COGNITIVE EVALUATION IN SILVER RUSSELL CHILDREN

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BACKGROUND and AIMS

▪Silver-Russell Syndrome (SRS) is a heterogeneous syndrome characterized by severe intrauterine and postnatal growth retardation, typical dysmorphic features *(E Wakeling et al, Diagnosis and management of Silver–Russell syndrome: first international consensus statement, Nature Reviews Endocrinology 2016).*

▪ Hypomethylation of paternal allele of 11p15 imprinting center region 1 is present in 50-60% of cases, and maternal uniparental disomy of chromosome 7 (mUPD7) in a minority of cases. Clinical diagnosis is confirmed if patient presents at least 4 out of the 6 criteria (table3) (*Azzi S et al A prospective study validating a clinical scoring system and demostrating phenotypical-genotypical correlations in Silver Russell Syndrome. J Med Genet 2015*)

METHODS

Neuropsychological assessments, including evaluation of intellectual efficiency, cognitive functions, and learning abilities, were performed in 30 patients (17 males, 13 females), aged 6 to 11 years (mean age 7,5 years) followed at Trousseau Pediatric Hospital (France) from 2008 to 2016.

Table 1. Neonatal parameters in the two groups of SRS patients

MEAN SD	TOTAL	11p15	UDP7
Gestational Age (Weeks)	36,4	36,7	35,9
Birth Weight (SDS)	-2,5	-2,8	-1,8
Birth Head Circumference (SDS)	-0,01	-0,4	0,8
Birth Lenght (SDS)	-3,72	-4,1	-2,8

Table 2. Results of Neuropsychological Evaluation in the 2 groups of SRS patients

MEAN SD	TOTAL	11p15	UDP7
FSIQ	93,4	94,6	90,7
VCI	101,1	106,1	90,7
PRI	93,4	95,8	92,2
PSI	93,9	94,7	92,4
WMI	92,9	92,1	94,6
Copy of Figures	8	9,1	6,3

FSIQ=Full Scale IQ; VCI=Verbal Comprehension Index; PRI=Perceptive Reasoning Index; PSI=Processing Speed Index; WMI=Working Memory Index.

RESULTS

The population consisted of 17 males and 13 females (20 patients in 11p15 group and 10 patients in mUDP7 group).
The mean NH-CSS scoring was 5,94 in 11p15 group and 4,6 in mUDP7 group.
Growth hormone treatment (GH) was given in 86,6% of patients.
The mean age at the beginning of GH treatment was 3,3 years.
Eleven (42%) patients had episodes of hypoglycemia (glycemia <2,4 mmol/L). No child presented seizures hypoglycemia-related. 13 patients (43%) needed enteral nutrition (gastrostomy tube feeding and nasogastric tube) .
Mean overall IQ score in the total SRS sample was 93.36 with a range between 52 – 118. 57% of all children needed speech therapy especially in UDP7 group (90% of mUDP7 children).
A correlation between low birth weight and low IQ has been found
We have found a correlation between severe hypoglycemia and low Percentual Reasoning Index (PRI) and a correlation between enteral nutrition and IQ and lower PRI. Verbal comprehension Index (VCI) is lower in mUDP7 children than in 11p15. 2 children with mUDP7 had myoclonus.
The link between myoclonus and mUDP7 should be explained by the lack of epsilon-sarcoglycan gene (SGCE) paternal allele located at 7q21.3.

Table 2. Netchine Harbison clinical scoring system (NH-CSS, Azzi et al, J Med Genet. 2015 Jul;52(7):446-53.)

Clinical diagnosis confirmed if patient scores at least 4 out of 6 of the following criteria

Clinical criteria	Definition
SGA (birth weight and/or birth length)	≤ -2SDS for gestational age
Postnatal growth failure	Height at 24±1 months ≤ -2SDS or Height ≤ -2SDS from mid-parental target height
Relative macrocephaly at birth	Head circumference at birth ≥ 1.5 SDS above birth weight and/or length SDS
Protruding forehead	Forehead projecting beyond the facial plane on a side view as a toddler
Body asymmetry	Leg length discrepancy (LLD) of ≥ 0.5 cm or arm asymmetry or LLD < 0.5cm with at least two other asymmetrical body parts
Feeding difficulties and/or low BMI	MI ≤ -2SDS at 24 months or use of a feeding tube or cyproheptadine for appetite stimulation

CONCLUSIONS

➢Cognitive evaluation is recommended in SRS patients and mUPD7 children should be monitored for the development of movement disorders
➢The early start of occupational therapy, speech therapy and school aids can improve many of these children's quality of life
➢We underline the importance to educate parents to prevent hypoglycemia with complex carbohydrate modules and avoid fasting, and to recognize the early signs of hypoglycemia
➢Finally it is very important that parents treat the child according to age and not depending on size because the physical and social expectations that a child perceives from the world gives him the framework for setting expectations for himself.

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