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Incomplete reversibility of selective hippocampal response after early and delayed shunting in adult kaolin-hydrocephalus – implications for early shunt treatment

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Background

In recent studies of adult kaolin hydrocephalus delayed selective neuronal response was evidenced by findings in the hippocampus. In the present study, it was investigated whether these findings might be reversed by shunting, and whether reversibility might be different when hydrocephalus was shunted at different stages.

Materials and Methods

In 20 adult SD-rats kaolin hydrocephalus was induced and immunostaining of neurofilament (NF68), neuronal nitric oxide synthase (NOS), synaptophysin (SYN38) and heat-shock-protein (HSP70) was performed at 2,4,6 and 8 weeks (5 controls). In further 30 hydrocephalic rats, a polyethylene-catheter (PE 10) was placed into the lateral ventricle allowing the CSF to be drained subcutaneously into the neck. Each 15 rats were shunted at 1 week (early) and at 3 weeks (late). Both groups were then investigated at 1,3 and 5 weeks of shunt implantation (5 sham). Immunoreactivity (%) was analysed with the aid of computerized image-analysis; $P < 0.01$.

Results

In the hydrocephalic rats selective neuronal responses were evidenced by the immunohistochemical changes found in the CA1 and CA3 sectors: In CA1, NOS staining was positive for all animals at all hydrocephalic weeks, whereas in CA3, HSP70 was positive at 2,4 and 6 weeks, and at 8 weeks, both sectors were stained. Furthermore, neurofilament staining in CA3 was significantly increased, however, not until 6 weeks. SYN38 staining was increased in both sectors already at 2 weeks; at 4 weeks, greater differences in the immunoreactivity levels have occurred. With an early shunt, NOS was only seen in a few animals. Also, neurofilament staining was reduced in both regions in the one week implantation group. HSP 70 in CA3 was significantly reduced compared to 6 and 8 weeks hydrocephalus whereas it remained increased in CA1. Also for synaptophysin the values for the three and five weeks implantation group were significantly decreased compared to all hydrocephalic weeks. With a late shunt, NOS staining was comparable to the hydrocephalic rats. Also, staining with HSP70 was comparable to 6 and 8 weeks hydrocephalus, while neurofilament staining was identical to that of 4 and 6 weeks hydrocephalus, but showed a good recovery at three and five weeks of implantation. In contrast, synaptophysin reactivity showed maintained increases in both the CA1 and CA3 sectors in all implantation groups.

Conclusions

Incomplete reversibility and only partial recovery of selective neuronal response after delayed shunting was evidenced by the findings in the hippocampus. The observed differences between the early and late shunt group might have important clinical implications for early shunting.