Behavioral Research Agenda in a Multietiological Approach to Child Obesity Prevention

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Background

Serious limitations have been found in the simple energy balance model (energy in–energy out) as the single or primary biological strategy for virtually all child obesity prevention interventions.^{1,2} Experts have criticized it for not reflecting the likely multifactorial nature of obesity.^{1,2} A substantial number of other possible, even likely, causes of obesity have been identified.³

Since the simple energy balance model is easy to understand and target, behavioral scientists have taken the initiative to identify factors that influence energy in and energy out, and design, implement, and evaluate behavior and/or environmental change interventions to prevent obesity accordingly. Unfortunately, most of these obesity prevention interventions have either not worked, or had small effects,⁴ not nearly enough to halt the epidemic. In the process, a serious disconnect has developed between advances in biological and in behavioral sciences in regard to obesity prevention.

Several investigators have proposed multietiological approaches to understanding obesity onset and thereby its prevention.^{3,5,6} A recent article specified infectobesity (*i.e.*, virus-related infection), dysbiosis (imbalance in phyla in the microbiome), and dys-synchrony in circadian and circannual rhythms as three etiologies for which ample and growing evidence exists for a role in the development of obesity in children.⁷ Behavioral- and prevention-oriented scientists have had minimal involvement in the delineation of these etiologies. However, behavioral and prevention scientists can make important contributions to child obesity prevention research based on these multiple etiologies, thereby reconnecting the biological, behavioral, and prevention sciences. In general, this prevention-oriented research agenda would involve assessing the in-

cidence of childhood obesity due to each problem, prioritizing the problems for research attention, specifying the behaviors that may be involved in the transmission or the prevention, developing models predicting the behaviors, and designing and evaluating interventions to minimize the problem, thereby preventing obesity. We briefly identify some of the research issues specific to each possible etiology to exemplify how behavioral or prevention researchers may begin to address such problems from a biobehavioral perspective.

Infectobesity

Several literature reviews and meta-analyses have indicated that infection with adenovirus 36 increases the risk of obesity for which children may be particularly susceptible.^{8,9} From a child obesity prevention perspective, it would be important to know how infection by adenovirus 36 occurs, for example, as an “outbreak” or “epidemic,” or the nature or process of person-to-person or environment-to-person transmission; the incidence of adenovirus 36 infection among children; the proportion of children infected who develop obesity; and the proportion of child obesity due to adenovirus 36 infection.

If we assume that not everyone who is infected becomes obese, it would be important to know the behaviors and other exposures that minimize or enhance viral infection immunity in general and resistance to adenovirus 36 in particular. Cause-specific interventions require testing to assess if they prevent transmission under controlled conditions in the laboratory, and then prevent transmission of infection in the field. For example, if adenovirus 36 infection spreads person-to-person by sneezing and coughing, then sneezing into the arm at the back of the elbow and hand washing should be useful child obesity prevention

strategies. Immunity and resistance enhancing strategies also need testing, specifically in regard to adenovirus 36.

If scientists developed an adenovirus 36 vaccine, programs to promote vaccination would need to be developed. Delayed child vaccinations with existing vaccines have become common,¹⁰ increasing the risk of infection. Thus, behavioral programs would need to be developed and tested to minimize potential resistance and enhance vaccination rates.

Microbiome

Imbalances in the bacterial (and maybe the viral, fungal, and eukaryotic) phyla in the microbiome can lead to obesity.^{11,12} The microbiome begins to develop (from the mother) in the immediate postnatal period and changes substantially early in life,¹³ due, in part, to diet¹⁴ and physical activity¹⁵ influences.

In parallel with infectobesity, understanding the population prevalence of dysbiosis and determining whether this differs by age, gender, socioeconomic status, ethnic group, or other demographic grouping variables become important. For example, the microbiome may vary early in life by any, and duration of, breastfeeding, formula feeding, and introduction of complementary foods.¹³ It would be important to develop an understanding of how different aspects of the diet (*e.g.*, dietary fiber, prebiotics, probiotics, vegetarian dietary patterns¹⁴), physical activity,¹⁵ and other behaviors influence the microbiome. The role of processed foods in the development of obesity has tweaked public health interest.¹⁶ The influence of processed food on the microbiome needs further understanding. Cannabis use has been related to obesity,¹⁷ but its influence on the microbiome is not clear. Antibiotic use, especially in the first 2 years of life, has been shown to influence the microbiome and increase the risk of childhood obesity.¹⁸ Further research on the possible effects of different types of antibiotics is needed so that some drugs may be used more safely early in life. At least one study demonstrated parental resistance to the use of antibiotics in children early in life to prevent obesity.¹⁹ Understanding and finding ways to minimize parental resistance are important behavioral research agendas. Household disinfectants²⁰ and acid suppression or prokinetic medications¹⁸ also have been shown to influence the microbiome and deserve research parallel to that on antibiotics. The internal and external validity of microbiome research in humans has been challenged.²¹ These are issues that prevention and behavioral scientists have usefully addressed.²²

Circadian and Circannual Rhythms

The body has multiple biological clocks synchronized in the brain to be in concert with external influences. Because of this synchronization, we are able to sleep, eat, and be active during evolutionarily advantageous times. Social demands such as school and work schedules, school holi-

days, and social obligations can affect the timing of sleep, physical activity, and eating patterns, which may lead to dys-synchrony between behavior and the internal clocks as well as within the internal clocks. Disruptions of, or dys-synchrony among, circadian rhythms have been demonstrated to lead to obesity.^{23,24} The interaction of circadian misalignment and children's circannual or seasonal rhythms in growth²⁵ has also been proposed as a cause of obesity among children, accounting for the summertime increases and school year decreases in adiposity in subsets of early elementary school children.^{26,27}

Following the same logic, research is needed on the incidence of childhood obesity in response to circadian or circannual disruptions, specifying the behaviors that contribute most to the dys-synchrony, and generating and evaluating interventions to change these behaviors and environmental influences on obesity. Sleep duration or disturbances have not been related consistently to obesity in children,²⁸ perhaps partially due to use of self-report measures. Exploring sleep within the context of indicators of circadian rhythm synchrony, for example, timing and amounts of melatonin release, using objective measures offers opportunities for testing hypotheses regarding the role of sleep in energy balance, hopefully leading to more effective behavioral interventions. Digital media at night disturbs circadian rhythms among children²⁹ and ways of minimizing those effects need to be developed.

While the timing of meals has been identified as a circadian rhythm issue,³⁰ the time and content of those meals (*e.g.*, macronutrients, caffeine, alcohol), and seasonal differences in timing and content need to be understood. Once the operative nutritional factors can be identified, the role of school and family influences on chronobiology, meal content, and timing may be determined. Longitudinal analyses of inter-relationships among diet, physical activity (PA), sedentary behaviors, sleep, and indicators of circadian rhythmicity are needed, including their impact on the microbiome.³¹ A more expansive research agenda in regard to summer-onset obesity in children has been suggested.²⁵

Multietiological Approach

Priority among the biological etiologies for behavioral obesity prevention research in early childhood must be established, based on their relative contribution to and severity of obesity. Subsets of children develop obesity at different ages,²⁶ suggesting that identifying such subsets and determining the size of the subsets and operational etiological influences would be an important approach. Analyses of large electronic health records might be a first step in identifying the subsets.^{32,33}

In a multietiological approach, any particular child may be subject to influence by multiple etiologies simultaneously. It is not clear how each etiology interacts with each other or with a complex dynamic energy balance model (including neurological and hormonal influences).³⁴ Diverse etiological influences on obesity may be mediated

by diet, physical activity, or sedentary behaviors, re-introducing behavioral factors in the multiple etiological approach, but based on different biological models.

Interventions for each causal factor related to the development of obesity can be designed, implemented, and evaluated. For targeted groups of children (*e.g.*, specific schools or day care centers in specific cities), the risk of obesity must be estimated for each potential etiology to apply the most likely to be effective interventions (likely multiple). These procedures need to be developed and tested.

Conclusions

We believe the above discussion delineates a substantial research agenda that holds promise of a beneficial contribution to child obesity prevention. As indicated before,³⁵ we welcome submission of articles on these issues for consideration for publication in *Childhood Obesity*.

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