INTRODUCTION

Del22q11.2 syndrome (OMIM # 192430) was first described in the 1950s, by Eva Sedlackova, and recognized in 1978 from the study published by Shprintzen and colleagues. In these studies, the authors described as an etiologic factor of this genetic condition the microdeletion on the long arm of chromosome 22 in the region q11.2, which leads to a set of clinical features first observed in 12 individuals, hypernasality as a result of multiple defects, including cleft palate, cardiac anomalies, learning disabilities and behavioral disorders.

This genetic condition has variable frequency, due to some cases are undiagnosed because they have mild phenotypic expression and clinical recognition difficult. Data from the United States reported frequency of 1:2000 live births. Until the present moment, there are no national epidemiological data. Since this is a condition resulting from microdeletion, it is necessary for the diagnosis of del22q11.2 syndrome, a cytogenetic evaluation often performed by the technique of Fluorescence in situ hybridization (FISH) to detect the absence of chromosomal segment in the region 22q11.2.

The phenotype of this syndrome presents wide variability among individuals, among the most common the presence of characteristic facial

ABSTRACT

Purpose: to characterize the behavioral problems and social competence of individuals with del22q11.2 syndrome and compare them with typically developing individuals, according to information from parents. Methods: participated in this study 24 parents of individuals of both sexes between 6 and 18 years, being 12 individuals with the syndrome del22q11.2 (sample group) and 12 individuals with typically developing (control group). The behavioral inventory “Child Behavior Checklist (CBCL)” was applied. Results: eight of the twelve patients with the syndrome were classified as “clinical” as the scales of behavior and Internalizing Problems. Five of the twelve individuals of sample group were “clinical” as the scales of behavior and Externalizing Problems. The skills of social competence, ten of the twelve individuals sample group were “clinical”. Conclusion: individuals with the diagnostic of the del22q11.2 syndrome, according with opinion their parents present behavioral and social problems in different degrees of commitment. Comparing the groups, was observed statistically significant differences in variables of externalizing and internalizing behaviors. Therefore, we conclude that the sample group presents more abnormal behavior compared to the control group.

KEYWORDS: Speech, Language and Hearing Sciences; Behavior; Interpersonal Relations; Communication; Social Behavior Disorders; DiGeorge Syndrome

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features: long face with prominent nose and broad nasal base, with square aspect; jaw alteration; retraction of the mandible; narrow palpebral fissures; minor ear alterations; velopharyngeal insufficiency and cleft palate; renal and skeletal abnormalities; cardiac abnormalities, representing about 90% of the cause of death in this syndrome\textsuperscript{4-5}; delayed acquisition of language\textsuperscript{6}; learning problems with significant deficits in tasks of arithmetic\textsuperscript{7}; and behavioral disorders\textsuperscript{8,9}.

The behavioral phenotype of del22q11.2 syndrome has been described in the literature with problems with aggression, depression, and difficulty in interacting and similar social problems to disorders of the autistic spectrum\textsuperscript{10,11}.

Psychiatric symptoms, mainly schizophrenic disorders are among the behavioral problems frequently cited as part of the phenotype of del22q11.2\textsuperscript{12,13} syndrome. The presence of schizophrenic symptoms has attributed to this genetic condition significant value as neurobiological research model of the genetic basis of schizophrenia, which has propelled the growing number of studies aimed at the characterization of the behavioral phenotype of this syndrome\textsuperscript{8-16}.

The discussion about aggravation of psychiatric disorders according to age group is still contradictory. Some authors argue that psychiatric disorders did not differ in age in del22q11.2\textsuperscript{8} syndrome, being identified both in children and in older individuals, but there are authors who argue that attention deficit disorder, anxiety, mood instability, hyperactivity, impulsivity, shyness or disinhibition aggravate according to age group\textsuperscript{17}.

The Child Behavior Checklist (CBCL) is one of the most used tools in the literature on the subject, since it enables, besides identifying problematic behaviors in specific populations, classify such problems due to the characteristics of the complaints in internalizing behaviors (e.g. problems become internalized as depressive thoughts, anxiety and somatic problems) and externalizing behaviors (e.g. related to the social context of individuals, such as social problems, thought problems, attention problems, presence of aggressive behavior and delinquency).

Behavioral studies using the CBCL in the population of individuals with del22q11, highlighted shifts in attention\textsuperscript{18,19}, changes in internalizing behavior and social competence\textsuperscript{20}. In another study, it was found through the application of behavioral inventory CBCL that individuals with the syndrome del22Q11.2 presented commitments in internalizing and externalizing behaviors when compared to a group of children with craniofacial abnormalities (ACF)\textsuperscript{21}.

Therefore, this research proposes to characterize the behavioral problems and social skills of individuals with the syndrome del22q11.2 and compare them with individuals with typical development, according to information from parents.

**METHODS**

This study was approved by the Research Ethics Committee (nº 0706/ 2013) with humans from the institution. All participants signed a Free and Informed Consent before entering the study. It is noteworthy that all ethical criteria were applied respecting the Resolution 196/96 of the National Health Council (CNS/196) on Regulatory Guidelines and Standards for Research Involving Humans, and the recommendations of the Research Ethics Committee.

This is an experimental and cross-sectional study, which compares the information reported by parents of 24 individuals aged 6-18 years old of both genders. These individuals were divided into two subgroups: Sample Group (SG) and the Control Group (CG), namely:

Sample Group (SA): 12 individuals, seven girls (58.3%) and five boys (41.7%) with a diagnosis of del22q11.2 syndrome, positive for the deletion in the 22q11.2 region, using the technique of Fluorescent In situ Hybridization (FISH), patients in the Center for Study of Education and Health (CEES) UNESP – Marília / SP or from the Hospital for Rehabilitation of Craniofacial Anomalies (HRAC), Bauru / SP. All patients in the sample perform dental treatment and speech therapy at HRAC and attend regular school.

Control group (CG): 12 individuals, paired with SA by gender and chronological age without clinical diagnosis of del22q11.2 syndrome, with negative history for genetic or psychiatric illness, no history of speech therapy or psycho-pedagogical treatment, and enrolled in public schools in the city of Marilia-SP.

For investigation of behavior problems and social skills, the instrument “Child Behavior Checklist for ages 6-18”\textsuperscript{22}, Brazilian version of a questionnaire for parents\textsuperscript{23}. The CBCL consists of 138 items: 118 related to evaluation of behavior problems and 20 for the assessment of the child or adolescent social skills.

The behavioral inventory was applied through direct interviews with parents or guardians gathering information from 113 items related to behavior problems. The informant should classify the behavior: false or absent (score = 0); partially or sometimes true (score = 1); and very true or often present (score = 2). Only behavioral problems identified by parents within the past six months prior to the date of the questionnaire\textsuperscript{23} were registered.
Behavior problems in CBCL are divided into eight behavioral scales: withdrawn, somatic complaints, anxious and depressed, social problems, thought problems, attention problems, rule-breaking behavior, delinquent and aggressive behavior. For each of these behaviors, the instrument provides a scoring system for rating scales, and the index should be $<60$ for non-clinical classification, $60 \leq 63$ for classification in borderline category and the clinical category $>63$.

The data were analyzed using the statistical package SPSS (Statistical Package for Social Sciences), in its version 21.0, to obtain the results. It was used for statistical analysis, the Mann-Whitney Test and Spearman correlation analysis, and the significance value ($p$) calculated in less than 5% ($0.050 / 0.005$).

**RESULTS**

The data from the sample group indicated that on the scales of behavior and Internalizing Problem $66.7\%$ of the individuals showed behavior rated as “clinical”, with a lower percentage for “borderline” ($25\%$) and “normal” ($8.3\%$). As for the Externalizing Problems scale, there is equivalence between the behaviors classified as “clinical” and “normal” ($41.7\%$ of the individuals each) and lower percentage for borderline behavior ($16.7\%$) (Figure 1).

As for skills of social competence, $83.3\%$ of the individuals with del22q11.2 syndrome were classified as “clinical”, $8.3\%$ as “borderline” and $8.3\%$ as “normal” (Figure 2).

![Figure 1 – internalizing and externalizing behaviours in group sample](legend: Clinical > 70, and Borderline $67 \leq 70$ Normal $< 67$ 0-9: number of individuals with the syndrome)
By comparing the sample groups (SG) and control (CG) using the Mann-Whitney test, there were significant differences among them (Table 1, Figure 3). It was registered a statistically significant difference between CG and SG for the variables “internalizing behaviors”, “withdrawn”, “social problems”, “attention problems” and “aggressive behavior.”

In order to better characterize the behavior problems presented by the SG and CG and check if they established a relation with each other, the Spearman correlation analysis (Table 2) was performed.

According to the data obtained for behavioral problems, it was noted that complaints of “anxious and depressed” presented positive relation to complaints of “aggressive behavior.” The same happened in the relation “anxious and depressed” with “the rule-breaking behavior”.

The variable “somatic complaints” had a positive relationship with “social problems” and “thought problems” where the variables “social problems” and “thought problems” also had a positive relation with each other.

The variable “anxious and depressed” had a positive relation to “activities”, related to social competence, and also with Internalizing Behaviors (“thought problems”, “withdrawn” and “somatic complaints”).

In order to verify possible differences between genders, a statistical correlation analysis was performed, in which it was not found a statistically significant difference for behavior problems and social competence in terms of male and female individuals in the SG (Figures 3 and 4).

### Table 1 – Behavioral problems of sample group and control group

|                       | M   | SD  | Min | Max  | Med. | p     |
|-----------------------|-----|-----|-----|------|------|-------|
| Anxiety / Depressed   |     |     |     |      |      |       |
| SG                    | 62.17| 7.68| 50  | 76   | 65   | 0.664 |
| CG                    | 59.67| 7.98| 50  | 72   | 58   |       |
| Withdraw              |     |     |     |      |      |       |
| SG                    | 67.42| 8.85| 54  | 85   | 68   | 0.013*|
| CG                    | 57.67| 7.34| 50  | 77   | 57   |       |
| Somatic Complaints    |     |     |     |      |      |       |
| SG                    | 61.58| 8.82| 50  | 78   | 63   |       |
| CG                    | 56.08| 4.66| 50  | 64   | 55.5 | 0.116 |
| Social Problems       |     |     |     |      |      |       |
| SG                    | 68.83| 7.69| 61  | 83   | 67   | <0.001**|
| CG                    | 56.17| 5.09| 50  | 66   | 56.5 |       |
| Thought Problems      |     |     |     |      |      |       |
| SG                    | 60.58| 7.56| 50  | 71   | 60   | 0.021 |
| CG                    | 54.00| 5.72| 50  | 69   | 51   |       |
| Attention Problems    |     |     |     |      |      |       |
| SG                    | 66.83| 6.90| 52  | 77   | 65   | 0.001**|
| CG                    | 54.08| 5.38| 50  | 66   | 52   |       |
| Hule-Breaking Behavior|     |     |     |      |      |       |
| SG                    | 55.75| 5.61| 50  | 66   | 55.5 | 0.276 |
| CG                    | 53.00| 3.41| 50  | 60   | 51   |       |
| Agressive Behavior    |     |     |     |      |      |       |
| SG                    | 61.42| 6.40| 50  | 69   | 64   | 0.020*|
| CG                    | 54.67| 5.31| 50  | 67   | 52   |       |
| Internalizing         |     |     |     |      |      |       |
| SG                    | 65.92| 6.81| 48  | 72   | 68.5 | 0.019*|
| CG                    | 56.67| 8.42| 48  | 72   | 53   |       |
| Externalizing         |     |     |     |      |      |       |
| SG                    | 59.08| 7.41| 44  | 67   | 61.5 | 0.052*|
| CG                    | 53.00| 5.89| 46  | 67   | 51   |       |

Mann-Whitney Test
p<.05*, p<.005**
Legend: M = Mean, SD= standard deviation, Min= Minimum, Max= Maximum, Med= Median, (p)= significance, SG = sample group, CG = control group
Table 2 – Degree of relationship between the variables (sample group)

|                      | Anx / Dep | Withdrawn | Somatic Complains | Social Problems | Thought | Attention | Rule-Breaking Behavior | Agressive Behavior | Internaliz | Externaliz |
|----------------------|-----------|-----------|-------------------|----------------|---------|-----------|------------------------|-------------------|------------|------------|
| **Anx / Depr**       | Coef. Corr. (r) | -0.339   |                   |                |         |           |                        |                   |            |            |
|                      | Sig. (p)   | 0.282     |                   |                |         |           |                        |                   |            |            |
| **Withdrawn**        | Coef. Corr. (r) | +0.529   | -0.112            |                |         |           |                        |                   |            |            |
|                      | Sig. (p)   | 0.077     | 0.728             |                |         |           |                        |                   |            |            |
| **Somatic Complains**| Coef. Corr. (r) | +0.327   | -0.353            | +0.549         |         |           |                        |                   |            |            |
|                      | Sig. (p)   | 0.300     | 0.261             | 0.065          |         |           |                        |                   |            |            |
| **Social Problems**  | Coef. Corr. (r) | +0.247   | -0.069            | +0.454         | +0.384  |         |                        |                   |            |            |
|                      | Sig. (p)   | 0.439     | 0.831             | 0.138          | 0.217   |         |                        |                   |            |            |
| **Thought**          | Coef. Corr. (r) | +0.137   | -0.110            | +0.332         | +0.637  | +0.450   |                        |                   |            |            |
|                      | Sig. (p)   | 0.672     | 0.733             | 0.292          | 0.026*  | 0.143    |                        |                   |            |            |
| **Attention**        | Coef. Corr. (r) | +0.153   | -0.250            | +0.565         | +0.576  | +0.481   | +0.263                 |                   |            |            |
|                      | Sig. (p)   | 0.634     | 0.433             | 0.056          | 0.050   | 0.113    | 0.409                 |                   |            |            |
| **Rule-Breaking Behavior** | Coef. Corr. (r) | +0.695   | -0.419            | +0.550         | +0.556  | +0.456   | +0.372                 | +0.643            |            |            |
|                      | Sig. (p)   | 0.012*    | 0.175             | 0.064          | 0.061   | 0.136    | 0.234                 | 0.024*            |            |            |
| **Agressive Behavior** | Coef. Corr. (r) | +0.629   | +0.093            | +0.895         | +0.480  | +0.377   | +0.107                 | +0.462            | +0.474    |            |
|                      | Sig. (p)   | 0.028*    | 0.775             | < 0.001**      | 0.114   | 0.227    | 0.741                 | 0.130             | 0.119     |            |
| **Internaliz**       | Coef. Corr. (r) | +0.420   | -0.340            | +0.670         | +0.618  | +0.543   | +0.360                 | +0.933            | +0.855    | +0.551    |
|                      | Sig. (p)   | 0.173     | 0.279             | 0.017*         | 0.032*  | 0.068    | 0.250                 | < 0.001**         | < 0.001** | 0.063     |
| **Externaliz**       | Coef. Corr. (r) | +0.467   | -0.340            | +0.723         | +0.866  | +0.665   | +0.577                 | +0.759            | +0.671    | +0.655    |
|                      | Sig. (p)   | 0.126     | 0.280             | 0.008*         | < 0.001**| 0.018*   | 0.050                 | 0.004**           | 0.017*    | 0.021*    |
| **Total**            | Coef. Corr. (r) | +0.467   | -0.340            | +0.723         | +0.866  | +0.665   | +0.577                 | +0.759            | +0.671    | +0.655    |
|                      | Sig. (p)   | 0.126     | 0.280             | 0.008*         | < 0.001**| 0.018*   | 0.050                 | 0.004**           | 0.017*    | 0.021*    |

**Legend:** Cor. Coef. (r)=Correlation coefficient, (p)= significance
Anx/depr: anxious and depressed

Figure 3 – Behavior problems as a function of gender for group sample
study del22q11.2 classified as “clinical”, i.e. out of the expected range for normality. One of the main features of schizophrenia and most common found in del22q11.2 syndrome is anxiety. The high incidence of schizoid symptoms in this particular genetic condition has been described as a neurobiological model of the investigation of genetic basis of schizophrenia that it was reported a subtype of del22q11.2 – Schizophrenia.

All the individuals were categorized with behaviors beyond expectations in at least one of the scales of the CBCL. The data obtained allowed to observe statistically significant differences between CG and SG for the variables “withdrawn”, “social problems”, “attention problems”, “aggressive behavior” and “internalizing behaviors” (e.g. anxious and depressed), thus confirming the hypothesis by previous studies that the presence of anxiety and depression would be frequent in children and adolescents with a diagnosis of del22q11.2 syndrome, which would cause impairments in adaptive functioning, e.g., a lack of ability of social nature in different areas.

The sample group also had higher rates of aggressiveness when compared to the control group, and the aggressiveness a feature commonly described in del22q11.2 syndrome. It was also observed the reported problems with anxiety and depression, thought problems and rule-breaking behavior presented positive relation to complaints of aggressiveness for the subjects of this study.

It was also proposed in this study to verify the possible distinctions based on gender, which it was observed there is no difference between the behavior.
problems and social competence between the male and female genders in the sample group, reinforcing the findings of Klaassen et al. Paradoxically, there are other researchers, who found higher proportions of behavior problems for boys, expressed by clinically significant scores in “internalizing behaviors” (withdrawn, somatic complaints, anxious and depressed) and about thought problems regarding the girls.

### CONCLUSION

Parents or guardians of individuals with diagnosis of del22q11.2 syndrome when responding to behavioral inventory CBCL, reported the presence of behavioral and social competence in different degrees of commitment.

When performed to compare the groups we observe statistically significant differences in variables of externalizing behaviors (i.e. aggressive behavior, social and attention problems) and internalizing behaviors (i.e. withdrawn, anxious and depressed). Thus, we conclude that the sample group presents more abnormal behavior compared to the control group.

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