# 1 **Casi clinici**

# Is theta/beta Neurofeedback effective for gambling disorder treatment? Insights from a case report

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Summary. Several studies showed the effectiveness of theta/beta Neurofeedback (NF) training (i.e., decrease theta power and simultaneously increase beta power) in treating different psychiatric conditions characterized by impaired cognitive control. However, investigations concerning Gambling Disorder (GD) have not yet been conducted. Thus, the main aim of the present study was to investigate the effectiveness of 11 theta/ beta NF sessions in the treatment of a patient with GD. A psychological and neuropsychological assessment was performed before and after NF. A general improvement in symptoms severity (i.e., general psychopathology, dissociative symptoms, and impulsivity) as well as in cognitive performance (i.e., executive functioning) was observed after NF. Moreover, a decrease of theta/ beta ratio (i.e., a marker of executive control and cognitive processing capacity) was mainly detected in the mid-frontal cortex at the end of NF training. Taken together our results provide preliminary evidence of the effectiveness of theta/beta NF in enhancing top-down cognitive control in patients with GD.

**Key words.** Cognitive control, EEG-Neurofeedback, gambling disorder, psychopathology, theta/beta ratio.

### Introduction

Gambling Disorder (GD) is an important global health issue<sup>1</sup> affecting around 0.2-12.3% of adolescents and young adults and about 0.4-8.1% of adults<sup>2,3</sup>. This pathological condition is caused by several biological, psychological, and social factors<sup>1</sup> and it is characterized by symptoms overlapping those met in substance disorders (e.g., impulsivity, emotional dysregulation, withdrawal and tolerance symptoms) leading to severe relational, social and economic problems<sup>4</sup>.

From a neurobiological point of view, GD is associated with different functional (e.g., decreased activity of the prefrontal cortex during cognitive tasks) Il theta/beta Neurofeedback è efficace nel trattamento del disturbo da gioco d'azzardo? Approfondimenti da un caso clinico.

Riassunto. Diversi studi hanno documentato l'efficacia del theta/beta Neurofeedback (NF) training (contemporaneo decremento del theta e incremento del beta power) nel trattamento di differenti condizioni psichiatriche caratterizzate da una compromissione nel controllo cognitivo. Tuttavia, indagini specifiche sul disturbo da gioco d'azzardo (DGA) non sono state ancora condotte. L'obiettivo del presente studio, perciò, è stato quello di indagare l'efficacia di 11 sedute di theta/beta NF nel trattamento di un paziente con DGA. Prima e dopo il trattamento di NF, è stato condotto un assessment psicologico e neuropsicologico. Dopo il trattamento con il NF è stato riportato un miglioramento nella gravità dei sintomi (ovvero psicopatologia generale, sintomi dissociativi e impulsività) così come nella performance cognitiva (ovvero nelle funzioni esecutive). Inoltre, dopo il trattamento, un decremento del rapporto theta/beta (ovvero un marker del controllo e di elaborazione cognitiva) è stato osservato principalmente a livello della corteccia prefrontale. Considerati nel loro insieme, i nostri risultati forniscono dei risultati preliminari circa l'efficacia del theta/beta NF nel miglioramento del controllo cognitivo top-down in pazienti con DGA.

**Parole chiave.** Controllo cognitivo, disturbo da gioco d'azzardo, EEG-Neurofeedback, psicopatologia, rapporto theta/beta.

and structural (e.g., decreased volume of amygdala, thalamus and putamen) brain anomalies, suggesting a global impairment of the cognitive control network, as well as of the reward system<sup>5</sup>.

Among functional alterations, electroencephalographic (EEG) studies showed that GD is characterized by several abnormalities<sup>6</sup>. Although some controversial findings are reported<sup>7</sup>, increased power of both slow and/or beta waves in the frontal and central areas has been frequently detected in patients with GD<sup>8-10</sup>. Of relevance, abnormal increased of both theta and theta/beta ratio (TBR) is considered a common biomarker associated to poor attentional control<sup>11</sup>.

To date, although different treatment options<sup>1</sup> for GD are available, there are no standardized practice guide-

lines<sup>12</sup>. In the last decades, feedback-based treatment, such as EEG-neurofeedback (EEG-NF), have been widely studied as an additional treatment modality for psychiatric disorders<sup>13</sup>. EEG-NF is an endogenous non-invasive brain stimulation technique based on operant conditioning aimed at improving individuals' well-being and cognitive performance<sup>14</sup>. Through a brain-computer interface, individuals learn to modify and regulate their brain activity using a continuous real-time visual or auditory feedback related to their own electrocortical indices<sup>13</sup>. Even though other neurofeedback modalities exist (e.g., the real-time functional magnetic resonance imaging-based NF), EEG-NF is still considered the preferred choice among clinicians<sup>15</sup>.

In particular, in the field of impulsive spectrum disorders, different studies showed the effectiveness of EEG-NF<sup>16,17</sup>. More specifically, theta/beta NF training (i.e., decrease theta power and simultaneously increase beta power) has been widely used to treat core symptoms of attention deficit hyperactivity disorder (ADHD<sup>17</sup>), showing promising results also in patients with substance use disorders<sup>18</sup>. Thus, theta/beta NF may represent a usefulness additional treatment to reduce GD symptomatology through an improvement of cognitive control. Despite this, to the best of our knowledge, no studies examined the effectiveness of EEG-NF in GD. Therefore, the main aim of the current study was to report the application of theta/beta NF in the treatment of a patient with GD.

## **Case illustration**

Walter (a pseudonym) is a 24 years old male who asked for psychological treatment for the first time.

In the initial session he underwent a comprehensive interview<sup>19</sup> performed by a trained clinician. Walter met both "A" (i.e., item #1, #2, #3, #4, #6, #8) and B criteria for GD diagnosis according to the Diagnostic and Statistical Manual of Mental Disorders 5th edition<sup>20</sup>. Although the patient's psychopathological suffering did not meet the criteria to pose other psychiatric diagnoses, emotional dysregulation, sleep problems, anxiety and depression symptoms were observed during the interview.

Walter reported to have developed problematic gambling behavior at the age of 16. He started with sport bets and online games on pay-per-view basis, and then began attending casinos to chase losses. Walter claims to feel obsessed with gambling and to become angry and aggressive when he loses money. Before starting NF and during the entire training no other psychological or pharmacological treatments were performed.

### **PSYCHOLOGICAL AND COGNITIVE ASSESSMENT**

A psychological and neuropsychological assessment before (T0) and after (T1) NF was conducted.

Walter was administered the Symptoms Check List 90-Revised (SCL-90-R)<sup>21</sup>, the Barratt Impulsiveness Scale-11(BSI-11)<sup>22</sup>, the Dissociative Experiences Scale-II (DES-II)<sup>23</sup>, the Symbol Digit Modalities Test (SDMT)<sup>24</sup> and the Trial Making Test A and B (TMT A-B)<sup>25</sup>. Gambling behavior was evaluated before each NF session using the following two questions: "Did you ever gamble last week?", "How often?".

The SCL-90-R consists of 90 items rated on a 5-point Likert scale  $(0-4)^{21}$ . It is a widely used self-report measure for the assessment of psychopathology composed by nine dimensions: somatization, phobic anxiety, hostility, interpersonal sensitivity, depression, psychoticism and obsessive-compulsive symptoms. A Global Severity Index (GSI), which reflect the general level of psychological distress, is obtained summing all items and dividing them by 90.

The BIS-11 is a 30-item multidimensional self-administered questionnaire assessing behavioral, psychological, and biological aspects of impulsivity<sup>22</sup>. Items are rated on a 4-point Likert scale (from "never/rarely"=1 to "almost always/always"=4) and investigate three main dimensions: i) attentional impulsivity, ii) motor impulsivity and iii) non-planning impulsivity.

The DES-II<sup>23</sup> is a 28-item multidimensional self-administered questionnaire assessing the frequency of three main dissociative experiences (i.e., absorption, amnesia, depersonalization/derealization). Items are rated on a 11-point Likert scale (from 0% to 100%) with higher scores indicating more dissociative symptoms.

The SDMT is a neuropsychological test assessing information processing speed<sup>24</sup>. More specifically, it investigates several crucial neurocognitive functions including attention, visual scanning, and motor speed<sup>24</sup>. Using paper and pencil, the subject must fill in as many boxes as possible with a number corresponding to a specific symbol. The symbol/number correspondences are shown in a table that can always be consulted at the top of the test. The score for each trial is the total number of correctly paired items (maximum= 110). Higher scores suggest better cognitive performance.

The TMT A and B<sup>25</sup> is used to evaluate graphomotor speed, visual scanning and executive functions. Using a pencil, the subject must connect 25 numerals in ascending order in part A, and alternately 25 numbers and 25 letters in alphabetical and ascending order, in part B. For the score correction of the test, the method validated by Giovagnoli et al. was used<sup>26</sup>. The B-A difference score was also computed as an index of executive functioning<sup>27</sup>.

### EEG ASSESSMENT PROCEDURE AND NF TRAINING SESSIONS

An EEG assessment was conducted before and after the NF treatment, using three electrodes (Fz, Cz, and Pz) placed according to the international 10-20 system. Two reference electrodes were also placed on the right and the left mastoid. The assessment was performed in two conditions: eyes-open RS (2 minutes) and eyes-closed RS (2 minutes).

Artifacts rejection, including eye-blink, was performed visually by adding markers to the beginning and end of the artifact on the raw EEG trace. Only artifact-free EEG data were analyzed. In the current study, TBR before and after NF has been investigated as a stable electrophysiological marker of executive control and cognitive processing capacity<sup>11,28</sup>. Amplitude calculation was performed using a Fast Fourier transformation applied for theta (4-7.5 Hz) and beta (13-21 Hz) frequencies on Fz electrode, where theta/ beta ratio is supposed to be maximum<sup>29</sup>, and on Cz electrode (i.e., the target of NF training). According to Schutte et al.<sup>29</sup>, TBR values were collapsed (i.e., using the average) across both eyes-open and eyes-closed condition.

After the initial assessment, Walter started a NF treatment consisting of 30 minutes sessions once a week for 11 weeks (i.e., 11 sessions in total). The aim of the NF training was to reinforce beta activity (13-21 Hz) simultaneously inhibiting high beta (21-35 Hz) and theta (4-7.5 Hz) activity. The inhibition of the high beta activity was implemented since it is typically associated with states of tension, anxiety, stress and hyper-arousal<sup>13</sup>.

The NF hardware Nexus 4 (MindMedia BV) linked by computer to the BioTrace+ software (MindMedia BV) was used. During each NF session the active electrode was placed on Cz, while the grounding and reference electrodes were located on the right and the left mastoid, respectively. Patient was sitting on a comfortable chair while the feedbacks were shown on a tv screen in front of him. The training was conducted with the software Brain Assistant as following: the patient had to focus on three guided concentration games of 10 minutes each, for a total of 30 minutes: i) the "Focus Master", where a monk swings upwards (positive feedback) or down (negative feedback); ii) the "Ocean Dive", where a white circle enlarges (positive feedback) or narrows (negative feedback) showing or blocking the ocean view; iii) the "Waterfall", where a dam opens (positive feedback) or closes (negative feedback) allowing or obstructing the water transfer. Feedback thresholds were set in order to reinforce or inhibit the targeted frequency bands. The beta was reinforced about the 60% of the time, while theta and high beta were inhibited the 40% of the time. Altogether, the percentage of success of the ratio reinforcement/inhibition was about 40%. Thresholds were adjusted automatically by the Biotrace+ software in order to optimize rewards and gradually increase the level of difficulty<sup>30</sup>.

Clinical, cognitive and EEG data were evaluated

using the percentage changes ( $\Delta$ %) according to the following formula:

$$\Delta\% = \frac{Post treatment value - Baseline value}{Baseline value} x 100$$

#### Results

The frequency of gambling activities during NF treatment decreased from 5-6 times a week to 0 (Walter stopped gambling behavior between the sixth and the seventh NF session).

A general improvement in symptoms severity as well as in cognitive performance was observed after the NF training (detailed modifications are reported in table 1). More specifically, a large decrease in the

**Table 1.** Pre-treatment (T0) vs. post-treatment (T1) results of self-report questionnaires, neuropsychological tests, and electrophysiological data. The percentage change score ( $\Delta$ %) is reported.

|                    | Т0   | T1   | $\Delta$ % |
|--------------------|------|------|------------|
| SOM                | 52   | 44   | -15.38     |
| oc                 | 60   | 45   | -25        |
| IS                 | 64   | 45   | -29.68     |
| DEP                | 70   | 44   | -37.14     |
| AXN                | 47   | 42   | -10.63     |
| HOST               | 61   | 41   | -32.78     |
| РНОВ               | 66   | 62   | -6.06      |
| PAR                | 58   | 41   | -29.31     |
| PSY                | 53   | 44   | -16.98     |
| GSI                | 1.11 | 0.33 | -70.27     |
| BIS-11             | 82   | 68   | -17.07     |
| DES-II             | 13.6 | 2.85 | -79.04     |
| SDMT               | 50   | 63   | 26.00      |
| TMT B-A            | 76   | 63   | -17.11     |
| Theta Fz           | 2.9  | 1.5  | -30.65     |
| Theta Cz           | 3.0  | 2.7  | -3.67      |
| Beta (13-21 Hz) Fz | 5.2  | 3.6  | -50.38     |
| Beta (13-21 Hz) Cz | 5.6  | 5.4  | -7.71      |
| Beta (21-35 Hz) Fz | 4.6  | 2.95 | -35.87     |
| Beta (21-35 Hz) Cz | 6.25 | 3.4  | -45.6      |
| Fz TBR             | 0.57 | 0.41 | -28.45     |
| Cz TBR             | 0.52 | 0.50 | -4.20      |

*Legend*: SOM= Somatization; OC= Obsessive-Compulsive; IS= Interpersonal Sensitivity; DEP= Depression; AXN= Anxiety; HOST= Hostility; PHOB= Phobic Anxiety; PAR= Paranoid Ideation; PSY= Psychoticism; GSI= Global Severity Index; BIS-11= Barratt Impulsiveness Scale-11; DES-II= Dissociative Experiences Scale-II; SDMT= Symbol Digit Modalities Test; TMT-A-B= Trial Making Test A-B; TBR= theta/beta ratio. GSI (-70.27%) and DES-II total score (-79.04%) was detected. A small decrease in the BIS-11 total score (-17.07%) was also reported. Moreover, an improvement in TMT B-A difference score (-17.11%) as well as in the SDMT total score (26.00%) was documented. Lastly, a decrease of TBR was detected on Fz electrode (-28.45%) and on Cz electrode (-4.20%) after NF training.

#### Discussion

The main aim of this study was to investigate the effectiveness of theta/beta NF in the treatment of a patient with GD. Results showed that NF training was associated with a decrease of TBR in frontal and central midline areas (i.e., Fz and Cz electrodes) as well as with an improvement of cognitive performance and executive functioning (i.e., increased SMDT score and decreased TMT B-A index). Moreover, a decrease of impulsivity, dissociative symptoms and psychopathological distress was also observed after the NF treatment.

Our results are in accordance with previous studies suggesting that the effectiveness of theta/beta NF appears to be associated with a general improvement of top-down control<sup>17</sup>. Indeed, it is known that cognitive control is associated with low frontal TBR<sup>11,28</sup>, especially in the mid-frontal cortex<sup>29</sup>. Similarly, the TMT B-A index is considered a good indicator of cognitive control and executive functioning<sup>27</sup>. Notably, although the aim of theta/beta training was to decrease theta and simultaneously increase beta power, a reduction in both frequency bands was observed at the end of NF treatment suggesting that the improvement of our patient may be more related to theta decrease than beta increase over time. This is in line with previous evidence showing that the improvement of cognitive performance and/or clinical outcomes following theta/beta NF can be driven by decreases of theta power<sup>31,32</sup>.

Furthermore, from a psychopathological point of view, we detected a small decrease in impulsivity and a large improvement of the general level of psychopathology and dissociative symptoms, which are known to play a critical role in development/maintenance of GD<sup>33,34</sup>. Impaired cognitive control is considered a transdiagnostic vulnerability to psychopathology<sup>35</sup> making it a critical target for the treatment in several mental disorders, especially in those characterized by impulsivity and emotional dysregulation<sup>36,37</sup>. Thus, taken together, our results seem to provide preliminary evidence of the effectiveness of theta/beta NF in enhancing top-down cognitive control in patients with GD, suggesting its use as possible additional treatment modality. Indeed, NF can be perfectly complemented with both pharmacological and psychotherapeutic approaches without side effects.

Although promising, some specific limitations should be highlighted in the current study. First, as a case report the efficacy of theta/beta NF in GD should be deeply investigated by double-blind randomized controlled trials (RCT). Second, although several domains of cognitive performance have been evaluated (e.g., attentions and executive functions), we have not investigated other relevant areas for GD, such as inhibitory control, assessed only with a selfreport scale (i.e., the BIS-11). Third, gambling behavior before and after NF was not evaluated using standardized measures and a long-term follow-up was not performed. Finally, we assessed EEG activity with only three electrodes (i.e., Fz, Cz and Pz). Thus, further high-density EEG investigations should be conducted to better understand the neurophysiological bases of theta/beta NF effects. Moreover, since other NF protocols (e.g., sensorimotor rhythm NF) showed promising results in reducing both impulsivity and addictive symptomatology<sup>38</sup>, future RCT should be performed in order to investigate the efficacy of different NF protocols in GD.

*Conflict of interests*: the authors have no conflict of interests to declare.

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