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The relation between memory and decision-making in multiple sclerosis patients

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ABSTRACT

Background. Impairments in long-term and working memory are widespread in Multiple Sclerosis (MS), setting on in early disease stages. These memory impairments may limit patients' ability to take informed and competent medical decisions, too. In healthy populations, memory abilities predict decision quality across a wide range of tasks. These studies suggest that higher working memory capacity supports decisions in cognitively taxing tasks, whereas better semantic memory facilitates decisions in tasks requiring knowledge retrieval. In individuals with MS, previous studies have linked less accurate decisions to memory deficits and reduced executive functioning, too. However, these studies focussed on decisions under risk and did not broadly assess decision making skills. We aimed to fill this gap in a cross-sectional study. **Methods.** Hundred thirty-seven participants with MS were recruited during their stay in an MS specialized rehabilitation centre. In a first test session, participants completed a standardized test battery for working memory and semantic memory, the inventory for memory diagnostics. In a second test session, participants filled out the Adult Decision Making Competence battery (A-DMC). This version of the A-DMC measured decision making competence on five subscales: Resistance to Framing Effects, Under/Overconfidence, Applying Decision Rules, Consistency in Risk Perception, and Resistance to Sunk Cost Effects. In addition, participants were screened for depression and cognitive fatigue. **Results.** Working memory was impaired in most participants, whereas semantic memory was not impaired. To understand which memory abilities underlie distinct components of decision making in people with MS, we used structural equation modelling. Replicating previous findings in a healthy sample, working memory capacity was associated with the ability to recall semantic knowledge. Participants with lower working memory capacity were less resistant to framing effects and adhered to decision rules less. In contrast, participants with worse semantic memory assessed their own knowledge less accurately, perceived risks less consistently, and made more errors in applying decision rules. Cognitive fatigue and depression unlikely explain these relationships. **Conclusions.** Taken together, our study suggests that the memory problems, frequently reported in MS patients, may reach out to higher-order cognitive functions, such as decision making skills. Supporting shared decision-making and patient autonomy within MS thus requires to take memory impairments into account and to match the information provided to the patient's memory abilities.

1. Introduction

One of the most prevalent and earliest symptoms of MS are cognitive dysfunctions, such as short-term and long-term memory impairments, with prevalence rates of 43–70% (Amato et al., 1995; Chiaravalloti and DeLuca, 2008; Rao et al., 1993). Previous research has, however, often neglected consequences of memory impairments for well-being, quality of life, and patient decisions (Rahn et al., 2012).

For instance, many patients prefer to take an active role in treatment decisions, especially those patients who experience more disabilities (D'Amico et al., 2016).

Importantly, cognitive abilities may interact with patients' ability to take informed and competent medical and life decisions. In healthy populations, memory abilities have been shown to predict decision quality and decision making skills across a wide range of cognitive tasks (Bruine de Bruin et al., 2007; Del Missier et al., 2010; 2013; Hoffmann

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et al., 2014; Lewandowsky, 2011) and real-life settings (Parker et al., 2018). In persons with MS, worse decisions have been traced back to deficits in processing speed, visual memory performance, reduced memory, and executive functioning (Farez et al., 2014; Muhlert et al., 2015). Most studies on persons with MS focussed on a narrow subset of decisions, namely decisions under risks (Kleeberg et al., 2004; Muhlert et al., 2015; Simioni et al., 2009) in which choice outcomes are known and realized with a predefined probability. Yet, decision making requires executing a variety of subprocesses: estimating the likelihood of outcomes, evaluating decision outcomes, integrating outcomes and beliefs into a decision, and metacognitive skills (Bruine de Bruin et al., 2007).

In healthy adults, working memory, the ability to simultaneously store and manipulate information (Atkinson and Shiffrin, 1968), likely underpins the evaluation of decision outcomes and the accurate integration of outcomes and beliefs into a decision. Specifically, evaluating decision outcomes requires to focus attention on the relevant information and to ignore irrelevant information, whereas integrating outcomes and beliefs requires mentally updating the information in working memory (Del Missier et al., 2012). In this vein, previous research has consistently shown that working memory predicts decision performance in tasks that require rule application (Del Missier et al., 2010; 2012; 2013; Hoffmann et al., 2014) or that require to ignore how a problem is described or framed (Resistance to Framing, Del Missier et al., 2013). Metacognitive skills, the ability to assess the quality of one's own knowledge and decisions, have been suggested to demand working memory (Del Missier et al., 2013), too. Especially, taking disconfirming evidence into account, a cognitively taxing process, should reduce overconfidence and lead to better calibrated judgments (Koriat et al., 1980). In contrast, semantic memory likely predicts performance in decision tasks that demand a high amount of background knowledge (Del Missier et al., 2013). For instance, assessing risks consistently requires the knowledge of the laws of probability and, thus, retrieval of knowledge from semantic memory. Similarly, ignoring unrecoverable investments requires the normative knowledge that future decisions should be independent of past costs. In line with this idea, semantic memory is predictive of the ability to perceive risks consistently as well as the ability to ignore unrecoverable investments (Del Missier et al., 2013). We aimed to replicate these relationships in individuals with MS and to examine how individual differences in memory abilities relate to five aspects of decision making competence, as measured by the multi-dimensional Adult Decision-Making Competence battery (A-DMC, Bruine de Bruin et al., 2007).

Memory impairments in MS may be caused by comorbid diseases, such as depression, or disease-related symptoms, such as cognitive fatigue, too. Depression may adversely impact on working memory (Arnett, 2005; Demaree et al., 2003), whereas cognitive fatigue has been related to alertness and vigilance (Hanken et al., 2015). If fatigue and depression impede memory performance, those impairments may in turn harm decision making skills.

2. Methods

2.1. Participants

Hundred thirty-seven participants with a MS diagnosis (98 women, 71.5%, $M_{Age} = 49.4$ years, $SD_{Age} = 10.4$ years, range: 19–76 years) were recruited during their stay in the Kliniken Schmieder Konstanz, Germany. The Kliniken Schmieder is a MS specialised neurological rehabilitation centre that admits MS patients for an interdisciplinary cognitive and physical rehabilitation treatment. To recruit participants, all incoming patients were screened for a MS diagnosis as the admission reason. Inclusion criteria were: a confirmed MS diagnosis according to the revised McDonald criteria (Polman et al., 2011), Age ≥ 18 , native German speakers, no severe visual deficits or other neurological diseases. Patients with a relapse or steroid treatment within the last four

weeks were excluded. All MS patients fulfilling these criteria were consecutively asked to participate in the study.

Educational background was comparable to the average population (18.2% Hauptschule, i.e. degree after grade 9, 44.5% Realschule, i.e. degree after grade 10, 37.2% Abitur, i.e. degree after grade 12–13). Eighty-five participants (62.0%) were diagnosed with RRMS, 37 (27.0%) with SPMS, and 15 (10.9%) with PPMS (Lublin and Reingold, 1996). Participants have been living with the disease on average for 17.5 years ($SD = 9.6$) with mostly mild to moderate disease symptoms (EDSS = 4.0, $SD = 2.1$, range: 1.0–8.0, EDSS = Expanded Disability Status Scale Kurtzke, 1983). Sixty-two participants were at least partially retired from work. Among these participants, 51 participants stated disability and 11 participants stated age as the reason for their retirement. A comparison with an unselected MS patient sample at the Kliniken Schmieder suggests that the recruited participants were representative for the patient population.

2.2. Memory tests

We assessed working memory and semantic memory with the inventory for memory diagnostics (Inventar zur Gedächtnisdiagnostik, IGD Baller et al., 2006), an established normed German memory battery.

2.2.1. Working memory

The four working memory tests (subtests A2–A5) measure the ability to shortly store information, to manipulate it, and to shift attention between different sources of information. In the digit span task, a sequence of digits is read out to each participant and the participant has to remember the digits in correct order. In the verbal working memory task, the participant has to remember all words containing the letter "r" from a list of 14 words read out to her. In the visual working memory task, participants remember the position and alignment of seven lines and later place the lines into a blank square. In the executive control task, nine boxes contain a different number of grey and black triangles and circles. Participants have to count and remember the number of grey items in each box with the color of triangles and circles alternating between boxes.

2.2.2. Semantic memory

The semantic memory tests (subtests B1–B4) measure previously acquired semantic knowledge across four domains: object, concept, word, and factual knowledge. For instance, the object knowledge task asks participants to map typical features (e.g., "weight": "100 kg", "12 kg", "1 g", "200 g", "1000 kg", "30 kg") onto five different objects (e.g., "feather", "car", "bike", "refrigerator", "pocketbook").

2.3. Decision-making competence

We translated the A-DMC to German according to a committee approach. A professional interpreter back-translated the German version to English. As in the Italian version, we modified some items because of cultural differences (Del Missier et al., 2010). A sample of healthy relatives ($n = 87$, 51 females, $M_{Age} = 48.9$, $SD_{Age} = 14.4$) completed the translated A-DMC in paper-pencil format. Reliabilities were comparable to previous studies (Del Missier et al., 2013), ranging from Cronbach's $\alpha = 0.51$ for Resistance to Sunk Costs to $\alpha = 0.78$ for Resistance to Framing.

2.3.1. Resistance to framing

How a decision problem is described or framed often affects decisions in formally equivalent problems (Tversky and Kahneman, 1981). The Resistance to Framing task measures how resistant people are to framing with seven attribute framing and seven risky-choice problems. In attribute framing, for instance, the effectiveness of a new condom is described with a 95% success rate in the positive frame and with a 5%

failure rate in the negative frame. Participants express endorsement on a 6-point Likert scale, ranging for instance from "Insecure" to "Secure". A lower mean absolute difference between the ratings for positive and negative frames indicates a higher resistance to the framing effect (reverse coded).

2.3.2. Under/overconfidence

The Under/Overconfidence task measures the degree to which the confidence in one's own knowledge reflects also its accuracy. Participants answered 34 true/false general knowledge statements (e.g., "There is no way to improve your memory.") and indicated how confident they were of their answer on a scale from 50% ("just guessing") to 100% ("absolutely sure"). A smaller absolute difference between the percentage of correct answers and average confidence reflects less under/overconfidence.

2.3.3. Applying decision rules

The Applying Decision Rules task assesses how accurately participants apply a specified decision rule. In ten multi-attribute decisions, participants choose between fictitious DVD players with different features (e.g., sound quality) according to a predefined decision rule. The complexity of the decision rules varies from rules considering only one attribute (e.g. sound quality) to rules integrating information from all presented attributes. Task performance is measured as the proportion of correctly chosen DVD-Players.

2.3.4. Consistency in risk perception

Participants judge the probability of ten events (e.g., dying in a terrorist attack) happening within a timespan of one and five years on a scale from 0% ("no chance") to 100% ("certain"). Probability judgments are scored based on their agreement with probability principles. For instance, participants should judge the probability for an event happening within the next year as lower as the probability of the same event happening within the next five years. Performance is evaluated by the proportion of correctly applied probability principles to the 20 event pairs.

2.3.5. Resistance to sunk costs

Normatively, one should ignore unrecoverable past investments and concentrate on the future consequences of a decision. One's ability to ignore prior invested unrecoverable financial and time costs (sunk costs) is measured by the Resistance to Sunk Costs scale (e.g., "... you ordered a big dessert..., after a few bites you find you are full: would you be more likely to eat more or to stop eating it?"). In ten problems, participants express a preference for the sunk-cost option (e.g., "most likely to continue eating") compared to the normatively correct option (e.g., "most likely to stop eating") on a 6-point Likert scale. Performance is calculated as the average rating for the normatively correct option.

2.4. Clinical assessments

Disability was assessed by experienced neurologists with the Expanded Disability Status Scale (EDSS Kurtzke, 1983). Medical data was collected from the clinical record. The subjective severity of cognitive fatigue was assessed with the cognitive functioning subscale from the Fatigue Scale for Motor and Cognitive Functions (FSMC Penner et al., 2009); the severity of a depressive disorder was measured with the Rasch-based Depression Screening (DESC-II Forkmann et al., 2011).

2.5. Procedure

Participants gave written informed consent in line with the Declaration of Helsinki after reading the study description on an information sheet and a personal meeting with one researcher.

Participants were tested in two sessions in their room. Testing times matched the participants' best daily performance. In the first session, participants were first tested on working memory, next semantic memory, and finally filled out the depression and cognitive fatigue scales. In the second session, participants filled out the A-DMC questionnaire in the order: (1) positively framed Resistance to Framing, (2) Under/Overconfidence, (3) Applying Decision Rules, (4) Consistency in Risk Perception, (5) Resistance to Sunk Costs, (6) negatively framed Resistance to Framing. Participants with physical problems received assistance in filling out the questionnaires. Participants received feedback about their test performance if desired.

2.6. Analysing the relationship between memory performance and decision making

To understand to what degree memory predicts decision making in individuals with MS, we first established a measurement model for "working memory" and "semantic memory" within a confirmatory factor analysis. This measurement model specified which memory tests measure the latent constructs "working memory" and "semantic memory" and estimated how strongly working memory and semantic memory are correlated.

In a next step, we tested in a regression-based structural model which memory construct predicted decision making as measured with each A-DMC subtest (Anderson and Gerbing, 1988; Del Missier et al., 2013; Kline, 2011). In line with previous studies (Del Missier et al., 2012; 2013), we predicted that working memory facilitates decisions in cognitive demanding tasks (Resistance to Framing, Under/Overconfidence, Applying Decision Rules), whereas semantic memory helps knowledge-based decisions (Consistency in Risk Perception, Resistance to Sunk Costs) or tasks requiring the comprehension of complex instructions (Applying Decision Rules). To test these assumptions, we compared the candidate model that, for instance, postulated a relationship between working memory and resistance to framing, against two competitors: A null model specifying that memory does not predict resistance to framing and a full-path model specifying that working memory and semantic memory contribute to resistance to framing. If only working memory predicts resistance to framing, then this candidate model should outperform the null model, but adding semantic memory as a predictor should not further improve model fit.

Regression weights were tested using χ^2 difference tests that compared the model with the hypothesised relationship to competitors without that relationship. All analyses were controlled for age and education.¹ Because of deviations from multivariate normality, we estimated all models using a maximum likelihood estimator with robust standard errors (MLM) and Satorra-scaled χ^2 values (scaling factor, SF, for χ^2 difference tests, Satorra and Bentler, 2001). Model fit was evaluated with several fit indices (reference thresholds in brackets): χ^2 , the standardized root-mean-square residual (SRMR < 0.06), the comparative fit index (CFI > 0.95), and the root-mean-square error of approximation (RMSEA < 0.05, Iacobucci, 2010; Kline, 2011).

3. Results

3.1. Descriptive statistics

Normed percentile ranks based on the inventory for memory diagnostics indicated that working memory was below average in participants ($M = 34.2\%$, $SD = 31.0$, Table 1 for descriptive statistics for all

¹Controlling in addition for EDSS did not alter any major conclusion. Semantic memory predicted slightly worse how accurately participants followed decision rules when accounting for individual differences in working memory, $\Delta\chi^2(1) = 2.7$, $p = .102$, but the estimated coefficient did not change in magnitude, $b = 0.25$ (0.13).

Table 1
Descriptive statistics for memory, decision-making competence, and clinical measures.

Measure	<i>M</i>	<i>SD</i>	Min	Max	Skewness	Kurtosis	Reliability
Working memory							
Digit Span	7.6	1.9	3	12	0.1	- 0.3	0.67 ^a
Verbal WM	15.2	3.6	2	21	- 0.9	0.7	
Visual WM	12.1	5.0	1	21	- 0.2	- 1.0	
Executive Control	14.5	5.7	2	25	- 0.1	- 0.8	
Semantic memory							
Object knowledge	97.2	3.4	68	100	- 5.0	38.4	0.67 ^a
Concept knowledge	97.3	4.2	73	100	- 2.3	7.7	
Word knowledge	18.4	1.9	11	20	- 1.8	3.3	
Factual knowledge	86.5	8.2	62	99	- 0.8	0.2	
A-DMC							
Resistance to Framing	3.9	0.7	1.2	5.0	- 0.9	1.5	0.72 ^b
Under/Overconfidence	0.90	0.07	0.71	1.00	- 0.7	- 0.4	0.56 ^b
Applying Decision Rules	0.67	0.16	0.13	0.93	- 0.5	0.1	0.68 ^b
Consistency in Risk Perception	0.77	0.13	0.35	1.00	- 0.6	0.3	0.59 ^b
Resistance to Sunk Costs	4.5	0.7	2.30	6.00	- 0.5	0.0	0.59 ^b
Clinical assessments							
Cognitive Fatigue	32.1	10.0	10	49	- 0.5	- 0.9	0.93 ^b
Depression	11.6	8.4	0	39	0.7	0.0	0.93 ^b
EDSS	4.0	2.1	1	8	0.2	- 1.1	— ^c

Note. WM = working memory; A-DMC = Adult Decision-Making Competence; EDSS = Expanded Disability Status Scale.

- ^a Composite reliability.
- ^b Cronbach's α .
- ^c EDSS score taken from medical record.

measures), but semantic memory was not impaired ($M = 47.5\%$, $SD = 36.5$). Our participants with diagnosed MS performed similar to healthy participants on decision making tasks (Bruine de Bruin et al., 2007; Del Missier et al., 2013). Most participants reported moderate ($N = 21$, 15.3%) or severe ($N = 73$, 53.3%) cognitive fatigue symptoms and only a few participants did not experience any ($N = 27$, 19.7%) or mild symptoms ($N = 16$, 11.7%). 63 participants could be classified as experiencing a depressive episode according to the Rasch-based depression screening (46%).

3.2. Measuring working and semantic memory

We expected that all working memory tests relate to the construct "working memory" and all semantic memory tests relate to the construct "semantic memory". In addition, participants with a better working memory may also possess a better semantic memory, that is, "working memory" and "semantic memory" are moderately correlated (Del Missier et al., 2012; 2013). Although this measurement model outperformed a model assuming that working and semantic memory are uncorrelated, $\Delta\chi^2(1) = 28.5$, $p < .001$, or a model assuming that working and semantic memory are identical, $\Delta\chi^2(1) = 10.2$, $p < .001$ (see Table 2 for fit indices), not all fit indices indicated a satisfying fit. Modification indices suggested an insufficient discriminant validity of word knowledge (MI = 12.9) so that we excluded word knowledge. The revised model without word knowledge proposed that participants with a better working memory more successfully retrieve knowledge from semantic memory (Fig. 1).

3.3. Predicting decision making with memory

In most cognitively demanding tasks, participants with higher working memory scored higher on decision making competence (see Table 3 for model fits). Participants with higher working memory more likely resisted framing effects, $\Delta\chi^2(1) = 12.2$, $p < .001$, but semantic memory did not increase resistance to framing further, $\Delta\chi^2(1) = 1.7$, $p = .189$. Likewise, in the over-/underconfidence task, working memory predicted how well participants' confidence ratings

Table 2
Confirmatory factor analysis of memory.

Model	SRMR	RMSEA	CFI	χ^2	<i>df</i>	SF	<i>p</i>
WM + SM	0.06	0.05	0.93	25.9	19	1.3	.133
WM + SM (uncorrelated)	0.21	0.13	0.52	68.9	20	1.3	< .001
Unitary	0.07	0.06	0.89	31.6	20	1.3	.047
WM + SM (revised)	0.05	0.04	0.97	15.4	13	1.0	.282

Note. WM = working memory; SM = semantic memory; SRMR = standardized root-mean-squared residual; RMSEA = root-mean-square error of approximation; CFI = comparative fit index; SF = Scaling Factor.

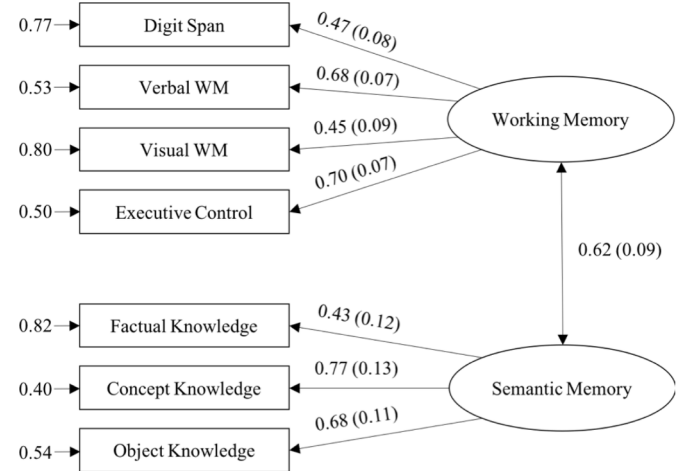


Fig. 1. The revised measurement model suggesting a correlation between working memory and semantic memory. Arrows indicate standardized factor loadings; double-headed arrows indicate correlations; residual variances are displayed at the arrows to the memory tests. Standard errors in parentheses.

represented their knowledge, $\Delta\chi^2(1) = 6.2$, $p = .01$. Predicting over-/underconfidence jointly with working and semantic memory further improved the prediction $\Delta\chi^2(1) = 15.2$, $p < .001$. Regression weights in this model suggest that participants with a better semantic memory successfully adjust their confidence ratings to the knowledge they possess, but working memory contributes little to well-calibrated confidence ratings. Finally, applying decision rules should draw on working memory and semantic memory. In line with this idea, participants with a higher working memory applied decision rules more accurately, $\Delta\chi^2(1) = 34.2$, $p < .001$, as did participants with a better semantic memory, $\Delta\chi^2(1) = 32.9$, $p < .001$. Jointly considering both memory abilities further improved model fit, $\Delta\chi^2(1) = 5.8$, $p = .016$, but the higher regression weight for working memory indicates that working memory may be more important for following decision rules.

In knowledge-based tasks, participants with a better semantic memory perceived risks more consistently, $\Delta\chi^2(1) = 9.5$, $p < .002$, but participants with a higher working memory did not, $\Delta\chi^2(1) = 3.7$, $p = .054$. Finally, a better semantic memory did not help to resist sunk costs, $\Delta\chi^2(1) = 0.5$, $p = .497$, nor did working memory explain better why people resist sunk costs, as indicated by the unsatisfying model fits. Thus, memory did not contribute to resisting sunk costs.

3.4. Cognitive fatigue and depression as predictors for memory

Depression and cognitive fatigue were expected to impede memory and, in turn, to be negatively correlated with decision making skills. Yet, neither cognitive fatigue, $\Delta\chi^2(2) = 2.8$, $p = .240$, nor depression, $\Delta\chi^2(2) = 1.4$, $p = .477$, predicted working and semantic memory (Table 4). Consequently, depression and cognitive fatigue unlikely explain why lower memory performance is associated with lower decision making skills in individuals with MS.

Table 3
Fit indices for models predicting decision making with memory.

DM	Model	SRMR	RMSEA	CFI	χ^2	df	SF	p	WM → DM	SM → DM
RCA	FP	0.05	0.02	0.98	19.4	18	1.0	.370	0.31 (0.13)	0.28 (0.19)
	WM	0.05	0.03	0.98	20.6	19	1.2	.359	0.53 (0.13)	—
	Null	0.14	0.08	0.77	36.7	20	1.5	.013	—	—
CAL	FP	0.05	0.01	1.00	18.1	18	1.1	.452	−0.11 (0.17)	0.52 (0.14)
	WM	0.07	0.07	0.86	30.7	19	1.0	.044	0.31 (0.11)	—
DR	Null	0.11	0.08	0.80	36.3	20	1.1	.014	—	—
	FP	0.05	0.04	0.95	22.7	18	1.1	.201	0.43 (0.15)	0.28 (0.13)
	WM	0.06	0.06	0.92	27.0	19	1.0	.104	0.65 (0.09)	—
RP	SM	0.06	0.05	0.92	26.5	19	1.2	.116	—	0.64 (0.08)
	Null	0.16	0.13	0.53	66.8	20	1.2	.001	—	—
	FP	0.05	0.02	0.99	19.1	18	1.0	.387	0.25 (0.14)	0.22 (0.13)
SC	SM	0.05	0.03	0.96	21.9	19	1.0	.291	—	0.41 (0.10)
	Null	0.12	0.07	0.82	34.2	20	1.2	.025	—	—
	FP	0.06	0.07	0.85	29.4	18	1.1	.044	−0.26 (0.14)	0.31 (0.19)
SM	SM	0.07	0.07	0.83	31.6	19	1.1	.035	—	0.11 (0.15)
	Null	0.07	0.06	0.88	29.4	20	1.2	.080	—	—

Note. The endorsed model is indicated in bold. Regression coefficients for memory on the decision task are indicated by →. Standard errors in parentheses. DM = Decision Making Task; RCA = Resistance to Framing; CAL = Under/Overconfidence; DR = Applying Decision Rules; RP = Consistency in Risk Perception; SC = Resistance to Sunk Costs; FP = full-path model; WM = working memory; SM = semantic memory; SRMR = standardized root-mean-squared residual; RMSEA = root-mean-square error of approximation; CFI = comparative fit index; SF = Scaling Factor.

Table 4
Fit indices for models predicting memory with the clinical assessments.

Scale	SRMR	RMSEA	CFI	χ^2	df	SF	p	CA → WM	CA → SM
Fatigue	0.07	0.07	0.83	42.4	25	1.0	.016	−0.11 (0.10)	0.06 (0.08)
Depression	0.08	0.07	0.82	43.6	25	1.0	.012	0.05 (0.09)	0.11 (0.10)
Null	0.08	0.07	0.82	45.6	27	1.0	.014	—	—

Note. The endorsed model is indicated in bold. Regression coefficients for clinical assessments on memory are indicated by →. Standard errors in parentheses. CA = Clinical Assessment; WM = working memory; SM = semantic memory; SRMR = standardized root-mean-squared residual; RMSEA = root-mean-square error of approximation; CFI = comparative fit index; SF = Scaling Factor.

4. Discussion

Making informed, competent treatment and life decisions may pose a challenge for individuals with MS (Cofield et al., 2017). Facilitating those decisions has recently attracted more attention because decision making skills affect treatment compliance and adherence (D’Amico et al., 2016; Gaissmaier et al., 2018; Reen et al., 2017). This study investigated to what degree memory deficits carry over to decision making in individuals with MS. Using an established memory battery (Baller et al., 2006), we replicated previous findings that individuals with MS show working memory deficits, whereas semantic memory is less impaired (Chiaravalloti and DeLuca, 2008). Working memory was associated with semantic memory, matching findings in a healthy sample (Del Missier et al., 2013).

Compared to previous studies, we assessed decision making competence with the broad, multidimensional A-DMC battery (Bruine de Bruin et al., 2007). Our analyses revealed that limited working memory capacity predicted resistance to framing as well as the capacity to follow decision rules (Del Missier et al., 2013). In combination, these results indicate that working memory deficits in MS may carry over to decisions that require to focus on relevant information and suppress irrelevant information. Framing and communicating decision alternatives, such as treatment options, thoroughly may thus be particularly important for MS patients with known working memory impairments.

Semantic memory predicted over- and underconfidence, consistency in risk perception as well as applying decision rules. Replicating previous findings (Del Missier et al., 2013), these associations highlight that every-day decision tasks often demand retrieving previously learned knowledge from long-term memory, ranging from understanding complex instructions to judging the likelihood of events. It is less clear why better semantic memory predicted a more accurate assessment of one’s own knowledge. Potentially, raised awareness to their

own memory failures helps individuals with good semantic memory to still keep track of their knowledge, but once semantic memory worsens, they are unable to assess their lack of knowledge. In a shared decision-making setting, this might imply that patients’ ability to monitor their disease-related knowledge worsens as a function of cognitive decline.

In contrast to previous work (Bruine de Bruin et al., 2012; Del Missier et al., 2013), we did not find any association between memory and resisting sunk costs. Potentially, depression in MS suppressed the affect-laden processes underlying sunk cost effects (Szanto et al., 2015). This result might be clinically relevant, as depressed patients might give up earlier on treatments that do not show fast initial success.

4.1. Limitations and future research

Although the majority of individuals with MS reported cognitive fatigue and depressive symptoms, our results do not provide any evidence that those clinical symptoms further aggravate memory impairments. These absent links resonate well with the notion that depression is not causally linked to cognitive abilities in MS (Arnett, 2005; Demaree et al., 2003) and that cognitive fatigue does not consistently predict cognitive abilities (Hanken et al., 2015). Still, objective measures of fatigue could provide a more fine-grained picture of the relationship between decision skills and memory impairments in individuals with MS.

In our study, we followed a cross-sectional confirmatory approach to test which memory components underlie decision making in individuals with MS. This approach comes at the cost of a comprehensive neurological and pharmacological assessment that may further shed light on the causes of memory and decision making problems within MS. Brain atrophy as well as widespread microscopic brain tissue damage have been associated with distinct patterns of cognitive decline (Amato et al., 2007; Vinciguerra et al., 2019) and may thus also impact

differentially on decision making. Unfortunately, our study lacks the necessary structural MRI data to further investigate the neurological underpinnings of decision making deficits in MS. In addition, it would be worthwhile to note if the memory impairments in MS give rise to more severe impairments in decision making than in a healthy control group, a conclusion that can only be drawn from a design with a healthy control group. Finally, we did not aim to cover all memory components. Future work may more thoroughly investigate to what degree measures of episodic memory or executive functioning, such as inhibition, contribute to accurate decisions. This may help to design treatment information in such a way that individuals with MS can process this information easily and reach a decision consistent with their goals and needs. Such a more naturalistic design may further shed light on how integrating information in working memory affects clinically relevant treatment decisions in MS.

5. Conclusion

Memory impairments are frequently reported in MS. Our study suggests that those impairments reach out to higher-order cognitive functions, such as decision making. Improving treatment decisions in MS thus likely benefits from acknowledging the patients' memory limits and match the information provided to the patient's memory abilities.

Declaration of Competing Interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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