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Brain damage in experimental neonatal hydrocephalus: correlations between diffusion tensor imaging and cytopathology

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Background

Diffusion tensor imaging (DTI) is an advanced non-invasive magnetic resonance imaging (MRI) technique used clinically to quantify white matter (WM) abnormalities in various pathologic conditions, and thus could be beneficial in detecting progressive brain damage in hydrocephalus. This study was designed to correlate DTI and cytopathology in a rat model of neonatal hydrocephalus.

Materials and methods

Obstructive hydrocephalus was induced by intracisternal injection of kaolin on postnatal day 1 (P1); age-matched control animals were either intact or received intracisternal injections of saline. Six animals (3 hydrocephalics and 3 intact controls) were imaged in vivo at 8-9 days of age (P8-9) and then sacrificed by cardiac perfusion of paraformaldehyde. Four animals (2 hydrocephalics and 2 saline controls) were sacrificed at postnatal day 21 (P21) and paraformaldehyde-fixed brains were imaged *ex vivo* with a Bruker 7 T MRI scanner. DTI was acquired in 6 directions to obtain measurements of the directionality of water diffusion through tissue (Fractional Anisotropy, FA; 0 = isotropic where water can move freely in any direction; 1 = anisotropic where water can move in only one direction) and the magnitude of diffusivity of water in tissue (Mean Diffusivity, MD). Values were computed bilaterally in the genu of the corpus callosum (gCC), external capsule (EC), internal capsule (IC), and cortical gray matter (Ctx).

Results

At P8-9 ventriculomegaly was severe and by P21 had progressed to where the periventricular white matter and internal capsule were so thin that DTI could only be reliably performed *ex vivo*. At both times FA values were significantly reduced in the gCC ($p < 0.001$) but not the EC, IC or Ctx. There was a trend toward higher FA values at P21 than at P8/9 for both hydrocephalic rats and normal controls. In contrast, MD values increased only in the EC. Conspicuous gliosis was prevalent in all structures examined but differed depending on cell type. Younger animals showed a more robust reaction of microglial cells compared to 21-day old hydrocephalics. Astrocytes exhibited the opposite pattern with a more robust reaction in the older animals.

Conclusion

These results demonstrate the feasibility of applying DTI to experimental hydrocephalus in neonatal rats, and reveal impairments in the corpus callosum and external capsule. The reduction in FA with hydrocephalus suggests that structural and perhaps physiological impairments exist in cortical connectivity. Whether the associated gliosis in these structures is causative or a response to axonal and myelin damage requires further study.