Grand Rounds Handout

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Key Takeaways

- Overall costs attributable to obesity in the US alone were nearly $260 billion in 2016.[1]
- Obesity disproportionately impacts Hispanics relative to non-Hispanic whites. Estimates indicate that 50.4% of Mexican Americans meet the criteria for obesity, compared with 42.2% of the non-Hispanic white population.[2]
- The majority-minority County of San Bernardino has one the highest proportions of overweight and obese adults in southern California (nearly 7-in-10 adults).[3] The significant disparities in obesity rates underscore the pressing necessity to investigate the fundamental mechanisms driving obesity in this vulnerable demographic.
- **Obesogenic behaviors,** pivotal contributors to the onset of obesity, stem from a multifaceted interplay of factors encompassing genetics, environment, psychology, and socio-cultural influences. A comprehensive understanding of the intricate connections between these elements is paramount for successfully developing and implementing interventions and policies to mitigate **obesity health disparities**.
- **Childhood adversity is highly prevalent in Hispanics/Latinos,** ranging from 64%[4] to 77%[5], surpassing the 58% prevalence observed among non-Hispanic Whites.[4]
- Recent data indicate that **Hispanics/Latinos** report a higher number of ACEs relative to non-Hispanic Whites.[6]
- Extensive empirical evidence spanning decades indicates a robust association between childhood adversity and health outcomes later in life. In the influential Childhood Adversity Study, **adverse childhood experiences (ACEs)** were defined as trauma- and household-centric, encompassing psychological, physical, and sexual abuse, as well as household dysfunction involving substance abuse, mental illness, criminal behavior, and domestic violence.[7]
- Some scholars have advocated for a broader conceptualization of adversity, encompassing experiences beyond the home, such as witnessing violence, living in an unsafe neighborhood, and encountering bullying. This expanded view incorporates adversities associated with racism (e.g., perceived discrimination) and poverty-related challenges (e.g., food insecurity, reliance on public assistance, residential instability, homelessness, and foster care placements).[8–11] This underscores an urgent need to determine how the unique experiences of Hispanics/Latinos confer risk *and resilience* against ACEs.
- Accumulating evidence indicates that the root cause of numerous chronic illnesses within marginalized minority communities may be linked to the *cumulative* impact of chronic psychological and physiological stressors.[12]
- **Childhood adversity is a documented risk factor for obesity and obesogenic behaviors in adults.**[11,13–15]
- Obesity is often associated with altered eating behaviors, including emotional eating, overeating, and binge eating. Adults with disordered eating frequently report adverse

childhood experiences that may include abuse, neglect, domestic violence, and traumatic loss and grief.[16–19]

- Scores on binge eating tendencies measures are consistently high among childhood trauma victims,[20] highlighting the importance of stressful experiences in the development of obesogenic eating behavior habits later in life.
- Emotional eating represents an important mechanism mediating the association between perceived stress and diet quality in Hispanic/Latino adolescents.[21]
- Despite compelling evidence indicating a connection between childhood adversity and obesity in Hispanic Americans,[5,22–24] the advancement of research in this field is hindered by the **limited knowledge of the mechanisms connecting childhood adversities to obesogenic behaviors is limited, hindering the development of tools for early detection, prevention, and therapy.**
- Our studies indicate that the brain-gut-microbiome system is a critical mechanism that anchors early-life stress to obesogenic behaviors. The gut microbiome is critical to digestion, metabolism, immune system development, brain function, and other host physiological functions.[25,26]
- Childhood adversity is associated with marked and persistent alterations in gut microbiome composition and diversity. We previously demonstrated that microbiome signatures in adults are shaped by exposure to traumatic stress, primarily when adversity occurs early in life.[27,28]
- Microbial imbalances or **dysbiosis** can lead to **(neuro)inflammation** and altered brain function,[25] which potentially contributes to maladaptive eating behaviors.[29] However, the causal relationships between adversity-induced pathological 'dysbiotic drift' and obesogenic behaviors are unclear. Determining the relationship between adverse environments and the gut-microbiome-brain system could reveal mechanisms and facilitate the identification of new targets for interventional and preventative strategies.
- Our laboratory has been at the forefront of exploring brain and behavioral susceptibilities to obesogenic conditions. We reported that access to an obesogenic diet during adolescence:
    - 1) reduces the volume of the hippocampus,[30]
    - 2) impairs the maturation of corticolimbic circuits,[31]
    - 3) enhances behavioral vulnerabilities to psychosocial stressors,[30,31] and
    - 4) increases oxidative stress and neuroinflammation,[32] even in the absence of an obesogenic phenotype.[33]
- Unpublished groundbreaking systems biology approaches reveal that the consumption of an obesogenic diet during adolescence leads to anxiety-like behaviors triggered by stress in adulthood.[28]
- Exposure to an obesogenic environment during adolescence alters indices of hippocampal microstructural integrity, synaptic integrity, and neuroinflammation in adult rats.[28]
- Obesogenic diet consumption and chronic stress exposure also contributed to selective gut microbiota dysbiosis.[28]
- The combination of an obesogenic diet and chronic stress act synergistically to expand putative pro-inflammatory microglia populations in the hippocampus.[28]
- These obesogenic conditions influence the methylation status of the hippocampal *Fkbp5* gene at specific loci. *FKBP5/Fkpb5* represents a potential molecular hub linking

adolescent obesogenic diet consumption to stress-related inflammatory dysregulation in microglia.[28]

Summary and implications

Our findings carry significant implications for elucidating the impact of early exposure to obesogenic environments, marked by high-fat diets and psychosocial stress, on the lifelong gut-brain pathways governing stress responses. These insights shed light on the risk factors for psychiatric comorbidities in individuals struggling with obesity. We foresee that this influential research will pave the way for identifying crucial biomarkers and developing interventions to enhance obesity and mental health care among vulnerable populations.[2]

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