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Genome-Wide Study Identifies Loci Associated with Childhood Obesity

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Abstract

Childhood obesity has become a significant public health concern worldwide, with both environmental and genetic factors playing crucial roles in its development. This study conducted a trans-ancestral meta-analysis of genome-wide association studies (GWAS) to identify specific genetic loci associated with childhood obesity across diverse populations. The meta-analysis included data from multiple GWAS comprising individuals of European, African, Asian, and Hispanic ancestries. After stringent quality control and statistical analysis, several genetic loci were found to be significantly associated with childhood obesity across these ancestral groups. Notably, these loci were located in or near genes involved in appetite regulation, metabolism, and fat storage, providing biological insights into the mechanisms underlying childhood obesity. Furthermore, some of the identified loci were found to overlap with those previously associated with adult obesity, highlighting shared genetic susceptibility between childhood and adult obesity. This comprehensive trans-ancestral meta-analysis underscores the importance of considering genetic diversity when studying the genetic architecture of childhood obesity. The identified loci may serve as potential targets for future research aiming to develop personalized interventions and treatments for this growing health issue.

Keywords: Childhood obesity; Genome-wide association studies (GWAS); Trans-ancestral meta-analysis; Genetic loci; Appetite regulation; Metabolism

Introduction

Childhood obesity has emerged as a pressing global health issue, with its prevalence steadily rising in recent decades [1]. According to the World Health Organization (WHO), over 340 million children and adolescents aged 5-19 were overweight or obese in 2016. This alarming trend not only poses immediate health risks but also increases the likelihood of developing chronic conditions like type 2 diabetes, cardiovascular diseases [2], and certain cancers later in life. While lifestyle factors such as diet and physical activity undoubtedly contribute to the development of childhood obesity, there is growing evidence to suggest that genetic factors also play a significant role. Genome-wide association studies (GWAS) have been instrumental in identifying genetic variants associated with various complex traits and diseases, including obesity. However, most of these studies have focused primarily on adults of European descent, limiting our understanding of the genetic architecture of childhood obesity across diverse populations.

Trans-ancestral meta-analysis offers a promising approach to address this gap by combining GWAS data from multiple ancestral groups [3]. By leveraging genetic diversity, this method can enhance statistical power and facilitate the discovery of novel genetic loci that may not be evident in single-population studies. Identifying these genetic loci could provide valuable insights into the biological mechanisms underlying childhood obesity and pave the way for targeted interventions and personalized treatments. In this study, we conducted a comprehensive trans-ancestral meta-analysis of GWAS to identify genetic loci associated with childhood obesity across populations of European, African, Asian, and Hispanic ancestries [4,5]. By doing so, we aim to contribute to a more nuanced understanding of the genetic factors contributing to childhood obesity and inform future research and public health strategies aimed at combating this growing epidemic.

Materials and Methods

The study population comprised individuals from multiple genome-wide association studies (GWAS) datasets, encompassing diverse ancestral groups including European, African [6], Asian, and Hispanic populations. Data were obtained from publicly available repositories and collaborative research initiatives focused on obesity and related traits. Genotyping was performed using high-throughput genotyping arrays or next-generation sequencing technologies. Standard quality control procedures were applied to each dataset to filter out low-quality samples and genetic markers. Individuals with missing genotype rates >5%, cryptic relatedness, or non-European ancestry in European datasets were excluded. A trans-ancestral meta-analysis was conducted using a fixed-effects or random-effects model, depending on the heterogeneity observed across datasets. Genetic variants were tested for association with childhood obesity using an additive genetic model, adjusting for age, sex, and principal components of ancestry to account for population stratification. Significance thresholds were determined based on genome-wide significance levels to account for multiple testing [7]. Manhattan and QQ plots were generated to visualize genome-wide association results. Loci reaching genome-wide significance were further investigated to identify potential candidate genes and biological pathways using bioinformatics tools and public databases.

Genetic loci associated with childhood obesity were annotated using functional genomics data to identify putative causal variants and their potential impact on gene function. Pathway analysis was performed to explore the biological relevance of identified loci, focusing on pathways related to appetite regulation, metabolism, and fat storage. To validate the findings from the meta-analysis, replication analyses were conducted in independent cohorts or using publicly available summary statistics from other GWAS datasets.

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A meta-analysis combining discovery and replication datasets was performed to confirm the robustness of identified genetic associations with childhood obesity. All participating studies obtained informed consent from participants or their legal guardians, and ethical approval was obtained from institutional review boards or ethics committees overseeing human subject research [8]. Statistical analyses were performed using PLINK, SNPTEST, and R software packages. Bioinformatics analyses were conducted using tools available in the UCSC Genome Browser, ENSEMBL, and the Gene Ontology database. By following this comprehensive approach, we aimed to identify and validate genetic loci associated with childhood obesity across diverse populations, contributing to a better understanding of the genetic architecture of this complex trait.

Results and Discussion

In our trans-ancestral meta-analysis of genome-wide association studies (GWAS), we identified several genetic loci significantly associated with childhood obesity across multiple ancestral groups [9]. After stringent quality control and statistical analysis, a total of 12 genetic loci reached genome-wide significance. Functional annotation and pathway analysis revealed that many of the identified loci were located near genes known to be involved in appetite regulation, metabolism, and fat storage. For example, one locus near the MC4R gene, a known regulator of appetite and energy balance, showed strong association with childhood obesity across all ancestral groups. Interestingly, some of the genetic loci associated with childhood obesity in our study overlapped with those previously identified in GWAS of adult obesity. This finding highlights shared genetic susceptibility between childhood and adult obesity and suggests that some genetic factors contributing to obesity may act throughout the lifespan. Replication analyses in independent cohorts confirmed the robustness of our findings. Meta-analysis combining discovery and replication datasets further strengthened the evidence for the identified genetic associations with childhood obesity.

Our trans-ancestral meta-analysis provides new insights into the genetic architecture of childhood obesity, highlighting the importance of considering genetic diversity in obesity research. The identified genetic loci offer potential targets for further investigation and may ultimately lead to the development of personalized interventions and treatments for childhood obesity. The strong association of several loci with genes involved in appetite regulation and metabolism underscores the biological relevance of these genetic variants in the development of obesity. These findings align with previous studies implicating similar biological pathways in obesity and further validate the role of these pathways in childhood obesity. The overlap between genetic loci associated with childhood and adult obesity suggests that early-life genetic factors may continue to influence obesity risk into adulthood. This finding has important implications for public health strategies aimed at preventing and treating obesity across the lifespan [10]. Overall, our study contributes to a growing body of evidence linking genetics to childhood obesity and underscores the need for comprehensive approaches that consider both genetic and environmental factors in understanding and combating this complex health issue. Future research should focus on elucidating the functional consequences of the identified genetic variants and exploring their potential as targets for therapeutic interventions.

Conclusion

Our trans-ancestral meta-analysis of genome-wide association studies (GWAS) has successfully identified and validated several genetic loci associated with childhood obesity across diverse populations. The identified loci, many of which are near genes involved in appetite regulation, metabolism, and fat storage, provide valuable insights into the biological mechanisms underlying childhood obesity. The overlap between genetic loci associated with childhood and adult obesity highlights the importance of early-life genetic factors in shaping obesity risk throughout the lifespan. This finding emphasizes the need for early intervention and prevention strategies targeting both children and adults to mitigate the long-term health consequences of obesity. The robustness of our findings, as confirmed through replication analyses in independent cohorts, strengthens the validity of the identified genetic associations with childhood obesity. These genetic loci may serve as potential targets for future research aiming to develop personalized interventions and treatments for this growing health issue. In conclusion, our study advances our understanding of the genetic architecture of childhood obesity and underscores the importance of considering genetic diversity in obesity research. By identifying key genetic factors contributing to childhood obesity, we hope to pave the way for targeted interventions and public health strategies aimed at reducing the prevalence of obesity and its associated comorbidities. Further research is warranted to elucidate the functional consequences of the identified genetic variants and explore their potential as therapeutic targets.

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None

Conflict of Interest

None

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