Cerebral palsy: synergism, pathways, and prevention

Editorial

The recently proposed definition and classification of cerebral palsy[1] (CP) is still up for debate – see the correspondence in this issue – and additional comments via the Castang website are warmly invited before the final version is completed next month (www.castangfoundation.net/workshops_washington_public.asp). The Castang Foundation funds 'research into the causes of CP and other neurodevelopmental disorders leading to their prevention'. Rightly, the document does not specify the 'non-progressive disturbances' to which CP is attributed, with the exception of cerebral dysplasia.[1] It is unclear why this should be picked out since in developed countries white matter disorders and perinatal vascular events currently appear more common.[2,3] Data from other parts of the world are less available, but emphasize the continuing importance of post-neonatal causes.[2-4] As the relative importance of different disturbances changes with medical knowledge, geography, and over time, a non-specific definition is understandable.

Most causal factors do not act in isolation, but synergize to make a disturbance more likely. Bilirubin encephalopathy has been used as a classic example, where a raised blood level of unconjugated bilirubin appears the obvious cause. However, acidosis and the integrity of the blood-brain barrier are important determinants of whether a particular level causes harm. This concept of synergism has been extended by including the antecedents (here blood group incompatibility) to create causal pathways.[3] If the antecedents of the other factors are added, a causal network appears. Successful prevention requires attention to all of these influences.

Recognizing a risk factor does not mean it can be successfully prevented. In the Swedish study nearly half the children with CP were born preterm. Unfortunately the causal pathways leading to preterm labour are poorly understood and attempts to intervene have not been particularly successful. However, improved neonatal intensive care, especially since the arrival of surfactant, means the risk to survival with CP is diminishing, and even the improved survival of neonates born extremely preterm is not leading to an increased number of cases.[2] Although white matter damage seems the major disturbance in this group of children, its causes are still obscure.

Hemiplegic CP is now one of the most common types with a prevalence of approximately 3 per 4000 live births.[2] This may often be due to vascular events. Perinatal strokes, defined as occurring between 28 weeks of gestation and 7 days of age, have an estimated incidence up to 1 in 4000 live births.[5] While this is the highest in childhood, the causal pathways are the least understood. In case series, trauma and alloimmune thrombocytopenia are the major recognized causes of antenatal strokes, but more than 50% do not have any recognized risk factors.[6] In later cases, embolic or thrombotic causes appear important. Some, but not all, studies have linked the more common genetically determined prothrombotic factors, Factor V Leiden or mutations in the prothrombin and methylenetetrahydrofolate reductase genes, to an increased risk of perinatal stroke or of an adverse outcome from stroke.[7-9] If they are causal, other factors must be synergistic.[10] As prothrombotic factors are linked to pre-eclampsia, intrauterine growth retardation, and placental infarction, they could influence other types of CP.[7] The data from Reid et al. in this issue supports this, but not all studies agree on the details.[11]

However, were the association causal, prevention remains difficult. Anticoagulating large numbers of pregnant mothers seems a relatively unlikely prospect. It might be worth examining possible treatable synergistic factors such as dehydration and stress during delivery. The role of birth asphyxia or sub-optimal delivery remains a difficult issue, as in other forms of CP, and would need a separate editorial. In the meantime Ms Hilda Castang's hope that understanding the cause of CP will lead to prevention is not as straightforward as it first appears.

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