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Neuronal Remodelling as a Predictor of Autism Spectrum Disorder Diagnosis

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Abstract

People with Autism Spectrum Disorder (ASD) are a neurodevelopmental symptom group characterized by significant deficits in information connectivity, mainly caused by specific genetic mutations affecting the fluency of the gamma-aminobutyric acid (GABAergic) system. This disruption, to a greater or lesser degree, hinders the interactive process of incoming stimuli with previously stored information, preventing working memory from fulfilling its role of facilitating access to information in permanent memory and later recovery. In addition to the genetic components, environmental processes occurring, above all, in early childhood, related to specific organic and severe psycho-emotional diseases can produce the same effects in the brain system as the genetic karyotypic component through the concept of neuronal remodelling. In this sense, this research aims to empirically show the influence of neuronal remodelling on the GABAergic pathway leading to the traits of autism spectrum behaviour.

A total of 175 participants from the three levels of ASD intensity have participated in this study. Data have been analysed through Linear Logistic Regression, which shows that both components, the genetic process and the environmental process, significantly influence the neural connective pathway that relates information, unlike other operationalized covariates, such as gender or age of the participants. Likewise, as shown by the Chi-Square Test, the interactions between genetic and environmental variables showed no differences in their interaction regarding the connectivity level that would explain the different levels of disorder. However, when there is a combination of genetic mutations in the diagnostic karyotype, there are significant differences between the genetic group and the environmental process over the neural network.

Keywords: autism spectrum disorder, diagnosis, neuropsychological information processing, perception-cognition, semantic memory.

1. Introduction

According to the American Psychiatric Association (APA) (2013) and the Centres for Disease Control and Prevention (CDC) (2012), autism spectrum disorder (ASD) is characterized by deficits related to social interaction and communication, as well as the occurrence of restrictive and stereotyped behaviours. These deficits are categorized into three levels of intensity, with level 1 being the lowest need level and level 3 being the highest symptomatic intensity level.

However, further empirical studies regarding the aetiology of this disorder have identified that ASD is delimited by the maintenance of basic deficits in the brain's synaptic processes, which involve the systemic processes regulated by the gamma-aminobutyric acid (GABAergic system), resulting in severe impairment at the cerebral network's connexional level. This impacts the fluidity and plasticity of stimulus reception and its relationship with previously available information in permanent memory, leading to severe effects on the emotional and behavioural components, both at the past-expressive level and at the dynamic level of behavioural action (Hadjikhani et al., 2015).

This group of features is determined by genetic mutations directly related to (Croen et al., 2011). It is caused by highly specific genetic karyotypes referring to several specific genes, amongst which, according to previous studies carried out by Ojea (2024a) and Castro & Ojea (2024), a specific group of genes related to the 15q11-q13 gene (27.04%), the SHANK 2-3 gene (3.47%), and the 7q11-q33 gene (3.22%) have been highlighted. These

genes are statistically significantly related to systemic connectional involvement involving the GABAergic neuropathway.

In addition, up-to-date experimental studies have enhanced our understanding of neural functioning, suggesting the prevalence of disrupted neural pathways in the brain processing characteristic of ASD (Dufour, McBride, Bartley, Juárez & Martínez- Cerdeño, 2023; Falcone et al., 2021), as well as impairments in cell proliferation and migration that occur prenatally (Wegiel et al., 2010). In this context, Adorjan et al. (2017), Amina et al. (2021), Ariza et al. (2018), Hashemi et al. (2017) and Lawrence et al. (2010) have precisely identified the brain's GABAergic constituents, which form a network that regulates most local glutamatergic pyramidal neuronal activity across multiple specific subtypes, particularly affecting neural-cerebral connectivity or connexional processing.

DeFelipe et al. (2013) have specified that when the disorder correlates with specific co-morbid processes, such as cognitive impairment or associated partial convulsive components or permanent epilepsies, it occurs in a highly significant number of cases. It has been widely demonstrated that genetic mutations and genetic karyotypic clusters specifically affect the neural connections that underlie the perceptual- cognitive characteristics regarding the particular neuropsychological information processing that characterizes people with ASD at different levels of intensity. However, there are also other environmental components that can produce effects on the GABAergic system similar to those of genetic karyotypic processing, which are related to conditions experienced, especially at an earlier age, both organic and psycho-emotional.

These conditions might be related to diseases such as encephalitis, meningitis, severe blood infections, or severe emotional processes, especially those related to significant anguish, anxiety, or depressive processes that involve the socio-familial relational system. These conditions produce an effect on brain plasticity similar to that caused by genetic components, owing to the process described as neuronal remodelling (Snyder, Kee & Wojtowicz, 2001).

Indeed, Dong & Greenough (2004) have argued that neuronal and non-neuronal plasticity is similarly affected by specific genetic factors influencing connectionist neuropathways, as well as by environmental factors and relational experiences throughout socio-familial development. Furthermore, these environmental experiences and intrinsic organic conditions have triggered a process of neuronal remodelling in the entire brain system, including alterations in the dimensions of the dendritic domain, synaptic processes, and their own synaptic morphology.

However, it is not just specific organic diseases in early life that can lead to this neuronal remodelling process; individual exposure to experiences perceived as severely traumatic also plays a role. This is due to the environmental complexity and interactions that occur during interpersonal interactions throughout the learning and development process, which may impair glial cells, including both astrocytes and oligodendrocytes, and consequently affect the regulation of the cerebral cortex and cerebellum.

These assertions, highly refuted in empirical scientific studies (Auvergne et al., 2002; Barnea-Goraly et al., 2003; Barnea-Goraly, 2004; Brown et al., 2003; Courchesne et al., 2001; Dierssen et al., 2003), have corroborated that synapse formation can also co- occur in the absence of glial cells, and the few cells that are formed are functionally immature, limiting or impairing a connective process for the efficient flow of information, which has also been refuted by other current studies (Van Praag et al., 2002; Volterra, Magistretti & Haydon, 2002; Vourc'h et al., 2002; Wang et al., 2004; Ullian, Sapperstein, Christopherson & Barres, 2001).

These incidents are mainly due to the considerable plasticity of the brain at the fetal level or in the first years of life, which is influenced by multiple organic- environmental factors and can lead to severe consequences in the cerebral- cerebellar systemic processes, involving the GABAergic pathways, through its influence on neurogenesis as a holistic system (Eriksson, 2003; Toda & Gage, 2018). Such experiences can lead, as shown by the studies of Turner, Lewis, & King (2003) and Ullian, Sapperstein, Christopherson & Barres (2001), among other consequences, to the creation of multiple differences in the number of synaptic elaborations for each neuron, as well as to significant changes in synaptic processes, which have a substantial influence on personal perception, cognition, and semantic memory.

In summary, this neuronal remodelling process is characterized by the influence of these affections on the new-born granule neurons, which severely affect neuronal plasticity in the hippocampal neural pathway. This new cell proliferation influences synaptic plasticity, shaping afferent inputs to the hippocampus and substantially affecting learning processes, particularly in semantic memory processes or the capacity to integrate relevant information. This integration allows new stimulus inputs to be related to previously stored long- term memory.

These factors are precisely the most decisive characteristics of the deficit in neuronal plasticity, which especially affects the functional elaboration of neuronal nodes that facilitate the relationship between information at the

cognitive level and leads to basic alterations at the perceptual- cognitive level, as well as in the processes of comprehension and elaboration of semantic content. Hence, the general characteristics indicated by the current international classifications in relation to the concept of the autism spectrum should be updated to reflect the current recurrent research and incorporate a third conceptual dimension in reference to all the contents of neuropsychological information processing, from the initial sensory- perceptual component to the information retrieval processes, focused on the personal semantic memory basis.

Nevertheless, this research seeks to justify the importance of organic-environmental factors as processes that generate neuronal remodelling similar to the effects of a specific genetic karyotype affecting the nodal connectivity of GABAergic composition. The study had two main aims. The first aim of this scientific study is to analyse whether the explanatory-predictive effects of the intersection of the variables operationalized as factors influencing ASD levels are statistically significant.

The second goal indicates that there are no statistically significant differences in the effects of genetic factors and environmental components as explanatory aetiological factors of ASD, according to the neuropsychological theories of neuronal remodelling. In this sense, the environmental factors considered refer to illnesses suffered, especially during early childhood, or to adverse relational circumstances arising from emotional states caused by severe stress or severe anguish- anxiety that are determined in early childhood, which could give rise to the same consequences as genetic conditions on the functioning of neuropsychological information processing as a whole cerebral system.

Now, therefore, the basic expected hypothesis is that the percentage frequencies of the variable "gene" (genetic karyotype) and the variable "disease" (environmental factors) don't differ with respect to the "nodes" variable (ability to establish conceptual and categorical relationships) at the ASD level. Therefore, the null hypothesis (H_o) could be accepted.

2. Method

2.1 Research Design

This study involves the psychometric analysis of a survey questionnaire constructed ad hoc regarding the aforementioned goals, with the questions available at the following online link (see Annex 1). Many responses were obtained directly through the survey application, via submissions from educational and health centres and institutions. Others were gathered from the review of the corresponding participants' psycho- pedagogical reports.

2.2 Participants

The participants of this project can be found in Table 1. Total quantified data (∑) and the corresponding percentages (*p*) have been shown in relation to ASD level, along with the age and sex of the study participants.

Table 1. level * age * sex (N: 175)

sex				age					
				2.1-5	5.1-8	8.1-12	12.1-15	>15.1	total
guys	level	level -1	∑	31	28	8	13	1	81
			p	38.3%	34.6%	9.9%	16.0%	1.2%	
		level- 2	∑	7	3	11	3	0	24
			p	29.2%	12.5%	45.8%	12.5%	.0%	
		level- 3	∑	2	3	3	1	1	10
			p	20.0%	30.0%	30.0%	10.0%	10.0%	
		Total	∑	40	34	22	17	2	115
			p	34.8%	29.6%	19.1%	14.8%	1.7%	
girls	level	level- 1	∑	10	6	11	3	4	34
			p	29.4%	17.6%	32.4%	8.8%	11.8%	
		level-2	∑	6	2	1	2	4	15
			p	40.0%	13.3%	6.7%	13.3%	26.7%	
		level- 3	∑	6	0	2	1	2	11
			p	54.5%	.0%	18.2%	9.1%	18.2%	
		total	∑	22	8	14	6	10	60
			p	36.7%	13.3%	23.3%	10.0%	16.7%	

As can be seen, a total of 175 participants were involved in this study, of which 115 were boys, with 81 in level 1, 24 in level 2, and 10 in level 3; there were also a total of 60 girls, with 34 in level 1, 15 in level 2, and 11 in level 3. For each level and sex of the participants, the age ranges and the specific percentages to which each group of participants belongs can also be observed.

2.3 Variables, Description and Values

The variables of this study, their meanings, and the values operationalized for the statistical analysis are as follows:

(1) “level,” ASD diagnostic level, with three levels according to the American Psychiatric Association (APA) international classification of diseases (2013, *ob. cit.*): "ASD level 1, 2, 3."

(2) “sex,” which indicates the sex of the participants, with two values: boys and girls.

(3) “age,” related to the age of the participants, distributed in the following age intervals: 2.1–5 years old, 5.1–8 years old, 12.1–15 years old, and the interval for participants older than 15.1 years old.

(4) “nodes,” which is the quantitative variable related to the participants' ability to elaborate relations between concepts, construct categories, and elaborate relations between several conceptual categories. The ordinal values measured are as follows, increasing as a function of the participants' level of difficulty in elaborating relationships: - no deficit, - very slight deficit, - slight deficit, - half deficit, - high deficit, and - very high deficit.

(5) “gene,” which was found to correspond to the presence of the karyotypic diagnosis of the participants. The genes proposed for analysis are the following: no deficit (not indicated), the 15q11-q13 gene, the 17q11-q22 gene, the 7q31-q33 gene, the SHANK2,3 gene, and combined (the karyotypic occurrence of several genes occurring jointly in the report).

(6) “disease,” which describes the environmental implications derived from the existence of childhood illnesses and relational difficulties associated with severe psycho-emotional issues. The values are as follows: no deficit (not indicated), encephalitis, meningitis, infections, convulsions (temporary or permanent epileptic episodes), emotional (psychological, social, or family relational stress suffered due to emotional tension, anxiety, depressive processes, or severe anguish), and combined (several diseases experienced jointly or successively).

2.4 Data Analysis

Variables were processed using the most recent version of the SPSS statistical package. The explanatory-predictive analysis has been conducted for the set of values of the variables found, taking the variable "level" of ASD diagnosis as the dependent variable (DV) of the study, while the other variables were included as explanatory factors or independent variables (IVs). The analysis was developed using Multinomial Ordinal Regression Analysis, which allows for the use of ordinal and nominal variables, through the Model Fitting Criteria (-2 Log Likelihood) and Likelihood Ratio Tests.

Also, Frequencies Cross Tables of the variables: "level," "nodes," "gene," and "disease" will be used to find the equality or difference in the interrelation of the data using the Chi-Square Test for dynamic variables.

2.5 Acknowledgements

I would like to thank all the Guidance Departments and specific services that have responded to this survey, either online through the website of the Autism Scientific Research Institute, as well as all those who have consented to interviews conducted directly or by making telephone calls.

2.6 Ethical Questions

All data, both from the survey and extracted from clinical and psycho-educational reports, are ensured to be completely anonymized, maintaining confidentiality regarding the participants and the institutions collaborating in this study.

3. Results

3.1 Predictive-explanatory analysis of ASD criteria

Although the genetic explanatory variance in the perceptual- cognitive components characteristic of ASD has been duly confirmed, it has been widely refuted due to brain connectionist limitations. Nevertheless, this study has been completed with the analysis of the effects of the operationalized genetic variables, with "level" being the dependent variable (DV) of the study. Other variables have also been incorporated into the analysis. The ordinal multinomial logistic regression analysis of the main effects model has been used for this study, as it allows for the analysis of ordinal and nominal variables simultaneously and determines the importance of the main effects of the variables gathered on the process of disorder diagnosis ("level") regarding the factor’s "gene" and "disease," while also considering "sex" and "age" as covariates in the regression analysis.

On the basis of the frequency count regarding DV, "level" can be seen in Table 2.

Table 2. Counting the frequencies of variables

Variables		N	*p*
level	level- 1	123	70.3%
	level- 2	39	22.3%
	level- 3	13	7.4%
sex	boy	115	65.7%
	girl	60	34.3%
age	2.1-5 y-o	62	35.4%
	5.1-8 y-o	42	24.0%
	8.1-12 y-o	36	20.6%
	12.1-15	23	13.1%
	>15.1 y-o	12	6.9%
nodes	slight deficit	4	2.3%
	half deficit	27	15.4%
	high deficit	25	14.3%
	very high deficit	119	68.0%
gene	no deficit	77	44.0%
	15q11-q13	65	37.1%
	17q11-q22	1	.6%
	7q31-q33	6	3.4%
	SHANK2,3	9	5.1%
	combined	17	9.7%
disease	no deficit	42	24.0%
	encephalitis	26	14.9%
	meningitis	20	11.4%
	infections	19	10.9%
	convulsions	5	2.9%
	emotional	36	20.6%
	combined	27	15.4%
Valid		175	100.0%
Missing			0
Subpopulation		98(a)	

a) The dependent variable has only one value observed in 82 (83,7%) subpopulations.

In the Frequency counting process, it is noteworthy that no value has been lost (valid for N: 175), with a delimitation of the subpopulation (83.7). Indeed, the Model Fitting Information from the Multinomial Logistic Regression of main effects has already shown that the final data from the analysis of the effects of all the variables of the study, as covariates, have found highly significant scores as predictive and explanatory of the effects produced on the DV "level" (Sig: .00) (see Table 3).

Table 3. Model Fitting Information

Model	Model fitting criteria			Likelihood ratio tests		
	AIC	BIC	-2 Log Likelihood	Chi-Square	df	Sig.
Intercept	263.94	270.27	259.94			
Final	238.11	364.70	158.11	101.83	38	.00

DV: "level".

The Akaike Information Criterion (AIC), as well as the Bayesian Information Criterion (BIC), also known as the Schwarz Goodness-Of-Fit Criterion, has been fitted to a significant statistic (Sig: .00, to 38 df.), which allows us to conclude that the variables operationalized as factors were significantly explanatory and predictive of the operationalized DV: "level." The Goodness-Of-Fit analysis has substantiated the values predicted by the model (see Table 4).

Table 4. Goodness-Of-Fit

	Chi-Square	df	Sig.
Pearson	129.891	156	.93
Deviance	124.241	156	.97

Indeed, the Pearson and Deviance statistics have indicated scores that allow us to accept the H_o of the predictive model, in that the expected scores do not differ from the scores found throughout this study, indicating that there has been a good fit regarding the final result (Pearson Sig: .93, and Deviance Sig: .97). The Pseudo-R-Squared statistic has also been analysed in order to corroborate whether the scores are similarly distributed (see Table 5).

Table 5. Pseudo R-Square

Cox and Snell	.44
Nagelkerke	.53
McFadden	.33

Data have been conclusive; the results are quite similar, and assuming Nagelkerke's correction, the factors explained 53.6% of all changes indicated by the final model found. Additionally, the similarity ratio explaining the significance of the predictors used in the Regression Model on its own has been observed (see Table 6).

Table 6. Likelihood Ratio Tests

Effect	Model Fitting Criteria			Likelihood Ratio Tests		
	AIC of reduced model	BIC of reduced model	-2 Log Likelihood of Reduced Model	Chi-Square	df	Sig.
Intercept	238.11	364.70	158.11(a)	.00	0	.
gene	248.41	343.35	188.41	30.29	10	.00
disease	255.49	344.10	199.49	41.38	12	.00
nodes	244.31	351.91	176.31	18.20	6	.00
age	236.14	337.41	172.14	14.03	8	.08
sex	235.66	355.92	159.66	1.55	2	.46

The chi-square statistic is the difference in -2 log-likelihoods between the final model and a reduced model. The reduced model is formed by omitting an effect from the final model. The null hypothesis is that all parameters of that effect are 0.

a) This reduced model is equivalent to the final model because omitting the effect does not increase the degrees of freedom.

As can be seen in the Model Likelihood analysis, the individual predictor levels can already be observed for each factor examined. The variable "gene" (Sig: .00), as well as the variables "disease" (Sig: .00) and "nodes" (Sig: .00), are significant explanatory predictors of the changes found in the dependent variable "level," while the factors represented by the variables "age" and "sex" do not show statistically significant predictive values. Thus, "age" did not show a significant prediction for the disorder (Sig: .08), nor did the variable "sex" (Sig: .46). In conclusion, as expected, it can be stated that the entire predictive model of the main effects of the "level" variable is influenced by the factors "gene," "disease," and "nodes."

3.2 Relationships between the Genetic-environmental and Nodal Domains

The second study goal is to observe whether there are differences in the relationships between the "gene" and "disease" variables concerning the cognitive capacity encoded by these variables, in relation to the cognitive capacity defined by the "nodes" variable. Previously, the frequencies indicated by the count (∑), regarding the three predictive factors, can be observed in Table 7.

Table 7. “gene” * “disease” * “nodes”

gene	nodes		disease							total
			no deficit	*encephalitis*	*meningitis*	*infections*	*convulsions*	*combined*	*emotional*	
no deficit		slight deficit	0	0	0	0	0	2	0	2
		half deficit	4	3	1	2	0	4	0	14
		high deficit	3	2	3	3	0	2	0	13
		very high deficit	2	12	6	8	3	9	8	48
	∑		**9**	**17**	**10**	**13**	**3**	**17**	**8**	**77**
15q11-q13	nodes	slight deficit	2	0	0	0		0	0	2
		half deficit	3	0	0	0		2	2	7
		high deficit	4	1	1	1		0	0	7
		very high deficit	22	4	6	0		6	11	49
	∑		**31**	**5**	**7**	**1**		**8**	**13**	**65**
17q11-q22	nodes	half deficit						1		1
	∑								**1**	**1**
7q31-q33	nodes	very high deficit			1			2	3	6
	∑					**1**		**2**	**3**	**6**
SHANK2,3	nodes	high deficit	0	0		1	0	0		1
		very high deficit	1	2		1	2	2		8
	∑			**1**	**2**		**2**	**2**	**2**	**9**
combined	nodes	half deficit	0	0	0	0		2	3	5
		high deficit	1	0	0	3		0	0	4
		very high deficit	0	2	2	0		4	0	8
	∑		**1**	**2**	**2**	**3**		**6**	**3**	**17**
TOTAL										175

This Cross- Count analysis has been essential for the corresponding chi-square analysis of factor interactions, which is fundamental for deciding whether to confirm or reject the H_o. Consequently, it allows us to affirm that there are no differences in the effect of the two variables, "gene" and "disease," on the relational connexional competence variable "nodes," thereby confirming the joint interaction at the diagnostic level. If these verifications are corroborated, it would confirm that both factors similarly affect the ability to elaborate cognitive connectionist relations, which is the basic feature of this disorder.

In other words, the impact on the GABAergic system that shapes the ability to connect concepts and conceptual categories from a perceptual-cognitive perspective in people with ASD has been tested. This analysis has been conducted using the Chi-Square statistical analysis for the Cross-Frequency table developed earlier, in which the values, degrees of freedom (df), and the statistical asymptotic significance level have been analysed in depth and specifically. The results can be seen in Table 8.

Table 8. Chi-Square Tests to “gene” * “disease” * “nodes”

gene		Value	df	Sig.
no deficit	Pearson Chi-Square	23.57(a)	18	.17
	Likelihood Ratio	25.37	18	.11
	Linear-by-Linear	1.09	1	.29
	Valid cases	77		
15q11-q13	Pearson Chi-Square	16.74(b)	15	.33
	Likelihood Ratio	16.66	15	.33
	Linear-by-Linear	.24	1	.61
	Valid cases	65		
17q11-q22	Pearson Chi-Square	(c)		
	Valid cases	1		
7q31-q33	Pearson Chi-Square	(d)		
	Valid cases	6		
SHANK2,3	Pearson Chi-Square	3.93(e)	4	.41
	Likelihood Ratio	3.50	4	.47
	Linear-by-Linear	.00	1	.94
	Valid cases	9		
combined	Pearson Chi-Square	26.63(f)	10	.00
	Likelihood Ratio	28.23	10	.00
	Linear-by-Linear	3.58	1	.05
	Valid cases	17		

a) 23 cells (82.1%) have expected count less than 5. The minimum expected count is .08.
b) 20 cells (83.3%) have expected count less than 5. The minimum expected count is .03.
c) No statistics are computed because nodes and disease are constants.
d) No statistics are computed because nodes is a constant.
e)10 cells (100.0%) have expected count less than 5. The minimum expected count is .11.
f) 18 cells (100.0%) have expected count less than 5. The minimum expected count is .24.

Indeed, the Chi-Square analysis has confirmed, in fundamental aspects, the study's H_o, i.e., that the interrelationship between the variable "gene" and the variable "disease" affects their relationship with the variable "nodes" differently. The possible effects produced by the "disease" variable in its relationship with the "nodes" variable are similar to the demonstrated effects shown between the genetics of the "gene" variable and the capacity for connectional fluidity of information encoded in the "nodes" variable.

These findings have partially supported the hypothesis of neuronal remodelling, as the effects produced on the GABAergic pathway by the karyotypic-genetic effect can also be produced by other organic-environmental components, which have been analysed by the variable "disease." The statistical significance values allow us to accept the H_o since there are no differences in the incidence processes.

However, in the combined value of the "gene" variable, the Chi-Square statistic and the Likelihood Ratio Test (Sig: .00) show significant differences between both variables in the analysis. This has allowed us to conclude that when the condition is very severe, resulting from the combination of multiple genes that affect the neuropsychological system, significant differences are produced in the cerebral effects in relation to the presence of a psycho- organic illness.

Therefore, not just the specifically genetic effects decisively affect the neural connections that lead to the specificity of ASD diagnostic, but psycho- organic diseases and environmental factors can also produce a similar effect as genetic involvement by remodelling the systemic process in the same or similar way as the specific genetic component itself does.

4. Conclusion

Firstly, the data found have corroborated that the criteria for autism spectrum disorder are strongly defined by limitations and breaks in the GABAergic connectionist pathway, which affects the fluidity of connectivity between incoming information and information previously stored in permanent memory. This severely affects cognitive-semantic memory, owing to factors related to the genetic-organic components that influence this connectivity. Additionally, environmental factors shaped by the occurrence of early illnesses or severe psycho-emotional and relational processes could produce the same consequences as the main genetic factors. This has been shown by the model fitting information with a significant critical level of explanation of the intersection of genetic and environmental variables on relational capacity, shaping the basic characteristics of the autism spectrum. (Sig: .00), significantly elevated Goodness-Of-Fit as indicated by Pearson's Chi-Square (129.89) and Deviance statistical (124.24).

This will confirm that expected scores indicate there are no differences between the genetic component and the environmental variables for the explanatory variance related to relational competence: "nodes," whose mean critical level for the two statistics, both Pearson's and Deviance, was markedly non-significant (μ-Sig: .95).

As a matter of fact, both components had a significant impact on the variable "level" (ASD diagnosis), as shown by the effects of the Multinomial Ordinal Logistic Regression Equation, with the critical level for the genetic and environmental components being statistically significant (Sig: .00), as well as the critical level of the ability to establish relationships being significantly significant (Sig: .00) in defining the ASD diagnosis. Meanwhile, the “sex” and “age” variables do not specifically influence the evaluation of ASD level, with “sex” (Sig: .08) and “age” (Sig: .46).

However, when these data are analysed in depth, it is observed that, in effect, there are no differences between the genetic and environmental components regarding their effect on the ability of perceptual- cognitive relations that configure the neuropsychological processing of information in people with ASD, in relation to the genes and the organic- emotional diseases analysed in this study, with critical levels that have not been differentially significant, all except in the subtype of genes: combined. That is, when the presence of a group of combined genetic mutations in individuals is indicated, there are significant differences in relation to the organic- environmental aetiology in influencing the neuropsychological relational capacity of "nodes," which occurred in 17 of the 175 cases in this study (9.71%) (Sig. of Pearson's statistic: .00).), although the Linear by Linear statistic of the Chi-Square itself has already been found to be at the limit of the significance critical level (Sig: .05).

Consequently, when the interaction of the three interrelated factors was analysed- namely, the genetic component, the environmental factor, and the relational capacity- it could be confirmed that, despite all the empirical constraints, environmental components derived from the presence of early organic and severe psycho- emotional illnesses may produce neuronal remodelling, restricting neuronal transmission in a manner similar to that produced by the genetic factor. This is with the exception of the ASD diagnosis with several genetic groups combined, which,

although constituting a low percentage, has shown significant differences in the interaction of the predictive components.

5. Discussion

The semantic memory concept that is severely affected as a consequence of limitations in the neurological processes of GABAergic connectivity is not an unrelated component of the brain system; rather, the whole mechanism of neuropsychological information processing in human beings revolves around this issue. In this way, high specificities that shape perception in a particular way in people with ASD are produced as soon as the information stimulus is input through the sensory pathway.

This conception is due to the fact that the sensory stimulus is not immediately related to the previously stored information in long- term memory. Consequently, the working memory does not have the immediate resources to access the specific previously learned information required to make this connection, as working memory, or short-term memory, is limited in establishing these conceptual or categorical- conceptual relationships. This limitation consequently characterizes this particular processing in individuals with ASD. More importantly, by not establishing these relationships correctly, the perceived sensory information could either be misidentified or simply lost.

In this sense, mediation generates anticonceptual links to establish relationships between these and their categories through the creation of nodes by means of specific learning programs. However, when this information needs to be used to establish new relations or relations of greater cognitive complexity, a similar effect will be produced in the inverse cognitive way. Again, the working memory will not find the necessary resources to backtrack the stored information to relate it to the new or higher cognitive information.

In this way, there is a very particular perceptual-cognitive processing process, which is a specific feature of functioning in people with ASD. This is as important, if not more so, than observable targeted behaviours, which may be very evident at levels 2+ and 3. However, developmental behaviours may go unnoticed at level 1 of the disorder.

When referring to the influence of neuronal remodelling on the GABAergic pathway, he is specifically addressing the processes of connectivity between information contents, which become more complicated as the intensity and complexity of the target concepts increase. This is especially true when these concepts must be retrieved in conceptual categories, as they always need to be categorized by working memory, primarily due to the spatial limitations of permanent memory.

Indeed, experimental biographical studies regarding the episodic memory of individuals with ASD (Ojea, 2024b) show the limitations of people with ASD in relating incoming information to previously learned stimuli, both narratives, textual, and visual. This is due to delays in linking the relational nodes of that content with previously learned information, which limits their overall semantic understanding. For this reason, in a secondary process, people with ASD describe more specific elements of the stimuli than neurotypical individuals in order to provide the semantic content that has not been automatically stated.

These insights are highly observable and have been investigated through studies of biographical episodic information retrieval (Henderson et al., 2009; Lombardo et al., 2007), in which deficits have been found to be associated with limited mentalization capacities regarding one's own actions in the environment or self-representation processes. These studies align with other relevant empirical research (Crane et al., 2010; Goddard et al., 2014; Robinson, Howlin & Russell, 2016; Spek et al., 2010), which is also corroborated by studies in the field of personal introspection (Dritschel et al., 2010; Mitchell & O'Keefe, 2008).

The analyses revealed layer- specific group differences on each measure that were consistent with other functional studies in Functional Magnetic Resonance Imaging and Electroencephalography. There was more complexity observed in typical development controls (TD) than in ASD individuals in frontal regions in the delta layer and occipital- parietal regions in the alpha band, and less complexity in TD than in ASD in delta (parietal regions), theta (central and temporal regions), and gamma (frontocentral border regions). Additionally, there was increased short- range connectivity in the frontal lobe in the delta layer and long- range connectivity in the temporal, parietal, and occipital lobes in the alpha band.

Ghambari et al. (2015) showed, perhaps most surprisingly, that group differences between ASD and TD in complexity and functional connectivity appear spatially complementary; where connectedness was high in ASD, complexity was lower (and conversely). The correlation of regional averaged complexity and connectivity node connectedness strength with symptom severity scores of ASD individuals supported the overall complementarity (with opposite signs) of connectivity and complexity measurements, suggesting that diminished connectivity leads

to high entropy owing to inhibitory mis-regulation or chaotic signals preventing effective measurement of interconnectivity.

That is, there are significant differences in the functional nodal connectionist processes in the parietal, central, and temporal regions, but especially in the gamma area, which corresponds to the frontocentral border regions. Connectivity signals in people with ASD are very limited and have a very short global range regarding the functional component in the delta range, with greater connectivity in the alpha region.

All these studies confirm the existing complexity in the nodal connectivity processes, which are severely limited in people with ASD. This means that the fundamental aetiology of the needs for the functionality of the perceptual-cognitive system shapes the practical cluster of semantic memory, or the storage and retrieval of information with comprehensive content. As a result, the executive processes for the development of higher-order cognitive traits are severely impaired.

According to these premises, the scientific research of the time should focus on the didactic processes that enable the creation of links or nodes between concepts in depth to allow the creation of conceptual categories, and to allow the working memory to be able to efficiently undertake the process of semantic elaboration of the meanings within its context. These issues are highly important in enabling the executive elaboration of higher- level psychological processes, thereby enhancing all areas of an individual's development within the environment of which they are an intrinsic member.

Moreover, further research with a greater sample size should corroborate, and verify the data found throughout this scientific study.

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Annex

Annex I: Questionnaire Interview

https://docs.google.com/forms/d/1x4J2i5nMy2E4GKon_463FjWypKqjS1MYNtPUZyGiJSc/edit