

BACKGROUND and AIM

There is little information on cognitive function in Silver Russell Syndrome (SRS) and no neuroimaging studies are available so far [1-4].

Aims of the study are to assess cognitive function and brain volumes in a cohort of genetically confirmed SRS patients and to compare the findings with those of controls.

SUBJECTS and METHODS

Subjects:

The study group comprised 45 Caucasian subjects, 38 of whom received a molecular diagnosis of SRS (11p15LOM in 18 subjects, mUPD7 in 18 subjects; 11cr duplication in 2 cases). Thirty patients with a mean age of 12.6±10 years were enrolled for cognitive assessment; in 23 of them, neuroimaging sequences were analyzed.

Methods

Cognitive assessment was performed by Wechsler Intelligence Scale

Brain magnetic resonance imaging (MRI) was performed on a 3-Tesla scanner. 3D-T1 weighted sequence and Voxel-based morphometry analysis were performed.

RESULTS

Cognitive evaluation showed significantly higher cognitive profiles in 11p15LOM group than in UPD7 group at the age of 6-16 years (Table 1; Table 2)

Table 1. Cognitive assessment based on age at the time of examination, and molecular findings in 30 SRS patients

	11P15LOM			mUPD7		
	2-5	6-16	17-48	2-5	6-16	17-48
Age range (years)	2-5	6-16	17-48	2-5	6-16	17-48
Number of Patients	N=2	N=9	N=4	N=5	N=7	N=3
Age at evaluation	3.5±0.7	8.9±3.4	29.8±12.5	3.7±0.9	9.2±3.3	24.2±3.1
IQ	77±1.4	96.7±11.6*	92.2±27.8	84.4±15.8	75.8±12.2*	90±20
VCI	83.5±7.7	100.2±8.3*	94±13.8	87.8±21.9	81.1±14.4*	81.3±16.1
PRI	78.5±14.8	94.1±13.3*	93.7±32.5	84.8±6.1	74.4±12.7*	89±10.4
WMI	72.5±2.1	100±9.6*	96.5±25.5	97.2±15.8	80.8±14.2*	98.3±28.5
PSI	-	94.2±21.8	92.2±18.2	-	92.2±14.6	106.6±15

IQ (p=0.003), VCI (p=0.004), PRI (p=0.009), WMI (p=0.006) were significantly higher in 11p15LOM group than in mUPD7 group at the age of 6-16 years.

Abbreviations : IQ: Intelligence Quotient; VCI: Verbal Comprehension Index; PRI: Perceptual Reasoning Index ; WMI: Working Memory Index; PSI: Processing Speed Index

Unpaired T test analysis:

- No significant difference in cognitive scores between 11p15LOM school-aged patients and the control group.
- The mUPD7 school-aged patients displayed a significantly lower cognitive profile compared to controls (IQ, 75.8±12.2 vs. 100.8±9.6, p<0.0001; VCI, 81.1±14.4 vs. 97.3 ± 7.2, p<0.0001; PRI, 74.4±12.7 vs. 102.2±14, p<0.0001; WMI, 80.8±14.2 vs. 100.9±17, p=0.008; PSI, 92.2±14.6 vs. 102.9± 15, p=0.001)

Table 3. Cognitive assessment based on age at the time of examination, and molecular findings in 23 SRS patients who performed Brain-MRI study.

	11P15LOM			mUPD7		
	2-5	6-16	17-48	2-5	6-16	17-48
Age range (years)	2-5	6-16	17-48	2-5	6-16	17-48
Number of Patients	N=2	N=7	N=3	N=3	N=6	N=2
	range	mean±SD	range	range	mean±SD	range
IQ	76-78	98.8±12.1*	74-133	58-91	78.8±10.3*	92-109
VCI	78-89	101.1±8.3*	84-114	51-98	84±13.4*	73-100
PRI	68-89	95±15*	79-137	76-90	76.3±12.8*	94-96
WMI	71-74	103.4±5.8*	77-134	83-103	81.7±6.3*	109-120
PSI	-	95.6±24.9	78-119	-	95±14	106-122

IQ (p=0.008), VCI (p=0.01), PRI (p=0.03), WMI (p=0.005) were significantly higher in 11p15LOM group than in mUPD7 group at the age of 6-16 years.

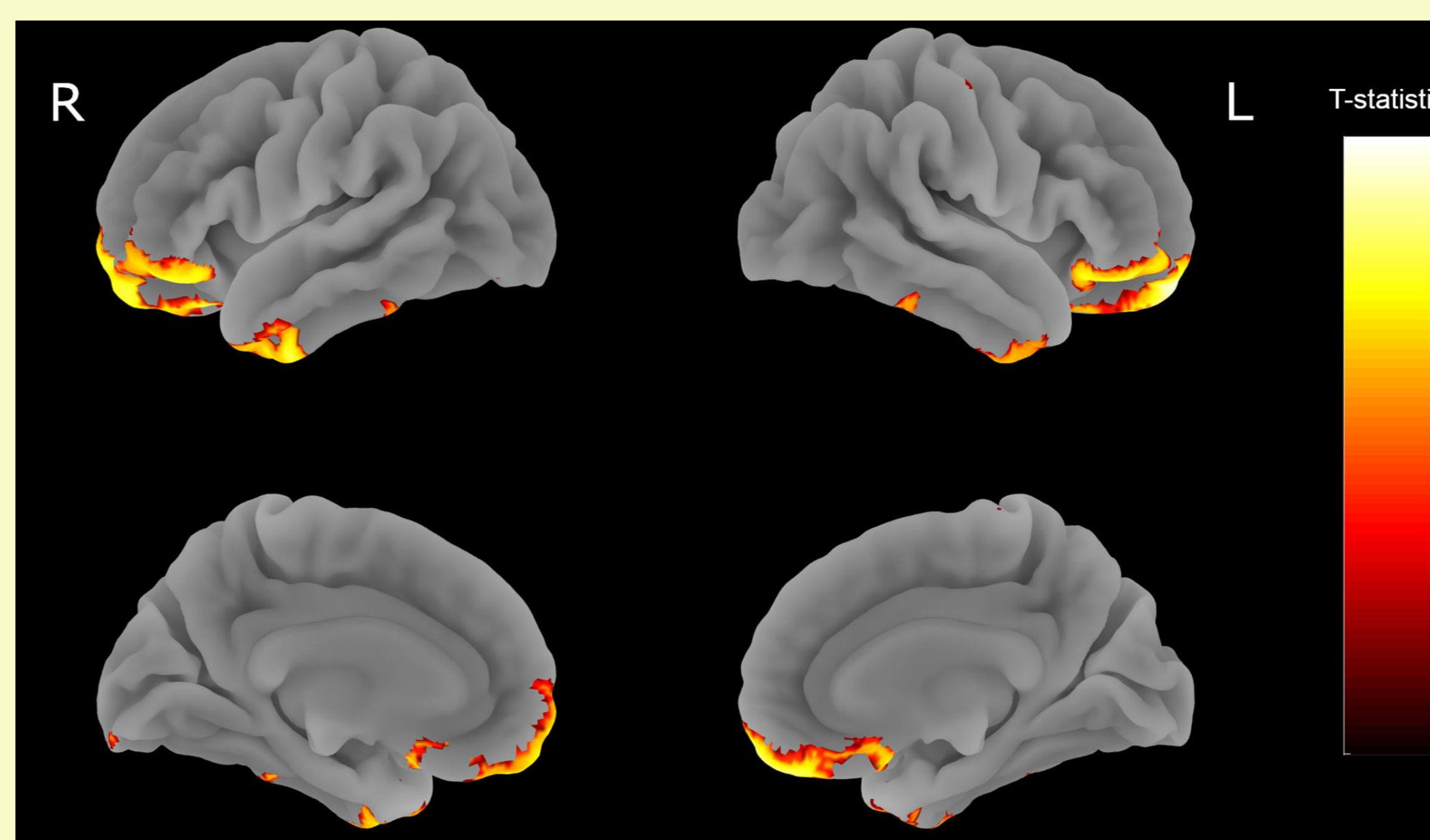
Abbreviations : IQ: Intelligence Quotient; VCI: Verbal Comprehension Index; PRI: Perceptual Reasoning Index ; WMI: Working Memory Index; PSI: Processing Speed Index

3 T- Brain MRI Findings

- No Neuroanatomical Anomalies
- No significant difference between SRS patients and controls in total brain volume, total gray matter volume and total white matter volume
- Grey Matter: Lower volume in the SRS group compared to controls at level of frontal (mean 2.556±0.401 cm³ VS 2.989±0.409 cm³, p<0.001) temporal (mean 7.434±1.354 cm³ VS 8.304±1.186 cm³, p<0.001) lobes and globi pallidi (Fig.1)
- Grey Matter volume: no significant regional differences between the 2 molecular groups
- White Matter volume: no significant regional differences between SRS and control groups

Figure 1. Differences of Gray Matter volume between SRS group and controls.

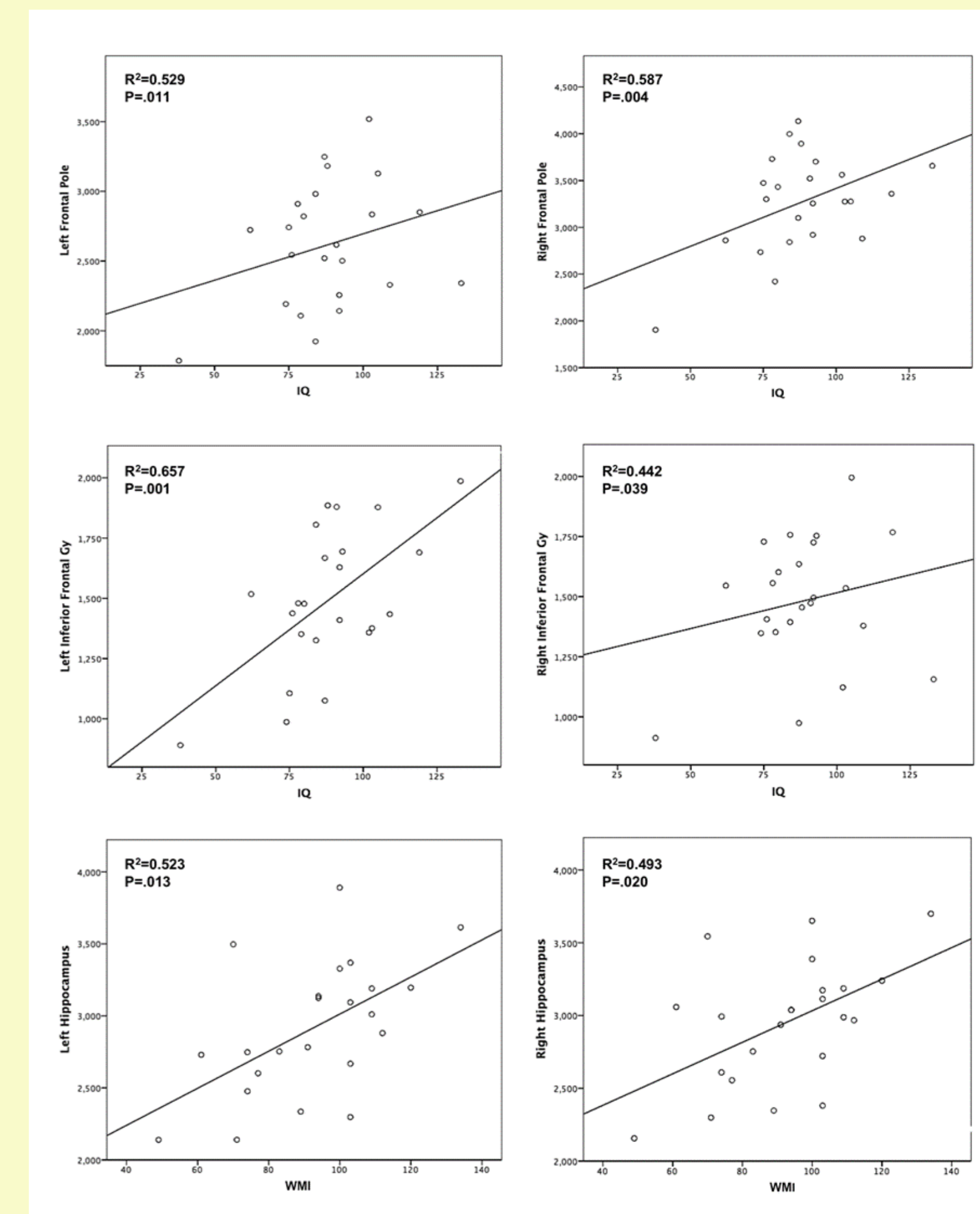
Color bar indicates T-statistic differences between groups (Controls>SRS patients). Six clusters were identified: in both frontal and temporal poles and at level of globi pallidi bilaterally



Significant correlation between

- IQ and gray matter volume in the frontal regions
- and between WMI and gray matter volume at hippocampi (Fig.2)

Figure 2. Relationship between the cognitive test scores and the regional brain volumes



CONCLUSIONS

- Our data showed that the cognitive profile of mUPD7 is impaired and that the brain volume of gray matter at the frontal and temporal lobes and globi pallidi is reduced in SRS patients.
- Cognitive evaluation is recommended in these patients, especially in mUPD7 group and early intervention is advisable to improve their quality of life
- No major neuroanatomical Anomalies were found
- No significant differences between SRS patients and controls in total brain volume (Brain Sparing?)
- More research is needed to unravel the pathophysiology of Lower gray matter volume in the SRS group at frontal/ temporal lobes and globi pallidi (Regional brain sparing over global?)

References

- [1] Wakeling EL et al, Nat Rev Endocrinol 2017
- [2] Lai KY et al, Arch Dis Child 1994
- [3] Noeker M et al, Dev Med Child Neurol 2004
- [4] Burgevin M et al, Appl Neuropsychol Adult 2019