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ABSTRACT

The phenotype of triple X syndrome comprises a variety of physical, psychiatric, and cognitive features. Recent evidence suggests that patients are prone to severe language impairments. However, it remains unclear whether verbal impairments are pervasive at all levels of language, or whether one domain is relatively more spared than others. Here we document the language profile of one patient with triple X, using standardized language tests and reports. Results concur in showing that impairments are noticeable both in expressive and receptive language skills, and in vocabulary as well as in structural components of language. Although receptive ability in some tests appears relatively spared, even here A's performance is clearly below average. This single case study further underscores that language and communication at all levels can be severely compromised in patients with triple X. Practitioners should be aware of the limited language abilities that possibly exist in patients with triple X.

Triple X syndrome (47,XXX) is characterized by the presence of an extra X chromosome in women.[1] Its prevalence is estimated to be 1/1000 females[2] or even lower[3;4]. Because triple X syndrome manifests itself differently in individuals, it is assumed that many women remain undiagnosed because their symptoms are too mild to warrant medical attention, while only 16% of women with triple X syndrome receive a diagnosis because they exhibit more severe symptoms or have been identified via prenatal screenings.[3–6]

The phenotype of triple X syndrome lists a variety of physical, psychiatric, and cognitive features [for reviews, see[6–9]]. The physical features are best understood: These are usually subtle and variable, and include long legs or tall stature, small head circumference, scoliosis, poor motor coordination, and infertility.[3,6] The psychiatric characteristics that are more frequent than in the general population include mood disorders (anxiety and depression), shyness, lower self-esteem, and attention deficits. Some researchers noted the similarities between patients with triple X syndrome and people with autism spectrum disorder (ASD) in their communicative abilities.[10] Indeed, cognitive limitations often manifest themselves in the verbal domain with delays in language [e.g.[11–14]] and in reduced executive functions.[15]

Although most research has focused on the physical and psychiatric problems in patients with triple X syndrome, one hypothesis holds that abnormalities in sex chromosomes may also lead to language problems.[16] A recent study documents that the majority of affected women experience marked general language problems, although there is substantial individual variation in the severity.[17] However, language acquisition is a multi-faceted process, comprising both production and perception of language, across different components of language: phonology (language sounds), mental lexicon (vocabulary), morpho-syntax (the rules of grammar) and pragmatics (the ways in which we use language in interactions). Hence, a relevant question to ask is whether the documented language problems in patients with triple X syndrome are only noticeable at the level of expressive vocabulary or pervade all levels of linguistic structure and processing.[18] It is here that we can appreciate as a first step the full-depth analysis that single-case studies can offer. The current case study aims to present a full language profile of a Dutch patient 'A' diagnosed with triple X syndrome prenatally, using standardized language tasks.

Materials & Methods

Patient A was 17;11 years old during testing. The patient was well acquainted with the experimenter, which was advantageous as she felt at ease, could signal the need for breaks, and was motivated to continue testing. Parental report revealed 1) no abnormalities at birth; 2) delayed onset of word production (around 3 years) compared to her siblings; 3) clear aversion to initiating conversations, reading and writing; 4) a history of enrollment in schools specialized in language delays. A's full-scale IQ at the age of 17;11, as determined with the Wechsler Adult Intelligence Scale-III ["WAIS-III",[19]] was 70, with a verbal IQ of 66 and a performance IQ of 74.

We used two widely used tests to assess A's language skills: the Clinical Evaluation of Language Fundamentals ["CELF,"[20] for Dutch:[21]] and the Peabody Picture Vocabulary Test- ["PPVT";[22] for Dutch: Schlichting, [23]], as well as a standardized report: the Children's Communication Checklist-2-NL ["CCC,"[24] for Dutch: Geurts, [25]].

The CELF is a battery of 16 subtests and two parental questionnaires, indexing various parts of language acquisition, to assess language abilities in children between the ages of 5 and 18 years. Norms are based on a sample of 1336 Dutch children aged between 5;0 and 15;11 years. Besides generating a general language score, the subtasks assess relative strengths and weaknesses: receptive vs. expressive language performance; vocabulary vs. language structure. The test further comprises subtasks that index the following underlying processes considered crucial in language processing: executive functions such as working memory and automation in naming tasks, as well as phonological awareness (how sounds combine into words).

The PPVT is used to assess a person's receptive vocabulary and can be taken as a proxy of verbal IQ.[26] Both the CELF and the PPVT have been standardized to create scores with 100 as the mean, and a standard deviation of 15 points. Clinicians usually consider scores of 1.5–2 standard deviations below the mean as a critical marker for language impairment (i.e., scores lower than 77 or 70). In contrast, the CCC does not measure a child's language abilities directly but is a 70-item questionnaire for adult informers who know the child well, rendering their assessment of the child's general communication skill, social interaction, and pragmatic abilities. Scores between 10 and 90 percentiles indicate typical development, while scores above 90 or below 10 percentiles give cause for concern. Both parents and A's adult brother filled in the CCC-questionnaires. Her scores were compared against the oldest age group available: 13;0–15;5 years.

Results

Clinical Evaluation of Language Fundamentals

Table 1 lists scores for all subscales (1A) and subtests (1B), with 95% confidence intervals (95% CI), and translates this to percentile rankings and age equivalents. A's general language score is 58 (95% CI 53–67), which is more than two standard deviations below the age-appropriate average. However, although all test scores are clearly below average, she does not show similar degrees of impairment on all tests. A comparison of the subscales indexing language components shows that receptive language (score 74) is relatively spared compared to expressive language (score 58): only 6% of the Dutch original sample shows a similar or larger difference score.[21] There is no reason to believe that vocabulary (language contents: score 60) is more impaired than language structure (score 59): a difference of 1 point is considered non-significant.

Table 1. Results from the Clinical Evaluation of Language Fundamentals -4.

A: Scales of the CELF	Raw score	Index score	[95% CI]	Percentile
General Language Score	12	58	53–67	0.3
Receptive Language Index	11	74	67–89	4.2
Expressive Language Index	13	58	53-69	0.3
Language Contents Index	13	60	55–72	0.4
Language Structure Index	9	59	54-73	0.3
Working Memory Index	12	76	70–86	5.5

B: Subtests of the CELF	Raw score	Norm score [95% CI]	Percentile score [95% CI]	Age equivalent	Domain affected
Sentence repetition	32	1 [1–3]	0.1 [0.1–2]	5;4	S
Sentence formulation	27	5 [2–8]	5 [0.4–25]	9;6	V, S
Word categories 2 – receptive	9	5 [2–8]	5 [0.4–25]	4;3	V, S
Word categories 2 – expressive	7	6 [4–8]	9 [2–25]	4;7	V, S
Word categories 2 – total	16	5 [2–8]	5 [0.4–25]	4;4	V, S
Word definitions	11	1 [1–3]	0.1 [0.1–1]	8;11	V
Understanding texts	2	1 [1–4]	0.1 [0.1–2]	n.a.	V
Sentence construction	1	3 [1–7]	1 [1–16]	7;6	V, S
Semantic relationships	13	6 [3–9]	9 [1–37]	9;7	V
Number repetition forwards	8	8 [4–12]	25 [0.1–91]	8;4	WM
Number repetition backwards	5	9 [4–14]	37 [16–98]	11;4	WM
List repetition	29	4 [1–9]	2 [0.1–37]	7;9	WM
Word associations	34	4 [1–8]	2 [0.1–25]	8;5	M, V
Rapid naming task-errors	0	9 [5–13]	37 [5–84]	n.a.	V
Rapid-naming task-timing	74 s	4[1–8]	2 [0.1–25]	10;2	V
Following instructions *	29			6;3	V
Active vocabulary *	34			7;0	Ph, M, V
Phonological awareness *	35			6;9	Ph

* Indicates that this subtest is typically only administered in younger ages; consequently, we started with a starting set that fitted the highest age group possible but which was below A's age.
n.a. (not available) indicates that no age equivalents could be obtained, either because this task was only administered at younger ages or because it was not normed at all.
Language domains: Ph = phonology; M = Morphology; S = Syntax; V = Vocabulary; WM = working memory.

She also performs poorly on tests of working memory: she has a score of 76, which is between 1.5 and 2 standard deviations below the group average. Table 1B lists performances for all subtasks and breaks down how each performance compares to her peers (percentile score) as well as for which age it is representative (age equivalent). When examining the tasks underlying linguistic ability we observe that most scores fall below 5%-percentile score, suggesting that they are more than two standard deviations below the population average. For phonological awareness, she functions at the lowest 5%-percentile compared to 8-year-olds. For tests indexing automatization (word associations, rapid naming), she scores at the lowest 2%.

Peabody Picture Vocabulary Task

The results from the PPVT confirm that A's vocabulary development is severely delayed. She has a verbal quotient of 62 ([58–72] 95% CI), which corresponds to the level of a 9.6-year-old ([9.0–11.3] 95% CI).

Children's Communication Checklist

Only the brother's report was consistent, whereas data from both parents failed the consistency check: their answers did not reflect the required distinction between the patient's weaknesses and strengths.[a] We therefore only report her brother's ratings (cf. Table 2). The test considers any percentile above 90 for all subscales as a clinical marker. Her general communication score (based on subscales A–H; see Table 2) is 115, which puts her beyond the 95th percentile of 4.0- to 15.6-year old children, that is, she ranks with children with a severe developmental language disorder. The subscales for structural processing (subscales A–D) reflect more atypical performances (e.g. in speech production, syntax, and coherence), whereas the subscales for pragmatics (language use; subscales E–H) mainly list typical performances (that is, inappropriate imitation, stereotypical language, and non-verbal communication). Indeed, a significantly negative social interaction score confirms that her problems are mainly in structural parts of language processing rather than in pragmatics.

Table 2. Results from the Child's Communication Checklist-2.

Subscale		Norm scores	Percentiles
A	Speech production	20	>99
B	Syntax	15	95
C	Semantics	13	80
D	Coherence	16	98
E	Inappropriate imitation	12	70
F	Stereotypical language	10	45
G	Use of context	16	98
H	Non-verbal communication	13	80
I	Social relationships	15	98
J	Interests	12	65
General Communication Score		115	> 95
Social Interaction Score		−12	<10
Pragmatics Score		51	85

[a]Checks for internal consistency are required when (corrected) strengths exceed 31 points (max is 60), suggesting that she sometimes shows signs of strong communicative behavior. Careful reading of the questionnaire revealed that while both parents consider her strengths as strong (mother: 51 points; father: 50 points), her father considered her weaknesses as noteworthy (problem score 54 out of 120 max) whereas her mother did not: (problem score 19 points out of 120 max).

Finally, there is a mixed picture for the subscales on characteristics of autism (I-social relationships; J-interests): for interests, she behaves like her peers (i.e., compared to oldest age range available: 13.0–15.6-year-olds) whereas for social relationships she is at the 98th percentile, which indicates atypical behavior.

Discussion & Conclusion

Even though females who receive their diagnosis of triple X syndrome prenatally (like our patient A) have a smaller risk of language disorders than those who receive their diagnosis postnatally [17,27], our results from the standardized language tests as well as her brother's report indicate that patient A's language is severely impaired compared to her peers. These results are in line with recent studies, showing that also children with prenatally diagnosed sex chromosome trisomies often have lower language scores than their age-matched controls,[17,28] which are noticeable from an early age.[14]

Her performances on the clinical tests remain far below average, even though A was familiar with the experimenter, and experimenter familiarity usually yields higher scores as it increases patients' motivation and attention.[29] As each of the tasks becomes increasingly more difficult, her unsteady performance in vocabulary might not only be due to the specific task at hand but could also be partly due to fatigue, which is one of the symptoms of triple X syndrome.[6] Indeed, the participant often complained about how tired the tasks made her feel. Nevertheless, we catered for fatigue: tasks were administered in a scope of 3 days with ample breaks upon request. We, therefore, believe that our results underscore that she is performing at least 8 years below her chronological age in her language abilities.

Our results further make clear that these language impairments are pervasive at all levels of language: at receptive versus expressive levels, at semantics versus structural components of language. She makes errors at all levels of language: not only in tasks assessing vocabulary but also in tasks assessing sentence construction (syntax), phonology, and morphology. Although the CELF suggests an imbalance between receptive and expressive language, it is clear that she is performing far below the mean in both levels. For pragmatics, it appears that she scores moderately low (CCC: 85th % percentile). Different underlying processes for language acquisition appear to be equally impaired: she scores far below her age on tasks such as phonological awareness and executive functions (working memory and task automation).

All three instruments report lower performances in vocabulary compared to age-matched peers, albeit that they provide different estimates. Her brother ranks her vocabulary as low but within normal bounds, whereas the clinical tests put her functioning as equivalent to a 4.3- (CELF) to 9.6-year-old (PPVT). It is, therefore, striking that her parents do not even

seem to notice this in daily conversations. This finding fits nevertheless with research documenting that parental reports for school-aged children are often more positive than teacher reports or language test scores.[30] Such findings show that even though parents are the ones who know the child best as they communicate with her on a daily basis, they can be prone to subjective biases and might vary in their ability to compare their child's language abilities to other children [but see[31]]. It is possible that some parents (like A's parents), and clinicians too, consistently overestimate a patient's verbal abilities while underestimating her weak points in communication. We, therefore, recommend that all patients with triple X be tested (ideally repeatedly at yearly intervals) on their language comprehension skills to compare them to typical development and to chart their development of language skills.

Of course, one of the limitations of this study is that it involves only one single case. Bishop and colleagues[17] suggest that two thirds of patients with triple X experience some form of developmental language disorder. It remains unclear whether all patients with triple X with language impairments are as compromised in their language at all levels as was the case with our patient. This study should, therefore, be taken as a first step arguing that language deficits can be one of the core symptoms of triple X. Practitioners should be aware of the compromised language and communication abilities that possibly exist in patients with triple X.

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