Memories of the fetal heart

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ONE OF THE MOST PROVOCATIVE recent findings in modern medicine has been the suggestion from Barker and colleagues (1) that problems of late adulthood, such as coronary heart disease, stroke, hypertension, and non-insulin-dependent diabetes, are associated with metabolic compromise and impaired growth in fetal life. Although the precise mechanisms of how adverse events in utero can program adult disease are unclear and some of the associations are likely to be indirect (6), many of these epidemiological data have now been replicated in experimental preparations (12). The current focus on disease, however, is perhaps a little misleading. In other areas of development, the central importance of early experience during defined windows of maturation for subsequent adult development is well known. The seminal work by Hubel and Wiesel (5), for example, demonstrated that correct visual experience is important for normal visual development, just as whiskers are essential for the development of barrels and peripheral factors are, of course, typically tightly coordinated, as shown by the observation that chronic intermittent hypoxia leads to an enhanced response to sympathetic stimulation, mediated by a decreased ability of NO to inhibit presynaptic norepinephrine release (9). Such studies demonstrate that programming results in complex and sustained alterations in physiological control mechanisms. What we now need to understand are the consequences of such alterations. The work by Broberg and colleagues has highlighted the concept that physiological “memory” of fetal experiences can have important influences on the adult heart, but, unlike other studies, they have shown that this can be beneficial. Of course, what determines whether such influences are in the long-term “good” or “bad” remains the fascinating question.

Previous short-term studies in the fetal sheep have shown that chronic hypoxia for just 24 to 48 h leads to progressive normalization of basal cardiac function but results in greater responses to acute events, consistent with augmentation of the chemoreflex (4). Furthermore, repeated hypoxia causes upregulation of immediate early genes in areas of the brain involved in regulation of sympathetic activity (10). Even in the adult human, acute hypoxia, but not hypercapnia, leads to long-lasting sympathetic activation (13). Central and peripheral factors are, of course, typically tightly coordinated, as shown by the observation that chronic intermittent hypoxia leads to an enhanced response to sympathetic stimulation, mediated by a decreased ability of NO to inhibit presynaptic norepinephrine release (9). Such studies demonstrate that programming results in complex and sustained alterations in physiological control mechanisms. What we now need to understand are the consequences of such alterations. The work by Broberg and colleagues has highlighted the concept that physiological “memory” of fetal experiences can have important influences on the adult heart, but, unlike other studies, they have shown that this can be beneficial. Of course, what determines whether such influences are in the long-term “good” or “bad” remains the fascinating question.

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