The long-term cognitive outcomes of Alzheimer's disease — influence of APOE genotype, NSAID therapy, and cholinesterase inhibitor treatment.

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The long-term cognitive outcomes of Alzheimer's disease — influence of APOE genotype, NSAID therapy, and cholinesterase inhibitor treatment

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Conclusions

In this 3-year AD study in routine clinical practice, the response to ChEI treatment and longitudinal cognitive outcome was better for those receiving a higher dose of ChEI, non-carriers of the APOE ε4 allele, and for patients treated with NSAIDs/acetylsalicylic acid. The type of ChEI did not influence the outcome.

Introduction and objectives

Heterogeneity in cognitive outcomes and response to treatment has been described in Alzheimer's disease (AD). Using the method of mixed models, higher resolution can be obtained to identify potential predictors of long-term outcomes. The aim of this presentation is to analyse the impact of the APOE genotype, non-steroidal anti-inflammatory drug (NSAID)/acetylsalicylic acid therapy, and cholinesterase inhibitor treatment (ChEI) on the longitudinal cognitive outcomes in AD.

Methods and subjects

The Swedish Alzheimer's Treatment Study (SATS) is a 3-year, open, prospective, non-randomized, multicentre study in a routine clinical setting. In total, 843 patients treated with donepezil, rivastigmine or galantamine were included in this study. At baseline and every 6 months, the patients were assessed using several rating scales, including the Alzheimer's Disease Assessment Scale–cognitive subscale (ADAS–cog), and the dose of ChEI was recorded. The mean dose used during the entire follow-up period was calculated for each patient, and the median values for this mean dose were used as the cut-offs (low vs high dose): donepezil 7.1 mg, rivastigmine 6.5 mg, and galantamine 16.0 mg. Sociodemographic and clinical characteristics were investigated. The relationships of the predictors to longitudinal cognitive ability were analysed using linear and non-linear mixed-effects models, adjusting for sex, age at onset and at baseline, years of education, and disease severity at baseline.

In this study, we used a mixed-effects statistical model. This method takes into account the correlation within subjects, variations in the number of follow-up assessments available for the participants, and the actual time intervals between the collected data points. Thus, the mixed models are especially suitable for longitudinal studies.

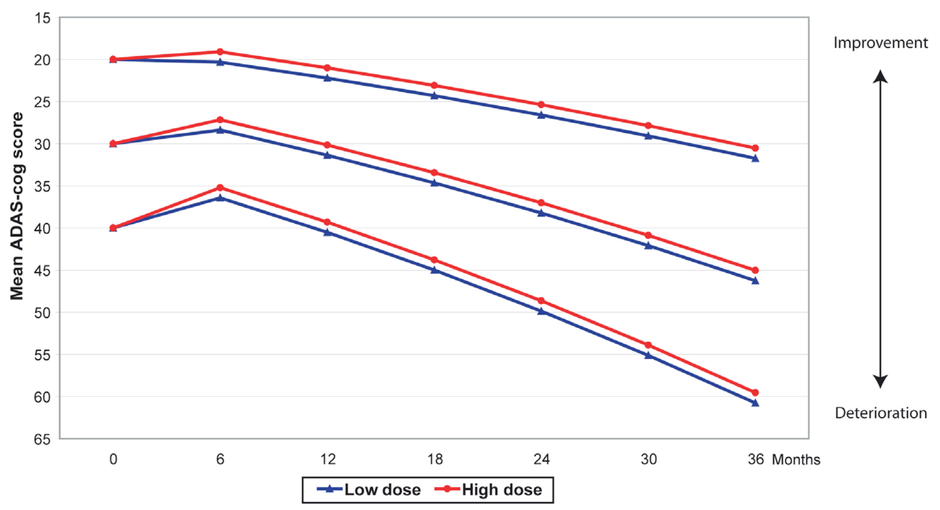
Baseline characteristics	
Number of patients (n)	843
Gender (males / females)	37% / 63%
APOE ε4 carrier	68%
NSAID/acetylsalicylic acid therapy	30%
Estimated age at onset[a]	71.9 ± 7.4
Age at start of ChEI treatment[a]	75.0 ± 7.1
Duration of AD, years[a]	3.0 ± 2.1
ADAS-cog, range 0 - 70[a]	20.6 ± 8.9

[a]mean ± SD.

Results

- The **type of ChEI agent** (donepezil, rivastigmine, galantamine) had **no impact on the outcome.**
- A **higher mean ChEI dose** was associated with an **improved 6-month response to treatment** and a **more positive long-term outcome** ($p < 0.001$), **Figure 1.**

Fig. 1. ChEI dose



The calculated outcomes displayed in Figure 1 were based on an average male patient aged 75 with 9 years of education and an IADL score of 16.
The 3-year mean outcome predicted by the models for different baseline ADAS–cog scores; 20, 30, and 40 were used as arbitrary examples.

- Patients with **lower cognitive ability** at baseline exhibited an **improved 6-month response to ChEI treatment.**
- Patients **receiving NSAID/acetylsalicylic acid therapy** showed an **improved 6-month response to ChEI treatment**, and a **more positive long-term outcome** ($p = 0.017$).
- **Non-carriers of the APOE ε4 allele** showed an **improved 6-month response to ChEI treatment** and a **more positive long-term outcome**, compared with ε4-carriers ($p = 0.012$). No significant difference regarding 1 or 2 ε4 alleles was observed.

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