discrete staining of cell bodies was found with type I sera in the newborn or 5-day-old rats. In the newborn there was a diffuse staining of the parenchyma of the developing cortex and other areas. Type II staining was observed, particularly in those cells with developed perikarya. By 9 days type I sera began to show, although only weakly, some cells in the cortex and hippocampus. At 14 days some of the cells in the dentate nucleus began to show type I staining, and by 21 days the staining pattern was as in the adult brain. Sera giving type II pattern of staining did so at all ages examined. One of the sera, which normally gave type I staining with adult brain, gave additional type II staining in the young brains.

Monoclonal antibodies against meningococcal polysaccharide with cross-reactivity against brain antigens

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Bacterial meningitis is a serious disease with a high mortality rate and a high rate of morbidity. The disease, produced by Neisseria meningitidis (meningococcus), occurs both endemically and epidemically in the population. The meningococci have been subdivided into a number of serogroups, each group being defined by their capsular polysaccharide. The chemistry and structure of the polysaccharides have now been determined. Vaccines have been prepared against the groups A and C and have proved effective in limiting epidemic disease due to these organisms. The group B meningococci share the same capsular polysaccharide antigen as Escherichia coli type K1, which is the principal agent of meningitis in the newborn. However, group B meningococci and E. coli K1 have been found to be poor immunogens and no really effective vaccines have yet been developed. The polysaccharide antigen of these organisms is a homopolymer of D-N-acetylneuraminic acid linked α2-8. This form of D-N-acetylneuraminic acid linkage occurs in the polysialoproteins found in the mammalian brain. It has been suggested that the poor immunogenicity of this bacterial polysaccharide is explained in part by the presence of similar structures in the host and hence immunization would require the breaking of tolerance. There is, in addition, the possibility that if produced such antibodies could, particularly in the infant, lead to autoimmune damage.

Evidence has already been published to show that polysialopeptides isolated from the foetal brain will bind to horse anti-meningococcal B serum, this binding being specifically blocked by polysaccharide from meningococci B or E. coli K1 (Finne, et al., 1983). By using a panel of monoclonal antibodies raised against purified bacterial polysaccharides we have further investigated the possibility of cross-reactivity with brain.

The initial screening of antibody binding to brain tissue has been attempted by a micro-e. l.i.s.a. procedure with brain microsomal preparations from adult and neonate mice and human foetal brain (18–20 weeks) as test antigens. The micro-e. l.i.s.a. procedure indicated that monoclonal antibody against the group B and the group W135 (4-O-α-D-galactopyranosyl-D-N-acetylneuraminic acid polymer) cross-react with foetal and to some extent with adult brain microsomes. Further studies concentrated upon the reactivity of the anti-B monoclonals tested three out of three gave positive immunofluorescence of cell surfaces after reacting them with live cultures of dissociated rat forebrain. A similar pattern of staining has been achieved with a polyvalent rabbit anti-meningococcal B serum. The cells which react with anti-B monoclonals are not stained by rabbit anti-glial fibrillary acid protein serum nor by rabbit anti-galactocerebroside serum, and are therefore neither astrocytes nor oligodendrocytes. They do bind rabbit anti-monomiosialganglioside antibodies. These observations plus the numbers of stained cells and their morphology suggest that they are neurons. Double staining with anti-B type monoclonals and anti-GT1b antibodies after 6 days culture shows that three groups of cells can be distinguished: (a) cells reactive with both anti-B antibodies and anti-GT1b; (b) cells reactive with anti-B monoclonals but not anti-GT1b; and (c) cells reactive with anti-GT1b but not anti-B type monoclonals.

After the pronase digestion of delipidated newborn rat brain as described by Finne (1982) a polysialopeptide fraction was isolated which on immune diffusion showed a line of identity with meningococcal B polysaccharide. The immunoblot procedure confirmed that foetal brain, but not adult brain, contained a high Mr, (>200000) antigen reactive with the anti-B monoclonals. It is quite likely that the cross-reactive brain molecule belongs to the class of proteins called neural cell adhesion molecules (Rutishauser, 1983), the antibodies reacting with the polysialic acid side chain of these molecules.

Abbreviations used: e.l.i.s.a., enzyme-linked immunosorbent assay; GT1b, trisialoganglioside.