Linguistic phenotype in a sample of Arabic speaking children with Williams and fragile X syndromes

Available online freely at www.isisn.org

Bioscience Research

Print ISSN: 1811-9506 Online ISSN: 2218-3973

Journal by Innovative Scientific Information & Services Network

RESEARCH ARTICLE BIOSCIENCE RESEARCH, 2018 15(2): 873-882. **OPEN ACCESS**

Linguistic Phenotype in a Sample of Arabic Speaking Children with Williams and Fragile X Syndromes

Neveen Hassan Nashaat[1,3], Nagwa A. Meguid[1,2], Ehab Ragaa Abdelraouf[1,3], Nivine A. Helmy[4], Ahmed A. Dardir [1], Vesna Stojanovik[5] and Aly A. El-Nofely[6]

[1]Research on Children with Special Needs Department, Medical Research Division, National Research Centre, Cairo, **Egypt**
[2] CONEM Egypt Child Brain Research Group, National Research Centre, Giza, **Egypt**.
[3]Learning Disability Research Clinic, Medical Research Centre of Excellence, National Research Centre, Cairo, **Egypt**
[4]Human Cytogenetics Department, Human Genetics and Genome Research Division, National Research Centre, Cairo, **Egypt.**
[5] School of Psychology and Clinical Language Sciences, University of Reading, **UK.**
[6] Department of Biological Anthropology, National Research Centre, Cairo, **Egypt.**

***Correspondence:** dr.neveennashaat@gmail.com **Accepted: 26** Feb. 2018 **Published online:** 08 June 2018

The detailed linguistic assessment of children with Williams syndrome (WS) in comparison to typically developing (TD) children and other genetic syndromes such as fragile X syndrome (FXS) could reveal the language specific difficulties and help in better designing of intervention plans. Aim: To investigate the linguistic abilities with detailed syntactic performance in a sample of Egyptian children with WS in comparison to TD and FXS children from the same pool. The participants (n=30) included WS, TD children of similar sex and age of WS group and FXS group matching the WS group for mental age. The linguistic assessment was established using the Wechsler intelligence scale for children-III, Vineland social maturity scale and the standardized Arabic language test. The linguistic abilities of WS group were delayed even in relation to their mental age and when compared to TD children. WS group manifested deficits in past verb tense, manner adverbs and in spatially related syntax. The overall WS group language profile differed from that of FXS group especially regarding Pragmatics. The cognitive assessment revealed differences between the groups. The in depth detailed language assessment supports the presence of certain profile in the Arabic speaking WS participants. Individuals with WS do need language and social intervention plans as early as possible in addition to the original required visuospatial improvement strategies.

Keywords: Williams syndrome, FXS, Arabic language, syntax, cognition.

INTRODUCTION

The linguistic and cognitive abilities of children with Williams syndrome (WS) have been investigated in different languages but not in Arabic. Broadbent et al. (2015) reported that visuospatial abilities in the population with WS are defective in relation to their language abilities. The linguistic abilities of Italian WS children were similar to their mental age matched typically developing children while the French individuals manifested morphosyntactic deficits even in adulthood (Karmiloff-Smith et al., 1997; Volterra et al., 2003). Children with this rare syndrome manifested delay in the use of morphemes concerning gender and poor grammatical receptive language abilities while similar lexical

comprehension when compared to younger normal children (Mervis and Klein-Tasman,2000). Moreover, comparison between linguistic abilities of WS and fragile X syndrome (FXS) children have been investigated to underpin the contrasts or similarities of their behavior to verify syndrome specific language profile (Di Nuovo and Buono, 2011). Fisch et al. (2007) observed similar linguistic abilities for WS and FXS although being non-significantly lower in WS. Receptive language abilities of FXS individuals were noticed to be a point of relative strength while the pragmatic abilities were impaired (Fung et al., 2012). The opposite was reported in WS children together with strengths in the paralinguistic domain [Paterson et al., 1999; Fung et al., 2012). Egyptian population is of special interest considering the unique geographic location of Egypt which is characterized by recurrent migration waves followed by gene flow. Furthermore, every population has their unique genotype and the gene-environmental interaction differs accordingly (Manni et al., 2002). Besides, mother language stores the national culture and defines personal identity which emphasizes the importance of investigating certain genetic insult in different populations (El-Nofely, 2014). Arabic is a language with complex morphology. Modern standard Arabic (MSA) is characterized by much inflection which originates by addition of prefixes and suffixes. It is characteristically endowed with the 'root' and 'pattern' system. The root is mostly formed of a skeletal structure of three consonants. By changing various vowel patterns, several stems emerge which express related concepts taking the form of different grammatical units [e.g. /ʔɛkɛl/, /ʔɛkl/ (ate, food) /ʃɛreb/, /ʃɛrɛ:b/ (drank, drink (n))]. Colloquial Egyptian Arabic (Cairene dialect) has the same criteria as MSA. However, there are few sounds that are not commonly used especially before school enrollment such as /q/ and diphthongs (Omar, 1973). There are 7 Arabic vowels in the colloquial Cairene dialect: 6 of them are used with long and short variants with another central one and this is the dialect used in the present study (Kotby et al., 2011).

The aim of this study was to assess the linguistic abilities in a sample of Egyptian Arabic speaking children with Williams syndrome in comparison to typically developing and FXS children, keeping in mind the cognitive-social performance of the participants. This would emphasize the importance of the detailed assessment of their abilities and its essentiality for the proper intervention and would verify the role of cultural and genotypic interaction in the final syndromic outcome.

MATERIALS AND METHODS

Participants:

The study was conducted in the out-patient clinic of the research on children with special needs department, Medical Research Centre of Excellence, National Research Centre (NRC), Cairo, Egypt. Written consents were obtained from the parents of all participants. The study was approved by the Medical Research Ethics Committee of the NRC. The WS group included 10 participants [7 males and 3 females, age range 6-12 (9.1±3) years] who were first-time visiting the outpatient clinic. Their enrollment in the study was based on the clinical picture especially the characteristic physical phenotype (preliminary diagnosis). The typically developing (TD) children group included 10 participants (IQ= 90-109; SQ 95-106) matched for chronological age, gender and socioeconomic class with the WS participants and were randomly selected among the relatives of cases visited the outpatient clinic. They did not have a history of delayed language development or neuropsychiatric disorders. The fragile X syndrome group included 10 males [age range 7-12.5 (10.4±2); IQ 37-74; SQ 43-72] who were mental age matched with WS group. Their diagnosis was confirmed by DNA analysis using polymerase chain reaction (PCR) (Saluto et al., 2005). None of the participants matched the DSM-IV-TR (American Psychiatric Association, 2000) diagnostic criteria for autism (otherwise excluded).

Methods:

The participants were evaluated by the language assessment protocol which was developed by Kotby and El-Assal (1995) which is based on elementary diagnostic procedures, clinical diagnostic aids and additional instrumental measure. Elementary diagnostic procedures included history taking, clinical examination including general, ear, nose, vocal tract examination and neurological examination. Clinical diagnostic aids included cognitive and social aptitudes evaluation by: the Wechsler intelligence scale for children (WISC) III (Wechsler, 1991; Melika, 1999), the Vineland social maturity scale (VSMS) (Doll, 1965; Alaguizi et al., 1982). The linguistic performance was assessed by the Arabic language test (Kotby et al., 1995). The Arabic language test is a standardized norm-referenced test that was

designed to evaluate Arabic speaking children whose ages are between 2 and 8 years. The attention of the child, the ability to imitate actions and sounds, the auditory memory span (AMS) of words and digits (up to 4 digits and up to five-word sentence), receptive and expressive semantics at word level, receptive syntactic abilities, expressive syntactic abilities, pragmatics, prosody and phonology were evaluated. The test utilizes cards of colored drawings and uses the dialect of people living in Cairo. This test was chosen for this study because it assesses the syntactic performance in details and because the raw scores obtained by it are transformed into a language age starting from 2 years. Moreover, it was the only test that was developed for evaluating the Arabic language of Egyptian population at the time when the study started.

The language test parameters helps to obtain language age for: semantics, receptive component of syntax, expressive component of syntax, pragmatics, prosody and a total language age. A score is given to each item within the test and the raw scores that belong to the same language parameter of the test were added together. Standardized tables were used to obtain a language age from the raw scores of the language test parameters. The language ages obtained range from 2 to 8 years and they gradually increase by 6 month in the test manual. The child's language performance is considered normally developed if the language age of the language parameter in the test matches the chronological age of the child. When the obtained language age of a test parameter was less than the child's age by 6 months or more, the child was considered to manifest a language delay in this parameter. It's noteworthy that the ceiling of the test is 8 years. So, if the participant's language age is 8 years in any parameter, it means that this language parameter is fully developed. This rule is applied even when the child's chronological age is more than 8 years. Therefore, the parameters of the language test were presented as a 100-point scale according to the relation between the participants' language age (dependent variable) and chronological age or 8 years if the chronological age is more than 8 years (independent variable for calculating this 100-piont scale). This 100-point score was obtained for each participant. Furthermore, some syntactic components raw scores were collected from the Arabic language test results of each participant. The sum of raw scores of receptive and expressive performance of the participant on the syntactic components such as superlatives was used to get another 100-piont scale for each participant. This 100-point scale was determined according to the relation between the sum of the raw scores that reflected the participant's performance in a syntactic component (the dependent variable) and the actual total scores of this syntactic component in the test (the independent variable for obtaining this 100-point score). For example, the relation between the participant's actual scores in plurals (on receptive and expressive levels) and the total raw scores of plurals in the test. This was performed in the present study to analyze the details of syntactic components separately. The auditory memory span (AMS) was assessed by scores from 0-6 within the test. The Additional instrumental measures included audiological evaluation, polymerase chain reaction (PCR), and Echo. Initial karyotypes and Fluorescent in Situ Hybridization (FISH) were performed according to Verma and Babu (1995) and Pinkle et al. (1986) to confirm the clinical diagnosis of WS participants.

Statistical analysis:

The statistical analysis of the data was performed by using SPSS 15 software package under Windows 7® operating system. Mann Whitney U and Kruskal-Wallis tests were used for data analysis. Probability level (p value) was assumed significant if less than 0.05. The statistical analysis was performed for comparison between WS and TD groups then between WS and FXS groups and finally between the 3 groups regarding the scores of social quotient, the 100-point scale scores of the language test parameters, the auditory memory span and the 100-point scale scores of the syntactic components.

RESULTS

Initial karyotypes of lymphocytes from peripheral blood samples evaluated using Giemsa-Trypsin-Giemsa (GTG) stained banding did not show visible abnormalities. Fluorescent in Situ Hybridization (FISH) revealed that all WS children showed a missed elastin (ELN) gene from one copy of chromosome 7 (haploinsufficiency).

The psychometric assessment for WS participants revealed: Total IQ: 50-75 (66.8±7.1); Verbal IQ: 60-100 (87.4±11.1); Performance IQ: 30-58 (46.4±10.3); SQ: 59-88 (76±8.8). They all showed better verbal than performance IQ. The

difference between the verbal and performance IQ ranged from 22- 61 IQ degrees. In the TD group, the difference between the verbal and performance IQ ranged from 2-9 in favor of the performance IQ. In FXS group, the difference between the verbal and performance IQ ranged from 10-36 in favor of performance IQ.

WS group manifested statistically significant delay in receptive syntactic and total language ages in relation to the mental age. The receptive syntactic language age mean was less than the expressive language age one. The delay in the expressive syntactic abilities almost reached significant levels (Table 1). None of the participants with WS manifested articulation errors except one child who showed multiple phonological processes in the form of weak syllable deletion, substitutions and assimilation.

Table 2 revealed that the difference between WS group and the TD group was statistically significant concerning the social quotient and all the language test parameters being lower in the WS group. The auditory memory span scores were less in WS group but with non-significant statistical difference.

The comparison between WS and TD group regarding the detailed syntactic abilities scores in table 3 revealed that the scores in WS group were less than those in TD group being statistically significant only in past verb tense, manner adverbs, superlatives and place indicators and almost significant in present verb tense and comparatives.

Comparison between WS and FXS groups showed that the performance of WS group was better than the performance of the FXS group regarding all language test parameters and AMS except the receptive syntactic language abilities. A significant difference between the groups was noticed only in social quotient and pragmatics. A discrepancy between the receptive and expressive syntactic language performance in WS and FXS groups was noticed. The receptive language abilities scores were less than the expressive language abilities in the WS group which is the opposite of what was noticed in the FXS group (Table 4). Comparison between the two groups regarding the detailed syntactic abilities scores was performed and revealed that the WS group scores were better than those of the FXS group in all syntactic parameters but with non-significant statistical difference.

Table 5 showed that the difference between the 3 groups of participants was statistically significant regarding SQ, receptive syntactic abilities, expressive syntactic abilities, semantics, pragmatics, prosody, total language performance, past verb tense, pronouns, superlatives and place indicators. The difference almost reached significant level for adjectives and manner adverbs.

Discussion

To our knowledge, this preliminary study is the first one that was addressed to investigate the linguistic and cognitive profile of Arabic speaking Williams syndrome children not to mention the special attention paid to the detailed syntactic abilities.

Syntactic deficits were evident for WS participants in this study even when the mental age of WS group was considered. Studies targeted other languages such as French, Italian and Hungarian reported no syntactic deficits in relation to mental age (Karmiloff-Smith et al., 1997; Volterra et al., 2003; Luka´cs, 2005). This relative language delay in the present study could stem from peculiarities of the Arabic language and environmental factors. The sociability of the children with WS and their good basic phonological development hide their language problem and hinder the parents from seriously considering it. This makes the parental attention directed more towards their scholastic achievement as they usually fail to cope. Our results agree with Mervis and Morris (2007) who reported deficits in language describing relational concepts for individuals with WS. According to Meyer-Lindenberg et al. (2006), the difficulty in temporal, spatial, and quantitative concepts could be related to abnormalities in the dorsal stream pathway of visual processing especially the area close to the intraparietal sulcus in WS individuals.

WS participants in this study further manifested special difficulty for the past tense although it has the least complicated morphemes in Arabic language (e.g. /**ʔɛkɛ**l/ is for [ate] while /Be**jɛkʊ**l/ is reflecting the present continuous tense [is eating] and /h**ɛjɛkʊ**l/ is for the future tense [will eat]. This deficit could be attributed to the impaired temporal domain of action which was considered a part of WS cognitive deficits. Clahsen and Almazan (1998) suggested that the cause of impaired irregular past tense production was the impaired access to lexical system in such population. This could be applied in Arabic as a second explanation for the delayed past tense performance despite the absence of irregular past tense forms in Arabic.

Table (1): The language performance of the Williams syndrome participants presented as language age in years in relation to their mental age

Language test items	Language age in years	Mental age	P value
Receptive syntactic age	3.1±1	5.7±1.8	0.000*
Expressive syntactic age	4.2±1.4	5.7±1.8	0.05
Semantics age	5±2.3	5.7±1.8	0.4
Pragmatics age	5.4±1.8	5.7±1.8	0.7
Prosody age	4.3±1.7	5.7±1.8	0.09
Total language age	3.1±1	5.7±1.8	0.000*

Table (2) : Comparison between WS and TD children groups regarding the social quotient, the language performance scores and the auditory memory span scores

Measures	Mean± SD for WS group scores	Mean± SD for TD children group scores	P value
Social quotient	76±8.8	101.2±4.04	0.000*
Receptive syntactic abilities	41.1±14.5	100±0	0.002*
Expressive syntactic abilities	57±18.3	100±0	0.002*
Semantics	63.2±31.7	100±0	0.007*
Pragmatics	71±25.9	100±0	0.007*
Prosody	57±21.1	100±0	0.002*
Total Language performance	56±23	100±0	0.002*
Auditory memory span scores	4.3±2	5.9±0.3	0.15

SD standard deviation TD typically developing WS Williams syndrome

Table (3): Comparison between WS and TD children groups regarding the scores of performance in syntactic abilities obtained by the Arabic language test.

Syntactic items	Mean± SD for WS group Scores	Mean± SD for TD children group Scores	P value
Future verb tense	71±46	100±0	0.14
Present verb tense	70.8±40	100±0	0.05
Past verb tense	54±29	100±0	0.00*
Pronouns	65±37	75±41.83	0.31
Adjectives	56±32	97.5±4.18	0.31
Manner adverbs	73±38	100±0	0.03*
Comparatives	71±40	100±0	0.05
Superlatives	73±37	100±0	0.03*
Time indicators	83±41	100±0	0.49
Place indicators	76±36	100±0	0.004*
Plurals	79.1±26	91±11	0.1

SD standard deviation TD typically developing WS Williams syndrome

Table (4) : Comparison between WS and FXS groups regarding the social quotient, the language performance scores, and the auditory memory span scores

Measures	Mean± SD for WS group Scores	Mean± SD for FXS group Scores	P value
Social quotient	76±8.8	57±7.8	0.00*
Receptive syntactic abilities	41.1±14.5	58±36	0.57
Expressive syntactic abilities	57±18.3	51±35	0.62
Semantics	63.2±31.7	60±37	0.87
Pragmatics	71±25.9	38±27	0.01*
Prosody	57±21.1	40±35	0.25
Total Language performance	56±23	56±37	0.87
Auditory memory span scores	4.3±2	3.5±2.3	0.5

FXS fragile X syndrome SD standard deviation WS Williams syndrome

Table (5) : Comparison between the 3 groups concerning social quotient, auditory memory span scores and performance in language test and syntactic components scores

Measures	Median of WS group	Median of TD children group	Median of FXS group	X^2	P value
Social Quotient	73.5	102	58.5	13.51	0.00*
Receptive syntactic abilities	39.55	100	50	9.22	0.01*
Expressive syntactic abilities	56.25	100	40.6	10.21	0.01*
Semantics	62.5	100	56.3	7.32	0.03*
Pragmatics	75	100	25	12.65	0.00*
Prosody	61.43	100	18.8	12.44	0.00*
Total Language abilities	62.5	100	43.8	8.74	0.01*
Auditory memory span	5	6	3.5	5.48	0.06
Future verb tense	100	100	75	3.56	0.17
Present verb tense	87.5	100	37.5	5.78	0.06
Past verb tense	62.5	100	50	7.84	0.02*
Pronouns	100	100	70.8	8.29	0.02*
Adjectives	100	100	100	6.14	0.05
Manner Adverbs	87.5	100	68.8	6.14	0.05
Comparatives	87.5	100	62.5	5.33	0.07
Superlatives	81.25	100	62.5	6.38	0.04*
Time indicators	68.75	100	12.5	3.21	0.20
Place indicators	62.5	100	60	7.06	0.03*
Plurals	68.75	100	12.5	3.21	0.20

FXS fragile X syndrome TD typically developing WS Williams syndrome

Their reliance on the present tense use instead of the past could be attributed to the impaired access to their lexicon. The deficit in the present verb tense almost reached significant level. The WS language system is suggested to develop under different constraints which may include atypical phonological representation which is required for complicated morphosyntax (Thomas et al., 2001).

The development of some linguistic domains such as semantics and plurals of young individuals with WS was suggested to be typical

but delayed (Martens et al., 2008). This was actually noticed in this study when using mental age as a reference. Concerning the prosody and pragmatics, despite of being less than normal, their prosodic and pragmatic abilities were better than their total language performance which accord with Stojanovik et al. (2007). Notwithstanding, Laws and Bishop (2004) identified pragmatic difficulties in children with WS. There were no detected articulation errors of the participants except the youngest one which is consistent with Bellugi et al. (2000) who suggested preservation of the phonological processing which is required for proper articulation in the individuals with WS.

Concerning the differences in language abilities between participants with WS and FXS, one could observe different patterns. The WS group showed better expressive than receptive syntactic abilities in contrast to the FXS group. This agrees with previous reports such as Paterson et al. (1999). Schmitt et al. (2001) presumed that the linguistic discrepancy in WS children could stem from the alteration of their cerebral shape with decreased parieto-occipital lobe volumes relative to frontal regions. They further reported that the cognitive and linguistic profile of WS was attributed to the lost genes in the deleted segment of chromosome 7 (7q11.23). These genes are involved in controlling the early cell development, tissue differentiation, and dorsal-ventral brain polarity. The linguistic criteria of FXS could be related to slower expressive than receptive language acquisition and to the regional cerebral abnormalities which were reported in those individuals such as: enlarged caudate nucleus volume and increased volume of grey matter in fronto-striatal regions (Gothelf et al., 2008; Hallahan et al., 2011). On the other hand, pragmatic abilities of the WS group were significantly better than those of the FXS group. Echolalia, perseveration and the difficulty in starting and ending of conversation have been reported to negatively impact pragmatics in FXS individuals (Visootsak et al., 2005). Furthermore, the FXS group manifested verbal short term memory deficits which are attributed to decreased attention and executive capacity (Munir et al., 2000). Nevertheless, past reports have shown that individuals with WS have preserved verbal short term memory (Hsu et al. 2007) which is in agreement with the present study and it is thought to be responsible for their relatively good verbal performance.

It was noticed that verbal IQ mean (87.4±11.1) was better than performance IQ mean (46.4±10.3) with a difference between the two means reaching about 40 IQ degrees in the WS group. The presence of great differences between the verbal and performance IQs in favor to verbal IQ is consistent with previous reports about WS cognitive characteristics (Martens et al., 2008). This discrepancy is not similar to what was noticed in the TD group in this study. TD group manifested difference between verbal and performance IQ but within 9 IQ degrees with the performance IQ being better than the verbal IQ. The FXS group manifested variable difference between verbal and performance IQs which sometimes exceeded the difference noticed in the TD group but was always with better performance than verbal IQ which is the opposite to WS group. The WS visuospatial construction deficits could explain this discrepancy and might be attributed to decreased grey matter concentration in the left parieto-occipital region and reduction of gyrification index in occipital lobes which was negatively correlated with their cognitive psychometric scores (Fahim et al., 2012). The frontal lobe, frontostriatal circuits and caudate nucleus aberrations were involved in the executive functions deficits which could explain the delayed cognitive performance of both syndromes (Fisch et al., 2007). Children with WS were sociable and engaging. Nonetheless, some abilities in the VSMS were found to be defective such as some items of reading, writing, working and self-directing.

The deficits in the VSMS for the children with FXS revealed similar deficits in the VSMS for WS group. Deficits in phonological awareness development in both syndromes have been reported (Menghini et al., 2004; Adlof et al., 2015) which could explain the reading disorders manifested by these children. However, FXS children manifested further deficits in relating and socializing tasks. This can be attributed to social anxiety, hypersensitivity to social and sensory stimuli, shyness and impairment in the processing and retention of information in social situations which characterize individuals with FXS (Visootsak et al., 2005). This could be explained by alterations in brain regions involved in social processing such as amygdala and fusiform cortex. The amygdala for example was found to be smaller than normal in FXS while larger than normal in WS (Fung et al., 2012). To sum up, WS, TD children and FXS groups differed in their linguistic and cognitive performance.

CONCLUSION

The linguistic and cognitive abilities of Egyptian Arabic speaking children with WS support the presence of a certain profile and go in line with some other languages. Considering that cultural identification is defined by language, the in depth detailed language assessment highlights the difference in culture-genotype interaction which interferes with the final syndrome outcomes. The individuals with WS do need language and social interventional plans as early as possible in addition to the original required visuospatial and executive functions improvement strategies. Moreover, linguistic problems of children with Williams and fragile X syndromes should not be viewed as a manifestation of a general cognitive impairment but rather as an expression of specific deficits with certain areas of strengths and weaknesses.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interests.

ACKNOWLEGEMENT

This research did not receive any specific grant from funding agencies.

AUTHOR CONTRIBUTIONS

All authors but VS shared in the practical work. All authors shared in analysis and interpretation of data, writing and critically revising the manuscript. All authors read and approved the final version.

REFERENCES

Adlof SM, Klusek J, Shinkareva SV, Robinson ML, Roberts JE, 2015. Phonological awareness and reading in boys with fragile X syndrome. J Child Psychol Psychiatry 56:30-39.

Alaguizi MY, Badari AH, Habashi NW, 1982. A study for standardization of Vineland Social Maturity Scale on an Egyptian sample. M. Sc. Thesis. Minia University, Minia, Egypt.

American Psychiatric Association, 2000. Diagnostic and statistical manual of mental disorders. 4th ed. text rev. American Psychiatric Association Publishing, Washington DC, USA.

Bellugi U, Lichtenberger L, Jones W, Lai Z, St George MI, 2000. The neurocognitive profile of Williams syndrome: a complex pattern of strengths and weaknesses. J Cogn Neurosci 12:7-29.

Broadbent HJ, Farran EK, Tolmie A, 2015. Sequential egocentric navigation and reliance on landmarks in Williams syndrome and typical development. Front Psychol 6:1-11.

Clahsen H, Almazan M, 1998. Syntax and morphology in Williams syndrome. Cognition 68:167-98.

Di Nuovo S, Buono S, 2011. Behavioral phenotypes of genetic syndromes with intellectual disability: comparison of adaptive profiles. Psychiatry Res189: 440-445.

Doll EA, 1965. Vineland Social Maturity Scale, Rev. ed. American Guidance Service Inc., Minnesota, USA.

El-Nofely A, 2014. Linguistic tolerance and national heritage: children and foreign language learning in a changing world. Int J Anthropol 29: 69-76.

Fahim C, Yoon U, Nashaat NH, et al., 2012. Williams syndrome: a relationship between genetics, brain morphology and behavior. J Intellect Disabil Res 56:879-94.

Fisch GS, Carpenter N, Howard-Peebles PN, et al., 2007. Studies of age-correlated features of cognitive-behavioral development in children and adolescents with genetic disorders. Am J Med Genet A 143A: 2478–2489.

Fung L, Quintin E, Haas B, Reiss A, 2012. Conceptualizing neurodevelopment disorders through a mechanistic understanding of fragile X syndrome and Williams syndrome. Curr Opin Neurol 25: 112-124.

Gothelf D, Furfaro JA, Hoeft F, et al., 2008. Neuroanatomy of fragile X syndrome is associated with aberrant behavior and the fragile X mental retardation protein (FMRP). Ann Neurol 63:40–51.

Hallahan BP, Craig MC, Toal F, et al., 2011. In vivo brain anatomy of adult males with

Fragile X syndrome: an MRI study. Neuroimage 54:16-24.

Hsu A, Karmiloff-Smith A, Tzeng O, Chain R, Wang H, 2007. Semantic knowledge in Williams syndrome: Insights from comparing behavioural and brain processes in false memory tasks. Paper presented at: 6th International Conference on Development and Learning; July 11, London, UK.

Karmiloff-Smith A, Grant J, Berthoud I, Davies M, Howlin P, Udwin O, 1997. Language and Williams syndrome: how intact is "intact"? Child Dev 68: 246-62.

Kotby MN, El Assal N, 1995. Results of a language intervention program in delayed language mentally retarded children. In N. Kotby, ed, Proceedings of the XXIII World Congress of the International Association of Logopedics and Phoniatrics. Cairo, Egypt.

Kotby MN, Khairy A, Barakah M, Rifaie N, El-Shobary A, 1995. Language testing of Arabic speaking children. In N. Kotby, ed, Proceedings of the XXIII World Congress of the International Association of Logopedics and Phoniatrics. Cairo, Egypt.

Kotby MN, Saleh M, Hegazi M, et al., 2011. The Arabic Vowels: Features and Possible Clinical Application in Communication Disorders. Folia Phoniatr Logop 63: 171–177.

Laws G, Bishop D, 2004. Pragmatic language impairment and social deficits in Williams syndrome: a comparison with Down syndrome and SLI. Int J Lang Comm Dis 39: 45-64.

Luka´cs A, 2005. Language Abilities in Williams Syndrome. Akade´miai Kiado, Budapest, Hungary.

Manni F, Leonardi P, Barakat A, et al., 2002. Y-chromosome analysis in Egypt suggests a genetic regional continuity in Northeastern Africa. Hum Biol 74: 645-658.

Martens M, Wilson S, Reutens D, 2008. Research Review: Williams syndrome: a critical review of the cognitive, behavioral, and neuroanatomical phenotype. J Child Psychol Psychiatry 49: 576–608.

Melika L, 1999. Wechsler intelligence scale for children, Ed 1. The Anglo Egyptian bookstore, Cairo, Egypt.

Menghini D, Verucci L, Vicari S, 2004. Reading and phonological awareness in Williams syndrome. Neuropsychology 18:29-37.

Mervis C, Klein-Tasman B, 2000. Williams syndrome: cognition, personality, and adaptive behavior. Ment Retard Dev Disabil Res Rev 6:148–158.

Mervis CB, Morris CA, 2007. Williams syndrome. In: Mazzocco MM, Ross J, eds, Neurogenetic Developmental Disorders: Variation of Manifestation in Childhood, Ed 1. MIT Press, Cambridge, UK.

Meyer-Lindenberg A, Mervis CB, Berman KF, 2006. Neural mechanisms in Williams syndrome: a unique window to genetic influences on cognition and behavior. Nat Rev Neurosci 7:380-93.

Munir F, Cornish KM, Wilding J, 2000. Nature of the working memory deficit in fragile-X syndrome. Brain cog 44:387-401.

Omar M, 1973. The acquisition of Egyptian Arabic as a native language, Ed 1. Mouton, The Hague, Netherlands.

Paterson SJ, Brown JH, Gsodl MK, et al., 1999. Cognitive modularity and genetic disorders. Science 286: 2355–2358.

Pinkle D, Gray J, Trask B, Van den Engh G, Fuscoe J, Van Dekken H, 1986. Cytogenetic analysis by in situ hybridization with fluorescently labeled nucleic acid probes, Cold Spring Harbor Symp. Quaut Biol 51:151-157.

Saluto A, Brussino A, Tassone F, et al., 2005. An enhanced polymerase chain reaction assay to detect pre- and full mutation alleles of the fragile X mental retardation 1 gene. J Mol Diagn 7: 605–612.

Schmitt JE, Eliez S, Bellugi U, Reiss AL, 2001. Analysis of cerebral shape in Williams syndrome. Arch Neurol 58:283–287.

Stojanovik V, Setter J, van Ewijk L, 2007. Intonation abilities of children with Williams syndrome: a preliminary investigation. J Speech Lang Hear Res 50:1606-1617.

Thomas M, Grant J, Barham Z, et al., 2001. Past tense formation in Williams syndrome. Lang Cogn Process16:143-176.

Verma R, Babu A, 1995. Tissue culture techniques and chromosome preparation. In Verma R, Babu A, eds, Human chromosomes: Principles and technique, Ed 2. Pergamon Press, New York, USA, pp 926-931.

Visootsak J, Warren ST, Anido A, Graham Jr JM, 2005. Fragile X syndrome: an update and review for the primary pediatrician. Clin Pediatr (Phila) 44:371-381.

Volterra V, Caselli MC, Capirci O, Tonucci F, Vicari S, 2003. Early linguistic abilities of Italian children with Williams syndrome. Dev

Neuropsychol 23:33-58.
Wechsler D, 1991. Wechsler Intelligence Scale for Children, Ed 3. Psychological Corporation, San Antonio, TX, USA.