UNIVERSITAT DE BARCELONA

Regulación emocional, impulsividad y compulsividad en los trastornos de la conducta alimentaria y el trastorno de juego

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UNIVERSITAT DE BARCELONA

TESIS DOCTORAL

REGULACIÓN EMOCIONAL, IMPULSIVIDAD Y COMPULSIVIDAD EN LOS TRASTORNOS DE LA CONDUCTA ALIMENTARIA Y EL TRASTORNO DE JUEGO

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Autorización de los directores de la tesis

El Dr. **Fernando Fernández Aranda** con DNI [redacted] y la Dra. **Susana Jiménez Murcia** con DNI [redacted] miembros del Programa de Doctorado Medicina e Investigación Traslacional, impartido por la Facultad de Medicina y Ciencias de la Salud de la Universidad de Barcelona, **AUTORIZAN** como directores de la doctoranda **Maria del Espino Lozano Madrid** con DNI [redacted] la presentación de la tesis doctoral titulada **"Regulación Emocional, Impulsividad y Compulsividad en los Trastornos de la Conducta Alimentaria y el Trastorno de Juego"**.

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Susana Jiménez Murcia

Barcelona, 30 de diciembre de 2020

A mis padres,

por su apoyo incondicional durante todos estos años.

“¿La ciencia ha prometido la felicidad? No lo creo.

Ha prometido la verdad,

y la cuestión es saber si con la verdad se conseguirá algún día la felicidad.”

Emilé Zola

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Índice

Glosario / Glossary

AN: Anorexia Nerviosa (*Anorexia Nervosa*)

BN: Bulimia Nerviosa (*Bulimia Nervosa*)

BSD: *Bulimic Spectrum Disorder*

DSM: Manual Diagnóstico y Estadístico de los Trastornos Mentales (*Diagnostic and Statistical Manual of Mental Disorders*)

ED: *Eating Disorder*

EDT: *Experiential Discounting Task*

EEG: Electroencefalograma

GD: *Gambling Disorder*

GWAS: Estudios de Asociación del Genoma Completo (*Genome-Wide Association Studies*)

IGT: Juego de Azar de Iowa (*Iowa Gambling Task*)

LPP: Potencial Positivo Tardío (*Late Positive Potential*)

SCWT: Test de Stroop (*Stroop Colour and Word Test*)

TA: Trastorno por Atracón

TCA: Trastornos de la Conducta Alimentaria

TCI-R: Inventario de Temperamento y Carácter-Revisado (*Temperament and Character Inventory-Revised*)

TJ: Trastorno de Juego

UPPS-P: *Urgency, Premeditation, Perseverance, Sensation Seeking-Positive Urgency*

WCST: Test de Clasificación de Cartas de Wisconsin (*Wisconsin Card Sorting Test*)

Relación de artículos incluidos

Esta Tesis Doctoral es presentada siguiendo el formato de compendio de artículos para optar al grado de Doctorado Internacional en Medicina e Investigación Traslacional otorgado por la Universidad de Barcelona.

La presente tesis está conformada por cinco estudios independientes, pero complementarios. Todos ellos llevados a cabo en la Unidad de Trastornos de la Conducta Alimentaria y la Unidad de Adicciones Comportamentales, Departamento de Psiquiatría, del Hospital Universitario de Bellvitge.

De los artículos incluidos en la presente tesis, cuatro han sido publicados en revistas internacionales de revisión por pares y uno de ellos se encuentra bajo revisión, sumando un Factor de Impacto Total de 13,811.

1) Mallorquí-Bagué N*, **Lozano-Madrid M***, Testa G, Vintró-Alcaraz C, Sánchez I, Riesco N, César Perales J, Francisco Navas J, Martínez-Zalacaín I, Megías A, Granero R, Veciana De Las Heras M, Chami R, Jiménez-Murcia S, Fernández-Formoso JA, Treasure J, Fernández-Aranda F. Clinical and Neurophysiological Correlates of Emotion and Food Craving Regulation in Patients with Anorexia Nervosa. J Clin Med. 2020;9(4):960.

IF 3,303; Q1 (Área: Medicine, General & Internal; 36/165)

2) Mallorquí-Bagué N, Testa G, **Lozano-Madrid M**, Vintró-Alcaraz C, Sánchez I, Riesco N, Granero R, Perales JC, Navas JF, Megías-Robles A, Martínez-Zalacaín I, Veciana de Las Heras M, Jiménez-Murcia S, Fernández-Aranda F. Emotional and non-emotional facets of impulsivity in eating disorders: From anorexia nervosa to bulimic spectrum disorders. Eur Eat Disorders Rev. 2020;28(4):410-422.

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4) **Lozano-Madrid M**, Clark Bryan D, Granero R, Sánchez I, Riesco N, Mallorquí-Bagué N, Jiménez-Murcia S, Treasure J, Fernández-Aranda F. Impulsivity, Emotional Dysregulation and Executive Function Deficits Could Be Associated with Alcohol and Drug Abuse in Eating Disorders. J Clin Med. 2020;9(6):1936.

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   IF 3,645; Q1 (Área: Clinical Psychology, 19/131).

***** *Primera autoría compartida*

Resumen

Regulación Emocional, Impulsividad y Compulsividad en los Trastornos de la Conducta Alimentaria y el Trastorno de Juego

INTRODUCCIÓN

En el ámbito de la psicología y la psiquiatría, se puede observar un creciente interés en el estudio de los trastornos mentales desde una perspectiva dimensional. Desde este marco conceptual, se ha postulado que la impulsividad y compulsividad desempeñan un papel central en numerosas psicopatologías, entre las cuales se incluyen los trastornos de la conducta alimentaria (TCA) y el trastorno de juego (TJ). Estos trastornos son englobados y situados a lo largo de un continuo conocido como espectro impulsivo-compulsivo, el cual incluye diferentes condiciones neuropsiquiátricas caracterizadas por importantes deterioros en los mecanismos de control de los impulsos.

La impulsividad ha sido relacionada con el TJ y con todos los subtipos de TCA, principalmente con la bulimia nerviosa (BN) y el trastorno por atracón (TA). Sin embargo, pese a que la impulsividad es considerada un constructo multifactorial, apenas encontramos trabajos empíricos que evalúen por separado sus principales dominios (i. e., rasgos impulsivos, impulsividad de elección e impulsividad de respuesta) en estas poblaciones clínicas. De forma similar, son escasas las investigaciones que estudian la compulsividad en los TCA y el TJ. Además, se observa una falta de consenso respecto a la evaluación de este complejo constructo, dificultando la investigación de sus diferentes dominios (i. e., flexibilidad cognitiva y rasgos compulsivos) en estos trastornos.

OBJETIVOS

El objetivo principal de esta tesis era proporcionar nuevas nociones acerca de los procesos de regulación emocional y los componentes de impulsividad y compulsividad implicados en los

TCA y el TJ. Como primer objetivo, investigamos distintos mecanismos de regulación emocional en la anorexia nerviosa (AN), explorando mediante técnicas psicofisiológicas los procesos neurales subyacentes. Después, examinamos diversos componentes de impulsividad en varios subtipos de TCA, analizando la potencial modulación emocional de los mismos. Seguidamente, se identificaron las similitudes y diferencias entre los TCA y el TJ en relación con distintos dominios impulsivos y compulsivos, explorando a su vez si presentaban diferencias asociadas al sexo en estas dimensiones. Se estudió también la posible vinculación de las características impulsivas y compulsivas con el abuso de alcohol y drogas en los TCA, así como su influencia en la respuesta al tratamiento en el TJ.

METODOLOGÍA

Todos los datos proporcionados en la presente tesis provienen de participantes reclutados en la Unidad de Trastornos de la Conducta Alimentaria y la Unidad de Adicciones Comportamentales del Hospital Universitario de Bellvitge (Barcelona). Los pacientes incluidos en las diferentes muestras fueron diagnosticados siguiendo los criterios diagnósticos del DSM-5 por psicólogos y psiquiatras con una vasta experiencia en este campo.

RESULTADOS PRINCIPALES

Estudio 1: Clinical and Neurophysiological Correlates of Emotion and Food craving Regulation in Patients with Anorexia Nervosa

El objetivo de este estudio era explorar las características clínicas y psicofisiológicas vinculadas a la regulación emocional y del *food craving* en una muestra de 20 mujeres con AN y 20 mujeres sin psicopatología.

Las pacientes con AN exhibieron niveles más elevados de disregulación emocional y un mayor uso de estrategias desadaptativas que el grupo control. En ningún grupo se pudo observar una reducción en la amplitud de los potenciales evocados (P300 y LPP) durante la tarea de regulación de emociones negativas. Estos resultados sugieren un posible fallo a nivel

neurofisiológico en los mecanismos de regulación emocional, tanto en pacientes como en controles.

El grupo con AN manifestó niveles más elevados de *food craving* que el grupo control en los cuestionarios autorreportados. No obstante, ambos grupos mostraron una correcta regulación del *food craving* a nivel neurofisiológico, evidenciada por una disminución en la amplitud del LPP durante esta tarea.

Estudio 2: Emotional and Non-Emotional Facets of Impulsivity in Eating Disorders: From Anorexia Nervosa to Bulimic Spectrum Disorders

Con este estudio se pretendía investigar varios componentes de la impulsividad (i. e., rasgos impulsivos e impulsividad de respuesta), así como la posible modulación emocional de los mismos en mujeres con TCA (17 con AN y 16 con BN/TA) y 20 mujeres controles.

Se observaron mayores niveles de impulsividad rasgo en las pacientes con TCA que en las controles, siendo por lo general superiores en la BN/TA. Los resultados subrayaron que la urgencia negativa es una característica común en la AN y la BN/TA, mientras que la falta de perseverancia solamente es un rasgo distintivo la BN/TA.

Las medidas conductuales y psicofisiológicas no mostraron diferencias en la impulsividad de respuesta entre los grupos con TCA y el grupo control, ni en el control inhibitorio general ni en aquel con componente afectivo. Tampoco se observó en ningún grupo una modulación del control inhibitorio ante la presencia de estímulos afectivos.

Estudio 3: Impulsivity and Compulsivity in Gambling Disorder and Bulimic Spectrum Eating Disorders: Analysis of Neuropsychological Profiles and Sex Differences

Mediante el uso de medidas autoreportadas y neurocognitivas, comparamos diferentes dimensiones de impulsividad y compulsividad en una muestra conformada por 59 pacientes con BN/TA (62.7% mujeres), 159 pacientes con TJ (20.1% mujeres) y 150 sujetos controles (82.0% mujeres). Pretendíamos enfatizar las diferencias y similitudes entre las dos muestras clínicas, además de analizar en cada dominio las posibles diferencias asociadas al sexo.

En comparación con los controles, los pacientes con TJ y BN/TA exhibieron niveles más elevados de impulsividad y compulsividad en todas las dimensiones. Sin embargo, ambas patologías mostraron diferencias en varios rasgos impulsivos, como una mayor búsqueda de la novedad en el TJ, y una menor persistencia y mayor evitación del daño en la BN/TA. Además, los pacientes con BN/TA también revelaron una tendencia más impulsiva en la toma de decisiones que aquellos con TJ.

Respecto a los efectos del sexo, las mujeres con TJ presentaron a nivel general mayores niveles de impulsividad y compulsividad que los varones con TJ. Sin embargo, no se encontraron diferencias de sexo en el grupo de BN/TA.

Estudio 4: Impulsivity, Emotional Dysregulation and Executive Function Deficits Could Be Associated with Alcohol and Drug Abuse in Eating Disorders

Este estudio compara mediante medidas clínicas y neurofisiológicas las características impulsivas y compulsivas de 145 pacientes con y sin síntomas de abuso de alcohol y/o drogas.

Aquellos pacientes con TCA que presentaban síntomas de abuso de alcohol y/o drogas mostraron mayores niveles de impulsividad rasgo (i. e., búsqueda de la novedad), mayor impulsividad de elección y menor flexibilidad cognitiva que los pacientes sin esta sintomatología adictiva.

Estudio 5: Trait Impulsivity and Cognitive Domains Involving Impulsivity and Compulsivity as Predictors of Gambling Disorder Treatment Response.

La presente investigación exploró a nivel longitudinal las asociaciones entre distintos dominios impulsivo-compulsivos y la respuesta al tratamiento en 144 varones con TJ.

Varias medidas de impulsividad rasgo predijeron peor respuesta al tratamiento. En concreto, una alta urgencia negativa predecía baja adherencia y recaídas a las 5 semanas de iniciar el tratamiento, mientras que la búsqueda de sensaciones se asociaba a mayor número de abandonos al final del tratamiento.

Los niveles de compulsividad también se asociaron a peores resultados en el tratamiento. Los déficits en flexibilidad cognitiva predecían una mayor tasa de abandonos al final del tratamiento, así como más abandonos, peor adherencia y recaídas en el seguimiento. La baja flexibilidad cognitiva también se asoció a menor tiempo transcurrido hasta la primera recaída y menor tiempo en abandonar.

CONCLUSIONES

En conjunto, estos estudios han subrayado las notables alteraciones en regulación emocional, impulsividad y compulsividad presentes en los pacientes con TCA y TJ, así como las similitudes y diferencias entre ambos trastornos. Nuestros hallazgos señalan la existencia de alteraciones a nivel clínico y neurofisiológico en los procesos de regulación emocional en pacientes con AN. Además, distintos subtipos de TCA parecen diferenciarse por la presencia de distintos rasgos impulsivos, siendo la BN y el TA los trastornos con una mayor personalidad impulsiva en general. También concluimos que el TJ y la BN/TA comparten alteraciones en distintos dominios impulsivo-compulsivos, mostrando algunas diferencias principalmente relacionadas con la personalidad. Nuestros hallazgos también sostienen que ser mujer podría ser un potencial factor de riesgo en el TJ, dado que los niveles de impulsividad y compulsividad parecen estar más exacerbados en mujeres con TJ que en varones. Finalmente, nuestros estudios sugieren que una acentuada impulsividad-compulsividad puede incrementar el riesgo de desarrollar sintomatología adictiva en el TCA, y parece influir negativamente en la respuesta al tratamiento en el TJ. Se espera que estos descubrimientos ayuden a expandir el conocimiento en el campo de los trastornos del espectro impulsivo-compulsivo, con la finalidad última de ofrecer novedosas intervenciones focalizadas en aquellos aspectos que caracterizan a estos trastornos.

Summary in English

Emotion Regulation, Impulsivity and Compulsivity in Eating and Gambling Disorders

INTRODUCTION

In recent years, a growing interest in studying mental disorders from a dimensional perspective has emerged in the fields of psychology and psychiatry. From this framework, it has been postulated that impulsivity and compulsivity have a core role in numerous mental pathologies, including eating (EDs) and gambling disorders (GD). These disorders are encompassed along a continuum known as the impulsive-compulsive spectrum, which includes different neuropsychiatric conditions distinguished by significant impairments in impulse control mechanisms.

Impulsivity has been linked with GD and with all the ED subtypes, especially with bulimic spectrum disorders (BSDs). Although impulsivity is considered a multidimensional construct, most of the empirical studies have rarely assessed its different domains (i.e., impulsive personality traits, response impulsivity and choice impulsivity) in these populations, leading to an inappropriate characterisation of an essential transdiagnostic risk factor for these disorders. Similarly, research focused on exploring compulsivity in EDs and GD is scarce. In addition, there is a lack of consensus regarding the assessment of this complex construct, resulting in difficulties to explore its different domains (i.e., cognitive flexibility and compulsive traits). Lastly, deficits in emotion regulation are also shared in GD and EDs, giving support to the notion of a dimensional continuum encompassing both disorders.

OBJECTIVES

The global aim of this thesis was to provide new insights into the emotion regulation mechanisms and the impulsivity-compulsivity features involved in the symptomatology of EDs and GD. We first aimed to delineate emotion regulation processes in anorexia nervosa

(AN) using clinical and neurophysiological measures. Second, several impulsivity domains were investigating in different ED subtypes, analysing the potential emotional modulation of impulsivity features. Next, we sought to compare the main impulsivity and compulsivity dimensions in GD and BSDs, emphasising the differences and similarities, and exploring the possible influence of sex. We also examined the potential association between impulsivity and compulsivity levels and the presence of alcohol and/or drug symptoms in EDs. Lastly, we aimed to assess the influence of impulsivity and compulsivity in response to treatment in GD.

METHODS

All the data provided in the present thesis come from participants recruited at the Eating Disorder Unit and the Pathological Gambling Unit within the Department of Psychiatry at Bellvitge University Hospital (Barcelona, Spain). All patients included in the different samples were formally diagnosed by experienced psychologists and psychiatrists according to the DSM-5 diagnostic criteria.

MAIN RESULTS

Study 1: Clinical and Neurophysiological Correlates of Emotion and Food craving Regulation in Patients with Anorexia Nervosa

The aim of this study was to investigate clinical and electrophysiological correlates of emotional and food craving regulation in a sample made up of 20 female patients with AN and 20 healthy females.

Patients with AN exhibited greater emotional dysregulation and use of maladaptive strategies than the control group. Neither group displayed a reduction in event related potential amplitudes (P300 and LPP) amplitudes during down-regulation of negative emotions, meaning a lack of successful emotion regulation at a neurophysiological level in both AN patients and controls.

The AN group showed enhanced self-reported food craving compared to controls. However, both groups indicated neurophysiological evidence of food craving regulation as evidenced by blunted LPP amplitudes during down-regulation of food craving.

Study 2: Emotional and Non-Emotional Facets of Impulsivity in Eating Disorders: From Anorexia Nervosa to Bulimic Spectrum Disorders

The study aimed to investigate several impulsivity components (i.e., impulsive traits and response impulsivity), as well as the potential emotional modulation of these components, in ED females (17 with AN and 16 with BSDs) and 20 female controls.

Higher trait impulsivity in ED patients than HC was observed, especially among BSD patients. Results highlighted negative urgency as a common feature of AN and BSDs, while lack of perseverance specifically characterises patients with BSDs.

Neither behavioural measures nor neural indexes showed differences in response impulsivity between any EDs group and controls, for either general or emotional-related response inhibition. Moreover, response inhibition did not differ in presence of neutral or negative stimuli in any group, indicating no emotional modulation of response impulsivity in either ED patients or healthy controls.

Study 3: Impulsivity and Compulsivity in Gambling Disorder and Bulimic Spectrum Eating Disorders: Analysis of Neuropsychological Profiles and Sex Differences

Using self-reported and neurocognitive measures, we compared different impulsivity and compulsivity features in 59 BSD patients (62.7% females), 159 GD patients (20.1% females) and 150 healthy controls (82.0% females). We aimed to emphasise the differences and similarities between the two clinical groups, and to analyse the potential influence of sex in these domains.

GD and BSDs exhibited elevated levels of impulsivity and compulsivity in all the dimensions compared to healthy controls. However, these disorders showed differences in several personality traits, such as high novelty seeking in GD, and low persistence and high harm

avoidance in BSDs. Moreover, patients with BSDs also displayed a trend towards greater impulsive choice than GD patients.

Regarding sex effects, GD women presented higher overall impulsivity and compulsivity than GD men. Nevertheless, no sex differences were found in BSDs.

Study 4: Impulsivity, Emotional Dysregulation and Executive Function Deficits Could Be Associated with Alcohol and Drug Abuse in Eating Disorders

This study compared, by means of clinical and neuropsychological measures, the impulsivity and compulsivity features of 145 ED patients (74.5% females) with and without alcohol and/or drug abuse symptoms.

Patients with alcohol/drug abuse symptoms showed higher levels of impulsive traits (i.e., novelty seeking) and impulsive choice, as well as lower cognitive flexibility than patients without abuse symptomatology.

Study 5: Trait Impulsivity and Cognitive Domains Involving Impulsivity and Compulsivity as Predictors of Gambling Disorder Treatment Response.

The present study longitudinally explored the associations between impulsivity-compulsivity domains and response to treatment in 144 male patients with GD.

Several impulsive personality traits predicted worse treatment outcome. Specifically, high negative urgency predicted low compliance and relapse at 5 weeks of treatment, while increased sensation seeking predicted dropout at the end of treatment.

Levels of compulsivity were also associated to poorer treatment response. In particular, deficits in cognitive flexibility predicted higher dropout rates at the end of treatment; dropout, low compliance and relapses at follow-up; and time to first relapse and time to dropout.

CONCLUSIONS

As a whole, the five studies included in the present thesis have underlined the relevance of emotional regulation mechanisms and impulsivity-compulsivity features on the symptomatology of populations with EDs and GD. Our findings suggest the existence of clinical and neurophysiological alterations in emotional regulation processes among AN patients. Moreover, ED subtypes, namely AN and BSDs, seem to differ by the presence of distinct impulsive personality traits, with BSDs being the group with greater impulsive personality overall. We also concluded that GD and BSDs share common alterations in all the impulsivity and compulsivity domains, displaying some differences mainly related to impulsive-compulsive traits. Our results also uphold that being female may be a potential risk factor in GD, since impulsivity and compulsivity levels are exacerbated in females with GD. Finally, our studies suggest that enhanced impulsivity-compulsivity may increase the risk of developing comorbid abuse symptomatology in EDs, and may negatively influence response to treatment in GD. Our findings hopefully may serve as a beneficial contribution to EDs and GD fields, and give support to the notion of a dimensional approach for mental disorders. Our aim is for our discoveries to eventually offer novel interventions that target specifically the observed problems in emotional regulation and impulsivity-compulsivity control mechanisms.

1. INTRODUCCIÓN

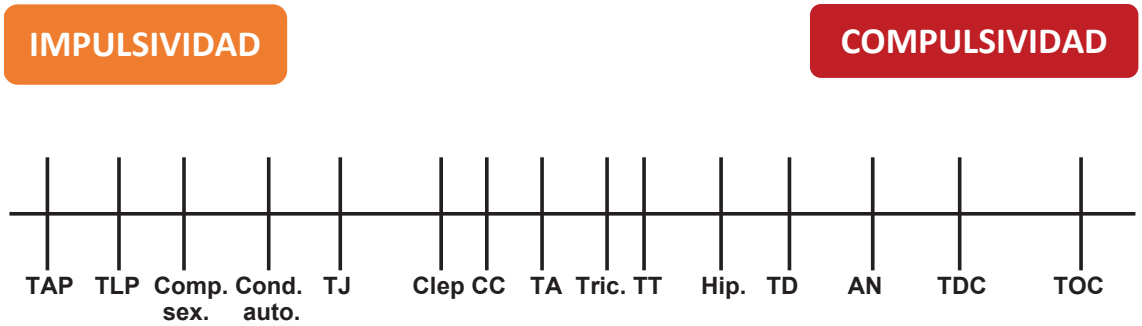
1.1. ESPECTRO IMPULSIVO-COMPULSIVO

La conceptualización de los trastornos mentales comenzó a redefinirse a partir de la década de 1980, momento en el cual el enfoque dimensional emergió con el propósito de suplir las deficiencias de la clasificación psiquiátrica existente [1–3]. De forma opuesta al enfoque categorial, donde los trastornos mentales son considerados entidades biomédicas concretas de diferente naturaleza, la perspectiva dimensional aboga por el carácter continuo de los trastornos mentales, los cuales no poseerían unos límites precisos [4–7]. Este enfoque permitiría agrupar dentro de un mismo continuo o *spectrum* a aquellos trastornos con características compartidas, como rasgos de personalidad, psicopatología o endofenotipos comunes [8–11]. Siendo éste el caso de los trastornos de la conducta alimentaria (TCA) y el trastorno de juego (TJ).

A simple vista, estas patologías pueden parecer muy dispares, principalmente por sus diferencias a nivel sociodemográfico, mientras que el TJ es más prevalente en varones, en los TCA sucede justo lo contrario [12]. Sin embargo, ambos trastornos presentan, no sólo similitudes clínicas, neurobiológicas y de comorbilidad [13–18], sino también otras características comunes relacionadas con la impulsividad y la compulsividad [19–22]. Por ejemplo, tanto los pacientes con TCA como los pacientes con TJ, muestran rasgos de personalidad impulsiva y dificultades en el control de los impulsos [14,23]. Asimismo, en ambos trastornos se observan conductas compulsivas (p. ej., juego, atracones, purgas, rituales con la comida, etc.), las cuales se realizan con el propósito de reducir emociones negativas como la ansiedad, la tristeza o el aburrimiento [21,22].

Siguiendo el enfoque dimensional, estos trastornos se ubicarían a lo largo de un mismo continuo denominado espectro impulsivo-compulsivo, donde la impulsividad, entendida como el deseo de obtener activación y gratificación, representaría un extremo, mientras que la compulsividad, entendida como el intento de aliviar la ansiedad y el malestar, representaría el otro [24–26]. En este continuo, aquellos trastornos con mayor presencia de conductas impulsivas, como el trastorno por atracón (TA) y el TJ, se encontrarían más cerca del polo impulsivo. Mientras que en el polo opuesto, se situarían los trastornos con una mayor compulsividad, como es el caso de la anorexia nerviosa (AN) [27–30] (ver **Figura 1**).

Figura 1. Espectro impulsivo-compulsivo.



Adaptado de Hollander & Rosen [31]. Nota. TAP: trastorno antisocial de la personalidad; TLP: trastorno límite de la personalidad; Comp. sex.: compulsiones sexuales; Cond. auto.: conductas autolesivas; TJ: trastorno de juego; Clep.: cleptomanía; CC: compra comulsiva; TA: trastorno por atracón; Tric.: tricotilomania; TT: trastorno de Tourette; Hip: hipocondrí; TD: trastorno de despersonalización; AN: anorexia nerviosa; TDC: trastorno dismórfico corporal; TOC: trastorno obsesivo-compulsivo.

Cabe destacar que a pesar de que la impulsividad y la compulsividad representan constructos diferenciados, en ambos se observa una dificultad por parte del individuo a la hora de inhibir su propio comportamiento, un elemento clave en los trastornos del espectro impulsivo-compulsivo. Asimismo, estos conceptos no son mutuamente excluyentes, pudiendo estar presentes al mismo tiempo o aparecer en diferentes momentos del curso de un mismo trastorno [25].

Finalmente, además de las semejanzas en impulsividad y compulsividad, los pacientes con TCA y TJ comparten otras singularidades, entre las que destacan los marcados déficits en regulación emocional [32–35]. En general, estos pacientes carecen de la habilidad para gestionar sus emociones, lo cual se traduce en una mayor sensibilidad emocional, un mayor afecto negativo y un elevado uso de estrategias inadecuadas de regulación emocional [36]. Los TCA y el TJ también comparten circuitos y bases neurológicas [14], así como altos índices de comorbilidad con las mismas psicopatologías, especialmente con los trastornos relacionados con sustancias y los trastornos del control de los impulsos [37–41]. Asimismo, es frecuente la presencia comórbida del TJ y los TCA [16,38], principalmente en los subtipos con conductas de atracón y/o purgas, lo cual implica un perfil clínico más complicado, con menor autoestima y mayor impulsividad [17,18].

1.2. TRASTORNOS DE LA CONDUCTA ALIMENTARIA

1.2.1. DEFINICIÓN Y CLASIFICACIÓN

Los TCA constituyen un conjunto de trastornos mentales caracterizados por una alteración persistente de la conducta alimentaria, la cual conlleva un deterioro significativo de la salud física y/o del funcionamiento psicosocial del individuo [12]. Es constante la presencia de cogniciones y/o comportamientos disfuncionales con relación a la comida, los cuales se asocian a una reducción significativa de la calidad de vida [42]. En muchos casos se observa una preocupación excesiva por el peso y la imagen corporal, lo cual da lugar a la aparición de comportamientos inadecuados para controlar el peso, como restringir la ingesta de comida o realizar conductas purgativas. Por otro lado, encontramos pacientes donde la ingesta de comida es excesiva y descontrolada, y en ocasiones seguida de conductas compensatorias [12].

De acuerdo con la quinta y última edición del "Manual Diagnóstico y Estadístico de los Trastornos Mentales" (DSM-5, *Diagnostic and Statistical Manual of Mental Disorders*) [12], los TCA se sitúan ahora dentro del apartado denominado "Trastornos de la conducta alimentaria y de la ingesta de alimentos". Constituyen así un heterogéneo grupo de trastornos donde se incluyen la AN, la bulimia nerviosa (BN), el TA, el diagnóstico de "otro trastorno alimentario o de la ingesta de alimentos especificado" y el de "trastorno alimentario o de la ingesta de alimentos no especificado". Este último se utilizaría cuando se presentan síntomas de TCA pero la información es insuficiente como para realizar un diagnóstico más específico [12]. Además, dentro de la AN encontramos distintas tipologías, la AN restrictiva y la bulímico-purgativa, dependiendo de la ausencia o presencia de conductas de atracón y/o purgas. Para una descripción detallada de cada cuadro clínico, consúltese la **Tabla 1**.

Por último, cabría destacar que existe un alto solapamiento entre los distintos grupos diagnósticos, siendo común que los síntomas varíen y el diagnóstico inicial se vea modificado, pasando el paciente a cumplir criterios para otro TCA. Esto sucede especialmente en la AN y el TA, donde una parte considerable de pacientes evolucionan hacia una BN [42–44].

Tabla 1. Criterios diagnósticos de los TCA adaptados del DSM-5 [77].

Diagnóstico	Sintomatología principal	Subtipos
Anorexia nerviosa	Restricción de la ingesta energética que conduce a un peso corporal significativamente bajo Miedo intenso a ganar peso o a engordar Alteración de la imagen corporal e influencia inapropiada del peso o la figura corporal en la autoevaluación.	Tipo restrictivo Tipo con atracones/purgas
Bulimia nerviosa	Episodios recurrentes de atracones. Comportamientos compensatorios inapropiados como el vómito, el abuso de laxantes o el ejercicio excesivo. La autoevaluación se ve excesivamente influida por la figura corporal y el peso.	
Trastorno por atracón	Episodios recurrentes de atracones. Malestar intenso respecto a los atracones. Ausencia de conductas compensatorias	
Otro trastorno alimentario o de la ingesta de alimentos especificado	AN con IMC>18.5 km/m^2	AN atípica
	BN con < 1 atracón-purga/semana	BN de frecuencia baja
	TA con < 1 atracón/semana	TA de frecuencia baja
	Purgas recurrentes en ausencia de atracones	Trastorno por purgas
	Episodios recurrentes de ingestión nocturna junto con malestar significativo	Síndrome de ingestión nocturna de alimentos
Trastorno alimentario o de la ingesta de alimentos no especificado	Categoría empleada cuando no se cumplen criterios para un TCA especificado	

1.2.2. EPIDEMIOLOGÍA

Se observa una mayor prevalencia de TCA en mujeres, sobre todo durante la adolescencia y la edad adulta temprana [43], aunque a lo largo de los últimos años se ha producido un aumento de la incidencia en varones [44]. Pese a que los TCA afectan a las personas independientemente de su situación socioeconómica o cultural, es más frecuente observarlos en sociedades occidentales industrializadas. En países occidentales, la prevalencia se eleva al 15.2% entre las mujeres adolescentes, mientras que en adultos se sitúa entre el 3% y el 9% [45,46].

La gravedad de estos trastornos se ve reflejada en su prolongada duración, así como en sus altos índices de cronicidad y mortalidad [47], especialmente en pacientes con AN, cuya tasa de mortalidad es una de las más elevadas dentro de los trastornos mentales [48]. Además, estos trastornos se asocian a elevados índices de comorbilidad, lo cual incrementa su severidad, cronicidad y la resistencia al tratamiento [49]. Entre los trastornos comórbidos más frecuentes destacan los trastornos del estado de ánimo, de ansiedad, relacionados con sustancias, del control de impulsos, y los trastornos de personalidad [13,47,50–53].

1.2.3. FACTORES DE RIESGO Y MANTENIMIENTO

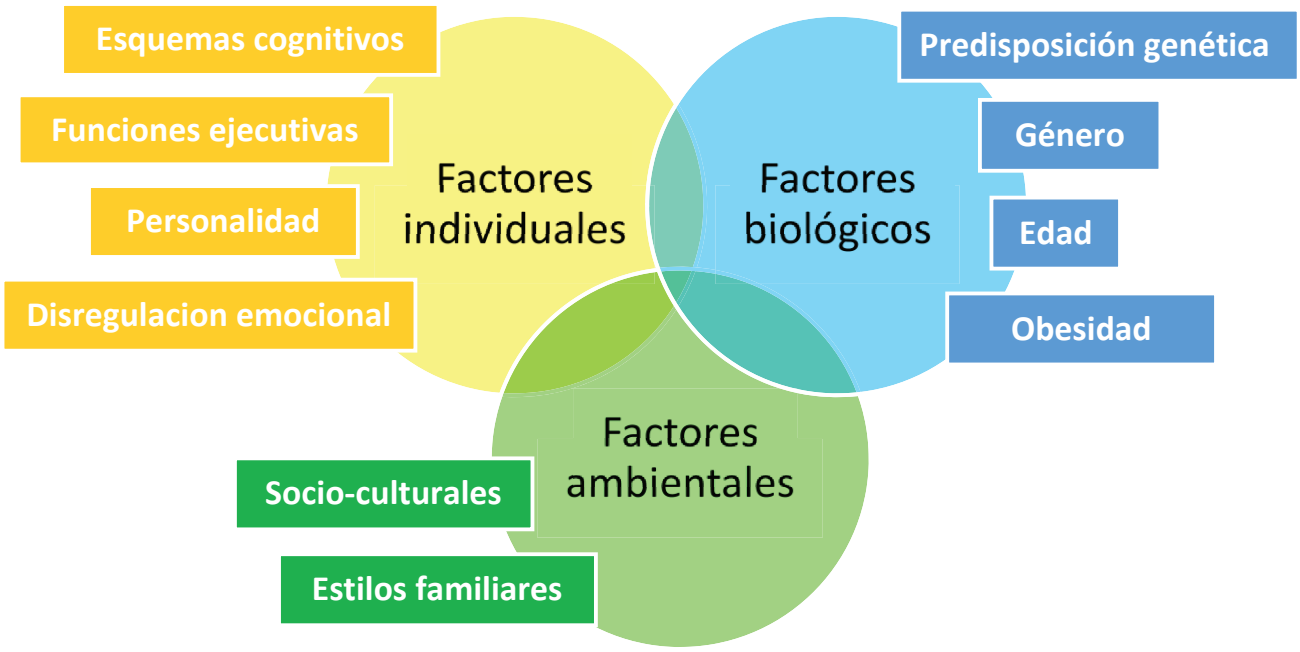
Los TCA son trastornos de carácter multifactorial, dado que numerosos factores influyen en su aparición, desarrollo y mantenimiento. Entre estos factores encontramos tanto biológico-genéticos como ambientales, individuales, e incluso rasgos específicos de personalidad [54]. En primer lugar, diversos estudios con gemelos y familiares apuntan a una alta predisposición genética [55–59]. Recientemente, se están llevando a cabo estudios de asociación del genoma completo (GWAS, *Genome-Wide Association Studies*), los cuales indican que, aunque parece haber ciertas variantes genéticas asociadas a los TCA, todavía es necesario seguir indagando en el conocimiento de estos posibles biomarcadores [60–62].

Por otro lado, los factores socio-culturales también desempeñan un papel relevante en la aparición de estos trastornos, principalmente en las sociedades occidentales. Aquí se observa una tendencia cultural a asociar la delgadez con la belleza, el éxito y la aceptación social, lo cual se refleja en los medios de comunicación [63–65]. Otro factor ambiental de riesgo serían

los estilos familiares, destacando la notable influencia de las críticas parentales relativas al peso y la apariencia física de los hijo/as [66–68].

Finalmente, factores individuales, como los esquemas cognitivos sobre el propio peso y figura, el bajo apoyo social percibido, la baja autoestima, la disregulación emocional, la rigidez cognitiva y otros déficits en las funciones ejecutivas, también propician su desarrollo [69–75]. Asimismo, tanto los rasgos como los distintos *clusters* de personalidad influyen de forma notable en la etiología y mantenimiento de los TCA [13,76,77] (ver **Figura 2**).

Figura 2. Factores de riesgo y mantenimiento en TCA.



1.3. TRASTORNO DE JUEGO

1.3.1. DEFINICIÓN Y CLASIFICACIÓN

El TJ es una adicción comportamental caracterizada por una conducta recurrente y problemática de juego, la cual persiste a pesar de las consecuencias negativas que de ésta derivan en el funcionamiento psicosocial del individuo [12]. Los pacientes con TJ presentan la necesidad de apostar mayor cantidad de dinero de la que se pueden permitir, así como una gran

dificultad para controlar esta conducta. Tanto la cantidad de dinero apostado como la frecuencia de las apuestas realizadas van aumentando gradualmente a medida que el trastorno evoluciona. Además, son recurrentes los pensamientos de juego, consistiendo en la recreación de experiencias pasadas con esta actividad, en las próximas apuestas o en cómo conseguir dinero para seguir jugando o poder saldar las deudas, dependiendo del curso del trastorno.

En definitiva, la conducta de juego tiene una relevancia muy significativa en la vida del individuo, desplazando cualquier otro interés, obligación o responsabilidad. Sin embargo, pese a ser un problema de gran gravedad, la detección del TJ suele ser tardía y compleja, dado que las personas afectadas suelen mentir con el objetivo de ocultar su grado de implicación en actividades de juego [12]. Por ello, realizar un diagnóstico certero del TJ es esencial para detectar de forma precisa su prevalencia en la población general, y así llevar a cabo una práctica clínica efectiva, especialmente en términos de evaluación clínica y respuesta al tratamiento [78].

Con este propósito, el DSM-III [79] fue la primera edición que consideró el TJ como un trastorno mental, entonces conceptualizado como juego patológico. Para cuando se preparó la siguiente versión, el DSM-IV [80], aún escaseaba la evidencia empírica sobre el TJ, lo cual explica que la lista de síntomas incluidos no fuera exhaustiva, aunque resultaba suficiente para la realización de un diagnóstico clínico [81]. Finalmente, la actual edición DSM-5 adopta notables cambios respecto a las versiones anteriores [78].

En primer lugar, el TJ ha dejado atrás su antigua nomenclatura de juego patológico y su ubicación dentro de los trastornos del control de los impulsos [82], pasando a clasificarse ahora como una adicción comportamental dentro de la sección de “Trastornos relacionados con sustancias y trastornos adictivos” [12]. Otro cambio significativo es la eliminación del criterio de comisión de actos ilegales. Pese a que hasta un 25% de las personas con TJ pueden llegar a cometer actos ilegales con la finalidad de continuar financiando su actividad de juego [83], este criterio no parece mejorar la precisión diagnóstica, aunque es un criterio con gran importancia clínica que suele indicar la severidad del cuadro [84]. Además, se ha establecido una duración mínima de 12 meses para poder realizar el diagnóstico, reduciendo el número mínimo de síntomas a cumplir de 5 a 4. Finalmente, se permite establecer distintos niveles de

severidad dependiendo del número de síntomas presentes [12]. Para una descripción detallada de los criterios diagnósticos, consúltese la **Tabla 2**.

Tabla 2. Criterios diagnósticos del JP adaptados del DSM-5 [77].

Sintomatología principal		
Juego patológico problemático persistente y recurrente, que provoca un deterioro o malestar clínicamente significativo y se manifiesta porque el individuo presenta cuatro (o más) de los siguientes criterios durante un período de 12 meses:		
❖ **Necesidad de apostar cantidades de dinero cada vez mayores para conseguir la excitación deseada.**		
❖ **Está nervioso o irritado cuando intenta reducir o abandonar el juego.**		
❖ **Ha hecho esfuerzos repetidos para controlar, reducir o abandonar el juego, siempre sin éxito.**		
❖ **A menudo tiene la mente ocupada en las apuestas (p.ej. reviviendo continuamente con la imaginación experiencias de apuestas pasadas, condicionando o planificando su próxima apuesta, pensando en formas de conseguir dinero para apostar).**		
❖ **A menudo apuesta cuando siente desasosiego (p.ej. desamparo, culpabilidad, ansiedad, depresión).**		
❖ **Después de perder dinero en las apuestas, suele volver otro día para intentar ganar ("recuperar las pérdidas).**		
❖ **Miente para ocultar su grado de implicación en el juego.**		
❖ **Ha puesto en peligro o ha perdido una relación importante, un empleo o una carrera académica o profesional a causa del juego.**		
❖ **Cuenta con los demás para que le den dinero para aliviar su situación financiera desesperada provocada por el juego.**		
Su comportamiento ante el juego no se explica mejor por un episodio maníaco.		
Subtipos		**Gravedad**
Episódico	En remisión inicial	Leve (4-5 criterios)
Persistente	En remisión continuada	Moderado (6-7 criterios) Grave (8-9 criterios)

1.3.2. EPIDEMIOLOGÍA

Los estudios epidemiológicos confirman una mayor prevalencia del TJ en varones [85], aunque esta diferencia por sexos parece estar estrechándose [86]. Si comparamos ambos sexos, podemos observar que los varones exhiben una edad de inicio más temprana [87–89], aunque la evolución del curso es más acelerada en el sexo femenino [90,91], lo que se conoce como efecto telescópico. Además, los varones muestran una mayor preferencia por los juegos estratégicos (p. ej., apuestas deportivas y juegos de cartas), mientras que las mujeres tienden a participar más en juegos no estratégicos (p. ej., máquinas tragaperras y bingo [92].

Asimismo, los estudios corroboran que la vulnerabilidad a desarrollar un TJ se incrementa durante la adolescencia y la edad adulta temprana [93,94]. Sin embargo, también se observa una alta prevalencia de TJ en personas de edad avanzada [95,96]. A diferencia de los pacientes jóvenes, que prefieren formas de juego como las apuestas deportivas, los adultos mayores desarrollan más problemas con las máquinas tragaperras [97,98].

En definitiva, se estima que la prevalencia del TJ oscila entre el 1% y el 6% en los países desarrollados [99]. Sin embargo, se espera que esta prevalencia aumente considerablemente en los próximos años, debido a la mayor accesibilidad de las actividades de juego, principalmente a través de internet, donde las plataformas de juego proliferan a un ritmo constante [100–102].

En lo relativo a la comorbilidad, los índices más elevados se observan con los trastornos relacionados con sustancias, cuya prevalencia en pacientes con TJ llega a rondar el 60% [103]. Otras psicopatologías frecuentes en el TJ son los trastornos del control de los impulsos, trastornos depresivos, trastornos de ansiedad y trastornos de personalidad [104–106]. En algunos individuos, principalmente mujeres, los trastornos depresivos y de ansiedad suelen preceder al TJ, el cual se manifiesta como una estrategia disfuncional de afrontamiento [87,107,108]. Por el contrario, es más frecuente que en los varones el TJ preceda a ciertas patologías, como los trastornos relacionados con sustancias [107,109].

1.3.3. FACTORES DE RIESGO Y MANTENIMIENTO

Desde una perspectiva biopsicosocial se han propuesto diferentes factores ambientales, biológicos e individuales que explican la heterogeneidad de perfiles en el TJ. En primer lugar,

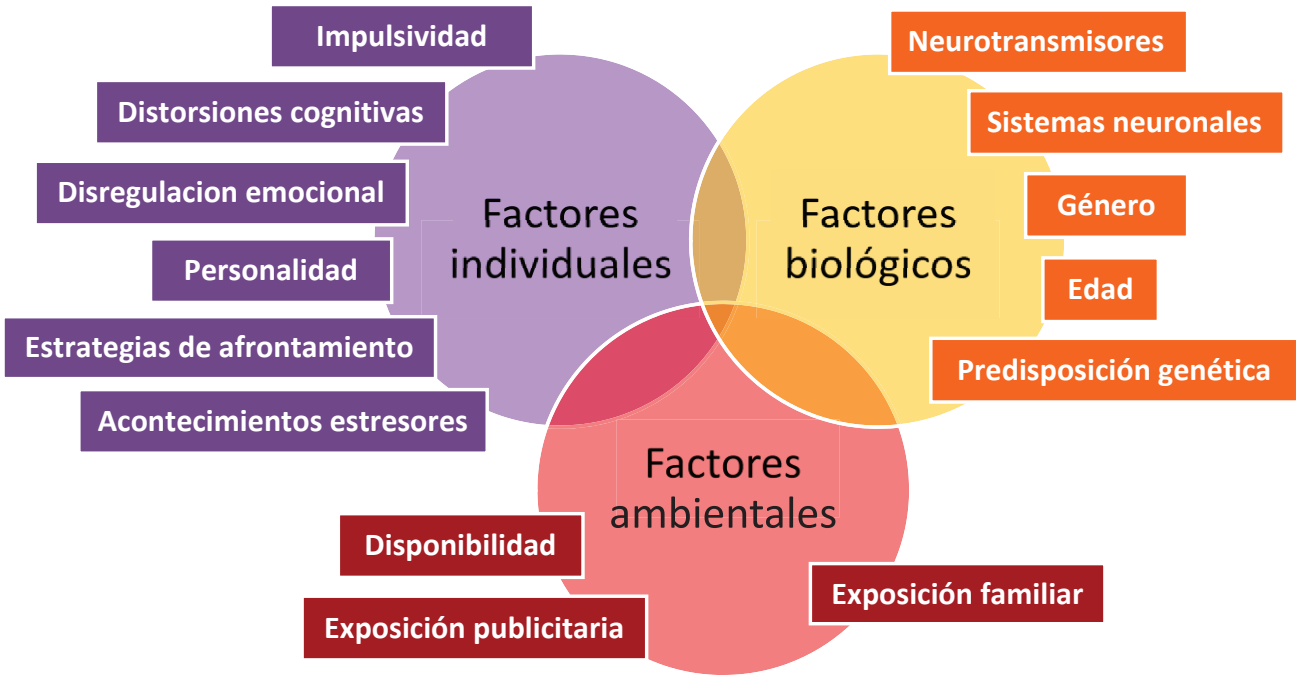
la creciente disponibilidad de oportunidades de juego se asocia a una mayor prevalencia del TJ en población general [110]. El nivel de exposición a la publicidad relacionada con las apuestas también podría estar influyendo, aunque su relación con el TJ aún no ha sido del todo establecida. Sin embargo, sí parece existir una relación entre la exposición a la publicidad en los más jóvenes y las personas que ya tienen un problema de juego [111,112]. También se ha demostrado el papel fundamental que desempeña en la iniciación de la conducta de juego, la exposición familiar temprana a esta conducta [113].

Con respecto a los factores biológicos, numerosos neurotransmisores parecen estar implicados en el TJ, destacando la noradrenalina, la dopamina, serotonina, los opioides, el cortisol y el glutamato [114,115]. Entre los sistemas neuronales implicados, múltiples estudios han observado una disminución de la activación de la corteza prefrontal ventromedial en individuos con TJ durante las fases anticipatorias de los procesos de recompensa [105,114]. Los factores genéticos también han comenzado a ser estudiados dada su relación con el desarrollo del TJ [30].

Dentro de los factores individuales predisponentes destacan el comportamiento impulsivo, las distorsiones cognitivas (p. ej., la ilusión de control), la disregulación emocional, las estrategias de afrontamiento disfuncionales, así como ciertos rasgos específicos de personalidad (p. ej., la búsqueda de novedad y la baja autodirección) [34,35,116–119]. Los acontecimientos estresores también suelen actuar como factores desencadenantes del TJ [120,121].

Finalmente, la impulsividad y compulsividad parecen desempeñar distintos roles en el desarrollo y mantenimiento del TJ. En las fases iniciales del curso del trastorno, la búsqueda de gratificación, refuerzo y excitación son los desencadenantes de la conducta de juego. Sin embargo, a medida que éste avanza, los pacientes emplean esta conducta para paliar sus estados de ánimo negativos o recuperar el dinero perdido previamente. De modo que, la impulsividad estaría más presente durante las primeras etapas del trastorno, considerándose más bien un factor de riesgo, mientras que la compulsividad aparecería en fases más avanzadas, actuando como factor de mantenimiento [116,117] (ver **Figura 3**).

Figura 3. Factores de riesgo y mantenimiento en JP.



1.4. REGULACIÓN EMOCIONAL

1.4.1. MECANISMOS DE REGULACIÓN EMOCIONAL

Durante los últimos años, el estudio de las emociones ha ido suscitando cada vez más interés, dado que preocupa saber cómo su inadecuado manejo puede favorecer el desarrollo de diferentes psicopatologías. Desde una perspectiva psicológica, las emociones pueden ser definidas como la combinación de dos factores; primero, los cambios fisiológicos producidos en el individuo como respuesta a los estímulos internos o externos; segundo, la interpretación que se realiza de estos estímulos atribuyéndoles un significado, lo cual daría lugar a estados afectivos negativos o positivos [122].

Normalmente, las emociones vienen acompañadas de cambios en la expresión facial, los cuales son universales y distintivos de cada emoción, al menos en las emociones básicas [123]. Además, las emociones no sólo tienen una función social informando acerca de las intenciones

o necesidades del individuo [124], sino que también le ayudan a adaptar su comportamiento al ambiente, dando lugar a conductas motivadas específicas [125]. Sin embargo, cuando perdemos el control sobre las emociones que experimentamos, pueden surgir respuestas inadecuadas que dificultan la consecución de nuestras metas. Con el objetivo de prevenir que nuestras emociones se conviertan en el determinante de nuestras conductas, recurrimos a diferentes procesos de regulación emocional.

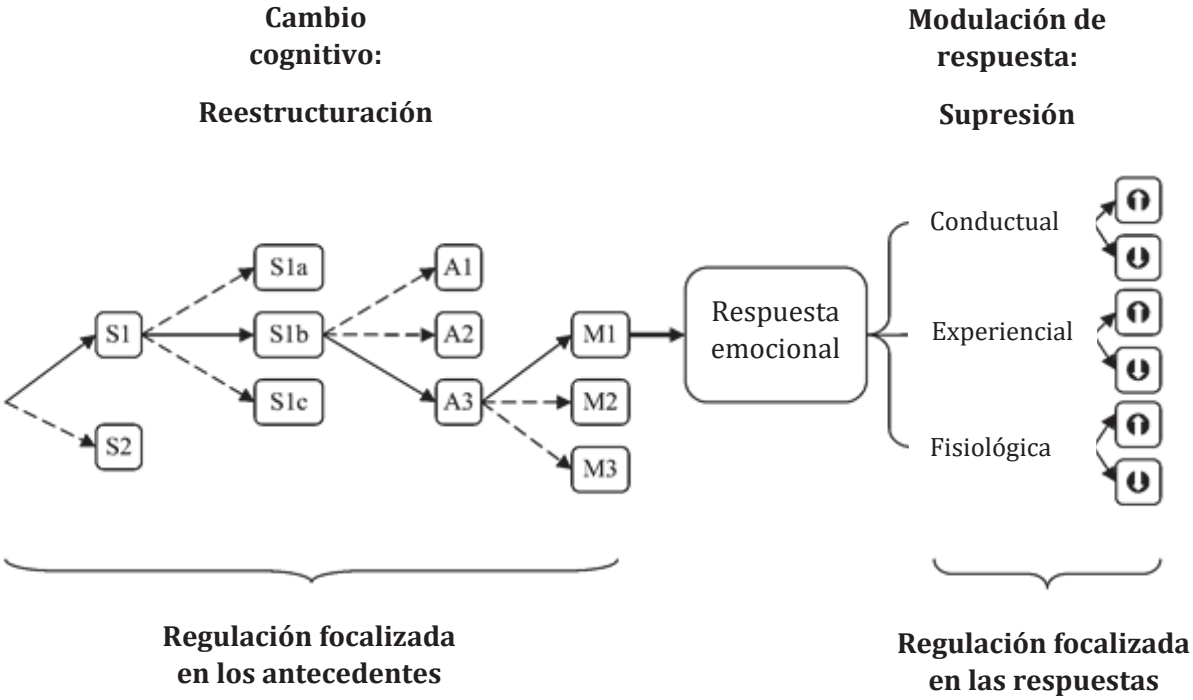
La regulación emocional es un concepto psicológico básico que hace referencia al conjunto de procesos automáticos y/o controlados a través de los cuales los individuos son capaces de modular la intensidad, duración, valencia y expresión de sus emociones [126]. Como prerrequisito para una adecuada regulación emocional, la persona ha de ser consciente de sus propias emociones, siendo capaz de identificar y diferenciar unas de otras. La finalidad de la regulación emocional es dirigir la conducta hacia la consecución de nuestros objetivos bajo estados emocionales intensos, se pretende adaptar nuestro comportamiento a las demandas específicas de la situación y controlar aquellas emociones e impulsos que transgreden nuestras metas [127].

Dentro de los mecanismos de regulación emocional podemos destacar dos tipos de estrategias, aquellas focalizadas en modificar los antecedentes o desencadenantes de la emoción (p. ej., la reevaluación cognitiva), y las estrategias centradas en la modificación de la respuesta emocional (p. ej., la supresión expresiva) [126,128]. Mientras que la reevaluación consiste en modificar el significado del estímulo desencadenante de la emoción, con el objetivo de interpretarlo de una forma más adaptativa; la supresión implicaría la inhibición o el enmascaramiento de las emociones experimentadas, evitando su expresión externa [128] (ver **Figura 4**).

La evidencia muestra que usar estrategias específicas de regulación emocional ayuda a lidiar con los estados emocionales intensos, y esto puede observarse en población con y sin trastornos mentales [129–134]. Sin embargo, no todas las estrategias de regulación parecen actuar como factores protectores ante la psicopatología, algunas de ellas son consideradas desadaptativas, dado que su uso se relaciona con la presencia de ciertos trastornos mentales [135].

Generalmente, la revaluación cognitiva resulta más efectiva que la supresión, dado que interviene de una forma más precoz en proceso de generación de emociones [136,137]. Además, se ha observado que la supresión de emociones negativas puede conducir a una mayor activación fisiológica, consiguiendo un efecto contrario al inicialmente deseado [138]. Aun así, cada estrategia tiene diferentes ventajas e inconvenientes dependiendo de la emoción y de la situación. Por lo que la flexibilidad a la hora de elegir una estrategia u otra dependiendo del contexto parece la forma más adecuada para regular las emociones [139–141].

Figura 4. Modelo de regulación emocional desarrollado por Gross.



Adaptado de Gross [126].

De hecho, diversos estudios han demostrado la eficacia de la regulación emocional mediante el empleo de técnicas psicofisiológicas, como el electroencefalograma (EEG) [142]. Esta técnica posibilita el estudio de los potenciales evocados, es decir, los cambios que se producen en la actividad cerebral ante estímulos sensoriales o cognitivos [143]. Entre los potenciales evocados más estudiados en el ámbito de la regulación emocional, encontramos los componentes P300 y el potencial positivo tardío (LPP, *Late Positive Potential*), ambos descritos como medidas de atención motivada y saliencia emocional [142,144,145]. Se ha

comprobado que la amplitud de estos componentes en respuesta a emociones positivas o negativas puede ser modulada por distintas estrategias de regulación emocional [146–150].

Por último, entre las principales estructuras neurales implicadas en el procesamiento de las emociones se encuentran la corteza prefrontal y ciertas regiones subcorticales, como la amígdala y la ínsula [151–153]. Además, tanto la corteza prefrontal como otras regiones más recientes a nivel evolutivo (i. e., corteza parietal y corteza cingulada anterior) estarían involucradas en la regulación emocional y en el uso explícito de las estrategias de regulación [154,155]. Cabe señalar que el foco de interés se halla principalmente en el estudio de las bases neuronales implicadas en la reevaluación cognitiva, dado que esta estrategia ha demostrado ser más adaptativa que el resto [156]. Tres sistemas neuronales parecen contribuir en la generación y ejecución de esta estrategia: la corteza prefrontal dorsolateral y posterior, la corteza cingulada anterior dorsal y la corteza prefrontal ventrolateral [157–160]. Asimismo, las regiones neuronales más comúnmente moduladas mediante la reevaluación cognitiva son la amígdala, el cuerpo estriado ventral, la ínsula y la corteza prefrontal ventromedial [161].

1.4.2. REGULACIÓN EMOCIONAL Y "FOOD CRAVING"

Diversos autores han propuesto que la combinación de emociones negativas y altos niveles de impulsividad daría lugar a un aumento del denominado comer emocional [162–164], entendido como una mayor ingesta de comida en respuesta a emociones intensas. Sin embargo, la evidencia también sugiere que más que las emociones en sí, sería nuestra forma de regularlas la que influiría. Por ejemplo, el uso de la rumiación y la supresión como estrategias regulatorias evocarían un mayor deseo de realizar atracones y un incremento del comer emocional en comparación con otras estrategias como la distracción y la reevaluación cognitiva [165–168].

Dado el indiscutible vínculo existente entre las emociones y la ingesta de comida, se han desarrollado diversos modelos explicativos [163,169,170]. Uno de ellos, originalmente conceptualizado para explicar la adicción a las drogas, postula que los estados emocionales negativos conducen a un sesgo en el procesamiento de la información, lo cual incrementa la saliencia de estímulos apetitivos como las drogas o ciertos alimentos [171]. Al aumentar la saliencia, la atención se dirige a estos estímulos de forma selectiva, conllevando un aumento en el deseo de consumirlos [172].

El deseo intenso por consumir ciertos alimentos, denominado *food craving* o ansia por la comida, es considerado un estado emocional que implica cambios a nivel conductual y fisiológico [173]. Frecuentemente conduce a la pérdida de control y a la ingesta del alimento deseado, aunque esto no siempre sucede [174]. El *food craving* puede observarse tanto en individuos sanos como en pacientes con TCA [175–177]. Incluso algunos estudios sugieren su presencia en pacientes con AN, especialmente en aquellos individuos con sintomatología bulímico-purgativa [178,179].

Como cualquier otro estado emocional, el *food craving* puede ser modulado mediante el uso de la regulación emocional [180–182]. De hecho, varios estudios de EEG han demostrado la eficacia de distintas estrategias de regulación. Por ejemplo, mediante la reevaluación cognitiva puede modificarse el significado emocional de la comida, incrementando o reduciendo su valor apetitivo [183]. Se ha comprobado que cuando individuos sanos visualizan imágenes de comida, las amplitudes de los componentes P300 y LPP aumentan si, a través de la reevaluación, los sujetos intentan incrementar el valor apetitivo del alimento visualizado [184]. Además, en personas sin TCA pero con conductas alimentarias restrictivas, se observó que tanto la reevaluación como la supresión tenían la capacidad de reducir las amplitudes de los potenciales evocados ante imágenes de comida [185]. Sin embargo, aún se desconoce la capacidad de estas estrategias para regular el *food craving* en pacientes con TCA.

1.4.3. REGULACIÓN EMOCIONAL EN LOS TRASTORNOS DE LA CONDUCTA ALIMENTARIA Y EL TRASTORNO DE JUEGO

Se ha observado una asociación significativa entre la aparición y mantenimiento de ciertos trastornos mentales y las dificultades a la hora de regular las emociones [135]. Por ello, la disregulación emocional es considerada un factor de riesgo transdiagnóstico implicado en el desarrollo de diversos trastornos [131,186].

En el caso de los TCA, los problemas de regulación emocional parecen subyacer a la sintomatología alimentaria central de estos trastornos [33,187]. De hecho, los pacientes con TCA normalmente hacen uso de conductas alimentarias inadecuadas para aminorar sus estados emocionales negativos [188–192]. En pacientes con AN, la restricción alimentaria y el ejercicio físico excesivo son empleados como medio para evadirse de los problemas

emocionales y recuperar la sensación de control sobre sus vidas [193]. De forma similar, los pacientes con BN y TA hacen uso de la ingesta de comida excesiva para regular sus estados emocionales [188]. Sin embargo, esto no parece contribuir a la reducción de sus emociones negativas, al contrario, éstas aumentan tras los episodios de atracón [194–196].

Asimismo, en todos los subtipos de TCA es frecuente el uso de estrategias de regulación desadaptativas (p. ej., la supresión). Por lo que, aunque experimentan más emociones negativas, tienen mayores problemas a la hora de reconocerlas y expresarlas [186,192,197]. En conjunto, todo apunta a que la disregulación emocional parece actuar como factor de mantenimiento en los TCA, dado que aquellos pacientes con mayores dificultades para regular sus emociones presentan una sintomatología alimentaria más severa con el paso del tiempo [198].

Las dificultades en regulación emocional también predisponen el inicio y mantenimiento de los problemas asociados al TJ [199–201]. Sabemos que los pacientes con TJ muestran dificultades para identificar sus propias emociones, lo cual les conduce a escoger estrategias inadecuadas para manejarlas, empleando la conducta de juego para reducir los estados emocionales negativos [202]. Además, se ha observado una estrecha relación entre la disregulación emocional y los sesgos cognitivos propios del TJ, como las expectativas poco realistas de ganar en el juego o la creencia de que jugar es el único medio para sentirse mejor [201]. Sin embargo, estos mecanismos de regulación son claramente disfuncionales y sólo contribuyen al aumento del malestar y al deterioro del paciente a medida que avanza el curso del trastorno [203].

1.5. IMPULSIVIDAD

1.5.1. DEFINICIÓN Y CONCEPTUALIZACIÓN

El manejo de la impulsividad es esencial en muchos aspectos cognitivos y conductuales del ser humano, siendo necesario controlar la interferencia de ciertos estímulos, pensamientos o repertorios de respuesta [204]. En la vida cotidiana, es relativamente fácil identificar ejemplos de impulsividad [205], sin embargo, este concepto es empleado con mayor frecuencia dentro

de la esfera de los trastornos mentales [206]. En las últimas décadas, han ido surgiendo numerosas dudas relacionadas con la conceptualización de la impulsividad en diversos ámbitos de la psicología [204], pudiendo observarse numerosos intentos de resolver estas cuestiones y posibilitar una mejor definición, medición y categorización de este constructo, especialmente en el campo de la neurociencia [207].

Desde una perspectiva biopsicosocial, la impulsividad se definiría como una tendencia a responder con acciones rápidas y no planificadas ante estímulos internos y externos, sin considerar las consecuencias negativas que esas acciones podrían conllevar [208]. Es esencial tener en cuenta que en la impulsividad, las respuestas surgen de forma repentina y se realizan sin valorar intencionalmente los riesgos, al contrario que en la compulsividad, donde la planificación precede a la conducta [208].

En los últimos años, diversas investigaciones sugieren que la impulsividad es un constructo complejo y multidimensional compuesto por tres dominios principales (i. e., impulsividad rasgo, impulsividad de respuesta e impulsividad de elección), los cuales no parecen solaparse en gran medida [206,209]. Es de vital importancia diferenciar estos dominios, dado que parecen estar vinculados a diferentes circuitos, sistemas de neurotransmisores y mecanismos genéticos [210].

1.5.1.1. IMPULSIVIDAD RASGO

La impulsividad puede ser definida como un rasgo de personalidad, reflejando así una predisposición o tendencia hacia los comportamientos impulsivos [211]. El concepto de impulsividad ha sido incluido en numerosos modelos de personalidad [212], como por ejemplo, el modelo de “Temperamento y Carácter” de Cloninger [8]. En base a este modelo se ha desarrollado el “Inventario de Temperamento y Carácter-Revisado” (TCI-R, *Temperament and Character Inventory-Revised*) [213], una escala autoadministrada que proporciona cuatro dimensiones de temperamento y tres de carácter.

La conducta impulsiva se relacionaría con cuatro rasgos de temperamento heredables (TCI-R): alta búsqueda de novedad (alta tendencia a responder activamente a los nuevos estímulos), baja evitación del daño (baja tendencia a evitar estímulos aversivos), reducida persistencia (baja

capacidad de invertir esfuerzos en tareas con dificultad) y baja dependencia de recompensa (baja tendencia a persistir en conductas ante señales de recompensa). Sin embargo, sería la alta búsqueda de novedad la que se asocia más estrechamente con la impulsividad, dado que hace referencia al entusiasmo y disposición a explorar nuevos estímulos o señales de recompensa [214] (ver **Tabla 3**).

Tabla 3. Evaluación de las diferentes dimensiones de impulsividad y compulsividad.

	Dimensión	Proceso implicado	Medida
Impulsividad	Impulsividad rasgo	Búsqueda de la novedad	TCI-R
		Urgencia negativa/positiva Premeditación Perseverancia Búsqueda de sensaciones	UPPS-P
	Impulsividad de respuesta	Control inhibitorio	Tareas Go/No-go
			SCWT
	Impulsividad de elección	Toma de decisiones	IGT
		Delay discounting	EDT
Compulsividad	Flexibilidad cognitiva	*Set-shifting*	WCST
	Rasgos compulsivos	Evitación del daño	TCI-R

Nota. TCI-R: Inventario de Temperamento y Carácter-Revisado; UPPS-P: Escala de Comportamiento Impulsivo UPPS-P; SCWT: Test de Stroop; IGT: Juego de Azar de Iowa; EDT*: Experiential Discounting Task*; WCST: Test de Clasificación de Cartas de Wisconsin.

Otro de los modelos desarrollados con el fin de conceptualizar y evaluar la impulsividad rasgo, es el modelo "*Urgency, Premeditation, Perseverance, Sensation Seeking-Positive Urgency*" (UPPS-P). Éste propone cinco factores de impulsividad, los cuales recoge la "Escala de

Comportamiento Impulsivo UPPS-P" [212]: urgencia negativa (tendencia a actuar de forma precipitada ante emociones negativas extremas), falta de premeditación (tendencia a actuar sin pensar en las consecuencias), falta de perseverancia (incapacidad para permanecer focalizado en una tarea), búsqueda de sensaciones (tendencia a buscar experiencias novedosas y excitantes) y urgencia positiva (tendencia a actuar de forma precipitada ante emociones positivas extremas) (ver **Tabla 3**).

Se ha comprobado que elevadas puntuaciones en la escala UPPS-P correlacionan con un amplio rango de manifestaciones conductuales de impulsividad [215,216]. Asimismo, el modelo UPPS-P subraya la importancia de los aspectos emocionales de la impulsividad [217,218]. De hecho, la urgencia positiva y negativa parecen estar relacionadas con una inadecuada evaluación de las emociones que preceden a los procesos de toma de decisiones, mientras que la búsqueda de sensaciones ha sido vinculada con la anticipación de recompensas y la falta de previsión de los riesgos implicados en la conducta. Sin embargo, la falta de premeditación y de perseverancia se relacionan en menor medida con las emociones [219,220].

A nivel neurobiológico, se ha sugerido que el volumen de materia gris y blanca correlaciona con los niveles de impulsividad rasgo [221]. También se la ha relacionado con alteraciones durante el procesamiento de recompensas, donde los individuos con mayor impulsividad presentan una mayor sensibilidad hacia las recompensas inmediatas [222]. En este sentido, se ha sugerido una asociación positiva entre la impulsividad rasgo y la activación del cuerpo estriado ventral durante el procesamiento de las recompensas y los procesos de anticipación [223].

1.5.1.2. IMPULSIVIDAD DE RESPUESTA

La impulsividad de respuesta hace referencia a la dificultad para retrasar, detener, interrumpir o inhibir respuestas conductuales inapropiadas [224,225]. La impulsividad de respuesta es un reflejo del control inhibitorio de cada individuo [225]. Éste es un aspecto muy importante del funcionamiento humano, dado que permite a los individuos evaluar las consecuencias de sus acciones y responder de forma adaptativa [226]. La impulsividad de respuesta reflejaría una tendencia motora de desinhibición, dado que no se realiza una evaluación adecuada del contexto o ambiente, especialmente cuando se producen cambios en él [226–228].

Para medir esta dimensión pueden emplearse tareas de tipo *Go/No-go*, las cuales evalúan la capacidad para inhibir respuestas motoras dominantes [229] (ver **Tabla 3**). Estas tareas combinan dos tipos de ensayos o condiciones. Durante los ensayos "*go*", los sujetos han de proporcionar una respuesta motora rápida (p. ej., presionar una tecla cuando determinada letra aparece en la pantalla); mientras que durante los "*no-go*", han de inhibir esa misma respuesta (p. ej., no presionar la tecla cuando un número aparece en la pantalla) [228]. Esta tarea nos proporciona una medida clave de impulsividad de respuesta o control inhibitorio, los "errores de comisión", que reflejan el número de veces que el sujeto no es capaz de inhibir la respuesta durante los ensayos "*no-go*" [228]. Además, se obtienen otro tipo de medidas relacionadas con la impulsividad, como el tiempo de reacción durante los ensayos "*go*" (tiempo requerido para proporcionar la respuesta), donde altos niveles de impulsividad conducirán a respuestas más rápidas e inmediatas [230].

También se ha utilizado el "Test de Stroop" (SCWT, *Stroop Colour and Word Test*) [231], que evalúa la capacidad de resistirse a la interferencia de los estímulos presentes en el ambiente (ver **Tabla 3**). En esta prueba es necesario inhibir una respuesta automática que interfiere con la ejecución de otra tarea novedosa. Esta interferencia se produce cuando el individuo ha de indicar el color de la tinta con la que está escrita una palabra, el cual no coincide con su significado. Aquí se produce una interferencia semántica a consecuencia de nuestra automaticidad en la lectura, donde el significado de la palabra interfiere en la tarea de nombrar el color de la tinta con la que está escrita.

La corteza orbitofrontral, la corteza cingulada anterior y el cuerpo estriado son regiones cerebrales vinculadas a este tipo de impulsividad [221,232]. Ciertas regiones fronto-parietales están particularmente implicadas en la capacidad de inhibir con éxito la respuesta motora, en concreto, la corteza cingulada anterior y la ínsula de ambos hemisferios, así como la corteza orbitofrontal derecha, la corteza prefrontal dorsolateral derecha y ciertas áreas motoras suplementarias del hemisferio derecho [233].

1.5.1.3. IMPULSIVIDAD DE ELECCIÓN

La impulsividad de elección puede ser definida como la falta de planificación y de consideración por las consecuencias futuras, mostrando una mayor tendencia de aproximación

a los estímulos y un estilo impulsivo de toma de decisiones [232,234]. Con el fin de evaluar si la toma de decisiones resulta impulsiva y desventajosa, diversos estudios han utilizado el "Juego de Azar de Iowa" (IGT, *Iowa Gambling Task*), una tarea basada en la toma de decisiones arriesgadas, donde el sujeto ha de aprender a realizar elecciones ventajosas en base a los castigos o las recompensas que conllevan estas elecciones [235] (ver **Tabla 3**). Para ello, se utiliza un juego de cartas donde los participantes han de optar entre diferentes barajas que proporcionan recompensas y castigos monetarios. Cuanto mayor es la recompensa monetaria, mayor es la posibilidad de recibir un castigo monetario elevado, por lo que la elección de estas barajas es más arriesgada y desventajosa.

Por otro lado, la impulsividad de elección también haría referencia a la incapacidad de retrasar la gratificación, mostrando mayor preferencia por pequeñas pero inmediatas recompensas en detrimento de recompensas mayores pero demoradas en el tiempo, lo cual ha sido denominado como *delay discounting* [236,237]. Se ha hecho uso de una amplia variedad de tareas para evaluar el *delay discounting,* como la *Experiential Discounting Task* (EDT) [238] (ver **Tabla 3**). Estas tareas se basan en la premisa de que la gente prefiere recibir recompensas cuantiosas e inmediatas en vez de demoradas y de menor cuantía. Sin embargo, cuando estas dos dimensiones se contraponen, es decir, recibir menos ahora o más luego, las elecciones se vuelven más complejas [237]. Se sabe que a medida que incrementa la demora para conseguir una recompensa más cuantiosa, el valor de la recompensa se degrada sistemáticamente [239,240]. El objetivo último es encontrar el punto en el cual dos recompensas (menos cuantiosa pero inmediata vs. más cuantiosa pero demorada) alcanzan aproximadamente el mismo valor [237].

Dada la complejidad de la impulsividad de elección, aún queda por esclarecer cómo las regiones neurales y los sistemas neuroquímicos contribuyen a esta dimensión [241]. La impulsividad de elección puede ser entendida como la manifestación de un desequilibrio entre ciertos sistemas neurobiológicos vinculados con la motivación y el control [242]. Entre las regiones cerebrales implicadas encontramos las áreas límbicas y prefrontales, las cuales subyacen a la toma de decisiones y a los procesos de recompensa [243,244]. En concreto, la impulsividad de elección ha sido vinculada con los circuitos mesolímbicos dopaminérgicos de

la corteza prefrontal medial, la corteza orbitofrontal, el cuerpo estriado ventral, el núcleo accumbens y la corteza cingulada posterior [221,241].

1.5.2. IMPULSIVIDAD EN LOS TRASTORNOS DE LA CONDUCTA ALIMENTARIA

La impulsividad parece ser una característica muy frecuente en los individuos con TCA, sobre todo en aquellos que muestran conductas de sobreingesta. Ésta parece subyacer a los sentimientos de pérdida de control característicos de los episodios de atracón [38,245]. Una mayor impulsividad en pacientes con TCA se ha asociado con una mayor severidad del trastorno, así como con mayores niveles de psicopatología general y peor respuesta al tratamiento [246,247].

Al examinar las tendencias o rasgos impulsivos con el TCI-R, se demostró que, mientras los pacientes con AN muestran una baja búsqueda de la novedad y una alta persistencia, aquellos con BN se caracterizan por altos niveles de búsqueda de la novedad y baja persistencia, mostrando una mayor personalidad impulsiva [77]. Cuando se emplea la escala UPPS-P, puede observarse que la urgencia negativa y la búsqueda de sensaciones son las dimensiones más vinculadas a los TCA con sintomatología bulímica [248]. Además, los pacientes con conductas de atracón y/o purgas muestran una mayor falta de premeditación y de perseverancia al ser comparados con pacientes de tipo restrictivo o sujetos sin sintomatología alimentaria [249]. Estos resultados sugieren que diferentes tipos de TCA podrían ser diferenciados en función de la presencia o ausencia de rasgos impulsivos, y que las conductas restrictivas y de atracón podrían ser entendidas como polos opuestos de un espectro de comportamientos impulsivos [23].

Respecto a la impulsividad de respuesta, mediante el uso de tareas *Go/No-go* se han observado numerosas dificultades en el control inhibitorio de los pacientes con TCA, especialmente en el TA, donde los pacientes muestran un mayor número de errores de comisión, y tiempos de reacción más precipitados [250,251]. El SCWT también ha reflejado importantes problemas de inhibición de respuesta en los TCA, especialmente en los subtipos bulímico-purgativos [252,253]. En general, los déficits en el control inhibitorio parecen especialmente notables

cuando se examinan estímulos relacionados con el trastorno, como estímulos de comida [252,254,255], lo cual parece contribuir al mantenimiento del trastorno [256].

Por otro lado, se ha observado que los pacientes con BN y TA muestran una mayor preferencia por las recompensas monetarias y de comida inmediatas en las tareas de *delay discounting* [257–259]. Esta incapacidad de resistirse a la tentación de las recompensas inmediatas puede tener una influencia muy desfavorable en la adherencia a las directrices alimentarias que incluyen los programas de tratamiento para la BN y el TA [260]. Por el contrario, los pacientes con AN se caracterizan por presentar elevados niveles de autocontrol y por focalizarse en la gratificación demorada del cumplimiento de sus objetivos a largo plazo [190,261–263]. De hecho, esta capacidad de priorizar las recompensas demoradas es considerada uno de los factores de mantenimiento del trastorno [264]. La inanición parecer ser un reforzador positivo y producir un reconfortante e inmediato sentimiento de control, y el objetivo a largo plazo de perder peso puede convertirse en algo irracionalmente sobrevalorado en la AN [265,266].

Con relación a la impulsividad de elección, todos los subtipos de TCA presentan déficits en la toma de decisiones evaluada mediante el IGT, reflejando una deficiente habilidad para aprender las contingencias de refuerzo o castigo de sus elecciones [74,267–271]. Estos hallazgos apuntan a que los pacientes con TCA muestran dificultades a la hora de sopesar las ventajas y desventajas de sus elecciones, mostrando una mayor tendencia a optar por las alternativas más arriesgadas, pero con mayores beneficios, pese a que conlleven mayores consecuencias negativas. Un claro ejemplo, son las conductas de restricción o los atracones, tanto los pacientes con AN como aquellos con BN y TA llevan a cabo estas conductas alimentarias desadaptativas que, a pesar de proporcionarles un gran reforzamiento positivo (p. ej., sensación de control o reducción de la ansiedad), tienen efectos nocivos para su salud [272,273].

1.5.3. IMPULSIVIDAD EN EL TRASTORNO DE JUEGO

La impulsividad rasgo ha sido asociada con el TJ mediante el uso de la escala UPPS-P [274–276]. En concreto, altos niveles de urgencia positiva y negativa, así como una alta falta de perseverancia, son algunas de las características distintivas de los pacientes con TJ [277,278]. Además, la falta de premeditación ha sido relacionada con una inadecuada toma de decisiones,

una característica relevante en el TJ [279,280]. La severidad del trastorno también parece estar relacionada con la impulsividad rasgo, sobre todo con los niveles de urgencia [281,282], posiblemente dada su relación con los mecanismos afectivos y ejecutivos, dos componentes esenciales del TJ [274,283–285]. La escala TCI-R también ha mostrado una alta impulsividad rasgo en el TJ, concretamente se han observado altos niveles de búsqueda de sensaciones y baja persistencia [18,100].

El TJ también ha sido vinculado con elevados niveles de impulsividad de respuesta y déficits de control inhibitorio, tanto en tareas *Go/No-go* como en el SCWT [286,287]. Y pese a que la asociación entre la impulsividad de respuesta y la severidad del TJ aún no ha sido estudiada en profundidad [230], algunos estudios sugieren que hay una relación positiva entre ambos [211,288].

Por último, diversos estudios han informado de una asociación entre la impulsividad de elección y el TJ, tanto en adultos como en adolescentes [289–291]. La conducta de juego es en sí una actividad arriesgada que entraña abundantes elecciones donde las probabilidades de ganar son muy bajas [292]. Se ha observado que la forma de evaluar los riesgos es diferente en los pacientes con TJ, los cuales muestras varios sesgos o distorsiones cognitivas (p. ej., la ilusión de control, la falacia del jugador, supersticiones relacionadas con el juego, etc.) [293]. Por este motivo, los pacientes con TJ continúan jugando a pesar de largas secuencias de pérdidas, dado que tienen la creencia irracional de que sus pérdidas van seguidas de ganancias [294]. Estos sesgos cognitivos tienen importantes implicaciones en la de toma de decisiones, sobre todo, cuando ésta conlleva un alto riesgo, como en el IGT, donde los individuos con TJ presentan grandes dificultades a la hora de elegir las opciones ventajosas [104,114,280,295,296]. Por otro lado, en las tareas de *delay discounting*, los individuos con TJ muestran una mayor tendencia a las recompensas inmediatas [280,297–299].

1.6. COMPULSIVIDAD

1.6.1. DEFINICIÓN Y CONCEPTUALIZACIÓN

Pese a que el concepto de compulsividad está menos extendido que el de impulsividad [227], algunos campos como la psiquiatría y la psicología se han interesado en este constructo dada su estrecha relación con más de una docena de condiciones clínicas [300]. Resulta esencial para el ámbito clínico y el de investigación poder clarificar la forma de evaluar la compulsividad. Sin embargo, este constructo aún resulta ambiguo y existen diferencias en su conceptualización dependiendo del trastorno [301].

Actualmente, en un intento por heterogeneizar las definiciones, la compulsividad es definida como la realización de comportamientos repetitivos y estereotipados, ya sean conductas manifiestas o actos encubiertos de tipo mental, los cuales, pese a no tener una funcionalidad, se realizan conforme a ciertas normas rígidas o como medio para evitar posibles consecuencias negativas [232,302]. La compulsividad representa el resultado de una lucha interna asociada a la falta de control sobre el propio comportamiento. Esto genera con frecuencia sentimientos de vergüenza, culpa, falta de autoestima y ansiedad [301].

La compulsividad ha sido asociada con la falta de flexibilidad cognitiva [227,232], es decir, la habilidad para cambiar nuestro foco de atención de unos estímulos a otros o de una tarea a otra (*set-shifting*) [303]. La flexibilidad cognitiva también hace referencia a la capacidad de modificar un comportamiento tras recibir retroalimentación negativa (*reversal learning*) y de aprender de los resultados de nuestras acciones (*habit learning*) [303]. Por tanto, los déficits en esta dimensión dan lugar a acciones automáticas y repetitivas [227,232].

Entre las medidas conductuales propuestas para evaluar *set-shifting* y flexibilidad cognitiva, encontramos el "Test de Clasificación de Cartas de Wisconsin" (WCST, *Wisconsin Card Sorting Task*) [304], prueba que consiste en ir cambiando de estrategias cognitivas en función de los cambios que se producen en las contingencias ambientales (ver **Tabla 3**). Una de las medidas clave de esta prueba, son los "errores perseverativos", una puntuación del número de veces en las que el sujeto no cambia de criterio o estrategia pese a la retroalimentación negativa que recibe. Puntuaciones altas en este índice serían, por tanto, un reflejo de déficits significativos en la flexibilidad cognitiva.

Las herramientas psicométricas utilizadas para evaluar la compulsividad son todavía muy escasas, y aquellas disponibles normalmente se basan en la conceptualización del trastorno

obsesivo-compulsivo [300]. Dada la falta de instrumentos transdiagnósticos, algunos autores han empleado la subescala de evitación del daño del TCI-R como una medida autoreportada de rasgos compulsivos [303,305] (ver **Tabla 3**). Sin embargo, sigue siendo necesaria la optimización de herramientas autorreportadas que permitan la evaluación de este constructo.

Con relación a las bases y circuitos cerebrales comprometidos, las conductas compulsivas parecen desencadenarse en el núcleo caudado, mientras que la corteza orbitofrontal tendría un papel inhibitorio sobre las mismas [227]. En concreto, la corteza prefrontal dorsolateral, la orbitofrontal y el núcleo caudado se han vinculado con el *reversal learning*; mientras que el área motora suplementaria, la corteza premotora y el putamen, han sido asociados con los procesos de *habit learnig* [199].

1.6.2. COMPULSIVIDAD EN LOS TRASTORNOS DE LA CONDUCTA ALIMENTARIA

El modelo teórico en el que se conceptualiza el espectro impulsivo-compulsivo, describe a la AN como uno de los trastornos con más características compulsivas [22,305]. La AN se caracteriza por la presencia de pensamientos persistentes e intrusivos relacionados con la comida y la ganancia de peso, que pueden conllevar el desarrollo de conductas compulsivas ritualizadas con el objetivo de reducir o eliminar la ansiedad asociada a estos pensamientos [306], tales como el control extremo de la ingesta, la restricción alimentaria y el ejercicio excesivo [266,307–310]. Aquellos individuos a los que les resulta imposible mantener este control excesivo, pueden acabar desarrollando episodios de atracón y conductas purgativas compensatorias, elementos también relacionados con la compulsividad [311].

Diversos estudios han evaluado la compulsividad en los TCA mediante el WCST, mostrado grandes déficits de flexibilidad cognitiva y altos niveles de rigidez en todos los subtipos, no sólo en la AN [75,267,312–316]. Ciertos factores mantenedores de la AN, como la incapacidad para cambiar las reglas y rituales relacionados con la comida, son un reflejo de los altos niveles de rigidez cognitiva observados en este trastorno [317]. Por otro lado, en los pacientes con BN y TA, los problemas de flexibilidad cognitiva estarían más relacionados con un decremento en el manejo del afecto negativo, dando lugar a la pérdida de control sobre la comida [318].

Finalmente, tanto la AN como el resto de TCA son patologías caracterizadas por una alta presencia de evitación del daño [18,77,319], rasgo compulsivo evaluado mediante el TCI-R. Es probable que los altos niveles de evitación del daño observados en estos trastornos sean la causa subyacente al uso de conductas compulsivas disfuncionales (p. ej., atracones y conductas purgativas) con el fin de evitar el afecto negativo y de aliviar el malestar emocional [22].

1.6.3. COMPULSIVIDAD EN EL TRASTORNO DE JUEGO

La compulsividad juega un papel fundamental en la comprensión del TJ, dado que la conducta de juego está en gran parte motivada por la necesidad de evitar estímulos aversivos [320,321]. No obstante, la investigación de la compulsividad en este trastorno continúa siendo escasa, al contrario de lo que ocurre con la impulsividad. Esto podría deberse, entre otras cosas, a la naturaleza multifacética de este concepto y a la escasez de medidas de evaluación [320].

Los pocos estudios realizados en este campo sugieren que el TJ está vinculado a un amplio rango de déficits en las funciones neuropsicológicas relacionadas con la compulsividad [320], y en especial, con alteraciones en la flexibilidad cognitiva [322,323]. Estas alteraciones podrían explicar la dificultad para aprender de los errores y encontrar métodos alternativos de solución de problemas [324], así como el uso de estrategias desadaptativas para lidiar con el afecto negativo [325]. También es reflejo de estos déficits la presencia de pensamientos persistentes y repetitivos sobre el juego, similares a aquellos presentes en el trastorno obsesivo-compulsivo [325], así como la presencia de conductas ritualizadas (p. ej., necesidad de "números de la suerte" u objetos supersticiosos que favorecerán los resultados de su juego) [326]. Los déficits neuropsicológicos encontrados en el TJ también se asociarían a otras conductas compulsivas no relacionadas directamente con la conducta de juego, pero que podrían estar contribuyendo a su desarrollo y mantenimiento [320].

Finalmente, algunos estudios han identificado una asociación positiva entre los errores que comenten estos pacientes en las tareas de compulsividad y las medidas de severidad del trastorno (p. ej., número de criterios presentes del DSM-5, frecuencia del juego, urgencia por jugar, cantidad de dinero apostado, etc.) [327]. También se ha observado una correlación positiva entre estos errores que reflejan falta de flexibilidad cognitiva y las puntuaciones de algunos cuestionarios autoreportados que miden compulsividad [327].

2. HIPÓTESIS

Teniendo en cuenta el contexto teórico expuesto anteriormente, el propósito de esta tesis se fundamenta en contrastar las siguientes hipótesis:

1. Los pacientes con AN presentarán mayores déficits en la regulación emocional y del *food craving* que los individuos sin psicopatología, estas dificultades se observarán tanto a nivel clínico como psicofisiológico (**Estudio 1**).

2. Los pacientes con TCA mostrarán una mayor impulsividad rasgo que los controles, siendo superior en los pacientes con BN/TA que en aquellos con AN (**Estudio 2**).

3. Existirán diferencias a nivel conductual y psicofisiológico entre el control inhibitorio de pacientes con TCA y controles, siendo más reducido en la BN/TA y más elevado en la AN (**Estudio 2**).

4. El procesamiento de estímulos con contenido afectivo interferirá con los mecanismos de control inhibitorio, especialmente en los pacientes con BN/TA, donde el control inhibitorio se verá disminuido al procesar estímulos afectivos (**Estudio 2**).

5. Los pacientes con BN/TA y TJ presentarán anomalías en la impulsividad y compulsividad respecto al grupo control, así como diferencias entre ellos en algunos dominios (**Estudio 3**).

6. Se observarán diferencias de sexo en algunos dominios de impulsividad y compulsividad en pacientes con BN/TA y TJ (**Estudio 3**).

7. Los pacientes con TCA y síntomas de abuso de alcohol y/o drogas mostrarán mayores niveles de impulsividad y compulsividad que los pacientes con sólo TCA (**Estudio 4**).

8. La presencia de altos niveles de impulsividad y compulsividad será predictora de una peor respuesta al tratamiento en pacientes con TJ, tanto en una fase temprana como una vez finalizada la intervención (**Estudio 5).**

3. OBJETIVOS

El **objetivo global** de esta tesis es avanzar en el conocimiento de los mecanismos de regulación emocional y los factores de impulsividad y compulsividad implicados en dos notorios trastornos del espectro impulsivo-compulsivo, los TCA y el TJ.

En primer lugar, se investigan los mecanismos de regulación emocional empleados por los pacientes con TCA, explorando mediante técnicas psicofisiológicas los procesos neurales subyacentes. A continuación, se examinan distintos dominios de impulsividad en varios subtipos de TCA, analizando la interferencia que los procesos emocionales pueden ejercer sobre éstos. Posteriormente, se estudian las similitudes y diferencias en impulsividad y compulsividad entre los TCA y el TJ, examinando las posibles diferencias asociadas al sexo. Se analiza también la posible vinculación de las características impulsivas y compulsivas con el abuso de sustancias en pacientes con TCA. Finalmente, se analiza la influencia de distintos factores de impulsividad y compulsividad en la respuesta al tratamiento en el TJ.

Con el propósito de lograr nuevos descubrimientos en el campo de los trastornos del espectro impulsivo-compulsivo, se diseñaron y desarrollaron cinco estudios con los siguientes **objetivos específicos**:

1. Explorar las características clínicas y psicofisiológicas vinculadas a la regulación emocional y del *food craving* en pacientes con AN (**Estudio 1**).

2. Investigar las diferencias en impulsividad rasgo entre pacientes con AN, con BN/TA y controles sin psicopatología (**Estudio 2**).

3. Explorar las diferencias a nivel conductual y psicofisiológico en el control inhibitorio de pacientes con AN, con BN/TA y controles, analizando la posible modulación emocional del mismo (**Estudio 2**).

4. Explorar las similitudes y diferencias en impulsividad y compulsividad en pacientes con BN/TA y pacientes con TJ, examinando a su vez diferencias asociadas al sexo (**Estudio 3**).

5. Comparar las características de impulsividad y compulsividad de los pacientes con TCA que presentan síntomas de abuso de alcohol y/o drogas y aquellos pacientes con sólo TCA (**Estudio 4**).

6. Explorar el valor predictivo de la impulsividad y compulsividad en la respuesta al tratamiento (i. e., adherencia, recaídas y abandonos) durante una intervención ambulatoria en pacientes con TJ (**Estudio 5**).

4. MÉTODOS Y RESULTADOS

ESTUDIO 1

CLINICAL AND NEUROPHYSIOLOGICAL CORRELATES OF EMOTION AND FOOD CRAVING REGULATION IN PATIENTS WITH ANOREXIA NERVOSA

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Objetivos:

Explorar las características clínicas y psicofisiológicas vinculadas a la regulación emocional y del *food craving* en pacientes con AN.

RESUMEN

Las dificultades en regulación emocional y regulación del *food craving* han sido vinculadas con la sintomatología alimentaria de la AN, así como con el mantenimiento de este trastorno. Con el objetivo de investigar los correlatos clínicos y neurofisiológicos de estos procesos, 20 mujeres con AN y 20 mujeres sin psicopatología completaron dos tareas computerizadas durante un registro de EEG. En estas tareas, las participantes fueron instruidas para tratar de reducir las emociones negativas y el *food craving* durante el visionado de imágenes negativas o imágenes de comida. Las participantes también cumplimentaron una serie de medidas autoreportadas de disregulación emocional y *food craving*. Como medida psicofisiológica, se analizaron los potenciales evocados P300 y LPP durante las distintas tareas de regulación. Las pacientes con AN reportaron niveles más elevados de disregulación emocional y un mayor uso de estrategias desadaptativas que el grupo control. En ningún grupo se pudo observar una reducción en la amplitud del P300 o el LPP durante la tarea de regulación de emociones negativas. Estos resultados sugieren un posible fallo a nivel neurofisiológico en los mecanismos de regulación emocional, tanto en pacientes como en controles. El grupo con AN manifestó niveles más elevados de *food craving* que el grupo control en los cuestionarios autorreportados. No obstante, ambos grupos mostraron una correcta regulación del *food craving* a nivel neurofisiológico, evidenciada por una disminución en la amplitud del LPP durante esta tarea. Asimismo, las participantes con AN mostraron una amplitud del P300 más reducida que el grupo control independientemente de la tarea, sugiriendo una menor activación psicofisiológica en general, probablemente debida a las deficiencias nutricionales. Sería de gran beneficio que futuras investigaciones describan los mecanismos asociados con esta reducción general de la amplitud del P300 en individuos con AN.

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Clinical and Neurophysiological Correlates of Emotion and Food Craving Regulation in Patients with Anorexia Nervosa

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Abstract: Background: Difficulties in emotion regulation and craving regulation have been linked to eating symptomatology in patients with anorexia nervosa (AN), contributing to the maintenance of their eating disorder. Methods: To investigate clinical and electrophysiological correlates of these processes, 20 patients with AN and 20 healthy controls (HC) completed a computerized task during EEG recording, where they were instructed to down-regulate negative emotions or food craving. Participants also completed self-report measures of emotional regulation and food addiction. The P300 and Late Positive Potential (LPP) ERPs were analysed. Results: LPP amplitudes were significantly smaller during down-regulation of food craving among both groups. Independent of task condition, individuals with AN showed smaller P300 amplitudes compared to HC. Among HC, the self-reported use of re-appraisal strategies positively correlated with LPP amplitudes during emotional regulation task, while suppressive strategies negatively correlated with LPP amplitudes. The AN group, in comparison to the HC group, exhibited greater food addiction, greater use of maladaptive strategies, and emotional dysregulation. Conclusions: Despite the enhanced self-reported psychopathology among AN, both groups indicated neurophysiological evidence of food craving

regulation as evidenced by blunted LPP amplitudes in the relevant task condition. Further research is required to delineate the mechanisms associated with reduced overall P300 amplitudes among individuals with AN.

Keywords: food craving; food addiction; emotion regulation; eating disorders; anorexia nervosa; event related potentials; EEG; neurophysiology; psychopathology

1. Introduction

Anorexia nervosa (AN) is recognized as a severe mental disorder characterized by restrained eating, dysfunctional thoughts, preoccupation concerning food and body image disturbance [1,2]. In addition to maladaptive cognitions and behaviours, difficulties in emotion regulation and food craving regulation have been linked to disordered eating symptomatology (i.e., binging, purging, or restriction), which are considered to be contributing factors to the maintenance of eating disorders [3–5].

Emotion regulation is understood as the process by which individuals are able to modulate the way they experience and express their emotions [6]. Two strategies have been of special interest when studying emotion regulation: suppression and reappraisal. Suppression consists of inhibiting the behavioural expression of an emotional response to a stressor, while reappraisal implicates reinterpreting the meaning of an emotional event [7]. Although the former is considered to be a maladaptive response, the latter is considered to be an adaptive strategy used to reduce the impact of negative emotional states evoked during stressful situations. In this sense, reappraisal appears to be particularly effective because it implies less physiological and cognitive costs, as well as less negative impact on memory compared to suppression [8].

It is hardly surprising that dysfunctional emotion regulation is considered to be a key mechanism underpinning numerous psychopathologies [9–12], among which we can find the whole spectrum of eating disorders [13–15]. Several studies suggest that, due to emotion regulation being adopted as a means of regulating negative emotions, difficulties in this area could be involved in the development and maintenance of problematic eating disorder-related behaviours [16,17]. Accordingly, emotion dysregulation has been exhibited as a trait among patients with AN, and also as a key element of their therapy [18,19].

Interestingly, food craving (i.e., intense desire for specific food), which is considered a hallmark of food addiction, has been recently proposed as an affective state involving behavioural and physiological changes [20]. Food craving is not necessary followed by increasing eating [21] and can be regulated like other affective states as suggested in recent studies in the non-clinical population [22–24]. In the eating disorder population, food craving and the related food addiction have been frequently reported [25], with a few studies suggesting the presence of these features even in patients with AN, especially those with binging/purging symptoms [26,27]. However, to our best knowledge, there is a lack of studies investigating food craving regulation in eating disorders, including AN.

Event-related potentials (ERPs) are electrical changes in electroencephalographic (EEG) recordings that are time-locked to sensory or cognitive events. Given the excellent time resolution, the event-related potential (ERP) technique has been adopted to investigate the time course of emotion regulation and craving regulation [28]. During late processing, the P300 component has been relevant to attention research as it increases with stimulus salience. Following it, the late positive potential (LPP) is thought to reflect motivated attention [7,29].

Previous ERP studies in the non-clinical population showed that the amplitude of the P300 and LPP components can be modulated by different emotion regulation strategies [30–38]. Due to the clinical relevance of emotions in daily life, numerous EEG studies have focused on down-regulation of P300 and LPP amplitudes in response to negative and positive emotions [30–38]. Although most studies point to a reduction of LPP amplitudes when participants try to down-regulate their

negative emotions [30–33,39,40], other research studies have found no significant modulation of this component [35,38], or even a modulation in the opposite direction [41]. Focusing on the eating disorders field, several ERP studies have shown emotion regulation difficulties among individuals with comorbidities, such as anxiety disorders and alexithymia [42,43]. Nevertheless, no studies to date have examined ERP modulations by emotion regulation in specific eating disorder populations such as AN.

On the other hand, several ERP studies have strived to demonstrate the efficacy of different emotion regulation techniques in modulating food craving in healthy individuals. For instance, using reappraisal in order to change the emotional meaning of food increased LPP amplitude when participants tried to focus on the long-term consequences of eating high-caloric food [44]. Reappraisal was also employed in another study in which participants were instructed to increase or decrease the appetitive value of food. Results showed that P300 and LPP amplitudes to food cues were larger when participants tried to increase the appetitive value of food in comparison to the condition of decreasing or just watching the images [45]. Moreover, research instructing restrained eaters to either reappraise cravings, suppress cravings, or watch food during a food task found that engaging in cognitive reappraisal or suppression significantly reduced ERP amplitudes compared to the food watch condition [46]. Although research has demonstrated the efficacy of emotion regulation techniques in normal-weight healthy individuals, up to date there is a lack of ERP research assessing regulation of food craving in AN patients [47]. Elucidating neurophysiological mechanisms of food craving regulation could pave the way for new treatment approaches for anorexia nervosa, in which emotion regulation techniques might be employed to alter the motivational value of certain foods.

The primary aims of the study were to explore clinical and electrophysiological features of emotion regulation and food craving regulation among patients with AN. As for the clinical profile, we hypothesized that individuals with AN would present higher self-reported emotion dysregulation and food addiction compared to a group of healthy control (HC). Regarding electrophysiological data, we hypothesize that there will be a significant reduction in LPP amplitudes during conditions requiring participants to down-regulate negative emotions or food craving, as opposed to neutral conditions. Based on previous clinical research reporting emotion and food craving regulation difficulties in AN, we also aim to explore between-group differences in ERP during down-regulation of emotion or food craving. Finally, we explored to which extent self-reported emotion regulation strategies (adaptive or maladaptive) correlates with ERP (i.e., P300, LPP) during down-regulation of food craving or negative emotions. Maladaptive strategies are expected to be predominant in AN and possibly correlate with brain response during down-regulation of emotions/food craving.

2. Materials and Methods

2.1. Participants

The present study involved two different groups: a clinical group of patients with anorexia nervosa (AN) and a healthy control group (HC). The AN clinical group was comprised of 20 female treatment-seeking patients diagnosed with AN (60% AN restrictive subtype, 40% AN binge/purging subtype) according to DSM-5 criteria (Body Mass Index (BMI) < 18.5) [48]. Recruitment was conducted at the Eating Disorders Unit within the Department of Psychiatry at Bellvitge University Hospital, a public health hospital certified as a tertiary care centre with a highly specialised unit for the treatment of eating disorders in Barcelona (Spain). The HC group consisted of 21 female participants who had no history of an eating disorder. Participant groups were matched by age and education level. All participants were recruited between June 2016 and July 2018.

Data from one healthy control participant had to be excluded due to poor EEG data quality. The final sample size consisted of 40 participants, of whom 20 were patients with AN (mean age = 22.7 years, SD = 6.51, age range 18 to 43, mean BMI = 16.6 kg/m^2, SD = 1.1), and 20 were HC (mean age = 21.0 years, SD = 5.12, age range 18 to 39; mean BMI = 20.7 kg/m^2, SD = 1.78). Among AN group, 9 patients

(45%) reported psychotropic treatment (antidepressants: n = 4, 20%; anxiolytics: n = 1 5%; both: n = 4, 20%). Exclusion criterion for all participants were: (a) being male, (b) younger than 18 years, (c) current or life-time history of chronic illness or neurological condition (abnormal EEG activity), which could influence electrophysiology and/or the neuropsychological assessment, (c) lifetime diagnosis of a severe mental health condition (bipolar disorder, lifetime diagnosis of psychotic disorder), (d) current substance dependence or any other mental disorder that could interfere cortical activity or the assessment. Additionally, in the HC group, an exclusion criteria was a lifetime diagnosis of any eating disorder, assessed by means of the Mini International Neuropsychiatric Interview (MINI) [49], being overweight/obese (Body Mass Index (BMI) ≥ 25), or underweight (BMI < 18.5).

Written informed consent was obtained before participation in the study, which was approved by the Ethics Committee of University Hospital of Bellvitge in accordance with the Helsinki Declaration of 1975 as revised in 1983. Participants received no compensation for taking part in the study.

2.2. Procedure

Patients who sought treatment for AN as their primary health concern were assessed by an experienced clinical psychologist as part of the Eating Disorders Unit protocol, which is based on DSM-5 criteria and includes height and weight measurements. All patients consecutively diagnosed with AN were screened for the inclusion criteria of the study and gave informed consent for voluntarily accepting to be part of the study. HC participants were recruited within a university campus and, if they were interested in taking part in the study, an eligibility screening was conducted prior to the initial face-to-face assessment session.

The variables explored in the present study were assessed in two separate sessions of approximately 90 minutes each. Firstly, participants were evaluated with the MINI to exclude those patients with any severe psychiatric condition. Afterwards, they completed a battery of self-reported questionnaires (DERS, ERQ, SCL-90-R, YFAS-2). Next, participants performed the experimental tasks (food craving and emotion regulation) during EEG acquisition. Participants were instructed to have a 'normal' meal 90 minutes before the session and then to refrain from eating or drinking coffee. Additional information was collected on the day of the experimental session, in order to control for a set of variables (i.e., food consumed on the day of the session, menstrual cycle, and alcohol or drugs consumption in the last 24h). In a second session, participants completed a different set of experimental neurophysiological tests (data will be reported in separate manuscript).

2.3. Clinical Assessment

The *Mini-International Neuropsychiatric Interview* (MINI) [49] is a short structured diagnostic interview for the major psychiatric disorders in DSM-III-R [50], DSM-IV [51] and DSM-5 [16] and ICD-10 [52]. Validation and reliability studies have been done comparing the MINI to the Structured Clinical Interview (SCID-P) [53] based on DSM-III-R [50] and the Composite International Diagnostic Interview (CIDI) [54], which is a structured interview developed by the World Health Organization. These studies showed that the MINI has similar reliability and validity properties to both instruments. With an administration time of approximately 15 minutes, it was designed to meet the needs for a short, yet accurate, structured psychiatric interview for multicentre clinical trials and epidemiology studies and to be used as a first step in outcome tracking in non-research clinical settings. The standard MINI assesses the 17 most common disorders in mental health. The disorders were selected based on current prevalence rates of 0.5% or higher in the general population in epidemiology studies. In the interest of brevity, it uses branching tree logic.

Difficulties in Emotion Regulation Scale (DERS; Spanish validation) [15,55,56] is a 36-item self-report scale that assesses relevant difficulties in emotion regulation on six subscales: non-acceptance of emotional responses, difficulties engaging in goal directed behaviour, impulse control difficulties, lack of emotional awareness, limited access to emotion regulation strategies and lack of emotional clarity. The measure yields a total score as well as scores on the six subscales. Higher scores indicate

greater problems with emotion regulation. Cronbach's α for the total score in the present study was 0.91.

Emotion Regulation Questionnaire, Spanish version (ERQ) [57] is a 10-item questionnaire to assess the respondents' tendency to implement two emotion regulation strategies: reappraisal and emotional suppression. For the present study it shows a Cronbach's α of 0.76 for the suppression scale, and 0.85 for the reappraisal scale.

Symptom Checklist-90 Revised (SCL-90; Spanish validation) [58,59] is a 90-item questionnaire which evaluates psychopathological symptoms. It also includes a global severity index (GSI), designed to measure overall psychological distress. Internal consistency for GSI scale in the present study sample was 0.98.

The Yale Food Addiction Scale Version 2.0 (YFAS-2) [25] is a 25 item self-report questionnaire to measure addictive food behaviours. It consists of seven scales which refer to the criteria for substance dependence: (1) tolerance, (2) withdrawal, (3) substance taken in larger amount/period of time than intended, (4) persistent desire/unsuccessful efforts to cut down, (5) great deal of time spent to obtain substance, (6) important activities given up to obtain substance, (7) use continued despite psychological/physical problems. The Cronbach's α value for the present study was 0.97.

2.4. Electrophysiological Assessment

Participants completed an emotion regulation task and a food craving regulation task during continuous EEG recording.

Emotion regulation task: The task stimuli consisted of 180 images, of which 120 were negative images distributed in two blocks of 60 images each and 60 were neutral images grouped in a third block. Stimuli were presented for 3000 ms, with an inter-trial interval ranging from 3500 ms to 4500 ms. Negative images and neutral images were matched on contrast, brightness, resolution and complexity. Images were taken from the International Affective Picture System (IAPS) [60] and each image was presented only once during the task. Stimulus presentation was carried out by Presentation®software (Version 16.0) [61]. Participants were seated approximately 60 cm in front of a computer screen and the images were shown serially and occupied 35.1° of visual angle horizontally and 28.1° vertically.

For negative images, participants were instructed to either view each picture and allow themselves to feel any emotional response it might elicit (from now on referred to as Observe Negative) or to view each picture and try to reduce the emotional response that it might elicit (from now on referred to as Regulate Negative). For neutral images, participants were instructed to view each picture and allow themselves to feel any emotional response it might elicit (from now on referred to as Observe Neutral) while viewing the images and feeling the elicited emotion.

Food craving regulation task: Task stimuli consisted of 180 images, of which 120 were highly palatable food images distributed in two blocks of 60 images each and 60 were neutral images (i.e., office items) grouped in a third block. Stimuli were presented for 3000 ms, with an inter-trial interval ranging from 3500 ms to 4500 ms. Food images and neutral images were matched on contrast, brightness, resolution and complexity. Images were taken from Food Pics [62] and each image was presented only once during the task. Stimulus presentation was carried out by Presentation®software (Version 16.0) [61]. Participants were seated approximately 60 cm in front of a computer screen. The images were shown serially and occupied 18.9° of visual angle horizontally and 17.1° vertically.

For food images, participants were instructed to either view each picture and allow themselves to feel any emotional response it might elicit (from now on referred to as Observe Negative) or to view each picture and try to reduce the emotional response that it might elicit (from now on referred to as Regulate Negative). For neutral images, participants were instructed to view each picture and allow themselves to feel any emotional response it might elicit (from now on referred to as Observe Neutral).

2.5. Electrophysiological Recording and Analysis

The electroencephalogram (EEG) was recorded continuously throughout the experimental task using PyCorder (BrainVision). 60 active Ag/AgCI electrodes were inserted into an EEG recording cap (EASYCAP GmbH), distributed after the 10–20 system; additional three electrodes were adopted for recording vertical and horizontal electrooculogram (EOG) and Cz was used as online reference. Impedances were kept below 20 KOhm using the SuperVisc high-viscosity electrolyte gel for active electrodes. Signals from all channels were digitized with a sampling rate of 500 Hz and 24 bit/channel resolution and online filtered between 0.1 and 100 Hz.

Offline EEG analyses were performed with Brain Vision Analyzer (Version 2.2.0) [63] consisting of the following steps: high pass filtering 0.1 Hz, low pass filtering at 30 Hz (Butterworth zero phase filter; 24 dB/octave slope) and notch filter at 50 Hz; raw data inspection for manual detection of artefact and screening for bad channels, semi-automatic eye-blink correction using independent component analysis (ICA); artefact rejection of trials with an amplitude exciding ±80 μV; and baseline correction adopting the pre-stimulus interval between −200 and 2000 ms. EEG data were segmented into 2200 ms epochs from 200 ms before to 2000 ms after stimulus onset. Data were baseline corrected against the mean voltage during the −200 pre stimulus period. Artefact free epochs were separately averaged for each subject in each experimental condition for each paradigm.

ERP analyses were based on visual inspection of the grand average waveforms and the existing literature [45,46]. ERP components were analysed in a central-parietal cluster (CP1, CP5, P3, P7, CP2, CP6, P4, P8). P300 mean amplitude (μV) was computed in the time-window between 280 and 400 ms; LPP mean amplitude (μV) was measured within two time-windows: at 500-1000 ms (LPP1) and 1000-1500 ms (LPP2) [64–66].

2.6. Statistical Analysis

Statistical analysis was carried out with Stata Statistical Software: Release 15 for Windows [67]. The variables of the study (ERQ, YFAS, DERS and SCL-90-R) were compared between groups using t-tests for quantitative measures and chi square (χ^2) tests for categorical measures. Comparisons were considered significant with $p < 0.05$ after Bonferroni-Finner correction to avoid Type-I errors (Finner, 1993). The effect size for the mean differences/proportions was measured through Cohen's-*d* coefficient (low/small effect size was considered for $|d| > 0.2$, moderate for $|d| > 0.5$ and large/high for $|d| > 0.8$; Kelly and Preacher, 2012). In this study, different dimensional and categorical measures for the YFAS 2.0 were analysed: firstly, the YFAS 2.0 dimensional symptom count, which measures the 11 DSM-5 SRAD criteria (raw scores are in the range of 0–11); and secondly, the categorical classification based on the dimensional symptom count, a threshold for food addiction (presents for individuals with at least two symptoms plus self-reported clinically significant impairment or distress, and absent for participants who did not meet these criteria). The capacity of the dimensional YFAS 2.0 symptom count to discriminate between the groups was tested through two sample T-test, and the capacity of the YFAS 2.0 categorical classifications to discriminate between the diagnostic sub-types was tested through chi-square tests (χ^2).

The mean amplitudes (μV) of the emotion regulation and food craving regulation tasks were analysed for each ERP component (P300, LPP1, LPP2) with independent 3 × 2 mixed design analyses of variance (ANOVA), with condition as the within-subject variable (Regulate Negative/Food, Observe Negative/Food, Observe Neutral) and group as the between subject variable (HC versus AN). Pairwise comparisons were used to follow up main effects (for non-significant interaction condition-by-group) and single effects (for significant interaction condition-by-group).

Pearson's correlations were calculated for each group to estimate correlations between ERPs in the "regulation" condition of the emotion/food craving regulation tasks and ERQ subscales (ERQ-suppression; ERQ-reappraisal). Due to the strong association between this model and the sample size, practical relevance was based on the own coefficient measure (effect size was considered low/poor for $|R| > 0.10$, moderate for $|R| > 0.24$ and large/high for $|R| > 0.37$) [66].

3. Results

3.1. Comparison of Clinical Profiles

There were no significant between-group differences in age (p = 0.364, $|d|$ = 0.29). As expected, the HC group had significantly greater BMIs ($p < 0.001$, $|d| = 2.79$), lower mean scores on psychopathological self-report measures (i.e., the SCL-90-R GSI, DERS and YFAS), and higher mean scores on ERQ-Reappraisal. The prevalence of participants with food addiction positive screening score was also higher in the AN group (70% vs. 0%, $p < 0.001$, $|d| = 2.16$) (See Table 1). When comparing food addiction between AN sub-types, significant higher scores were displayed by the AN-BP subtype on the YFAS total score (p = 0.031, $|d|$ = 1.00) and in all the YFAS criteria with exception of "withdrawal symptoms" (See Table 2).

Table 1. Comparison of the clinical profile between groups.

	HC (n = 20)		**AN (n = 20)**		***T-stat***	***p***	***|d|***
	Mean	***(SD)***	***Mean***	***(SD)***			
Age (years-old)	21.00	(5.12)	22.70	(6.51)	0.92	0.364	0.29
BMI (current, kg/m^2)	20.72	(1.78)	16.63	(1.06)	8.82	**<0.001** *	**2.79** †
SCL-90-R: GSI score	0.65	(0.45)	1.59	(0.70)	5.10	**<0.001** *	**1.61** †
DERS: Total score	73.30	(16.12)	114.25	(23.36)	6.45	**<0.001** *	**2.04** †
ERQ: Reappraisal	33.50	(5.94)	24.25	(6.69)	4.62	**<0.001** *	**1.46** †
ERQ: Suppression	13.45	(5.71)	15.75	(4.64)	1.40	0.170	**0.51** †
YFAS2 total score	0.75	(1.12)	4.35	(3.73)	4.13	**<0.001** *	**1.31** †
	n	(%)	*n*	(%)	χ^2	*p*	*|d|*
FA positive screening (YFAS-2)	0	(0.0%)	14	(70.0%)	21.54	**<0.001** *	**2.16** †

Note. SD: standard deviation. HC: healthy control. AN: anorexia. FA: food addiction. * Bold: significant parameter (.05 level). † Bold: effect size into the mild/moderate ($|d| > 0.80$) to large/good range ($|d| > 0.80$).

Table 2. Comparison of the FA measures between AN sub-types.

	AN-R (n = 12)		**AN-BP (n = 8)**		χ^2	***p***	***|d|***
	n	**(%)**	***n***	**(%)**			
Substance taken in larger amount	4	33.3%	4	50.0%	0.56	0.456	0.34
Persistent desire	3	25.0%	4	50.0%	1.32	0.251	**0.53** †
Much time-activity to obtain, use, recover	5	41.7%	6	75.0%	2.15	0.142	**0.72** †
Social or occupational affectation	7	58.3%	7	87.5%	1.94	0.163	**0.69** †
Use continues despite consequences	4	33.3%	5	62.5%	1.65	0.199	**0.61** †
Tolerance	0	0.0%	5	62.5%	10.00	**0.002** *	**1.83** †
Withdrawal symptoms	5	41.7%	5	62.5%	0.83	0.361	0.43
Continued use despite social problems	1	8.3%	4	50.0%	4.44	**0.035** *	**1.03** †
Failure to fulfil major rule obligations	1	8.3%	4	50.0%	4.44	**0.035** *	**1.03** †
Use in physically hazardous situations	3	25.0%	4	50.0%	1.32	0.251	**0.53** †
Craving, or a strong desire or urge to use	2	16.7%	4	50.0%	2.54	0.111	**0.76** †
Clinically significant impairment-distress	8	66.7%	7	87.5%	1.11	0.292	**0.51** †
FA positive screening score	8	66.7%	6	75.0%	0.16	0.690	0.18
	Mean	*(SD)*	*Mean*	*(SD)*	*T-stat*	*P*	*|d|*
FA dimensional (YFAS2 total)	2.92	2.39	6.50	4.47	2.34	**0.031** *	**1.00** †

Note. AN-R: anorexia restrictive subtype. AN-BP: anorexia bulimic-purgative subtype. FA: food addiction. SD: standard deviation. * Bold: significant parameter (.05 level). † Bold: effect size into the mild/moderate ($|d| > 0.80$) to large/good range ($|d| > 0.80$).

3.2. ERP Results: Emotion Regulation Task

P300. The mixed design ANOVA yielded a significant main effect of condition (Regulate Negative, Observe Negative, Observe Neutral; F:27.7, df = 2/38, $p < 0.001$; $\eta^2 = 0.421$) and a significant main effect of group (HC versus AN; F = 10.9, df = 1/38, $p = 0.002$; $\eta^2 = 0.223$). No significant group x condition interaction was detected (F = 1.51, df = 2/37, $p = 0.229$; $\eta^2 = 0.038$). Post-hoc t-tests revealed that the main effect of condition was due to higher P300 mean amplitude in Observe Negative and in Regulate Negative conditions compared to the neutral one (Observe Negative vs. Observe Neutral $p < 0.001$; Regulate vs. Observe Neutral $p < 0.001$). With regards to the main effect of group, the AN group showed significantly smaller mean P300 amplitudes compared to HC group ($p = 0.002$).

LPP1. The mixed design ANOVA showed a significant main effect of condition (F = 51.7, df = 2/38, $p < 0.001$; $\eta^2 = 0.577$), but no significant main effect for group (F = 3.04, df = 1/38 $p = 0.089$; $\eta^2 = 0.074$) or group x condition interaction (F = 1.01, df = 2/37, $p = 0.369$; $\eta^2 = 0.026$). Post hoc t-tests for the main effect of condition showed higher LPP1 amplitudes in the Observe Negative and Regulate Negative conditions, compared to Neutral condition (Observe Negative vs. Observe Neutral $p < 0.001$; Regulate vs. Observe Neutral $p < 0.001$).

LPP2. The mixed design ANOVA showed a significant main effect of condition (F = 13.1, df = 2/38, $p < 0.001$; $\eta^2 = 0.256$), but no main significant effect of group (F = 0.22, df = 1/38, $p = 0.643$; $\eta^2 = 0.006$) or group x condition interaction (F = 0.05, df = 2/37, $p = 0.954$; $\eta^2 = 0.001$). Post-hoc t-tests revealed that the effect of condition was due to higher mean LPP2 amplitudes in both the Observe Negative and Regulate Negative conditions, compared to the neutral one (Observe Negative vs. Observe Neutral $p = 0.002$; Regulate Negative vs. Observe Neutral $p < 0.001$).

Means and standard deviations of the ERP amplitudes (μV) for each component (P300, LPP1, LPP2) are reported in Table 3 (see also Figure 1).

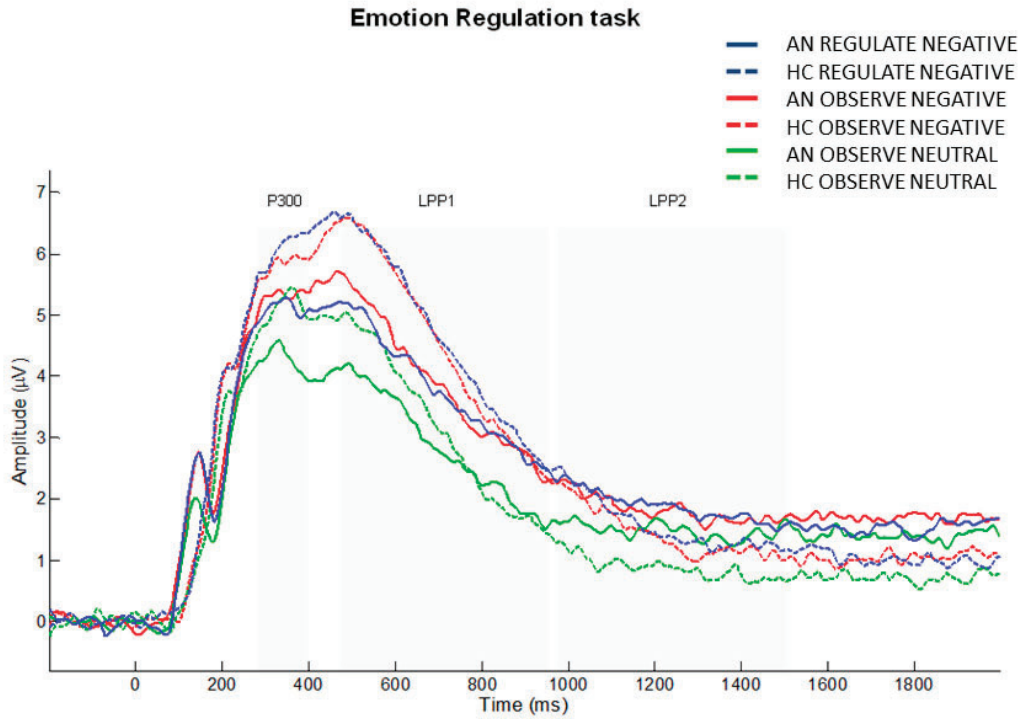

Figure 1. Grand average waveforms of the ER task, for each experimental condition (Regulate Negative, Observe Negative, Observe Neutral) and group (HC, AN), in the centro-parietal cluster of electrodes.

Table 3. Mean (SD) amplitudes (μV) of P300, LPP1 and LPP2 during the emotion regulation task.

	HC (n = 20)		AN (n = 20)	
	Mean	**(SD)**	**Mean**	**(SD)**
P300:				
observe negative	6.53	(2.72)	4.85	(1.97)
regulate negative	6.96	(2.93)	4.44	(1.84)
observe neutral	5.17	(1.86)	3.10	(1.44)
LPP1:				
observe negative	4.71	(2.59)	3.69	(1.63)
regulate negative	4.81	(2.27)	3.65	(1.49)
observe neutral	2.34	(1.53)	1.83	(1.20)
LPP2:				
observe negative	1.77	(2.16)	2.03	(1.48)
regulate negative	2.04	(2.04)	2.16	(1.11)
observe neutral	0.86	(1.47)	1.08	(1.10)

Note. HC: healthy control. AN: anorexia. SD: standard deviation.

3.3. ERP Results: Food Craving Regulation Task

P300. The mixed design ANOVA showed a significant main effect of condition (Regulate Food, Observe Food, Observe Neutral; F = 47.2, df = 2/38, $p < 0.001$; $\eta^2 = 0.560$) and a significant main effect of group (HC versus AN; F = 6.72, df = 1/38, $p = 0.014$; $\eta^2 = 0.154$), but no significant group x condition interaction (F = 1.40, df = 2/37, $p = 0.252$; $\eta^2 = 0.037$). Post-hoc t-tests for the main effect of condition showed higher amplitude in Observe Food and Regulate Food compared to the Observe Neutral condition (Observe Food vs. Observe Neutral $p < 0.001$; Regulate Food vs. Observe Neutral $p < 0.001$). Moreover, the AN group showed significantly smaller mean P300 amplitudes compared to the HC group ($p = 0.014$).

LPP1. The mixed design ANOVA showed a significant main effect of condition (F = 38.5, df = 2/38, $p < 0.001$; $\eta^2 = 0.504$), but no significant main effect of group (F = 0.73, df = 1/38, $p = 0.397$, $\eta^2 = 0.019$) or a significant group x condition interaction (F = 0.25, df = 2/37, $p = 0.778$; $\eta^2 = 0.007$). Post-hoc t-tests for condition revealed higher LPP1 in both Observe Food and Regulate Food compared to the Observe Neutral condition (Observe Food vs. Observe Neutral $p < 0.001$; Regulate Food vs. Observe Neutral $p < 0.001$), and higher LPP1 in Observe Food compared to Regulate Food ($p = 0.040$).

LPP2. The mixed design ANOVA showed a significant main effect of condition (F = 23.3, df = 2/38, $p < 0.001$; $\eta^2 = 0.380$), but no significant main effect of group (F = 0.13, df = 1/38, $p = 0.911$, $\eta^2 = 0.001$) or group x condition interaction (F = 0.10, df = 2/37, $p = 0.906$, $\eta^2 = 0.003$). Post-hoc t-tests for condition revealed higher LPP1 in both Observe and Regulate compared to the Observe Neutral condition (Observe Food vs. Observe Neutral $p < 0.001$; Regulate Food vs. Regulate Neutral $p < 0.001$), and higher LPP1 in Observe Food compared to Regulate Food ($p = 0.008$).

Mean and standard deviations of the ERP amplitudes (μV) for each component (P300, LPP1, LPP2) are reported in Table 4 (see also Figure 2).

Table 4. Mean (SD) amplitudes (μV) of P300, LPP1 and LPP2 during the food craving regulation task.

	HC (n = 20)		AN (n = 20)	
	Mean	**(SD)**	**Mean**	**(SD)**
P300:				
observe food	5.23	(2.39)	3.82	(1.47)
regulate food	5.60	(2.64)	3.67	(1.52)
observe neutral	3.68	(2.46)	2.32	(1.13)
LPP1:				
observe food	3.20	(1.91)	2.73	(1.38)
regulate food	2.86	(2.14)	2.38	(1.38)
observe neutral	1.49	(1.59)	1.25	(0.97)
LPP2:				
observe food	1.71	(1.45)	1.75	(1.19)
regulate food	1.26	(1.62)	1.21	(1.07)
observe neutral	0.42	(1.24)	0.54	(0.83)

Note. HC: healthy control. AN: anorexia. SD: standard deviation.

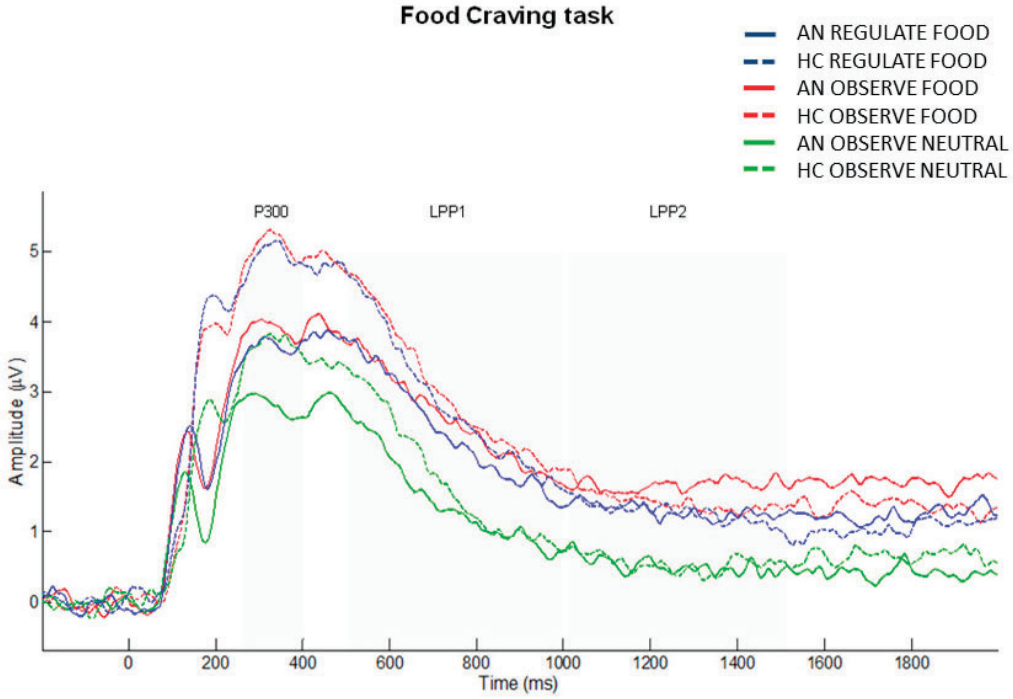

Figure 2. Grand average waveforms of the FRC task, for each experimental condition (Regulate Food, Observe Food, Observe Neutral) and group (HC, AN), in the centro-parietal cluster of electrodes.

3.4. Correlations between ERPs and Self-reported Emotional Regulation Strategies

Emotion Regulation Task and ERQ. In the HC group, reappraisal, as measured using the ERQ, was positively correlated with mean LPP1 amplitudes, while suppression was negatively correlated with mean LPP2 amplitudes. No significant correlations were found in the AN group.

Food Craving Regulation Task and ERQ. ERQ-reappraisal was positively correlated with mean LPP2 in the HC group, but not in the AN group. ERQ-suppression was negatively correlated with mean LPP1 and LPP2 amplitudes among patients with AN, but not in the HC group.

Table 5 shows the correlation matrix measuring the correlation between self-report measures of emotion regulation strategies (ERQ-suppression; ERQ-reappraisal) and ERPs amplitudes during emotion regulation (Regulate Negative) and food craving regulation (Regulate Food).

Table 5. Pearson's correlation between the amplitudes (μV) of the P300, LPP1, LPP2 during the "regulate" condition of the emotion regulation and the food craving regulation tasks.

	Emotion Regulation Task				Food Craving Regulation Task			
	HC (n = 20)		AN (n = 20)		HC (n = 20)		AN (n = 20)	
	ERQ reappr.	ERQ suppr.	ERQ reappr.	ERQ suppr.	ERQ reappr.	ERQ suppr.	ERQ reappr.	ERQ suppr.
P300	0.003	−0.195	0.119	−0.051	0.201	−0.187	0.101	0.018
LPP1	**0.247** †	−0.205	0.130	−0.103	0.144	−0.207	0.204	**−0.258** †
LPP2	0.196	**−0.281** †	0.173	−0.058	**0.396**†	−0.129	0.215	**−0.370** †

Note. HC: healthy control. AN: anorexia. † Bold: effect size into the mild/moderate (|R| > 0.24) to large/good range (|R| > 0.37). Sample size: Healthy control = 20; Anorexia = 20.

4. Discussion

In the present study, clinical and electrophysiological features of emotion regulation and food craving regulation among patients with AN were investigated by means of self-report and ERP measures.

Results from self-report measures of emotion regulation, confirmed greater difficulties in emotion regulation in patients with AN compared to the HC group (as suggested by DERS scores). This is in line with previous studies comparing AN with HC using the same questionnaire [5,68–70]. In addition, in the ERQ subscales, differences between groups were found, suggesting that patients with AN most frequently implemented maladaptive strategies (i.e., suppression) than adaptive strategies (i.e., reappraisal). This latter results corroborated previous findings suggesting dysfunctional emotion regulation strategies (e.g. suppression, avoidance) in populations with eating disorder [71–73], as is the case with other psychiatric disorders [74]. Moreover, problematic eating behaviours, such as binging, purging, and restriction, can be seen as maladaptive strategies to avoid or suppress negative emotions [68,75,76]. With regards to food addiction, a higher score was detected in the AN, as opposed to the HC group. Additional comparisons within the AN sub-types suggested higher scores in multiple dimensions of food addiction in AN-BP compared to AN-R. The present findings portray evidence of the relevance of food addiction to AN, specifically in patients with binging/purging symptoms. It is important to note that food addiction scores have been more typically described in patients with binge-subtype eating disorder [77–80], with some inconclusive or less evident results in AN. In a previous study exploring food addiction in eating disorders, patients with AN binge/purging subtype showed the highest prevalence of food addiction although half of the AN patients with restrictive type also positively scored for food addiction [27].

Results from electrophysiological measures collected in the emotional regulation task indicated enhanced mean P300 and LPP amplitudes in presence of pictures depicting negative emotions compared to neutral pictures in both AN and HC groups. This suggested enhanced processing of emotional stimuli, potentially due to their evolutionary salience, in accordance with previous ERP literature on 'healthy' populations [7,81–85]. Based on our results, we can suggest that, similarly to HC, patients with AN display a facilitated processing of stimuli with negative emotional valence. Although a previous ERP study reported altered processing of emotional stimuli in patients with AN [86], these controversial findings could be explained by the use of different types of stimuli and task (i.e., recognition of emotional faces).

Despite of the reported ERP indices of emotional processing, the instruction to down-regulate negative emotions did not elicit significant differences in mean P300 and LPP amplitudes when compared to passive viewing of negatively valenced emotional stimuli in any group. Since a reduction in LPP amplitude has been previously shown during emotion down-regulation in healthy population [30–33,39,40], the lack of this effect can be explained by a failure in emotion down-regulation that occurred in both AN patients and controls. This can be due to the fact that participants were not instructed to adopt a specific regulation strategy (e.g. reappraisal; suppression), which makes it

more difficult to successfully achieve emotion regulation. However, adopting visual analogue scales to measure self-reported down-regulation is necessary to avoid premature conclusions.

During the food craving regulation task, pictures of food elicited greater mean P300 and LPP amplitudes compared to neutral non-food pictures in both AN and HC groups. This can be interpreted as motivated attention, meaning a higher amount of attentional resources allocated to process food stimuli [87]. However, we did not find higher motivated attention toward food in patients with AN when compared to HC, suggesting similar allocation of attentional resources toward food-stimuli, at latest stages of attentional processing. This is in accordance with a previous study in which patients with AN did not display enhanced P300/LPP toward high-caloric food, but only for low-caloric food pictures when compared with HC [88]. Since we were interested in investigating regulation of food craving, which is generally experienced in response to "forbidden foods" (i.e., high caloric), low-caloric food was not included in our study.

Interestingly, smaller LPP amplitudes were detected during down-regulation of craving compared to passing viewing food pictures, possibly suggesting successful down-regulation of food craving in both groups. This result is in line with a previous study in non-clinical 'restrained' eaters, showing that P300 and LPP amplitudes were reduced during down-regulation of food craving compared to the passive viewing of food-related pictures [46]. As the first ERP study which explores food craving regulation in patients with AN, we could observe that, despite AN reported greater "food addiction" symptomatology, these subjects were able to regulate food craving, as depicted at a neurophysiological level. Nevertheless, differential ERP response during food craving regulation may be expected between AN-BP and AN-R. Thus, further research in larger sample sized including different AN sub-types is needed to deeply understand the neurophysiological mechanisms underpinning this craving modulation in AN.

Finally, differences in ERP between patients and controls were depicted by smaller P300 amplitudes in the AN group. This overall reduction in mean P300 amplitudes was consistent in both tasks and regardless of experimental condition. Reduced neurophysiological response in AN could reflect neurocognitive alterations, possibly as a secondary effect of malnutrition which consequently affect cognitive functioning [89]. Accordingly, cognitive difficulties have been suggested in patients with AN, especially in memory, attention and executive functions (i.e. decision-making, set-shifting [90–92]. Similarly to our findings, previous ERP studies adopting different tasks showed reduced P300 in AN compared to controls, regardless of the emotional relevance of the stimuli [93,94].

Exploratory correlations in each group were performed in order to explore how emotion regulation strategies modulate both emotion and food craving regulation at a neurophysiological level. As for the emotion regulation task, our findings suggest that, only among HC, the tendency to suppress emotions correlated with larger LPP amplitudes, while the tendency to reappraise emotions correlated with lower LPP amplitudes. This may suggest that the tendency to adopt different emotion regulation strategies (i.e. reappraisal or suppression) is related with different modulation of the LPP amplitude while regulating emotions, at least in healthy individuals. Since the modulation of LPP amplitude has been linked to reappraisal of negative emotions in HC [30–33,39,40], the present results may further suggest a link between neurophysiological markers of emotion regulation and the tendency to adopt reappraisal as cognitive strategy to down-regulate negative emotions in the non-clinical population. By contrast, LPP response did not significantly correlate with emotion regulation strategies among patients with AN.

Similarly to the emotion regulation task, the LPP amplitude during down-regulation of food craving was positively related to ERQ-reappraisal in HC. By contrast, LPP amplitudes negatively correlated with ERQ-suppression in patients with AN. These latter results could suggest that neurophysiological response during down-regulation of food craving is related to different emotion regulation strategies in patients as compared to controls, which is in line with the differences observed in ERQ scores among groups. Interestingly, significant correlations with suppression in AN were specifically present in the food craving regulation task, and this can be linked to the fact that patients tend to adopt dysfunctional

eating behaviours (e.g. bingeing/purging, restriction) as maladaptive strategies to regulate negative emotions, as showed by higher scores in ERQ-suppression.

It is important to consider some limitations when interpreting the results of the present study. Firstly, our sample size is rather low, which might have decreased the likelihood of detecting a significant difference if it existed [95]. Further studies with larger samples would be required to confirm our findings. Moreover, the small size of the sample did not allow us to distinguish and compare restrictive and purging AN sub-types. Given that different AN sub-types may exhibit different neurobiological correlates [96], future studies with larger samples should explore neural correlates of emotion regulation and food craving in different AN sub-types. In addition, our sample only consisted of female participants, which limits the generalizability of the results to a wider population. Additionally, we did not expose individuals to real food stimuli, which would have mimicked real-life situations and perhaps elicited stronger emotional and physiological reactions than food pictures [97]. Given the nature of the paradigms, another limitation of the study is the lack of eye-tracking and the lack of arousal tracing. Additional studies should further control eye-movements and attention focus during the image presentation. Furthermore, a proportion of patients with AN were under psychopharmacological medication (i.e., antidepressants, neuroleptic drugs, and benzodiazepines) and our sample did not allow us to control for medication. Finally, the present study design is cross-sectional in nature and claims regarding causality cannot be made. Future longitudinal studies are required to examine the extent to which the repetitive use of emotion regulation and food craving regulation techniques might modify the long-term neurophysiological responses in AN patients.

5. Conclusions

To conclude, previous ERP findings did not appear to mirror clarifying findings regarding eating disorders' aetiology and functioning. Therefore, to this date, they might not be used as accurate parameters or biomarkers that could be directly employed in the diagnosis or treatment of eating disorders [98]. To our knowledge, this is the first study which has examined the electrophysiological features of emotion and food craving regulation among patients with AN. Interestingly, ERP results suggest a successful down-regulation of food craving in AN, despite the fact that AN reported greater food addiction symptomatology. Nevertheless, further research including different AN sub-types is needed to deeply understand the neurophysiological mechanisms underpinning this craving modulation in AN.

Furthermore, although ERP did not depict differential response between AN and HC while down-regulating emotions or food craving, reduced P300 mean amplitudes were detected in AN when compared to HC. This result might reflect a general alteration in the neurophysiological responses of AN patients, which is possibly related to their prolonged state of malnutrition [99]. In this regard, this study provides an objective parameter of those impairments which long-lasting malnutrition might be occasioning in the neural systems of AN patients. Previous research has also found neurophysiological dysfunctions in AN, which do not always seem to be normalised after weight gain [98]. In that respect, it would be of great interest that future studies explore not only if neurophysiological alterations remain or, on the contrary, are ameliorated after patients' recovery, but also investigate the factors which might contribute to normalise neural responses in AN (e.g., weight gain, pharmacological treatments, specific psychological interventions, etc.).

On the other hand, clinical measures showed that patients with AN were characterized by food addiction symptoms and difficulties in emotion regulation with the tendency to use maladaptive techniques (i.e., suppression) to manage negative emotions. Moreover, this is the first study which relates the use of suppression strategies to smaller ERP amplitudes during food craving regulation in AN patients. This possibly reflects their tendency to adopt dysfunctional eating behaviours as maladaptive strategies to regulate negative emotions. Future interventions should focus on implementing more effective emotion regulation techniques such as reappraisal, which act through a reinterpretation of

emotional situation in order to reduce its emotional impact. Reappraisal has shown a better capacity to decrease negative emotional experience, consequently reducing distress [100].

Further research with larger samples and considering AN sub-types is needed to deeply understand the neurophysiological mechanisms underpinning emotion and food craving modulation in AN.

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ESTUDIO 2

EMOTIONAL AND NON-EMOTIONAL FACETS OF IMPULSIVITY IN EATING DISORDERS: FROM ANOREXIA NERVOSA TO BULIMIC SPECTRUM DISORDERS

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Objetivos:

Investigar las diferencias en impulsividad rasgo entre pacientes con AN, con BN/TA y controles sin psicopatología.

Explorar las diferencias a nivel conductual y psicofisiológico en el control inhibitorio de pacientes con AN, con BN/TA y controles, analizando la posible modulación emocional del mismo.

RESUMEN

La impulsividad y las dificultades de regulación emocional son consideradas dos características transdiagnósticas de los TCA. Este estudio pretendía investigar varios componentes de la impulsividad (i. e., rasgos impulsivos e impulsividad de respuesta), así como su posible modulación emocional en los TCA. Para ello, 20 mujeres con TCA (17 con AN y 16 con BN/TA) y 20 mujeres controles, tras completar la escala de impulsividad UPPS-P, realizaron una tarea de control inhibitorio con componente afectivo mientras se registraba su actividad neuronal con EEG. Se observaron mayores niveles de impulsividad rasgo en las pacientes con TCA que en el grupo control, siendo por lo general superiores en la BN/TA. Por otro lado, ni las medidas conductuales ni las psicofisiológicas mostraron diferencias en la impulsividad de respuesta entre los grupos con TCA y el grupo control, esto sucedía tanto en la tarea de control inhibitorio general y como en aquella con componente afectivo. En conclusión, nuestros resultados subrayaron que la urgencia negativa es una característica común en la AN y la BN/TA, mientras que la falta de perseverancia sólo se halla presente en las pacientes con BN/TA. Tampoco se observó a nivel psicofisiológico y conductual ninguna alteración del control inhibitorio en pacientes con TCA, ni una modulación del mismo ante la presencia de estímulos afectivos.

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RESEARCH ARTICLE

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Emotional and non-emotional facets of impulsivity in eating disorders: From anorexia nervosa to bulimic spectrum disorders

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Abstract

Objective: Impulsivity and difficulties in regulating emotions are considered to be transdiagnostic characteristics of patients with eating disorders (EDs). The study aimed to investigate trait impulsivity and inhibitory components of impulsivity, related or unrelated to emotions in patients with EDs.

Method: A total of 17 patients with anorexia nervosa (AN), 16 patients with bulimic-spectrum EDs (BSD) and 20 healthy control (HC) participants completed an impulsivity scale (UPPS-P) before performing an emotional inhibitory control task during electroencephalography (EEG) acquisition.

Results: Higher trait impulsivity in EDs than HC (with higher scores among BSD patients) was observed. However, no differences in behavioural measures or neural indexes [event-related potential (ERP)] of emotional and non-emotional inhibitory control were observed between patients and HC.

Conclusion: The present results highlighted negative urgency, an impulsive personality trait related to emotions, as a common feature of AN and BSD. Lack of perseverance, a trait which is less related to emotions, specifically characterises patients with BSD. On the other hand, behavioural and ERP data

Núria Mallorquí-Bagué and Giulia Testa contributed equally to this study.

did not show altered inhibitory control in EDs, for either general or emotional-related response inhibition.

KEYWORDS

eating disorders, event-related potentials, inhibitory control, negative urgency, trait impulsivity

1 | INTRODUCTION

Impulsivity and difficulties in regulating emotions are considered to be transdiagnostic characteristics of patients with eating disorders (EDs) (Mallorquí-Bagué et al., 2018; Wolz et al., 2015). At a clinical level impulsive behaviours are typically related to the bulimic-spectrum of EDs, encompassing bulimia nervosa (BN), binge eating disorder (BED) and anorexia nervosa binge-eating/purging subtype (AN-BP) (Atiye, Miettunen, & Raevuori-Helkamaa, 2015; Lavender et al., 2015; Waxman, 2009; Wolz et al., 2015); although impulsive behaviours have also been found in the restrictive subtype of anorexia nervosa (AN-R) (Favaro & Santonastaso, 2000). Similarly, patients with EDs show difficulties in recognising and regulating emotions (Harrison, Sullivan, Tchanturia, & Treasure, 2009). It has been suggested that patients with EDs engage in dysregulated eating behaviours (e.g., bingeing, purging and even restricting) in a maladaptive attempt to regulate negative emotions (Brockmeyer et al., 2014; Corstorphine, 2006; Harrison et al., 2009; Lavender et al., 2014). Moreover, an intense emotional state (both negative and positive) often precedes binge episodes in patients with BN or BED (Bongers, Jansen, Houben, & Roefs, 2013; Gianini, White, & Masheb, 2013; Leehr et al., 2015; Nicholls, Devonport, & Blake, 2016). These patterns of emotion dysregulation and some forms of impulsivity seem to be strongly interrelated in patients with EDs. Impulsivity, defined as the tendency to act quickly without enough consideration of the action consequences, is a multifaceted construct comprising personality traits, and behavioural and cognitive factors. Emotions seem to have a central role in the characterisation of certain domains of impulsivity, thus a distinction between emotional and non-emotional components of impulsivity has been suggested (Barratt, 1993; Perales, Verdejo-Garcia, Moya, Lozano, & Perez-Garcia, 2009).

With regards to impulsive personality traits, the UPPS model has emerged as a successful factorial account (Verdejo-García, Lozano, Moya, Alcázar, & Pérez-García, 2010) and has shown to be useful to identify impulsive behaviours associated with different psychopathologies, including the EDs spectrum (Claes, Vandereycken, & Vertommen, 2005). The UPPS-P (Whiteside & Lynam, 2001) includes five main dimensions: positive urgency (i.e., the tendency to act impulsively when undergoing positive affect), negative urgency (i.e., the propensity to act impulsively when experiencing negative affect), sensation seeking (i.e., the disposition to seek exciting experiences), lack of perseverance (i.e., the tendency to not persist in an activity that can be arduous or boring) and lack of premeditation (i.e., the tendency to act without considering the consequences of an action). Of these five dimensions, sensation seeking as well as negative and positive urgency are the ones mostly linked to emotional factors (Torres et al., 2013). Current studies conducted with EDs draw special attention to emotional impulsive traits and especially to negative urgency, which is strongly suggested as a key component of bingeing and purging behaviours whereas the association of bingeing with other impulsivity dimensions shows small effect sizes (Cyders & Smith, 2008; Fischer, Smith, & Anderson, 2003; Kenny, Singleton, & Carter, 2019). However, some studies report the link of non-emotional impulsive traits with these eating behaviours. For instance, patients with binge purging behaviours consistently showed less premeditation and perseverance than patients with AN together with more negative urgency and sensation seeking (Claes et al., 2005).

From a behavioural perspective, one of the main components of impulsivity is inhibitory control which refers to the ability to suppress, interrupt or delay an activated behaviour or cognitive course of action (Bartholdy, Dalton, O'Daly, Campbell, & Schmidt, 2016). The underlying mechanisms of inhibitory control and its related brain network seems mostly non-emotional (Rubia et al., 2001), yet the evidence indicates that the brain regions involved in the network changes as a function of the response to be inhibited. Thus, when emotional responses are implicated, brain networks related to emotional salience (e.g., limbic system, amygdala, insula) are involved (Banich et al., 2009; Compton et al., 2003; García-García et al., 2016). Response inhibition tasks (e.g., go/no-go; stop signal) have been most commonly used to investigate motor components of inhibitory control. Affective version of these tasks (e.g., emotional go/no-go) can be adopted to study emotional modulation of response inhibition (Drevets & Raichle, 1998; Schulz et al., 2007).

Time-locked electroencephalography (EEG) or event-related potential (ERP) helps capture neural activity related to both sensory and cognitive processes. Given its excellent temporal resolution, ERP technique is well suited to study neurophysiological correlates of inhibitory control and emotional modulation of this process. ERP components which have been consistently associated with inhibitory control mechanisms are: the no-go N2, which is a negative deflection occurring 200–350 ms following the no-go stimuli (Bruin, Wijers, & van Staveren, 2001; Kiefer, Marzinzik, Weisbrod, Scherg, & Spitzer, 1998; Pfefferbaum, Ford, Weller, & Kopell, 1985) linked to effortful attention, detection of response conflict, and action monitoring (Donkers & van Boxtel, 2004; Nieuwenhuis, Yeung, van den Wildenberg, & Ridderinkhof, 2003; Yeung, Botvinick, & Cohen, 2004); and the no-go P3, a positive deflection occurring at 300–600 ms following no-go stimuli, which has been primarily related to the inhibitory process itself (Bruin et al., 2001; Smith, Johnstone, & Barry, 2008). A few ERP studies investigated inhibitory control in presence of emotional stimuli in healthy population, with some showing emotional modulation of the no-go P3 component (Albert, López-Martín, & Carretié, 2010; Chiu, Holmes, & Pizzagalli, 2008). Interestingly, larger no-go P3 has been reported for emotional than neutral stimuli in individuals with higher trait impulsivity (Messerotti Benvenuti, Sarlo, Buodo, Mento, & Palomba, 2015), whereas larger no-go N2 in an emotional go/no-go task has been reported in individuals with higher emotional intelligence (Megías, Gutiérrez-Cobo, Gómez-Leal, Cabello, & Fernández-Berrocal, 2017).

In patients with EDs, altered inhibitory control appears to be implicated in the development and maintenance of the disorder. Specifically, poor inhibitory control contributes to the inability to control the urges to binge or to purge, whereas excessive inhibitory control is reported in AN (Brooks, Rask-Andersen, Benedict, & Schiöth, 2012). A meta-analysis of studies on response inhibition tasks in patients with EDs reported general deficits in bulimic-type eating disorders, although with small effect size (Wu, Hartmann, Skunde, Herzog, & Friederich, 2013). Overall, current literature presents divergent findings with some studies suggesting lower general response inhibition in patients with AN (Galimberti, Martoni, Cavallini, Erzegovesi, & Bellodi, 2012), BN (Wu, Giel, et al., 2013) and BED (Svaldi, Tuschen-Caffier, Trentowska, Caffier, & Naumann, 2014), while other studies do not report evidence for reduced response inhibition in EDs (see for a review: Bartholdy et al., 2016). Nonetheless, more consistent findings in patients with BN showed deficits when response inhibition is specifically measured for disorder-relevant stimuli (e.g., food; body-shape) (Wu, Hartmann, et al., 2013). This may suggest that difficulties in response inhibition among EDs may be particularly affected in relation to specific stimuli rather than general stimuli. Given the alteration in emotional processing and regulation suggested in EDs, it could be expected that the emotional context would differently modulate inhibitory control in patients with EDs compared to the general population. However, there is a lack of studies assessing emotion-related inhibitory control in patients with EDs.

In the present study, we aimed to investigate different components of emotional and non-emotional impulsivity in patients with AN and bulimic-spectrum EDs (BSD; i.e., including BN and BED) as compared to HC. More specifically, we explored: (a) trait impulsivity, assessed according to the UPPS-P model; (b) inhibitory control, assessed through an emotional go/no-go task and neurophysiological correlates of response inhibition. We hypothesised higher trait impulsivity in ED patients compared to HC, with higher impulsivity in BSD than AN. Based in previous literature, we specifically expected negative urgency to be the trait more highly linked to ED patients in general but even more in patients from the bulimic-spectrum. We also expected to observe a tendency to higher sensation seeking scores together with lower perseverance and premeditation scores in BSD patients. As for response inhibition, we expected to detect lower accuracy in no-go trials compared to go trials, which would be reflected at a neurophysiological level by larger N2 and P3 amplitudes in no-go trials. In particular, we expected to detect differences in behavioural and ERP indices of response inhibition in patients with EDs compared to controls, possibly expecting reduced ability to withhold inappropriate motor responses in BSD and higher control ability in AN compared to HC. Emotional images (positive and negative) are expected to interfere with inhibitory control mechanisms, at least in HC. This is the first study investigating emotional-inhibitory control in ED patients; however, based on emotional difficulties described in EDs, emotional stimuli may lead to reduced response inhibition in BSD, while lower interference of emotional stimuli on response inhibition may be expected in patients with AN.

2 | METHODS

2.1 | Participants

In the present study, the sample was comprised of two clinical groups and a HC group: (a) patients with AN (b) patients with BSD (including BN and BED) and (c) a HC group. The clinical groups were comprised of

20 female treatment seeking patients diagnosed with AN according to DSM-5 criteria (American Psychiatric Association, 2013) and 20 female treatment seeking patients diagnosed with any BSD (70% BED and 30% BN, according DSM-5) who attended to the ED Unit within the Department of Psychiatry at Bellvitge University Hospital—a public health hospital certified as a tertiary care centre with a highly specialised unit for the treatment of ED in Barcelona (Spain). The HC group consisted of 21 female participants who had no history of an ED. Participant groups were matched by education level. All participants were recruited between June 2016 and July 2018.

Data from eight participants (one HC, three AN and four BSD) had to be excluded due to poor EEG data quality. The final sample size consisted of 53 participants, of whom 17 were patients with AN (mean age = 22.7 years, *SD* = 6.51, age range 18—43, mean BMI = 16.63 kg/m^2, *SD* = 1.0), 16 were patients with a BSD (mean age = 40.18 years, *SD* = 9.93, age range 22–56, mean BMI = 37.81 kg/m^2, *SD* = 7.2) and 20 were HC (mean age = 20.81 years, *SD* = 4.84, age range 18–39; mean BMI = 20.8 kg/m^2, *SD* = 1.61). Exclusion criterion for all participants were: (a) being male, (b) younger than 18 years, (c) current or life-time history of chronic illness or neurological condition (abnormal EEG activity), which could influence electrophysiology and/or the neuropsychological assessment, (d) lifetime diagnosis of a severe mental health condition, (e) current substance dependence or any other mental disorder that could interfere with cortical activity or the assessment. Additionally, in the HC group, an exclusion criterion was a lifetime diagnosis of any ED, assessed by means of the Mini International Neuropsychiatric Interview (MINI, (Sheehan et al., 1998), or being obese [Body Mass Index (BMI) $\geq$ 30] or underweight (BMI < 18.5).

All participants gave written informed consent for being part of the study and the study protocol and procedures were approved by the Ethics Committee of University Hospital of Bellvitge in accordance with the Helsinki Declaration of 1975 as revised in 1983. Participants received no compensation for taking part in the study.

2.2 | Procedure

Patients who sought treatment for AN, BED or BN as their primary health concern were assessed by an experienced clinical psychologist as part of the ED unit protocol, which is based on DSM-5 (American Psychiatric Association, 2013) criteria and includes height and weight measurements. All patients consecutively diagnosed with AN, BED or BN were screened for the inclusion criteria of the study and gave informed consent for voluntarily accepting to be part of the study. HC participants were recruited following a snowball sampling method via researchers' social media, Internet posting and advertising in university campuses (i.e., Granada University campuses). If they were interested in taking part in the study, an eligibility screening was conducted prior to the initial face-to-face assessment session.

The variables explored in the present study were evaluated as part of a bigger assessment which took part in two separate sessions of approximately 90 min each. Firstly, participants were evaluated with the MINI (Sheehan et al., 1998) to exclude those patients with any severe psychiatric condition. Afterwards, they completed a battery of self-reported questionnaires (including UPPS-P). Next, participants performed the experimental tasks (emotion go/no-go task and two extra tasks which are reported in a separate manuscript, Mallorquí-Bagué et al., 2020) during EEG acquisition. Participants were instructed to have a 'normal' meal 90 min before the session and then to refrain from eating or drinking coffee. Additional information was collected on the day of the experimental session, in order to control for a set of variables (i.e., food consumed the day of the session, menstrual cycle, and alcohol or drugs consumption in the last 24 hr). In a second session, participants completed a different set of experimental neurophysiological tests (data will be reported in a separate manuscript).

2.3 | Measures

2.3.1 | Clinical and self-reported measures

The Mini-International Neuropsychiatric Interview (MINI; Sheehan et al., 1998) is a short structured diagnostic interview for the major psychiatric disorders in the DSM-IV (American Psychiatric Association, 1994) which has shown good reliability and validity properties. With an administration time of approximately 15 min, it was designed to meet the need for a short but accurate structured psychiatric interview for multicentre clinical trials and epidemiology studies and to be used as a first step in outcome tracking in non-research clinical settings. The standard MINI assesses the 17 most common disorders in mental health. The disorders investigated are the most important to identify in clinical and research settings. The disorders were selected based on current prevalence rates of 0.5% or higher in the general population in epidemiology studies.

The UPPS-P Impulsivity Scale (Whiteside, Lynam, Miller, & Reynolds, 2005) is a 59-item questionnaire to

assess five different features of impulsive behaviour: lack of premeditation, lack of perseverance, sensation seeking, negative urgency and positive urgency. The UPPS-P has satisfactory psychometric properties in terms of both convergent and discriminative validity and its Spanish adaptation also shows adequate psychometric properties (Verdejo-García et al., 2010). The α values for the different UPPS-P scales in our sample are: lack of premeditation (.842), lack of perseverance (.872), sensation seeking (.879), positive urgency (.924) and negative urgency (.884).

2.3.2 | Emotional go/no-go task

Participants completed an emotional go/no-go task which consisted of the visual presentation of affective pictures as go (i.e., blue framed affective pictures) and no-go stimuli (i.e., yellow framed affective pictures). The task was compiled and run using E-PrimeTM software (Psychology Software Tools, Inc., Pittsburgh, PA) and the images were selected from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 2005) on the basis of their standardised ratings of affective arousal and valence ratings. Images were divided into three emotional valence categories: 200 pleasant, 200 neutral and 200 unpleasant. The mean (*SD*) normative valence ratings and the mean (*SD*) normative arousal ratings respectively were 7.58 (0.31) and 4.79 (0.87) for pleasant images; 5.17 (0.27) and 3.25 (0.61) for neutral images; 2.08 (0.37) and 5.96 (0.73) for unpleasant images.

The task required participants to monitor 600 stimuli presented individually in the centre of a computer screen and respond as rapidly as possible (while trying not to make errors) by pressing a mouse button to target stimuli (go cues) and withholding responses to non-target stimuli (no-go cues). The emotional and non-emotional go/no-go task consisted of three blocks. Each block contained 200 images, of which 75% were go cues ('press the left side of the mouse as fast as you can when you see a blue frame') and 25% were no-go cues ('do not press the left side of the mouse when you see a yellow frame'), resulting in a total of 600 images (450 go cues and 150 no-go cues). Trial order of the presentation of the images in the task was counterbalanced within each block and blocks' order presentation was also randomised. Images were presented in the centre of the screen (w = 75%; h = 75%; the remaining 25% corresponds to y/b frame) for 200 ms each. The interstimulus interval (ISI) was pseudorandomized from 1,500 to 1,700 ms to discourage anticipatory responses; a fixation cross was displayed in the centre of the screen during the ISI. Instructions were presented on the computer screen before each block started and participants pressed a mouse button when ready to begin. In order to ensure that participants processed each picture's content; they were required to keep the eyes fixed on the centre of the screen. Before the beginning of the task, participants underwent a practise block of eight trials (75% go and 25% no-go), to ensure they understood task instructions.

Reaction times (RTs) in go trials and accuracy in go and no-go trials were calculated for each emotional category (i.e., positive, negative and neutral). The RTs data for the go trials were calculated after the deletion of incorrect responses and outliers for each individual (i.e., RTs below 150 ms or above 1,500 ms).

2.3.3 | Electrophysiological (EEG) recording and data reduction

The electroencephalogram (EEG) was recorded continuously throughout the experimental task using PyCorder (BrainVision). Sixty active Ag/AgCI electrodes were placed into an EEG recording cap (EASYCAP GmbH), distributed according to the 10–20 system; additional three electrodes were adopted for recording vertical and horizontal electrooculogram (EOG) and Cz was used as online reference. Impedances were kept below 20 k**Ω** using the SuperVisc high-viscosity electrolyte gel for active electrodes. Signals from all channels were digitised with a sampling rate of 500 Hz and 24 bit/channel resolution and online filtered between 0.1 and 100 Hz.

Offline EEG analyses were performed with Brain Vision Analyser consisting in the following steps: high pass filtering 0.1 Hz, low pass filtering at 30 Hz (Butterworth zero phase filter; 24 dB/octave slope) and notch filter at 50 Hz; raw data inspection for manual detection of artefact and screening for bad channels, semi-automatic eye-blink correction using independent component analysis (ICA); artefact rejection of trials with an amplitude exciding ±80 μV; EEG data were segmented into 1,500 ms epochs from 500 ms before to 1,000 ms after stimulus onset. Data were baseline corrected against the mean voltage during the 200-ms pre-stimulus periods. Artefact free epochs were separately averaged for each subject in each experimental condition (go, no-go) and stimulus type (positive, negative, neutral).

ERP analyses were based on visual inspection of the grand average waveforms and the existing literature. Peak amplitudes for the N2 and P3 components were computed in fronto-central cluster (FC1, FC2, Fz, C3, C4, Cz), in the time windows between 200–380 ms and 300–500 ms, respectively (Figure 1).

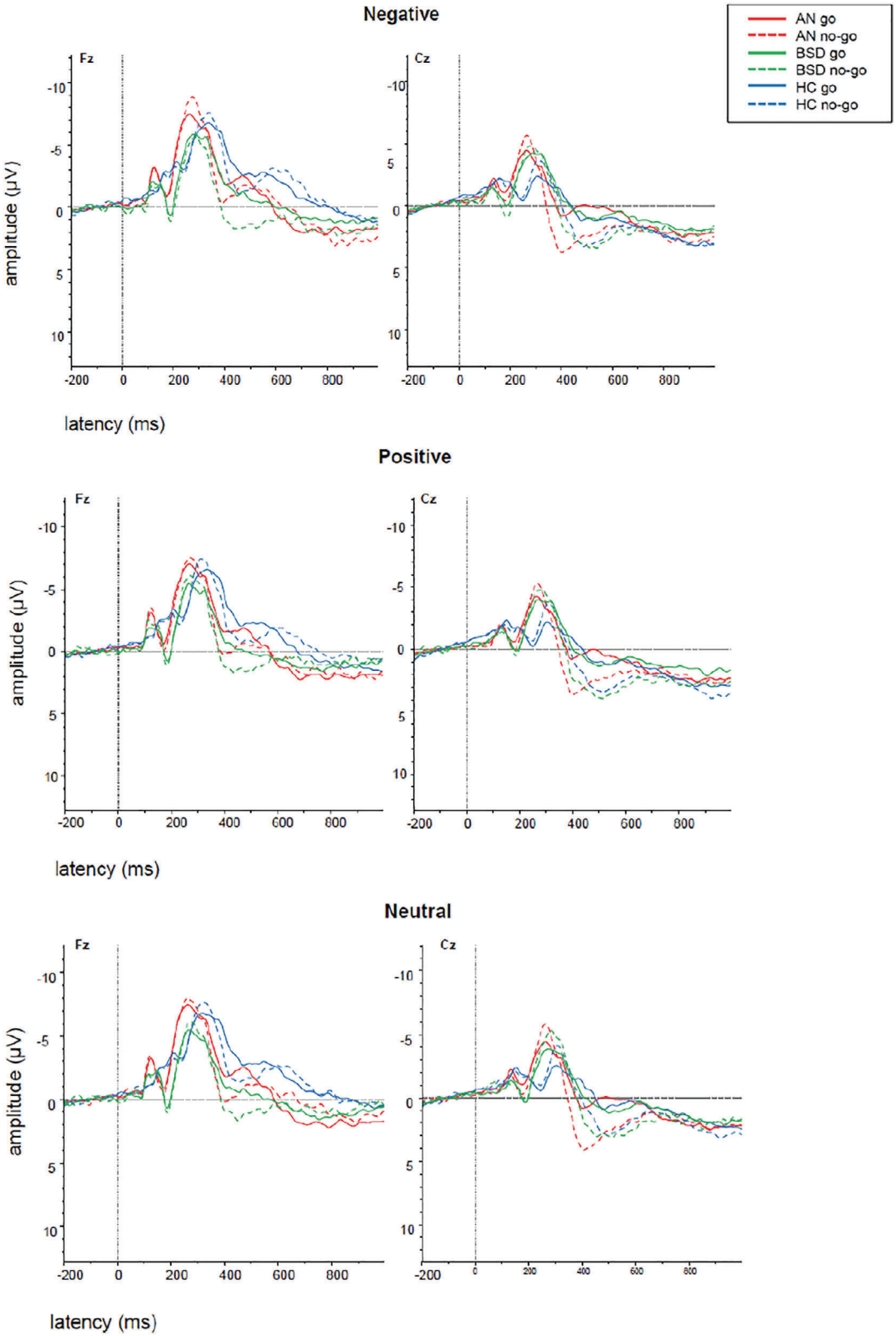

FIGURE 1 ERP amplitudes (μV) and latencies (ms) for each group (AN, BSD, HC), condition (go, no-go), and type (positive, negative, neutral). AN, anorexia nervosa; BSD, Bulimic spectrum disorder; ERP, event-related potential; HC, healthy control [Colour figure can be viewed at wileyonlinelibrary.com]

2.3.4 | Statistical analysis

Statistical analysis was carried out with Stata16 for Windows. The impulsivity levels (UPPS-P scores) were compared between groups using analysis of variance (ANOVA), adjusted by the participants' age [Analysis of covariance (ANCOVA)]. Effect size for pairwise comparisons was measured through Cohen's *d* coefficient (low/poor effect size was considered for $|d| > 0.2$, moderate for $|d| > 0.5$ and large/high for $|d| > 0.8$; (Kelley & Preacher, 2012).

Accuracy and ERP components (N2, P3) of the go/no-go task were compared through $2 \times 3 \times 3$ mixed ANOVA, defining as within-subjects the factors 'condition' (go vs. no-go) and 'type' (positive, negative and neutral) and as between-subjects factor the 'group' (HC, AN, and BSD). Pairwise comparisons estimated main effects (for non-significant interaction parameters) and simple effects (for significant interaction parameters). In this analysis, eta-squared coefficient (η^2) was obtained to measure the effect size for the ANOVA (values of 0.01, 0.06 and 0.14 were interpreted as low-poor, moderate-medium and large-high effect size) (Levine & Hullett, 2002).

3 | RESULTS

3.1 | Self-report measures

Table 1 contains the results of the ANCOVA (adjusted by age) measuring the mean differences in the UPPS-P scores between the groups. Lack of perseverance was higher in the BSD group compared to both AN ($T = 3.07$, $p = .004$, $|d| = 1.52$; $\eta^2 = 0.164$) and HC ($T = 4.06$, $p = .001$, $|d| = 2.45$; $\eta^2 = 0.256$). Sensation seeking scores were not significantly different between the groups, but a moderate effect size was obtained in the comparison between BSD and AN (higher mean in the BSD group: $T = 1.21$, $p = .232$, $|d| = 0.63$; $\eta^2 = 0.030$). Regarding negative urgency, the group that presented higher mean scores was the BSD group, followed by the AN and the HC groups all pairwise comparisons achieved statistical significance and/or mild to large effect size; HC versus AN: $T = 1.96$, $p = .056$, $|d| = 0.69$, $\eta^2 = 0.074$; HC versus BSD: $T = 2.83$, $p = .007$, $|d| = 1.48$, $\eta^2 = 0.143$; AN versus BSD: $T = 1.56$, $p = .126$, $|d| = 0.80$, $\eta^2 = 0.048$).

Table S1 includes the results of assessing for potential differences between the AN subtypes [restrictive (AN-R) vs. bulimic-purgative (AN-BP)] in the impulsivity profile. Statistical differences appeared in the negative urgency domain: higher mean score in the AN-BP compared to AN-R (35.3 vs. 28.0, $p = .041$, $|d| = 1.24$).

Table 2 shows the means and standard deviations of the RTs and accuracy in the go/no-go task, as well as the amplitudes (μV) for each ERP component (N2 and P3). Table S2 includes the complete results obtained in the mixed ANOVA.

3.1.1 | Emotional go/no-go task

RTs in go trials

The mixed design ANOVA yielded a quasi-significant main effect of group $F = 2.84$, $df = 2/48$, $p = .068$; $\eta^2 = 0.104$, a non-significant main effect of the type ($F = 0.73$, $df = 2/49$, $p = .469$, $\eta^2 = 0.015$), and a non-significant group × type interaction ($F = 0.80$, $df = 4/49$, $p = .517$, $\eta^2 = 0.031$). Post hoc pairwise comparisons revealed that the main effect of the group was related to the higher means in the reaction time registered in the HC compared to the AN ($p = .023$).

Accuracy

The mixed design ANOVA yielded a significant main effect of condition ($F = 11.82$, $df = 1/49$, $p < .001$;

TABLE 1 Comparison of the clinical profile between groups: ANCOVA adjusted by age

	HC (*n = 20*)		AN (*n = 17*)		BSD (*n = 16*)		HC vs. AN		HC vs. BSD		AN vs. BSD	
	Mean	***SD***	**Mean**	***SD***	**Mean**	***SD***	***p***	***|d|***	***p***	***|d|***	***p***	***|d|***
UPPS-P lack premeditation	21.1	5.3	21.2	5.8	21.6	5.8	.953	0.02	.861	0.09	.893	0.07
UPPS-P lack perseverance	16.1	4.5	18.7	6.4	27.2	4.5	.146	0.46	.001*	2.45[a]	.004*	1.52[a]
UPPS-P sensation seeking	28.5	8.4	24.7	7.1	29.5	8.1	.138	0.49	.791	0.13	.232	0.63[a]
UPPS-P positive urgency	23.8	5.7	24.9	8.6	26.8	12.6	.745	0.14	.544	0.30	.694	0.18
UPPS-P negative urgency	26.1	6.4	30.6	6.8	36.4	7.5	.056	0.69[a]	.007*	1.48[a]	.126	0.80[a]

Abbreviations: AN, anorexia; BSD, bulimic spectrum disorder; HC, healthy control.

[a]Effect size into the mild/moderate ($|d| > 0.50$) to large/good range ($|d| > 0.80$).

*Significant parameter (.05 level).

TABLE 2 Means and *SD* for behavioural and ERP measures during the go/no-go task

			HC ($n = 20$)		AN ($n = 17$)		BSD ($n = 16$)	
Measure	**Condition**	**Type**	**Mean**	***SD***	**Mean**	***SD***	**Mean**	***SD***
RTs	Go	Positive	389.9	57.3	349.8	46.2	369.7	66.2
		Negative	391.4	56.0	344.0	56.1	391.4	73.0
		Neutral	390.8	58.0	349.1	49.4	374.2	70.7
Accuracy	Go	Positive	0.99	0.03	0.99	0.04	0.94	0.07
		Negative	1.00	0.01	0.99	0.02	0.94	0.07
		Neutral	1.00	0.03	0.99	0.03	0.93	0.08
	No-go	Positive	0.86	0.11	0.83	0.12	0.75	0.12
		Negative	0.87	0.10	0.83	0.11	0.75	0.12
		Neutral	0.86	0.11	0.81	0.13	0.73	0.13
N2-amplitude	Go	Positive	−4.27	2.05	−4.46	2.38	−5.53	2.30
		Negative	−4.44	2.26	−5.32	2.30	−5.82	2.51
		Neutral	−4.59	2.04	−5.07	2.33	−5.49	2.10
	No-go	Positive	−3.49	2.37	−4.91	2.20	−6.18	2.99
		Negative	−5.16	2.56	−5.92	3.01	−6.75	2.51
		Neutral	−5.47	2.27	−6.14	2.40	−6.43	2.42
P3-amplitude	Go	Positive	1.14	2.02	1.24	1.86	1.45	1.49
		Negative	1.10	1.75	0.95	1.76	1.10	1.52
		Neutral	0.81	2.07	0.76	1.47	1.74	1.98
	No-go	Positive	3.34	2.60	3.25	2.04	3.11	1.69
		Negative	3.10	2.51	3.20	2.32	2.97	2.23
		Neutral	3.10	2.46	3.24	2.44	3.01	2.21

Note: Results adjusted by the participants' age.
Abbreviations: AN, anorexia; BSD, bulimic spectrum disorder; HC, healthy control; RTs, reaction times.

$\eta^2 = 0.194$), a significant main effect of group ($F = 5.88$, $df = 2/49$, $p = .005$, $\eta^2 = 0.193$) and a non-significant effect of type ($F = 1.35$, df = 2/49, $p = .264$, $\eta^2 = 0.027$). No significant interaction parameters were obtained (group × condition: $F = 0.61$, $df = 2/49$, $p = .547$, $\eta^2 = 0.024$; group × type: $F = 0.38$, $df = 4/49$, $p = .817$, $\eta^2 = 0.015$; condition × type: $F = 0.89$, $df = 2/49$, $p = .415$, $\eta^2 = 0.018$; and group × condition × type: $F = 0.11$, $df = 4/49$, $p = .977$, $\eta^2 = 0.005$). Post hoc pairwise comparisons revealed that the main effect of condition was due to higher means registered in the go trials compared to the no-go trials ($p < .001$), and that the main effect for the group was related to the lower means in the BSD compared to HC ($p = .001$) and AN ($p = .013$).

N2-amplitude

The mixed design ANOVA yielded a significant main effect of condition ($F = 4.92$, $df = 1/49$, $p = .031$; $\eta^2 = 0.091$), and a non-significant main effect of type ($F = 1.04$, $df = 2/49$, $p = .357$, $\eta^2 = 0.021$) and group ($F = 1.08$, $df = 2/49$, $p = .349$, $\eta^2 = 0.042$). No significant interaction parameters were obtained (group × condition: $F = 1.04$, $df = 2/49$, $p = .337$, $\eta^2 = 0.043$; group × type: $F = 0.95$, $df = 4/49$, $p = .438$, $\eta^2 = 0.037$; condition × type: $F = 0.44$, $df = 2/49$, $p = .611$, $\eta^2 = 0.009$; and group × condition × type: $F = 1.77$, $df = 4/49$, $p = .152$, $\eta^2 = 0.067$). Post hoc pairwise comparisons revealed that the main effect of condition was due to more negative means (higher N2 negativity) registered in the go trials compared to the no-go trials ($p < .001$).

P3-amplitude

The mixed design ANOVA yielded a significant main effect of condition ($F = 4.36$, $df = 1/49$, $p = .042$; $\eta^2 = 0.082$), and a non-significant main effect of type ($F = 0.60$, $df = 2/49$, $p = .547$, $\eta^2 = 0.012$) and group ($F = 0.01$, $df = 2/49$, $p = .989$, $\eta^2 = 0.001$). No significant interaction parameters were obtained (group × condition: $F = 0.68$, $df = 2/49$, $p = .597$, $\eta^2 = 0.027$; group × type: $F = 0.24$, $df = 4/49$, $p = .913$, $\eta^2 = 0.010$; condition × type: $F = 0.19$, $df = 2/49$, $p = .821$, $\eta^2 = 0.004$; and group × condition × type: $F = 0.82$, df = 4/49, $p = .510$, $\eta^2 = 0.033$). Post hoc pairwise comparisons

revealed that the main effect of condition was due to more positive amplitude registered in the go trials compared to the no-go ($p < .001$).

4 | DISCUSSION

The present study explored trait impulsivity and emotion-related inhibitory control in patients with BSD and AN, and compared them with a normal-weight group of HC. Trait impulsivity was assessed using the UPPS-P scale; an emotional go/no-go task during EEG recording was used to assess inhibitory control in presence of emotional (positive and negative) and neutral stimuli. Results demonstrated higher trait impulsivity in EDs than HC (with even higher scores among BSD patients) and lower response accuracy in the go/nogo task among BSD patients; however, no group differences were detected in neural or behavioural indices of inhibitory control, neither in presence of emotional or neutral stimuli.

With regards to trait impulsivity, as hypothesised results displayed higher negative urgency in both ED groups compared to HC, with BSD showing higher negative urgency than AN. Patients with BSD also showed the highest score in lack of perseverance compared to both AN and HC, and a mean value for the sensation seeking domain higher than AN (with an effect size into the mild/moderate range). No significant differences were observed for the lack premeditation or positive urgency. Our results support those of previous studies reporting negative urgency as a key component of BSD (Fischer, Peterson, & McCarthy, 2013; Magel, 2019; Steward et al., 2017) and add some extra evidence on the role of lack of perseverance in this disorder. Therefore, in patients with BSD, it appears as remarkably relevant to specifically target and assess negative emotions during treatment as well as to target and assess low perseverance as it could be an indicator of bad prognosis and worse treatment outcome (Dalle Grave, Calugi, Brambilla, & Marchesini, 2008).

In the emotional go/no-go task, RTs in go trials were not modulated by positive or negative images, which may suggest a lack of emotional bias, at least over motor responses. As for accuracy, significantly lower accuracy was present in no-go trials compared to go trials, indicating that the task was effective in inducing a pre-potent tendency to respond. However, again, emotional images do not affect accuracy in no-go trials, in neither HC nor EDs subjects, suggesting that in our task incidental emotional stimuli with positive or negative valence do not interfere with response inhibition. Interestingly, BSD patients showed lower task accuracy, and this seems to be particularly evident in the no-go trials (see Table 2). Unfortunately, the interaction between group and condition was not significant thus it did not support the hypothesis of lower inhibitory control in patients with BSD. Still these results may be due to reduced statistical power. As compared to previous literature, some of the behavioural studies of inhibitory control, did not show differences between patients with EDs (including AN, BED, BN and EDNOS) and HC (Claes, Nederkoorn, Vandereycken, Guerrieri, & Vertommen, 2006; Mole et al., 2015; Wu, Hartmann, et al., 2013) although contrasting findings are present (Bartholdy et al., 2016; Wierenga et al., 2014; Wu, Hartmann, et al., 2013). Overall, it has been suggested that specific elements of inhibitory control may be differently affected among ED subtypes. For instance, proactive component of inhibitory control (i.e., a form of inhibitory control related to the preparation or initiation of a response) is augmented in patients with AN (Bartholdy et al., 2017). By contrast, no differences in reactive inhibitory control (i.e., withhold a motor response in reaction to a cue) were detected in patients with BN, BED or AN compared to controls, suggesting that specific elements of inhibitory control may be differently affected in different EDs. Additionally, the fact that the participants scored high on negative urgency with no significant interactions in the go-no go task which could be due to a compensatory effect. This would go in line with the data reported by Chester et al. (2016), who found that in their sample negative urgency predicted greater PFC activity during negative-valence inhibition but greater PFC activity compensated for urgency's inhibitory deficits. Further investigating these differences with experimental paradigms may allow the development of specific inhibitory control trainings adapted for different EDs.

Concerning ERP measures, N2 and P3 amplitudes in no-go trials were larger than in go trials, in line with the typical go/no-go effect, also observed at behavioural level. However, and similarly to behavioural results, no differences were shown across groups in neural index of response inhibition (e.g., no-go N2/P3 amplitudes). Neither patients nor controls showed differences in ERP between emotional and non-emotional trials of the task, further confirming the lack of emotional modulation of inhibitory control. In a previous study in HC, results showed emotional modulation of no-go P3 only in individuals with high traits impulsivity, measured by the BIS-11 scale (Messerotti Benvenuti et al., 2015). This suggests that, at least in healthy individuals, emotional context may interfere with inhibitory control as a function of trait impulsivity. Given this, the lack of differences in emotional or non-emotional inhibitory control between patients and HC may be partially explained by variability

in impulsivity traits observed in the HC group. Thus, impulsivity trait seems to be an important factor to assess in healthy population.

It is also worth noting that there are no previous ERP studies assessing emotional inhibitory control in EDs, which makes the present findings difficult to compare and contextualise. Only a recent ERP study in patients with BED measured food-related inhibitory control using an anti-saccade paradigm with food stimuli (Leehr et al., 2018), after inducing negative mood. Despite of methodological differences (e.g., mood induction; task; sample of EDs; food-related stimuli), ERP results did not show reduced inhibitory control in BED, as showed by similar N2 amplitudes between patients and controls. By contrast, at behavioural level more errors were detected in BED, suggesting food-specific inhibitory control difficulties.

The current study should be considered under some limitations. First of all, the cross-sectional design of this study cannot imply causality. Additionally, the limited sample size may have an effect on the external validity of the study (and therefore in the capacity to infer conclusions to the original populations) as well as on the statistical power analyses (the capacity to identify relationships between the variables is limited). However, it must be maintained that the conclusions of the current study were not only based on the significance tests but also on the standardised measures used to calculate the effect sizes (Cohen's *d* values, which are not affected by samples sizes). Likewise, it should be considered that the assessment conducted in this study is difficult to perform in clinical samples, and therefore researches in this area are scarce, include low sample sizes and perform extra caution for controlling potential biases in the statistical analyses. Given that the assessment of the present study mainly focuses on some aspects of the impulsivity, our results are not generalizable to all facets of impulsivity which should be explored in future studies. Finally, current findings should not be generalised to men with EDs, as only women were recruited in the current sample.

In conclusion, the present results highlighted negative urgency, an impulsive personality trait related to emotions, as a common feature of AN and BSD. Lack of perseverance, a trait which is less related to emotions d, specifically characterises patients with BSD. On the other hand, behavioural and ERP data did not show altered inhibitory control in EDs, for neither general nor emotional-related response inhibition. Other facets of impulsivity and inhibitory control should be further investigated in future studies in larger clinical samples, to better elucidate cognitive profiles of EDs and developing specific treatments.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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ESTUDIO 3

IMPULSIVITY AND COMPULSIVITY IN GAMBLING DISORDER AND BULIMIC SPECTRUM EATING DISORDERS: ANALYSIS OF NEUROPSYCHOLOGICAL PROFILES AND SEX DIFFERENCES

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Objetivos:

Explorar las similitudes y diferencias en impulsividad y compulsividad en pacientes con BN/TA y pacientes con TJ, examinando a su vez diferencias asociadas al sexo.

RESUMEN

El TJ y los trastornos del espectro bulímico (BN y TA) no sólo comparten características psicopatológicas y neurobiológicas, ambos también se asemejan en la presencia de conductas inapropiadas relacionadas con la impulsividad y la compulsividad. Mediante el uso de medidas autoreportadas y neurocognitivas, comparamos diferentes dimensiones de impulsividad y compulsividad en una muestra conformada por 59 pacientes con BN/TA (62.7% mujeres), 159 pacientes con TJ (20.1% mujeres) y 150 sujetos controles (82.0% mujeres). Pretendíamos enfatizar las diferencias y similitudes entre las dos muestras clínicas, además de analizar en cada dominio las posibles diferencias asociadas al sexo. En comparación con los controles, los pacientes con TJ y BN/TA exhibieron niveles más elevados de impulsividad y compulsividad en todas las dimensiones. Sin embargo, estos trastornos mostraron diferencias en varios rasgos impulsivos, como mayor búsqueda de la novedad en el TJ, y menor persistencia y más evitación del daño en la BN/TA. Además, los pacientes con BN/TA también mostraron una tendencia más impulsiva en la toma de decisiones que aquellos con TJ. Respecto a los efectos del sexo, las mujeres con TJ presentaron a nivel general mayores niveles de impulsividad y compulsividad que los varones con TJ. Sin embargo, no se encontraron diferencias de sexo en el grupo de BN/TA. Las investigaciones clínicas deberían considerar y abordar estos déficits a través de tratamientos complementarios, esto podría beneficiar y acelerar la recuperación de los pacientes. Nuestros resultados también dan soporte a la relevancia del sexo en el TJ, otro factor a tener en cuenta en futuros estudios.

Impulsivity and Compulsivity in Gambling Disorder and Bulimic Spectrum Disorders: Analysis of Neuropsychological Profiles and Sex Differences

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ABSTRACT

Gambling disorder (GD) and bulimic spectrum eating disorders (BSDs) not only share numerous psychopathological, neurobiological and comorbidity features, but also are distinguished by the presence of inappropriate behaviours related to impulsivity and compulsivity. This study aimed to emphasise the differences and similarities in the main impulsivity and compulsivity features between GD and BSD patients, and to analyse the potential influence of sex in these domains. Using self-reported and neurocognitive measures, we assessed different impulsive-compulsive components in a sample of 218 female and male patients (59 with BSD and 159 with GD) and 150 healthy controls. We observed that GD and BSDs exhibited elevated levels of impulsivity and compulsivity in all the dimensions compared to healthy controls. Moreover, these disorders showed differences in several personality traits, such as high novelty seeking in GD, and low persistence and high harm avoidance in BSDs. In addition, patients with BSDs also displayed a trend towards greater impulsive choice than GD patients. Regarding sex effects, GD women presented higher overall impulsivity and compulsivity than GD men. Nevertheless, no sex differences were found in BSDs. Clinical interventions should consider these deficits to enhance their effectiveness, including adjunctive treatment to target these difficulties. Our findings also provide support to the relevance of sex in GD, which should also be considered in clinical interventions.

INTRODUCTION

Gambling disorder (GD) and eating disorders (EDs) are mental conditions characterised by persistent maladaptive patterns of gambling behaviour and abnormal eating, respectively [1]. Despite representing very different entities with specific clinical symptoms, these disorders share numerous psychopathological, neurobiological and comorbidity features [2,3]. GD and EDs are also distinguished by the presence of inappropriate behaviours related to impulsivity and compulsivity [4–6], and are considered to map into the impulsive-compulsive spectrum, a continuum encompassing different neuropsychiatric conditions characterised by impairments in impulse control mechanisms [7].

Recent research suggests that impulsivity (i.e. rapid unplanned responses performed without regard to their negative consequences) can be conceptualized as a multidimensional construct composed of three major domains: “choice impulsivity”, “response impulsivity” and “impulsive personality traits” [8]. **Choice impulsivity** is understood as impulsive decision-making without neither planning nor regard for future consequences [8], and is usually measured with the Iowa Gambling Task (IGT) [9]. Numerous studies have shown decision-making impairments in all EDs, but especially in bulimic spectrum disorders (BSDs) [10,11], meaning higher impulsive choice in these ED subtypes. Similarly, decision-making deficits have been observed in GD [12,13], mainly when taking risk-reward choices, in which GD patients display high difficulty to choose the advantageous options [14].

The second form of impulsivity is referred to as **response impulsivity**, and reflects the inability to inhibit a prepotent motor response [8]. The Stroop Colour and Word Test (SCWT; Golden, 1978, 2001), widely used to measure inhibitory control, has shown significant deficits in EDs, mainly in BSD patients [17,18]. These deficits are particularly outstanding when examining stimuli related to the disorder (e.g., food consumption) [19], suggesting they may constitute a maintenance factor [20]. GD has also been linked with decreased inhibitory control, especially in certain cognitively demanding situations (e.g. gambling activities) [21,22].

Impulsive personality traits are the last form of impulsivity, and refer to dispositional tendencies toward impulsive behaviour [8]. Novelty seeking, assessed using the Temperament and Character Inventory-Revised (TCI) [23], is the trait most closely related to impulsivity, since it refers to the search of new stimuli and rewards. Among EDs, the highest levels of novelty seeking are displayed by patients with BSDs [24,25], reflecting a more impulse personality. Similarly, high novelty seeking has been identified as an outstanding feature in GD [26,27]. Lastly, another impulsive trait highlighted in GD and particularly in BSDs is low persistence [28], indicating lack of perseverance in the presence of adversities [23].

Similarly to impulsivity, compulsivity (i.e. repetitive maladaptive behaviours performed to avoid negative consequences) can be described as a multifactorial construct made up of different dimensions [29,30]. **Cognitive flexibility** is one of the most relevant components of compulsivity. It refers to the ability to adapt cognitive strategies in response to feedback [31], and is commonly measured by the Wisconsin Card Sorting Task (WCST) [32]. Numerous studies have displayed poor cognitive flexibility in patients with BSDs [10,33,34] and GD [35,36], reflecting high levels of cognitive rigidity and compulsivity in both disorders. On the other hand, due to the lack of psychometric tools to measure compulsivity, some authors have suggested the use of harm avoidance (TCI-R) to assess **compulsive traits** [31,37]. In this regard, several studies have shown that BSD and GD patients display higher levels of harm avoidance than healthy controls (HCs) [24,25,38].

Despite the similarities between GD and BSDs, only a few studies have explored impulsivity and compulsivity comparing both disorders. Studies focused on personality traits observed that GD patients show higher novelty seeking than BSD patients [26,28,39–41], while the latter group display lower persistence [28] and higher harm avoidance [26,28]. Only one research compared the neuropsychological performance of GD and BN patients [35], revealing that GD patients exhibit poorer cognitive flexibility. Finally, although sex differences are especially highlighted in these pathologies at a clinical and neuropsychological level [42–45], most of the cited studies did not consider the effect of sex on their results, possibly leading to a bias.

Given that numerous impulsive and compulsive features overlap across GD and BSDs, there is a need for comparative studies which examine differences and similarities between both. Thus, this study aimed to compare impulsivity and compulsivity dimensions among HCs and patients with BSDs and GD. We hypothesised that both clinical groups would display abnormalities in these domains relative to HCs. We also expected to find some differences between GD and BSDs, specifically, GD patients would show the lowest cognitive flexibility and the highest novelty seeking, while BSD patients would display the lowest persistence and the highest harm avoidance. Secondly, we aimed to examine sex effects on the impulsivity and compulsivity of GD and BSD patients.

METHODOLOGY

Participants

The final sample consisted of 368 participants (52.2% females) aged between 18 and 72 years old, of which 59 were diagnosed with a BSD (62.7% females) and 159 with a GD (11.6% females) according to the DSM-5 diagnostic criteria [1]. The control group was made up of 150 individuals without a lifetime mental disorder. BSDs subsample comprised of bulimia nervosa (47.5%) and binge eating disorder patients (52.5%).

Participants were recruited at the *Eating Disorder Unit* and the *Pathological Gambling Unit* within the Department of Psychiatry at Bellvitge University Hospital (Barcelona, Spain). They were diagnosed by psychologists/psychiatrists with over 10 years' experience by means of a semi-structured interview. All participants were informed about the research procedures and gave their informed consent in writing. Procedures were approved by the Ethical Committee of the above-mentioned institution in accordance with the Helsinki Declaration of 1975 as revised in 1983 (reference: PR146/14). Exclusion criteria were the following: (1) history of chronic medical illness or neurological condition that might affect cognitive function; (2) head trauma with loss of consciousness for more than 2 min; (3) learning disability or intellectual disability; (4) use of psycho-active medications or drugs; (5) age under 18.

Procedure and assessment

All individuals who arrived at the hospital and were diagnosed with an ED or a GD, were screened for the inclusion criteria. Those included in the study underwent a clinical and neuropsychological assessment within the first week of their outpatient treatment. The instruments included were specifically selected to cover a wide range of impulsivity and compulsivity domains. Additional sociodemographic information was also taken.

Instruments

The Spanish adaptation of the Symptom Checklist-90 Revised (SCL-90-R) [46,47] assesses psychopathological symptoms grouped as: somatization, obsessive-compulsive, interpersonal sensitive, depression, anxiety, hostility, phobic anxiety, paranoia and psychotic. Additionally, this scale contains a global severity index (GSI), that measures overall psychological distress. Cronbach's alpha in this study was good to excellent (between a = 0.77 for phobic anxiety to a = 0.93 for depressive symptoms).

The Spanish validation of the Temperament and Character Inventory Revised (TCI-R) [23,48] is a reliable questionnaire composed by 240 items. It includes four dimensions of temperament (novelty seeking, harm avoidance, reward dependence and persistence) and three of character (self-directedness, cooperativeness and self-transcendence). In this study sample, Cronbach's alpha was good to excellent (between a = 0.73 for novelty seeking to a = 0.89 for self-directedness).

The Stroop Colour and Word Test (SCWT) [15,16] is a neuropsychological tool that evaluates inhibitory control. It comprises three different lists: a word list containing names of colours, a colour list that comprises letter Xs printed in colour, and a colour-word list composed of names of colours in a colour ink that does not match the written name. Three scores are calculated using the number of items correctly read from each list in 45 seconds. An additional "interference score" is obtained using all three lists. Better capacity of inhibitory control is related to higher scores in the colour-word list and in the interference score.

The Wisconsin Card Sorting Test (WCST) [32] is a computerized set-shifting task which allows assessing cognitive flexibility. Participants have to sort each of the 128 cards provided in one of the four available decks. Each card presents a figure with different properties (colour, shape and number). The aim is to select the correct deck considering one of the properties. When participants select a deck, a feedback ("correct" or "incorrect") is displayed, hence they can deduce the selection criteria. The rule changes after completing a category (10 consecutive correct sorts) or if this is not discovered after six trials. The task finishes when all 128 cards are sorted or after six categories are completed. The main variable related to compulsivity is perseverative errors (i.e., failures to change sorting strategy after negative feedback).

The Iowa Gambling Task (IGT) [9] is a computerized task designed to assess decision making processes and impulsive choices [49]. The task involves 100 trials in which participants have to select one of the four presented decks (A, B, C or D); afterwards, a specified amount of play money is awarded or subtracted. Two of the decks result in money wins (C, D), while the others result in losses (A, B). Participants are instructed to gather as much money as possible. The test score is computed by subtracting the number of times that participants selected the disadvantageous decks from the number of advantageous decks choices. Lower scores translate to impulsive decision-making.

Statistical analysis

Statistical analysis was carried out with Stata16 for Windows [50]. Firstly, the frequency distribution of the sociodemographic and clinical variables was based on chi-square tests (χ^2) for categorical variables and analysis of variance (ANOVA) for quantitative measures. The effect size of the mean differences was tested through Cohen's-*d* coefficient, considering low-poor effect for $|d| > 0.20$, moderate-medium for $|d| > 0.5$ and large-high for $|d| > 0.8$ [51]. The effect size of the proportion differences was estimated through Cohen's-*h* coefficient, obtained as the difference of the arcsine transformation for the proportions observed in each group; it was interpreted with the same threshold ranges as Cohen's-*d* measure [52]. The comparison of the impulsivity and compulsivity measures was based on 3×2 ANOVA procedures, controlling for the covariates chronological age and education. Two between-subjects factors were defined: group (with 3 levels: HCs, BSDs and GD) and sex (with 2 levels: women and men).

In addition, Finner-correction was used to control the increase in the Type-I error due to the multiple statistical comparisons [53], which is a family-wise procedure that has demonstrated higher power than classical Bonferroni-correction.

RESULTS

Characteristics of the sample

Table 1 contains the comparison of the sociodemographic and clinical profile of the three groups. Statistical differences emerged for all the measures among all three groups, with most effect sizes within the moderate to high range (|*d*|>0.50 or |*h*|>0.50).

Table 1. Descriptive of the sample

		HC		BSD		GD		BSD *versus*		GD *versus*		BSD *versus*	
		n=150		*n=59*		*n=159*		HC		HC		GD	
		n	%	*n*	%	*n*	%	*p*	|*h*|	*p*	|*h*|	*p*	|*h*|
Sex	Women	123	82.0%	37	62.7%	32	20.1%	**.003***	0.44	**.001***	**1.33†**	**.001***	**0.90†**
	Men	27	18.0%	22	37.3%	127	79.9%						
Education	Primary	8	5.3%	4	6.8%	75	47.2%	**.001***	0.06	**.001***	**1.05†**	**.001***	**0.99†**
	Secondary	85	56.7%	17	28.8%	52	32.7%		**0.57†**		**0.51†**		0.08
	University	57	38.0%	38	64.4%	32	20.1%		**0.53†**		0.40		**0.93†**
		Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*p*	|*d*|	*p*	|*d*|	*p*	|*d*|
Age (years-old)		30.67	13.68	35.24	11.08	41.10	11.34	**.016***	0.37	**.001***	**0.83†**	**.002***	**0.52†**
Onset of disorder		---	---	25.81	11.43	29.61	11.27	---	---	---	---	**.029***	0.33
Duration of disorder		---	---	7.98	4.73	5.23	5.28	---	---	---	---	**.001***	**0.55†**
SCL-90-R													
Somatization		0.62	0.47	1.73	0.90	1.01	0.83	**.001***	**1.53†**	**.001***	**0.57†**	**.001***	**0.82†**
Obsessive-comp.		0.76	0.56	1.88	0.98	1.25	0.80	**.001***	**1.40†**	**.001***	**0.70†**	**.001***	**0.70†**
Interp. sensitive		0.63	0.54	1.99	1.07	1.11	0.81	**.001***	**1.60†**	**.001***	**0.70†**	**.001***	**0.92†**
Depressive		0.64	0.51	2.19	1.06	1.66	0.86	**.001***	**1.87†**	**.001***	**1.45†**	**.001***	**0.55†**
Anxiety		0.48	0.42	1.66	1.00	1.09	0.80	**.001***	**1.54†**	**.001***	**0.96†**	**.001***	**0.62†**
Hostility		0.44	0.51	1.36	0.97	0.96	0.81	**.001***	**1.19†**	**.001***	**0.77†**	**.001***	0.45
Phobic anxiety		0.12	0.27	1.08	0.86	0.48	0.58	**.001***	**1.50†**	**.001***	**0.78†**	**.001***	**0.82†**
Paranoid		0.53	0.54	1.40	0.91	1.00	0.78	**.001***	**1.16†**	**.001***	**0.71†**	**.001***	0.47
Psychotic		0.29	0.31	1.36	0.85	0.93	0.70	**.001***	**1.68†**	**.001***	**1.20†**	**.001***	**0.55†**
GSI score		0.55	0.40	1.73	0.83	1.14	0.68	**.001***	**1.81†**	**.001***	**1.05†**	**.001***	**0.78†**
PST score		21.25	6.69	57.32	19.13	48.71	20.92	**.001***	**2.52†**	**.001***	**1.77†**	**.001***	0.43
PSDI score		1.44	0.31	2.34	0.64	1.92	0.57	**.001***	**1.79†**	**.001***	**1.06†**	**.001***	**0.69†**

Note. HC: healthy controls. BSD: bulimic spectrum disorders. GD: gambling disorder. SD: standard deviation. *Bold: significant comparison (.05 level). †Bold: effect size into the range mild-moderate (|*h*| or |*d*| higher than 0.50) to high-large (|*h*| or |*d*| higher than 0.80).

Comparison of the impulsivity and compulsivity measures

Table 2 includes the results of the 3×2 ANOVA comparing the impulsivity and compulsivity measures among the three groups, controlling for age and education. Multivariate tests showed a significant effect of the factor group in most variables. When single effects were estimated, differences between HCs and the clinical groups were found for most measures, except for the following: IGT block 1, SCWT interference, TCI-R reward dependence and WCST conceptual. Comparisons between BSDs and GD reported differences only for TCI-R novelty seeking (higher in GD) and harm avoidance (higher in BSDs).

Table 2. Comparison of the impulsivity and compulsivity measures: 3×2 ANOVA adjusted for age and education

	HC		BSD		GD		Women		Men		Multivariate tests†			Post-hoc compar.†		
	n=150		*n=59*		*n=159*		*n=192*		*n=176*		Factor	Factor	Inter.	BSD	GD vs	BSD
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	Group	Sex		vs HC	HC	vs GD
IGT																
Block 1	-1.17	7.58	-2.08	6.02	-2.07	8.11	-2.05	6.26	-1.49	4.80	.508	.468	.826	.355	.319	.998
Block 2	0.85	9.23	-1.72	7.32	-0.19	9.87	-0.67	7.74	-0.04	6.44	.095	.497	**.001***	**.030***	.345	.231
Block 3	4.34	10.60	0.47	8.41	1.23	11.33	1.50	8.15	2.52	8.21	**.006***	.342	.211	**.005***	**.014***	.606
Block 4	3.51	11.78	0.34	9.35	2.74	12.59	1.82	9.16	2.57	8.83	.110	.526	**.010***	**.037***	.583	.144
Block 5	4.78	12.43	-0.76	9.86	1.24	13.28	1.10	9.82	2.41	9.09	**.001***	.297	.903	**.001***	**.017***	.248
Total	12.38	33.67	-3.75	26.71	2.97	35.99	1.69	28.21	6.04	24.29	**.001***	.203	**.020***	**.001***	**.019**	.151
SCWT																
Words	105.16	21.13	102.86	16.76	98.89	22.58	103.57	16.21	101.04	16.89	**.045***	.237	**.010***	.397	**.013***	.177
Colours	72.84	16.43	68.26	13.03	68.29	17.56	71.44	13.03	68.15	12.43	**.025***	**.049***	**.030***	**.030***	**.020***	.988
Words-colours	47.19	13.32	43.67	10.56	43.76	14.23	44.76	11.39	44.98	10.71	**.039***	.869	.674	**.040***	**.031***	.962
Interference	4.45	10.29	2.98	8.17	3.62	11.00	2.68	8.23	4.69	8.23	.517	.054	.312	.266	.497	.656
TCI-R																
Novelty seeking	101.39	17.84	103.97	14.15	110.17	19.07	104.86	13.72	105.50	13.60	**.001***	.725	.262	.260	**.001***	**.013***
Harm avoidance	91.43	22.84	118.25	18.12	105.64	24.42	108.60	20.77	101.62	18.00	**.001***	**.003***	.520	**.001***	**.001***	**.001***
Reward depend.	101.62	19.06	97.92	15.12	100.57	20.37	102.57	14.52	97.51	14.06	.319	**.009***	.052	.132	.643	.319
Persistence	111.85	23.95	103.73	19.00	107.35	25.60	104.99	18.88	110.29	17.42	**.026***	**.030***	.287	**.009***	.115	.278
WCST																
Trials	88.93	24.86	100.81	19.72	100.74	26.57	99.08	20.30	94.57	20.90	**.001***	.075	.576	**.001***	**.001***	.984
Persev. errors	8.99	14.24	14.99	11.29	14.90	15.22	14.57	11.04	11.35	11.30	**.001***	**.027***	.948	**.001***	**.001***	.964
Non-per.	10.52	16.07	15.21	12.74	16.78	17.17	16.24	13.86	12.10	12.28	**.003***	**.011***	.266	**.023***	**.001***	.481
Conceptual	64.49	20.17	62.95	16.00	60.30	21.56	59.77	16.17	65.39	14.29	.218	**.006***	.820	.554	.081	.344
Categ.comp.	5.60	2.11	4.94	1.67	4.83	2.25	4.76	1.79	5.49	1.55	**.004***	**.001***	.305	**.016***	**.003***	.715
Trials 1st categ.	16.30	32.80	22.04	26.02	30.87	35.06	31.00	31.14	15.14	19.00	**.001***	**.001***	.065	.174	**.001***	.053

Note. SD: standard deviation. HC: healthy controls. BSD: bulimic spectrum disorders. GD: gambling disorder. *Bold: significant parameter. †*p-value*

Regarding the sex factor, differences between men and women were obtained for all the WCST measures, except for WCST trials, men showing a better performance relative to women. Compared to women, men achieved lower scores in SCWT colours, TCI-R harm avoidance and reward dependence, but higher levels in TCI-R persistence.

Multivariate tests also displayed a significant interaction sex-by-group for some variables: IGT block 2 and 4, IGT total, SCWT words and SCWT colours. Single effects were estimated (see Table 3.).

Table 3. Post-hoc comparisons (*p*-value) for the interaction sex-by-group adjusted for age and education

	HC				BSD				GD				Group within sex†						Sex within group†		
	Women		Men		Women		Men		Women		Men		Within women			Within men			HC	BSD	GD
	n=123		*n=27*		*n=37*		*n=22*		*n=32*		*n=127*										
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	BSD HC	GD HC	BSD GD	BSD HC	GD HC	BSD GD	W-M	W-M	W-M
IGT																					
Block 1	-1.12	6.71	-1.23	6.13	-2.44	5.86	-1.71	5.67	-2.61	6.17	-1.54	6.29	.222	.273	.912	.775	.814	.900	.932	.633	.359
Block 2	3.54	8.17	-1.84	7.47	-3.62	7.13	0.17	6.91	-1.94	7.51	1.57	7.66	**.001***	**.001***	.360	.323	**.031***	.396	**.002***	**.042***	**.013***
Block 3	5.14	9.38	3.53	8.58	-0.28	8.19	1.21	7.94	-0.36	8.62	2.82	8.79	**.001***	**.004***	.967	.320	.693	.396	.416	.486	**.050***
Block 4	5.87	10.42	1.14	9.53	-1.51	9.10	2.19	8.82	1.08	9.58	4.39	9.77	**.001***	**.024***	.268	.684	.107	.296	**.031***	.119	.067
Block 5	4.04	10.99	5.53	10.05	-1.72	9.60	0.20	9.30	0.97	10.10	1.51	10.30	**.001***	.169	.276	.052	.059	.556	.519	.443	.778
Total	17.4	29.8	7.3	27.2	-9.6	26.0	2.1	25.2	-2.8	27.4	8.8	27.9	**.001***	**.001***	.312	.479	.801	.266	.106	.087	**.025***
SCWT																					
Words	108.9	18.7	101.5	17.1	106.4	16.3	99.3	15.8	95.5	17.2	102.3	17.5	.415	**.001***	**.009***	.647	.811	.428	.060	.097	**.034***
Colours	75.1	14.5	70.5	13.3	72.3	12.7	64.2	12.3	66.9	13.4	69.7	13.6	.221	**.005***	.100	.082	.758	.064	.133	**.016***	.271
Words-colours	47.2	11.8	47.2	10.8	44.3	10.3	43.1	10.0	42.9	10.8	44.7	11.0	.125	.070	.596	.162	.266	.507	.995	.665	.374
Interference	2.86	9.11	6.05	8.33	1.42	7.95	4.55	7.70	3.76	8.37	3.49	8.53	.329	.626	.252	.508	.146	.563	.096	.132	.863
TCI-R																					
Novelty seeking	98.8	15.8	103.9	14.4	105.0	13.8	103.0	13.3	110.8	14.5	109.6	14.8	**.017***	**.001***	.100	.807	.066	**.039***	.124	.582	.654
Harm avoidance	93.0	20.2	89.9	18.5	122.3	17.6	114.2	17.1	110.5	18.6	100.8	18.9	**.001***	**.001***	**.001***	**.001***	**.005***	**.001***	.460	.079	**.006***
Reward depend.	101.1	16.9	102.1	15.4	103.7	14.7	92.2	14.3	102.9	15.5	98.2	15.8	.353	.596	.849	**.018***	.230	.078	.778	**.003***	.106
Persistence	111.7	21.2	112.0	19.4	100.9	18.5	106.5	17.9	102.3	19.5	112.4	19.9	**.002***	**.030***	.767	.302	.928	.174	.950	.246	**.007***
WCST																					
Trials	90.5	22.0	87.4	20.1	101.9	19.2	99.7	18.6	104.9	20.2	96.6	20.6	**.001***	**.001***	.545	**.025***	**.030***	.482	.505	.666	**.030***
Persev. errors	10.6	12.6	7.4	11.5	16.3	11.0	13.7	10.7	16.8	11.6	13.0	11.8	**.005***	**.015***	.859	**.045***	**.022***	.788	.228	.359	.081
Non-per.	12.1	14.2	8.9	13.0	15.9	12.4	14.5	12.0	20.7	13.1	12.9	13.3	.096	**.003***	.135	.117	.153	.573	.291	.655	**.002***
Conceptual	61.8	17.8	67.1	16.3	60.8	15.6	65.1	15.1	56.6	16.4	64.0	16.7	.729	.148	.291	.643	.363	.765	.160	.300	**.017***
Categ.comp.	5.31	1.86	5.88	1.71	4.74	1.63	5.15	1.58	4.24	1.71	5.43	1.75	.057	**.005***	.237	.114	.208	.455	.144	.331	**.001***
Trials 1st categ.	20.9	29.0	11.7	26.5	27.7	25.3	16.3	24.5	44.4	26.7	17.4	27.2	.147	**.001***	**.011***	.519	.311	.860	.131	.086	**.001***

Note. SD: standard deviation. HC: healthy controls. BSD: bulimic spectrum disorders. GD: gambling disorder. *Bold: significant parameter. †*p-values*

Figure 1 contains the learning curve of each group in the IGT, HCs reporting the best performance. When the two clinical groups were compared, GD displayed a trend toward better performance.

As a summary, Figure 2 illustrates the radar-chart for the variables measuring impulsivity and compulsivity features (z-standardized means are plotted to allow an easier interpretation).

Figure 1. Learning curves in the IGT

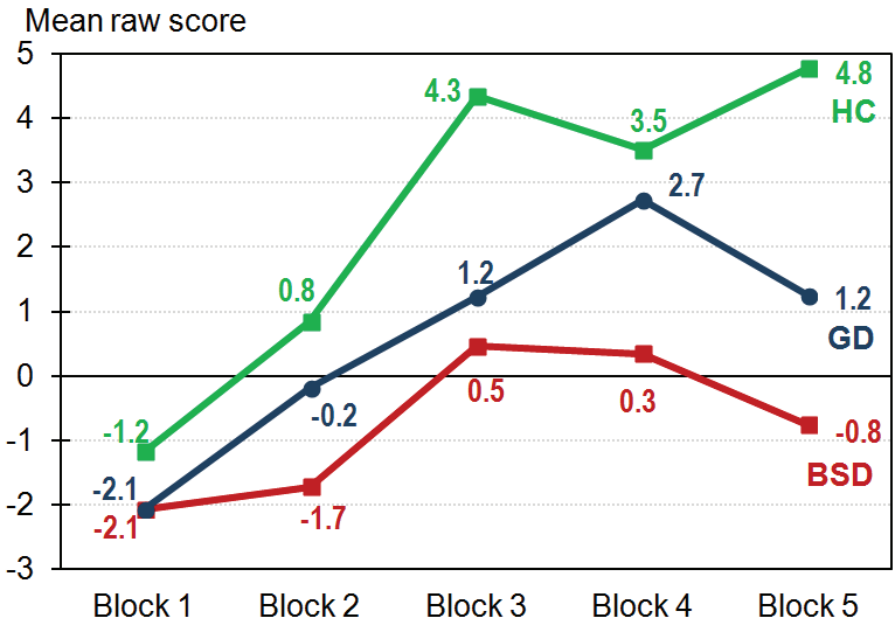
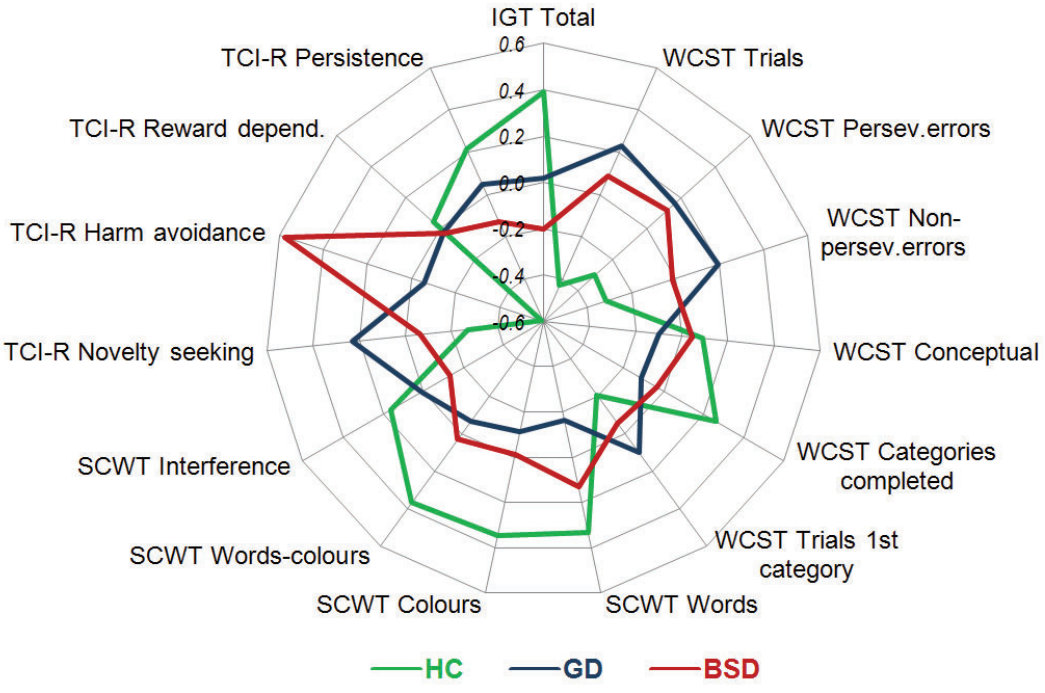


Figure 2. Summary of the results: radar-chart (z-standardized mean scores)



Note. HC: healthy controls. GD: gambling disorder. BSD: bulimic spectrum disorders.

DISCUSSION

In this study we aimed to compare, through self-reported and neurocognitive measures, impulsivity and compulsivity among HCs, GD and BSDs, emphasising the differences and similarities between the two clinical groups. We also aimed to analyse the potential influence of sex in these impulsive and compulsive domains.

Firstly, when exploring general psychopathology, we observed notable differences among the three groups in all the SCL-90-R subscales. In agreement with previous studies [28,40,41], HCs exhibited the lowest levels of global psychopathology and specific symptomatology, while BSD patients displayed the highest levels. This could be interpreted as an increased perception of psychopathological distress in BSDs.

Regarding **choice impulsivity**, our results illustrated that GD and BSD patients had a worse IGT performance than HCs, indicating a reduced capacity to learn the reward/punishment contingencies of their choices [54]. In addition, BSD patients performed slightly worse than patients with GD, demonstrating a trend to more impulsive decision-making. Attending to earlier findings, it was expected that both clinical groups presented difficulties in decision-making [10,11,55]. Evidence also indicates that GD and BSD patients share a preference for immediate rewards (i.e. binging or gambling) regardless of future consequences [56,57]. This might be a reflection? of their increased choice impulsivity, which appears to be slightly enhanced in BSDs. When comparing women and men, significantly increased choice impulsivity was displayed by women only in GD, although BSD women also showed a trend to higher choice impulsivity than men. Previous studies failed to find sex differences in the decision-making of AN patients [34], indicating that sex influences might be only noticeable in ED patients with binge-purging symptoms. Regarding GD, several metanalyses failed to find any sex effect on this domain [55,58], which is likely to be explained by methodological issues (e.g. metanalyses compared female samples to male samples). We also observed that men exhibited similar choice impulsivity regardless of the diagnostic group; however, among women, both clinical groups displayed higher choice impulsivity than HCs. Altogether, our results indicate that enhanced choice impulsivity might be highlighted only in female patients.

Another dimension of impulsivity examined in this work was **response impulsivity**. Our results revealed that both clinical groups showed lower inhibitory control than HCs, as observed in the SCWT word-colour scores. Recent research also remarked significant inhibitory control deficits in GD and BSDs [17,18,22], and the only study which compared both disorders also found analogous outcomes [35]. These similarities in response impulsivity found in GD and BSDs, may be related to common underlying processes involving impairments in behavioural inhibition systems [3]. Finally, women and men did not differ in inhibitory control, neither in the whole sample nor within each clinical group. There is no research in BSDs exploring sex differences in inhibitory control, and very little evidence examined these effects in GD, presenting similar evidence to this work [44,58].

The results of this work also illustrated that, in terms of **impulsive personality traits**, patients with GD showed the highest levels of novelty seeking in the TCI-R, differing from BSD patients and HCs. In addition, BSD patients showed lower levels of persistence compared to HCs. It is noted that, although BSDs are considered to be the EDs with the highest impulsive personality [24,25], BSD patients displayed similar novelty seeking to HCs. Our finding is consistent with former investigations [25,28,38,39], and suggests that novelty seeking might not be a core factor of impulsive personality in BSDs, other traits being more relevant such us low persistence. As a whole, these findings give support to previous research [26,28,39–41] and uphold the notion that impulsive personality in GD and BSDs appears to be from a different nature, high novelty seeking being the distinctive trait in GD, and low persistence in BSDs. Concerning sex, no differences in novelty seeking were found within the clinical groups, although lower persistence was displayed by women in the GD group. Prior studies in GD and EDs partially support our findings, since no sex differences were yielded in any of these impulsive traits [42,43]. In addition, although earlier studies reported novelty seeking differences between GD and BSDs in both sexes [38–41], our study only displayed differences among men. This might indicate that, regarding impulsive traits, GD and BSDs may be more closely associated in females than in males. However, future research exploring sex differences in these disorders would be required to make solid assumptions.

Another finding to emerge from the present study are the differences in **cognitive flexibility**. Compared to HCs, patients with GD and BSDs displayed a worse performance in

most measures of the WCST, including perseverative errors, meaning less cognitive flexibility and more compulsivity. This outcome is in line with previous research [10,33,35,36,59–61] and might explain the inability of GD and BSD patients to learn from mistakes and handle negative affect, increasing loss of control over gambling or eating [62–65]. Contrary to our hypothesis, we did not succeed in identifying greater cognitive flexibility impairments in GD compared to BSDs. A former work had revealed such results [35], although they were considered preliminary, due to the fact that the sample was considerably small and only included females. Since comparative studies of compulsivity in BSDs and GD are extremely scarce, solid conclusions still cannot be made. Focusing on sex effects, worse cognitive flexibility in females than males was observed in the whole sample. Nevertheless, when examining each diagnostic group, this pattern only remained present in the GD group. Only a prior study had explored sex differences in compulsivity between women and men with GD, showing similar results [44]. Moreover, when comparing GD and BSDs within each sex, the clinical groups showed lower cognitive flexibility than HCs in both sexes. As a whole, these results reveal that females with GD appear to have more compulsivity features in common with BSD females than with GD males.

Regarding **compulsive personality traits**, differences in harm avoidance were observed among all three groups, with BSD patients showing the highest scores, followed by GD patients. Our findings dovetail with previous reports and uphold that compulsive traits are a distinguishing feature in these pathologies [38], especially in BSDs [26,28]. Therefore, the elevated compulsivity noted in these pathologies is likely to underlie the use of abnormal behaviours (e.g. binge eating, compensatory purging, gambling) with the aim of avoiding negative affect and relieving emotional distress [5,6]. Finally, when we explored sex effects on harm avoidance, higher scores were displayed by women in the overall sample and within the GD group. These results are in line with previous research [43] and with our findings in cognitive flexibility, indicating that GD women may differ from GD males and present a specific profile characterised by higher compulsivity. These findings could be indirectly related to the increased emotion regulation difficulties found in women with GD when compared to male patients [66]. Finally, differences among all three groups emerged when exploring women and men separately. As observed in the overall sample, the highest harm

avoidance was displayed by BSDs, followed by GD. These results indicate that high levels of compulsive traits are noticeable in both GD and BSD patients regardless of their sex, being significantly highlighted in female and male patients with BSDs.

These findings should be interpreted in light of some limitations. Firstly, our study sample comprised mostly young adults, not allowing for generalisation to older populations. Moreover, although results have been controlled for age and education, other confounding variables might be affecting. The subgroup sizes are relatively large but not evenly distributed. This study also included participants receiving pharmacotherapy without considering its potential influence. Lastly, the cross-sectional nature of this study does not allow for cause-effect inferences.

CONCLUSIONS

In conclusion, GD and BSDs seem to be distinguished by elevated levels of impulsivity and compulsivity in all the dimensions, showing differences in some domains mainly related to personality. In this regard, these pathologies show distinct impulsive personality traits, such as high novelty seeking in GD and low persistence in BSDs. Moreover, BSDs are characterised by higher compulsive personality traits as well as a trend towards greater impulsive choice. Given the lack of neuropsychological and clinical studies comparing GD and BSDs, future research would be needed to consolidate our findings. Nevertheless, clinical interventions should consider these deficits to enhance their effectiveness, for instance, including adjunctive treatment to target these difficulties, such as inhibitory control training [67], emotion regulation training [68] or cognitive remediation therapy [69]. Finally, it seems that GD women present higher difficulties than GD men in almost all the impulsivity and compulsivity components, displaying in some cases more similarities with BSD women than with GD men. This finding is in line with former research providing support to the relevance of sex in GD [70], which should also be considered in clinical interventions.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest. The funders had no role in the design of the study; in the collection, analyses or interpretation of data; in the writing of the manuscript or in the decision to publish the results.

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ESTUDIO 4

IMPULSIVITY, EMOTIONAL DYSREGULATION AND EXECUTIVE FUNCTION DEFICITS COULD BE ASSOCIATED WITH ALCOHOL AND DRUG ABUSE IN EATING DISORDERS

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Objetivos:

Comparar las características de impulsividad y compulsividad de los pacientes con TCA que presentan síntomas de abuso de alcohol y/o drogas y aquellos pacientes con sólo TCA.

RESUMEN

La evidencia señala una alta comorbilidad entre los TCA y los trastornos relacionados con sustancias. Estos trastornos también comparten numerosas características clínicas y neurológicas. Sin embargo, hasta el momento no se han investigado las características neuropsicológicas de aquellos pacientes que presentan esta comorbilidad. Este estudio comparó, mediante medidas clínicas y neuropsicológicas, las características de impulsividad y compulsividad de pacientes con TCA con y sin síntomas de abuso de alcohol y/o drogas. Para ello, 145 participantes (74,5% mujeres) diagnosticados con algún subtipo de TCA se sometieron a una evaluación clínica y neuropsicológica. Aquellos pacientes con TCA que presentaban síntomas de abuso de alcohol y/o drogas, mostraron mayor personalidad impulsiva (i. e., alta búsqueda de la novedad), una toma de decisiones más impulsiva, y menor flexibilidad cognitiva que los pacientes sin esta sintomatología. También presentaron mayores niveles de somatización y dificultades para reconocer sus propias emociones y sensaciones. En conclusión, parece que los pacientes con TCA se distinguirían por presentar un fenotipo específico caracterizado por una mayor impulsividad rasgo, mayor disregulación emocional y mayores daños en distintas funciones ejecutivas relacionadas con la impulsividad de elección y la compulsividad. Los pacientes con estas características podrían correr un mayor riesgo de desarrollar en un futuro un trastorno de abuso de sustancias.

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Article

Impulsivity, Emotional Dysregulation and Executive Function Deficits Could Be Associated with Alcohol and Drug Abuse in Eating Disorders

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Abstract: Background: Empirical data suggests a high comorbid occurrence of eating disorders (EDs) and substance use disorders (SUDs), as well as neurological and psychological shared characteristics. However, no prior study has identified the neuropsychological features of this subgroup. This study examines the prevalence of alcohol and/or drug abuse (A/DA) symptoms in ED patients. It also compares the clinical features and neuropsychological performance of ED patients with and without A/DA symptoms. Methods: 145 participants (74.5% females) with various forms of diagnosed EDs underwent a comprehensive clinical (TCI-R, SCL-90-R and EDI-2) and neuropsychological assessment (Stroop, WCST and IGT). Results: Approximately 19% of ED patients (across ED subtypes) had A/DA symptoms. Those with A/DA symptoms showed more impulsive behaviours and higher levels of interoceptive awareness (EDI-2), somatisation (SCL-90-R) and novelty seeking (TCI-R). This group also had a lower score in the Stroop-words measure, made more perseverative errors in the WCST and showed a weaker learning trajectory in the IGT. Conclusions: ED patients with A/DA symptoms display a specific phenotype characterised by greater impulsive personality, emotional dysregulation and problems with executive control. Patients with these temperamental traits may be at high risk of developing a SUD.

Keywords: eating disorder; alcohol and/or drug abuse; substance use disorder; executive functions; impulsivity; emotional dysregulation

1. Introduction

Eating disorders (EDs) are mental illnesses characterized by abnormal eating behaviours, which normally lead to significant impairments in physical health and psychosocial functioning [1]. EDs often co-occur with other untreated mental conditions such as substance use disorders (SUDs) [2], summarised as the inability to control the usage or craving of substances despite problems related to their use [1]. A recent meta-analysis of 43 studies estimated that the lifetime prevalence of any SUD among adults with EDs is 25.4%, with tobacco, caffeine and alcohol most commonly abused [2]. The prevalence of substance abuse varies according to demographic factors (e.g., age, sex, ethnicity) and ED diagnostic subtype [2–4]. According to the above-mentioned meta-analysis [2], the lifetime prevalence of SUDs seems to be higher in female-sample studies (26%) compared to mixed studies (15%), in adult populations (26%) compared to young adults (19%) and in primarily Caucasian samples (24%) compared to Asian samples (7%). Similarly, several studies have reported a stronger association between substance abuse and bulimia nervosa (BN) compared to anorexia nervosa (AN) [3,4]. Overall, it seems that those ED patients with purging behaviours are at higher risk of developing a comorbid SUD [2,5].

This comorbidity might be due to shared biological and psychological endophenotypes [6]. Genetic studies reveal that EDs and SUDs share overlapping genetic risk factors, especially those ED subtypes characterized by binge-purge behaviours [7,8]. Personality traits such as impulsivity are also shared [9–11], as are the elevated rates of psychopathology (especially social anxiety, antisocial behaviour, and cluster B and C personality disorders) and emotional dysregulation [12–14]. Neuropsychological impairments are another common feature [15–27], especially in executive functions (i.e., high-level cognitive processes implicated in the formation of successful goal-directed behaviours [28]). Difficulties in decision-making, cognitive flexibility and inhibitory control have been reported in all ED subtypes [15–20], as well as in SUD patients [21–27]. However, no studies have explored neuropsychological performance in ED patients with substance abuse comorbidity.

Empirical data on the comorbidity of EDs and SUDs, as well as their biological and psychological shared characteristics are available. However, there are no prior studies which have assessed the neuropsychological profile in ED patients with substance abuse symptomatology. Identifying these neuropsychological features might help to develop specific treatments that target these deficits with the purpose of preventing the later evolution into a SUD. As such, the first aim of this study was to examine the prevalence of alcohol and/or drug abuse (A/DA) symptoms in a heterogeneous series of ED patients. Our hypothesis was that A/DA symptoms would be most common in those with binge-purge behaviours. A second aim was to compare clinical (i.e., eating symptomatology, general psychopathology and personality traits) and neuropsychological features (i.e., decision-making, cognitive flexibility and inhibitory control) of patients with or without A/DA symptoms. Our hypothesis was that ED patients with A/DA symptoms will display higher impulsivity and emotional dysregulation, along with poorer executive functions.

2. Materials and Methods

2.1. Participants

The total sample comprised of 145 participants (74.5% females) aged between 18 and 60 years old. All participants were diagnosed with an ED by experienced clinicians according to the DSM-5 diagnostic criteria [1]. The final sample included: AN-restrictive subtype [AN-R] (n = 57), AN-binge/purge subtype [AN-BP] (n = 26), BN (n = 28), binge eating disorder [BED] (n = 22) and other specified feeding or eating disorder [OSFED] (n = 12).

Participants were recruited at the *Eating Disorders Unit* within the Department of Psychiatry at Bellvitge University Hospital (Barcelona, Spain), where they were receiving outpatient treatment. All participants were informed about the research procedures and gave their informed consent in writing. Procedures were approved by the Ethical Committee of the above-mentioned institution in accordance with the Helsinki Declaration of 1975 as revised in 1983 (reference: PR146/14). Exclusion

criteria were the following: (1) history of chronic medical illness or neurological condition that might affect cognitive function; (2) head trauma with loss of consciousness for more than 2 min, learning disability or intellectual disability; (3) use of psycho-active medications or drugs; (4) age under 18 or over 60 (to discard neuropsychological deficits associated with the age).

2.2. Procedure and Assessment

As part of the protocol, all patients who arrived at the *Eating Disorders Unit* seeking treatment for an ED were assessed by experienced clinicians using a semi-structured clinical interview based on the DSM-5 diagnostic criteria [1]. All patients consecutively diagnosed with an ED were screened for the inclusion criteria of the study. Those who met the criteria and voluntarily accepted to be part of the study underwent a comprehensive neuropsychological and clinical assessment within the first week of their outpatient treatment. Weight and Body Mass Index (BMI) were measured for all subjects on the day of assessment. Additional sociodemographic information was also taken. The neuropsychological tests were selected to cover various aspects of executive functions including decision-making, response inhibition, strategic planning and cognitive flexibility and were administered by a trained psychologist in a single session and in a randomised order. Finally, information regarding the presence or absence of impulsive behaviours (including alcohol abuse, drugs abuse, binge episodes, theft, kleptomania and compulsive buying) was taken from the semi-structured clinical interview. The presence of A/DA symptoms was defined as the confirmation of current or lifetime behaviours of alcohol abuse, illicit drug abuse or both, causing significant distress or impairments in daily functioning.

2.2.1. Psychopathological/Personality Measures

Semi-structured clinical interview: This interview is based on the ED module of the Structured Clinical Interview for DSM-5 (SCID-5 [29]) and is used to ascertain the presence of a current ED according to the DSM-5 criteria. It provides specific information regarding the symptomatology and course of the ED. It also includes other questions in relation to the impulsive behaviours frequently found in ED patients, such us alcohol abuse, drug abuse, theft, compulsive buying, etc.

The *Temperament and Character Inventory-Revised* (TCI-R [30]; Spanish validation [31]) is a reliable and valid 240-item questionnaire that measures seven personality dimensions: four temperament dimensions (novelty seeking, harm avoidance, reward dependence and persistence) and three about character (self-directedness, cooperativeness and self-transcendence). The scales in the revised version showed a mean internal consistency of 0.87 (α coefficient).

The *Symptom Checklist-90 Revised* (SCL-90-R [32]; Spanish validation [33]) is a 90-item questionnaire which evaluates psychopathological symptoms; these are grouped as follows: somatization, obsessive-compulsive, interpersonal sensitive, depression, anxiety, hostility, phobic anxiety, paranoia and psychotic. It also includes a global severity index (GSI), designed to measure overall psychological distress. This instrument has demonstrated satisfactory psychometric properties in the Spanish version, obtaining a mean internal consistency of 0.75 (α coefficient).

The *Eating Disorders Inventory-2* (EDI-2 [34]; Spanish validation [35]) is a 91-item self-report questionnaire that assesses the following ED factors: drive for thinness, bulimia, body dissatisfaction, ineffectiveness, perfectionism, interpersonal distrust, interoceptive awareness, maturity fears, asceticism, impulse regulation and social insecurity. This instrument was validated in a Spanish population with a mean internal consistency of 0.63 (α coefficient).

2.2.2. Neuropsychological Measures

The Stroop Colour and Word Test (SCWT [36]; Spanish version [37]) is an extensively used neuropsychological test to assess inhibitory control (including response inhibition and interference control). It consists of three different lists: a word list containing the names of colours printed in black ink, a colour list that comprises letter Xs printed in colour and a colour-word list comprised of names of colours in a colour ink that does not match the written name. Three final scores are obtained

based on the number of items that the participant is able to read on each of the three lists in a time window of 45 s. An interference score is computed from all three lists. A higher score is interpreted as better inhibitory control.

The Wisconsin Card Sorting Test (WCST [38]) is a computerized set-shifting task for assessing cognitive flexibility. It includes 128 cards that vary according to three attributes: number (N), colour (C) and shape (S). The participant has to pile the cards beneath four reference cards that also vary along these same dimensions, and in order to succeed, they have to settle upon a predetermined sorting rule. The only feedback given to the participant is the word "right" or "wrong" after each sorting. Initially, C is the correct sorting category, and positive feedback is given only if the card is placed in the pile with the same colour. After 10 consecutive correct sorts, the rule changes. Thus, the positive feedback is only given when the sorting matches the new category. By trial and error, the participant must learn to change the sorting categories according to the given feedback. There are up to six attempts to derive a rule, providing rule shifts in the following category sequence: C-S-N-C-S-N. Participants are not informed of the correct sorting principle and that the sorting principle shifts during the test. The test is completed when all 128 cards are sorted or after the six full categories are completed. The number of completed categories, the percentage of perseverative errors (i.e., failures to change sorting strategy after negative feedback) and the percentage of non-perseverative errors are recorded.

The Iowa Gambling Task (IGT [39]) is a computerized task to evaluate decision-making, which has also been proposed as a measure of choice impulsivity [40]. It involves a total of 100 turns distributed across four decks of cards (A, B, C and D), and each time the participant selects a deck, a specified amount of play money is awarded. The interspersed rewards among these decks are probabilistic punishments (monetary losses with different amounts). Participants are instructed that the final aim of the task is to win as much money as possible and to avoid losing as much money as possible. Moreover, they may choose cards from any deck, and switch decks at any time. This test is scored by subtracting the number of cards selected from decks A and B from the number of cards selected from decks C and D. Decks A and B are not advantageous as the final loss is higher than the final gain; however, decks C and D are advantageous since the punishments are smaller. Higher scores indicate better performance on the task.

2.3. Statistical Analyses

Statistical analysis was carried out with Stata16 for Windows [41]. The comparisons between the groups with and without A/DA symptoms were based on T-TEST procedures for quantitative variables and chi-square tests (χ^2) for categorical variables. The effect size of the mean differences in the clinical variables was estimated with Cohen's-*d* coefficient, considering null effect for $|d| < 0.20$, low-poor for $|d| > 0.20$, moderate-medium for $|d| > 0.5$ and large-high for $|d| > 0.8$ [42]. The significance tests were complemented with other standardised measures of the effect size: partial eta-squared coefficients (η^2), which measures the proportion of the total variance in a criterion associated with the membership of the different groups, defined by the independent variable once the potential effects of other predictors and interactions are partialled out (in one way ANOVA, eta-squared and partial eta-squared come out the same, but in multivariate ANOVA, their values differ). The comparisons between the proportions were based on the Cohen's-*h* coefficient, a standardised measure of the distance between the proportions obtained in two groups; it is estimated as the difference of the arcsine transformation for the two probabilities [43]. In addition, and due the multiple statistical comparisons performed on the clinical and neuropsychological variables, Finner-correction was used to control the increase in the Type-I error [44]. Finner-method uses a stepwise multiple comparisons procedure, which solves the monotonicity of the critical values by means of an inequality for the distribution function of the statistic range, using the principle of family-wise Type I correction. The post-hoc power calculation was also conducted for each observed effect based on the sample size and the parameter estimates, defining an alpha value $\alpha = 0.05$.

A 2 × 5 mixed analysis of variance was obtained to analyse the learning curve in the IGT test. For this analysis, the group was defined as the between-subjects factor (2 levels: with versus without A/DA) and the IGT-block as the within-subjects factor (5 levels: blocks 1 to 5). Tests of within-subjects included polynomial contrasts for assessing the presence of trends in the mean estimates (linear, quadratic, cubic and order-4). Effect size of the parameter estimates were assessed with eta-squared values (η^2).

3. Results

3.1. Characteristics of the Sample

Most participants were women (108, 74.5%), born in Spain (130, 89.7%) and single (105, 72.4%). Mean chronological age was 30.3 years (SD = 10.3), age of ED onset was 22.7 years (SD = 9.1) and duration of the ED symptoms 7.7 years (SD = 7.4). The prevalence of impulsive behaviours was 43.1% for binges episodes, 18.6% for theft, 3.4% for kleptomania and 11.0% for compulsive buying. No participants reported instances of problematic gambling behaviours.

Table 1 shows the comparison between the groups with and without A/DA symptoms. Statistical differences were found for the presence of impulsive behaviours (higher prevalence among patients with A/DA).

Table 1. Descriptive of the sample.

		Without A/DA		**With A/DA**		*p*
		***n* = 118**		***n* = 27**		
		n	**%**	***n***	**%**	
Sex	Women	88	74.6%	20	74.1%	0.957
	Men	30	25.4%	7	25.9%	
ED subtype	Anorexia restrictive	49	41.5%	8	29.6%	0.751
	Anorexia binge/purge	20	16.9%	6	22.2%	
	Bulimia	21	17.8%	7	25.9%	
	Binge eating disorder	18	15.3%	4	14.8%	
	Other specified feeding eating dis.	10	8.5%	2	7.4%	
Education	Primary	30	25.4%	10	37.0%	0.438
	Secondary	52	44.1%	11	40.7%	
	University	36	30.5%	6	22.2%	
		Mean	SD	Mean	SD	*p*
Age (years-old)		30.30	10.13	30.56	11.22	0.907
Onset of the ED (years-old)		22.94	8.99	21.59	9.83	0.491
Duration of the ED (years)		7.36	7.58	8.96	6.72	0.312
BMI (kg/m^2)		21.70	8.47	22.50	8.87	0.663
Other impulsive behaviours		*n*	%	*n*	%	*p*
Binges episodes		46	39.3%	16	59.3%	0.049 *
Theft		18	15.3%	9	33.3%	0.029 *
Kleptomania		2	1.7%	3	11.1%	0.045 *
Compulsive buying		10	8.5%	6	22.2%	0.040 *

A/DA: alcohol and/or drugs abuse symptoms. ED: eating disorder. BMI: body mass index. SD: standard deviation. *: significant comparison (0.05 level).

3.2. Prevalence of A/DA in ED Patients

The number of patients with A/DA symptoms was 27 (prevalence = 18.6%). Table 2 compares prevalence estimates between ED subtypes and gender. No differences by gender (women (18.5%) and men (18.9%) ($\chi^2 = 0.01$, $df = 1$, $p = 0.957$)) or subtype (14.0% for AN-R, 23.1% for AN-BP, 25.0% for BN,

18.2% for BED and 16.7% for OSFED ($\chi^2 = 1.92$, $df = 4$, $p = 0.751$)) were found. The highest effect size for the comparison between AN-R and BN was a Cohen's-h into the low range $|h| = 0.28$.

Table 2. Prevalence estimate of A/DA depending on ED subtype and gender.

Total		AN-R		AN-BP		BN		BED		OSFED		Women		Men	
n = 145		*n* = 57		*n* = 26		*n* = 28		*n* = 22		*n* = 12		*n* = 108		*n* = 37	
n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
27	18.6%	8	14.0%	6	23.1%	7	25.0%	4	18.2%	2	16.7%	20	18.5%	7	18.9%
	χ^2	1.92	(*df* = 4)									0.01	(*df* = 1)		
	p	0.751										0.957			

AN-R: anorexia restrictive. AN-BP: anorexia binge/purge. BN: bulimia. BED: binge eating disorder. OSFED: other specified feeding eating disorder. df: degrees of freedom.

3.3. Comparison of the Clinical and Neuropsychological Profile of Patients with and without A/DA

Table 3 compares the clinical measures of patients with and without A/DA symptoms. Those with A/DA had higher levels of interoceptive awareness (EDI-2), somatisation (SCL-90-R) and novelty seeking (TCI-R). Internal consistency in the sample of the study was between good to excellent for all the psychometrical scales (Cronbach's alpha values).

Table 3. Comparison of the clinical profile between groups with and without A/DA.

		Without A/DA		With A/DA					
	α	*n* = 118		*n* = 27		*p*	|*d*|	η^2	Power
		Mean	SD	Mean	SD				
EDI Drive for thinness	0.846	11.24	6.65	12.10	6.50	0.544	0.13	0.003	0.093
EDI Body dissatisfaction	0.922	13.35	8.86	15.66	7.70	0.213	0.28	0.011	0.237
EDI Interoceptive awareness	0.868	8.98	7.13	12.10	5.95	0.036 *	0.52 †	0.030	0.556
EDI Bulimia	0.791	4.92	5.20	6.51	4.83	0.148	0.32	0.015	0.303
EDI Interpersonal distrust	0.824	5.59	4.84	5.92	4.47	0.752	0.07	0.001	0.061
EDI Ineffectiveness	0.905	8.61	6.89	10.78	6.91	0.142	0.32	0.015	0.312
EDI Maturity fears	0.841	7.54	5.08	7.58	5.89	0.975	0.01	0.001	0.050
EDI Perfectionism	0.842	5.31	4.40	5.16	4.54	0.878	0.03	0.001	0.053
EDI Impulse regulation	0.850	5.43	5.85	5.60	4.43	0.886	0.03	0.001	0.052
EDI Ascetic	0.703	5.99	4.37	6.92	3.76	0.307	0.23	0.007	0.175
EDI Social insecurity	0.825	6.37	5.17	7.28	5.72	0.417	0.17	0.005	0.127
EDI Total score	0.974	83.33	48.73	95.62	42.19	0.228	0.27	0.010	0.225
SCL-90R Somatization	0.857	1.45	0.90	1.82	0.77	0.049 *	0.44	0.026	0.497
SCL-90-R Obsessive-compulsive	0.909	1.57	0.98	1.78	0.89	0.308	0.22	0.007	0.174
SCL-90-R Interpersonal sensitive	0.912	1.76	1.04	1.94	0.91	0.416	0.18	0.005	0.128
SCL-90-R Depression	0.946	2.00	1.05	2.21	0.82	0.329	0.22	0.007	0.164
SCL-90-R Anxiety	0.911	1.38	0.95	1.66	0.74	0.145	0.34	0.015	0.307
SCL-90-R Hostility	0.774	1.17	0.88	1.25	0.97	0.672	0.09	0.001	0.071
SCL-90-R Phobic anxiety	0.854	0.78	0.87	0.86	0.73	0.667	0.10	0.001	0.072
SCL-90-R Paranoia	0.875	1.27	0.89	1.32	0.81	0.821	0.05	0.001	0.056
SCL-90-R Psychotic	0.893	1.17	0.77	1.28	0.67	0.529	0.14	0.003	0.096
SCL-90-R GSI	0.980	1.50	0.82	1.69	0.68	0.257	0.26	0.009	0.204
SCL-90-R PST	0.980	56.61	19.91	63.15	17.64	0.119	0.35	0.017	0.345
SCL-90-R PSDI	0.980	2.20	0.66	2.32	0.42	0.383	0.21	0.005	0.140
TCI-R Novelty seeking	0.797	94.68	13.80	103.37	13.83	0.004 *	0.63 †	0.057	0.834
TCI-R Harm avoidance	0.925	112.31	20.84	116.07	21.50	0.402	0.18	0.005	0.133
TCI-R Reward dependence	0.700	101.21	15.47	102.56	17.33	0.691	0.08	0.001	0.068
TCI-R Persistence	0.860	114.12	20.30	107.33	24.13	0.133	0.30	0.016	0.323
TCI-R Self-directedness	0.908	125.72	21.84	119.33	24.19	0.181	0.28	0.012	0.266
TCI-R Cooperativeness	0.831	136.66	17.28	135.89	15.97	0.832	0.05	0.001	0.055
TCI-R Self-transcendence	0.893	63.16	15.28	63.37	18.91	0.951	0.01	0.001	0.050

SD: standard deviation. Cronbach's alpha in the sample. *: significant comparison (0.05 level). †: effect size into the moderate ($|d| > 0.50$) to high range ($|d| > 0.80$). *p*-values with Finner-correction.

Table 4 shows the comparison of the neuropsychological profile. Higher scores in perseverative errors (WCST) and in the first block of the IGT and lower scores in the Stroop-words measure were found.

Table 4. Comparison of the neuropsychological profile between groups with and without A/DA.

	Without A/DA		With A/DA		p	$\|d\|$	η^2	Power
	n = 118		n = 27					
	Mean	SD	Mean	SD				
Stroop Words	104.43	19.39	95.61	24.53	0.045 *	0.40	0.028	0.521
Stroop Colour	75.84	16.06	80.24	19.74	0.221	0.24	0.010	0.231
Stroop Words-colour	48.27	11.75	46.50	9.33	0.467	0.17	0.004	0.112
Stroop Interference	5.09	8.99	4.42	7.92	0.725	0.08	0.001	0.064
WCST Total trials	94.42	20.72	100.55	20.70	0.168	0.30	0.013	0.280
WCST Correct	67.83	10.87	68.06	14.02	0.924	0.02	0.001	0.051
WCST Perseverative errors	12.40	10.33	18.54	19.41	0.023 *	0.39	0.036	0.629
WCST Non-perseverative errors	14.20	15.25	14.22	11.91	0.993	0.01	0.001	0.050
WCST Conceptual	60.64	16.54	59.18	19.97	0.692	0.08	0.001	0.068
WCST Categories completed	5.10	1.80	4.88	1.98	0.577	0.12	0.002	0.086
WCST Trials completed 1st categ.	20.36	24.17	26.73	31.78	0.248	0.23	0.009	0.210
IGT Block 1	−2.59	4.21	−0.62	2.84	0.023 *	0.55 †	0.036	0.629
IGT Block 2	−1.11	4.91	0.32	4.41	0.165	0.31	0.013	0.284
IGT Block 3	0.29	5.80	−1.39	3.55	0.152	0.35	0.014	0.298
IGT Block 4	0.38	6.69	0.68	6.67	0.834	0.04	0.001	0.055
IGT Block 5	0.51	7.78	0.06	5.42	0.777	0.07	0.001	0.059
IGT Total	−2.52	20.79	−0.95	11.51	0.704	0.09	0.001	0.067

SD: standard deviation. *: significant comparison (0.05 level). †: effect size into the moderate ($|d| > 0.50$) to high range ($|d| > 0.80$). p-values with Finner-correction.

The results of the mixed ANOVA obtained to analyse the learning curve in the IGT showed a quasi-significant interaction parameter IGT-by-Group ($F_{(3.42;488.5)} = 2.02$, $p = 0.091$, $\eta^2 = 0.014$; Greenhouse–Geisser adjusted) as well as a main effect of the IGT-block ($F_{(3.42;488.5)} = 2.65$, $p = 0.041$, $\eta^2 = 0.018$). Figure 1 shows the adjusted mean net scores in the blocks, showing a learning trajectory only for patients without A/DA symptoms: Among this group, polynomial contrasts for the IGT-block showed a significant linear trend ($F_{(1;117)} = 18.3$, $p < 0.001$, $\eta^2 = 0.135$) and a significant quadratic trend ($F_{(1;117)} = 6.97$, $p = 0.009$, $\eta^2 = 0.056$), while non-significant results were found for the cubic ($F_{(1;117)} = 0.01$, $p = 0.931$ $\eta^2 = 0.001$) and order 4 ($F_{(1;117)} = 0.59$, $p = 0.442$, $\eta^2 = 0.005$) trends. In patients without A/DA symptoms, post-hoc pairwise comparisons defining the difference-type contrasts (based on comparing each block with the previous) showed statistical differences between blocks 2 versus block 1 ($p = 0.008$) and block 3 versus block 2 ($p = 0.011$), while no statistical differences were found between blocks 4 versus block 3 ($p = 0.886$) and block 5 versus block 4 ($p = 0.832$). However, patients with A/DA symptoms did not have significant results (linear: $F_{(1;26)} = 0.27$, $p = 0.607$, $\eta^2 = 0.010$; quadratic: $F_{(1;26)} = 0.06$, $p = 0.815$, $\eta^2 = 0.002$; cubic: $F_{(1;26)} = 0.01$, $p = 0.988$, $\eta^2 = 0.001$; order 4: $F_{(1;26)} = 2.30$, $p = 0.141$, $\eta^2 = 0.081$). No statistical differences were found in the post-hoc pairwise comparisons comparing the IGT blocks among patients who reported the presence of A/DA.

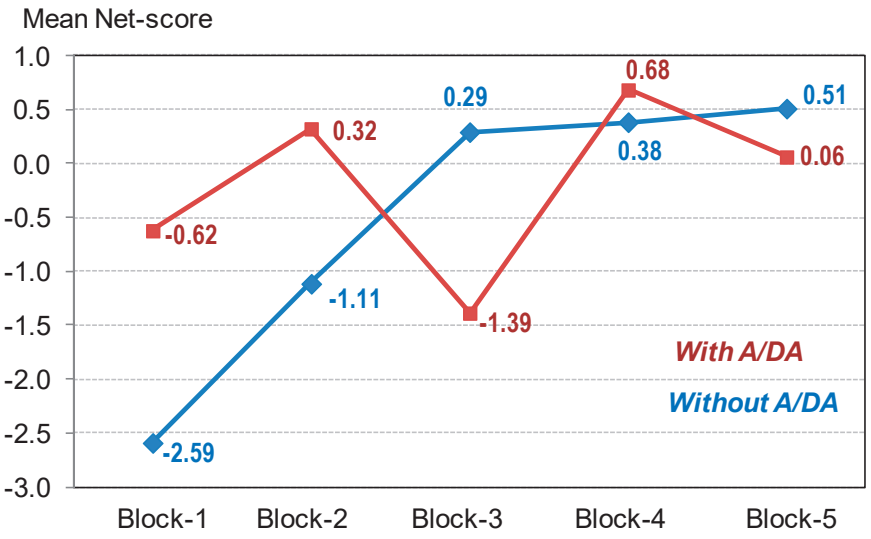

Figure 1. Learning curve in the IGT measure. Note. A/DA: alcohol and/or drug abuse. Sample size: $n = 145$.

4. Discussion

The first aim of this study was to assess the prevalence of A/DA symptoms in a sample of patients across the range of ED diagnoses. The lifetime A/DA prevalence was similar to that found previously in ED patients [2], although slightly lower. This small difference could be explained by the fact that we only assessed symptoms of alcohol and illicit drugs abuse, whereas previous studies considered other substances such as tobacco and caffeine [2]. Although this study had insufficient power to detect differences between subtypes, the trends were in the same direction as previous studies, with BN patients showing the highest prevalence [2–5] and those with AN-BP higher than those with AN-R [45], confirming our first hypothesis based on previous studies. We failed to find the gender difference in prevalence observed in a previous systematic review [2]; however, this might be a question of low power and methodology. While our study compares female and male patients within the same sample, Bahji et al. [2] compared the prevalence observed in female sample studies to mixed studies.

When comparing the clinical profile, the A/DA group scored higher on interoceptive awareness subscale (EDI-2), which indicates a poorer ability to recognise and differentiate between hunger and satiety and emotional states [34]. In ED patients, emotional dysregulation is associated with difficulties in controlling impulsive behaviours (e.g., compulsive binging, purging and overeating) in both negative and positive states [46,47], and this may lead to abuse of alcohol and drugs [13,14]. Indeed, the weaker interoceptive awareness previously found in individuals with BN [48] may explain their higher vulnerability to develop comorbid A/DA symptoms [3,4].

Moreover, the A/DA group had higher levels of somatisation (SCL-90-R), the experience of psychological distress in the presence of unexplained physical symptoms [49]. It is suggested that patients experiencing high levels of somatising symptoms use substances to numb uncomfortable experiences [49]. Furthermore, somatising symptoms are closely associated with symptoms of substance intoxication or withdrawal, but whether they are a cause or effect of substance abuse remains unclear [50]. In any case, our results seem to reflect this association between somatising and substance abuse symptoms, yet longitudinal studies would be needed to clarify the direction of these interactions.

The group with A/DA symptoms had higher scores for the novelty seeking trait (TCI-R), mainly related to impulsivity [30]. Our findings align with other neurobehavioural research, which suggests that novelty seeking is associated with vulnerability to substance abuse [10,11] and with the finding of a higher prevalence of binge episodes, theft, kleptomania and compulsive buying in this subgroup. Strong associations among all the impulsive behaviours mentioned above are documented in the literature. For instance, ED patients who engage in binge-purge behaviours frequently display high

prevalence of SUD [2–5,45] and compulsive buying [51,52]. Similarly, several studies have reported high rates of SUDs in individuals with kleptomania and compulsive buying [53,54].

The neuropsychological assessment results revealed that ED patients with A/DA symptoms display significantly lower scores in the Stroop-words measure, demonstrating a poorer reading ability in terms of speed and accuracy [36]. Contrary to expectations, no differences between groups were found in the Stroop-interference measure, meaning no differences in inhibitory control [36]. Impairments in inhibitory control are found to be a core deficit among binge/purge-type EDs [15,16] and SUDs [21,23], especially when examining stimuli related to each disorder (e.g., food, body shape, use of substances, etc.) [15,55,56]. Since inhibitory deficits seem to represent a risk factor for the development of both disorders separately, we expected to find greater inhibitory control impairments when both disorders co-occur. The fact that we failed to find this result might be explained because of the limited statistical power of this study. Further studies with larger samples are needed to clarify this issue.

In addition, patients with A/DA symptoms made more perseverative errors (WCST). Previous research demonstrated that individuals with EDs perform worse on set-shifting tasks than healthy individuals, which translates to poorer cognitive flexibility and higher rigidity [17,18]. Reduced cognitive flexibility has also been observed in individuals with SUDs, which may negatively impact on their problem-solving strategies [24,25]. In summary, poor cognitive flexibility is shown to be a common feature in EDs and SUDs, and our results point out that it might be highlighted when both disorders are present at the same time. However, due to the relatively small sample size of one of the groups and the low statistical power, our results should be interpreted with caution until more evidence is available.

Lastly, even though no differences between groups were found on the IGT total score, both groups displayed an impaired decision-making performance in comparison to healthy population [18,57,58]. However, when comparing the learning curve of both groups, patients with A/DA symptoms showed a weaker learning trajectory and greater difficulties to learn the reward/punishment contingencies of their choices [59]. Our results point out that decision-making problems seem to be present in ED patients [18–20], particularly in those with comorbid substance abuse symptomatology. Once again, future studies are needed to confirm this finding.

The results of this study should be interpreted in the context of some limitations. First, although our sample size is relatively large, the subgroups vary in size, and one of them is relatively small, leading to a low statistical power. Studies with small samples are severely underpowered, which might represent a concern if the "null hypothesis" cannot be rejected. For this reason, the significance tests were complemented with other standardized measure of the effect size. In any case, the results of this study should be interpreted with caution and considering this limitation. Furthermore, because the design is cross-sectional, claims regarding causality cannot be made. Future longitudinal studies should examine the extent to which psychopathology and cognitive function improve after treatment. Another limitation was the lack of a formal diagnosis of SUD in our sample. Finally, our sample was largely made up of young adults, and it would be of clinical interest to explore whether similar impairments in neuropsychological functioning are present in older samples.

5. Conclusions

To conclude, although previous studies have explored comorbidity between EDs and SUDs, this is the first study to explore gender differences. Moreover, it is the first to assess the neuropsychological profile in ED patients with A/DA symptoms. We found that this subgroup displays a specific phenotype characterised by greater impulsivity (i.e., high novelty seeking and difficulties to control impulsive behaviours), noticeable emotional dysregulation (i.e., decreased interoceptive awareness) and more impaired executive control (i.e., low cognitive flexibility and poor decision-making). Of future benefit would be the consolidation of our findings in larger samples and clarifying if these deficits are involved in the development and maintenance of substance abuse comorbidity. As such, this subgroup of ED

patients might benefit from augmented treatment that targets these problems, such as inhibitory control training [60], emotion regulation training [61] or cognitive remediation therapy [62]. This may reduce the present substance abuse symptomatology and prevent later evolution into a SUD, as previous studies have reported that ED patients who do not receive any adjunctive treatment for substance abuse are at high risk for switching from one problematic behaviour to the other, especially during the recovery process [2].

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ESTUDIO 5

TRAIT IMPULSIVITY AND COGNITIVE DOMAINS INVOLVING IMPULSIVITY AND COMPULSIVITY AS PREDICTORS OF GAMBLING DISORDER TREATMENT RESPONSE

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Objetivos:

Explorar el valor predictivo de la impulsividad y compulsividad en la respuesta al tratamiento (i. e., adherencia, recaídas y abandonos) durante una intervención ambulatoria en pacientes con TJ.

RESUMEN

El TJ es una condición altamente heterogénea con grandes tasas de cronicidad, recaídas y abandonos en el tratamiento. La presente investigación exploró a nivel longitudinal las asociaciones entre distintos dominios impulsivo-compulsivos y la respuesta al tratamiento en 144 varones con TJ que habían recibido terapia cognitivo-conductual a nivel ambulatorio. Se llevó a cabo una exhaustiva evaluación clínica y neuropsicológica que comprendía distintos componentes de impulsividad-compulsividad. Varias medidas de impulsividad rasgo predijeron respuesta al tratamiento. En concreto, una alta urgencia negativa predecía baja adherencia y recaídas a las 5 semanas de tratamiento, mientras que la búsqueda de sensaciones se asociaba a más abandonos en etapas finales. Los niveles de compulsividad también se asociaron a peores resultados. Los déficits en flexibilidad cognitiva predecían una mayor tasa de abandonos al final del tratamiento, así como más abandonos, peor adherencia y recaídas en el seguimiento. La baja flexibilidad cognitiva también se asoció a menor tiempo transcurrido hasta la primera recaída y menor tiempo en abandonar. Podemos concluir que los niveles de impulsividad-compulsividad parecen influir en la respuesta al tratamiento en el TJ, representando un posible foco de interés para mejorar el abordaje terapéutico en esta patología.

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Trait impulsivity and cognitive domains involving impulsivity and compulsivity as predictors of gambling disorder treatment response

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HIGHLIGHTS

- Impulsivity and compulsivity cognitive related variables play an important role in relapse, dropout and treatment compliance.
- Trait impulsivity (namely negative urgency and sensation seeking) predicts poorer treatment outcomes.
- Worse cognitive flexibility delays dropout but as treatment progresses it increases risk of dropout and lower compliance.

ARTICLE INFO

Keywords:
Gambling disorder
Impulsivity
Treatment
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Cognitive flexibility
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ABSTRACT

Background and aims: Gambling disorder (GD) is a highly heterogeneous condition with high rates of chronicity, relapses and treatment dropout. The aim of this study was to longitudinally explore the associations between trait impulsivity, impulsivity-compulsivity related cognitive domains, and treatment outcome in an outpatient sample of adult patients with GD.

Methods: 144 adult male participants diagnosed with GD undergoing cognitive-behavioural treatment (CBT) at a specialized outpatient service completed a series of neuropsychological tests to assess executive functioning (including cognitive flexibility, inhibition control and decision making) and psychometric questionnaires.

Results: Trait impulsivity predicted low compliance [UPPS-P negative urgency (B = 0.113; p = 0.019)] and relapse [UPPS-P negative urgency (B = 0.140; p = 0.015)] at 5 weeks of treatment and dropout at the end of treatment [(UPPS-P sensation seeking B = 0.056; p = 0.045)]. Cognitive flexibility performance predicted: dropout rates at the end of treatment [WCST perseverative errors (B = 0.043; p = 0.042)]; dropout [WCST categories completed (B = −1.827; p = 0.020)] and low compliance or relapses at follow-up [WCST perseverative errors (B = 0.128; p = 0.020)]; and time to first relapse [WCST failure to maintain set (B = −0.374; p = 0.048)] and time to dropout [WCST perseverative errors (B = 0.0198; p = 0.019)].

Conclusions: Our findings indicate impulsivity-compulsivity levels may influence response to GD treatment (i.e.: low compliance and dropout or relapse rates) thus representing a potential target for improving treatment outcomes.

1. Introduction

Gambling disorder (GD) is a prevalent mental health condition characterized by persistent and recurrent problematic gambling behaviour that leads to a clinically significant impairment and distress. In the fifth edition of the Diagnostic and Statistical Manual of the American Psychiatric Association (DSM-5), GD was included within the substance related and addictive disorders chapter as a "non-substance-

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related disorders" (American Psychiatric Association, 2013). GD is a very heterogeneous mental condition and 96% of individuals with GD present a lifetime psychiatric condition (Yau & Potenza, 2015), with substance related addictions and mood or anxiety disorders being the most frequent. It also presents high rates of chronicity (Abbott, Romild, & Volberg, 2017) and frequent relapses and dropout from treatment (Aragay et al., 2015; Jiménez-Murcia et al., 2015).

GD has been conceptualized as being placed within an impulsive-compulsive spectrum, in which gambling gains saliency through reward-based learning processes evolving into a compulsive behaviour often triggered by anxiety or stressful events (Brewer & Potenza, 2008). In fact, although many factors can contribute to the development and maintenance of GD, high levels of impulsivity (a tendency to carry out risky behaviours usually linked to maladaptive decision making patterns and to inhibitory control alterations) and compulsivity (a tendency to repeatedly perform acts in a habitual way to prevent perceived negative consequences, even if the act itself can lead to negative consequences) stand out (Fauth-Bühler, Mann, & Potenza, 2017; Savvidou et al., 2017; Yau & Potenza, 2015). It must be noted that both impulsivity and compulsivity constructs imply impaired impulse control, however, while individuals with GD tend to score high across different domains of impulsivity, compulsivity impairments appear more limited to decreased control over mental activities and to fears of losing control over motor behaviours (Yau & Potenza, 2015).

Impulsivity is a complex construct that can be defined along three different domains: choice impulsivity, motor impulsivity and trait impulsivity (Sharma, Markon, & Clark, 2013). Trait impulsivity is a stable personality characteristic related to difficulties in inhibiting inappropriate behaviours, for example acting prematurely in situations that have undesirable consequences or acting without previous reflection of the consequences derived from one's own behaviour (Griffin, Lynam, & Samuel, 2017; Rodenacker, Hautmann, Görtz-Dorten, & Döpfner, 2017). Therefore, trait impulsivity encompasses different cognitive domains and refers to the difficulty to autoregulate dominant preferences (Leshem, 2016). In this line, the UPPS-P model is one of the most accepted theoretical approaches for measuring trait impulsivity and it covers five different dimensions: lack of premeditation, lack of perseverance, sensation seeking, as well as positive and negative urgency (Berg, Latzman, Bliwise, & Lilienfeld, 2015; Canale, Rubaltelli, Vieno, Pittarello, & Billieux, 2017). Positive urgency describes the propensity to act impulsively when undergoing positive emotions; negative urgency reflects the tendency to act impulsively when experiencing negative affect; lack of perseverance refers to the tendency to not persist in an activity that can be boring; lack of premeditation shows the tendency to act without considering the consequences of a behaviour; and sensation seeking indicates one's disposition to seek exciting and new experiences (Verdejo-García, Lozano, Moya, Alcázar, & Pérez-García, 2010). Of these five dimensions, urgency seems to be most highly related to comorbid psychopathology and GD severity (Savvidou et al., 2017).

When examining impulsivity and compulsivity on an endophenotypic level, neurocognitive research suggests that the impulse control deficits observed in GD are highly linked to executive function (EF) impairments (Hinson, Jameson, & Whitney, 2003; Mallorquí-Bagué et al., 2017). EF performance is crucial for the formation of successful goal-directed behaviours (Lezak, Howieson, Bigler, & Tranel, 2012) and difficulties in this cognitive domain can lead to different maladaptive behaviour patterns. Mainly, patients with GD display impaired response inhibition (Odlaug, Chamberlain, Kim, Schreiber, & Grant, 2011) and poor self-regulation together with deficits in planning, cognitive flexibility and decision-making (Forbush et al., 2008; Goudriaan, Oosterlaan, De Beurs, & Van Den Brink, 2008; Hodgins, Stea, & Grant, 2011; Ledgerwood et al., 2012; Zhou, Zhou, & Zhu, 2016). The observed decision making difficulties seem to extend to both the learning process and the whole decision making performance when assessed with the Iowa Gambling Task (IGT; Mallorquí-Bagué et al., 2016), and are characterized by myopia for the future, deficits in immediate/delayed reinforcements and reward/punishment, as well as poor cognitive flexibility (Ochoa et al., 2013). It should be noted that poor cognitive flexibility (set-shifting) is robustly associated with high compulsivity and with disordered compulsive behaviours (Potenza, 2007). In GD, poor cognitive flexibility seems to be partially explained by a greater difficulty in learning from mistakes and finding alternative methods of problem-solving (Marazziti et al., 2008) when assessed with the Wisconsin Card Sorting Task (WCST: Alvarez-Moya et al., 2009; Forbush et al., 2008).

In reference to the association between impulsivity and treatment outcome, previous studies in the field of substance addiction suggest that inhibitory control and choice impulsivity are both relevant facets of impulsivity when treating addiction and maintaining abstinence (Mitchell & Potenza, 2014); still this has not been robustly explored in GD. Regarding impulsivity levels, a current meta-analysis has proposed that negative urgency and lack of premeditation are both associated with poorer psychotherapy outcomes in substance-related addictions when measured with the UPPS-P (Hershberger, Um, & Cyders, 2017); however, there is a lack of studies examining association between the five dimensions of UPPS-P and GD treatment outcome. From a neuropsychological level, findings on the association between impulsivity-compulsivity and GD treatment outcomes are still scarce (Verdejo-Garcia & Manning, 2015). So far, studies seem to point towards the implication of EF impairments in relapse rates and dropouts. For instance, self-regulatory impairments and executive dysfunction have been found to predict treatment dropout (Alvarez-Moya et al., 2011) and two recent studies have suggested that impaired decision making as well as higher disinhibition can predict relapse rates (Goudriaan et al., 2008; Yau & Potenza, 2015). Additionally, better performance on decision-making tasks (as assessed with the IGT) predicted GD recovery, regardless of the type of therapy that was implemented (Rossini-Dib, Fuentes, & Tavares, 2015). Yet, these findings are still controversial: several studies have conversely suggested that there is no clear association between decision-making and GD treatment outcome. One study found that poor decision-making was only associated with higher risk of dropouts and not associated with relapse (Alvarez-Moya et al., 2011). The reported inconsistent findings across studies are likely to reflect methodological issues relating to the measurement instruments. Likewise, other authors have reported that Card Playing Task performance is a significant predictor of relapses, whereas performance on the IGT is not (Goudriaan et al., 2008).

In sum, although impulsivity and compulsivity have been widely described in GD, the limited existing research prospectively examining the link between these constructs and treatment outcome on an endophenotypic level is still inconclusive. Therefore, the aim of this study was to longitudinally explore the impact of impulsivity and compulsivity on GD treatment outcome. The specific objective was to determine the predictive power of EF and trait impulsivity on therapy compliance, relapse and dropouts during outpatient treatment of GD.

2. Methods

2.1. Sample

The final sample consisted of 144 adult male participants diagnosed with GD, according to the DSM-5 criteria (American Psychiatric Association, 2013) (see supplementary material for the flowchart diagram specifying the initial number of male participants who accepted to be part of the study but were excluded for not meeting DSM-5 criteria or for not starting treatment). All participants were consequently referred through general practitioners or via another health care professional for problematic gambling to the Gambling Disorder Unit within the Department of Psychiatry at Bellvitge University Hospital. This public hospital oversees the treatment of very complex cases as it is certified as a tertiary care centre for the treatment of addictive

behaviours. Experienced psychologists conducted two face-to-face clinical interviews before a diagnosis was given and before starting outpatient treatment. Only patients who sought treatment for GD as their primary health concern were admitted to this study and all participants were over 18. GD is more frequent in men than women (Granero et al., 2009) thus very few women seek treatment for GD at our unit; consequently, only males were included in this study. Exclusion criterion for being part of the treatment protocol were: (1) history of chronic medical illness or neurological condition that might affect cognitive function; (2) brain trauma, a learning disability or intellectual disabilities; (3) age under 18 or over 65.

All participants provided signed informed consent and received no additional compensation for being part of the study. In accordance with the Helsinki Declaration of 1975 as revised in 1983, the Ethics Committee of Bellvitge University Hospital approved the study.

2.2. Measures

Patients individually completed the assessment required for this study (requiring approximately 80 min) before initiating outpatient treatment. Apart from the self-report questionnaires and neuropsychological tasks listed below, additional sociodemographic and clinical information was taken.

2.2.1. Semi-structured face-to-face clinical interview, psychopathology and gambling disorder measures

Patients presenting GD were assessed using the DSM-5 criteria (American Psychiatric Association, 2013) via a face-to-face clinical interview. However, patients that were assessed before the release of the DSM-5, were diagnosed with pathological gambling if they met DSM-IV-TR criteria (American Psychiatric Association, 2000). These patients were then reassessed and remodified post hoc and only patients who met DSM-5 criteria for GD were included in our analysis. Demographic and social variables related to gambling were also measured.

The South Oaks Gambling Screen (SOGS) (Lesieur & Blume, 1987) is a 20-item diagnostic questionnaire to ascertain gambling disorder severity. It discriminates between probable pathological, problem and non-problem gamblers. The Spanish validation of this self-reported tool showed excellent internal consistency ($\alpha = 0.94$) and test-retest reliability ($r = 0.98$) (Echeburúa, Báez, Fernández, & Páez, 1994). Internal consistency in the present study sample was 0.76.

Symptom Checklist-90 Revised (SCL-90-R; Derogatis, 1994) is a 90-item questionnaire which evaluates a broad range of psychological problems and psychopathological symptoms. It measures nine primary symptom dimensions: somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism. It also includes three global indices: a global severity index (GSI), designed to measure overall psychological distress; a positive symptom distress index (PSDI), to measure the symptom intensity; and a positive symptom total (PST), which reflects self-reported symptoms. This scale has been validated in a Spanish population, with a mean internal consistency of 0.75 (Derogatis, 2002). Internal consistency in the present study sample was between good ($\alpha = 0.75$ for phobic anxiety) to excellent ($\alpha = 0.98$ for the global composite scores).

2.2.2. Trait impulsivity and neuropsychological assessment

The UPPS-P Impulsivity Scale (Whiteside, Lynam, Miller, & Reynolds, 2005) is a 59-item questionnaire to assess five different features of impulsive behaviour: negative urgency, lack of perseverance, lack of premeditation, sensation seeking and positive urgency. The UPPS-P has satisfactory psychometric properties in terms of both convergent and discriminatory validity (Cyders & Smith, 2008; Smith, Hay, Campbell, & Trollor, 2011). The Spanish adaptation of the scale has adequate psychometric properties (Verdejo-García et al., 2010). The α values for the different UPPS-P scales in our sample are as follows: lack of premeditation (0.88), lack of perseverance (0.88), sensation seeking (0.83), positive urgency (0.93) and negative urgency (0.87).

The Stroop Colour and Word Test (SCWT; Golden, 1978, 2001) is a extensively used neuropsychological test to assess one's cognitive ability to override the dominant behavioural response to a stimuli, namely inhibitory control (including response inhibition and interference control). It consists of three different lists: a word list containing the names of colours printed in black ink, a colour list that comprises letter Xs printed in colour, and a colour-word list constituted of names of colours in a colour ink that does not match the written name. Three final scores are obtained based on the number of items that the participant is able to read on each of the three lists in a time window of 45 s. In addition, there is also an interference score that is computed with all three lists that enables the assessment of individual's cognitive flexibility and the ability to inhibit cognitive interference. Higher scores in this index suggest better inhibitory control.

The Wisconsin Card Sorting Test (WCST; Lezak et al., 2012) is a computerized set-shifting task for assessing cognitive flexibility. It includes 128 cards that vary according to three attributes: number (N), colour (C) and shape (S). The participant has to pile the cards beneath four reference cards that also vary along these same dimensions and, in order to succeed they have to settle upon a predetermined sorting rule. The only feedback given to the participant is the word “right” or “wrong” after each sorting. Initially, C is the correct sorting category, and positive feedback is given only if the card is placed in the pile with the same colour. After 10 consecutive correct sorts the rule changes. Thus, the positive feedback is only given when the sorting matches the new category. By trial and error, the participant must learn to change the sorting categories according to the given feedback. There are up to six attempts to derive a rule, providing rule shifts in the following category sequence: C-S-N-C-S-N. Participants are not informed of the correct sorting principle and that the sorting principal shifts during the test. The test is completed when all 128 cards are sorted or after the six full categories are completed. The number of completed categories, the percentage of perseverative errors (i.e., failures to change sorting strategy after negative feedback) and the percentage of non-perseverative errors are recorded.

The Iowa Gambling Task (IGT; Bechara, Damasio, Damasio, & Anderson, 1994; Bechara, Tranel, & Damasio, 2000) is a computerized task to evaluate decision-making. It involves a total of 100 turns distributed across four decks of cards (A, B, C and D) and each time the participant selects a deck, a specified amount of play money is awarded. Still, the interspersed rewards among theses decks are probabilistic punishments (monetary losses with different amounts). Participants are instructed that the final aim of the task is to win as much money as possible and to avoid losing as much money as possible. Also, they may choose cards from any deck, and switch decks at any time. This test is scored by subtracting the number of cards selected from decks A and B from the number of cards selected from decks C and D. Decks A and B are not advantageous as the final loss is higher than the final gain; however, decks C and D are advantageous since the punishments are smaller. Higher scores indicate better performance on the task while negative scores indicate persistently choosing disadvantageous decks.

2.2.3. Outpatient treatment protocol

The outpatient treatment at our unit is a manualized cognitive behavioural therapy (CBT) protocol which consists of 16 weekly group sessions lasting 90 min each; each treatment group has a maximum of 14 patients when the treatment starts. In addition, the current prospective study not only assesses the changes during the 16 weeks of treatment but also the changes observed at the three follow-up sessions that take place during the 6 months after completing treatment. CBT groups were led by an experienced clinical psychologist as well as a clinically trained co-therapist. The main goal of the intervention was to train patients to implement CBT strategies in order to minimize GD

maladaptive behaviours and to eventually reach full abstinence. For this purpose, the general topics addressed included psychoeducation regarding the disorder (its course and phases, vulnerability factors, diagnostic definition, etc.), stimulus control (such as money management and avoidance of potential triggers), reinforcement and self-reinforcement, response prevention, skills training, cognitive restructuring focused on illusions of control over gambling, and relapse prevention techniques. This treatment protocol has previously been described (Jiménez-Murcia, Aymamí-Sanromà, Gómez-Peña, Álvarez-Moya, & Vallejo, 2006) and its short- as well as mid-term effectiveness has been reported for GD (Jimenez-Murcia et al., 2012; Jiménez-Murcia et al., 2007), with an abstinence rate of 76.1% at the end of treatment and of 81,5% at 6 months follow-up. For the present study, the occurrence of a gambling episode once treatment had begun was considered a relapse. A dropout was defined as a patient missing therapy sessions on three or more occasions without previously notifying the clinician. Finally, a breach of 4 or more intersession tasks (such as recording their spending, avoiding risky situations and controlling their spending by presenting receipts) was considered low therapy compliance.

2.3. Statistical analysis

Statistical analysis was carried out with Stata15 for Windows. All the analyses were adjusted for age, education and psychopathological symptoms (measured through the SCL-90R, GSI scale) to avoid potential biases due to cofounding effects with the variables of interest.

Three main treatment outcome measures were analyzed in the study: dropout, relapse and therapy compliance. Given that the time to first relapse or dropout presented censoring data (namely some participants did not dropout or relapse), an initial descriptive survival analysis estimated its cumulative survival functions (through Kaplan-Meier methods). In the present study, the survival function S(t) is interpreted as the probability of "surviving" longer than a time t, that is, the probability of not presenting a dropout or a relapse (Collett, 2003). Secondly, a preliminary bivariate analysis based on an analysis of variance (ANOVA, adjusted for the covariates age, education and psychopathological symptoms) compared the means of the results obtained in the neuropsychological measures between patients with (or without) dropout from treatment, with (or without) relapse, and with adequate (or low) therapy compliance. Effect size for the mean differences in the ANOVA models were estimated through Cohen's-d coefficient (low effect size, $|d| > 0.20$; moderate-medium effect size, $|d| > 0.50$; large-high effect size, $|d| > 0.80$ (Cohen, 1990)). Next, predictive models of patient responses to treatment were implemented with the potential independent variables, namely trait impulsivity and EF measures. Logistic regressions were used with the binary dependent variables: dropout (yes vs. no), therapy compliance (low vs. adequate) and relapse (yes vs. no) (goodness-of-fit was valued through Hosmer-Lemeshow test, considering $p > 0.05$ to be good fit). Cox's regressions were performed with the censored criteria: time to first relapse and time to dropout during treatment. Each final model was adjusted in two step-blocks: the first one included and fixed the covariates (age, psychopathological symptoms and education; ENTER procedure), the second automatically selected and added the EF predictive variables with significant contribution to the treatment outcomes (STEPWISE procedure).

Given that multiple statistical comparisons were implemented, Finner correction was applied (Finner, 1993) to avoid an increase of Type-I error. Finner correction is included in the familywise error rate system and it is more powerful than Bonferroni correction.

3. Results

3.1. Sample characteristics

The first part of Table 1 includes sociodemographic and GD-related variables. The mean age in the sample was 42.6 years (SD = 9.6) and the majority of the participants had not been treated for gambling problems before. The most preferred gambling activity was slot machines (67.4%), followed by internet games (11.8%), casinos (7.6%) and lotteries (6.3%). The second column in Table 1 includes the distribution of the EF measures, trait impulsivity and psychopathological symptoms.

Table 2 includes the distribution of patients by treatment outcomes (i.e.: dropout, relapse and therapy compliance) at three treatment stages: at early change (at 5 weeks of treatment (Nazar et al., 2017)), at the end of treatment (after 16 weeks) and at 1 to 6 months follow-up. At the early-change stage, there were few remaining patients with relapses (48.6% with no relapse, 3.5% with 1 relapse and 5.6% with 2 or more relapses) and 42.4% dropped out from treatment. At the end of treatment stage, the percentage of remaining patients with relapse increased (34.0% with no relapse, 6.9% with only 1 relapse and 9.0% with at least 2 relapses) and 50% of patients dropped out. At the treatment follow-up stage, a total of 16.7% of the patients reported relapses and 40.3% of the patients failed to attend the sessions.

3.2. Survival analysis of dropout and relapse during treatment

The first cumulative survival corresponds to the time elapsed until the first relapse (Fig. 1). The risk of relapse during treatment was 39.6% (considering the total sample, 57 individuals reported at least one relapse). First relapses were registered during the first week of treatment: 7 participants indicated at least one episode, which represented 4.9% of the sample. Consequently, the cumulative survival probability at this time point was 95.1%. During the second week of treatment, 45 participants (31.3%) did not present relapses; thus the cumulative survival probability of relapse at this time point was 68.7%. The next relapses were registered from weeks 3 to 6. After week 6, there were no more relapse episodes.

The second cumulative survival corresponds to the time elapsed until dropout (Fig. 1). The risk of dropout during treatment was 50%. The survival function shows that the highest risk of dropout was at the beginning of the treatment: 26 patients (18.1% of the sample) only attended the first session, thus the cumulative survival probability for dropout was 81.9% at this time point. The rest of the dropouts were distributed rather regularly from weeks 2 to 11. During the rest of the sessions (12 to 16) no additional dropouts were registered.

3.3. Predictive capacity of impulsive-compulsive related measures with treatment outcomes

Tables S1, S2 and S3 (Supplementary material) include the results of the preliminary bivariate analyses comparing the means of the impulsive-compulsive related measures between patients who completed and did not complete (registered as dropouts) treatment, who reported high versus low treatment compliance, and who reported or not reported relapses. Table 3 includes the final predictive logistic regressions and Cox's regressions (adjusted for the age, education and psychopathological symptoms-SCL-90R). At the early-change stage, the risk of low compliance and relapse was increased for patients with high scores in negative urgency. At the end of treatment, the risk of dropout was increased for participants with higher sensation seeking scores on the UPPS-P and higher perseverative errors on the WCST. At follow-up, the logistic model obtained for the risk of dropouts showed that the probability of dropping out of treatment was increased for patients with lower response errors and lower categories completed in the WCST. Risk of low compliance or relapse at follow up was also increased for patients with higher perseverative errors on the WCST. All the logistic models obtained goodness-of-fit ($p > 0.05$ in Hosmer-Lemeshow test). With regards to the Cox's regressions adjusted for censoring data, the survival time elapsed until the first relapse was increased for patients with low failure to maintain set on the WCST and time to dropout was increased with higher perseverative errors in the WCST. That is, the

Table 1
Sample characteristics (n = 144).

Sociodemographic measures				Iowa Gambling Test (IGT)	Mean	SD
Origin; n-%	Immigrant	6	4.2%	Block 1	−1.02	5.15
	Spanish	138	95.8%	Block 2	1.53	6.75
Education; n-%	Primary	71	49.3%	Block 3	2.11	8.45
	Secondary	61	42.4%	Block 4	3.95	8.63
	University	12	8.3%	Block 5	0.56	9.85
Civil status; n-%	Single	47	32.6%	Total	7.12	23.97
	Married/in couple	74	51.4%	Wisconsin Card Sorting Test (WCST)		
	Separated/divorced	23	16.0%	Response errors	29.64	22.43
Employment; n-%	Unemployed	67	46.5%	Perseverative errors	14.69	13.86
	Employed	77	53.5%	Conceptual level responses	62.09	16.38
GD-related variables				Number categories completed	5.17	1.63
Previous treatment for GD; n-%	No	121	84.0%	Trials complete 1st category	20.16	20.42
	Yes	23	16.0%	Failure to maintain set	0.72	1.02
Main GD activity; n-%	Slot machines	97	67.4%	Stroop		
	Bingo	7	4.9%	Word reading	97.82	18.83
Internet games		17	11.8%	Colour naming	69.83	12.96
	Lotteries	9	6.3%	Colour/word naming	43.18	10.72
	Casinos	11	7.6%	Interference	3.11	7.52
	Cards	3	2.1%	UPPS-P		
Duration of GD (years); mean-SD		5.06	5.30	Lack of premeditation	24.14	6.44
Maximum bets-episode (€); mean-SD		913.0	2241.9	Lack of perseverance	21.97	5.34
Mean bets-episode (€); mean-SD		106.8	198.0	Sensation seeking	27.65	8.15
Cumulate debts gambling (€); mean-SD		32,519.9	251,145.8	Positive urgency	32.18	10.50
SOGS: total score; mean-SD		11.03	3.11	Negative urgency	32.99	7.85
DSM-5 criteria: total; mean-SD		7.09	1.91	Psychopathology (SCL-90R)		
Use-abuse of substances				Somatization	0.87	0.77
Tobacco use; n-%	No	55	38.2%	Obsessive-compulsive	1.09	0.77
	Yes	89	61.8%	Interpersonal sensitivity	0.98	0.78
[1]Tobacco (cigarettes-day); mean-SD		17.0	9.11	Depressive	1.54	0.80
Alcohol use-abuse; n-%	No	111	77.1%	Anxiety	0.96	0.72
	Yes	33	22.9%	Hostility	0.93	0.81
Illegal drugs use-abuse; n-%	No	129	89.6%	Phobic anxiety	0.40	0.54
	Yes	15	10.4%	Paranoid ideation	0.90	0.74
Drug: cannabis; n-%	No	133	92.4%	Psychoticism	0.87	0.67
	Yes	11	7.6%	GSI	1.03	0.64
Drug: cocaine; n-%	No	139	96.5%	PST	47.21	20.64
	Yes	5	3.5%	PSCI	1.82	0.54

Note. SD: standard deviation. GSI: global severity index. PSDI: positive symptom distress index. PST: positive symptom total [1]Distribution of the participants who reported tobacco use.

time until the presence of the first relapse was higher for patients with lower failure to maintain set and the time until dropout was higher for patients with high perseverative errors.

4. Discussion

The present study aimed to explore the role that impulsivity and compulsivity play in GD treatment outcomes by specifically targeting trait impulsivity and EF. In general terms, our results show that high trait impulsivity and poor cognitive flexibility (highly linked to compulsivity) are both predictors of treatment response (i.e.; low compliance, relapse and dropout); no associations were found between decision making and treatment response.

The results of the present study point towards an implication of both impulsivity and compulsivity in treatment outcome. People with GD are characterized by high levels of impulsivity (Mitchell & Potenza, 2014) and it has also been suggested that GD may change over time, starting as being a more reward-driven behaviour and evolving into a more compulsive one (Brewer & Potenza, 2008; El-Guebaly, Mudry, Zohar, Tavares, & Potenza, 2012; Hollander, Kim, Khanna, & Pallanti, 2007; Koob & Volkow, 2010). However, compulsivity has not only been reported as part of prolonged gambling behaviour but also, as recent studies maintain, as part of the onset of the disorder (Potenza, 2007); thus GD shows common features with disorders that could be located on the compulsive end, mainly obsessive-compulsive disorder (Potenza, 2007). Likewise, several studies agree on the overlap between impulsivity and compulsivity in terms of phenomenology, brain circuitry and neurocognition (Everitt & Robbins, 2013; Grant & Kim, 2014; Guo, Chen, & Feng, 2017); both constructs are characterized by deficits in self-control or response inhibition (Chamberlain, Stochl, Redden, Odlaug, & Grant, 2017) and are maintained, among other factors, by a reinforcement process (the former positive and the latter negative). In this regard, a systematic review by Moccia et al. (2017) concluded that alterations in the orbito- and ventromedial prefrontal cortex influenced affective and the motivational aspects, which in turn contribute to the decreased cognitive control observed in GD.

From an impulsivity perspective, and in accordance with previous research on substance use disorders (Hershberger et al., 2017), our results uphold a positive association between impulsivity traits and GD treatment outcome at three different stages: early change, end of treatment and 6-months follow-ups. Namely, as previously reported in substance use disorders (Hershberger et al., 2017), negative urgency predicted greater relapse risk and lower therapy compliance in early-change treatment response. Negative urgency is the propensity to act impulsively when experiencing negative emotions such as frustration, fear, anxiety or sadness (Verdejo-García et al., 2010); it is associated with greater vulnerability to negative affect and suggested to correlate with greater GD severity (Billieux et al., 2012). The present results lead us to postulate that patients with GD could be more prone to experience negative emotions, which in their turn also trigger higher impulsivity. Thus, the risk of experiencing a new gambling episode increases.

At the end of treatment, sensation seeking was the dimension of trait impulsivity that best predicted dropout. This finding seconds the struggles described in patients with high trait impulsivity when trying to engage in long-term rewarding aims (i.e.: health improvement and treatment) while being faced with short-term rewards (i.e.: gambling)

Table 2
Distribution of patients by treatment outcomes at three treatment stages: early change, end of treatment and 1 to 6 months follow-up.

Early change (5 weeks therapy)			
Complete therapy without relapses		70	48.6%
Complete therapy with only 1 relapse		5	3.5%
Complete therapy with 2 or more relapses		8	5.6%
Dropout		61	42.4%
Completers (n = 83);	Low therapy compliance; n-%	15	18.1%
	Relapses; n-%	13	15.7%
Relapses (n = 13);	Maximum bets in relapse-episodes; mean-SD	146.7	191.4
	Mean bets in relapse-episodes; mean-SD	34.7	42.5
Outcomes-during the therapy (16 weeks)			
Complete therapy without relapses		49	34.0%
Complete therapy with only 1 relapse		10	6.9%
Complete therapy with 2 or more relapses		13	9.0%
Dropout		72	50%
Completers (n = 72);	Low therapy compliance; n-%	11	15.3%
	Relapses; n-%	23	31.9%
Relapses (n = 23);	Maximum bets in relapse-episodes; mean-SD	428.0	1038.5
	Mean bets in relapse-episodes; mean-SD	46.4	123.7
One-month follow-up (attending: n = 72)			
Low therapy compliance; n-%		5	6.9%
Relapses; n-%		2	2.8%
Low therapy compliance or relapses; n-%		5	6.9%
Three-month follow-up (attending: n = 50)			
Low therapy compliance; n-%		5	10.0%
Relapses; n-%		6	12.0%
Low therapy compliance or relapses; n-%		6	12.0%
Six- month follow-up (attending: n = 45)			
Low therapy compliance; n-%		5	11.1%
Relapses; n-%		4	8.9%
Low therapy compliance or relapses; n-%		6	13.3%
Dropout between final therapy and 6-months follow-up (attending: n = 72)			
Dropout during final therapy to 1-month follow-up; n-%		10	13.9%
Dropout during 1-month to 3-months follow-up; n-%		12	16.7%
Dropout during 3-months to 6-months follow-up; n-%		7	9.7%

Note. SD: standard deviation.

(Ramos-Grille, Gomà-i-Freixanet, Aragay, Valero, & Vallès, 2015). Lastly, it is important to note that no significant results were obtained when exploring the association with inhibition of cognitive interference (STROOP effect) and treatment outcome. Previous cross-sectional GD studies have reported worse performance on the STROOP task (Kertzman et al., 2006) but literature of its implication in treatment outcome is lacking. The present results could indicate that the observed difficulties in interference control are not relevant when it comes to treatment outcomes. Still, this fact should be further explored and replicated as it might just be constrained to our sample or to difficulties in properly assessing different impulsivity features (Verdejo-Garcia & Manning, 2015).

From a compulsive perspective and in agreement with previous studies, patients with GD present poor cognitive flexibility (Alvarez-Moya et al., 2009; Forbush et al., 2008). Cognitive flexibility difficulties (based on higher perseverative errors) were associated with lower treatment compliance as well as dropouts at the end of treatment, and with lower compliance as well as relapses at follow-up assessments. Fewer categories completed, and response errors were also linked to dropout rates at follow-up assessments. Finally, time to dropout was predicted by higher perseverative errors, and time to first relapse was predicted by lower failure to maintain set (better ability to continue with a strategy that has been successful), which indicates that higher cognitive rigidity may at first be an advantageous characteristic in terms of dropouts. However, once the treatment progresses and the first dropout or relapse takes place this characteristic predicts higher risk of dropout and lower compliance. All in all, poor cognitive flexibility (particularly perseverative errors, which are highly linked to compulsive behaviours) seems to play an important role in treatment response.

Finally, previous longitudinal studies have reported contradictory results when exploring decision making as a predictive factor of treatment response in GD patients (Alvarez-Moya et al., 2011; Goudriaan et al., 2008). Our results go in line with the studies reporting that although there are decision-making impairments in GD, these difficulties are not a risk factor for poor treatment outcome. The lack of agreement between studies could be due to different decision-making measures or to differences with treatment outcome assessments. For example, a previous study reported that the performance on the Card Playing Test predicted the number of relapses but the performance on the IGT did not predict them (Goudriaan et al., 2008).

The present study reports impulsivity-compulsivity related variables that play a role in predicting treatment outcome. The results have the potential to provide more promising treatment responses (e.g.: improve treatment adherence and reduce relapses) by adapting current treatment protocols to specifically enhance an individual's cognitive flexibility and trait impulsivity (specifically urgency and sensation-seeking dimensions). However, the results of this study should be interpreted according to some limitations. First of all, trait impulsivity was assessed by means of self-reported measures. Although the UPPS-P is a well-established and validated measure for impulsivity, future studies should incorporate different behavioural measures to further evaluate different impulsivity domains (e.g.: choice impulsivity). Secondly, this study only explored males from a highly specialized unit that usually deals with severe cases of GD. Before results can be generalized, future

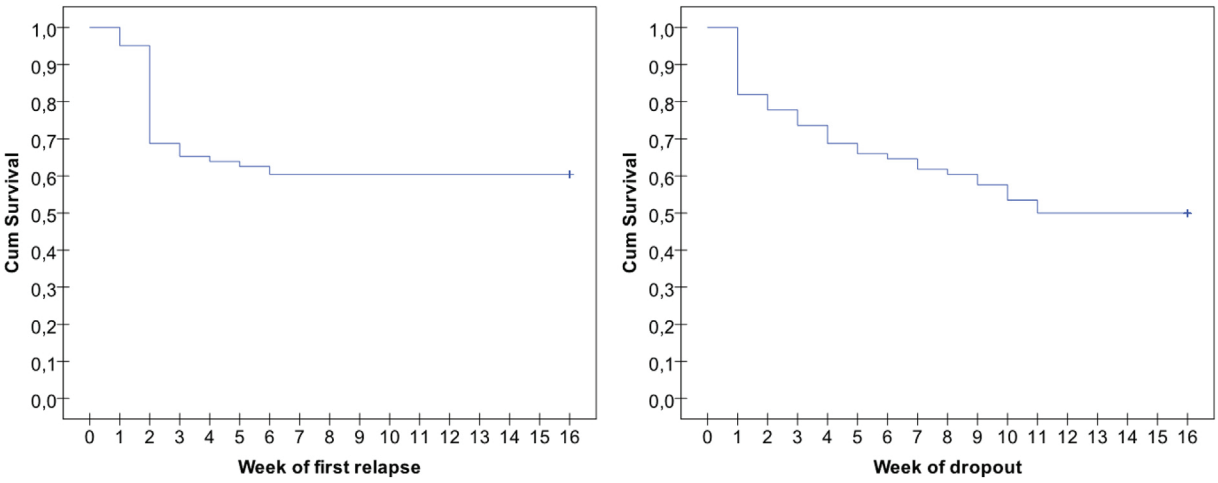

Fig. 1. Cumulative survival analysis of relapse and dropout during treatment.

Table 3
Predictive models: logistic and Cox's regressions adjusted for age, education and psychopathological symptoms.

Logistic regressions	Criteria	Predictors	B	SE	p	OR
5 weeks therapy	Dropout	No significant predictors				
	Low compliance	UPPS-P: negative urgency	0.14	0.07	.034	1.15
	Relapses	UPPS-P: negative urgency	0.15	0.08	.048	1.16
Final therapy (16 weeks)	Dropout	WCST: perseverative errors	0.04	0.03	.046	1.05
		UPPS-P: sensation seeking	0.06	0.03	.049	1.06
1 to 3 months follow-up	Dropout	WCST: response errors	−0.09	0.04	.021	0.91
		WCST: categories completed	−1.28	0.55	.020	0.28
	Low compliance or relapses	WCST: perseverative errors	0.11	0.06	.046	1.12
Cox's regressions	Criteria	Predictors	B	SE	p	OR
	Time to first relapse	WCST: failure to maintain set	−0.35	0.21	.046	0.71
	Time to dropout	WCST: perseverative errors	0.02	0.01	.023	1.12

WCST: Wisconsin Card Sorting Test.

studies should include samples from other health attention centres and should also include women. It is also important to note that there are substantial differences when defining dropout and relapse rates in the literature, with some studies defining relapse as more than simply a single incidence of resumption of the target behaviour (Ledgerwood & Petry, 2006). In this regard, our study takes a conservative perspective by defining relapse as only one incidence of gambling behaviour and results might have been different if a different approach had been taken. Additionally, our unit includes more than one practitioner and this could create a bias in itself; in this regard, measures were taken to guarantee that the clinical assessment and treatment of the patients were sufficiently reliable across practitioners. Finally, the IGT is designed to assess real life decision-making, however the participants' decisions have no real-life impact and future studies could test more naturalistic decision-making paradigms.

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Contributors

NMB, SJM, FFA, JMM and RG, designed the experiment based on previous results and the clinical experience of AP-M, MG-P, NA, TM-M, C-VA. RG, NM-B, GM-B, ML-M, FFA and SJM conducted the experiment, analyzed the data, and wrote a first draft of the manuscript. SJ-M, NM-B, GM-B, RG, M-LM and FF-A further modified the manuscript. TS conducted the language proofreading of the manuscript and provided further advice.

Conflict of interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.addbeh.2018.07.006.

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5. DISCUSIÓN

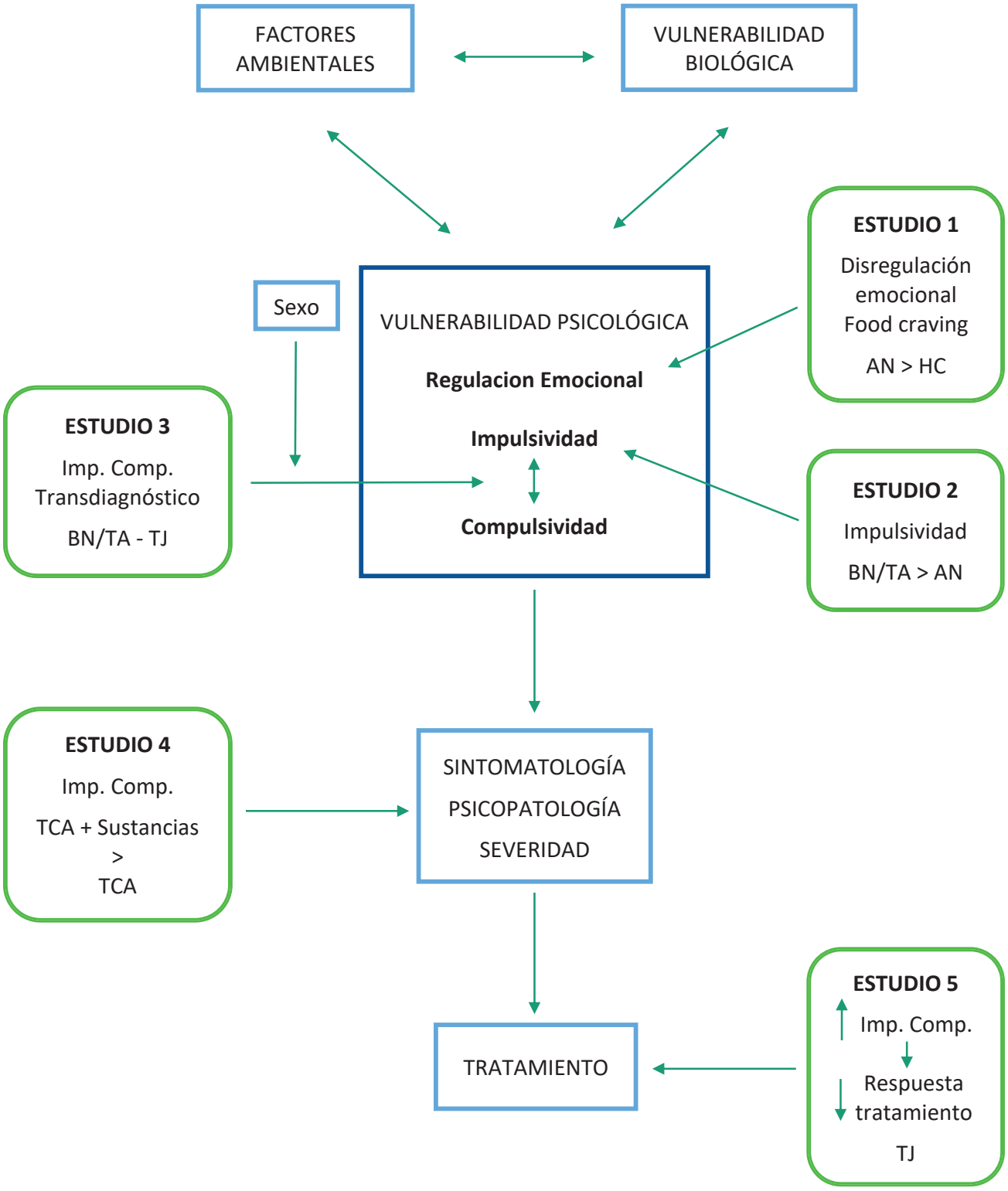
5.1. DISCUSIÓN GENERAL

Siguiendo un enfoque dimensional, los TCA y el TJ han sido englobados dentro de un mismo continuo impulsivo-compulsivo [22–24]. Además, se ha postulado que estos trastornos muestran semejanzas no sólo a nivel neurobiológico y clínico [13–18], sino también en ciertos aspectos implicados en su desarrollo y mantenimiento, como los mecanismos de regulación emocional y las características de impulsividad y compulsividad [19–22,32–35] [18–21,31–34]. Con esto en mente, el principal propósito de esta tesis era estudiar las posibles alteraciones en la regulación emocional y en la impulsividad-compulsividad de pacientes con TCA y TJ, así como su impacto a nivel psicopatológico y su influencia en el resultado al tratamiento.

En esta sección se discutirán de forma conjunta los principales hallazgos obtenidos en los cinco estudios que componen esta tesis (ver **Figura 5**). Desde esta perspectiva general, estos estudios han subrayado los notables déficits en regulación emocional, así como los niveles disfuncionales de impulsividad y compulsividad presentes en los TCA y el TJ. También han ilustrado las similitudes y diferencias en las características impulsivo-compulsivas de estos trastornos, esclareciendo las diferencias de sexo asociadas. Finalmente, se ha puesto de manifiesto la vinculación de estas alteraciones con la presencia de mayor psicopatología (i. e., consumo de sustancias) y una peor respuesta al tratamiento.

En primer lugar, nuestros hallazgos confirmaron la presencia de importantes dificultades de regulación emocional, así como el uso de estrategias de regulación disfuncionales en pacientes con AN (**Estudio 1**). En la AN, los déficits en regulación emocional parecen subyacer a los síntomas alimentarios característicos de esta patología [33,187]. De hecho, las conductas alimentarias alteradas que muestran estos pacientes, como la restricción y el ejercicio excesivo, pueden ser vistas como estrategias desadaptativas con las que evitan o suprimen el afecto negativo [193]. Nuestros resultados avalan la visión de la disregulación emocional como un factor de riesgo transdiagnóstico que participa en el desarrollo de diversas psicopatologías [131], incluidos los TCA [139,186]. Además, sugieren que la inhabilidad para gestionar las emociones podría acrecentar el afecto negativo y el uso de estrategias disfuncionales como la supresión [36].

Figura 5. Modelo integrativo de los principales hallazgos.



Nota. TAP: AN: anorexia nerviosa; BN: bulimia nerviosa; TA: trastorno por atracón; TJ: trastorno de juego.

Cabría también la posibilidad de que estas dificultades pudieran vincularse a una alteración en los sustratos neurales subyacentes a los procesos de regulación emocional [154,155]. En sujetos sin psicopatología se habían observado parámetros psicofisiológicos de regulación emocional [146–148,328–330]. Sin embargo, nuestros resultados señalan que los pacientes con AN no parecen mostrar estos parámetros, indicando un posible déficit en el manejo de las emociones a nivel psicofisiológico. No obstante, dado que este hallazgo se detectó tanto en los pacientes con AN como en los controles, no podemos descartar que fuera debido a otros factores. Por ejemplo, el no emplear una estrategia concreta de regulación emocional podría haber dificultado la consecución de regulación a nivel psicofisiológico. Pese a no haber llegado a resultados del todo concluyentes, esta tesis ha aportado un factor novedoso, como es el uso de técnicas psicofisiológicas para estudiar los procesos de regulación emocional en los TCA, abriendo una puerta a futuras investigaciones que quieran seguir en esta misma línea.

Asimismo, se confirmó que los pacientes con AN muestran niveles más elevados de *food craving* que los sujetos sin psicopatología, siendo superiores en la AN bulímico-purgativa que en la restrictiva. Aunque el *food craving* ha sido comúnmente asociado a pacientes con TA y BN [331–334], varios estudios habían reportado su presencia en la AN, sobre todo en el subtipo bulímico-purgativo [178,179,335,336]. No obstante, pese a los elevados niveles de *food craving* obtenidos en la AN, pudimos comprobar su adecuada regulación a nivel psicofisiológico. Resultados similares habían sido observados en personas con conductas alimentarias restrictivas [185], pero nunca se había explorado el *food craving* en los TCA con técnicas psicofisiológicas. En general, nuestros hallazgos remarcarían la relevancia del *food craving* en la AN, especialmente en la AN bulímico-purgativa, aunque la posible etiología neurofisiológica del mismo aún estaría pendiente de confirmar. Desde una perspectiva clínica, este hallazgo podría suponer un indicador de mayor predisposición en este grupo de pacientes a evolucionar con el tiempo hacia una BN, por lo que evaluar este rasgo de forma precoz se configuraría como una estrategia adecuada en clave preventiva.

Otro de los factores de riesgo más mencionados y estudiados dentro del ámbito los TCA y el TJ es la impulsividad. Al ser considerada un constructo multidimensional, cada uno de sus dominios podría asociarse en mayor o menor medida a estas patologías [337]. En lo que respecta a la impulsividad rasgo, ésta es comúnmente evaluada con las escalas TCI-R y UPPS-

P, las cuales han demostrado tener un gran apoyo empírico [214,338]. Basándonos en ambos modelos teóricos, en la presente tesis se han observado mayores niveles de impulsividad rasgo en pacientes con TCA y TJ que en población general (**Estudios 2 y 3**). Sin embargo, cada trastorno se caracteriza por la presencia o ausencia de diferentes rasgos impulsivos (ver **Figura 5**).

Por un lado, se identificaron altos niveles de urgencia negativa en la AN y la BN/TA. Ésta se asocia a un incremento en la sintomatología bulímica y a una pérdida de control en la ingesta [339], convirtiéndose en un componente distintivo de los trastornos del espectro bulímico, incluida la AN bulímico-purgativa [248,340–342]. No obstante, ambos trastornos difieren en algunos rasgos impulsivos, la BN/TA se caracteriza por altos niveles de falta de perseverancia y la AN por una baja búsqueda de la novedad. La literatura sostiene que los pacientes con conductas bulímico-purgativas muestran una mayor falta de perseverancia que los pacientes de tipo restrictivo o los sujetos sin sintomatología alimentaria [249], mientras que la AN es identificada como el TCA con niveles más reducidos de búsqueda de sensaciones [77]. Estos resultados sugieren que los distintos subtipos de TCA presentan tendencias diferenciadas de impulsividad rasgo, y que la sintomatología alimentaria (p. ej., restricción o sobreingesta) puede ser entendida como los extremos opuestos de un mismo espectro de comportamientos impulsivos [23].

De manera similar, al comparar el TJ, con la BN/TA, patologías todas ellas caracterizadas por una alta impulsividad [27–30], pudimos observar que, mientras en el TJ la impulsividad rasgo se asociaría más con una alta búsqueda de la novedad, en la BN/TA se asociaría con una baja persistencia, además de la falta de perseverancia y la alta urgencia negativa comentados anteriormente. Nuestros hallazgos concuerdan con numerosos estudios que habían identificado altos niveles de búsqueda de la novedad en el TJ [13,14,18,40,346], pero no en la BN/TA [14,319,346,347], pese a ser considerados los TCA con más rasgos impulsivos [77,319,348]. Asimismo, la literatura sostiene que los pacientes con TCA muestran niveles más bajos de persistencia que las personas sin psicopatología y los pacientes con TJ [346], a pesar de que en esta línea podrían identificarse diferencias si se consideran los distintos tipos de juegos problemáticos. En general, los juegos presenciales y de tipo no estratégico se asocian a menor búsqueda de novedad y menor persistencia. En cambio, los juegos más estratégicos, como las

apuestas deportivas (presenciales y online), se relacionan con perfiles de pacientes con mayores niveles de persistencia. En cualquier caso, es importante tener en cuenta este tipo de variables a la hora de explicar estos hallazgos. En definitiva, nuestros resultados avalan de nuevo la perspectiva dimensional del continuo impulsivo-compulsivo [18,21,40], confirmando que tanto la BN/TA como el TJ son patologías con una alta impulsividad rasgo, aunque difieran en los rasgos impulsivos que los caracterizan.

Se observó además en el **Estudio 3** que el sexo juega un papel importante en este dominio impulsivo, principalmente en el TJ. Aunque hasta el momento no se habían encontrado diferencias de sexo en ningún rasgo impulsivo al estudiar el TJ [276], este estudio desveló que las mujeres con TJ mostraban una persistencia más baja que los varones con TJ. Por otro lado, nuestros hallazgos sugieren que, en lo que respecta a la búsqueda de la novedad, la BN/TA y el TJ parecen guardar una mayor semejanza en mujeres que en varones. Estas diferencias resaltan la necesidad de considerar la perspectiva de género como una variable a tener en cuenta en el abordaje de estos trastornos, con el fin de mejorar la respuesta a las terapias al uso (ver **Figura 5**).

La presente tesis analizó también la posible vinculación de la impulsividad rasgo con otros factores, como la psicopatología y la respuesta al tratamiento (**Estudios 4 y 5**). Según nuestros resultados, aquellos pacientes con TCA que además presentan psicopatología de abuso de alcohol y/o drogas parecen exhibir una mayor búsqueda de la novedad y, consecuentemente, mayor impulsividad rasgo. Estos hallazgos coinciden con la evidencia previa [343,344], y sugieren que altos niveles de búsqueda de la novedad se asociarían a una mayor vulnerabilidad a desarrollar sintomatología adictiva. Asimismo, la alta urgencia negativa y alta búsqueda de sensaciones parecen estar asociadas a una peor respuesta al tratamiento en el TJ, lo cual concuerda con la evidencia previa [345] y con aquellos estudios que asocian la impulsividad rasgo a una mayor sintomatología y severidad en el TJ [346–348]. De forma similar, otros rasgos de personalidad, como la baja dependencia a la recompensa o la baja auto-dirección, también han sido relacionados con una peor respuesta al tratamiento, subrayando así el importantísimo papel que ejerce la personalidad dentro de este trastorno. Concluyendo, nuestros hallazgos ponen de manifiesto la relevancia de los rasgos impulsivos en el desarrollo y mantenimiento de estos trastornos, así como la necesidad de intervenciones especializadas

focalizadas en subsanar estas alteraciones. Por ello, estrategias complementarias de tratamiento orientadas a mejorar la capacidad de regulación emocional y el autocontrol pueden ser de gran utilidad en estos trastornos, como se ha demostrado en estudios previos [349,350]. Estas estrategias terapéuticas, algunas de ellas basadas en las nuevas tecnologías, como los *serious games,* han demostrado buenos resultados en trastornos del espectro impulsivo-compulsivo como los TCA y el TJ [203,351] (ver **Figura 5**).

De forma similar a los rasgos impulsivos, la impulsividad de respuesta ha sido identificada en la mayoría de los trastornos del espectro impulsivo-compulsivo, especialmente en aquellos situados en el polo impulsivo [250,286]. En esta tesis, se emplearon varios tipos de tareas para medir esta dimensión, y los resultados sugieren que las alteraciones en la impulsividad de respuesta podrían estar supeditadas al tipo de tarea empleada para su medición (**Estudios 2 y 3**). Mientras que con una tarea de tipo *Go/No-go*, no se aprecian diferencias en el control inhibitorio de pacientes con TCA y de sujetos sin psicopatología, al emplear la prueba SCWT sí que observamos un control inhibitorio inferior en los TCA. A este respecto, se ha sugerido la posibilidad de que únicamente ciertos elementos específicos del control inhibitorio puedan estar afectados en pacientes con TCA, lo cual explicaría estos resultados contradictorios [352]. Igual que sucede en los TCA, se observa un peor control inhibitorio en el TJ mediante el uso del SCWT. Recientes investigaciones habían subrayado la presencia de déficits de control inhibitorio en el TJ [286,353,354] y los TCA [252,253,355,356], pero tan sólo un estudio había comparado ambas patologías [322], obteniendo resultados análogos a los nuestros. Los altos niveles de impulsividad de respuesta semejantes en los TCA y el TJ podrían estar relacionados con procesos subyacentes comunes, los cuales implicarían deficiencias en el sistema de inhibición conductual [357]. Estos resultados refuerzan de nuevo la idea anteriormente expuesta de que ciertos tratamientos complementarios focalizados en el control de respuestas impulsivas y en la autoregulación emocional podrían beneficiar enormemente a los pacientes con TCA y TJ, especialmente a aquellos con un perfil más impulsivo.

Por otro lado, la impulsividad de respuesta es la única dimensión impulsiva que, en patologías como los TCA y el TJ, no parece guardar relación con factores como el sexo, el abuso de sustancias o la respuesta al tratamiento (**Estudios 3, 4 y 5**). Tampoco parece que en los TCA los mecanismos de regulación emocional interfieran con esta dimensión (**Estudio 2**), indicando

que en estos trastornos los mecanismos neuronales implicados en el control inhibitorio son en su mayoría no emocionales. En este sentido, estudios previos ya habían señalado que este dominio impulsivo era el único que no se había podido asociar a factores tales como la severidad en el TJ [230,347]. Teniendo en cuenta que no todas las dimensiones de la impulsividad están asociadas del mismo modo con factores como el sexo, la psicopatología, la respuesta al tratamiento o la regulación emocional, sería posible considerarlas como entidades independientes, aunque parcialmente interrelacionadas.

La evidencia empírica también ha enfatizado la relevancia de la impulsividad de elección en distintas patologías, incluyendo los TCA [267,269], las adicciones a sustancias [358,359] y las adicciones comportamentales como el TJ [289–291]. Esta tesis corroboró la presencia de una alta impulsividad de elección en pacientes con TJ y pacientes con BN/TA, siendo ésta ligeramente más elevada en los últimos (**Estudio 3**). Numerosos estudios ya habían informado de importantes déficits en los procesos de toma de decisiones en pacientes con BN/TA [267–269] y con TJ [289–291], sugiriendo déficits en la habilidad para sopesar las ventajas y desventajas de sus elecciones. A nivel clínico, esto se observa en las conductas desadaptativas (p. ej., atracones, purgas, juego, etc.) que llevan a cabo sin atender a las consecuencias negativas, focalizándose únicamente en el reforzamiento positivo y negativo que estas conductas proporcionan, ya sea proporcionando placer inmediato o aliviando los estados emocionales negativos [258,273,298,360]. Siendo el primer estudio en analizar este dominio comparando TJ con BN/TA, nuestros hallazgos apuntan a una elevada impulsividad de elección en ambas patologías, ligeramente más acentuada en la BN/TA.

Al explorar la potencial influencia del sexo en el **Estudio 3**, sólo en el TJ las mujeres mostraban una mayor impulsividad de elección que los varones. Estos resultados coinciden con los comentados anteriormente en impulsividad rasgo, y confirman que las mujeres con TJ presentarían en general mayores niveles de impulsividad que los varones con el mismo diagnóstico. Desde una perspectiva clínica, se subraya así la importancia de considerar el factor sexo como una variable potencialmente relevante en el TJ. En este sentido, el juego de apuesta ha sido tradicionalmente una actividad de ocio más frecuente en los varones que en las mujeres. Muestra de ello son las prevalencias de juego social, problemático y patológico (TJ), que indican los estudios epidemiológicos [361]. Las muestras de varones suelen estar sobre-

representadas en la literatura científica internacional, y a menudo se llegan a conclusiones generales respecto a la identificación de fenotipos, perfiles de riesgo, y respuesta al tratamiento en el TJ que, en realidad, responden mayoritariamente a hallazgos identificados en varones. Por ello, la caracterización del trastorno en mujeres es bastante desconocida. Así, observar que las mujeres con TJ presentan elevados niveles de impulsividad de elección y rasgo, superiores incluso a los de varones, es un resultado importante que contribuye de forma destacada al avance del conocimiento de esta patología, tanto desde la clínica (diseño de programas de tratamiento específicos que tomen en consideración las diferencias de género) como desde la prevención.

Por su parte, aunque la impulsividad de elección no parece tener un valor predictivo en la respuesta al tratamiento de pacientes con TJ (**Estudio 5**), sí estaría vinculada a un mayor abuso de sustancias en los TCA (**Estudio 4**). Nuestros resultados sugieren que, en los TCA, los altos niveles de impulsividad de elección se asocian a una mayor dificultad para aprender de las contingencias negativas o positivas de las elecciones [381], lo cual puede derivar en el desarrollo de conductas desadaptativas de abuso de sustancias [375,382,383]. En definitiva, aunque la elevada impulsividad de elección está presente en ambas patologías (**Estudio 3**), es posible que ésta suponga un mayor factor de riesgo para los TCA que para el TJ, tal cual indican los resultados de los **Estudios 4 y 5**. Además, en el caso del TJ, tanto la evidencia previa como los resultados comentados anteriormente parecen indicar que serían otras variables, como los rasgos impulsivos o incluso otros rasgos de personalidad (dependencia a la recompensa y autodirección), las más implicadas en una pobre respuesta a los programas de intervención.

En último lugar, a pesar de que el concepto de compulsividad está menos extendido que el de impulsividad [227], cada vez más se investiga su implicación en numerosas patologías [300]. Dada su estrecha relación con los TCA y el TJ, esta tesis perseguía el objetivo de clarificar el papel que desempeña la compulsividad en estos trastornos, intentando identificar semejanzas y diferencias entre ambos (**Estudio 3**). A este respecto, tanto en el TJ como en la BN/TA, se observó una baja flexibilidad cognitiva y una alta evitación del daño, siendo este rasgo compulsivo superior en la BN/TA. Tanto los hallazgos en flexibilidad cognitiva [75,267,323,362] como los resultados en evitación del daño [18,363,364] coinciden con la

evidencia previa, poniendo de manifiesto los mayores niveles de compulsividad que caracterizan a estas patologías, especialmente a la BN/TA. Esta alta compulsividad podría subyacer al uso de conductas desadaptativas con el fin de evitar el afecto negativo y aliviar el estrés emocional [21,22]. Además, los problemas en flexibilidad cognitiva podrían explicar la incapacidad de estos pacientes para aprender de los errores y gestionar el afecto negativo, conduciendo a una pérdida del control sobre la comida o el juego [314,318,324,325].

Centrándonos en los efectos del sexo, las mujeres con TJ mostraron una menor flexibilidad cognitiva y una mayor evitación al daño que los varones (**Estudio 3**). Esta diferenciación por sexo en la compulsividad de pacientes con TJ ya había sido identificada en ambos dominios [365,366]. Estos hallazgos, junto con los comentados previamente en impulsividad, indican que las mujeres con TJ presentarían un perfil específico caracterizado por una impulsividad y compulsividad más acentuadas, lo cual encajaría con las diferencias asociadas al sexo observadas en otros factores relevantes en esta patología, como las dificultades de regulación emocional [367]. Además, igual que sucedía en la impulsividad rasgo, nuestros resultados también sugieren que las mujeres con TJ podrían asemejarse más en flexibilidad cognitiva a las mujeres con BN/TA que a los varones con TJ. En su conjunto, nuestros hallazgos resaltan el importante papel que ejerce el sexo en la impulsividad-compulsividad de estas patologías, pudiendo observarse distintos efectos dependiendo del dominio analizado. Asimismo, justifican el uso y la utilidad de los modelos diagnósticos dimensionales frente a los categoriales, tal y como estudios previos centrados en el espectro impulsivo-compulsivo también han demostrado [18,21,40].

Para finalizar, los resultados que emergieron de los **Estudios 4 y 5** subrayan la relevancia de la compulsividad en el mal pronóstico de los TCA y el TJ, dado que parece asociarse a la presencia de conductas altamente disfuncionales (p. ej., consumo de alcohol y/o drogas) en los TCA, y a un mayor número de abandonos, recaídas y peor adherencia al tratamiento en el TJ. En relación a los TCA, estos pacientes presentan dificultades en la flexibilidad cognitiva [267,312], las cuales parecen tener un impacto negativo en sus estrategias de resolución de problemas y regulación de emociones negativas [21,22], pudiendo acentuar el desarrollo de conductas adictivas. Por otro lado, la evidencia apunta a que las dificultades en flexibilidad cognitiva son un factor distintivo en el TJ [322,323]. También cabe destacar que la conducta

de juego en sí misma es considerada un comportamiento compulsivo de evitación del afecto negativo [21], por lo que es esperable que la alta compulsividad muestre ser un factor predictor de peor respuesta al tratamiento en este trastorno.

5.2. CONSIDERACIONES GLOBALES

Desde una amplia pero integrativa perspectiva, los resultados de esta tesis reflejan las notables alteraciones en regulación emocional, impulsividad y compulsividad que caracterizan a los pacientes con TCA y TJ (ver **Figura 5**). A grandes rasgos, parece que los TCA, especialmente la BN y el TA, comparten numerosas características impulsivo-compulsivas con el TJ. Sin embargo, pueden apreciarse algunas diferencias significativas principalmente vinculadas con la impulsividad y compulsividad rasgo. Por su parte, la AN presenta un patrón característico de disregulación emocional y dificultades para regular el *food craving*, lo cual es apreciable en ambos subtipos, el restrictivo y el bulímico-purgativo. Sin embargo, a pesar de la relevancia de las emociones y su manejo en los TCA, estos procesos no parecen interferir con los mecanismos de control inhibitorio o impulsividad de respuesta de los pacientes con TCA. No obstante, lo que sí se ha demostrado en esta tesis es que esos déficits en impulsividad y compulsividad están vinculados a otros factores relevantes para ambas patologías, como el sexo, la psicopatología y la respuesta al tratamiento. Por lo que sería de vital importancia abordar estos trastornos desde una perspectiva integrativa que tuviese en cuenta todos estos aspectos. Se espera que estos hallazgos puedan contribuir a expandir el conocimiento en el campo de los trastornos del espectro impulsivo-compulsivo, con la finalidad última de ofrecer novedosas intervenciones focalizadas en aquellos aspectos que caracterizan a estos trastornos.

5.3. LIMITACIONES

Los resultados expuestos en la presente tesis deben ser interpretados con cautela y en consideración de ciertas limitaciones. En primer lugar, la generalización de resultados a otras poblaciones es limitada dada la modesta muestra de algunos de los trabajos incluidos (**Estudio 1 y 2**), y el hecho de que todos los pacientes fueron reclutados en el mismo centro, lo cual no reflejaría a la población clínica en su conjunto. Segundo, incluimos pacientes recibiendo

tratamiento farmacológico, factor que podría estar sesgando nuestros resultados. Tercero, a excepción del **Estudio 5**, todos los estudios tienen un diseño transversal, lo cual no permite determinar causalidad en las variables evaluadas. Sería conveniente el uso de estudios longitudinales con suficiente poder estadístico para poder determinar si las alteraciones identificadas persisten tras la recuperación de los pacientes o si precedían al inicio de la enfermedad. En cuarto lugar, parte de los datos analizados fueron recogidos de forma retrospectiva y autoreportada, lo cual puede ser susceptible a la deseabilidad social y el recuerdo, pudiendo generar sesgos en la validez y fiabilidad de los resultados. Quinto, la mayoría de los estudios, excepto el **Estudio 3**, incluían muestras formadas exclusivamente por mujeres con TCA o por varones en el caso del TJ, lo cual limitaría la generalización de resultados a poblaciones clínicas del sexo opuesto. Finalmente, no se emplearon instrumentos validados de cribado para detectar otras comorbilidades psiquiátricas distintas a los TCA o al TJ en los grupos control. Sería necesario que las futuras investigaciones evaluasen este aspecto en profundidad.

5.4. FUTURAS LÍNEAS DE INVESTIGACIÓN

Sería muy beneficioso para el ámbito de la psicología, que nuevas investigaciones se adentrasen el estudio de los trastornos mentales desde una perspectiva dimensional, tal cual se ha planteado en esta tesis. Esto ayudaría a solventar las limitaciones presentes en las aproximaciones categóricas, y proporcionaría nuevas nociones en el tratamiento y abordaje de las distintas psicopatologías. Centrándonos en el campo de los TCA y el TJ, resultaría de gran utilidad investigar el rol que desempeñan los déficits en regulación emocional y control de los impulsos desde diseños longitudinales que permitan aportar datos de causalidad y efectos de estabilidad temporal. También serían necesarios estudios de respuesta al tratamiento que aportasen valor empírico a la necesidad de abordar estas dificultades en la práctica clínica. Todo apunta a que los pacientes con TCA y el TJ se podrían beneficiar de tratamientos complementarios a la terapia cognitiva-conductual, focalizados en suplir estos déficits emocionales y neurocognitivos (p. ej., control inhibitorio, toma de decisiones y flexibilidad cognitiva). Además, sería interesante incluir estudios de neuroimagen que analizasen todos estos procesos a nivel neural, complementando así los resultados aportados en la presente tesis.

Asimismo, nuestros hallazgos han puesto de manifiesto que los déficits en impulsividad y compulsividad observados en estos trastornos pueden verse agravados por factores como el sexo. Resulta por tanto de vital importancia considerar este factor al estudiar estas patologías, incluyendo mayores muestras de varones en el campo de los TCA y de mujeres en el TJ, supliendo así una limitación muy mencionada por la mayoría de los estudios realizados hasta el momento. Finalmente, futuros estudios deberían tener en consideración otras variables importantes, como la toma de psicofármacos, los cuales pueden estar modulando, no sólo la sintomatología manifestada por los pacientes, sino también otras variables cognitivas y de personalidad.

6. CONCLUSIONS

Based on the results depicted in this thesis, the following conclusions may be drawn:

1) Emotion dysregulation in anorexia nervosa (AN) has been confirmed at a clinical and a neurophysiological level, suggesting that neural mechanisms and structures underlying emotion regulation processes might be altered in AN.

2) Despite the enhanced self-reported *food craving* observed in AN, especially in the bulimic-purging subtype, neurophysiological evidence indicates successful achievement of *food craving* regulation at a neural level.

3) AN and bulimic spectrum disorders (BSDs) seem to be distinguished by the presence or absence of different impulsive personality traits, showing BSDs the highest overall impulsive personality.

4) Behavioural and neurophysiological data do not appear to show altered response impulsivity in AN or BSDs, at least when assessing motor inhibition by a *Go/No-go* task. Moreover, emotional modulation of response inhibition has not been proven in either AN or BSDs.

5) Alterations in response impulsivity seem to be dependent on the type of task employed to measure this dimension, since BSD patients only exhibit increased response impulsivity as measured by an interference control task such as the SCWT.

6) Both gambling disorder (GD) and BSDs display elevated levels of impulsivity and compulsivity in all the studied domains: impulsive/compulsive personality traits, response impulsivity, choice impulsivity and cognitive flexibility.

7) Differences between GD and BSDs have been highlighted in some impulsivity and compulsivity dimensions, mainly in those related to personality. Specifically, patients with GD exhibit higher novelty seeking, while BSD patients display lower persistence, higher harm avoidance and a trend towards greater impulsive choice.

8) Sex is a relevant factor to consider when studying impulsivity and compulsivity in GD, since women with GD present greater abnormalities than GD men in all the impulsivity and compulsivity components, except for response impulsivity. In addition, GD women

seem to be even more closely related to BSDs women than to GD men in several domains, such as choice impulsivity and cognitive flexibility, supporting the perspective of the dimensional impulsive-compulsive spectrum.

9) ED patients with alcohol and/or drug abuse symptoms display a specific phenotype characterised by greater impulsive personality, enhanced choice impulsivity and decreased cognitive flexibility.

10) Impulsivity and compulsivity features may influence response to treatment in GD. Specifically, high impulsive traits and low cognitive flexibility seem to predict low therapy compliance, relapse and dropout at early change-stage, at the end of treatment and at follow-up.

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8. ANEXO

CURRÍCULUM VITAE

María del Espino Lozano Madrid

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Education

September 2014 – Present **University of Barcelona, Spain**

PhD in Medicine: "Neurocognitive functioning under extreme weight conditions (from Obesity to Anorexia nervosa): Detection of specific endophenotypes and their association with therapy response".

September 2014 – July 2016 **University of Granada, Spain**

Master's Degree in Clinical Psychology.

Master's dissertation regarding processing of food stimuli in eating disorder patients assessed with different psychophysiological measures.

September 2010 – July 2014 **University of Granada, Spain**

Bachelor's degree in Psychology specializing in Clinical Psychology.

Extraordinary Award in the Bachelor's degree in Psychology.

Award in Excellence in Academic Performance granted by the University of Granada and Caja Rural de Granada.

Professional experience

September 2016 – Present

PhD researcher contracted by the Bellvitge Biomedical Research Institute (IDIBELL). Supported by a predoctoral grant of the Ministerio de Educación, Cultura y Deporte (FPU15/02911).

Research fellow in the CIBER of Obesity and Nutrition (CIBERobn), Instituto Carlos III - Ministry of Health.

Center: Eating Disorders Unit coordinated by Dr F. Fernández Aranda, Department of Psychiatry, Bellvitge University Hospital, Barcelona, Spain.

September 2013 – May 2014

Research assistant at the Department of Personality, Assessment and Psychological Treatment of the University of Granada.

Supported by a research grant of the Vicerrectorado de Política Científica e Investigación - University of Granada.

Centre: Brain, Mind, and Behavior Research Center, University of Granada, Granada, Spain.

Teaching activities

September 2016 – Present **University of Barcelona, Spain**

Course: Psychology in Health Sciences

Medical School: Faculty of Medicine and Health Sciences, Bellvitge Health Sciences Campus

Teaching hours: 180 (18 ECTS)

Courses: 2016/17; 2017/18; 2018/19; 2019/20; 2020/21

Research Fellowships

August 2018 – November 2020

Pre-doctoral Research Fellowship at the Section of Eating Disorders of the Institute of Psychiatry, Psychology and Neuroscience - King's College London, United Kingdom.

Supervisor: Prof. Janet Treasure.

June 2019 – November 2019

Pre-doctoral Research Fellowship at the Section of Eating Disorders of the Institute of Psychiatry, Psychology and Neuroscience - King's College London, United Kingdom.

Supervisor: Prof. Janet Treasure.

Publications

Journal Articles

1. Mallorquí-Bagué N, Mestre-Bach G, **Lozano-Madrid M**, Granero R, Vintró-Alcaraz C, Fernández-Aranda F, Gómez-Peña M, Moragas L, Del Pino-Gutierrez A, Menchón JM, Jiménez-Murcia S.

Gender and gambling disorder: Differences in compulsivity-related neurocognitive domains. Addict Behav. 2021 Feb 1;113.

2. Estévez A, Jauregui P, Lopez-Gonzalez H, Macia L, López N, Zamora L, Onaindia J, Granero R, Mestre-Bach G, Steward T, Fernández-Aranda F, Gómez-Peña M, Moragas L, Mena-Moreno T, **Lozano-Madrid M**, del Pino-Gutiérrez A, Codina E, Testa G, Vintró-Alcaraz C, Agüera Z, Munguía L, Baenas I, Valenciano-Mendoza E, Mora-Maltas B, Menchón JM, Jiménez-Murcia S. Exploring the Predictive Value of Gambling Motives, Cognitive Distortions, and Materialism on Problem Gambling Severity in Adolescents and Young Adults. J Gambl Stud. 2020;

3. Estévez A, Jauregui P, Granero R, Munguía L, López-González H, Macía L, López N, Momeñe J, Corral S, Fernández-Aranda F, Agüera Z, Mena-Moreno T, **Lozano-Madrid M**, Vintró-Alcaraz C, del Pino-Gutierrez A, Codina E, Valenciano-Mendoza E, Gómez-Peña M, Moragas L, Casalé G, Mora-Maltas B, Mestre-Bach G, Menchón JM, Jiménez-Murcia S. Buying-shopping disorder, emotion dysregulation, coping and materialism: a comparative approach with gambling patients and young people and adolescents. Int J Psychiatry Clin Pract. 2020;1–9.

4. **Lozano-Madrid M**, Clark Bryan D, Granero R, Sánchez I, Riesco N, Mallorquí-Bagué N, Jiménez-Murcia S, Treasure J, Fernández-Aranda F. Impulsivity, Emotional Dysregulation and Executive Function Deficits Could Be Associated with Alcohol and Drug Abuse in Eating Disorders. J Clin Med. 2020 Jun 21;9(6):1936.

5. Granero R, Jiménez-Murcia S, del Pino-Gutiérrez A, Mena-Moreno T, Mestre-Bach G, Gómez-Peña M, Moragas L, Aymamí N, Giroux I, Grall-Bronnec M, Sauvaget A, Codina E, Vintró-Alcaraz C, **Lozano-Madrid M**, Camozzi M, Agüera Z, Martín-Romera V, Sánchez-González J, Casalé G, Sánchez I, López-González H, Munguía L, Valenciano-Mendoza E, Mora B, Baenas-Soto I, Menchón JM, Fernández-Aranda F. Gambling Phenotypes in Older Adults. J Gambl Stud. 2020 Sep 1;36(3):809–28.

6. Chami R, Treasure J, Cardi V, **Lozano-Madrid M**, Eichin KN, McLoughlin G, Blechert J. Exploring Changes in Event-Related Potentials After a Feasibility Trial of Inhibitory Training for Bulimia Nervosa and Binge Eating Disorder. Front Psychol. 2020 May 27;11.

7. Estévez A, Jáuregui P, Lopez-Gonzalez H, Mena-Moreno T, **Lozano-Madrid M**, Macia L, Granero R, Mestre-Bach G, Steward T, Fernández-Aranda F, Gómez-Peña M, Moragas L, del Pino-Gutierrez A, Codina E, Testa G, Vintró-Alcaraz C, Agüera Z, Munguía L, Baenas I, Valenciano-Mendoza E, Mora B, Menchón JM, Jiménez-Murcia S. The Severity of Gambling and Gambling Related Cognitions as Predictors of Emotional Regulation and Coping Strategies in Adolescents. J Gambl Stud. 2020;

8. Granero R, Jiménez-Murcia S, Fernández-Aranda F, Del Pino-Gutiérrez A, Mena-Moreno T, Mestre-Bach G, Gómez-Peña M, Moragas L, Aymamí N, Giroux I, Grall-Bronnec M, Sauvaget A,

Codina E, Vintró-Alcaraz C, **Lozano-Madrid M**, Camozzi M, Agüera Z, Sánchez-González J, Casalé-Salayet G, Sánchez I, López-González H, Valenciano-Mendoza E, Mora B, Baenas I, Menchón JM. Presence of problematic and disordered gambling in older age and validation of the South Oaks Gambling Scale. PLoS One. 2020 May 1;15(5).

9. Granero R, Valero-Solis S, Fernández-Aranda F, Gómez-Peña M, Moragas L, Mena-Moreno T, Del Pino-Gutierrez A, Codina E, Martín-Romera V, Casalé G, Agüera Z, Baenas-Soto I, Valenciano-Mendoza E, Mora-Maltas B, Sánchez I, **Lozano-Madrid M**, Menchón JM, Murcia SJ. Response trajectories of gambling severity after cognitive behavioral therapy in young-adult pathological gamblers. J Behav Addict. 2020 Apr 7;9(1):140–52.

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11. Guerrero-Vaca D, Granero R, Fernández-Aranda F, Mestre-Bach G, Martín-Romera V, Mallorquí-Bagué N, Mena-Moreno T, Aymamí N, del Pino-Gutiérrez A, Gómez-Peña M, Moragas L, Agüera Z, Vintró-Alcaraz C, **Lozano-Madrid M**, Menchón JM, Tárrega S, Munguía L, Jiménez-Murcia S. Explicit and Implicit Emotional Expression in Gambling Disorder Measured by a Serious Game: A Pilot Study. J Gambl Stud. 2020;

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Declaración de códigos éticos

El Dr. **Fernando Fernández Aranda** con DNI **46040411T** y la Dra**. Susana Jiménez Murcia** con DNI **40432581F,** miembros del Programa de Doctorado Medicina e Investigación Traslacional, impartido por Facultad de Medicina y Ciencias de la Salud de la Universidad de Barcelona, **DECLARAN QUE** como directores de la doctoranda **María del Espino Lozano Madrid** con DNI **70588974**-L, nos consta que en el desarrollo de esta tesis titulada **"Regulación emocional, Impulsividad y Compulsividad en los Trastornos de la Conducta Alimentaria y el Trastorno de Juego"**, se han cumplido los códigos éticos y de buenas prácticas y no tenemos conocimiento de que se haya producido ningún plagio.

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Declaración de no plagio

Yo, Dª **María del Espino Lozano Madrid** con DNI **70588974**-L, estudiante del Programa de Doctorado Medicina e Investigación Traslacional, impartido por Facultad de Medicina y Ciencias de la Salud de la Universidad de Barcelona, en el curso 2019-2020, como autora de este documento académico, titulado **"Regulación emocional, Impulsividad y Compulsividad en los Trastornos de la Conducta Alimentaria y el Trastorno de Juego"**, y presentado como Tesis Doctoral para la obtención del título correspondiente, **DECLARO QUE** esta memoria de tesis es fruto de mi trabajo personal, que no he copiado y que no he empleado ideas, formulaciones, citas integrales o ilustraciones extraídas de cualquier obra, memoria, etc. (versión impresa o electrónica), sin mencionar de forma clara, estricta y explícita su origen, tanto en el cuerpo del texto como en la bibliografía.

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