences began in the 1990s. The first tractographic images demonstrating the multi-dimensional directional information of the curved neural tracts in the brain were obtained in 1991 by Filler et al. when they submitted their patent descriptions on imaging a series of patients in the UK (Tso and Macdonald, 2014). Subsequently they were published in the World Intellectual Property Organization in 1993 (Tso and Macdonald, 2014). The very first images of DTI were published in the proceedings of the Society for Magnetic Resonance in Medicine annual meeting in Berlin in August 1992 (Zhang, 2014; Tso and Macdonald, 2014). Prior to 1992 the clinical community believed that the strategy of application of diffusion MRI to trace brain white matter tracts did not have any potential. The discoveries of Filler, Howe and Richards in London, England and Seattle demonstrated the feasibility of diffusion MRI in producing linear neural images of the white matter tracts of the brain in late 1991 and then were reaffirmed by investigators LeBihan and Basser in Bethesda in 1992 (Tso and Macdonald, 2014).

The initial interest in tract tracing was to study the evolution of higher function in humans from the early hominoids as for example speech (Filler, 1994; Filler et al., 2010). This was the original impetus to generate images of tracts in the brain. Diffusion nuclear magnetic resonance has been around for decades. It is yet another source of obtaining contrast in individual voxels based on the rate of signal decay that related to the degree of water to diffuse anisotropically (in a primary direction) as opposed to isotropically (in all directions) (Le Bihan, 1991). This is the basis for diffusion weighted MRI that has been utilized to demonstrate ischemic stroke for several years now (Kakuda et al., 2008; Lansberg et al., 2001). DTI is a fundamental modification in MRI data processing that allows each voxel to produce not only signal intensity data but also directional data that show the tensor (3D complex vector) direction in a 3 dimensional space. Each voxel represented by a single arrow is then collated into an array of directional arrows in the orientation of neural tracts. These directional arrows are then strung together by graphic techniques to produce linear images of nerve tracts (Filler, 2009).

Traditionally the fiber streamlines were reconstructed utilizing deterministic (Mori et al., 1999) or probabilistic methods (Jones and Pierpaoli, 2005; Lazar and Alexander, 2003; Parker et al., 2003). These methods of white fiber analysis have several limitations. When fiber pathways are being mapped at locations of intersections the traditional analysis methods are unable to display the full dispersion of the pathways. A good example of this situation is the mapping of fibers that pass through complex white matter like the centrum semiovale, where pyramidal tract, superior longitudinal fasciculus and the corpus callosum are known to intersect. As has been demonstrated by Bucci et al. these issues can be overcome by High Angular Resolution Diffusion Imaging (HARDI) technique that allows unraveling of the intersecting fibers to enable separate fiber tracking (Bucci et al., 2013). They documented feasibility of this technique in 12 patients with brain tumors

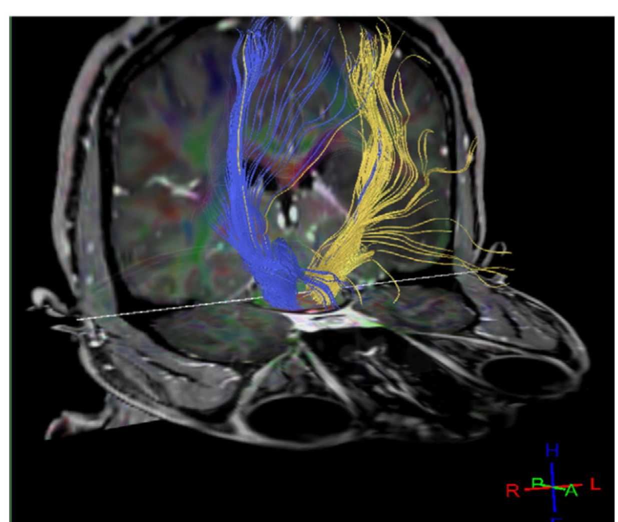

Fig. 1. 32 direction bilateral normal corticospinal tracts processed image from 3 T MRI on a human subject performed at the authors' institution. This demonstrates the current ability to perform diffusion tensor tractography on human subjects.