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EDITORIAL

Neonatal Encephalopathy or Hypoxic-Ischemic Encephalopathy? Appropriate Terminology Matters

In 1976, Sarnat and Sarnat (1) published a proposed staging system for neonatal encephalopathy. They carefully used the term "neonatal encephalopathy" in the title. However, in the abstract, they wrote about "postanoxic encephalopathy" and about "ischemic-anoxic encephalopathy" in the article itself. Infants were >36wks GA, and all had "a well-defined episode of fetal distress or an Apgar score of 5 or less at one or five minutes after delivery" (1). Apparently, much of the evidence that hypoxia and/or ischemia were indeed the causes of the encephalopathy was indirect and far from solid. Today, 35 y later, the term "hypoxic-ischemic encephalopathy" is widely used standard terminology, and we and others (2,3) strongly believe that it should not be.

In this issue of *Pediatric Research*, Drs. Borlongan and Weiss (4) summarize their vision of how stem cell therapy in stroke could be translated into the setting of perinatal brain damage. During the process of reviewing, revising, and editing their most interesting piece, some of us realized that we often not only seem to make inferences from adult to newborn disease but also from the name a clinical entity bears to its purported etiology.

In the article on Baby STEPS, it occurred to us that the authors frequently used the terms "hypoxic-ischemic encephalopathy" and "hypoxic-ischemic brain damage," although such single cause attribution (5) is not only unproven but sometimes unprovable. We called the authors and suggested to replace the term "HIE" with "neonatal encephalopathy" (2). We are grateful that Drs. Borlongan and Weiss agreed to revise their article accordingly, because their major reason to use the HIE terminology was to be in sync with common usage, not to make a statement about etiology. Here are multiple reasons why we are grateful they agreed.

First and foremost, ***we often do not know*** when hypoxia-ischemia is indeed the cause of neonatal encephalopathy. It remains utterly unclear what proportion of cases of neonatal encephalopathy is due to hypoxia and/or ischemia. Indeed, it is very difficult to even establish brain hypoxia-ischemia in the individual newborn except in select cases of neonatal stroke, so that current definitions and classification rely not on brain oxygenation and blood flow, but, for example, on blood pH or associated seizures. In our view, we can talk about hypoxia-ischemia only in controlled animal experiments, for only in those cases are we likely to be correct in our assumption that it is the cause for the brain damage we see. Of note, our ability to produce, by exposing animals to hypoxia-ischemia, brain damage that mimics what is observed in neonatal encephalopathy does not mean that a significant proportion of human neonatal encephalopathy is of hypoxic-ischemic origin.

Second, ***we do not need*** to use etiologic labels for disease entities. Descriptive terminology is completely sufficient to communicate which entity is referred to. We have struggled with this concept with the term "cerebral palsy," which describes a condition, not an etiology (6).

Third, ***we create obstacles*** for research by assuming etiology. By attaching an etiologic or pathogenetic label to a disease entity, we offer the illusion that the pathogenesis is known. Research programs are then designed to further elucidate the mechanisms of the purported pathogenesis with the goal of increased understanding and the subsequent design of preventive, therapeutic, or regenerative interventions. Still, we have not seen promising pharmacological fruits from >3 decades of research into the molecular details of hypoxia-ischemia. We are still hopeful that such will eventually become available; however, we are less than hopeful that they will be helpful in a large proportion of infants with what we think should not be called HIE. It is still unclear how the one intervention that seems to be promising in neonatal encephalopathy, brain cooling, works (7).

Fourth, ***we might do harm*** by attributing a cause (hypoxia-ischemia) to the disorder (encephalopathy) without having measured cerebral oxygenation and blood flow. Written mention of "HIE" in a newborn's chart will potentially be used as evidence against the obstetrician who is sued for not having done the C-section 20 min earlier if that newborn later develops a disability.

Thus, ***we should care*** because words are important, especially when words become terminology. In the case at hand, we want to distinguish, with Blackburn,

> "between the brute and conventional association of a term with a property which supplies its meaning, and the subsequent description in which the property is said to hold of something. The former can be as conventional as we like, while the latter, applying properties to things, putting them under descriptions, brings in correctness and incorrectness, truth or falsity. It is conventional that the word 'horse' refers to horses, but once that is fixed, it is information, true or false, that the animal over there is a horse." (8)

We believe that by simply calling "neonatal encephalopathy" what is now called "HIE," we might not only help reduce the number of unjustified convictions of obstetricians, midwifes, nurses, and hospitals but also increase the amount of much needed research in perinatal brain injury not necessarily related to the hypoxia-ischemia paradigm. For the same reason,

we suggest dropping etiologic language from our radiologic and pathologic vocabularies when pathogenetic mechanisms are unproven. We hope that authors of future submissions to *Pediatric Research* agree and are ready to follow in Drs. Borlongan's and Weiss' footsteps by acknowledging that appropriate terminology matters.

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