

VOL IV

Ciências da Saúde:

Investigação e Prática



Dr. Guillermo Julián González-Pérez
Dra. María Guadalupe Vega-López
(organizadores)



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2025

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**EDITORIA
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PRÓLOGO

La obra *Ciências da Saúde: Investigação e Prática IV* reúne un conjunto plural y profundamente significativo de 17 estudios que reflejan la complejidad, la urgencia y la diversidad de los desafíos contemporáneos en salud.

Elaborado por autoras y autores de distintos países iberoamericanos - Argentina, Colombia, Chile Ecuador, México y Portugal-, con trayectorias académicas y profesionales igualmente diversas, este volumen se consolida como un espacio de diálogo interdisciplinario, en el que confluyen perspectivas de la salud pública, la clínica, la salud mental, la enfermería, la fisioterapia, la farmacéutica, las tecnologías en salud y la epidemiología.

Estructurado en cuatro grandes ejes, el libro recorre escenarios que abarcan desde los determinantes sociales y ambientales de la salud hasta la aplicación de tecnologías emergentes para el diagnóstico, el monitoreo y el cuidado.

En el eje **Salud pública, ambiente y sistemas de salud**, se presentan reflexiones y evidencias sobre problemáticas colectivas que afectan a poblaciones enteras: el control de vectores, la exposición a contaminantes tóxicos, las características de los accidentes en el hogar, las desigualdades persistentes tanto en la sociedad como en los sistemas de salud y su impacto en el comportamiento de indicadores como la mortalidad materna. Los estudios aquí reunidos iluminan cómo factores sociales, ambientales y políticos moldean las condiciones de vida, riesgo y bienestar, reforzando la necesidad de políticas integradas de prevención y equidad.

El eje **Salud mental, bienestar y psicología de la salud** incluye investigaciones sobre los aspectos emocionales, conductuales y psicosociales que influyen en la vida académica, profesional y social. Se destacan análisis sobre satisfacción con la vida, estilos de vida saludables, intervenciones terapéuticas innovadoras, estilos educativos y de afrontamiento así como sobre las adicciones de nuevo tipo. Sus contribuciones revelan una comprensión ampliada y actualizada del cuidado en salud mental, siempre guiada por la evidencia y la sensibilidad humana.

En el eje **Clínica, diagnóstico y tecnologías en salud**, se presenta un conjunto de trabajos que exploran herramientas clínicas, protocolos diagnósticos, procesos de esterilización, estudios neurobiológicos de los trastornos alimentarios y modelos basados en inteligencia artificial para el apoyo a la toma de decisiones en entornos críticos. Estos capítulos dan cuenta del avance continuo de la innovación tecnológica y de su capacidad para transformar las prácticas asistenciales, promover la seguridad y ampliar la eficiencia de los servicios de salud.

Finalmente, el eje **Enfermería, familia y comunidades de cuidado** aborda la intervención clínica y relacional de profesionales que trabajan directamente con las familias, personas mayores y grupos comunitarios. Son aportes que evidencian el papel estratégico de la enfermería en la promoción de la autonomía, la funcionalidad, la salud emocional y la construcción de redes de apoyo – elementos esenciales para el cuidado integral.

Este libro, por lo tanto, no solo reúne resultados de investigación: materializa una visión contemporánea de la salud como un campo interdisciplinario, integrado y profundamente humano. Celebra la producción científica latinoamericana e ibérica, fomenta nuevas discusiones e invita a profesionales, estudiantes e investigadores a reflexionar sobre prácticas, desafíos y posibilidades emergentes.

Que estas páginas inspiren nuevas miradas, nuevas preguntas y formas de cuidar.
Buena lectura.

Guillermo Julián González-Pérez

María Guadalupe Vega-López

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SEQUENCE ANALYSIS OF FIVE EXONS OF *SLC6A4* GENE IN MEXICAN PATIENTS WITH ANOREXIA NERVOSA AND BULIMIA NERVOSA¹

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ABSTRACT: Background: Accumulating evidence indicates that alterations in the serotonin system are related to changes in eating behavior. The serotonin transporter is encoded by the *SLC6A4* gene and has been an interesting candidate for anorexia nervosa-restrictive type (AN-R) and bulimia nervosa (BN). Interestingly, functional variants have been identified in the coding region that could contribute to understand the role of this gene in eating disorders. The aim was to identify genetic variants in five exons of *SLC6A4* gene

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using Sanger-sequencing in anorexia nervosa-restrictive and bulimia nervosa patients, and a control group. **Method:** The sample consisted of 86 patients and 50 control subjects. We obtained DNA samples from all subjects and performed Sanger-sequence analysis of the 1, 2, 3, 8 and 9 exons. The sequences were compared with the reference sequence of the *SLC6A4* gene. **Results:** The sequence analysis of the five exons of the gene identified several variants. In the AN-R, we observed two novel variants (g.130delA and c.1740G>A), three synonymous variants (rs57172732, rs55908624, rs74478645) and a missense variant (L90F) reporting a probably deleterious and damaging variant. In BN, we identified two novel variants (g.295C>G and c.1725G>A), and the non-synonymous (rs28914832/1425V), reported as benign. Interestingly, we observed the 425V variant in three patients in the BN, variant that previously was reported in patients with a spectrum obsessive-compulsive disorder. **Conclusion:** The results of our study suggest that variants of the *SLC6A4* gene are related with a possible damaging or gain-of-function and may be involved in the susceptibility to AN-R and BN patients. However, the present findings should be considered as preliminary until replicated in large samples.

KEYWORDS: anorexia nervosa; bulimia nervosa; sequencing; *SLC6A4*; genetic variants.

ANÁLISIS DE LA SECUENCIA DE CINCO EXONES DEL GEN *SLC6A4* EN PACIENTES MEXICANOS CON ANOREXIA NERVIOSA Y BULIMIA NERVIOSA

RESUMEN: Antecedentes: La evidencia acumulada indica que las alteraciones en el sistema serotoninérgico están relacionadas con cambios en la conducta alimentaria. El transportador de serotonina está codificado por el gen *SLC6A4* y ha sido un candidato interesante para la anorexia nerviosa restrictiva (AN-R) y la bulimia nerviosa (BN). Resulta interesante que se hayan identificado variantes funcionales en la región codificante que podrían contribuir a comprender el papel de este gen en los trastornos de la conducta alimentaria. El objetivo fue identificar variantes genéticas en cinco exones del gen *SLC6A4* mediante secuenciación Sanger en pacientes con anorexia nerviosa restrictiva y bulimia nerviosa, y en un grupo control. **Método:** La muestra consistió en 86 pacientes y 50 sujetos control. Se obtuvieron muestras de ADN de todos los participantes y se realizó el análisis de secuenciación Sanger de los exones 1, 2, 3, 8 y 9. Las secuencias se compararon con la secuencia de referencia del gen *SLC6A4*. **Resultados:** El análisis de la secuencia de los cinco exones del gen identificó varias variantes. En el grupo AN-R, se observaron dos variantes nuevas (g.130delA y c.1740G>A), tres variantes sinónimas (rs57172732, rs55908624 y rs74478645) y una variante de cambio de sentido (L90F), que se describe como probablemente deletérea y dañina. En el grupo BN, se identificaron dos variantes nuevas (g.295C>G y c.1725G>A) y la variante no sinónima (rs28914832/1425V), descrita como benigna. Cabe destacar que se observó la variante 425V en tres pacientes con BN, variante que previamente se había descrito en pacientes con un trastorno obsesivo-compulsivo del espectro. **Conclusión:** Los resultados de nuestro estudio sugieren que las variantes del gen *SLC6A4* están relacionadas con una posible alteración o ganancia de función y podrían influir en la susceptibilidad a la anorexia nerviosa restrictiva (AN-R) y la bulimia nerviosa (BN). Sin embargo, estos hallazgos deben considerarse preliminares hasta que se repliquen en muestras de mayor tamaño.

PALABRAS CLAVE: anorexia nerviosa; bulimia nerviosa; secuenciación; *SLC6A4*; variantes genéticas.

1. INTRODUCTION

Anorexia nervosa (AN) and bulimia nervosa (BN) are mental disorders characterized by severe disturbance of body image and meal patterns (DSM-5). AN is defined by an intense fear of gaining weight, or persistent behavior that interferes with weight gain, even though underweight. AN restrictive (AN-R) type is defined by severe restrictions on the amount and type of food they consume, obsessive rules and rigid thinking related with gain weight. BN is an eating disorder characterized by binge eating followed by inappropriate compensatory behaviors to prevent weight gain (DSM-5). The etiology is unknown, but the genetic influences contribute in the onset and development of the disease (Thornton et al., 2010).

Evidence supports altered serotonergic neurotransmission in the physiology of AN and BN. Studies in animal models and humans indicate that alterations of the serotonin system result in changes in emotional states and altered satiety signaling in the brain.

The serotonin transporter (5-HTT) is a protein key in the serotonergic system; it is on the pre-synaptic membranes of nerve terminals in the midbrain and in the brain stem raphe nuclei. The synaptic activity of 5-HTT mediates rapid removal and recycling of released serotonin following neuronal stimulation in the brain and terminates the action of serotonin, playing a role in mediating the regulation of the availability of serotonin to other receptors of serotonergic systems. Additionally, the 5-HTT is regulated by protein kinase-associated pathways, including protein kinase C (PKC), protein kinase G (PKG), and p38 mitogen-activated protein kinase (MAPK). The PKC-dependent phosphorylation and down-regulation of the 5-HTT protein is sensitive to extracellular serotonin, which plays a regulatory role in the transporter of 5-HT. (Murphy et al., 2008).

The 5-HTT is encoded by the *SLC6A4* gene located on chromosome 17q11.1-q12 and is composed of 14 exons, spanning 40 kb. The sequences of the transcript codified a protein comprising 630 amino acid and has twelve transmembrane domains. Common variants, minor allele frequency (MAF) $\geq 5\%$, low-frequency variants ($0.5 \leq \text{MAF} < 5\%$), and rare variants ($\text{MAF} < 0.5\%$) have been identified in Mexican-American population (Glatt et al., 2001).

AN- are highly heritable suggesting that genetic variations play an important role in the pathogenesis (Bulik et al., 2006). The whole exome sequencing (WES) studies have identified variants that may have a major contribution in the development to diseases. Previously, one study analyzed two large families with multiple members with AN, identifying two rare variants, rs200039730 and rs61754648 in *HDAC4* and *ESRRA* genes respectively, increasing the risk of the developed eating disorders (Cui et al., 2013). In

addition, an excessive burden of novel damaging variants was identified in 186 genes in restricted-eating group and in 245 genes in the binge-eating group, with an implication of the genes involved in neuropeptide/neurotrophic pathways implicated in appetite regulation, including the neurotensin-glucagon-like peptide-1 and *BDNF* signaling (Lutter et al., 2017). More recently, were identified missense variants in the *DRD4*, *CCKR*, *NMS* genes that are highly expressed in the hypothalamus system, and co-segregate with AN (Bienvenu et al., 2019).

Genetic studies of *SLC6A4* polymorphisms reported in Mexican patients an association between S/Lg alleles and BN (Camarena et al., 2018). An association was reported between BN and variable number tandem repeat polymorphism VNTR located in intron 2. Other research found differences between subtypes of anorexia nervosa and the SNPs rs1872924 and rs3794809, located in introns 2 and 3 (Kiezebrink et al., 2010). Similarly, a study in multiple families with eating pathology analyzed SNPs located in introns 2, 3, 4, and a 3' untranslated region, but no significant associations were found between any genetic variant and ED-related phenotypes such as binge eating and weight/shape concern (Munn-Chernoff et al., 2012). We analyzed the G56A variant (rs6355) that presents amino acid changes and affects the transportation function and regulation, reporting an over-transmission of the 56A allele in families with AN (Camarena et al., 2012). Finally, other study identified functional variants in the exons 8 and 9, which were associated with obsessive-compulsive behaviors and anorexia nervosa (Ozaki et al., 2003). Interesting, this trait has been observed in AN-R patients, suggesting a common etiology (Anttila et al., 2018).

The variants identified in exons can have a structural and functional impact in the gene causing a gain or loss of function of the protein. Also, p.G56A, p.L605A, and p.I425V polymorphisms revealed high levels of basal 5-HT transporter in transfected and natively expressing cells (Prasad et al., 2008). Additionally, it was reported that p.G56A and p.L605A showed an altered pattern of regulation by multiple Ser/Thr kinases known to regulate SERT in native and transfected cells. Thus, both variants demonstrate insensitivity to activators of protein kinase G (PKG) and p38 mitogen-activated protein kinase (MAPK), stimuli that normally trigger elevated surface expression or enhancement of SERT catalytic rates (Blakely et al. 2005). It is interesting to identify other genetic variants in eating disorders; therefore, the aim of the study was to perform the sequencing of five exons of *SLC6A4* in AN-R and BN patients.

2. METHODS

2.1. SUBJECTS

The participants were recruited from the Clinic of Eating Disorders at the Instituto Nacional de Psiquiatria Ramon de la Fuente Muñiz. The local Institutional Ethics Committee approved the study. All participants and healthy controls gave written informed consent for participation at the time of recruitment.

The total sample included 86 female patients, 36 with anorexia nervosa-restrictive type (AN-R) and 50 with bulimia nervosa (BN) according to DSM-5 criteria.

Exclusion criteria included psychotic symptoms and significant medical and/or neurological illness.

The control group comprised 50 healthy females without current or past psychiatric history, screened using the Spanish version of the Diagnostic Interview Schedule (DIS). All individuals were over the age or risk for ED. All participants were Mexican Mestizos with a family background of three generations born in Mexico. All the participants provided written informed consent by the Ethics Committee of the Institute.

2.2. ASSESSMENT

Patients were evaluated and diagnosed according to DSM-5 (*Diagnostic and Statistical Manual of Mental Disorders, 5th edition*) criteria for ED using the Structured Clinical Interview for Mental Disorders v2.0 (SCID-1. We measured the presence of impulsivity using the Plutchik's impulsivity scale, Spanish version (Páez et al., 1996), the severity of preoccupations and rituals using the Spanish-language version of the Yale Brown-Cornell Eating Disorders Scale (YBC-EDS) (Caballero et al., 2003), and the evaluation of behavior and psychological traits in eating disorders using the Eating Disorder Inventory EDI-2 (Garcia et al., 2003).

2.3. DNA ISOLATION AND EXON SEQUENCING

Genomic DNA was extracted from whole blood using the Wizard Genomic DNA Purification Kit. Five primer pairs were used to amplify the exons 1, 2, 3, 8, and 9 (Kraft et al., 2005). The amplification was performed in a final volume of 25 µl containing 100 ng genomic DNA template, 5% DMSO, 1X KAPA HiFi HotStart ReadyMix (Kappa Biosystems), and 0.50 µM of each primer. PCR conditions were 96°C for 3 min, followed by 25 cycles at 96°C for 15 sec at 60°C for 15 sec (exception exon 9, which was 65°C) and finally 72°C for 30 sec. After amplification, the samples were visualized in 1.5% agarose Metaphor and

1.5% agarose gel and the size of the PCR product was confirmed using a 50 and 1000 bp DNA ladder. The remaining PCR product was cleaned up using enzyme Exonuclease 1 and Shrimp Alkaline Phosphatase (ExoSAP-IT).

The sequencing of amplicons was carried out using Big Dye™ chemistry (BigDye Terminator, Version 3.1; Applied Biosystems, Foster City, CA, USA). PCR products of the samples were sent to Genewiz Global Headquarter South Plainfield, NJ., USA (<https://www.genewiz.com>), for Sanger sequencing with a 373xL DNA Analyzer. The DNA sequence was analyzed using the Bioedit software version 7.2.5. Each sequence was subjected to an individual BLAST search to verify its identity to the GenBank mRNA sequence NM_001045.5.

2.4. IN SILICO ANALYSIS

To evaluate the effect of the coding variants in protein, we used two software, the SIFT (<http://sift.jcvi.org>), which is a sequence homology-based tool that predicts the deleterious and tolerant and the Polyphen-2 (<http://genetics.bwh.harvard.edu/pph2/>), which is a sequence and structure evolutionary conservation-based tool to classify damaging effect of amino acid substitutions and estimates position specific independent count score demonstrating 0-1 probably damaging index.

3. RESULTS

3.1. CLINICAL CHARACTERISTICS

The sample included 36 patients with AN-R, 50 with BN and 50 control subjects. The patients included in the study did not experience a diagnostic transition between eating disorders. In terms of clinical characteristics of the sample, we observed differences in the age, ($F=114.4$, $P=0.00$), and BMI ($F=70.4$, $P=0.00$) between AN-R, BN and control group. Also, we observed less impulsivity in the AN-R (mean 15.63 SD 8.11) than BN (mean 27.36 SD 6.72). Also, the severity of the preoccupations and rituals was minor score in AN-R (mean 15.87 SD 8.72) and major in BN (mean 21.21 SD 4.30) (Table 1). In the sample, 47 patients (55%) had a comorbidity, 5 (14%) and 13 (26%) had anxiety disorders; 12 (33%) and 19 (38%) had major depressive disorder, in AN-R and BN patients, respectively.

Table 1. Clinical characteristics of the sample.

Variable	Restrictive-eating (n=36)		BN-binge-eating (n=50)		t	p-Value
	Mean	SD	Mean	SD		
Age (years)	18.08	3.89	20.0	4.30	-2.15	0.03
BMI (kg/m ²)	15.66	1.51	24.61	4.41	-13.30	0.00
Age_of onset (years)	14.40	2.50	13.48	2.84	1.67	0.09
Time_evolution (weeks)	185.8	196	339.6	224	-3.33	0.00
Presence sustance_abuse	9.1% (2)		90.9% (22)	-		0.00
HAM-D	11.66	8.42	20.24	10.49	-2.56	0.00
HAM-A	14.83	13.84	24.75	14.25	-3.29	0.01
Plutchik's scale	15.63	8.11	27.36	6.72	-2.85	0.00
YBC-EDs scale	15.87	8.72	21.21	4.30	-2.72	0.01
EDI-2						
Drive for thinness	10.35	7.92	16.90	5.48	-4.18	0.00
Bulimia	1.85	5.58	10.14	5.91	-6.51	0.00
Body dissatisfaction	10.55	4.98	16.48	5.28	-5.21	0.00
Interoceptive awareness	8.85	9.32	15.94	7.97	-3.62	0.00
Total score	62.53	41.39	93.78	34.49	-3.62	0.00

SD: Standard deviation. **HAMA-D:** Scale of Hamilton depression. **HAM-A** Scale of Hamilton Anxiety. **YBC-EDs:** Scale Yale-Brown of Cornell Eating Disorders. **EDI-2:** Eating Disorders Inventory.

3.2. GENETIC VARIANTS

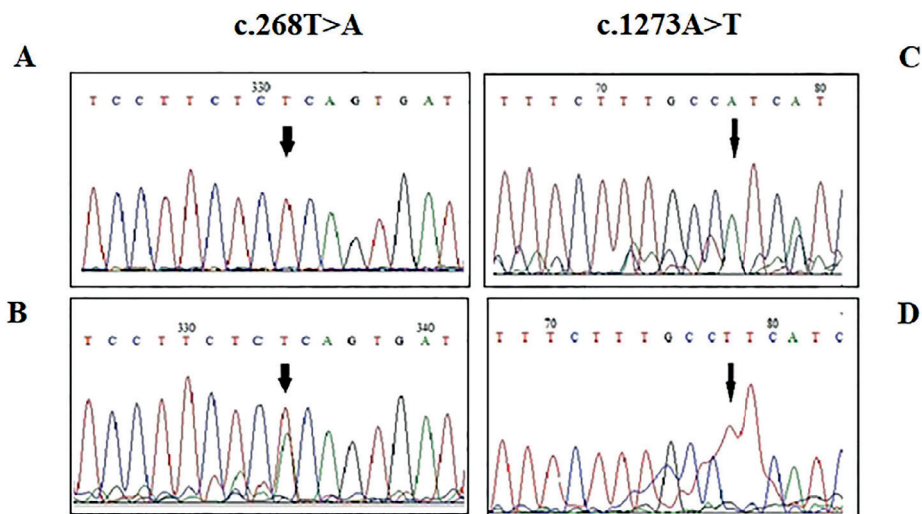
3.2.1. Anorexia nervosa-restrictive type

In the analysis of the five exons of the gene, there were alignment of the sequences of the patients and the control group (Table 2). Among the discovered variants in the patients, two were novel variants, g.130delA and c.1740G>A, located in exons 1 and 8 respectively, and they have not been reported yet in public databases (gnomAD, dbSNP, 1000 Genomes). In addition, we detected variants to the gnomAD database, three synonymous variants, rs57172732, rs55908624, and rs74478645 located in the exons 3 and 8, and could not affect the amino acid. Finally, we observed one missense variant, rs118308811, in the exon 2, this variant c.268A>T causes the amino acid change from leucine to phenylalanine (L90F); the change did not affect the length of the protein, but in the analysis of prediction of protein, the change of amino acid was reported as probably deleterious and damaging (SIFT score=0.01; Polyphen score=1). In total, 3/36 individuals in our restricted eating group were heterozygous for the L90F variant of the gen (Figure 1a, b).

Tabla 2. Variants of *SLC6A4* identified in *restrictive-eating*.

Gene región	References dbSNP	Nucleotide change	Amino acid	Prediction		No. of subjects	
				SIFT	PolyPhen	Restrictive- eating n=36	Controls subjects n=50
Exon 1	New	g.130delA	-	-	-	0.03	0
Exon 1	New	g.136delC	-	-	-	1	1
Exon 2	rs769651028	c.139_140insAC	p.T47fs	-	-	1	1
Exon 2	rs202152288	c.148G>C	p.V50L	Tolerant	Benign	1	1
Exon 2	rs118308811	c.268T>A	p.L90F	Deleterious	Damaging	0.04	0
Exon 2	rs140436169	c.121C>T	p.G41A	Deleterious	Damaging	1	1
Exon 3	rs34542731	c.1179dupA	p.V394fs	-	-	1	1
Exon 3	rs57172732	c.411G>A	p.L137	-	-	0.01	0
Exon 8	rs55908624	c.1149C>T	p.L383	-	-	0.01	0
Exon 8	rs74478645	c.1164G>A	p.G388	-	-	0.01	0
Exon 8	New	c.1740G>A	-	-	-	0.01	0

Figure 1. Sequencing results of the forward strand of the variants in the exons. Arrows denote the variant. The results in the exon 2, (A) Control subjects c.268T>A; (B) Patients were heterozygous of the restrictive-eating. Results of the forward strand of the variant in the exon 9. (C) control subjects c.1273A>T; (D) Patients homozygous of the BN-binge eating.



3.2.2. Bulimia nervosa

In the analysis of sequencing, there were alignment of the sequences of the patients and control group (Table 3). Among the discovered variants, two novel variants, g.295C>G and c.1725G>A located in the exons 1 and 8 respectively, and not been reported yet in public databases, and we observed one missense variant, rs28914832, found in

exon 9; transversion changes of the variant (A>T) cause the amino acid change from isoleucine to valine in position 425. However, the change did not affect the length of the protein; in the analysis of prediction of protein, the change of amino acid was reported as tolerant and benign (SIFT score=0.63; PolyPhen score=0.06). The potential impact of this variant was also interpreted according to current standards and guidelines, which suggested that the variant is pathogenic (Richards et al., 2015). Additionally, we observed that 3/50 patients were homozygous 425V (Figure 1c, d).

Finally, we observed variants shared among AN-R, BN and control groups, for a total of five variants: one novel variant g.136delC, located in the exon 1, two missenses, rs202152288 and rs140436169, identified in exon 2, and two frameshift insertions, rs769651028 and rs34542731, in exons 2 and 3 (Table 2 and 3).

4. DISCUSSION

Previous studies have identified genetic variants of the *SLC6A4* gene, which are associated with ED (Calati et al., 2011; Camarena et al., 2018). In the present study, we reported the findings of Sanger sequencing in individuals with AN-R, BN and a control group. We identified a higher number of variants in exons 1, 2, and 8, and a lower number in exons 3 and 9, those coding highly conserved regions in the *SLC6A4*. In general, we reported functional variants, as frameshifts insertion (p.T47fs and p.V394fs) that could be introduced an early stop codon of the protein, and functional variants (p.V50L, p.L90F, p.G41A, and I425V) that together could have an effect on the protein transporter, as confer a gain of function of the protein or a poor affinity to the 5-HT (Murphy et al., 2008). In particular, we identified three patients in the AN-R group heterozygous for p.L90F, located in the exon 2, a change of amino acid that could modulate the exonic splicing enhancer or silencer after bioinformatics prediction. Interestingly, we previously reported a variant p.G56A in the same exon in a AN-R, which has been reported as a gain-of-function variant; therefore, it is possible that two variants could have a critical role in the serotonin transporter activity in the brain (Prasad et al., 2008). Despite the limitation of GWAS findings for serotonin risk-conferring genes in AN-restrictive type, different studies have identified functional variants in the serotonin transporter with a major role in anorexia nervosa (Kiezebrink et al., 2010; Camarena et al., 2012; Solmi et al., 2016). WES reports identified functional variants in genes that are expressed in the lateral parabrachial and ventral tegmental areas of the hypothalamus, which plays a key role in the regulation of appetite; therefore, some functional variants identified in *SLC6A4* could confer biological vulnerability to develop an eating behavior as for example, the identification of damaging variants in patients with anorexia nervosa restrictive (Negraes et al., 2017; Lutter et al., 2017).

Interestingly, the present study reported a minor number of variants in the BN group compared with control subjects. We identified three patients homozygous for 425V, a functional variant that was previously associated with the spectrum rigid-compulsive behaviors (Delorme et al., 2005). A family association study reported an over-transmission of the 425V variant in patients with anorexia nervosa and OCD with perfectionist and compulsive behaviors related with food and exercise. These observations might indicate that several disorders partially overlap in clinical comorbidity and in causality, including genetic transmission of the p.I425V that may operate as an aggravating factor for the severity of these disorders (Ozaki et al., 2003). Also, WES study identified a functional variant in the *ESRRA* and *HDAC4* genes in families with multiple persons affected with anorexia and bulimia nervosa with a high comorbidity with OCD and perfectionism personality trait (Cui et al., 2013).

We observed comorbidity with anxiety disorder and major depression disorder according with previous studies (Kaye et al., 2004; Stice et al., 2004). Interestingly, *SLC6A4* gene reported association with bulimia nervosa and comorbid psychopathology (Richardson et al., 2008; Steiger et al., 2008); therefore, gene variants of *SLC6A4* could have a pleiotropic effect in AN-R, BN and phenotypes that co-occur with eating disorders such as anxiety disorder and major depressive disorder.

It has been suggested that functional variants have been overrepresented in the brain and predispose to the spectrum of complex serotonergic phenotypes and can be related to serotonin dysfunction (Anttila et al., 2018). The expectation that syndromes with a restrictive form should be characterized by an exaggeration of dysphoric mood relational with increased serotonergic tone, whereas syndromes characterized by binge-purge type would correspond to increased impulsivity, disinhibition of eating behavior, and other features associated with low serotonergic tone (Steiger H., 2004).

The present study has several limitations. First, the small sample size in our analysis resulted in limited power to identify rare variants; second, we only sequenced five exons of the gene, it could be interesting to explore the complete sequence of *SLC6A4*; and third, we did not include other eating disorder subtypes, which may miss some valuable findings about the role of *SLC6A4* in the eating disorders.

5. CONCLUSIONS

The results of our study suggest that variants of the *SLC6A4* gene are related with a possible damaging or gain-of-function and may be involved in the susceptibility in AN-R and BN patients.

6. AUTHOR CONTRIBUTIONS

SH designed the study and wrote the manuscript. **BC**, **MF**, and **AA**: helped in the preparation and editing of the manuscript. **LG** and **AC**: carried out the clinical evaluation of the patients. All authors read and approved the final version.

REFERENCES

- Anttila, V., Bulik-Sullivan, B., Finucane, H.K., Walters, R.K., Bras, J., Duncan, L., 2018. Analysis of shared heritability in common disorders of the brain. *Science*, 360(6395), p.eaap8757. DOI:10.1126/science.aap8757
- Bienvenu, T., Lebrun, N., Clarke, J., Duriez, P., Gorwood, P., Ramoz, N., 2019. Exome sequencing in a familial form of anorexia nervosa supports multigenic etiology. *J. Neu. Trans.*, pp.1-7. DOI:10.1007/s00702-019-02056-2
- Blakely, R.D., DeFelice, L.J., Galli, A., 2005. Biogenic amine neurotransmitter transporters: just when you thought you knew them. *Physiology*, 20(4), pp.225-231. DOI:10.1152/physiol.00013.2005
- Bulik, C.M., Sullivan, P.F., Tozzi, F., Furberg, H., Lichtenstein, P. and Pedersen, N.L., 2006. Prevalence, heritability, and prospective risk factors for anorexia nervosa. *Archives of general psychiatry*, 63(3), pp.305-312. DOI:10.1001/archpsyc.63.3.305
- Caballero, A.R., Sunday, S.R., Halmi, K.A., 2003. A comparison of cognitive and behavioral symptoms between Mexican and American eating disorder patients. *Int. J. Eat. Disord.*, 34(1), pp.136-141. DOI:10.1002/eat.10150
- Camarena, B., González, L., Hernández, S., Caballero, A. 2012. *SLC6A4* rare variant associated with eating disorders in Mexican patients. *J. Psych. Res.*, 8(46), pp.1106-1107. DOI:10.1016/j.jpsychires.2012.04.011
- Camarena, B., Hernandez, S., Gonzalez, L., Flores, G., Luna, D., Aguilar, A. et al., 2018. Association Study Between the Triallelic Polymorphism of *SLC6A4* Gene and Eating Disorders. *Am. J. Psych. Neurosc.*, 6(4), p.104.
- Calati, R., De Ronchi, D., Bellini, M., Serretti, A. 2011. The 5-HTTLPR polymorphism and eating disorders: a meta-analysis. *Int. J. Eat. Disord.*, 44, 191-199. DOI:10.1002/eat.20811
- Cui, H., Moore, J., Ashimi, S.S., Mason, B.L., Drawbridge, J.N., Han, S., et al., 2013. Eating disorder predisposition is associated with *ESRRA* and *HDAC4* mutations. *J.Clin. Invest.*, 123(11). DOI:10.1172/JCI71400
- Delorme R, Betancur C, Wagner M, Krebs MO, Gorwood P, Pearl P, et al., 2005. Support for the association between the rare functional variant I425V of the serotonin transporter gene and susceptibility to obsessive compulsive disorder. *Mol. Psychiatry*. Dec;10(12):1059-61. DOI:10.1038/sj.mp.4001728
- First, M. B., Williams, J. B. W., Karg, R. S., Spitzer, R. L. 2015. Structured clinical interview for DSM-5 (SCID-5 for DSM-5). Arlington, VA: American Psychiatric Association.
- García-García, E., Vázquez-Velázquez, V., López-Alvarenga, J.C. and Arcila-Martínez, D., 2003. Internal validity and diagnostic utility of the Eating Disorder Inventory, in Mexican women. *Salud publica de Mexico*, 45(3), pp.206-210. PMID: 12870422
- Glatt, C.E., DeYoung, J.A., Delgado, S., Service, S.K., Giacomini, K.M., Edwards, R.H., et al., 2001. Screening a large reference sample to identify very low frequency sequence variants: comparisons between two genes. *Nat. Gen.*, 27(4), p.435. DOI:10.1038/86948

Kaye WH, Bulik CM, Thornton L, Barbarich N, Masters K. 2004. Price Foundation Collaborative Group. Comorbidity of anxiety disorders with anorexia and bulimia nervosa. *American Journal of Psychiatry*. 2004 Dec 1;161(12):2215-21. DOI:10.1176/appi.ajp.161.12.2215

Kiezebrink, K., Mann, E.T., Bujac, S.R., Stubbins, M.J., Campbell, D.A. Blundell, J.E., 2010. Evidence of complex involvement of serotonergic genes with restrictive and binge purge subtypes of anorexia nervosa. *World J. Biol. Psych.,11*(6), pp.824-833. DOI:10.3109/15622975.2010.484550

Lutter, M., Bahl, E., Hannah, C., Hofmann, D., Acevedo, S., Cui, H., et al., 2017. Novel and ultra-rare damaging variants in neuropeptide signaling are associated with disordered eating behaviors. *PLoS one, 12*(8), p.e0181556. DOI:10.1371/journal.pone.0181556

Munn-Chernoff, M.A., McQueen, M.B., Stetler, G.L., Haberstick, B.C., Rhee, S.H., Sobik, L.E., et al., 2012. Examining associations between disordered eating and serotonin transporter gene polymorphisms. *Int. J. Eat Disord 45*(4), pp.556-561. DOI: 10.1002/eat.22001

Murphy, D.L., Fox, M.A., Timpano, K.R., Moya, P.R., Ren-Patterson, R., Andrews, A.M., et al., 2008. How the serotonin story is being rewritten by new gene-based discoveries principally related to SLC6A4, the serotonin transporter gene, which functions to influence all cellular serotonin systems. *Neuropharma, 55*(6), pp.932-960. DOI: 10.1016/j.neuropharm.2008.08.034

Negraes, P. D., Cugola F. R., Herai, C. A. Trujillo, A. S. Cristino, T. Chailangkarn, A. R. 2017. Modeling Anorexia Nervosa: Transcriptional Insights from Human iPSC-Derived Neurons. *Translational Psychiatry 7* (3): e1060. DOI:10.1038/tp.2017.37

Ozaki, N., Goldman, D., Kaye, W.H., Plotnicov, K., Greenberg, B.D., Lappalainen, J., et al. 2003. Serotonin transporter missense mutation associated with a complex neuropsychiatric phenotype. *Molecular psychiatry, 8*(11), p.933. DOI:10.1038/sj.mp.4001365

Páez, F., Jiménez, A., López, A., Ariza, J.P.R., Soto, H.O. Nicolini, H., 1996. Estudio de validez de la traducción al castellano de la Escala de Impulsividad de Plutchik. *Salud Mental, 19*(Supl 3), pp.10-12.

Prasad, H.C., Steiner, J.A., Sutcliffe, J.S. and Blakely, R.D., 2008. Enhanced activity of human serotonin transporter variants associated with autism. *Phil. Transc.Royal Soc. B: Biol. Sci., 364*(1514), pp.163-173. DOI:10.1098/rstb.2008.0143

Richardson J,Steiger H,Schmitz N,Joober R,Bruce KR,Israel M, et al.2008. Relevance of the 5-HTTLPR polymorphism and childhood abuse to increased psychiatric comorbidity in women with bulimia-spectrum disorders. *J Clin Psychiatry; 69*:981-990. DOI:10.4088/jcp.v69n0615

Solmi, M., Gallicchio, D., Collantoni, E., Correll, C.U., Clementi, M., Pinato, C., et al. 2016. Serotonin transporter gene polymorphism in eating disorders: Data from a new biobank and META-analysis of previous studies. *World. J. Biol. Psych., 17*(4), pp.244-257. DOI:10.3109/15622975.2015.1126675

Steiger, H., 2004. Eating disorders and the serotonin connection: state, trait and developmental effects. *Journal of Psychiatry and Neuroscience, 29*(1), p.20. PMID:PMC305267

Steiger H, Joober R, Gauvin L, Bruce KR, Richardson J, Israel M, et al.2008. Serotonin-system polymorphisms (5-HTTLPR and -1438G/A) and responses of patients with bulimic syndromes to multimodal treatments. *J Clin Psychiatry. 69*:1565-1571. DOI:10.4088/jcp.v69n1006

Stice E, Burton EM, Shaw H. 2004. Prospective relations between bulimic pathology, depression, and substance abuse: unpacking comorbidity in adolescent girls. *Journal of consulting and clinical psychology. Feb;72*(1):62. DOI: 10.1037/0022-006X.72.1.62

Thornton, L.M., Mazzeo, S.E. Bulik, C.M., 2010. The heritability of eating disorders: methods and current findings. In *Beh. Neurobiol.Eating Disorders* (pp. 141-156). Springer, Berlin, Heidelberg. DOI: 10.1007/7854_2010_91

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