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NEURAL ARCHITECTURE OF OBESITY: INTERFACES BETWEEN GENETICS, BEHAVIOR, AND NEUROSCIENCE IN SUPPORTING WEIGHT LOSS

Rafael Luís Marchetti
Cardiologist, Postgraduate Degree in Exercise and Sports Medicine
Heráclito Research and Analysis Center (CPAH), Department of Neuroscience and Genomics, Brazil & Portugal
https://orcid.org/0000-0002-5487-5852

Jacy Maria Alves
Master's Degree in Internal Medicine, Endocrinologist, Specialist in Neuroscience and Behavior.
Heráclito Research and Analysis Center (CPAH), Department of Neuroscience and Genomics - Cardioendocrine & Lifestyle Medicine. Curitiba
https://orcid.org/0009-0009-4199-1174

Fabiano de Abreu Agrela Rodrigues
Post-PhD in Neuroscience, Specialist in Genomics
Heráclito Research and Analysis Center (CPAH), Department of Neuroscience and Genomics, Brazil & Portugal
https://orcid.org/0000-0002-5487-5852

Abstract: This article reviews the complex interaction between neuroscience, behavior, and genetics in the etiology and treatment of obesity, highlighting the limitations of traditional metabolic models. It presents the Deep Wide-ranging Intellectual Interference (DWRI) model, which integrates genetic, neurobiological, and cognitive-behavioral factors to explain dysfunctional eating patterns. The review emphasizes the role of neuroplasticity and precision medicine in the development of individualized and sustainable therapeutic interventions. Techniques such as brain stimulation and cognitive therapies are discussed as promising tools for restructuring the neural circuits involved in food control. The article concludes that multidisciplinary and personalized approaches are essential for advances in the clinical management of obesity.
Keywords: obesity, neuroscience, eating behavior, genetics, precision medicine, neuroplasticity, DWRI

INTRODUCTION

Obesity is a multifaceted global health challenge with complex causes and significant consequences for physical and mental health (World Health Organization, 2021). Beyond an imbalance between energy intake and expenditure, it is currently understood as a multifactorial disorder, whose determinants involve complex interactions between genetic predispositions, neurobiological circuits, and behavioral patterns influenced by the environment (Berthoud, 2011; Volkow et al., 2008).

Limiting obesity to a purely metabolic condition reveals an epistemological flaw that ignores its neurogenetic and behavioral basis. This fragmented understanding compromises the effectiveness of therapeutic models. In this scenario, a more integrative framework is needed, such as the concept of 'Broad Intellectual Interference Architecture' (DWRI). Over the last two decades, studies have been developed on the interaction between genes, neural networks, and eating behavior patterns, culminating in the concept of DWRI as a theoretical model for understanding the functional imbalances involved in compulsive eating and weight maintenance (Rodrigues, 2023a).

Given the multifactorial complexity of obesity, this article proposes to analyze how neurobiological, behavioral, and genetic factors interact in its etiology and treatment. Specifically, it seeks to: (i) investigate the brain circuits involved in appetite regulation; (ii) explore the influence of gene-environment interaction; and (iii) discuss the therapeutic implications of this approach for the development of individualized and sustainable strategies.

NEUROBIOLOGY OF OBESITY

The brain exercises central control over food intake, integrating homeostatic (physiological hunger) and hedonic (pleasure in eating) signals. Structures such as the hypothalamus, nucleus accumbens, prefrontal cortex, and ventral striatum participate in regulating this balance. Functional neuroimaging studies show that obese individuals exhibit hyperactivation of these regions in response to high-calorie foods. This pattern is associated with dopaminergic dysfunction and reduced sensitivity to satiety, compromising dietary self-control (Volkow et al., 2008; Carnell et al., 2012).

Dopamine is related to reward seeking and motivation to eat, serotonin modulates satiety and mood, while norepinephrine regulates alertness and stress. Dysregulation of these neurotransmitters can increase eating impulsivity and hinder emotional control in the face of high-calorie stimuli (Berthoud, 2011; Blundell & Tremblay, 1985).

Therefore, in contexts of chronic stress, the interaction between dopaminergic dysfunction and reward system hyperactivity

compromises dietary self-regulation. This understanding underpins psychotherapeutic interventions that aim to increase self-control and desensitize individuals to rewarding food stimuli.

GENETICS AND GENE-ENVIRONMENT INTERACTION

Genetic predisposition is a relevant factor in obesity. Genome-wide association studies (GWAS), which identify correlations between genetic variants and diseases, have highlighted genes such as FTO (related to appetite control), MC4R (involved in satiety), and LEPR (receptor for leptin, a hormone that regulates metabolism and fat accumulation) (Locke et al., 2015). However, the expression of these genes is modulated by environmental factors such as dietary patterns, physical inactivity, and chronic stress (Hill & Peters, 1998).

Gene-environment interaction can accentuate dysfunctional eating patterns. One example is the Taq1A polymorphism in the DRD2 gene, which reduces the density of D2 dopaminergic receptors in the striatum—a structure linked to the reward system—and promotes compulsive eating of high-calorie foods (Stice et al., 2008).

PHENOTYPIC CLASSIFICATION AND PRECISION MEDICINE IN OBESITY

Obesity is a heterogeneous condition resulting from genetic, neurobiological, behavioral, and clinical variations. The identification of these subtypes or phenotypes allows for the development of individualized therapeutic strategies. For example, patients with impulsive obesity associated with compulsive eating may require neurobehavioral approaches that differ from those with metabolic obesity resistant to satiety (Rodrigues, 2023b).

Phenotypes can be defined based on eating behavior patterns, body fat distribution, presence of comorbidities, and response to different treatment modalities. This classification applied to clinical practice improves diagnostic accuracy and guides more effective interventions, in line with the proposal of precision medicine, which aims to maximize therapeutic response and reduce variability in clinical outcomes.

NEUROSCIENTIFIC INTERVENTIONS: BRAIN STIMULATION AND BEHAVIORAL TECHNIQUES

The application of neuroscience to clinical practice has driven new forms of intervention for obesity management. Among them are transcranial direct current stimulation (tDCS) and transcranial magnetic stimulation (TMS), non-invasive techniques that aim to alter the activity of specific brain regions. tDCS uses low-intensity electrical currents to stimulate the prefrontal cortex, promoting greater inhibitory control and a lower response to food impulses. TMS, in turn, applies magnetic pulses to modulate the activity of reward circuits, reducing the desire for caloric foods (Boggio et al., 2009; Gluck et al., 2021).

Behavioral interventions, such as mindfulness training and cognitive restructuring, have been shown to be effective in reducing episodes of binge eating. These approaches work by modulating the activity of the dorsolateral prefrontal cortex, promoting greater self-control. In addition, they promote neuroplasticity by reconditioning automatic responses to food, consolidating healthier food choice patterns (Katterman et al., 2014).

NEUROPLASTICITY AND WEIGHT LOSS MAINTENANCE

Maintaining weight loss involves activating brain areas related to motivation, executive control, and positive reinforcement. Neuroimaging studies reveal that individuals who

sustain weight loss activate the ventromedial prefrontal cortex and anterior cingulate gyrus more frequently, while exhibiting a lower response of the anterior insula to food stimuli (Rosenbaum et al., 2018).

These findings suggest that sustaining weight loss requires more than one-off interventions: it demands the consolidation of new cognitive patterns through neuroplasticity, continuous reinforcement, and prolonged behavioral reeducation. The concept of "Broad Intellectual Interference Architecture" (DWRI), developed by Rodrigues (2023a), offers an integrative model that considers the interactions between genes, neural networks, and eating behavior patterns. This model provides a theoretical basis for intervention strategies based on neuroplasticity and lasting behavioral reeducation.

TREATMENT OF OBESITY

The treatment of obesity requires a multifaceted approach that combines behavioral changes, clinical interventions, and, when necessary, pharmacological resources. Drug therapy may be indicated for patients who are unsuccessful with lifestyle interventions, acting to reduce appetite, increase satiety, or decrease fat absorption (Yan et al., 2021). However, its use must be carefully individualized, considering the risks, benefits, and clinical profile of each patient.

Even so, the long-term effectiveness of these strategies may be limited, with a high rate of weight regain. For cases of severe obesity, other strategies may be necessary, such as long-term pharmacological therapy or bariatric surgery, although these also have limitations and associated risks (Yan et al., 2021).

THE DWRI MODEL: AN INTEGRATIVE ARCHITECTURE OF OBESITY

The Broad Intellectual Interference Architecture (DWRI) is a theoretical model developed by Rodrigues (2023a) that seeks to understand obesity from an integrative perspective, centered on neuroplasticity. The model proposes that eating behavior is shaped by a network of cognitive, emotional, and genetic interferences that affect decision-making, self-regulation, and the perception of satiety. These interferences form a dysfunctional functional circuit, which perpetuates compulsive patterns and prevents weight loss maintenance.

The DWRI model is based on the premise that there is an overlap between dopaminergic genetic circuits (such as DRD2), patterns of neuronal activation (such as striatal hyperactivity and prefrontal cortex hypoactivity), and learned cognitive traits (such as impulsive eating and low frustration tolerance). This overlap creates a field of interference that reduces cognitive autonomy in the face of food stimuli. DWRI analyzes this architecture as a dynamic network, where small changes—such as behavioral, pharmacological, or neurostimulatory interventions—can trigger major changes in the functional configuration of eating behavior (Stice et al., 2008; Volkow et al., 2008; Davis et al., 2010).

In clinical practice, the DWRI model provides a basis for more precise and individualized interventions. By identifying the predominant type of interference—emotional, impulsive, reinforcing, or cognitive—it is possible to select more effective therapeutic strategies. For example, patients with reward system hyperactivity may benefit more from brain stimulation or dopaminergic drugs (Gluck et al., 2021; Boggio et al., 2009), while those with low prefrontal activation may respond better to interventions such as cognitive

restructuring or mindfulness (Katterman et al., 2014). Thus, DWRI allows the treatment of obesity to go beyond prescribing diet and exercise, acting to reorganize brain response patterns.

METHODOLOGY

This is an integrative review of the literature, with a qualitative approach, whose objective was to synthesize evidence on the neurobiological, genetic, and behavioral mechanisms of obesity, as well as therapeutic strategies based on neuroscience. Systematic searches were performed in the PubMed, Scopus, and Web of Science databases between January and March 2025. The descriptors used included the terms: 'obesity', 'neuroscience', 'dopamine', 'eating behavior', 'treatment', 'neuroplasticity', and 'genetics', combined with the Boolean operators AND and OR.

Articles published in the last 15 years were included, with an emphasis on systematic reviews, clinical trials, observational studies, and theoretical conceptual articles on the DWRI model. The inclusion criteria involved: (i) articles published in English or Portuguese; (ii) access to the full text; and (iii) relevance to the neurobiological, behavioral, or genetic aspects of obesity. The analysis was conducted through critical reading and thematic categorization of the main findings, focusing on identifying recurring patterns, gaps, and emerging proposals for personalized clinical intervention.

DISCUSSION

Obesity should be understood as the result of complex interactions between genetic predispositions, brain circuits of motivation and reward, and learned behavioral and/ y patterns. Neuroscience offers a robust framework for understanding how changes in functional connectivity and neuroplasticity directly influence food regulation mechanisms.

The interaction between genetic and environmental factors modulates not only eating behavior but also how individuals respond to clinical interventions. This variability justifies the adoption of personalized approaches, such as those proposed by precision medicine and clinical phenotyping, which allow therapeutic strategies to be aligned with each patient's neurobehavioral profile.

The Broad Intellectual Interference Architecture (DWRI) proposal offers an operational model for articulating knowledge of neuroscience, genetics, and behavior. By mapping the points of interference between neural structures, genetic predispositions, and maladaptive eating habits, the model allows for more precise and effective reconfiguration of clinical interventions.

As the biological substrate of behavioral change, neuroplasticity plays a central role in dietary re-education and sustainable weight loss. Strategies that stimulate self-control circuits and inhibit impulsive responses, such as attentional training and behavioral reinforcement, are essential for consolidating these changes in the long term.

The combination of brain stimulation, psychoeducational interventions, and mindfulness-based cognitive therapies allows the principles of DWRI to be applied in a practical and tailored manner. This convergence represents an important step toward sustainable therapeutic strategies aligned with the individual patient's profile.

CONCLUSION

Obesity is a complex, multifactorial, and heterogeneous phenomenon, whose etiology involves an intricate interaction between neurobiological, genetic, and behavioral factors. This article highlighted the importance of an integrative approach that goes beyond simplistic metabolic models and incorporates advances in neuroscience and genetics in the understanding and clinical management of obesity.

The Deep-Wired Regulatory Interference (DWRI) model offers a robust and innovative theoretical framework for understanding the dysfunctional patterns that underlie compulsive eating and difficulty in maintaining weight loss. Combined with precision medicine, which enables the individualization of interventions based on phenotypic , and genetic profiles, DWRI proposes promising paths for more effective and lasting treatments.

Neuroplasticity emerges as an essential biological foundation for dietary re-education and sustainable weight loss. Strategies that combine brain stimulation, cognitive therapies, and behavioral interventions offer the potential to reconfigure the neural circuits involved in food control, reinforcing the need for multidisciplinary and continuous approaches.

Advances in the integration of neuroscience, genetics, and behavior open new perspectives for the development of personalized therapeutic protocols. Continued research and the incorporation of these innovative clinical models can transform the landscape of obesity treatment, promoting lasting health and quality of life.

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