

Results: The presence of MS was significantly associated with worse apathy ($\beta=.34$, $p < .001$) and it remained significant after adjusting for covariates ($\beta=.19$, $p=.03$). Additionally, apathy was negatively associated with global cognition in persons with MS ($\beta=-.32$, $p=.01$) and this association remained significant after adjusting for covariates ($\beta=-.33$, $p=.01$) except depression ($\beta=-.27$, $p=.08$). The association of apathy and global cognitive functioning was not significant in healthy controls ($\beta=.01$, $p=.95$).

Conclusions: This study is the first to report worse apathy symptoms in older persons with MS compared to healthy controls. Additionally, worse apathy symptoms were associated lower global cognitive functioning in older adults with MS but not in healthy controls.

Categories: Multiple

Sclerosis/ALS/Demyelinating Disorders

Keyword 1: apathy

Keyword 2: cognitive functioning

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44 Low Modularity Contributes to Reduced Semantic Network Organization in Multiple Sclerosis

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Objective: Word finding difficulty is a prevalent cognitive symptom in multiple sclerosis (MS). Word finding relies on retrieving concepts and word forms from the long-term store.

Neuropsychological assessment of word finding difficulty in persons with MS (pwMS) is typically characterized by semantic errors and decreased speed in naming tests, along with decreased semantic verbal fluency scores. Despite this, there is significant heterogeneity in the detection of verbal fluency deficits across studies in the MS literature. This may be partially due to disease-related heterogeneity and/or low sensitivity of commonly used scoring approaches. We investigate the latter in the present study.

Semantic network analysis, derived from graph theory, provides a fine-grained approach to understanding semantic retrieval by utilizing information about the co-occurrence of words produced on semantic verbal fluency tasks.

Analysis results in a graphical quantification of the conceptual-lexical store. A preliminary study found that semantic networks from Spanish-speaking pwMS had fewer associative connections and more central connective pathways, which if affected, may lead parts of the network to become inaccessible for retrieval. However, their investigation was limited in the generalizability of their findings, as they excluded pwMS who have cognitive impairment (CI), which represents a significant proportion of pwMS. We sought to investigate network differences in an English-speaking MS sample, without exclusion based on CI, using widely-used metrics of micro-, meso-, and macroscopic structure. We hypothesize the MS network will be less efficiently organized, thus characterized by higher average shortest path length (ASPL), lower clustering coefficient (CC) and lower modularity (Q).

Participants and Methods: 53 persons with MS and 44 neurologically healthy controls (HC) were recruited as a part of an ongoing study (NMSS RG-1907-34364 & RG-1901-33304). As a part of a larger battery, participants were administered the semantic verbal fluency subtest of the Controlled Oral Word Association Test. Responses were analyzed using a network-analysis R suite.

Results: The MS and HC networks were characterized by having similar average shortest path lengths (ASPL MS = 2.466, ASPL HC = 2.463, $F(1,1997)=0.281$, $p=0.596$), indicating they require similar numbers of edges to be traversed to reach other nodes in the network. This suggests similar efficiency of information transfer. Clustering coefficient was not significantly different between the MS and HC networks (CC MS = 0.742, CC HC = 0.742, $F(1,1997)=0.10$, $p=0.919$), suggesting similar local interconnectivity. The MS network had significantly lower modularity compared to the HC network (Q MS = 0.497, Q HC = 0.502, $F(1,1997)=16.678$, $p<0.001$). This means that sub-communities of the network were less segregated into densely connected sub-graphs.

Conclusions: Contrary to expectation, ASPL and CC were not significantly different between groups. The absence of finding lower CC was consistent with prior findings. Consistent with our hypothesis, the MS network had lower modularity. This may suggest that pwMS were unable to use categorical clustering to aid in retrieval from the lexicon. Specifically, low modularity coupled with similar CC may suggest the structure of the MS lexicon is characterized

by intact clustering on a microscopic scale but less strong organization into distinct clusters on a larger scale.

Categories: Multiple

Sclerosis/ALS/Demyelinating Disorders

Keyword 1: multiple sclerosis

Keyword 2: language

Keyword 3: fluency

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45 A systematic review of cognitive correlates of fatigue in pediatric-onset multiple sclerosis

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Objective: Fatigue is common in pediatric-onset multiple sclerosis (POMS), yet causal factors and correlates of fatigue are poorly understood in this population. A 2016 review suggested an association between fatigue and emotional difficulties, sleep disturbance, and reduced quality of life in POMS. Information regarding the potential association between fatigue and cognitive challenges is limited and mixed. Through this systematic review, we searched for relationships between fatigue, cognition, and mental health.

Participants and Methods: Systematic review methodology and PRISMA guidelines were followed. Five electronic databases were searched: Ovid: Medline, Ovid: EMBASE, Ovid: PsycInfo, Web of Science and CINAHL. Search terms were specific to each database. Reference lists of included studies were also hand-searched. We included empirical studies that were published in English after 2001, included a sample with confirmed diagnoses of POMS using McDonald criteria, and measured fatigue, cognition and clinical factors including mental health outcomes. Cognition had to be

assessed using a standardized assessment tool and studies must have examined associations between outcomes of interest either descriptively or by assessing bivariate or multivariate relationships.

Covidence was used to complete the screening, extraction, and quality assessment. Two independent researchers (i.e., T.L.F, and/or S.D, and/or M.G) reviewed each paper included in the title and abstract screen and full text review. S.D and M.G completed the extraction and quality assessments. Conflicts at all stages were resolved by the lead author (T.L.F). The University of Adelaide JBI critical appraisal checklist for analytical cross-sectional studies was used to ensure the scientific rigor of each included study.

Sample characteristics and measures of fatigue, clinical and cognitive variables were extracted. A narrative synthesis was conducted.

Results: We identified 1025 abstracts through our initial search and retained 119 articles for full text review. One hundred and six of these studies were excluded during the full text review including six studies which did not examine the relationship between the outcomes of interest. Fifty-one additional studies were identified from hand-searching reference lists of included studies, of which 24 were retained for full text review. A total of 15 studies were extracted and analyzed. Overall, a positive relationship was found between fatigue and mental health outcomes (i.e., anxiety and depression), whereas results were mixed regarding the association between fatigue and performance-based measures of cognition as well as fatigue and other clinical characteristics (e.g., disease duration, EDSS, treatment with DMDs, relapse rate, age at disease onset). In some studies, fatigue and executive functioning performance were negatively related; the relationship was less clear in others (e.g., both fatigued and non-fatigued MS patients demonstrated cognitive challenges, an association between fatigue and executive functioning was identified at follow-up but not baseline). Eleven of the 15 included studies (73%) did not identify associations between fatigue and cognition.

Conclusions: While studies are mixed, fatigue in children has been associated with aspects of cognition. Understanding the relationship between fatigue, cognition, and mental health and identifying gaps in the existing literature, have implications for informing interventions for this clinical population.