Effects of pre- and postnatal glucocorticoid exposure on the cognitive function of children and adolescents with congenital adrenal hyperplasia

V Messina, L Karlsson, T Hirvikoski, A Nordenström and S Lajic

Karolinska Institutet/Karolinska University Hospital, Department of Women´s and Children´s health, Stockholm, Sweden

Conclusions

- This study indicates that children and adolescents with CAH, diagnosed via the neonatal screening program and treated with hydrocortisone, have normal psychometric intelligence and executive functions.
- Prenatal treatment with DEX may effect cognition in girls.
- These findings may thus question future DEX treatment of congenital adrenal hyperplasia.

Background

Patients with CAH are treated postnatally with life-long glucocorticoid (GC) replacement therapy. Existing evidence indicate that GC treatment may have negative effects on cognitive and affective functions.

Long-term cognitive effects were studied in adolescents and children with CAH and in a small cohort of patients with CAH and who were prenatally treated with dexamethasone (DEX).

Study population

Mean age: 11.8 years, range 7-17 y.

Patients with CAH n= 45

- Females n= 23
  - CAH n= 17
  - CAH-DEX n= 6
- Males n= 22
  - CAH n= 17
  - CAH-DEX n= 5
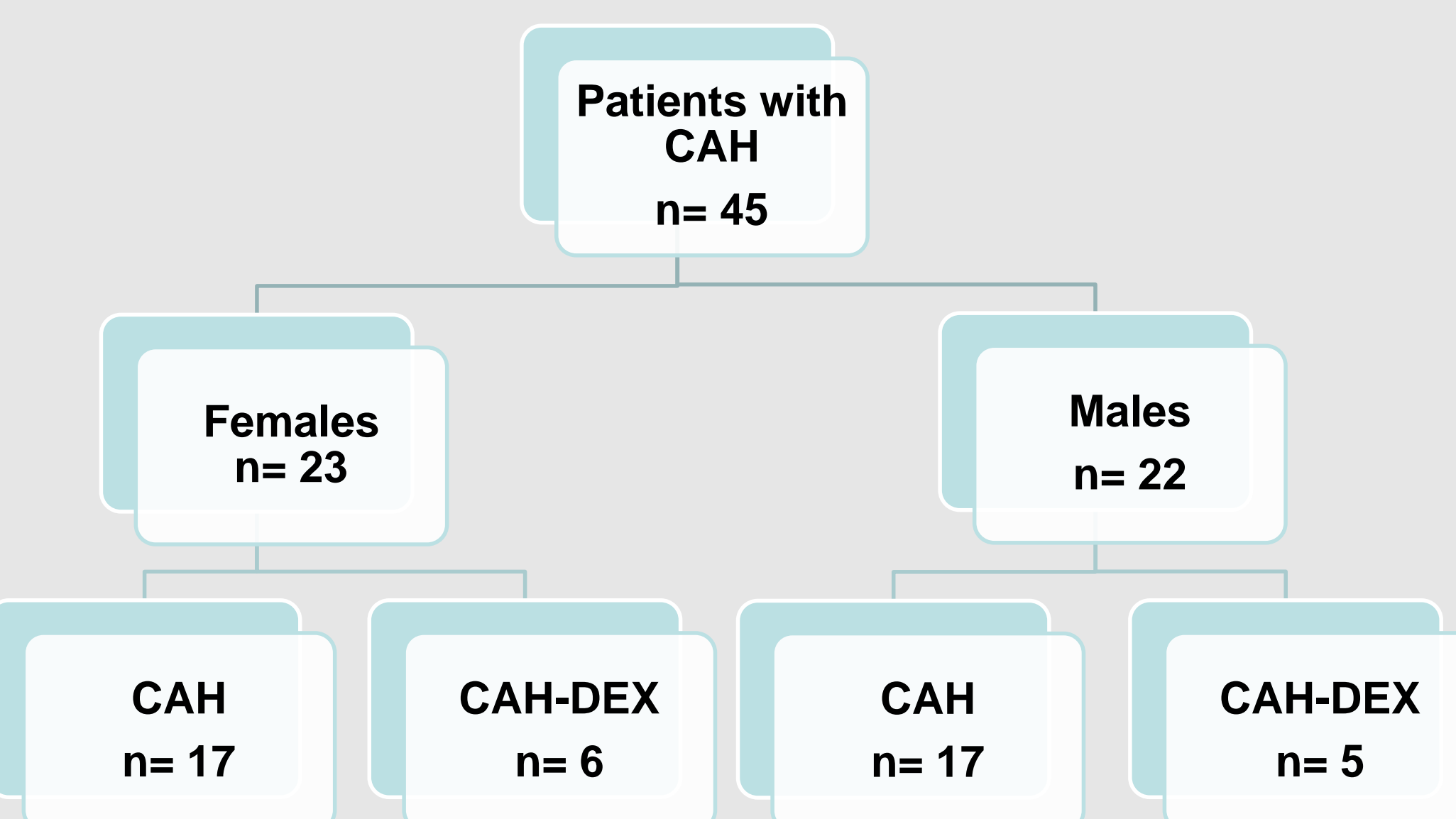
Phenotype: SW n=28; SV n=14
Genotype: non-null n=31; null n=11
Control group: n =66 (36 f, 30 m)

Methods

Standardized neuropsychological tests (WISC-III, Span board, Stroop and NEPSY) were administered to measure general intellectual ability, executive functions and learning and long term memory.

Table 1

	Females		Males		[CAH]			[CAH x Sex]	
	CAH (n=17) M (SD)	Control (n=36) M (SD)	CAH (n=17) M (SD)	Control (n=30) M (SD)	Effect size (Cohen's d)	F statistics	p	F statitics	p
General intellectual ability (estimated IQ)									
WISC-III Block Design (S)	10.8 (3.5)	11.7 (2.9)	11.4 (2.8)	11.1 (2.9)	-0.18	0.30	0.582	1.05	0.307
WISC-III Vocabulary (S)	11.3 (2.7)	10.7 (2.3)	11.8 (1.6)	10.6 (2.2)	0.57	3.63	0.060	0.34	0.560
Executive functions									
WISC-III Coding (S)	11.6 (2.8)	12.0 (3.1)	10.5 (2.0)	9.4 (2.4)	0.11	0.32	0.569	1.71	0.194
WISC-III Digit Span(S)	9.2 (2.7)	10.8 (2.9)	10.5 (3.1)	10.4 (3.1)	-0.36	1.32	0.252	2.10	0.151
Span Board Forward (T)	51.2 (10.5)	53.7 (8.9)	55.4 (9.8)	49.4 (10.3)	0.22	0.72	0.400	4.31	**0.041**
Span Board Backward (T)	56.1 (8.8)	56.0 (7.9)	58.7 (8.5)	54.6 (8.1)	0.34	1.51	0.222	1.35	0.248
Stroop interference (T)	54.8 (4.1)	52.7 (5.2)	51.4 (8.4)	51.4 (3.6)	0.22	0.74	0.390	0.76	0.385
Learning and long-term memory									
NEPSY List Learning (S)	12.4 (2.1)	11.4 (2.9)	11.8 (2.4)	10.5 (2.7)	0.62	4.07	**0.046**	0.14	0.705

Table 1: Neuropsychological test results for the CAH cohort.
S, scaled scores. T, T scores.

Table 2

	Females			Mann Whitney U test		Males			Mann Whitney U test	
	CAH-DEX (n=6)	CAH (n=17)	Effect size (Cohen's d)	U	p	CAH-DEX (n=5)	CAH (n=17)	Effect size (Cohen's d)	U	p
General intellectual ability (estimated IQ)										
WISC-III Block Design (S)	9.2 (3.2)	10.7 (3.5)	-0.68	37.00	0.354	11.0 (3.4)	11.4 (2.8)	-0.19	35.50	0.719
WISC-III Vocabulary (S)	8.0 (2.7)	11.4 (2.7)	-1.73	20.00	**0.030**	11.0 (1.6)	11.82 (1.5)	-0.73	29.00	0.319
Executive functions										
WISC-III Coding (S)	10.0 (2.9)	11.6 (2.8)	-0.80	31.00	0.231	11.6 (2.1)	10.5 (2.1)	0.75	28.50	0.354
WISC-III Digit Span (S)	9.3 (1.8)	9.2 (2.8)	0.06	47.50	0.812	8.6 (3.6)	10.6 (3.1)	-0.82	32.50	0.446
Span Board Forward (T)	47.8 (7.5)	51.2 (10.5)	-0.52	44.50	0.658	49.7 (17.4)	55.4 (9.8)	-0.57	30.50	0.763
Span Board Backward (T)	52.8 (3.4)	56.1 (8.7)	-0.70	33.00	0.227	49.5 (7.7)	58.8 (8.5)	-1.61	14.50	0.081
Stroop interference(T)	56.0 (6.4)	54.8 (4.1)	0.31	37.50	0.842	54.6 (3.3)	51.5 (8.5)	0.687	24.50	0.208
Learning and long-term memory										
NEPSY list learning (S)	10.7 (3.6)	12.4 (2.1)	-0.84	37.50	0.842	12.0 (2.0)	11.9 (2.4)	0.08	40.00	1.000

Table 2: Neuropsychological test results for the CAH-DEX cohort.

Results

There were no differences in general intellectual ability and executive functions between patients with CAH and controls. A significant CAH by SEX interaction effect was observed in the Span Board Forward subtest (p=0.04) but the effect no longer remained significant when separate post hoc analyses were performed for girls and boys (p>0.05) (Table 1).

The CAH cohort performed significantly better than the controls in the NEPSY List Learning subtest (p= 0.05).

In the CAH-DEX group girls performed worse than non-DEX treated girls with CAH in most measures, but the difference only reached statistical significance in the subtest Vocabulary (WISC-III) (p=0.03) (Table 2).

Discussion:

All patients with CAH were treated with HC and were detected through the Swedish national neonatal screening program. Early diagnosis and treatment in our screening-detected cohort could account for the normal performance in children with CAH. At present, it is not known whether the long term effects on cognitive function differ between different GC regimens in the context of CAH treatment.

Although our study group is small, the present study further suggests that there may be a sex difference in vulnerability to prenatal DEX treatment. Girls seem to be more vulnerable than boys.

Karolinska Institutet

Valeria Messina

MSc • Pediatric endocrinology unit

valeria.messina @ki.se

3--P1

57ESPE

Adrenals and HPA Axis

Valeria Messina

Poster presented at:

57th ESPE 2018 Meeting ATHENS GREECE