

# Analysis of influences on cognition and fatigue in patients with relapsing-remitting multiple sclerosis (RRMS) – a two-year observational study

H. Schreiber<sup>1</sup>, C. Lang<sup>1</sup>, K. Kiltz<sup>2</sup>, M. Lang<sup>1</sup>, P. Flachenecker<sup>3</sup>, H. Meißner<sup>3</sup>, M. Freidel<sup>4</sup>, H. Herbst<sup>5</sup>, E. Scholz<sup>6</sup>, W. Hofmann<sup>7</sup>, E. Schlegel<sup>8</sup>, W. Elias<sup>9</sup>, K. Gehring<sup>10</sup>, U. Eckhardt<sup>11</sup>, A. Bergmann<sup>12</sup>, G. Reifschneider<sup>13</sup>, S. Ries<sup>14</sup>, C. Ring<sup>15</sup>, S. Schlegel<sup>15</sup>



NTD Study Group on Multiple Sclerosis Ulm<sup>1</sup>, Kaltenkirchen<sup>4</sup>, Stuttgart-Böblingen<sup>5,6</sup>, Aschaffenburg<sup>7</sup>, Siegen<sup>8</sup>, Hamburg<sup>9</sup>, Itzehoe<sup>10</sup>, Rottweil<sup>11</sup>, Neuburg<sup>12</sup>, Erbach<sup>13</sup>; Marienhospital, Abt. Neurologie, Stuttgart<sup>2</sup>, Neurol. Rehabilitationszentrum Quellenhof, Bad Wildbad<sup>3</sup>; University of Ulm, Dept. of Biomedical Statistics, Ulm<sup>15</sup>

## Objective

- (1) To evaluate how and to what extent clinical, behavioral and psychobiological factors may influence cognition and fatigue in MS
- (2) To define whether and how these variables are influenced by fatigue in the long-term course of the disease

## Methods

### Study Design:

Monitoring of clinical, behavioral, neuropsychological and psychological (mood, personality) variables in RRMS patients with (MS-F) and without MS-associated fatigue (MS-NF) over 2 years. Inclusion criteria: 18-50 yr, RRMS/McDonald, EDSS 0-3.5, interferon beta-1b therapy (>3 months, no longer than 2 yr).

### Study Cohort:

At FU24 (after 2 yr), 78 patients (31m, 47f, mean 37.3 yr) and 25 controls (9m, 16f, mean 35.9 yr) were available for testing compared to 102 RRMS and 30 matched controls at baseline (BL). Stratification of RRMS-patients was done by the "Würzburger Erschöpfungsinventar in MS" (WEIMuS) to

- ▶ RRMS with MS-associated fatigue (MS-F; N=54) and
- ▶ RRMS without MS-associated fatigue (MS-NF; N=24)

### Data profile:

- **Clinical & behavioral domain:** EDSS, MSFC, fatigue (WEIMuS), IQ (MWT-B), quality of life (FAMS), ADS (depression), Epworth Sleepiness Scale (ESS).
- **Neuropsychology:** TAP attention battery comprising subtests of alertness, divided attention, mental flexibility, executive control, sustained attention and working memory, plus PASAT, visual and verbal memory (VVM) and self-perception of cognitive and attentional dysfunction (FEDA).
- **Disease Coping:** Freiburger Disease Coping Questionnaire, self assessment (FKV-SE).
- **Personality Profile:** Freiburger Personality Questionnaire (FPI-R).
- **Statistics:** Mixed linear models were calculated to assess the effects of time, EDSS, IQ, mood, fatigue, personality and disease coping on cognition and fatigue.

## Results

Among the neuropsychological variables, only very few were significantly and consistently influenced by factors of the mixed linear model. This held true above all for aspects of non-verbal (visual) memory (VVM) and sustained attention. Most consistently, a significantly negative effect of disease course (time) and disease progression (EDSS) was found for the delayed recall of the non-verbal VVM (Table 1). Consistent influences of personality traits or disease coping mechanisms on verbal and non-verbal memory suggesting a special profile were not found.

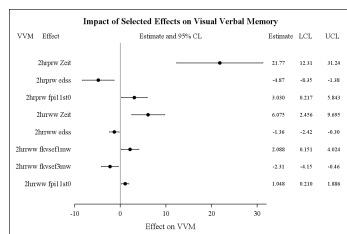


Table 1: Effect-factors significantly influencing visual and verbal memory test (VVM). 2hrprw, non-verbal reproduction rate after 2 hours (percent range); 2hrprw, non-verbal reproduction rate after 2 hr (raw score); Zeit/time, disease course; edss, disease progression; fpi11st0, FPI, subscale "extraversion"; fkvsef1mw, FKV, subscale depressive coping; fkvsef3mw, subscale deviation; LCL, lower confidence level; UCL, upper confidence level (Forest Plot).

The factors significantly influencing sustained attention are summarized in Table 2. The most interesting effect is the time\*fatigue interaction occurring in several time segments of the test and indicating that both fatigue and longer disease course (Zeit/time) interact and both enhance reaction times of TAP sustained attention subtest (negative influence). Overall, there was no consistent influence of personality and

disease coping on sustained attention.

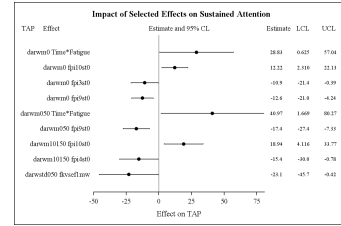


Table 2: Factors influencing TAP battery, sustained attention subscore darwm0 (reaction time (RT) raw score 0-5 min interval); darwm050, RT raw score 5-10 min interval; darwm10150, RT raw score 10-15 min. fpi10st0, FPI subscore "social desirability"; fpi3, "performance orient." fpi9, "healthy worries"; fpi4, "inhibition"; fkvsef1mw, disease coping, depressive coping".

In contrast to the objectively measured neuropsychological variables, there were multiple significant effects of clinical, behavioral and psychological variables on the self-assessment of distraction, tiredness and slowing during cognitive processing and practical activities (FEDA). Significantly negative influences on FEDA were shown by depression (adstw) and several personality traits, i.e. "social orientation" (fpi2), "social desirability" (fpi10) and "somatic distress" (fpi8), positive influences by "extraversion" (fpi11), "life satisfaction" (fpi1) & "somatic distress" (fpi8)

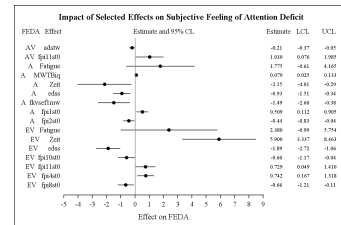


Table 3: Factors significantly influencing the self-assessment of distraction, tiredness and slowing (FEDA) during cognitive processing (AV) and practical activities (EV), and attention (A)

Fatigue was significantly influenced by disease progression (edss), depression (ads), some personality traits, i.e. performance orientation (fpi3), strain (fpi7), social desirability (fpi10), and active disease coping (fkvsef2mw), but not disease duration. For details refer to Table 4.

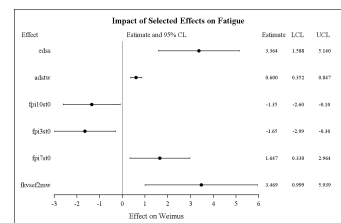


Table 4: Factors significantly influencing fatigue. Edss, disease progression; adstw, depression scale; fpi10st0, FPI subscore "social desirability"; fpi3, "performance orientation"; fpi7, "strain"; fkvsef2mw, disease coping, subscore active coping.

## Conclusions

- (1) Cognitive and attentional performance in early MS is not consistently influenced by clinical, behavioral and psychological variables. This correlates with the observation that cognitive decline in early MS is slow and distributed to certain areas.
- (2) Fatigue does not impair cognitive performance, only aspects of sustained attention, and above all self-perception of deficits.
- (3) Fatigue in early MS is influenced by personality traits, disease coping, depression and clinical status.