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 (mUDP7) in a minority of cases. Clinical diagnosis is confirmed if patient presents at least 4 out of the 6 criteria (Azzi S et al A prospective study validating a clinical scoring system and demonstrating 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 Length (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            |

**RESULTS**

The population consisted of 17 males and 13 females (20 patients in 11p15 group and 10 patients in mUDP7 group).

- The mean NH-CSI 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.

**CONCLUSIONS**

- Cognitive evaluation is recommended in SRS patients and mUDP7 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.

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

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

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