

# Mild Cognitive Deficits in Patients with Stable Treatment for Primary Adrenal Insufficiency: a Case-Control Study

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## Introduction

Patients with primary adrenal insufficiency (PAI) require daily and lifelong substitution with hydrocortisone (HC). Patients with PAI report impairments in quality of life (QoL), with persistent physical and psychological complaints<sup>1</sup>, which have been attributed, at least in part, to intrinsic imperfections of hormone replacement therapy<sup>2</sup>.

The brain is a major target area for cortisol considering its high density of glucocorticoid receptors and previous studies in patients treated for Cushing's disease (CD) that have been exposed to cortisol excess suggest that hypothalamic-pituitary-adrenal axis dysregulation is related to cognitive impairment<sup>3</sup>.

## Aim

The aim of the present study was to evaluate cognitive functioning in patients with PAI and to examine the possible effect of postponing early morning hydrocortisone intake on cognition. Furthermore, we aimed to assess cognitive functioning of patients with PAI relative to patients in remission of CD.

## Design

**Subjects:** We included a total of 60 patients with PAI. Thirty-one of these patients were matched with a healthy control. The other 29 patients were asked to postpone their morning HC intake until after the study. Cognitive functioning scores of patients in remission of CD (using HC) were obtained from previous research<sup>3</sup>.

**Assessment of cognitive functioning:** Several tests were used to evaluate global cognitive functioning, memory, and executive functioning: Wechsler memory scale (WMS), Verbal learning test of Rey, Rey complex figure, Letter-digit substitution test, Sustained attention to response task (SART), Verbal fluency FAS test, Trail making test, Synonyms subtest GIT, and Stroop color-word test.

Z-scores were calculated for each patient group by comparison with their own matched control group, with Z=0 indicating the scores of the matched controls.

## Conclusions

Patients with stable treatment for PAI demonstrate mild cognitive deficits compared to controls, and perform generally similar to patients in remission of CD. Patients who postponed their regular morning HC intake did not perform differently compared to patients with their regular HC intake.

## Future directions

Future studies in animal models and (functional) MRI research in patients with PAI could provide more insight into the underlying mechanisms of the found cognitive impairments.

## Results

### PAI (with HC intake) versus healthy controls ↓

Patients with PAI performed worse on all memory tests and two executive functioning test compared with healthy matched controls ( $P < 0.05$ ).

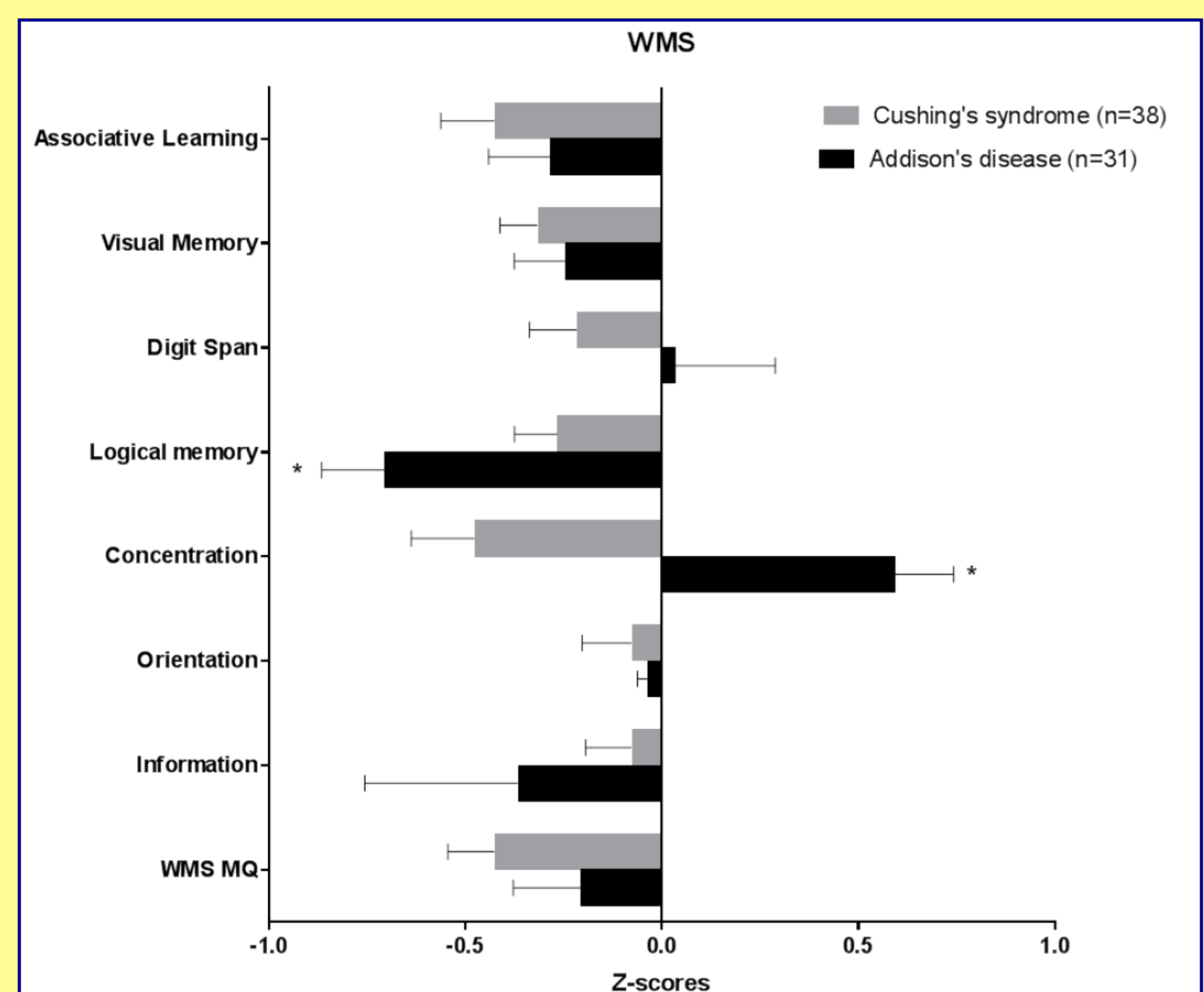
	PAI Patients n=31	Healthy matched controls n=31	P-value
<b>Memory</b>			
Wechsler Memory Scale			
MQ	110.9 (13.7)	113.7 (13.9)	.394
Concentration	7.9 (1.2)	7.1 (1.4)	.015
Logical memory	6.4 (2.3)	8.1 (2.4)	.006
Rey Auditory Verbal Learning Test			
Imprinting total	5.3 (1.7)	6.5 (2.5)	.024
Immediate total	7.9 (1.8)	9.7 (2.5)	.001
Delayed total	7.5 (2.6)	9.2 (3.4)	.016
Rey Complex Figure Test			
Immediate	18.7 (6.5)	22.2 (7.7)	.009
Delayed	18.6 (6.9)	22.8 (7.8)	.007
<b>Executive Functioning</b>			
Verbal Fluency Test (FAS)			
No. correct	33.6 (12.8)	33.3 (12.9)	.931
No. repeats	1.1 (1.2)	0.4 (0.6)	.003
Trail Making Test			
Trail A, time	0.3 (0.1)	0.3 (0.2)	.237
Trail A, errors	0.1 (0.3)	0.2 (0.4)	.041
Trail B, time	0.9 (0.4)	0.7 (0.4)	.012
Trail B, errors	0.3 (0.7)	0.2 (0.5)	.282

### PAI with HC intake versus PAI with postponed HC intake

Patients who postponed their regular morning HC intake did not perform differently compared to patients with their regular HC intake (results not shown).

### Z-scores PAI versus Cushing ↓

Patients with PAI performed generally similar to patients with CD, except for one memory task ( $P = .048$ ) and a concentration task ( $P = .001$ ). Furthermore, patients with PAI demonstrated more repeats during the verbal fluency task ( $P = .024$ ).



#### References

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