# The Impact of Hydrocephalus in Experimental Meningitis

C. Brandt[1], H. J. Simonsen[2], L. Vejby Søgaard[2], O. B. Paulson[2], I. J. Rowland[2]

[1]Statens Serum Institut, Copenhagen, Denmark, [2]Danish Research Centre for Magnetic Resonance, Copenhagen University Hospital, Hvidovre, Denmark

## Background

Bacterial meningitis remains a life-threatening disease with significant mortality and morbidity. Development of acute hydrocephalus is a well-known disease characteristic complicating the course of bacterial meningitis and is associated with a mortality of ~50%. The early discovery of ventricular dilation preceding severe acute hydrocephalus could lead to the identification of efficient treatments other than surgical intervention. The aims of this study were to follow the evolution of experimental meningitis in a rat model and to identify critical events in the disease process using MR imaging methods. This work focuses on the influence of ventricular enlargement on clinical and motor function in an experimental model of meningitis in rats.

## Materials and Methods

Meningitis was induced by intracisternal injection of ~3 x $10^5$ CFU/ml *S. pneumoniae* serotype 3 bacteria (n=29) or an equal volume of saline. Rats were randomized and sacrificed (4 infected, 2 saline inoculated at each time) after 6, 12, 24, 30, 36, 42 and 48 h post-infection. Prior to imaging rats were clinically assessed and a clinical and motor performance score obtained (1,2). MR Images were acquired using a SISCO 4.7T imaging system. T1W, T2W, quantitative diffusion, dynamic MRI and post contrast (0.5 mmol/kg GdDTPA) T1W measurements were performed. Three coronal MR images corresponding to the frontal, mid-frontal and mid-brain were selected in all rats. Total area of the brain and total area of lateral- and third ventricles were determined using T2W images and the ventricular-brain ratio (V-B) calculated as ventricular area divided by total brain area.

## Results

Comparison of infected rats with V-B values above and below that of the control group mean +2SD (group mean=0.028, group mean +2SD=0.047) showed a close relationship to time and thereby developmental stage of disease (Mann-Whitney test, mean 18.4 hours versus 39.9 hours, P<0.0001 and Spearman rank correlation r=0.83, P<0.0001). Highly significant correlations were found between clinical assessment (figure 1), motor performance score (figure 2) and V-B (rho=0.83, P<0.0001 and rho=0.82, P<0.0001 respectively). Infected rats with V-B> 0.047 had decreased ADC values compared to meningitis rats with V-B<0.047 (P=0.043). The impact of ventricular dilation on ADC values was also reflected by the significant downwards slope of the regression line in figure 3 (P=0.023).

Figure 1

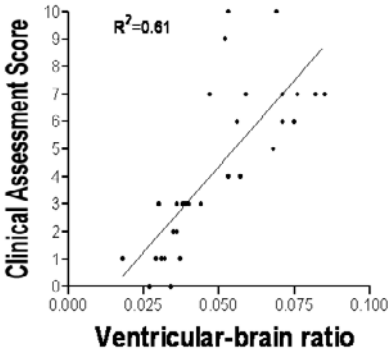



Figure 2

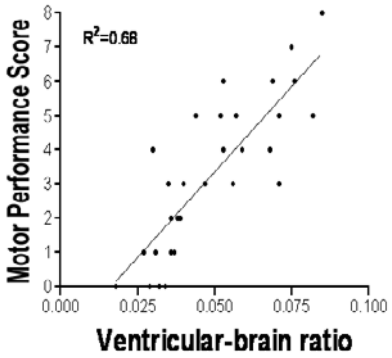
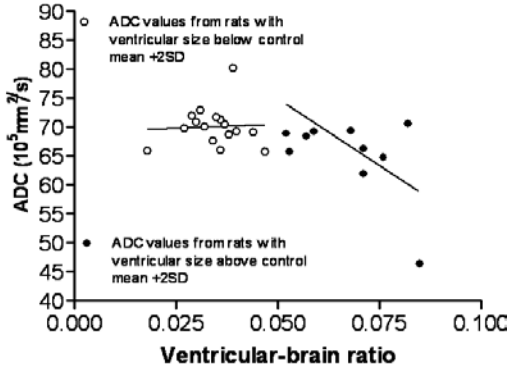



Figure 3




## Discussion

Production and re-absorption of cerebrospinal fluid is compromised in bacterial meningitis probably due to obstruction by bacteria/pus leading to acute hydrocephalus. In this experimental model of meningitis, expansion of the ventricles is detected at an early stage of the disease. The observed gradual increase in ventricular size was closely associated with the deterioration in clinical assessment and motor performance. Reduced ADC values, normally indicative of cytotoxic oedema, were related to ventricular size suggesting that expansion of the ventricles leads to compression, reduced perfusion and damage to cortical tissue. The assessment of ventricular size in patients with meningitis and prompt intervention may assist in the reduction of sequelae and the severe consequences associated with obstructive hydrocephalus.

## References

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## Acknowledgment

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