

Child Neuropsychological Assessment—Genetic Neurodevelopmental Disorders: True Microcephaly

Yolanda Benito

“Huerta del Rey” Psychological and Educational Centre, Valladolid, Spain

True Microcephaly is classified within neurodevelopmental disorders with well defined etiology. This clinical case study focuses on Ana, a child of 8 years and 6 months of age. She has been diagnosed with True Microcephaly. True Microcephaly is a genetic disorder that affects the autosomes, and due to its low incidence, it is classed as a “rare disease”. We have organised this text in several sections: the main text in this article is dedicated to the description and analysis of the clinical case. We have included the data and/or the results of the medical tests and the educational psychology reports that we considered most relevant in a summarised manner. We also attached a synopsis of the neuropsychological tests used in the diagnostic assessment and its results. In addition, as we developed this account, we inserted boxes which summarise and explain content related to the main text. The case studies (ideographic approach), as well as the single-case designs, have been an important source of information for Neuropsychology; information which would have otherwise been difficult to obtain from the designs describing a wide range of subjects (homothetic approach). This study widens our knowledge of possible anomalies affecting white matter and those cerebral regions connected to executive functions in people who have an attention deficit disorder and hyperactivity, as well as the cerebellum’s role in cognitive functions.

Keywords: neuropsychological assessment, True Microcephaly, ADHD, developmental dysphasia, pachygyria, autosomal recessive primary microcephaly, Williams Syndrome

Introduction

Neuropsychology is one of the disciplines, within Neuroscience, that studies the relationship between the higher cognitive processes and the brain. Its key purpose is to learn how human beings function, which would explain its special links with Psychology. Children’s Neuropsychology is a discipline that includes knowledge from Developmental Neuroscience and Classical Developmental Psychology.

A neuropsychological assessment is always a part of the psychological assessment, since it helps in making a diagnosis, determining a comorbidity diagnosis, measuring the degree of deterioration or the level of development of the child and quantifying the child’s strong and weak points. This information is essential both to set up interventions with a specific aim, and to develop recommendations which will enhance strong areas and compensate the weaker ones. Moreover, establishing a basal evaluation allows the subsequent repetition of tests in order to monitor the child’s development throughout time and to assess the effectiveness of the

Yolanda Benito, Director of the “Huerta del Rey” Psychological and Educational Centre. Registry number for Health Centres of CyL 47-C22-0114 Valladolid (Spain). Doctor in Psychology from the University of Radboud in Nijmegen (The Netherlands). Specialised in Child and Adolescent Psychology and Neuropsychology. E-mail address: c_h_rey@cop.es

intervention. This article, as well as a great number of the articles we have written since the publishing of our first book in 1990, has been based on the analysis of a clinical case. In Luria's posthumous work, he finishes wishing to gain back a romantic perspective for science, which is reflected in the detailed descriptions of clinical cases made by Charcot, Pierre Marie, Wernicke or Korsakov, among others in the 19th century; these views were afterwards confronted by the classical understanding reigning in the 20th century. According to Luria, classical scientists "considered facts depending on their parts", with a great deal of details. On the other hand, a romantic doesn't want to turn vital truths into concepts which are too abstract. Perhaps they were inspired by more intuitive methods; basing it on the description of the clinical analysis more than in the explanation. However, this way they can "see a fact from a wider range of perspectives" (Preface: Arnedo, Bembibre, Montes y Triviño, 2015, p. XIII)

Child neuropsychology has increased our knowledge in developmental neuroscience and in clinical and developmental psychology. It has designed specific assessment tests and appropriate interventions for the child population who suffer from acquired brain damage or neurodevelopmental disorders.

Genetic Neurodevelopmental Disorders: True Microcephaly

General Approach to the Case: Ana, 8 Years and 6 Months of Age

The parents arrived at the examination room so that their child would undergo the neuropsychological tests requested by paediatric neurologist, Dr. Martín Fernández-Mayoral. They provided medical and educational psychology records. The father, just as had been previously reported, informed that she had "*Developmental delays caused by Microcephaly Pachygyria*". According to the mother, she presented "*Autosomal recessive microcephaly. Diagnosis Pachygyria. The main consequence of this is a developmental delay and intellectual disability*".

They are both deeply concerned with the child's future and her present integration with other people (at school, with family...). The greatest difficulties have been observed when she is engaging in a conversation; she struggles to understand abstract concepts and she presents impulsive reactions when faced with a negative.

The condition has existed since her birth, but obviously, her difficulties have become clearer since the second year of pre-school (5 years old). She has received early stimulation from 6 months of age until she began attending school. They have consulted specialists, neurologists, endocrinologists, orthopaedic specialists and psychologists. She receives psychological therapy, speech therapy and she has a tutor at home. She slowly progresses toward maintaining a conversation.

They have tried to help their daughter with patience, love, stimulation, effort, understanding, cooperation, strengthening her self-esteem and giving her their full attention. Both parents agree that the child's situation causes more worry and distress to the mother. They are consistent, understanding and caring parents. They appear to agree, generally, on the way they want to raise their daughter. The emotional relationship is close and loving. The members of their family are the parents and Ana. Both parents have completed higher education and are graduates in Law. Both parents are employed.

Cranial growth disorders are anomalies in the cranial size, consequence of an abnormality of the cranial bones, or the Central Nervous System. The anomaly can be congenital or acquired. Among these are craniostenosis, macrocephaly, microcephaly and other alterations with cranial deformities which disrupt head

circumference and morphology. Microcephaly has been defined as an abnormal growth of the head circumference, which would be below 3 DS and lower than the age and gender averages. One of the common symptoms associated to all kinds of microcephaly is intellectual delay; except in the case of family microcephaly.

Etiology: cranial growth is intimately connected to cerebral growth; therefore, deficient cerebral growth, whether primary (in primary brain diseases) or a growth standstill secondary to intercurrent processes, will determine the presence of microcephaly for microencephaly. In both cases microcephaly can be harmonic if it is associated with weight and height delay. Primary microcephaly is present at birth, which means it is a static cerebral disorder, whereas secondary microcephaly appears after birth and it has a progressive nature. Essential Primitive, or True Microcephaly; Autosomal Recessive Primary Microcephaly; the Genetic Seckel Syndrome; and neuronal migration Disorders, according to their etiology and pathogenesis, are classified within microcephalies due to primary disorders in brain development, since it implies a lower number and size of the neurons for genetic reasons (Protocolo de la Asociación Española de Pediatría. Martí y Cabrera, 2008 p.190).

Box 1. Autosomal recessive primary microcephaly (MCPH, which stands for “Microcephaly Primary Hereditary”) is a rare disorder, genetically heterogeneous, of cerebral neurogenic development, characterised by a reduction of head circumference (HC) since birth. There are no macroscopic anomalies of the brain structure, and cognitive deficit has various degrees.

The exact incidence of non syndromic microcephaly is unknown. MCPH is more frequent in Asian and Middle Eastern populations than in Caucasian population, in which the annual incidence has been described as 1/1,000,000.

The diagnosis is based on clinical findings. Common diagnostic criteria are a reduction of the occipitofrontal circumference or HC, with moderate cognitive deficit, without any other malformations and with average or low height. The MR shows a normal brain, proportionately small and with certain simplification of the cerebral convolutions; also known as simplified gyral pattern. MCPH and Seckel Syndrome belong to a clinical continuum, since the mutation in some genes (CEPJ, CEP152) cause both phenotypes. The difference between both conditions is based on the history distinction between microcephaly patients with normal and low height (Verloes, 2012).

Box 2. Neuronal migration disorders: Pachygyria

Within neuronal migration disorders, the diseases which have been better identified include: schizencephaly, lissencephaly, pachygyria, polymicrogyria and neuronal heterotopia. Very often these diseases are accompanied by agenesis of the corpus callosum, although it isn't itself a neuronal migration disorder.

Pachygyria. Pachygyria is closely related to lissencephaly. It occurs in the later stages of development, probably around the fourth month of pregnancy.

The term lissencephaly means “smooth brain”, and it refers to a deficiency in the development of brain gyri and sulci; it is part of a group of neuronal migration disorders.

Agyria is the absence of convolutions in the cerebral cortex and is synonymous with “severe lissencephaly”; whereas pachygyria is the presence of few, ample and smooth convolutions, name which can be replaced with the term “mild lissencephaly”. Pachygyria can be focal or diffuse. When it is focal it is almost always bilateral and generally posterior. When it is diffuse, it is usually linked to areas with agyria and it is more severe in the parietooccipital region (Mota, Valdivieso, Quiroz y Criales, 2005).

Box 3. Performed medical tests and diagnosis.

Karyotype in amniotic fluid (4 month pregnancy): Cytogenetic studies with G banding showed a chromosomal formula of 46, XX in the 20 analysed metaphases. These results are consistent with those of a chromosomally normal woman.

Xr Cranial AP and Lateral (25-08-05). Newborn: All sutures can be seen. There are no signs of craniosynostosis; control (05-09-05): No changes to the previous one. Cranial ultrasound: No visible structural variation. The studies conducted so far are normal. On discharge (14-day-old newborn), the examination is normal except for the evident microcephaly.

Programme for the early detection of congenital disorders; the detection tests for Hypothyroidism and Phenilketonuria that were carried out on the child (1 month old) were considered normal.

Radiological study, NMR, brain structure and myelinization both normal. This study does not show significant alterations; the ventricular system appeared to have a normal size. The cavum subaracnoideale is large, as is regular at the patient’s age (2 months old). The corpus callosum can be identified. The degree of myelinization matches the age of the patient.

Paediatrics (Outpatient consultation), XR CRANEUM: Sutures and open fontanelle. CLINICAL JUDGEMENT: Some features are compatible with Seckel syndrome, but it is presently not possible to confirm (3 months of age).

Paediatrics (Outpatient consultation): Additional Exams: Xr of pelvis and knees: no pathological alterations. CLINICAL JUDGEMENT: Microcephaly. Morphological features corresponding to Seckel without clinical correlation (7 months of age)

Paediatrics, head control 2-3 months. Seated position 6 months. Wide smile 2 months. Slow weight gain and good growth speed. Hyporexia. Propensity to vomit. No convulsions. No dermatopathy. Calm sleep. Good relationship with her environment. Subjectively, normal hearing. Correct vaccines. No known allergies. Examined, suspected Seckel syndrome. No goitre. Normal muscle tone. DTR normal. Psychism currently normal. Dentition: 0/0. Ortolani test negative. Pes valgus. DIAGNOSIS: AUTOSOMAL RECESSIVE MICROCEPHALIA (9 months of age).

Clinical Genetics Unit; 22 month-old girl referred to us for assessment and study; suspected diagnosis of Nijmegen Syndrome. Karyotype at 18 months (normal female: 46, XX). Her size has developed throughout percentile 3; her weight has been gradually progressing further from said percentile from the age of 6 months. Her cranial circumference has been far below percentile 3 since the beginning; it has significantly deviated and it has come to a standstill in the last 10 months. Initial psychomotor development seemed quite appropriate (seated position at 6 months, crawling at 9-10 months, walking at 14-15 months);

however, she now has some motor unsteadiness and language delay. No seizure crisis and good health. Normal genitalia. Extremities, hands, feet, fingers and toes are normal. **DIAGNOSTIC IMPRESSION:** Primary microcephaly connected to growth restriction does not really suggest isolated recessive microcephaly. Facial features do not suggest Seckel syndrome either. Clinical manifestations, standstill of cranial growth and its connection with low levels of gammaglobulin are all fitting factors in the suspected diagnosis of Nijmegen Syndrome. This genetic disorder of recessive autosomal inheritance is due to mutations in the NBS1 gene, located on the long arm of chromosome 8. In most cases it is caused by a common mutation (657de15) in this gene.

Stichting Klinisch-Genetisch Centrum Nijmegen **RESULTS:** No pathogenic mutation detected in the coding part and splice sites of NBS1 gene by sequence analysis. **CONCLUSION:** These results make the diagnosis Nijmegen Breakage syndrome caused by mutations in the NBS1 gene unlikely (2 years and 5 months old).

Paediatric endocrinology unit. Paediatric department **CLINICAL JUDGEMENT:** history of growth delay, both in weight and stature; with size recovery and important microcephaly. Slight psychomotor delay with favourable progress (2 years and 7 months old).

Outpatient consultation. Paediatric endocrinology, girl aged 4 years and one month. Congenital microcephaly; at the moment head circumference is within normal parameters. Mild psychomotor and language delay with concentration difficulties. Harmonic and uniform growth pattern connected to a 2 year bone development delay, size prediction is appropriate to parental and demographic size patterns. **ADDITIONAL EXAMS:** Bone age: 2 years more/less 8 months. **CLINICAL JUDGEMENT:** Growth below normal limits. Bone developmental delay.

Outpatient consultation. Paediatric endocrinology, girl aged 5 years and 22 days. **ADDITIONAL EXAMS:** Bone age: 3 years more/less 8.6 months. **CLINICAL JUDGEMENT:** Growth below normal limits. Bone development delay. Failure to thrive.

Outpatient consultation. Paediatric endocrinology, girl aged 6 years and 1 month. No incidents since last check-up. She has a varied diet, but in small amounts; she needs caloric supplements for her proper nutrition. **CLINICAL JUDGEMENT:** She has normal growth regarding weight and stature. Bone development delay.

Outpatient consultation. Paediatric endocrinology, girl aged 6 years and 7 months with true microcephaly. Connection to bone development delay, size prediction is appropriate to parental and demographic size patterns. No incidents since last check-up. She has a varied diet, but in small amounts; she needs caloric supplements for her proper nutrition. **ADDITIONAL TESTS:** Bone age of 5 years. **CLINICAL JUDGEMENT:** She has normal growth regarding weight and stature. Bone development delay.

Specialist in Neurology and Clinical Neurophysiology, girl aged 6 years, 5 months and 12 days. Treated at Early Care; incorporated early into pre-school; she has always had therapy and psychopedagogic support; however, her learning curve has been deficient, which is why she is now repeating the third year of pre-school, still with support each evening; speech therapy, general stimulation and social abilities. Nocturnal enuresis, and frequently diurnal as well. Not very independent when dressing herself; evident family overprotection. No dysmorphic features, dermatoglyphs seem normal. Muscle tone, motility and coordination are normal, no signs of pyramidal symptoms, neither extrapyramidal nor cerebellar. Eyeground

normal. Good social contact. She has mild mental delay. In CONCLUSION, it appears to be True Microcephaly, which entails developmental delay due to a smaller amount of cerebral neurons. It would be recommended to repeat the magnetic resonance of the brain, since it was done when she was only a few months old. Maintain all the current therapies, and remove family overprotection. She has received trial treatment, 10mg of methylphenidate (Rubifen) with breakfast on her three school days to attempt to increase her attention and motivation.

Radiological Report: Commentary: The study (MRI) was conducted while the girl was under anaesthetics due to her age (6 years, 11 months and 28 days old). There is proof of alterations connected to microcephaly: disproportion of the cranium and face, as well as reduced cerebral size; the cerebellum is disproportionately big in comparison to the other cerebral hemispheres. Another noteworthy finding was the decrease of the number and depth of the sulci on the occipital and temporal lobes and in part of the frontal lobes where we have identified gyri which are wider than usual. The thickness of the cerebral cortex exceeds the limit of normality in several areas. The increase of thickness in the cortex suggests pachygyria more than a simplified gyral pattern.

There are no visible alterations in the morphology of other structures that could be affected in the context of microcephaly: corpus callosum, basal ganglia and brainstem have a normal appearance. The myelination pattern is normal. The ventricles have normal characteristics. The angio-MR study of the intracranial arteries is normal. CONCLUSION: Congenital abnormality of the gyral pattern which suggests cortical dysplasia).

Paediatric (Outpatient consultation), girl aged 7 years, 0 months and 10 days. She has never had epileptic seizures. From the psychomotor perspective, she appears to have difficulties both in gross and fine motor control; their development has improved. Verbal expression and comprehension are appropriate, although she struggles to maintain attention in a continued way. She repeated the third year of nursery school which improved her academic performance, according to the parents. She receives speech therapy, stimulation, extracurricular support and she attends a psychopedagogic centre. She requires corrective lenses because she suffers from astigmatism and hyperopia. Normal hearing. Nocturnal sleep is appropriate for her age. She is independent in daily-life activities. Severe microcephaly. Not very cooperative. Wandering attention. Appropriate eye-contact. Appropriate social interaction. PIN. Normal cranial nerves. Strength, tone and trophism of the 4 extremities are normal without asymmetries. Patellar reflex and Achilles reflex: symmetrical and normal. Plantar reflex: Bilateral flexor. Walking and variations normal. Gowers sign negative. Romberg test negative. No limb length discrepancy nor alterations in other cerebellum functions. No abnormal movements. CLINICAL JUDGEMENT: Developmental congenital malformation: Pachygyria. Severe microcephaly. EEG Anomalies: Psychomotor delay.

CLINICAL RECORD: In January 2014, Dr. Daniel Martín Fernández-Mayoralas, a child and adolescence neurologist of the QUIRÓN Hospital Group in Madrid (Spain), issued a report in which pertained to, among other topics, the following:

This is an 8-year-old patient. Intrauterine IUGR. Low height and microcephaly. No diagnosis.

EA: she started speaking late. Blood test good. Normal XX karyotype.

No renal, cardiac nor vaginal problems. Pes talus valgus treated with insoles. Amniocentesis normal. Suspected Nijmegen Breakage Syndrome (ruled out even because of sequences of the NBS10 gene). TORCH

negative. Immunology study. Deficit in practical semantics. ADHD symptoms, she finds it hard to understand rules in games. She is not hyperactive, but as a younger child she would not be still. Impulsive. She was seen by Dr. Herranz, who suggested the same diagnosis and treatment as I did.

Clinical Judgement:

TRUE MICROCEPHALY

SIGNS OF ADHD.

INTELLECTUAL DISABILITY.

Box 4. Genetic birth defects: True Microcephaly

The forms with isolated microcephaly or True Microcephaly. Diagnosis of this condition is based on the absence of any other systemic anomalies; and a history of microcephaly in the mother's and father's sides of the family. Characteristic facial features are: receding front hairline, corners of the eyelids (palpebral) turned upward, and relatively large, protruding ears. The MR shows a small, well formed brain.

Hereditary recessive autosomal forms (in this particular form it is necessary for the baby to inherit the two defective genes from the father and the mother) are usually associated with neurological signs and the studies of cerebral imaging are variable (Infogen, 2013).

Box 5. Performed psychopedagogic tests and diagnosis.

Final report of Early Care (chronological age 3 years and 0 months) from the "Regional Office for Family and Equal Opportunities"; the reason she finished the programme is she turned three years old and she was schooled under the Direct Care System: Stimulation measures, signed by the Team from the Centro Base de Atención a Personas con Discapacidad (Care Centre for Disabled People), dated the 28th of August 2008:

Initial situation: Girl assigned to our centre with 11 months of age because she was diagnosed with autosomal recessive congenital microcephaly. At that moment her developmental progress was within the parameters of normality.

Diagnosis: Psychomotor development within limits of normality. Slight delay in the development of oral language skills. Orientations: Normal schooling without special support for ACNES -Students with special educational needs (according to the Psychopedagogic Ruling of Education).

However, it would be advisable to monitor the development of her Oral Language skills throughout the next school year; the purpose of this would be to observe her hypothetical improvements from the perspective of phonetics, morpho-syntactic and practical.

Psychopedagogic reports of the Autonomous Region (chronological age 5 years and 6 months)

Diagnostic Conclusion, dated on the 14th of March 2011

Medical report: --/--/2005 DIAGNOSIS MICROCEPHALY

Main group: Students with special educational needs.

Typology: Physical disability; motor and nonmotor.

Category: Nonmotor physical disability.

From a medical perspective we observe microcephaly. During the first cycle of pre-school she seems to be within the normal parameters of development. We have observed a slight delay in the development of expressive language.

We observe some deficit in most skills. She is weaker in areas related to cognitive and linguistic levels, and fine motor skills. Even though it is an area which is advisable to re-evaluate when the child is 6 or 7 years old, the cognitive assessment (IQ) showed some maturative delay of approximately a year; this means she is within the medium-lower band. During the tests we have observed a low comprehension level (which could be connected with her difficulty understanding basic concepts).

Psychopedagogic report of the Autonomous Region (Chronological age of 6 years and 9 months)

Diagnostic conclusion, dated on the 30th of May 2012

Medical report: --/--/2005: DIAGNOSIS MICROCEPHALY

Main group: Students with special educational needs.

Typology: Physical disability; motor and nonmotor.

Category: Nonmotor physical disability.

Secondary group: Communication and language alterations.

Typology: Communication and language disorder.

Category: Dysphasia (mixed)

From a medical perspective we observe microcephaly. During the first cycle of pre-school she seems to be within the normal parameters of development. We have observed a slight delay in the development of expressive language. At the present moment, we have observed a significant deficit in several areas.

There is a deficit in most skills, however, we have seen an improvement since her autonomous stage began. Her weak areas appear at a linguistic level; scarce or nonexistent syntactic constructions and some substitutions. As we reviewed her cognitive assessment (IQ), we observed certain deficit, although it seems to be within the norm (VIQ = 97 PIQ = 90). The subtests have revealed a low level of comprehension in spoken instructions, which could be connected to her difficulty understanding basic concepts.

Box 6. Early care.

Early care is defined as a set of interventions, aimed at a young population, between 0 and 6 years old, as well as their family and environment. The purpose of it is to address as soon as possible the transient or permanent needs that might arise with children who have development disorders or are at risk of developing them. These interventions, which should take into consideration the entirety of the child's situation, should be planned by a team of professionals specialised in interdisciplinary or transdisciplinary guidance.

Early care can be classified as pre-emptive at three levels: a) primary, before the disorder or disease appears, with a universal nature; b) secondary, early detection of the disorder or of risk situations. and c) tertiary, actions directed to remedy or alleviate the consequences of an established disorder or disability (Martín, Pons y Pontes, 2015, p. 50).

Box 7. Developmental dysphasia, a specific dysfunction of congenital language development.

Expressive: expressive language disorder.

Mixed: comprehension and expression disorder (Narbona y Chevrie-Muller, 1997, p.187).

Concept: Several papers have attempted to narrow the clinical features that would be the same as in the TELD, and which could be classed as dysphasia. Aforementioned features are: the severity of the symptoms; their persistence throughout the entire lifetime, even; the unusual (not simply the poorness) quality of linguistic utterances (Narbona y Chevrie-Muller, 1997, p.252).

Aphasia is defined as language deterioration consequence of a acquired brain injury. Even though there have been descriptions of delays in the language development sequence of lactating and very young children after a brain injury; generally we don't use the term aphasia unless the injury has occurred after the acquisition of language, that is, after two years of age (Narbona y Chevrie-Muller, 1997, p. 278).

Grounds for Assessment

Among the reasons why the Neurology Services transfer children to us in Neuropsychological Assessment, the most frequent one is diagnosis. We deal with children with known brain injuries or neurological dysfunctions for which they are attempting to confirm a diagnosis. In order to do this, through referral they ask for a neuropsychological report in addition to the neurological exam.

Assuming that the whole neuropsychological assessment expects to obtain an abilities profile, in said profile weak and strong areas would be described according to the deteriorated abilities (in certain extent) and those which are intact. A given profile, in which certain neuropsychological abilities (behavioural and cognitive) are selectively deteriorated, can turn out to be compatible with the detected neurological alteration. If it were so, the diagnostic purpose would be able to confirm at a behavioural and/or cognitive level the deterioration that follows already detected alterations in the nervous system through neurological exploration and the application of electro-physiologic techniques (e.g., the EEG) or neuroimaging techniques (e.g., MRI). In this sense neuropsychological assessment is an additional contribution that the paediatric neurology specialist can take from the specialist in clinical child neuropsychology (Manga y Fournier, 1997, p.23).

The parents came to our practice with the purpose of carrying out the neuropsychological assessment requested by the Child and Adolescence Neurologist, Dr. Daniel Martín Fernández-Mayoralas from the QUIRON Hospital Group in Madrid (Spain). Through referral we request a neuropsychological report in addition to the neurological exam. Request made by Dr. Child and Adolescence Neurologist in March 2014:

PLAN. NEUROPSYCHOLOGICAL TESTS:

WISC-IV.

ATTENTION TEST CPT2 or AULA, CSAT, ENFEN.

READING or language tests according to IQ and psychologist assessment.

WHATEVER THE PSYCHOLOGIST CONSIDERS APPROPRIATE, AS WELL.

Assessment Procedure:

Initial interview and testing throughout six sessions. The parents completed questionnaires and so did the teacher.

General Description of the Case

Developmental progress, initial learning and family level.

Mother diagnosed with hyperprolactinemia, which was treated for a month; she was diagnosed with pregnancy after a month interval of the last dose. Pregnancy with hyperemesis gravidarum, treated during the first trimester (Rexert, Idalprem, Orfidal) The only month when the mother did not suffer from vomiting was the fourth one. Amniocentesis was normal. Induced labour after 37 weeks of pregnancy because ultrasound showed intrauterine IUGR in the third trimester. The Apgar score at one minute was of 9 and of 10 at ten minutes. Weight at the time of birth was 2.197 kilograms. She was admitted into Neonatology, she had moderate microcephaly. She was in the incubator for 8 days. Natural breastfeeding during approximately two months, she could latch on well onto the breast but she suckled small amounts. She vomited frequently. She slept very well and plenty but she had difficulties feeding. After the first year she started eating better with purées, although she has needed dietary supplements since her birth until the endocrinologist discharged her on September last year (chronological age 7 years) because her percentile was within normality. She presently eats all kinds of food and in normal quantities. She eats and sleeps well. As to disorders and diseases, only highlight what has been said earlier: growth delay; both in weight and stature, with size recovery; microcephaly; urine infection at six months of age; vision problems and bone development delay.

Motor development within normality, she could walk without support at fifteen months. Language development within normality, at fifteen months she built simple sentences and understood commands. Aged 4 and one month she presented a slight psychomotor language delay and she had difficulties concentrating. Primary sporadic nocturnal enuresis. She has had secondary diurnal enuresis until the present time; there are periods when it appears more frequently and periods when it is less frequent. The girl's reactions to noise and pain are normal.

Ana is considered a lively and restless; she is curious about everything, and she learns by observing and mimicking. It used to be hard for her, and still is, to remember past events, to learn songs and anything that requires her to retain or memorise. It is difficult for her to maintain her attention and it becomes necessary to change activities constantly; otherwise she would get easily distracted, and she still does. She finds it difficult to focus. Since she was 4 years old approximately, she feels curious about her surroundings and asks questions: "What is that?", "what does that mean?", "what does it say here?", "what are you doing?"; she is also interested in events: "What has happened?", "why?".

She attended early childhood intervention and always had an appropriate vocabulary for her age, and it increased normally throughout time. She started reading when she was 3 years old, however, she could not keep up with the other children her age, although she does have an interest in reading. She reads with difficulties, but she voluntarily makes a great effort to improve. She has not shown special interest in time; she is currently learning how to use the clock and dates. It is hard for her to understand irony and jokes need to be explained to her, otherwise she feels insulted and offended. She is still in the process of learning; she does not understand jokes or pranks. She has no tolerance for frustration, any setback provokes very intense reactions and she acts impulsively. She has no tolerance for criticism either; in family environment her reactions are of denial and refusal. Outside of the family environment, she reacts with withdrawal and inactivity. She is of a distracted nature; she finds it hard to finish tasks, even more so if she thinks they are difficult. Her utterances show immaturity, her thoughts are childish; the parents understand they are consistent with her cognitive delay.

The parents consider that their daughter's talents reside in the curiosity she has regarding her surroundings and the sensitivity in her feelings towards others. Her behaviour toward family has been described by the

parents as adaptive and her autonomy is normal. However, even though she knows how to do things, someone has to be nagging her to do them. When she is with other people, she is very polite and completes tasks autonomously. She is rather protected at home and it is difficult to increase her independence. She is sometimes impulsive when she is at home; she does not accept frustration and she will throw tantrums which they consider excessive and disproportionate. She is untidy, occasionally she finds it hard to obey and she loses her temper easily. Ana will ask for help with tasks she can complete on her own; sometimes she lies, cries easily, she is excitable and impulsive; and, occasionally she will constantly change activities. The **parents have noticed** the child is irritable and lack of attention.

School environment:

She attended Early Care since she was eleven months old until she started the first year of nursery school. Her progress was very positive during her attendance to Early Care; when she stopped, when she was 3 years and 0 months old, her psychomotor development was within normality and her language development had a slight delay. From ages 2 to 3 she went to pre-school, two hours per day. **Ana** really enjoyed being with other children. She interacted well. Her adjustment to school, where she started nursery school, was also normal. She had the same teacher during the three years of nursery school and, even though she received several therapies and psychopedagogic support throughout these years, her learning was not sufficient, which meant she had to repeat the third school year.

The girl's delay became evident in the second year of nursery school. Her teacher stressed her lack of attention; she required constant attention from the teacher to complete tasks and she needed an adult's approval. She repeated third year of nursery school with another teacher; that year her academic performance improved and she made a special friend.

She started the first year of primary school in her current school, and she adapted to it normally. She had a teacher in the first year of primary school and a different one on her second year of primary school. The school has 6 hours of educational support conducted by a Support Teacher and by a Language and Hearing Teacher. According to her teacher, she has excessive motor restlessness; she has difficulties with school learning, she is easily distracted, she pays little attention, she has her head in the clouds, she occasionally leaves tasks uncompleted, she is consistent, respectful and accepts the teacher's guidance. Generally, Ana expresses happiness regarding school. She is in the appropriate year and her attendance is regular.

Since she was 4 years old, she gets speech therapy, stimulation, extracurricular support and she psychopedagogic office. Once a week she goes to speech therapy and she also attends psychological therapy focused on fostering social abilities and stimulating cognitive functioning. Five days per week she receives support at home to help her with schoolwork. It is worth noting that there is communication and coordination among the different professionals who are treating the girl in school and extracurricular environments. The child's "working" day is very long and she has very little time to play.

Social environment:

Ana is sensitive, empathetic and affectionate. Sociable and open. She interacts very well with adults. At this time she tends to spend more time with other children her age, but on the whole, she used to go with smaller children because she had trouble understanding the language. They believe she is aware of her own language difficulties, which is why she prefers to spend time with younger children; she enjoys playing with her smaller cousins (5 years old).

According to her teacher, she does not bother other pupils in class, she struggles with cooperative

activities. She admits to her mistakes, she does not argue nor fight, she is accepted by the rest of the group, she understands the notion of “fair play” and she is on friendly terms with most of her classmates. According to her parents, she is generally shy in her interactions with others and she has some difficulties.

She lives with her parents in a city which has appropriate social and cultural resources, she can participate in various activities organised by the City Council, the Community, several clubs, associations, etc. She participates in sports as an **extracurricular activity**: Karate, tennis and swimming in the summer.

Conduct Observation During the Assessment:

Ana adapts to the assessment situation, she cooperates in what she is asked. Her appearance is clean and neat. Sociable, restless, communicative and affectionate. She maintains appropriate eye contact and it is easy to establish a positive relationship with the girl.

She enjoys working but she tires easily and it is necessary to switch activities frequently in order to maintain her attention and motivation in the tasks. She endures frustration and she adjusts to the rules. The girl is aware that there are some things she can't do: “*I don't know how to do that*”.

We have observed difficulties in expressive-comprehension language; she tries to explain using gestures, occasionally it is difficult to understand her if we do not know the context of what she is talking about.

The Basic Behavioural Repertoire for learning is developed. During Assessment, her attention span and power of concentration depend on the task at hand. She requires adult supervision to complete tasks, she likes people to pay close attention while she carries them out and to receive the adult's approval.

Summary and Findings: Test Applied to the Neuropsychological Assessment.

During the Assessment we must bear in mind the Mental Age, since, according to the DSM-IV-TR and DSM-5, the Attention deficit disorder with hyperactivity diagnosis, and the Learning and language disorders diagnoses require that the attention difficulties and/or development of instrumental learning be below expected according their intellectual capacity.

a) Intelligence assessment

Ana is a girl with “Far below average” intelligence, WISC-IV, Total IQ = 58; GAI = 67 Stanford-Binet (Form L-M), Total IQ = 70. Her Mental Age is of 6 years and two months.

Her Abstract Reasoning Ability is Very Low, she appears to have mild learning difficulties. Raven's Test, Colour Progressive Matrices, percentile 60 (scale for 6-year-old children).

She took the K-BIT (Kaufman Brief Intelligence Test), and she obtained in crystallised intelligence an IQ = 87, and in fluid intelligence an IQ = 76; Composite IQ = 76.

WISC-IV: Basic tests

Cubes	Pt = 5	Equivalent age: <6 years and two months
Similarities	Pt = 5	Equivalent age: <6 years and two months
Digits	Pt = 3	Equivalent age: <6 years and two months
Concepts	Pt = 6	Equivalent age: <6 years and two months
Keys (B)	Pt = 6	Equivalent age: <7 years and ten months
Vocabulary	Pt = 5	Equivalent age: <6 years and two months
Numbers and letters	Pt = 5	Equivalent age: <6 years and two months
Matrices	Pt = 4	Equivalent age: <6 years and two months

Medium Low 4	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Medium Low 4
Low 3	X	X	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Low 3
Very Low 2 1	<input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>	Very Low 2 1

Conclusion: the girl is unable to complete the 'grey pathway' test (non assessable), the 'colour pathway' (non assessable) nor the "Rings" test (non assessable); this indicates dysfunction in prefrontal areas. Ana has problems with behavioural sequences and difficulty to organise her short term behaviour **below her mental age**. Low scores in "phonological fluency" and in "semantics fluency" (scales 1 or 2) almost always correspond to children with child dysphasia. Scores below the average, as she has obtained (scales 3 or 4), taking into consideration her mental age, denote a mild language deficit and they are associated with children with learning difficulties, specific language disorders or mild attention problems. She obtained normal scores in "interference", considering her mental age, she does not appear to have a deficit in impulse control and she has normal mental flexibility.

c) Attention assessment

In the Conners' Kiddie Continuous Performance Test (K-CPT V.5), she obtained the following results (scale for 4 and 5 year-old):

The discriminating function of the CPT indicates that the results are consistent with a clinical profile of ADHD. The calculated confidence index could be described as follows: there is a 58.30% chance that there is a significant attention problem. Ana showed difficulties with attention self-control. The test did not reveal any impulsivity. We did not observe a low alertness level.

She obtained the following results in the Children Sustained Attention Test, CSAT (scale for 6-year-old females): Attention capacity or sensitivity index (d'): Score T = 4 (0-8), which indicates a very low attention capacity (normal scores are around 50; meaning the ratio of right and wrong answers are similar to those of the reference group).

The assessment of Visual Perceptual Attention Abilities is conducted with the EMAV-1, which evaluates attention-related abilities or skills (scale for 5 and 6 year-olds).

Aim: To assess attention-related abilities or skills.

Quality of Visual Perceptual Attention (efficiency in focusing and coding visual stimuli) is very low (percentile = 5).

Sustained Visual Perceptual Attention (ability to focus and code visual stimuli during a particular period of time), is very low (percentile = 5).

Conclusion: in the neuropsychological tests regarding attention control, we have observed results significantly below her Mental Age in attention self-control, sustained attention, visual perceptual attention and a low level of alertness.

d) Information processing assessment

Her Perceptual Development is low, it matches an approximate age of 5 years (Reversal Test, number of

errors, 18; errors expected at her age, 3; percentile = 33).

Her Visual Motor Skills are low (Bender Test, number of errors, 10; number of errors expected at her age, 2.4; equivalent age, approximately 5 years and six months old). We have observed markers that indicate a dysfunction in visual motor perception, omission of angles in figures 7 and 8; and lines instead of dots in figure 5.

Her Associative Speed is low [WISC-IV Key (Key A), equivalent age of 6 years and six months].

Conclusion: She displays signs of a dysfunction in her visual motor perception and she has low perceptual development. Her associative speed is within the expected parameters for her Mental Age.

e) Academic competence

Ana is currently in the second year of Primary Education (pupils 7 and 8 years old); she is not achieving the goals and acquiring the content taught in school in a satisfactory way.

Her academic abilities in developing and achieving goals and content from the second school year of Primary Education are not appropriate:

Her comprehensive Vocabulary Development reaches an approximate age of 6 years (PPVT-III Peabody, equivalent age of 6 years and eight months, Percentile = 9, IQ 80; WISC-IV, expressive Vocabulary Pt = 5, equivalent age of <6 years and two months), she displays a greater ability in comprehensive Vocabulary (Peabody) than in expressive Vocabulary (WISC-IV, Vocabulary).

Her Numerical Reasoning skills and Automatic Symbol Management is very low (Arithmetic in WISC-IV, Pt = 3, equivalent age <6 years and two months).

Learning of Basic Concepts in Spanish is instrumental in order to learn and perform at school. In the Test of Basic Concepts (Boehm Test), the level of knowledge is low. The girl achieved a 76% of correct answers, she still needs to learn twelve of the 50 concepts covered in the test: “right”, “before”, “farther”, “part”, “each”, “less”, “group”, “third”, “pair”, “jump”, “left” and “same”.

Psychomotor Development; she took the McCarthy Scales (MSCA) and in “Leg coordination” and in “Arm coordination” she had a development level of 6 year and a half. When it comes to Laterality, she uses her right hand to write and draw. She uses her right hand to throw and catch objects. We observe non defined eye laterality.

Academic abilities; the Cognitive aptitude tests are a series of integrated tests which attempt to assess the factors that most influence academic learning from pre-school until the beginning of university age. The score obtained by the pupil was low in the Primary-R I test, scale for pupils coursing first year of primary school, aged 6 and 7; percentile score = 20.

In the Psychopedagogical Tests of Instrumental Learning, she scored the following (scale for pupils in the first year of Primary Education, aged 6 and 7, scores from 1 to 10):

- a) Reading
 - a.1.) Reading speed, Pt = 2 (well read words per minute: 17)
 - a.2.) Reading comprehension Pt = 8
- b) Writing (Dictation):
 - b.1.) Spelling, Pt = 3.5
- c) Calculus
 - c.1.) Calculation speed, additions, Pt = 3
 - c.2.) Calculation speed, subtractions, Pt = 3

Conclusion: The pupil has a academic and instrumental learning development aptitude level (reading,

writing and calculus) below her Mental Age, which is in accordance to her academic abilities, approximately at the beginning of the first year of primary school (pupils are 5 or 6 years old).

f) Behavioural assessment

In Connor's Behaviour Rating Scale for teachers, her teacher observes her excessive motor restlessness, academic learning difficulties, scarce attention, and she occasionally leaves tasks uncompleted. She is constant, respectful and she accepts well her teacher's instructions. From a social perspective, according to her teacher, she does not bother other pupils in class, she struggles with cooperative activities. She admits to her mistakes, she does not argue nor fight, she is accepted by the rest of the group, she understands the notion of "fair play" and she is on friendly terms with most of her classmates.

In the Conner's Behaviour Rating Scale for teachers, the pupil does not score above the cut-off point from which the factor is considered pathological, not in Attention Deficit, not in Hyperactivity, not in Behaviour Disorder; albeit the girl's score, according to observation, are close to the cut-off point in Attention Deficit: Cut-off point = 10, pupil's score = 9.

The Behaviour Assessment System for Children (BASC), assesses a wide range of pathological dimensions (behavioural problems, emotional disorders, personality disorders...) and adaptive dimensions (social skills, leadership...) which are quite useful in order to get to know the children and teenagers.

Her parents, in the scales of observation for behavioural problems, perceived hyperactivity in her. The Hyperactivity scale measures two of the three symptoms of ADHD: hyperactivity and impulsivity.

Within Overall Dimensions, which are useful in obtaining overall conclusions in accordance to different types of behaviour. The parents highlight low scores in adaptive abilities; which refers to the ability to adapt to changes in routine and to new teachers, to change from one activity to another and to share toys or other belongings with other children, as well as social skills.

Summary and Clinical Judgement

Summary

Ana is a girl aged 8 years and 6 months with "Below average" intelligence. Her mental age is of 6 years and two months according to the Stanford-Binet (Form L-M) Total IQ = 70, recommended test at an international level in order to measure intelligence, WISC-IV Total IQ = 58, GAI = 67.

With the girl's Neuropsychological Tests we have observed problems with behavioural sequence and difficulties organising short term behaviour; which suggest a dysfunction in the prefrontal areas, as seen in the ENFEN test. In neuropsychological tests about attention control, results are evidently low for attention control, sustained attention, visual perceptual attention and low alertness; this suggests a dysfunction in the frontal dorsolateral as seen in the EMAV and CPT2. Ana displays a visual motor perceptual dysfunction as seen with the Bender test; low perceptual development as observed with the Reversal Test; and low phonological fluency and semantic fluency which all suggest a dysfunction in the motor cortex (Peabody assessment, Basic Concepts, Academic Ability tests and Instrumental Learning).

When the brain injury occurs during neurogenesis (until the 5th month of pregnancy), certain subsequent recovery has been observed in the affected area, although at the expense of worse general performance. That is to say, an injury in this stage, as seems to be the case with this girl, will never result in a focal dysfunction. Therefore, the injury occurred during neurogenesis seems to stimulate an overproduction of new neurons, even though total volume is less and the reorganisation of all the functions with a fewer number of neurons (obtain

more with less) lead to a decrease in intellectual quotient. The earlier and wider the injury is in this phase, greater will the intellectual disability be (Arnedo, Bembibre, Montes y Triviño, 2015, p.20). In Ana's case it is possible that the injury is small and/or that it happened at a later period. It is also possible that this fact conditioned her deficit not being observed significantly until she was 4 and 5 years old.

Language difficulties have also been substantially more noticeable since she was four years old. It is interesting to consider that towards the sixth month of her life there was an increase in the dendritic arborization in the frontal left operculum connected to language motor processing, which surpasses that of the right hemisphere. From that moment onward and during her first five years, the anterior perisylvian regions developed unevenly in each hemisphere, being the dendritic system more complex in the left hemisphere. In fact, when she was around six years old, the left Broca area reached the developmental stage of an adult. As the linguistic circuits of the left hemisphere grow and improve, children's abilities to understand and use more complex syntactical structures do so as well.

We believe the girl's language-related limitations are mostly located in short term phonological storage or in auditory working memory. Phonological representations decay quickly, so Ana is unable to order the elements and structure the word. This interferes with expressive and comprehensive language, as well as reading, writing and arithmetic. Expressive language tasks which are more complex (word association or category formation) don't only depend on Broca areas but also they activate the cingulate cortex (motivation processes, beginning of activities and sustained attention control) in both frontal lobes.

From an emotional perspective she displays anxiety. Lying, enuresis and fears are symptomatic of anxiety in children. We believe the anxiety is caused by stress at school; which would be connected to her difficulties keeping up with the rhythm and/or lessons; and in understanding and/or adapting to the games and interests of her classmates. It is noteworthy her behaviour of self-control in the school environment, where, according to her teacher, she does not show maladapted behaviours.

Within family environment she has been noted to have feelings of inadequacy. On the topic of Behaviour, the parents have determined behaviours connected to hyperactivity and with low Adaptive Skills (BASC scale).

Clinical Judgement

To our clinical judgement and according to the DSM-5, she has Mild Intellectual Disability (intellectual developmental disorder), in comorbidity with Attention Deficit Hyperactivity Disorder (combined presentation). In the neuropsychological tests, the girl's scores in attention self control are significantly below her Mental Age.

Ana has learning difficulties (reading, writing and calculus are below expected according to her Mental Age) and language difficulties (dysphasia) both expressive and in comprehension. (Language comprehension development is below her Mental Age, expressive language development is more affected).

Attention difficulties (ADHD) mildly affect intelligence (from a psychometric perspective 3.41 points in the TIQ of the WISC-IV); however it greatly impacts performance and the way in which they approach, plan and complete tasks. Voluntary attention control is the way into executive functions, and these, in turn, the centre for intelligence display (Goicoechea, 2015, p.199)

Anomalies have been detected in the white matter of people affected by attention deficit disorder and hyperactivity, bipolar disorder, language disorders associated to age, Alzheimer's disease and mythomania (Douglas, 2008, p.60).

Within neurobiological factors, neuroimaging techniques have shown that in ADHD, cerebral regions connected to executive functions, emotions, coordination and motor behaviour control are affected: the prefrontal and parietal cortices, the cerebellum, basal ganglia (caudate nucleus and putamen), limbic structures and the anterior cingulate; because of their reduced size and decreased or anomalous activity pattern of dopamine or noradrenaline neurotransmitters (Miranda, Colomer y Roselló, 2015, p.315).

The Magnetic Resonance Ana was given when she was 7 years old indicated that she had a normal myelination pattern. We did not observe any morphological anomalies in the corpus callosum, basal ganglia nor the brainstem. There were abnormalities in the parietal and prefrontal cortex, and in the cortical limbic structures.

One of the most noteworthy findings was the disproportionately augmented size of the cerebellum in comparison to the other cerebral hemispheres. It is also important to mention that Ana's neurological exam supports the thesis about language in children with Williams Syndrome. In the Williams syndrome, deletion seems to make anatomical changes (abnormal accumulation of neurons in visual areas) that alter spatial perception. However, the chromosomal defect doesn't seem to affect the network that covers the frontal and temporal lobes and the cerebellum. This preserved network could serve as a neuroanatomical scaffolding of sorts for the excellent and unexpected language abilities displayed by patients suffering from Williams Syndrome.

Other research, for example, have indicated that short term memory for spoken language sounds, or phonological memory, which is apparently involved in language learning and comprehension; is preserved rather well in patients with Williams Syndrome.

The discovery that the neocerebellum is preserved in patients suffering from Williams Syndrome is even more curious when contemplated within the context of other research. Until recently it was accepted that the cerebellum was mainly associated with movement. The team is led by Steven E. Petersen, from Washington University, proved that the neocerebellum is activated when someone tries to make a word association between a verb and a particular noun (as in "sitting" and "chair"); not only this, but also when patients are tested for cerebellar injuries alterations in cognitive functions emerge, as well as motor alterations.

The average cortical volume in individuals affected by Williams Syndrome (they have a richer and more extensive vocabulary than would be expected with their mental age) or Down (evident alteration in language acquisition and language development) is less than in normal individuals of the same age, however, the volumes of different regions differ. While the volume of the cerebellum is smaller in patients with Down Syndrome, in those with Williams it is normal (Lenhoff, Wang, Greenberg y Bellugi, 1998, p.23)

Average cortical volume in True Microcephaly is also less than in normal individuals of the same age. In this case of True Microcephaly, unlike children with Williams Syndrome and children with Down Syndrome, the size of the cerebellum is disproportionately augmented in relation to the cerebral hemispheres.

As well as in children with Down Syndrome, Ana displays evident abnormalities in language acquisition and development, but unlike children with Down Syndrome, whose communicative difficulties are noticeable during their pre-linguistic phase (first months of their lives), these alterations weren't noticed until the linguistic phase (from 2 years of age).

Child brain injuries have a non-specific nature, unlike adults; since children's brain dynamics themselves mean that the consequences of any cerebral damage will cause more diffuse cognitive disorders. Also, as was Ana's case, the deficit becomes more evident with the increase of school and social demands. Even though in

1949 Donald Hebb published a paper that revealed the severe long-term consequences suffered by children with early injuries in the frontal lobe, it wasn't until the decade of 1990 that the systematic view of "earlier is not always better, and sometimes, it is worse" began to be observed (Kolb y Whishaw, 2006, p. 20).

References

- Apgar Test. (2000). Manual Merck, Edición Centenario. Barcelona: Harcourt. Section, 19.
- Arnedo, M., Bembibre, J., Montes, A. y Triviño, M. (2015). Neuropsicología Infantil. A través de casos clínicos. Madrid: Editorial Médica Panamericana.
- Bender, L. (1938). Test Gestáltico Visomotor de Laureta Bender. Paidós Ibérica (1985).
- Benton, A. L. (1986). Visual Retention Test (TRVB). Madrid: TEA Ediciones.
- Boehm, A. E. (1986). Test Boehm de Conceptos Básicos – 3. Adaptación española de Pearson (2012).
- Canals, R. (1988). Pruebas Psicopedagógicas de Aprendizajes Instrumentales. Barcelona: Onda.
- Conners, C. K. (1969). A teacher rating scale for use in drug studies with children. *Am J Psychiatry*. Adaptada y validada por A. Farré y J. Narbona (1997, 2000).
- Conners, K., & MHS Staff: Conners' Kiddie Continuous Performance Test CPT (K-CPT V.5).
- Conners, K., & MHS Staff: Conners' Continuous Performance Test II (CPTII V.5).
- Corral y otros (2005): Adaptación española de TEA Ediciones, del WISC-IV, Wechsler Intelligence Scale for Children. Technical and Interpretative Manual (2003). Harcourt Assessment, San Antonio, Texas.
- Douglas, R. (2008). ¿Qué función cumple la sustancia blanca? Investigación y Ciencia. Mayo.
- DSM-IV-TR (Diagnostic and statistical Manual of Mental Disorders: DSM-IV-TR, 2000). Versión española de J.J. López-Ibor (2002). Manual diagnóstico y estadístico de los trastornos mentales. Barcelona: Masson, 56.
- Dunn, L. M. (1981). Peabody Picture Vocabulary Test (PPVT). Madrid: Mepsa Ediciones.
- Edfeldt, A. W. (1988). Reversal Test. Barcelona: Herder.
- García, E. M., & Magaz, A. (2000). EMAV-1 y 2 (Escala Magallanes de Atención Visual). Baracaldo: Grupo Albor-Cohs.
- Goicoechea, N. (2015). Diagnóstico del TDAH en niños con superdotación intelectual. Tesis Doctoral 2014, Universidad de Burgos. Ideacción 35, Valladolid.
- Infogen (2013). Defectos del nacimiento. Microcefalia. Recovered on 22/06/2016: <http://infogen.org.mx/microcefalia>
- Kaufman, A. S., & Kaufman, N. L. (1990). Kaufman Brief Intelligence Test, K-BIT, Minnesota: American Guidance Service: Circle Pines. Traducido "Test Breve de Inteligencia de Kaufman" por TEA Ediciones.
- Kolb, B., & Whishaw, I. Q. (2006). Neuropsicología Humana. Madrid: Editorial Médica Panamericana.
- Lenhoff, H. M.; Wang, P. P.; Greenberg, F., & Bellugi, U. (1998). Síndrome de Williams. Investigación y Ciencia. Febrero.
- López-Ibor, J. J. (2002): DSM-IV-TR. Manual diagnóstico y estadístico de los trastornos mentales. Masson, Barcelona (Diagnostic and statistical Manual of Mental Disorders: DSM-IV-TR, 2000).
- McCarthy Test McCarthy Scales of Children's Abilities (1986). Madrid: TEA Ediciones.
- Manga, D., & Fournier, C. (1997). Neuropsicología clínica infantil. Madrid: Editorial Universitas.
- Martí, M., & Cabrera, J. C. (2008). Macro- y microcefalia. Trastornos del crecimiento craneal. Asociación Española de Pediatría, Protocolos actualizados año 2008.
- Martín, M., Pons, A., & Montes, A. (2015). Atención Temprana y otros dispositivos especializados en la infancia. En M. Arnedo, J. Bembibre, A. Montes, and M. Triviño, Neuropsicología Infantil. A través de casos clínicos. Madrid: Editorial Médica Panamericana.
- Miranda, A., Colomer, C., & Roselló, B. (2015). Neurobiología y neuropsicología del trastorno por déficit de atención con hiperactividad. En M. Arnedo, J. Bembibre, A. Montes, and M. Triviño, Neuropsicología Infantil. A través de casos clínicos. Madrid: Editorial Médica Panamericana.
- Mota, V., Valdivieso, O. F., Quiroz, L., & Criales, J. L. (2005). Lisencefalia. Recovered on 28/08/2016: http://www.scielo.org.mx/scielo.php?pid=S0016-38132005000500014&script=sci_arttext&tlng=pt
- Narbona, J., & Chevie-Muller, C. (1997). El lenguaje del niño. Barcelona: Masson.
- Portellano, J. A., Martínez, R., & Zumárraga, L. (2009). ENFEN. Evaluación Neuropsicológica de las Funciones Ejecutivas en niños. Madrid: TEA Ediciones, 23, 14-22.
- Raven, J. C., Court, J. H., & Raven, J. (2011). Raven Matrices Progresivas CPM – SPM – APM. Madrid: Pearson.

- Reynolds, C., & Kamphaus, R. W. (1992). Behavior assessment system for children, BASC. Minnesota: Circle Pines: American Guidance Service. Traducido "BASC (Sistema de Evaluación de la Conducta de niños/adolescentes)" por TEA Ediciones.
- Servera, M. y Llabrés, J. (2004). CSAT Tarea de Atención Sostenida en la Infancia. Madrid: TEA Ediciones.
- Terman, L. M., & Merrill, M. A. (1976). Stanford-Binet Intelligence Scale: Form L-M (SB: L-M). Madrid (1976) Espasa Calpe.
- Thorndike, R. C., Hagen, E., & Lorge, I. (1968). Cognitive Abilities Tests, Primary I and II, Form 1". Adaptación española "Test de Aptitudes Cognoscitivas, Primaria-R", Madrid: TEA Ediciones.
- Verloes, A. (2012). Microcefalia primaria autosómica recesiva. Recovered on 22/06/2016: http://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=ES&Expert=2512
- Wechsler, D. (2003). Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV). San Antonio, Texas: The Psychological Corporation. (Corral et al., 2005). Manual Técnico español. Madrid: TEA Ediciones, 25 y 26.