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FACTORS INFLUENCING NEUROLOGICAL OUTCOME OF CHILDREN WITH BACTERIAL MENINGITIS

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Background and aims: Acute bacterial meningitis is a life-threatening illness with possible long-term neurocognitive sequelae. Aim of the study was to identify clinical and biological factors associated with death or neurological sequelae in a retrospective cohort of children with bacterial meningitis.

Methods: Retrospective cohort study. Inclusion criteria were bacterial meningitis beyond 1 month of age; and death or long-term (>10 yrs) follow-up. Clinical and biological data at admission were retrieved from medical charts.

Results: Eighty-nine patients (age at diagnosis 1 month - 15 years) were enrolled between 1990 and 1999. Nineteen (21%) died, two of them suffered from chronic diseases. At diagnosis, the following variables were associated with survival: absence of seizures ($p < 0.05$), absence of respiratory distress ($p < 0.001$), GCS>12 ($p < 0.001$), platelets> 150,000/mm3 ($p < 0.001$), WBC > 5,000 ($p< 0.01$) and blood neutrophils >1,500 ($p< 0.01$), no need for mechanical ventilation ($p < 0.001$). Among children who survived: 42 (60%) did not show any neurocognitive problems; 15 (21.4%) developed hearing loss, 10 (14.2%) mild mental retardation, 8 (11.4%) motor problems, 6 (8.5%) epilepsy, 2 (2.8 %) sleep disorders. None developed psychiatric disorders.

Conclusion: Some factors were significantly associated with survival in children with bacterial meningitis. The overall prognosis was good in more than half of the long-term survivors. The main limit of our study is its retrospective nature. However, since the routine use of vaccines, the incidence of bacterial meningitis has decreased so that prospective studies are difficult to conduct in developed countries.

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TNF-A INDUCTION OF INFANT MURINE BRAIN INFLAMMATION VIA IKK/NF KAPPA B SIGNALLING: A POTENTIAL MODEL FOR PAEDIATRIC NEUROINFLAMMATION

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Introduction: Many paediatric neurological conditions have a significant inflammatory component. Post-mortem brain samples of those affected often display neuroglial irritation and the presence of inflammatory markers within the cerebrospinal fluid. The underlying molecular mechanisms behind these breakdown products are largely unknown, and further knowledge in this area would enhance treatment options and prognosis.

Methods: Using our novel pressure chamber we stimulated murine neural tissue with the inflammatory cytokines IL-1α, IL-1β, IL-6 and TNF-α to represent an inflammatory process. Subsequently we quantified the change in volume of brain samples. Inflammation was compared using established histochemical techniques and statistics were performed with ANOVA (Tukey-Kramer multiple comparisons test), using Sigma Plot 5.

Results: We demonstrated significant variation in expansion of different brain regions. Whole brain preparations demonstrated a 30% increase. The frontal (17±1.2%) and temporal (15±0.8%) lobes demonstrated the greatest susceptibility to inflammation showing significant volumetric increases over 24 hours. This can be compared to the cerebellum (7±0.6%) and brain stem (5±0.7%) volume increases. Furthermore, this inflammation was noted to be a result of aberrant signalling of the NF-κB/IKK pathway. Using standard inhibitors this inflammation could be both inhibited and reversed.

Conclusions: These results suggest that NF-κB represents a potential therapeutic target for improvement of many paediatric neurological conditions. They illustrate the varying susceptibility of different lobes of the brain and promote further research into the role of inflammation in paediatric

neurology affecting these areas. Finally, we have established a novel and cost-efficient technique for quantification of neuroinflammation in a laboratory setting.

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INFLAMMATION INDUCED PH MODIFICATIONS IN AUTISM

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Introduction: There are many paediatric neurological conditions that have a significant inflammatory component which have been demonstrated most notably by an increase in microglia populations. In a number of degenerative conditions, these changes are associated with a reduction in brain pH. Due to this potential overlap between the low pH and the increased brain microglia, we decided to investigate whether the increased populations of microglia in autistic tissue caused the reduced brain pH.

Methods: Age, sex and cause of death matched prefrontal cortex sections were donated by the Institute of Psychiatry, King's College London. In vitro models were performed by stimulating murine neural tissue with inflammatory cytokines. Tissues were analysed using established histochemical techniques.

Results: An ~1 pH unit of difference between age, sex and cause of death matched tissue, and displayed a ±0.03 standard deviation within replicates. Staining with pH sensitive dyes suggested that the pH differences were located in lysosome-like structures in putative microglial cells. However, more significantly we demonstrated using a novel in vitro mouse model that we could induce such a pH change and subsequently reverse it by inactivation of the NF-κB/IKK signalling pathway.

Conclusions: These results suggest that NF-κB represents a potential target for the therapeutic improvement of outcome in autism spectrum disorder. Furthermore, the identification of an association with pH changes opens scope for not only therapeutic interventions but the possibility of diagnostic imaging based on these preliminary results.

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OPTIMAL THERAPY IN INFANTILE SPASMS

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Introduction: Infantile spasms is an epileptic syndrome composed of epileptic seizure, spasms and hypsarrythmia on EEG, associated with psychomotor delay. NICE guidelines offer two first line treatments: hormonal therapy or vigabatrin.

Objectives: To analyse current experimental literature, specifically RCTs, comparing vigabatrin with hormonal therapy. The outcomes looked at included spasm control, EEG resolution, relapse rates, subsequent seizures, side effects, and psychomotor delay.

Methods: PubMed - searched with MeSH term "infantile spasms", additional terms; "vigabatrin", "ACTH" or "tetracosactide".

Results: The combined data from three RCTs comparing vigabatrin with hormonal therapy suggests that in terms of cessation of spasms (OR 0.42, 95%CI 0.21 to 0.80) and EEG resolution (OR 0.38, 95%CI 0.15 to 0.99), hormone treatment is effective in a significantly greater proportion of infants. There was no significant difference in terms of relapse rates, subsequent seizures, number of infants with side effects, and psychomotor development. However, there was a significant improvement in psychomotor development when comparing infants with and without spasm cessation (p=0.008).

An RCT comparing vigabatrin with hydrocortisone in tuberous sclerosis patients suggests that vigabatrin is effective in more cases (OR13.8, 95%CI 2.21 to 86.35)