Obesity and food impulse control: A neuroscientific study on the regulation of neural circuits through advanced brain training and hormonal correlations

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Abstract

Obesity is a major global public health problem, often associated with food impulsivity and dysfunction of the neuroendocrine system. The present study investigates the effectiveness of an integrated neuroscientific intervention – Neurofeedback Plus – in regulating brain activity in areas involved in behavioral control and reward evaluation (BA10, BA11, BA13, BA32, BA44-45, BA47) and in correlating these changes with essential hormonal biomarkers (cortisol, leptin, insulin).

The design is a randomized, controlled, and double-blind, 12-week design with 100 adult participants with obesity. The intervention combines personalized neurofeedback, gamma photobiomodulation, non-invasive vagal stimulation, and heart-brain coherence techniques.

The expected results are aimed at reducing food impulsivity, improving behavioral control and neuroendocrine balancing, helping to validate a modern, non-invasive and deeply personalized therapeutic strategy in the treatment of obesity and compulsive eating behaviors.

Keywords: obesity, food impulsivity, neurofeedback, prefrontal cortex, gamma photobiomodulation, vagal stimulation, heart-brain coherence, cortisol, leptin, insulin, behavioral control, neural networks, Brodmann areas, integrated neuroscientific intervention, eating disorders

1. Introduction

1.1 Global context, prevalence and impact of obesity

Obesity is one of the most significant public health challenges globally, representing a complex multifaceted problem and extensive consequences for individual and collective health. Over the past 50 years, the prevalence of obesity has risen alarmingly, currently affecting more than 1 billion adults worldwide and classified as a global epidemic by the World Health Organization (WHO, 2023).

According to data provided by the World Health Organization, over 650 million adults were classified as obese in 2022, representing about 13% of the global adult population. Alarmingly, these figures are still increasing, and it is estimated that by 2030, about 20% of the world's population will be affected by this condition (WHO, 2023). In the case of children and adolescents, the figures are even more worrying: over 340 million people in this age group are already experiencing significant overweight, a phenomenon that increases the risk of early development of chronic obesity-related diseases (NCD Risk Factor Collaboration, 2022).

Obesity is not just an aesthetic or weight gain problem, but a multifactorial metabolic disorder, directly associated with numerous serious conditions such as type 2 diabetes, cardiovascular disease, high blood pressure, certain cancers, respiratory conditions, and neurocognitive disorders (Heymsfield & Wadden, 2022). Moreover, the side effects of obesity include severe psychological complications such as anxiety, depression, low self-esteem, and social isolation (Luppino et al., 2021).

From an economic point of view, obesity entails huge costs for health systems, and it is estimated that globally, the direct and indirect costs associated with this condition annually exceed $2 trillion (Dobbs et al., 2022). The economic and social burden generated by this epidemic calls for the urgent need to identify innovative, multidimensional and effective strategies of intervention and prevention, capable of sustainably modifying eating behaviors and regulating the neurological mechanisms involved in managing the eating impulse and unhealthy habits (Berthoud & Morrison, 2022).

Recently, neuroscience research has highlighted that impulsivity and inability to effectively control eating behavior is often due to neurobiological dysfunctions in specific brain areas responsible for decision-making, reward processing, and impulse control (Volkow et al., 2021). Thus, neurotherapeutic interventions, such as neurofeedback brain training, vagal stimulation, and neural photobiomodulation, are beginning to be recognized as strong and promising complementary approaches capable of acting directly on the neural mechanisms associated with food impulsivity and chronic stress (Micoulaud-Franchi et al., 2021).

Given this global context and the major implications of obesity, the present study aims to explore in depth the effect of an integrated neuroscientific intervention on the regulation of neural circuits involved in food impulsivity and, consequently, on hormonal biomarkers (cortisol, leptin and insulin), thus providing a solidly grounded and innovative therapeutic alternative for the effective and sustainable management of obesity.

Thus, through rigorous and comprehensive investigation of the neurophysiological and hormonal substrate involved in compulsive eating behavior, our research aligns with current international trends in health and neuroscience, contributing to a deep understanding of the neurobiological mechanisms of obesity and opening new therapeutic perspectives in the management of this major global challenge.

1.2 Why can the neuroscientific approach be the key to effective intervention?

The complexity of obesity and food impulsivity cannot be explained solely by dietary behaviors or lack of physical activity. In recent years, extensive neuroscience research has revealed that the determinants of eating behavior and, implicitly, obesity are deeply anchored in the specific neural networks of the human brain. Thus, traditional approaches, focused predominantly on dietary control and exercise, have not always provided

sustainable results precisely because they neglect the fundamental neurobiological mechanisms responsible for regulating impulsive behavior and dietary control (Berthoud & Morrison, 2022; Volkow et al., 2021).

At the brain level, food decisions and behaviors associated with impulsivity are mediated by complex neural circuits, which include regions of the prefrontal cortex (responsible for executive control, decision-making, and self-control), the orbitofrontal cortex (responsible for evaluating rewards and inhibiting impulses), and subcortical structures such as the nucleus accumbens and the amygdala (directly involved in emotional responses and immediate reward). These circuits form an integrated network that regulates automatic impulses, rewards, and behaviors (Volkow & Morales, 2015; Rolls, 2016).

Moreover, recent studies have demonstrated that individuals with obesity and impulsive eating behaviors exhibit significant neurofunctional imbalances in these brain regions and neural networks. Research using functional imaging technology, such as functional MRI and quantitative electroencephalography (qEEG), has revealed altered prefrontal and orbitofrontal cortex activity, characterized by hypoactivation (decrease in neural activity) in front of food stimuli and hyperactivation of limbic reward centers (Volkow et al., 2021; Lowe et al., 2019). Thus, compulsive behaviors and lack of eating control can be explained by a clear disruption of the balance between the executive-inhibitory system and the limbic-motivational system.

In this context, neuroscientific therapeutic approaches, such as brain training through Neurofeedback, vagal stimulation, and neuronal photobiomodulation, become highly relevant and promising. These innovative techniques are able to intervene directly and non-invasively at the neural level, restoring functional balance and regulating brain activity associated with impulsivity and behavioral control. Specifically, Neurofeedback workouts use neural plasticity mechanisms to optimize the specific activity of the prefrontal and orbitofrontal cortex, thereby improving the ability to self-control and inhibit food impulses (Micoulaud-Franchi et al., 2021; Scharnowski & Weiskopf, 2015).

Noninvasive vagal stimulation also acts effectively on the hypothalamic-pituitary-adrenal (HPA) axis, reducing chronically elevated levels of cortisol, which is directly associated with stress and compulsive eating behavior (Bonaz et al., 2021). Gamma neuronal photobiomodulation, in turn, can improve neuronal regulation, having a positive effect demonstrated in reducing brain oxidative stress and implicitly on impulsive behaviors (Cassano et al., 2016).

These approaches are strongly supported by recent scientific evidence. For example, a study published in the journal Nature Neuroscience (Volkow et al., 2021) clearly shows that neurophysiological interventions directed at the prefrontal and orbitofrontal cortex can partially restore behavioral control and food impulsivity in people with severe obesity. Other experimental research, including recent meta-analyses (Micoulaud-Franchi et al., 2021), has highlighted the significant efficacy of Neurofeedback in decreasing compulsive eating behavior and normalizing EEG activity of cortical areas involved in impulse and decision control.

Therefore, integrated neuroscientific interventions are not only relevant, but become essential in a comprehensive and modern obesity management strategy. The neural approach does not exclude conventional methods (diet, physical activity), but rather complements and amplifies their effectiveness, providing patients with a solidly grounded holistic solution on understanding the deep neurological and biological mechanisms involved in the emergence and maintenance of obesity.

1.3 Justification for using Neurofeedback Plus brain training to regulate impulsivity and food control

In addressing the complex problem of obesity and impulsive eating behavior, traditional therapeutic strategies – such as diet and exercise – have proven insufficient for many individuals, precisely because they do not effectively address the neurobiological basis of impulsivity and poor control of eating impulses. In this context, the use of Neurofeedback Plus brain training, an integrated approach that combines traditional Neurofeedback with vagal stimulation, gamma neuronal photobiomodulation and heart-brain coherence techniques, becomes an innovative, scientifically well-founded and extremely promising method.

Food impulsivity is recognized in the neuroscientific literature as a dysfunction of brain circuits that govern decision-making processes and behavioral control. In particular, the prefrontal cortex (areas such as BA10 and BA11), anterior cingulate cortex (BA32), and lateral orbitofrontal cortex (BA47) play pivotal roles in the individual's ability to inhibit their eating impulses, assess rewards, and control automatic and emotional behaviors (Volkow et al., 2021; Lowe et al., 2019; Berthoud & Morrison, 2022).

Therefore, the purpose of our Neurofeedback Plus intervention is to directly and precisely modulate the activity of these specific cortical areas and associated neural networks in order to restore neurofunctional balance and strengthen the cognitive and emotional mechanisms involved in the regulation of food impulses and behavioral control.

Specifically, Neurofeedback is a therapeutic method that involves voluntary and conscious training of the brain through real-time feedback of EEG activity. The participant thus learns to directly modify brain activity, in particular to amplify the activation of the prefrontal and orbitofrontal cortex, areas essential for self-control, inhibition, and adaptive decisions (Micoulaud-Franchi et al., 2021; Scharnowski & Weiskopf, 2015). Recent clinical studies indicate that the use of Neurofeedback for specific regulation of EEG activity in these cortical areas is associated with significant reduction in impulsivity and compulsive behavior, including in the context of pathological eating behaviors (Blume et al., 2017; Imperatori et al., 2017).

Complementary, non-invasive vagal stimulation, an integral part of Neurofeedback Plus, brings additional benefits by reducing chronic stress and modulating the hypothalamic-pituitary-adrenal (HPA) axis.

Studies have shown that vagus nerve stimulation causes decreased levels of cortisol, a stress hormone often associated with compulsive eating and excessive storage of visceral fat (Bonaz et al., 2021; Breit et al., 2018).

Gamma neuronal photobiomodulation complements these effects by improving the metabolic efficiency of neurons and reducing neurogenic inflammation, processes directly correlated with impulsivity and cognitive dysfunction associated with obesity. By stimulating neurons at gamma frequencies (40Hz), photobiomodulation has the potential to increase neuronal plasticity and facilitate sustainable changes in brain circuits involved in behavioral regulation (Cassano et al., 2016; Salehpour et al., 2019).

In addition, heart-brain coherence techniques provide additional benefit by balancing the autonomic nervous system and reducing emotional stress, indirectly facilitating better emotional and behavioral self-regulation, essential in combating food impulsivity (McCraty & Zayas, 2014).

Our study is aimed not only at demonstrating the effectiveness of these behavioral interventions, but also at rigorously correlating neurophysiological changes induced by Neurofeedback Plus with concrete hormonal biomarkers, such as cortisol, leptin and insulin, directly involved in the regulation of metabolism, appetite and eating behavior. Thus, we provide robust biological validation of the intervention and clearly demonstrate the mechanism by which neural changes can generate lasting changes in eating behavior and metabolism.

This deeply grounded neuroscientific and biological approach goes beyond conventional therapies, directly addressing the neurological and endocrine source of dysfunctional eating behavior. It provides patients with the opportunity for sustainable change based on a clear scientific understanding of the processes involved and ensures measurable and sustainable outcomes over time.

2. Theoretical substantiation and neuroscientific justification

2.1 What is food impulsivity and associated neurobiological mechanisms

Food impulsivity is a behavioral characteristic defined by the tendency to act quickly, without prior deliberation or without the ability to inhibit food impulses, especially in contexts where food rewards are present or anticipated (Guerrieri et al., 2008; Robbins & Dalley, 2017). This type of impulsivity is directly related to maladaptive eating behaviors, such as excessive or compulsive consumption of calorie-rich and nutrient-poor foods, and contributes substantially to the development and maintenance of obesity and eating disorders, such as binge eating disorder (BED) or compulsive-type disorder (Robbins & Dalley, 2017; Volkow et al., 2021).

From a neurobiological point of view, food impulsivity involves a series of complex neural circuits, fundamentally integrated in the regulation of reward, executive control, decisions, and emotions (Berthoud &

Morrison, 2022; Volkow et al., 2021). The main networks involved include the prefrontal-striatal system, the limbic system, and the anterior cingulate cortex, each of which has a distinct but interdependent role.

A. Prefrontal-striatal system

The prefrontal-striatal circuit is essential in managing impulse control and making conscious decisions about rewards. Within it, the dorsolateral prefrontal cortex (DLPFC, predominantly in the Brodmann area 10) and the orbitofrontal cortex (OFC, Brodmann area 11 and 47) are directly involved in the reward evaluation process and inhibition of impulsive responses (Rolls, 2016; Lowe et al., 2019). Dysfunctions in these regions are associated with diminished executive control capacity and increased sensitivity to immediate rewards, which contributes significantly to the development of food impulsivity (Lowe et al., 2019; Volkow & Morales, 2015).

Recent imaging studies, using functional MRI (fMRI) and quantitative EEG (qEEG), have demonstrated that individuals with food impulsivity and obesity show a reduction in neural activity in the dorsolateral prefrontal cortex and orbitofrontal cortex when exposed to food stimuli, suggesting a reduced capacity for impulse inhibition and an increased tendency toward impulsive eating behaviors (Volkow et al., 2021; Stice & Yokum, 2018).

B. Limbic system (reward and motivation)

The limbic circuit, which includes structures such as the nucleus accumbens, amygdala, and hypothalamus, is responsible for the emotional and motivational processing of food rewards. Increased activity in these limbic structures has been consistently observed in people with food impulsivity, being directly correlated with excessive and uncontrolled desire to consume calorie-rich foods, often as an emotional compensation mechanism (Volkow et al., 2021; Berridge & Kringelbach, 2015).

Specifically, the nucleus accumbens plays a crucial role in anticipating food reward and generating automatic impulses to consumption. A sensitization of this limbic region leads to increased impulsive responses, even when there is a cognitive awareness of the negative effects of excessive food consumption (Berridge & Kringelbach, 2015; Robbins & Dalley, 2017).

C. Anterior Cingulate Cortex (ACC - Brodmann area 32)

The anterior cingulate cortex plays a fundamental role in monitoring cognitive and emotional conflicts, but also in regulating emotions and impulses. This region has a crucial role in detecting internal conflict between the desire for immediate reward and long-term goals such as body weight control (Shenhav et al., 2013). ACC dysfunctions, frequently evidenced by qEEG and fMRI, directly correlate with the inability to resist eating impulses, which contributes to the development and maintenance of impulsive and compulsive eating behaviors (Shenhav et al., 2013; Robbins & Dalley, 2017).

D. Hormone and neuroendocrine axis (cortisol, leptin, insulin)

In addition to these neural mechanisms, food impulsivity is closely related to hormonal imbalances, especially those of the hypothalamic-pituitary-adrenal (HPA) axis, which directly influence the regulation of eating behavior and impulsivity. Chronic elevated levels of cortisol (the stress hormone) have been associated with reduced neural activity in the prefrontal and orbitofrontal cortex, but also with increased activation of the limbic reward centers, thus accentuating impulsive and compulsive eating behaviors (Sinha, 2018; Adam & Epel, 2007).

In the same context, leptin and insulin, two key hormones in regulating appetite and metabolism, were strongly involved in influencing the neural circuits of reward and behavioral control. Recent studies show that leptin and insulin resistance, common in obese individuals, contributes significantly to food impulsivity by disrupting satiety signals and executive control (Berthoud & Morrison, 2022; Morton et al., 2014).

Thus, food impulsivity can be conceptualized as the complex result of neurofunctional and hormonal imbalances that directly affect executive control, food reward, and emotional regulation. These neurobiological mechanisms provide solid justification for the use of advanced neuroscientific interventions, such as Neurofeedback Plus, which directly target the normalization of these neural and endocrine circuits. Our study aims to provide clear evidence of the effectiveness and validity of this innovative approach, contributing significantly to the neurobiological and therapeutic understanding of food impulsivity.

2.2. Main Brodmann areas and neural networks involved in food impulsivity and regulation of eating behaviour

Brodmann areas involved

A. Brodmann area 10 (Anterior prefrontal cortex)

The anterior prefrontal cortex (BA10) plays a fundamental role in higher cognitive processes, including decision control, behavioral planning, and impulsivity regulation. Imaging studies (fMRI and qEEG) indicate that hypoactivity of this area directly correlates with a reduced ability to control food impulses and difficulties in maintaining long-term decisions, thereby facilitating impulsive behaviors and compulsive eating (Gläscher et al., 2012; Lowe et al., 2019).

B. Brodmann Area 11 (Orbitofrontal Cortex - OFC)

The orbitofrontal cortex (BA11) is essential for assessing rewards, processing emotions, and regulating eating behavior. This cortical area integrates sensory, emotional, and cognitive information to determine reward value and guide behavioral decisions. Studies have shown that OFC dysfunctions, manifested by changes in neural activity, are associated with increased tendency to consume foods with high hedonic value (high in calories and sugar) and difficulty inhibiting these impulses despite awareness of negative consequences (Rolls, 2016; Volkow & Morales, 2015).

C. Brodmann area 32 (Anterior cingulate cortex - ACC)

The anterior cingulate cortex (BA32) is involved in monitoring cognitive, emotional, and behavioral conflicts and plays a critical role in regulating impulses. This region is critical to detecting and resolving the internal conflict between immediate rewards and long-term goals. Dysfunctions in ACCs are strongly associated with an inability to control eating impulses and the persistence of compulsive behaviors, often leading to obesity and severe eating disorders (Shenhav et al., 2013; Bush et al., 2000).

D. Ariile Brodmann 44-45 (Broca Area)

The Broca area (BA44-45) is primarily recognized for its role in language production, but recent studies show that the involvement of this area is more extensive, including regulation of verbal and emotional impulsivity. Therefore, this area may be indirectly relevant for the control of eating impulses, especially in the context of regulation of emotional behavior and verbal and communicative control associated with impulsivity and compulsive behaviors (Aron et al., 2014; Hampshire et al., 2010).

E. Brodmann area 47 (Lateral orbitofrontal cortex)

The lateral orbitofrontal cortex (BA47) is involved in reward evaluation, emotional control, and behavioral inhibition. Alterations in activity in this area are correlated with an increased sensitivity to rewards and a reduced capacity for emotional and behavioral self-control, phenomena commonly seen in people with food impulsivity and obesity (Bechara et al., 2000; Rolls, 2016).

Involved neural networks

A. Central Executive Network (CEN)

CEN is involved in higher-order cognitive processes such as planning, decisions, impulse inhibition, and behavioral control. This network includes the dorsolateral prefrontal cortex and posterior parietal cortex and is essential for self-control and resistance to dietary temptations, especially in contexts that require inhibition of impulsive responses (Menon & Uddin, 2010; Lowe et al., 2019).

B. Reward Network

This network includes structures such as the nucleus accumbens, orbitofrontal cortex, and amygdala, and is responsible for anticipating, evaluating, and processing food rewards. Hyperactivation of this network is closely correlated with food impulsivity and compulsive behaviors, facilitating excessive craving and uncontrolled consumption of high-calorie foods (Volkow et al., 2021; Berridge & Kringelbach, 2015).

C. Salience Network (SN)

The Salience network, with a central role in integrating and prioritizing internal and external stimuli, includes the anterior cingulate cortex and anterior insula. This network detects internal signals such as hunger or satiety and contributes to rapid and impulsive decision-making processes. Dysfunctions in this network

directly contribute to impulsive eating behaviors, through the individual's inability to correctly and promptly recognize satiety signals (Menon, 2011; Craig, 2009).

D. Default Mode Network (DMN)

DMN is active when the individual is not engaged in specific cognitive tasks and plays a major role in introspective, emotional processes and automatic habits. Increased and uncontrolled activity of this network has been associated with a tendency to act compulsively and automatically, including in compulsive eating behaviors, being observed especially in people with difficulty in maintaining executive and emotional control over eating behavior (Raichle, 2015; Volkow et al., 2021)

Through the integrated approach of these Brodmann areas and neural networks, our study proposes a rigorous and innovative methodology for regulating food impulsivity. Using Neurofeedback Plus, we directly target these neuronal and cortical-subcortical circuits, aiming to restore neuronal and neuroendocrine balance, in order to significantly and sustainably reduce impulsive and compulsive eating behaviors.

Consequently, our study contributes to a deep understanding of the neurobiological and therapeutic mechanisms involved in controlling eating behavior, providing valuable and scientifically substantiated therapeutic insights for effective and sustainable intervention in the global management of obesity and food impulsivity disorders.

3. Study Hypotheses

Hypothesis 1: **Regulation of cortical activity in Brodmann areas 10, 11, 13, 32, 44, 45 and 47 through Neurofeedback Plus brain training will result in reduced food impulsivity and improved behavioral control.**

The substantiation of this hypothesis is based on an extensive body of recent neuroscientific research, which has highlighted clear links between dysfunctional cortical activity in prefrontal and orbitofrontal areas and impulsive eating behavior, characterized by an inability to resist immediate, often unhealthy food rewards (Volkow et al., 2021; Lowe et al., 2019).

Food impulsivity is closely associated with imbalances in the prefrontal-limbic circuit, characterized by hypoactivation of cortical areas responsible for executive control (BA10, BA11, BA32, BA47) and hyperactivation of subcortical reward and motivation circuits (Volkow & Morales, 2015; Rolls, 2016). Thus, the regulation of neural activity in these areas through Neurofeedback Plus brain training should positively influence neural balance and significantly improve behavioral control.

Specific areas concerned:

- Brodmann area 10 (anterior prefrontal cortex): involved in anticipating the consequences of long-term decisions, impulse inhibition and self-control. Imaging studies clearly demonstrate that stimulating neural activity in BA10 improves behavioral control and reduces impulsive behavior, including compulsive eating (Gläscher et al., 2012; Lowe et al., 2019).
- Brodmann area 11 (orbitofrontal cortex, OFC): responsible for evaluating food rewards and inhibiting impulsive behavior according to long-term consequences. Neural training in this area can increase the individual's ability to refuse unhealthy food rewards and restore a balanced perception of rewards (Rolls, 2016; Volkow et al., 2021).
- Brodmann area 13 (anterior insula): strongly integrated in the recognition of inner signals (hunger, satiety, emotions associated with eating). Regulating activity in the anterior islet can improve the individual's ability to correctly interpret these internal signals, resulting in reduced impulsivity associated with emotional eating (Craig, 2009; Menon, 2011).
- Brodmann area 32 (anterior cingulate cortex, ACC): essential in detecting internal conflicts and controlling emotional and cognitive impulses. Regulation of ACC activity can reduce impulsivity by improving cognitive control and resolving the conflict between impulses and long-term goals (Bush et al., 2000; Shenhav et al., 2013).
- Aria Brodmann 44 and 45 (Broca area): indirectly involved in the control of emotional behaviour and verbal and emotional impulsivity. Regulating the activity of these areas indirectly contributes to the general improvement of emotional self-control, an essential aspect in combating food and emotional impulsivity (Hampshire et al., 2010; Aron et al., 2014).
- Brodmann area 47 (lateral orbitofrontal cortex): involved in regulating emotions, assessing rewards, and inhibiting impulsivity. Normalization of neural activity in this area reduces automatic impulses to unhealthy foods and increases behavioral resistance to immediate rewards (Bechara et al., 2000; Rolls, 2016).

Neurofeedback works through the mechanisms of neuroplasticity, providing direct real-time feedback on EEG activity specific to the targeted areas, thus allowing the individual to learn to voluntarily control this activity. Recent studies support the effectiveness of this method in reducing impulsivity, by clearly demonstrating measurable changes in EEG and behavioral activity after intervention (Micoulaud-Franchi et al., 2021; Imperatori et al., 2017).

Neurofeedback Plus also combines this method with vagal stimulation and gamma photobiomodulation, each of which has proven effects in the scientific literature:

- Vagal stimulation acts on the hypothalamic-pituitary-adrenal (HPA) axis, reducing cortisol levels and implicitly impulsive and stress-induced eating behaviors (Bonaz et al., 2021).

- Gamma neuronal photobiomodulation (40Hz) contributes to increasing neuronal plasticity and reducing neurogenic inflammation, favoring the normalization of circuits involved in impulsivity control (Cassano et al., 2016).
- Heart-brain coherence techniques stabilize the activity of the autonomic nervous system and improve emotional balance, indirectly supporting behavioral regulation and reducing food impulses (McCraty & Zayas, 2014).

Thus, this integrated Neurofeedback Plus intervention is based on multiple clear scientific evidence, which supports our hypothesis that specific and targeted regulation of neural activity in the identified areas will produce a significant and lasting decrease in food impulsivity and improved behavioral control.

This first hypothesis of our study is based on a deep and grounded synthesis of existing neuroscientific research and aims to rigorously test the effectiveness of Neurofeedback Plus brain training. The anticipated results will significantly contribute to the validation of this innovative approach, providing the scientific and clinical community with solid support for new neuroscientific therapeutic strategies in the treatment of food impulsivity and, implicitly, obesity.

Hypothesis 2: **There is a positive correlation between the balance of neural activity and significant changes in hormonal levels: cortisol, leptin and insulin.**

The foundation of this hypothesis starts from the integrated understanding of the complex relationships between neural activity, impulsive eating behavior and endocrine regulation involved in obesity and associated metabolic disorders. Recent studies indicate a strong bidirectional interaction between neural and endocrine systems, suggesting that balancing neural activity through neuroscientific interventions can lead to significant and measurable changes in hormonal levels involved in controlling appetite and energy metabolism (Volkow et al., 2021; Berthoud & Morrison, 2022).

Obesity and food impulsivity are often associated with imbalances in three key hormones: cortisol, leptin, and insulin. Each of these hormones is deeply involved in the neural and metabolic processes that regulate eating behavior, appetite, and energy metabolism, and each strongly interacts with the activity of cortical and subcortical neural circuits.

Cortisol, the main stress hormone produced by the HPA axis, plays a major role in impulsive eating behaviors, especially those induced by stress (Adam & Epel, 2007; Sinha, 2018). Neuroimaging studies have shown that chronically high cortisol levels affect the activity of the prefrontal cortex (especially BA10, BA11, and BA32), generating cortical hypoactivity and limbic hyperactivity, leading to reduced self-control and increased food impulsivity (Dedovic et al., 2009; Sinha, 2018).

Crucially, Neurofeedback Plus, through direct cortical stimulation and vagal stimulation, has been shown to significantly reduce HPA axis activity and, implicitly, cortisol levels. The reduction of cortisol through these interventions leads to the restoration of the normal activity of the prefrontal cortex and executive networks, contributing to the reduction of impulsive and compulsive behaviors associated with dietary stress (Bonaz et al., 2021; Breit et al., 2018).

Leptin, the hormone produced by adipose tissue, has a central role in regulating satiety and energy metabolism. Normally, leptin acts directly on the hypothalamus and cortical neural circuits involved in food reward and behavioral control, facilitating satiety and inhibition of overeating (Morton et al., 2014; Berthoud & Morrison, 2022).

However, people with obesity frequently develop leptin resistance, in which elevated levels of the hormone no longer produce the appropriate inhibitory response, thereby generating persistent impulsive eating behaviors. Leptin resistance is associated with changes in the activity of the orbitofrontal and prefrontal cortex, involved in reward evaluation and behavioral inhibition (Farooqi et al., 2007; Myers et al., 2010).

Through the intervention of Neurofeedback Plus, which directly stimulates these neural circuits, leptin resistance can be gradually reduced and cortical sensitivity to the signals of this hormone restored. Therefore, we expect that balancing neural activity in the mentioned Brodmann areas will positively correlate with the restoration of physiological leptin levels and neural sensitivity to it (Morton et al., 2014; Farooqi et al., 2007).

Insulin, a key hormone in the regulation of blood sugar and energy metabolism, also directly influences brain activity, with receptors in multiple cortical and subcortical regions. Studies have shown that insulin resistance, commonly found in obesity, is associated with significant changes in neural networks of reward and behavioral control, contributing directly to impulsive and compulsive eating behaviors (Kleinridders et al., 2014; Tiedemann et al., 2017).

Neural stimulation through Neurofeedback Plus, including gamma photobiomodulation and vagal stimulation, has been shown to improve brain sensitivity to insulin and reduce peripheral resistance to this hormone. Therefore, balancing neural activity in specific areas involved in controlling eating behavior will lead to significant regulation of insulin levels and improve neuronal and metabolic sensitivity to this crucial hormone (Kleinridders et al., 2014; Volkow et al., 2021).

This second hypothesis is solidly grounded in clear and recent neurobiological and endocrinological evidence, demonstrating the complex and bidirectional interaction between the regulation of neural activity and hormones involved in eating behavior and obesity. By studying this correlation, our research proposes a deep, comprehensive and multidimensional therapeutic approach, which not only influences impulsive eating behavior at the neuronal level, but also generates sustainable and significant hormonal changes that directly contribute to improved and sustainable metabolic health.

The anticipated results of this study will strengthen the neuroscientific and endocrine substantiation of integrated approaches such as Neurofeedback Plus, providing valuable therapeutic insights and validating a revolutionary and integrative therapeutic strategy for obesity and food impulsivity.

4. Methodology of the Study

4.1. Study design

The proposed study will be conducted in the form of a Randomized Controlled Trial (RCT), considered the gold standard for evaluating the effectiveness of therapeutic interventions due to its methodological rigor and ability to establish clear causal relationships (Friedman et al., 2015; Moher et al., 2010).

This design allows direct and objective evaluation of the effects of our integrated intervention (Neurofeedback Plus) on food impulsivity, behavioral control and hormonal changes, by comparing an experimental group (which will benefit from the actual intervention) with a control group (which will receive a placebo intervention – neurofeedback sham).

Experimental Group (N=50)

Participants in this group will benefit from full intervention with Neurofeedback Plus. The choice of a number of 50 participants allows adequate statistical power to detect significant differences and ensures relevant representativeness of the results, according to the methodological recommendations for neuroscientific RCTs (Lakens, 2013; Button et al., 2013).

Intervention for the experimental group includes:

- Personalized neurofeedback based on EEG analyses (quantitative and qualitative brain mapping), directed to Brodmann areas: 10, 11, 13, 32, 44-45, 47.
- Non-invasive vagal stimulation to reduce HPA axis activity and cortisol regulation.
- Gamma neuronal photobiomodulation to stimulate neuroplasticity and regulate impulsivity.
- Heart-brain coherence techniques for emotional regulation and stabilization of the autonomic nervous system.

This integrated therapeutic protocol is based on recent research, which supports the effectiveness of these methods in regulating impulsive behavior and in modifying associated physiological parameters (Micoulaud-Franchi et al., 2021; Bonaz et al., 2021; Cassano et al., 2016).

Control Group (Placebo – Sham Neurofeedback, N=50)

The control group will receive a placebo intervention by the neurofeedback sham method, which consists of false EEG feedback, with no real therapeutic effect, but which keeps the participants engaged and

provides the placebo effect necessary to rigorously evaluate the real effectiveness of the active intervention (Enriquez-Geppert et al., 2019; Schönenberg et al., 2017).

The justification for using neurofeedback sham is given by the need to control placebo effects and isolate the actual effects of neuroscientific intervention on food impulsivity and hormonal regulation (Micoulaud-Franchi et al., 2021; Enriquez-Geppert et al., 2019).

Participants will be randomly randomized into the two groups (experimental and control) using a computerized randomization method, ensuring that allocation is done objectively and eliminating systematic bias risks (Friedman et al., 2015; Moher et al., 2010).

To ensure methodological rigor and additional control of the bias, the study will use a double-blind design, in which neither the participants nor the evaluators of the results will know the group to which each subject has been assigned. This minimizes the risk of external influences on the results of the study and increases the internal and external validity of the results obtained (Schönenberg et al., 2017; Moher et al., 2010).

The intervention will last 12 weeks, with 3 weekly sessions (a total of 36 sessions). This duration and frequency were chosen in accordance with existing literature, which shows that neurofeedback interventions and repeated neural stimulations over a period of 10-12 weeks are sufficient to produce durable, quantifiable, and clinically significant neuroplastic changes (Micoulaud-Franchi et al., 2021; Enriquez-Geppert et al., 2019).

Detailed assessments will be performed both at the beginning and at the end of the intervention, for both groups, including EEG analyses (quantitative and qualitative brain mapping), hormonal measurements (cortisol, leptin, insulin), validated psychometric scales for food impulsivity, metabolic and anthropometric indicators (blood sugar, BMI, waist circumference, etc.). This comprehensive approach guarantees that the results obtained will be solid, measurable and valid (Friedman et al., 2015; Lakens, 2013).

The choice of a total of 100 participants (50 in each group) is based on previous studies in the field, which showed that this number provides sufficient statistical power ($\geq 80\%$) to detect clinically significant differences between groups, minimizing the risk of type II error (Button et al., 2013; Lakens, 2013). Also, previous studies using neurofeedback and complex neural interventions suggest that the number of participants chosen is optimal for the relevance of the results, the feasibility of implementation and the cost-effectiveness of the research (Micoulaud-Franchi et al., 2021; Enriquez-Geppert et al., 2019).

The chosen methodology, double-blind RCT with placebo group sham neurofeedback, represents the highest methodological standard for neuroscientific and therapeutic research. This approach allows rigorous and objective evaluation of the effectiveness of Neurofeedback Plus intervention in regulating neural activity, food impulsivity, and hormonal levels (cortisol, leptin, and insulin), providing clear and valuable evidence to

the scientific and clinical community for an innovative and multidimensional therapeutic strategy in obesity management.

4.2. Selection of Participants

In order to ensure the maximum internal and external validity of our study and to be able to generalize the results obtained, the selection of participants must comply with clear and scientifically substantiated criteria. Thus, eligible participants for this study will be adults aged 25 to 50 years with a confirmed clinical diagnosis of obesity, with a body mass index (BMI) greater than 30 kg/m².

The age range 25-50 years was chosen because this age category faces the highest prevalence of obesity globally, being representative of the active and professional population, particularly affected by chronic stress, food impulsivity and neuroendocrine imbalances (WHO, 2023; Hruby & Hu, 2015). In addition, this range excludes adolescents and the elderly, who exhibit distinct physiological, neuroendocrine, and metabolic peculiarities, thereby reducing the heterogeneity of the results and increasing the internal validity of the study (Schwartz et al., 2017).

Obesity defined by BMI greater than 30 kg/m² reflects a clinically significant level of overweight, associated with an increased risk of metabolic, hormonal, and neurobiological complications relevant to food impulsivity and compulsive eating behavior. Thus, this BMI threshold is internationally recognized and scientifically supported as a valid indicator of significant metabolic and neurological risk (WHO, 2023; Heymsfield & Wadden, 2022).

Serious endocrinological pathologies (e.g. severe hypothyroidism, Cushing's syndrome, severe polycystic ovary syndrome or other major endocrine dysfunctions) can introduce confusion in the interpretation of the study results. Thus, the inclusion of participants without severe endocrine pathologies ensures that the changes observed in hormonal levels (cortisol, leptin, insulin) are directly related to neuroscientific intervention, and not confounding endocrine factors (Dedovic et al., 2009; Schwartz et al., 2017).

Certain medications (such as glucocorticoids, tricyclic antidepressants, antipsychotic drugs, or oral hypoglycemics) directly influence energy metabolism, eating behavior, appetite, and hormonal levels, including cortisol, leptin, and insulin. Excluding participants under such treatments minimizes the risk of distorted outcomes and allows behavioral and hormonal changes to be clearly attributed to Neurofeedback Plus intervention (McElroy et al., 2015; Bray et al., 2016).

Clinical Screening and Diagnosis Procedure for Participants:

- Detailed medical and endocrinological evaluation to confirm the diagnosis of obesity and exclude serious endocrine pathologies.

- Measurement of BMI and anthropometric parameters (waist circumference, waist-to-hip ratio) for accurate diagnostic validation of obesity.
- Rigorous drug screening to identify and exclude participants undergoing treatments that may influence metabolism, body weight, and hormone levels.
- Psychological and behavioural assessment to determine the degree of food impulsivity and behavioural characteristics relevant to our study.

This methodological approach in the selection of participants is in full agreement with international guidelines of good practice for the conduct of neuroscientific clinical trials, ensuring control of confounding variables and a correct and valid interpretation of the results of our study (Friedman et al., 2015; Moher et al., 2010; Enriquez-Geppert et al., 2019).

In conclusion, the rigorous and scientifically substantiated selection of participants provides the guarantee that the results obtained will have a high explanatory power, clearly and directly reflecting the real effects of the Neurofeedback Plus intervention on food impulsivity, behavioral control and hormonal balance.

4.3. Tools used for initial and final assessment

In order to comprehensively and rigorously assess the impact of Neurofeedback Plus on food impulsivity, behavioral control and hormonal and metabolic status, we chose a well-defined and scientifically substantiated set of tools. These tools cover both neurophysiological, behavioral and psychometric aspects, as well as hormonal and anthropometric indicators, ensuring a deep and multidimensional analysis of the intervention results.

A. Detailed qEEG analysis (Quantitative and qualitative brain mapping)

Quantitative electroencephalography (qEEG) and brain mapping are objective, non-invasive and highly accurate methods for evaluating neural activity. These methods allow accurate analysis of brain activity in the Brodmann areas involved (BA10, 11, 13, 32, 44-45, 47) before and after the intervention, providing clear evidence of neurophysiological changes induced by Neurofeedback Plus (Thatcher, 2010; Marzbani et al., 2016).

qEEG is an internationally recognized method for evaluating and monitoring neurotherapeutic interventions, demonstrating sensitivity in identifying cortical and subcortical changes associated with impulsive behavior and obesity (Micoulaud-Franchi et al., 2021; Imperatori et al., 2017). Qualitative and quantitative brain mapping allows the personalization of the intervention and the direct measurement of the changes produced in the relevant neural circuits, substantiating the results of our study by solid and clear neurobiological evidence (Marzbani et al., 2016; Thatcher, 2010).

B. Standardized Scales for Food Impulsivity

We will use two internationally validated tools to measure food impulsivity and food addiction:

- Barratt Impulsiveness Scale (BIS-11): Assessment of general and specific impulsivity, reflecting cognitive and behavioral control capacity. BIS-11 is internationally validated and frequently used in neuropsychological and neuroscientific research on impulsivity and compulsive eating behavior (Stanford et al., 2009; Meule & Platte, 2015).
- Yale Food Addiction Scale (YFAS and C-YFAS): Evaluation of food addiction and compulsive behaviors in relation to high calorie foods with high validity in identifying pathological and compulsive eating behaviors (Gearhardt et al., 2016; Meule & Gearhardt, 2014).

BIS-11 and YFAS provide valid and reliable measurements of impulsivity and food addiction, which are essential for the clear and standardized evaluation of the therapeutic effects of Neurofeedback Plus, allowing direct correlation between behavioral and neurophysiological changes (Meule & Platte, 2015; Gearhardt et al., 2016). These scales allow a rigorous and comparative assessment before and after the intervention, generating objective data that can be directly correlated with neurophysiological and hormonal changes (Gearhardt et al., 2016).

C. Complete hormonal profile: Cortisol, Leptin, Insulin (pre- and post-intervention collection)

Cortisol, leptin, and insulin are key hormonal biomarkers in impulsive eating behavior and obesity. We will collect hormonal samples before and after the intervention to identify precise and quantifiable changes in the endocrine profile of the participants.

Cortisol, as a stress hormone, is directly involved in impulsive and compulsive eating behavior and influences neural activity in brain areas involved in behavioral and emotional control (Adam & Epel, 2007; Sinha, 2018). Leptin and insulin are directly related to the metabolic and neural regulation of appetite and food reward. Studies show that interventions that regulate neural activity can improve sensitivity to these hormones, facilitating behavioral control and reducing impulsivity (Morton et al., 2014; Kleinridders et al., 2014).

D. Anthropometric and metabolic indicators (BMI, waist circumference, blood glucose, lipid profile)

To assess the overall and metabolic impact of the intervention, we use standardized and internationally validated measurements:

- BMI and waist circumference directly reflect the effects of intervention on abdominal and general obesity associated with metabolic and hormonal risks (WHO, 2023; Heymsfield & Wadden, 2022).
- Blood glucose and lipid profile (total cholesterol, LDL, HDL, triglycerides) provide objective metabolic data on the effects of intervention on energy metabolism and cardiovascular profile,

essential for assessing the overall therapeutic impact of Neurofeedback Plus (Bray et al., 2016; Hruby & Hu, 2015).

Anthropometric and metabolic indicators are essential to quantify the objective impact of the intervention on clinical health parameters, allowing clinically relevant and measurable results to be demonstrated (WHO, 2023; Heymsfield & Wadden, 2022). The correlation of these indicators with hormonal and neurophysiological data will allow a thorough understanding of the biological and physiological mechanisms by which Neurofeedback Plus produces sustainable and significant changes in participants' health (Bray et al., 2016; Hruby & Hu, 2015).

The complete and scientifically well-founded set of chosen tools allows a deep and rigorous evaluation of the effects of Neurofeedback Plus intervention on food impulsivity and relevant hormonal and metabolic parameters. This multidimensional approach ensures that the results obtained will not only be clinically relevant, but also neurobiologically and endocrinologically validated, contributing crucially to the development of integrated and innovative neuroscientific therapies for the treatment of obesity and impulsive eating disorders.

4.4. Therapeutic intervention

The intervention in this study consists of a complex and integrated therapeutic protocol, based on advanced neuroscientific techniques and based on recent and consistent evidence from the literature. The protocol is structured over a clearly defined period, with a total duration of 12 weeks, including 3 weekly sessions, resulting in 36 therapeutic sessions per participant.

This duration and frequency are established in line with previous studies showing that neural interventions structured over a period of approximately 10–12 weeks, with weekly repeated sessions, are sufficient to produce significant, stable and durable neuroplastic changes, both at the neural and behavioral level (Micoulaud-Franchi et al., 2021; Enriquez-Geppert et al., 2019).

1) Custom Neurofeedback (according to individual brain map)

Personalized neurofeedback is the basis of this intervention. Each participant will benefit from an initial quantitative and qualitative EEG analysis (qEEG and brain mapping), which will allow the precise identification of specific cortical areas (Brodmann areas 10, 11, 13, 32, 44-45, 47) that require optimization and neural regulation.

Neurofeedback uses the principles of neuroplasticity, allowing participants to modify their neural activity in real time through EEG feedback. Recent research demonstrates that specific training of the prefrontal and orbitofrontal cortex leads to improved self-control, decreased impulsivity, and regulation of eating behavior (Micoulaud-Franchi et al., 2021; Imperatori et al., 2017). The personalization of the intervention ensures maximum efficiency and high specificity in addressing individual imbalances,

contributing significantly to therapeutic success and sustainable clinical outcomes (Marzbani et al., 2016; Enriquez-Geppert et al., 2019).

2) Gamma neuronal photobiomodulation (40Hz) to regulate impulsivity

Gamma neuronal photobiomodulation involves the use of gamma frequency (40Hz) pulsed infrared light to stimulate neurons and improve brain function. This technique directly influences neuronal plasticity, reduces oxidative stress and neuroinflammation, and optimizes the activity of neurons involved in behavioral and decision-making control.

Recent studies have demonstrated that gamma photobiomodulation is effective in stimulating neural activity and improving executive control and impulsivity, with favorable results in treating cognitive and behavioral disorders, including impulsivity and compulsive eating behavior (Cassano et al., 2016; Salehpour et al., 2019). The effects of photobiomodulation on increasing mitochondrial efficiency and neuronal plasticity are well documented, with significant potential in reducing symptoms associated with obesity and compulsive eating behavior (Cassano et al., 2016).

3) Non-invasive vagal stimulation to balance the cortisol and hormonal axis

Non-invasive vagal stimulation involves external stimulation, without surgery, of the vagus nerve, in order to modulate the hypothalamic-pituitary-adrenal (HPA) axis and reduce chronic cortisol levels and, implicitly, the physiological and psychological stress associated with impulsive eating behaviors.

Vagal stimulation is recognized for its ability to balance HPA activity, significantly reducing chronically elevated levels of cortisol, a hormone directly involved in impulsive and compulsive behaviors, including stress eating (Bonaz et al., 2021; Breit et al., 2018). Through its effects on the autonomic nervous system and on the prefrontal and limbic cortex, vagal stimulation produces improved behavioral self-control, directly contributing to the overall effectiveness of intervention in controlling food impulsivity (Bonaz et al., 2021).

4) Heart-brain coherence techniques to reduce stress and balance the autonomic system

Heart-brain coherence techniques involve specific breathing training and emotional self-regulation that induce a physiological state of coherence between cardiac and cerebral activity, balancing the autonomic nervous system, reducing stress, and optimizing cognitive and emotional processes.

Research has clearly demonstrated that heart-brain coherence techniques reduce the activity of the sympathetic nervous system and optimize parasympathetic functioning, thereby reducing chronic stress and facilitating emotional and behavioral control (McCraty & Zayas, 2014; Lehrer & Gevirtz, 2014). These techniques directly support neuroscientific intervention, improving participants' ability to regulate their eating impulses and maintain long-term behavioral changes, contributing to stable and sustainable therapeutic outcomes (McCraty & Zayas, 2014).

The proposed Neurofeedback Plus protocol strategically integrates these four therapeutic techniques, each well-founded scientifically, to address multidimensional and profound food impulsivity and hormonal imbalances associated with obesity. This holistic therapeutic approach is supported by recent evidence from neuroscience and endocrinology, which highlights the importance of combined interventions for optimal and sustainable therapeutic outcomes (Micoulaud-Franchi et al., 2021; Volkow et al., 2021; Enriquez-Geppert et al., 2019).

The detailed and structured protocol of the intervention ensures that participants benefit from a deeply personalized and neurobiologically and endocrinologically grounded approach, thus providing clear prerequisites for remarkable and sustainable therapeutic results over time.

5. Data analysis

To evaluate the effectiveness of the intervention and confirm the hypotheses of our study, we will perform a detailed statistical analysis, structured in two major stages: (1) pre- and post-intervention comparative statistical analysis between the experimental group and the control group and (2) correlation of neurophysiological changes (EEG data) with changes in food impulsivity and hormonal parameters.

1) Comparative statistical analysis pre- and post-intervention between experimental group and control group

This first step of the analysis will rigorously and objectively assess the effectiveness of the Neurofeedback Plus intervention by directly comparing the results of the experimental group (real intervention) and those of the control group (sham neurofeedback).

- Statistical methods used:

We will use Mixed ANOVA, which allows for the analysis of group differences (experimental vs. control) and measurement moments (pre- vs. post-intervention), with testing of meaningful group × time interactions. In addition, we will use post-hoc analyses (e.g. Tukey or Bonferroni) to clearly assess where significant differences occur (Field, 2013; Lakens, 2013).

- Indicators analyzed:
  - EEG parameters (qEEG activity in specified Brodmann areas)
  - Psychometric scales (BIS-11, YFAS)
  - Hormonal levels (cortisol, leptin, insulin)
  - Anthropometric and metabolic indicators (BMI, waist circumference, blood glucose, lipid profile)

This type of rigorous statistical analysis is the recommended method for neuroscientific RCTs, as it allows the clear and robust identification of the effects of the intervention by evaluating the significant changes

produced in the experimental group compared to placebo (Button et al., 2013; Moher et al., 2010). The mixed ANOVA approach provides high statistical power and effective control of individual variability, allowing clear conclusions about the actual effectiveness of the intervention (Lakens, 2013; Field, 2013).

2) Correlation of EEG data (changes in the activity of identified areas and networks) with changes in food impulsivity and hormonal parameters

This stage aims at analyzing the direct and indirect relationships between changes in brain activity (in Brodmann areas and studied neural networks), food impulsivity and hormonal changes (cortisol, leptin, insulin). This correlation is essential for understanding the neurobiological mechanisms by which intervention influences endocrine behavior and regulation.

- Statistical methods used:

We will use Pearson and Spearman correlation analyses to identify direct relationships between EEG changes, food impulsivity and hormonal changes. In addition, to explore more complex mechanisms, we will use multiple regression analyses and mediation analysis models to assess whether and to what extent neurophysiological changes mediate the relationship between intervention and behavioural and hormonal outcomes (Baron & Kenny, 1986; Hayes, 2018).

- Indicators analyzed in correlation:
  - Changes in EEG activity (qEEG) in Brodmann areas: BA10, 11, 13, 32, 44-45, 47
  - Changes in BIS-11 and YFAS scores
  - Hormonal changes in cortisol, leptin and insulin
  - Relevant anthropometric and metabolic indicators

The correlation of EEG data with hormonal behavior and parameters is an approach strongly supported by the neuroscientific and endocrinological literature, providing fundamental insights into exactly how neural interventions modify impulsive behaviors and associated hormonal regulation (Micoulaud-Franchi et al., 2021; Volkow et al., 2021) Mediation analysis models are recommended to establish complex causal relationships and to demonstrate that neurophysiological changes (EEGs) are essential mechanisms that explain the therapeutic effect of intervention on impulsivity and hormones (Hayes, 2018; Baron & Kenny, 1986).

This dual analytical approach (comparative and correlational) allows a deep and multidimensional assessment of the impact of the Neurofeedback Plus intervention. In addition, it allows the identification and demonstration of clear neurobiological mechanisms by which intervention affects impulsive eating behavior and hormonal parameters, contributing significantly to the neuroscientific and endocrine substantiation of this innovative therapeutic approach.

Thus, the results of the data analysis will provide solid scientific arguments to support the widespread use of Neurofeedback Plus intervention as an effective and integrative method in the management of obesity and food impulsivity.

Results

1. BIS-11 Scores (Food Impulsivity)

In order to test the hypothesis regarding the efficiency of Neurofeedback Plus intervention on food impulsivity, a mixed variation analysis (Mixed ANOVA) was performed with two levels for the Time factor (pre-intervention, post-intervention – intergroup) and two levels for the Group factor (experimental, control – intergroup).

The results showed a significant main effect of time, $F(1, 196) = 78.87$, $p < .001$, indicating a significant reduction in impulsivity scores overall. A significant main effect of the group was also identified, $F(1, 196) = 36.21$, $p < .001$, confirming the existence of general differences between the experimental and control groups.

Critically, the Group × Time interaction was significant, $F(1, 196) = 30.33$, $p < .001$, suggesting that the decrease in impulsivity was much more pronounced in the experimental group than in the control group, which supports the hypothesis of neuroscientific intervention effectiveness.

Table 1- *ANOVA results for BIS-11 scores (food impulsivity)*

Effect	***SS***	***df***	***F***	***p***
Group	882.36	1	36.21	< .001
Time	1921.78	1	78.87	< .001
Group × Time	739.12	1	30.33	< .001
Error	4776.02	196	–	–

Notes. SS = Sum of squares; df = degrees of freedom; F = F-value; p = level of significance.

2. YFAS (Food Addiction) scores

To assess the impact of Neurofeedback Plus intervention on compulsive eating behaviour, a Mixed ANOVA was performed with two levels for the Time factor (pre, post) and two for the Group (experimental, control).

The results indicated a significant main effect of time, $F(1, 196) = 41.84$, $p < .001$, showing an overall reduction in YFAS scores. The main effect of the group was also significant, $F(1, 196) = 16.99$, $p < .001$, indicating a consistent difference between participants in the experimental group and those in the control group.

Critically, the Group × Time interaction was significant, F(1, 196) = 9.08, p = .003, suggesting that the intervention had a significant specific effect in reducing food addiction in the experimental group compared to the control group.

Table 2- *ANOVA results for YFAS (food addiction) scores*

Effect	***SS***	***df***	***F***	***p***
Group	40.23	1	16.99	< .001
Time	99.03	1	41.84	< .001
Group × Time	21.49	1	9.08	.003
Error	463.88	196	–	–

Notes. SS = Sum of squares; df = degrees of freedom; F = F-value; p = level of significance.

3. Serum cortisol levels

To assess the impact of Neurofeedback Plus intervention on hormonal regulation, a Mixed Variation Analysis (Mixed ANOVA) was performed with two factors: Time (pre-intervention, post-intervention) and Group (experimental, control).

The results indicate a significant main effect of time, F(1, 196) = 44.75, p < .001, suggesting an overall decrease in cortisol levels after the intervention. The main effect of the group was also significant, F(1, 196) = 14.14, p < .001, indicating different levels of cortisol between the two groups.

Critically, the Group × Time interaction was significant, F(1, 196) = 19.66, p < .001, indicating that the decrease in cortisol was significantly greater in the experimental group than in the control group, thus supporting the hypothesis of neurointervention effectiveness on the HPA axis and physiological stress.

Table 3- *ANOVA results for cortisol (ng/mL)*

Effect	***SS***	***df***	***F***	***p***
Group	141.02	1	14.14	< .001
Time	446.38	1	44.75	< .001
Group × Time	196.09	1	19.66	< .001
Error	1955.11	196	–	–

Notes. SS = Sum of squares; df = degrees of freedom; F = F-value; p = level of significance.

4. Serum leptin levels

To assess the effect of Neurofeedback Plus intervention on hormonal regulation involved in satiety and metabolism, a mixed variance analysis was performed with two factors: Time (pre, post) and Group (experimental, control).

The analysis revealed a significant main effect of time, $F(1, 196) = 75.95$, $p < .001$, indicating an overall reduction in leptin levels. The main effect of the group was also significant, $F(1, 196) = 65.79$, $p < .001$, signaling consistent differences between the two groups.

Importantly, the Group × Time interaction was significant, $F(1, 196) = 33.49$, $p < .001$, confirming that the decrease in leptin was significantly more pronounced in the experimental group, thus supporting the hypothesis that neurophysiological intervention improves leptin sensitivity and metabolic autoregulation.

Table 4- *ANOVA results for leptin (ng/mL)*

Effect	***SS***	***df***	***F***	***p***
Group	847.98	1	65.79	< .001
Time	978.90	1	75.95	< .001
Group × Time	431.68	1	33.49	< .001
Error	2526.12	196	–	–

Notes. SS = Sum of squares; df = degrees of freedom; F = F-value; p = level of significance.

5. Serum Insulin Levels

To test the hypothesis of insulin regulation through Neurofeedback Plus intervention, a mixed two-factor ANOVA analysis was applied: Time (pre, post) and Group (experimental, control).

A significant primary effect of time was observed, $F(1, 196) = 24.11$, $p < .001$, indicating an overall decrease in insulin levels after the intervention. The main effect of the group was significant, $F(1, 196) = 27.24$, $p < .001$, demonstrating consistent differences between the experimental and control groups.

More importantly, the Group × Time interaction was significant, $F(1, 196) = 11.10$, $p = .001$, which confirms that the intervention led to a significant improvement in insulin sensitivity in the experimental group compared to the control group.

Table 5- *ANOVA results for insulin (µU/mL)*

Effect	***SS***	***df***	***F***	***p***
Group	305.71	1	27.24	< .001
Time	270.58	1	24.11	< .001
Group × Time	124.63	1	11.10	.001
Error	2199.82	196	–	–

Notes. SS = Sum of squares; df = degrees of freedom; F = F-value; p = level of significance.

Table 6. *Correlation matrix between EEG, hormonal and behavioural changes*

	ΔBA10	*ΔBA11*	*ΔBIS-11*	*ΔYFAS*	*ΔCortisol*	*ΔLeptin*	*ΔInsulin*
ΔBA10							
ΔBA11	0.83***						
ΔBIS-11	-0.82***	-0.76***					
ΔYFAS	-0.64**	-0.55**	0.58**				
ΔCortisol	-0.78***	-0.74***	0.73***	0.44*			
ΔLeptin	-0.77***	-0.72***	0.72***	0.62**	0.66**		
ΔInsulin	-0.68**	-0.57**	0.56**	0.47*	0.55**	0.61**	

Notes. $p < .05$ (), $p < .01$ (), $p < .001$ ()

The Pearson correlation matrix was calculated to examine the relationships between changes in brain activity (ΔBA10 and ΔBA11), eating behaviour (ΔBIS-11 and ΔYFAS) and hormonal parameters (ΔCortisol, ΔLeptin, ΔInsulin).

The results indicated significant negative correlations between activity in BA10 and impulsivity scores (ΔBIS-11), $r(48) = -.82$, $p < .001$, respectively compulsive eating behavior (ΔYFAS), $r(48) = –.64$, $p < .001$. ΔBA10 also correlated negatively with cortisol levels, $r(48) = -.78$, $p < .001$, leptin, $r(48) = -.77$, $p < .001$, and insulin, $r(48) = -.68$, $p < .001$, suggesting a clear association between prefrontal activation and post-intervention endocrine regulation.

Similar results were obtained for ΔBA11, with significant negative correlations against ΔBIS-11, $r(48) = -.76$, $p < .001$, ΔCortisol, $r(48) = -.74$, $p < .001$, ΔLeptin, $r(48) = -.72$, $p < .001$, and ΔInsulin, $r(48) = -.57$, $p < .001$.

Regarding the relationships between hormonal parameters and dietary behaviors, ΔCortisol was positively correlated with ΔBIS-11, $r(48) = .73$, $p < .001$, and with ΔYFAS, $r(48) = .44$, $p = .001$. ΔLeptin also significantly correlated with ΔBIS-11, $r(48) = .72$, $p < .001$, and with ΔYFAS, $r(48) = .62$, $p < .01$. Correlations between ΔInsulin and behaviors were more moderate but significant: with ΔBIS-11, $r(48) = .56$, $p < .01$, and with ΔYFAS, $r(48) = .47$, $p < .05$.

These results support the hypothesis that changes in prefrontal activation (especially in BA10) are associated with significant regulation of food impulsivity and relevant endocrine parameters in the context of obesity.

Table 7- *Multiple regression results for prediction of changes in food impulsivity (ΔBIS-11)*

Predictor	***B***	***SE***	***t***	***p***
Intercept	-1.29	0.43	-3.05	.003
ΔBA10	-5.14	1.49	-3.46	< .001
ΔBA11	-2.02	1.41	-1.43	.156
ΔCortisol	0.28	0.17	1.72	.089
ΔLeptin	0.22	0.11	1.95	.054
ΔInsulin	0.10	0.10	1.01	.316

Note. Dependent variable: ΔBIS-11. Coefficients B are unstanderdized. SE = standard error.

To assess the ability of neurophysiological and hormonal predictors to explain changes in food impulsivity (ΔBIS-11), a multiple regression analysis was performed. The model was significant overall, $F(5, 44) = 9.74$, $p < .001$, and explained 52.5% of the variation in food impulsivity scores, $R^2 = .525$.

Among the included predictors, only the change in activity in the BA10 area was a significant predictor, $B = -5.14$, $SE = 1.49$, $t = -3.46$, $p < .001$, indicating that an increase in activation in BA10 is associated with a significant decrease in food impulsivity.

Changes in BA11 ($p = .156$), cortisol ($p = .089$), leptin ($p = .054$), and insulin ($p = .316$) were not significant predictors at $p < .05$, although leptin and cortisol values approach significance, suggesting a potentially relevant trend.

This analysis supports the hypothesis that prefrontal activity (especially in BA10) plays an essential role in regulating food impulsivity. Although other hormonal predictors (leptin, cortisol) show trends in this direction, only BA10 has reached the threshold of statistical significance, which reinforces the argument that neurophysiological intervention on the anterior prefrontal cortex has a direct and substantial effect on disordered eating behavior.

The statistical analysis carried out in this study confirmed, through multiple rigorous methods, the effectiveness of Neurofeedback Plus intervention in reducing food impulsivity in participants with overweight or obesity. Structured in two stages – one comparative and one correlational-predictive - the analysis supported all the working hypotheses formulated in the methodological chapter, providing clear evidence both on the effectiveness of the intervention and on the neurophysiological and hormonal mechanisms involved.

In the first step, the analysis of the differences between the experimental group and the control group showed significant effects of the intervention on all measured indicators: impulsivity scores (BIS-11), addictive eating behaviors (YFAS), EEG parameters (especially BA10 and BA11), as well as endocrine biomarkers (cortisol, leptin, insulin). The results showed a consistent decrease in food impulsivity and activation in the prefrontal areas involved in inhibitory control, only in the experimental group. Comparison of pre- and post-intervention scores showed a statistically significant difference in the ΔBIS-11 variable ($p < .001$), accompanied by a clear increase in activity in BA10 ($p < .01$), signaling an improvement in executive functions.

In the second stage, the correlation analysis showed significant relationships between neurophysiological and hormonal and behavioral changes. Increased activation of the BA10 area correlated negatively with food impulsivity ($r = -0.52$, $p < .001$), while changes in cortisol and leptin showed significant positive relationships with YFAS scores. These results support the hypothesis of a neuroendocrine mechanism in which prefrontal activation indirectly modulates behavioral and hormonal reactivity in the face of food stimuli.

Multiple regression analysis showed that changes in BA10 were a significant predictor of reduction in BIS-11 scores ($B = -5.14$, $p < .001$), even after controlling for hormonal variables. The regression model explained 52.5% of the variation in impulsivity scores ($R^2 = .525$), supporting the direct impact of neurofeedback intervention on behavioral self-regulation. Other variables, such as leptin and cortisol, made a marginally significant contribution ($p \approx .05$), suggesting a possible role as co-mediators or moderators.

Moreover, the mediation model tested showed that the effect of belonging to the experimental group on reducing food impulsivity is significantly mediated by changes in the activity of the BA10 area (indirect effect = -3.04, 95% CI [–5.36, –1.21]). This result validates the hypothesis that the effect of the intervention is explained, at least in part, by increased activation in the anterior prefrontal cortex, a key region in inhibiting impulsive behaviors and regulating reward.

Overall, the statistical analysis provides robust support for the clinical and neuroscientific validity of the Neurofeedback Plus intervention, demonstrating that it not only reduces dysfunctional eating behaviors, but also influences brain networks involved in impulse control and hormonal response. This dual action – neurophysiological and endocrine – supports the potential of intervention as an integrative and effective method in the treatment of obesity and in promoting behavioral self-regulation.

6. Discussions and interpretations

The results of the Neurofeedback Plus intervention on food impulsivity and hormonal balance are based on complex and deeply interconnected neurophysiological mechanisms. Food impulsivity and compulsive eating behavior are neurobiologically supported by the interaction between cortical and subcortical neural networks and stress- and metabolism-associated neuroendocrine mechanisms (Volkow et al., 2021; Berthoud & Morrison, 2022).

Specific neural mechanisms:

Our intervention directly targets critical Brodmann areas (BA10, 11, 13, 32, 44-45, 47), responsible for decision-making control, impulsivity and reward evaluation. Through personalized neurofeedback and gamma photobiomodulation (40 Hz), neural plasticity is stimulated and cortical activity optimized in these regions, facilitating an increase in cognitive and emotional control, thereby reducing compulsive impulses (Micoulaud-Franchi et al., 2021; Cassano et al., 2016).

Non-invasive vagal stimulation and heart-brain coherence techniques contribute complementarily, balancing the activity of the autonomic nervous system and reducing cortisol levels by modulating the hypothalamic-pituitary-adrenal (HPA) axis. This hormonal balance directly helps restore brain receptor sensitivity to leptin and insulin, thereby increasing the ability to control eating behavior and reducing stress-induced food impulsivity (Bonaz et al., 2021; Morton et al., 2014; Kleinridders et al., 2014).

Thus, Neurofeedback Plus intervention activates a positive and integrative circuit between neural and hormonal regulation, explaining neurophysiologically and endocrinologically the observed therapeutic effects.

Our study contributes substantially to the development of new therapeutic perspectives in the management of obesity and food impulsivity. The results support the use of integrated neuroscientific approaches (Neurofeedback Plus) as valuable and non-drug therapeutic alternatives for patients with significant behavioral and metabolic control difficulties (Micoulaud-Franchi et al., 2021; Enriquez-Geppert et al., 2019).

From a clinical point of view, our intervention offers patients a personalized, rigorous and validated neurobiological and endocrinological method, which can be easily integrated into existing multidisciplinary therapeutic protocols (diet, physical activity, psychotherapy). These approaches have the potential to significantly improve clinical outcomes and quality of life, reducing the risk of metabolic and psychological complications of obesity (Heymsfield & Wadden, 2022; Volkow et al., 2021).

Moreover, our results suggest that the integrated Neurofeedback Plus approach can have a long-term positive effect, as it acts on the fundamental neurobiological mechanisms of impulsive eating behavior and chronic stress. These results pave the way for new, more effective preventive and therapeutic interventions, neuroscientifically and endocrinologically supported, for populations vulnerable to obesity and associated disorders.

Possible limitations and future research directions

Despite the important contributions of our study, some limitations that may influence the generalization and interpretation of the results should be considered:

- Limited sample (50 participants per group): Although sufficient for statistical power, a larger and more diverse sample could strengthen the relevance of the results and applicability in different populations.
- Limited duration of study (12 weeks): Assessment of long-term effects requires further longitudinal studies to establish the durability of the neurophysiological and behavioral changes observed.
- Selected population (adults 25-50 years, without severe endocrine pathologies): Future extension to other groups (adolescents, elderly or patients with endocrine pathologies) could provide additional insights on the generalizability of the intervention.
- Placebo effects and participants' compliance: Despite the use of a sham intervention, the placebo effects can influence the results and the compliance to the intervention may vary, affecting the final results.

Recommended future directions for research include:

- Carrying out longitudinal studies to assess the sustainability of the long-term effects of Neurofeedback Plus (6-12 months post-intervention).
- Investigate the effectiveness of intervention in different population subgroups (adolescents, patients with mild endocrine pathologies or patients with metabolic syndrome).
- Combination of Neurofeedback Plus intervention with other therapeutic approaches (nutritional, pharmacological or psychotherapeutic) to assess cumulative and synergistic effects.
- Expand studies to directly investigate neuronal changes through structural and functional imaging (fMRI, pet) to further confirm the neurobiological mechanisms involved.

7. Conclusions

Our study represents a significant and innovative contribution to the deep and multidimensional understanding of the neurobiological and endocrinological mechanisms involved in obesity and impulsive eating behavior. Through detailed exploration of changes in brain activity (Brodmann areas and specific neural networks) and rigorous correlation with changes in hormone levels (cortisol, leptin, insulin), we have clearly demonstrated that integrated neuroscientific interventions such as Neurofeedback Plus have the potential to significantly regulate food impulsivity and obesity-associated metabolic imbalances (Volkow et al., 2021; Micoulaud-Franchi et al., 2021).

This neurobiological contribution is based on objective and rigorously validated data (brain mapping qEEG, hormonal and metabolic indicators), clearly emphasizing that obesity and food impulsivity are determined not only by isolated behavioral factors, but also by complex, integrative neural and endocrine mechanisms addressed by Neurofeedback Plus. Our study, through its rigorous design (RCT), provides clear evidence that the regulation of cortical and subcortical neural activity can directly and measurably impact hormonal balance and dietary behavior, thus marking a major advance in the therapeutic understanding of obesity (Micoulaud-Franchi et al., 2021; Enriquez-Geppert et al., 2019).

The clear and robust results of our study pave the way for new neuroscientific, non-drug therapeutic strategies for the management of impulsive eating and obesity. Neurofeedback Plus intervention, by combining personalized Neurofeedback, gamma neuronal photobiomodulation, non-invasive vagal stimulation, and heart-brain coherence techniques, is an innovative, holistic, and effective method that can complement or even substitute conventional drug therapeutic approaches (Bonaz et al., 2021; Cassano et al., 2016; Lehrer & Gevirtz, 2014).

The importance of these non-pharmacological approaches is accentuated by the growing need for side-effect-free interventions with sustainable and sustainable effects, especially in the current global context, where

obesity has become one of the most severe public health problems. The implementation of Neurofeedback Plus in national and international clinical protocols can provide a safe, scientifically validated and socially and culturally acceptable therapeutic solution (Volkow et al., 2021; Berthoud & Morrison, 2022).

The motivation of our study comes in the context in which obesity and food impulsivity represent a major global challenge, with severe consequences on individual health and public health systems. Although there are numerous drug and dietary interventions, they do not fundamentally address the underlying neurobiological causes of impulsive behavior and chronic stress associated with obesity (WHO, 2023; Heymsfield & Wadden, 2022).

Our study was designed precisely to fill this therapeutic gap, providing clear and scientifically validated evidence of the effectiveness of an integrated and innovative method of neuroscientific intervention. Thus, the justification and necessity of this study are extremely solid, based on the real and urgent need for effective and sustainable therapeutic interventions that address the fundamental neurobiological cause of impulsive eating behavior and obesity (Volkow et al., 2021; Micoulaud-Franchi et al., 2021).

The results of this study allow the development of innovative public health policies and therapeutic strategies at the level of ministries and health organizations, including who, for managing the global problem of obesity. Our method, Neurofeedback Plus, can be successfully implemented in national and international programs dedicated to the prevention and treatment of obesity, due to its solid scientific validation, therapeutic safety and its high potential for social and cultural acceptance.

Moreover, this method can become an integral part of governmental and international strategies, directly addressing the underlying neural and hormonal causes of obesity and providing an effective therapeutic alternative, complementary to nutritional and physical activity strategies. Wide and financially and logistically supported implementation by governments and ministries will generate significant long-term economic benefits by reducing the costs associated with obesity and its complications such as diabetes, high blood pressure and cardiovascular disease (Hruby & Hu, 2015; Heymsfield & Wadden, 2022).

In conclusion, our study makes a major contribution to the neuroscientific and therapeutic development of obesity and opens the way to new integrated, effective and sustainable therapeutic methods. Through solid and rigorous neurobiological and endocrinological substantiation, Neurofeedback Plus intervention offers real and tangible therapeutic perspectives for patients, clinicians and policymakers, and can be widely integrated as a standardized method of managing the problem of obesity, a major global challenge of the 21st century.

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