Factors Associated with a Decline in Subjective Cognition: Results from an RA Observational Cohort Study

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Introduction

- Previous studies have suggested that RA confers an increased risk for worsened cognition later in life compared with the general population.
- Research in dementia has indicated that the presence of subjective cognitive complaints may be an indicator of cognitive decline.
- Little is known about the inflammatory, psychological, and functional factors associated with worsening of subjective cognitive complaints among RA patients.

Aims

- Assess factors associated with subjective cognitive complaints in RA patients.
- Evaluate whether a change in risk factors for subjective cognitive complaints overtime affects perceived cognitive function.

Methods

Study Population:

- RA patients enrolled in the Brigham and Women's Rheumatoid Arthritis Sequential Study (BRASS) with at least two study visits.
- Data Collection includes joint exams, serological analyses and patient reported outcome measures annually.
- Patients were asked to report the degree of their cognitive complaints concerning the following questions annually:
  - Do you have any of the following symptoms NOW?
    - Poor Memory (Not at all, Sometimes, Often)
    - Poor Concentration (Not at all, Sometimes, Often)
    - Word-finding Difficulty (Not at all, Sometimes, Often)

Statistical Analyses:

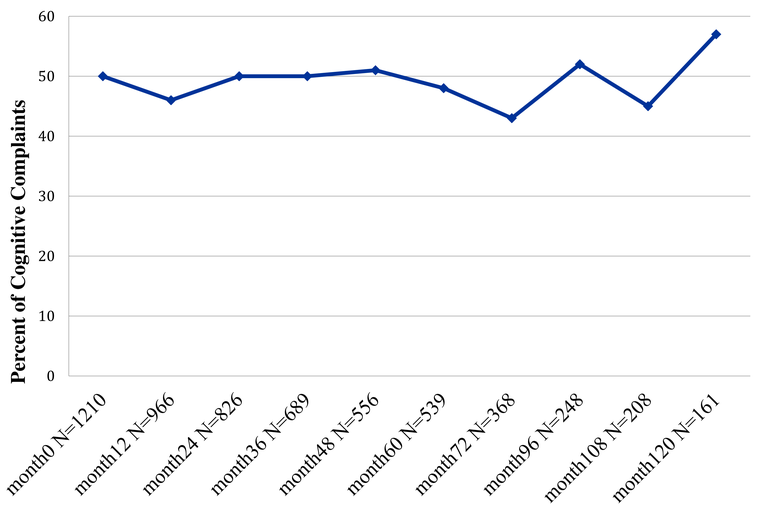
- Percent of participants reporting cognitive complaints over 10 years (Figure 1).
  - Define cognitive complaint as a report of "often" to one of the cognitive questions or reporting "sometimes" on at least two of the cognitive questions.
- Dependent variable for the univariate and multivariate analyses defined as Δ cognitive complaint (range =-6 to 6). Higher = increase in cognitive complaint.
- Mixed Model univariate analysis to assess known factors associated with cognitive decline.
  - Covariates included: age, gender, ethnicity, education, CV Risk Score (Desai et al, 2012).
  - Computed variables that measure the past year's change in MDHAQ depression, MDHAQ fatigue, MDHAQ sleep, exercise level (METS), DAS28-CRP4, corticosteroid use.
- Multivariate backwards elimination mixed model using univariate factors with a p<0.10 (Table 2).

Results

Table 1. Baseline Demographics (N=1343)

Variable	
Gender (female) (N,%)	1106 (82.4%)
Age, years (M,SD)	56.5 (14.1)
Education (College or more) (N,%)	731 (55%)
Race (White) (N,%)	1228 (92.1)
Steroid Use (N,%)	402 (30%)
Anti-TNF Use (N,%)	472 (35.1%)
METS >15 (N,%)	91 (9.8%)
DAS28-CRP4 (M, SD)	3.81 (1.62)
Fatigue (MDHAQ) (M,SD)	41.8 (29.4)
Sleep Problem (MDHAQ) (M,SD)	0.87 (0.85)
Depression (MDHAQ) (M,SD)	0.44(0.63)
MHI-5 (M,SD)	73.0 (17.8)
CV Risk Score (0-9) (M,SD)	1.57 (1.65)

Figure 1. Percentage of Participants Reporting Subjective Cognitive Complaints at Annual Study Visits



- Univariate analysis the following covariates were statistically significant and met the criteria to be entered into the multivariate mixed model:
  - CV Risk Score, Δ MHHAQ Sleep, Δ MDHAQ depression, Δ Corticosteroid use, Δ MDHAQ Fatigue, Δ anti-TNF use.
  - Age, gender, ethnicity, education and ΔDAS28-CRP4 were forced into the model.

Results

Table 2. Clinical and Psychological Factors Associated with a One Unit Increase in Subjective Cognitive Complaints

Multivariate Mixed Model*	B coefficient	Standard Error	P-Value
Age (continuous)	0.0006	0.002	0.74
Sex (Male)	**0.15**	**0.06**	**0.02**
Ethnicity (White)	0.01	0.10	0.91
Education (college and above or not)	0.05	0.05	0.35
Worse MDHAQ Depression (-3,3)	**0.20**	**0.05**	**<0.0001**
Worse MDHAQ Fatigue (-100, 100)	**0.006**	**0.001**	**<0.0001**
Addition of corticosteroids	**0.27**	**0.07**	**0.0002**
Decrease in DAS28-CRP4	-0.003	0.02	0.83

*Dependent variable (Δ cognitive complaint) -6-6, higher equals increased cognitive complaints

- Males reported more cognitive complaints than women (P=0.02).
- Worsening in MDHAQ depression and MDHAQ fatigue were statistically associated with an increase in cognitive complaints (P<0.0001).
- Adding corticosteroids as a treatment was also associated with an increase in subjective cognitive complaints (P=0.0002).

Strengths/Limitations

- Study included a large number of subjects with longitudinal data.
- First study to assess how change in factors associated with cognitive decline affects report of cognitive difficulties.
- Did not use neuropsychological measures to assess cognitive function.
- Analysis did not have a non-RA comparator group.

Conclusions

- Subjective cognitive complaints are associated with the following: being male, worsening of depression, worsening of fatigue and adding corticosteroids as a treatment.
- Future studies should focus on whether corticosteroid use and fatigue levels may be markers of subclinical disease activity that might make patients more likely to report cognitive difficulties.

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