

# Can Hypothalamic Obesity be Treated with Stimulants?

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## Introduction

Published case reports (1) and anecdotal experience suggest a positive effect of Dexamphetamine on impetus and weight in patients with hypothalamic obesity. Based on these observations, patients presenting to our obesity clinic with hypothalamic obesity are offered off-label treatment with dexamphetamine.

## Methods

Between 2010 and 2013, patients starting dexamphetamine treatment were enrolled in a prospective observation study. BMI-SDS was determined and impetus was rated at baseline and every three months. A retrospective chart review was conducted to establish BMI-SDS development prior to treatment initiation. Dexamphetamine administration was initiated at a single dose of 5mg per day, and titrated to effect up to a dose of 20mg/day in 2-3 single doses. Side effects were recorded in a standardized fashion.

## Results

9 Patients (3 males) mean age 17.2 years (range: 13.0-23.8) were included in the study. The primary diagnosis was craniopharyngeoma in 6 patients, ganglioglioma WHO 01 in one patient, neonatal meningitis in one patient and astrocytoma in one patient. Time from initial CNS insult to initiation of dexamphetamine treatment was 5.7 years on average (range 4 mo-17.4 yrs). All patients demonstrated a steady increase in BMI-SDS from the time of initial diagnosis up until the initiation of treatment. Of the nine Patients, two were excluded from the evaluation because of proven non-compliance. Baseline BMI-SDS of the remaining 7 patients was +3.1 (1.9-4.4). After a mean treatment duration of 2 years (0.6-4.5), BMI-SDS decreased on average by 0.4 (0-1.3) and the mean score for impetus improved from 1.3 to 2.8. No significant side effects were reported.

### BMI-SDS: craniopharyngeoma group

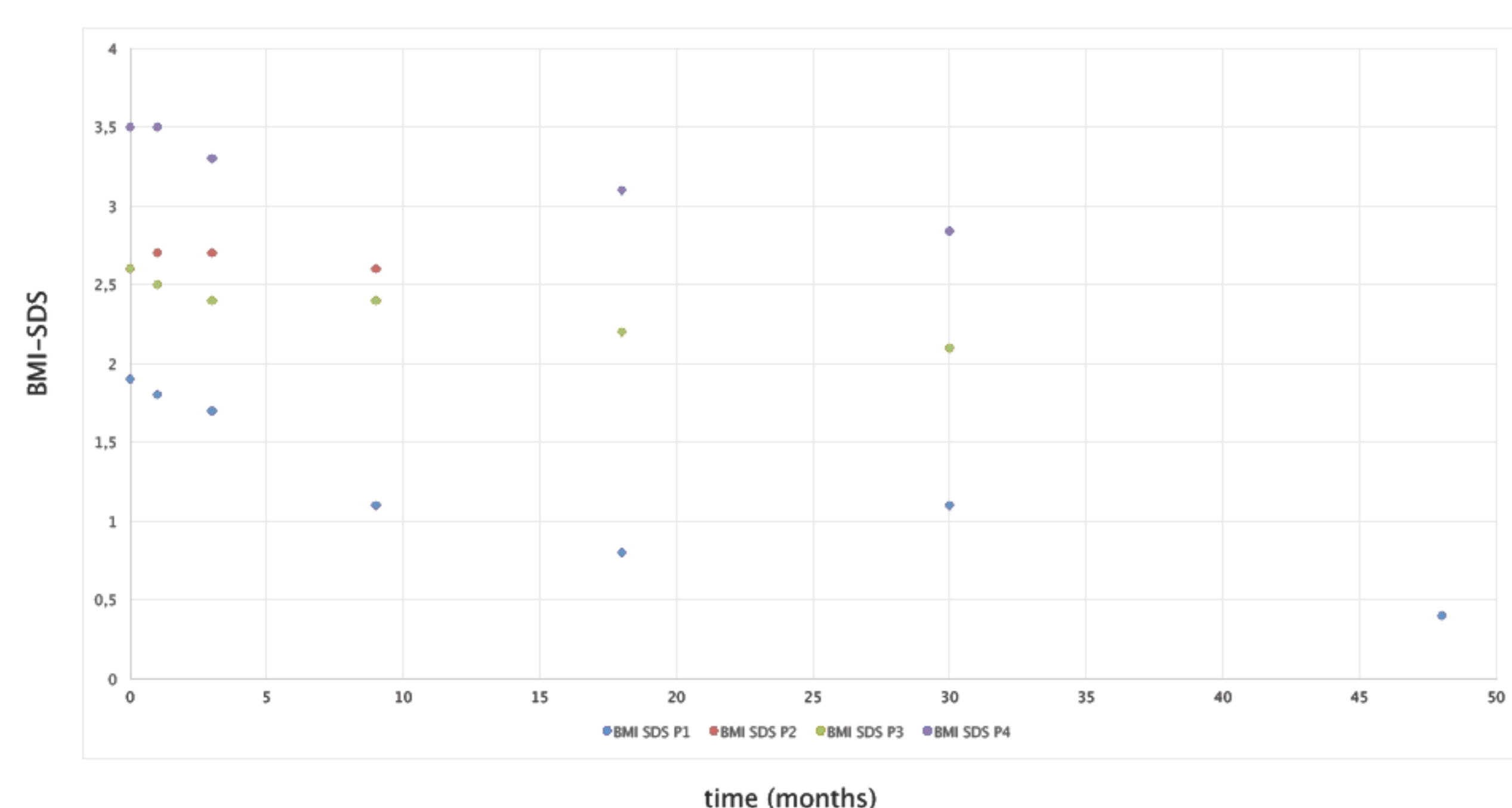


figure 1 Course of BMI-SDS in n=4 patients with craniopharyngeoma treated with dexamphetamine; treatment initiated at timepoint 0 months. For patient details see below.

#### Patient 1

24 4/12 year old male with complete resection of craniopharyngeoma, at age 14 9/12. BMI at treatment start 29.9 kg/m<sup>2</sup>, BMI-SDS 1.9. BMI-SDS after 4,5 years of treatment markedly reduced at 0.6.

#### Patient 2

15 9/12 year old female with complete resection of craniopharyngeoma at age 14 8/12. BMI at treatment start 32,0 kg/m<sup>2</sup>, BMI SDS 2.6. BMI-SDS after 9 months of treatment stable at 2.6.

#### Patient 3

26 11/12 year old female with complete resection of craniopharyngeoma at age 21 1/12. BMI at treatment start 41.2 kg/m<sup>2</sup>, BMI-SDS 2.6. BMI-SDS after 3 years of treatment reduced at 2.2.

#### Patient 4

19 2/12 year old female with complete resection of craniopharyngeoma at age 11 1/12. BMI at treatment start 43.2 kg/m<sup>2</sup>, BMI-SDS 3.5. BMI-SDS after 16 months of treatment reduced at 2.8.

### BMI-SDS: other causes of hypothalamic obesity

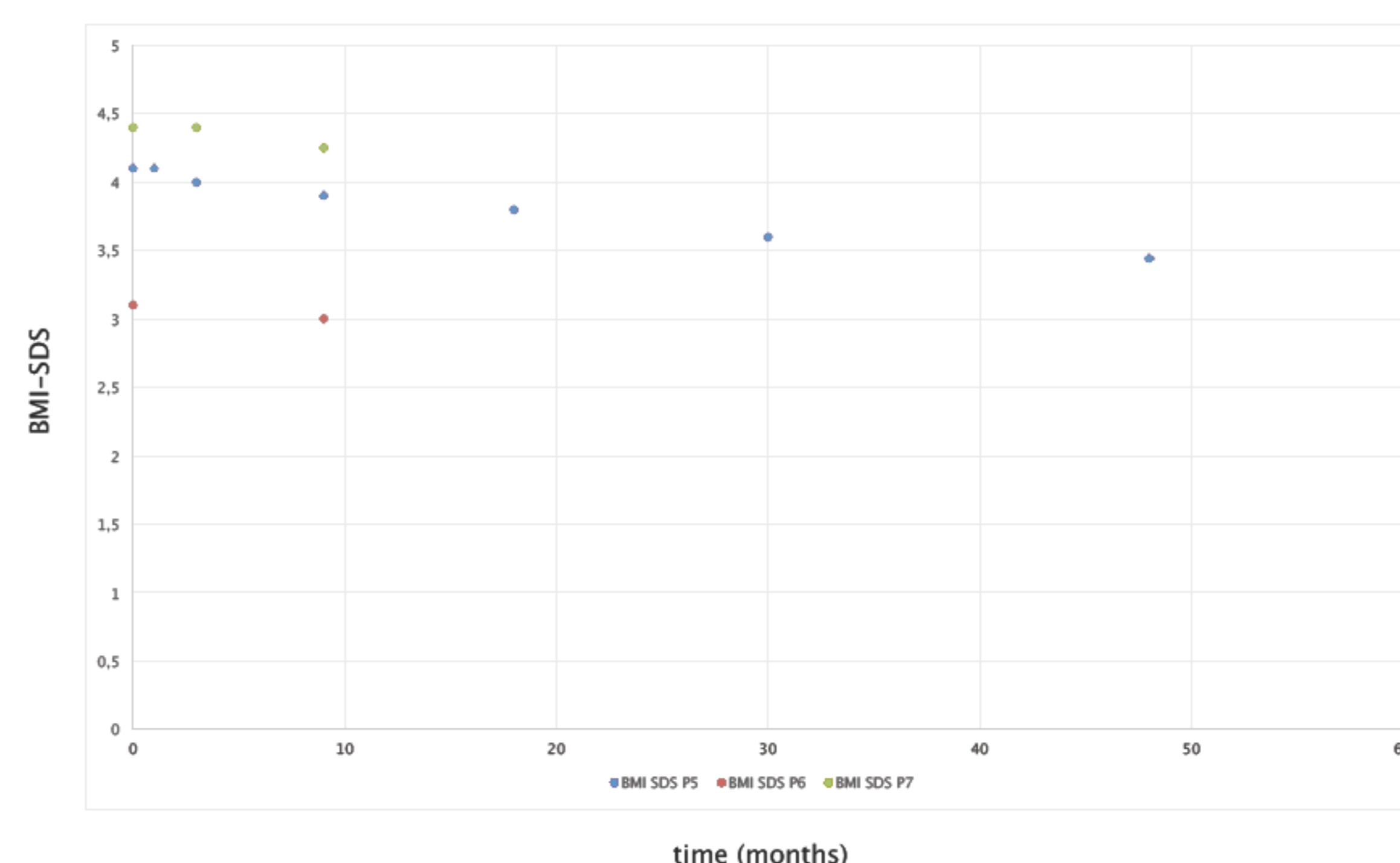


figure 1 Course of BMI-SDS in n=3 patients with other causes of hypothalamic obesity treated with dexamphetamine; treatment initiated at timepoint 0 months. For patient details see below.

#### Patient 5

22 4/12 year old female with meningococcal meningitis in infancy. BMI at treatment start 59.5 kg/m<sup>2</sup>, BMI-SDS 4.1. BMI-SDS after 3 years of treatment reduced at 3.7.

#### Patient 6

13 7/12 year old female with complete resection of ganglioneuroma at age 11 9/12. BMI at treatment start 36,4 kg/m<sup>2</sup>, BMI-SDS 3,1. BMI-SDS after 7 months of treatment reduced at 3.0.

#### Patient 7

20 4/12 year old male with incomplete resection of astrozytoma (localisation chiasma opticum and third venticle) at age 12 6/12. BMI at treatment start 64,2 kg/m<sup>2</sup>, BMI-SDS 4,4. BMI-SDS after 8 months of treatment reduced at 4,3

## Discussion

Hypothalamic obesity is caused by an insult to the hypothalamus resulting in loss of catabolic signaling and autonomic instability (2). Features include hyperphagia, decreased resting energy expenditure and mobility, and hyperinsulinemia. The hypothalamic (homeostatic) system of intake regulation is closely interrelated with the dopaminergic (non-homeostatic) system.

We postulate that dexamphetamine ameliorates hypothalamic obesity by 2 mechanisms. 1. by increasing sympathetic tone and thus energy expenditure, and 2. by increasing CNS dopamine concentration and thereby modifying cerebral satiety signals.

## References

1. Ismail D et al. J. Pediatr Endocrinol Metab. 2006; 19(2):129-134.
2. Pinkney J et al., Obesity Reviews 3 2001; 27-34

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