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Review: Is rapid fat accumulation in early life associated with adverse later health outcomes?

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ABSTRACT

This review discusses ways in which the maternal environment and placental function affect the birth weight and adult health outcomes of offspring. These maternal and placental factors have varying and sometimes opposing effects on birth weight, resulting in infants that are born small for gestational age (SGA), large for gestational age (LGA) or preterm. However, all these alterations in weight have similar effects on adult health, increasing the risk of obesity and its associated cardiovascular and metabolic disorders. While birth weight has been used as a marker for risk of adverse adult health, we propose that a common feature of all these scenarios – early accumulation of excess body fat – may be a better marker than birth weight alone. Furthermore, altered neonatal fat accumulation may be more closely related to the mechanism by which maternal environment and placental adaptation mediate effects on adult health. We suggest that more research should be focussed on early fat accretion, factors that promote fat accretion and if it can be avoided, and whether it would be beneficial to try to reduce fat accumulation in early life.

Contents

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1. Introduction

It is now well established that early life events play an important role in the development of obesity and its associated cardiovascular and metabolic disorders. Maternal and placental factors that alter fetal nutrient availability are associated with later adiposity in the offspring. Postnatal alterations in nutrient availability are also associated with adverse later health, particularly in infants born prematurely. The mechanisms behind these associations are still the subject of much research. While it has been established that low or high birth weight, and high postnatal growth rate are associated with later adverse health outcomes, it is likely that weight is only a marker for other metabolic changes that are responsible for long-term programming changes. We propose that early alterations in body composition may provide a better marker of adverse future health, and may be more closely related to the mechanisms of these changes than weight alone. This review will examine the evidence that there is a relationship between altered adiposity during fetal life or the first year of postnatal life and markers of later adverse health.

2. The obesity epidemic

Obesity is a major global health concern today. With the continuing rise in the prevalence of obesity, there has been an accompanying increase in the prevalence of associated cardiovascular and metabolic diseases [1]. Obesity and obesity-related diseases lead to a significant social and economic burden on society. According to recent global estimates, more than 2 billion people were overweight or obese in 2013, of whom 671 million were obese [2]. In Australia, obesity was estimated to generate a direct cost of $3.8 billion during 2011–12 [3]. Considering the enormous impact of obesity at both the individual and societal level, it is imperative that we find interventions to prevent, or at least reduce, the incidence of obesity and obesity-related outcomes.

Adiposity as measured by absolute fat mass or fat mass proportion has been closely associated with a spectrum of disorders including hypertension, type 2 diabetes, dyslipidemia (especially hypercholesterolemia), coronary arterial and cerebrovascular atherosclerosis and chronic renal dysfunction, which have been linked under the collective term ‘metabolic syndrome’ [4]. Understanding the origins of obesity may help uncover strategies for timely and effective intervention in some of these conditions. We propose that the inclusion of measures of neonatal body composition into research in this area will assist in understanding the origins of obesity.

3. The developmental origins of health and disease (DOHaD) hypothesis

It is becoming increasingly recognised that an early life component may play an important role in the development and progression of obesity and its associated disorders. This concept was initially proposed by David Barker and colleagues in what has come to be known as the ‘developmental origins of health and disease (DOHaD)’ hypothesis [5]. In epidemiological studies into the origins of cardiovascular disease, Barker and colleagues observed that areas in Britain with the highest infant mortality rates in the early 1900s were the same areas in which, decades later, there were the highest rates of mortality from coronary heart disease [5]. The data suggested that low birth weight may be associated with an increased risk of coronary heart disease in later life [6]. Until this point, research into etiological factors of chronic adult diseases was largely focussed on adult behaviours such as smoking, exercise and diet, rather than on early life exposures. Subsequent studies across various populations worldwide have confirmed an inverse association between birth weight and coronary heart disease [7–10]. Similar findings have been replicated within diverse ethnic cohorts with respect to a variety of other diseases including stroke [11], hypertension [12–14] and type 2 diabetes [15,16].

The inverse association between low birth weight and later cardiovascular and metabolic disease risk could be explained by the DOHaD hypothesis: inadequate nutrition *in utero* could “program” the fetus with permanent changes in structure, physiology and metabolism to increase short-term survival. However, when exposed to the *ex utero* environment, where the nutrient supply may be more abundant, these adaptations are mismatched, conferring an increased risk of later disease.

However it is not only inadequate nutrition in fetal life that leads to altered metabolic function. Although many studies have reported an inverse association between birth weight and later disease outcomes, there have also been studies that have found a non-linear association. A study by Baker et al. found a U-shaped association between birth weight and adult mortality, with both the low and high ends of the weight distribution associated with a significantly increased risk [17]. Some studies have even found the strongest association to be not with birth weight, but with other anthropometric measures that may indicate adiposity, such as birth length or ponderal index (birth weight/height^3) [18,19]. The results of these studies suggest that while birth weight may provide a summary measure of fetal growth, it may not necessarily play a causal role in itself. It may be the case that birth weight is a surrogate for an alternative, more comprehensive marker of fetal health, such as changes in body composition.

4. The intrauterine environment

It has since been acknowledged that the DOHaD hypothesis, with its key assertion that “the baby's nourishment before birth and during infancy influences its susceptibility to diseases in later life” [20], may hold an important role in our understanding of disease development. The intrauterine environment is a critical determinant of fetal growth, and in turn relies on maternal and placental function to deliver nutrients and oxygen from the maternal compartment, across the placenta, to the fetus [21,22]. This occurs in a series of steps referred to as the “fetal supply line” [23].

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