**Diffusion Changes in Normal Pressure Hydrocephalus**

Terry Chun, Christopher G. Filippi, Norman Relkin, Robert D. Zimmerman, Aziz M. Uluğ
Weill Medical College of Cornell University, New York, New York

**Introduction**

Normal pressure hydrocephalus (NPH) is a clinical syndrome characterized by enlargement of the brain's ventricular spaces without obstruction of cerebrospinal fluid (CSF) flow or elevation in CSF pressure. This condition may develop from a variety of processes that cause decreased resorption or over-production of CSF. The net effect of NPH is a reduction in the compliance of the brain parenchyma resulting in an increased susceptibility to brain injury. NPH is often associated with disturbances in gait, urinary continence and cognitive abilities (1).

The diffusion of water in the periventricular region is altered in hydrophilic patients due to transependymal resorption of CSF. This fluid diffuses away from the ventricular surface, producing increased extracellular water in the periventricular white matter (PVWM). The average diffusion constant ($D_{av}$) of the periventricular white matter in hydrophilic patients is increased compared to normals (2). In this study, we tested the hypothesis that transependymal resorption of ventricular fluid may lead to edema throughout the brain not only in PVWM regions. We quantified the mean brain diffusion constant in NPH patients and make comparisons to age-matched normative values.

**Methods**

In this study, we retrospectively examined the MR images of 7 patients with NPH. Diagnosis was made on the basis of clinical and imaging findings. The age range of the patients is 22-84 years with a mean age of 54.2 ± 21.3 years. The group of patients included 3 females and 4 males.

Using a 1.5 T GE Signa Echospeed scanner, images were obtained for each patient. An EPI multi-slice sequence (TE=100ms, TR=6s, 128x128, FOV=22cm, 5mm thick, 30 slices) was used to acquire axial diffusion images of entire brain. Diffusion was measured in 3 directions (x, y, z) for 4 subjects with a b-value of 100,000 $s/cm^2$ in each direction. An image without diffusion gradients also was acquired. For 3 patients, we measured diffusion in 7 directions (x, y, z, xy, xz, yz, xyz) with a b-value of 100,000 $s/cm^2$. Orientation independent diffusion maps ($D_{av} = \text{Trace}/3 = [D_{xx} + D_{yy} + D_{zz}]/3$) were calculated from the diffusion-weighted images. A C program was then used to calculate diffusion histograms (bin-width=0.02x10$^{-5}$cm$^2$/s) from the entire brain. The histograms were fitted to a double compartment model which allowed partial voluming between compartments. This model recognizes the brain tissue compartment and the high diffusion compartment consisting of CSF and non-brain tissue such as the eyes and scalp. For the brain tissue compartment, peak location (mean of the brain tissue compartment and mode of the entire distribution) and its distribution width ($\sigma$) were determined from the fitted data. The peak location was interpreted to be mean diffusion constant for the entire brain (BD$_{av}$). The BD$_{av}$ measurements for the NPH patients were compared with age-matched normative values. We also measured the $D_{av}$ values of the periventricular white matter by placing regions of interest (ROI) on the diffusion maps.

**Results**

A summary of our brain diffusion measurements is shown below. All measured diffusion parameters (in units of 10$^{-5}$cm$^2$/s) were increased in NPH patients (n=7) compared to controls (n=31). The reported changes are all statistically significant (p<0.05).

\[
\begin{array}{ccc}
\text{PVWM } D_{av} & \text{BD}_{av} & \sigma \\
0.94 \pm 0.13 & 0.81 \pm 0.02 & 0.24 \pm 0.04 \\
\end{array}
\]

increase compared 23.2% 7.3% 29.6% to controls

Entire brain $D_{av}$ histogram from an NPH patient is shown. The mean of the tissue compartment distribution (BD$_{av}$) and its width ($\sigma$) are marked. The high diffusion compartment and the pixels with partial voluming give rise to the broad tail to the right. The fit to the entire distribution is also shown (solid line).

**Discussion**

Histogram analysis is an effective technique for assessing overall brain diffusion changes. By sorting pixels according to $D_{av}$, contaminating factors such as lacunes and Virchow-Robin spaces can be removed. These regions are sometimes unintentionally included in ROI measurements, causing elevation of $D_{av}$ values. Histograms distribute these pixels of high diffusion intensity to the right, removing their effect on tissue $D_{av}$ measurements. Our histograms have a gaussian distribution of $D_{av}$ for brain tissue which is expected for the brain with a relatively homogeneous distribution of tissue water.

We evaluated diffusion changes in brain tissue of 7 NPH patients. Periventricular white matter measurements showed that the mean $D_{av}$ for this region is elevated for the patients when compared to controls. There was a statistically significant increase in the mean diffusion constant measured from the entire brain tissue (BD$_{av}$) for hydrophilic patients compared to age-matched controls. These results support our hypothesis that NPH may lead to increased water content throughout the entire brain. The mean diffusion distribution width of our 7 patients showed an increase over normative values. This is likely to be caused by variably increased water content throughout the brain tissue. Distribution width $\sigma$ also is dependent on brain microstructure, and the increased $\sigma$ may indicate the presence of anatomical changes other than edema alone.

**References**