780. PATHOLOGICAL, PROBABLY PATHOLOGICAL OR OF UNCERTAIN SIGNIFICANCE COPY NUMBER VARIANT IN A POPULATION OF PATIENTS WITH NEURODEVELOPMENTAL DISORDERS WITH EPIDEMIOLOGICAL REPRESENTATION.

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BACKGROUND:

The array CGH studies are recommended for the etiological diagnosis of neurodevelopmental disorders (ND), showing the best cost-effectiveness diagnostic method at present (1,2).

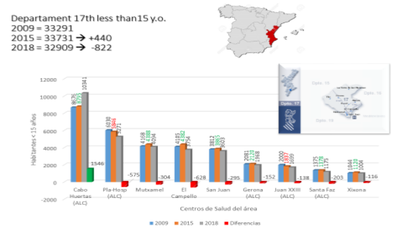
The array CGH compares the patient's genome against a reference genome identifying the differences named Copy Number Variants (CNV)which can explain ND such as developmental delay(DD) and ASD (3,4).

The proportion of pathological, probably pathological (P&PP) or of uncertain significance (US) findings varies depending on the biases introduced by the level of referral of patients to the centers in which they are performed.

OBJETIVES:

To detect the frequency of CNV in a controlled reference population of patients with neurodevelopmental disorders.

Figure 1



PATIENTS AND METHODS:

Cross-sectional frequency study has been carried out in a reference area This department, has a pediatric care population of 32,909 children under 15 years of age (Figure 1). Its primary assistance, universal and extended to any migrant residing in the area, is distributed in nine health centers. All assistance, are made and recorded in two common computer systems, to which access has been obtained with the corresponding permits.

The study focuses on array CGH (750-K) studies carried out between 2017 and 2021. 510 studies, 1.55% of the reference population, were diagnosed of DD or ASD From those, 372 were boys (3/1)

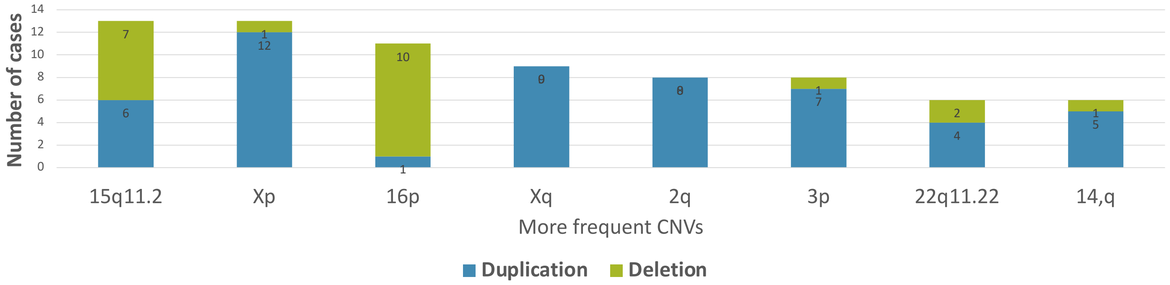
The results of the CNV of the CGH Arrays were categorized into the 5 usual levels: Pathological, probably pathological (P&PP) of uncertain significance (US), only these were considered in this study. We included pediatric patient from Department 17, referred for study due to DD or ASD. The exclusion criteria were: ND symptoms due to acquired factors and defined syndromic pictures with known genetic cause.

All data were collected with the corresponding authorization for this type of study, Analysis was done with Epi Info (CDC App statistical package).

RESULTS:

Of the 510 studies performed, 334 (65.4%) did not present CNV or were benign or probably benign CNV; of uncertain significance (US) 141 (27.6%) and pathological or probably pathological (P&PP) were 36 (7%). All other CNV are listed in Table 1.

Figure 2. Differences between duplications and deletions of the most frequent CNVs.



CONCLUSIONS:

1) The proportion of boys/girls with DD-ASD ranged from 3/1 to 4/1.

2) From the 1.55% of our with DD-ASD being tested for arrays CGH we could justify a genetic etiology in the 34.7% of cases.

3) 15q CNV both in q11.2 and p13.3 variations remains as a hot point explaining DD-ASD.

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Table 1. Frequency distribution of the CNV detected.

CNV/n	CNV	n	CNV	n	CNV	n	CNV	n	CNV	n
	10p12.31	1	16p13.3	4	20q13.33	1	5p13.2	1	9p24.1	1
	10p15.1	1	16q23,3	1	21q22.3	1	6p21.1	1	9p24.3	2
	10q21,3	1	17p12	1	22q11,22	6	6p21.33	1	9p22.1	1
	10q21.1	1	17p13.2	1	2p13,2	1	6p22.3	1	9q22.33	1
	10q23.1	1	17q11.1	2	2p15-p14	1	6q11.1	1	9q33,1	2
	10q25.3	1	17q24.2	1	2p16.3	1	6q12-q13	1	Cromosoma 18	1
	10q25.3	1	17q25.3	1	2p21	1	6q26	1	Cromosoma Y	3
	11q25	2	18p11.31-p11.23	1	2p24.1	1	7p15.3p14.3	1	Disomía uniparental 8p	1
	12q14,3	1	18p11.32	1	2q11.1-2q11.2	1	7p21.2	1	Xp11.22	1
	12q21.31	2	18q12.2	1	2q12.1	1	7p21.3	1	Xp21.1	1
	13q12.12	1	19p13.2	1	2q13	2	7p22.1	1	Xp21.2	1
	13q31.1-q34	1	19q13.41	1	2q14.3	1	7p22.1-p21.3	1	Xp22.31	1
	13q31.3	1	19q13.42	1	2q21.2	1	7q11.22	1	Xp22.33	8
	13q33.3-q34	1	1p34.1	1	2q24.1-q24.2	1	7q22.1	1	Xp28	1
	14q13.3-q21.1	1	1p36,22-p36,21	1	2q35	1	7q31	1	Xq12	1
	14q23.1	1	1p36.32	1	3p14.3	7	7q31,1	2	Xq13.3	1
	14q24.2	1	1p36.33	1	3q11.2	1	7q34	2	Xq23	1
	14q31.2-q31.3	1	1q21.1q21.2	2	3q13.13	1	7q35	1	Xq25	1
	14q31.3-q32.11	1	1q31.1	1	3q21,2-q21,3	1	7q36.3	1	Xq27.2	1
	14q32,12	1	1q32.1	2	4p15.3	1	8p22	1	Xq28	3
	15q11,2	13	1q32.2	1	4p16.3	1	8q11.23	1		
	15q13,3	4	1q42.3	1	4q13.1	1	8q21.2-q21.3	1		
	15q25.2	1	20p12.1	3	4q13.3	1	8q22,3	2		
	16p12.2	4	20p12.2	1	4q21.21	1	8q23.3	1		
	16p13.11	1	20q11.21	1	4q34.3	1	9p24,3	1		

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