ORIGINAL ARTICLE

Improvement of medical judgments by numerical training in patients with multiple sclerosis

L. Zamarian[a,*], M. Delazer[a,*], R. Ehling[b], M.-T. Pertl[a], G. Bsteh[a], J. Wenter[b], S. Glatzl[b], C. Brenneis[b], T. Benke[a] and T. Berger[a]

[a]*Medical University of Innsbruck, Innsbruck; and* [b]*Clinic for Rehabilitation Münster, Münster, Austria*

Keywords:
cognition, decision making, intervention, multiple sclerosis, relapsing-remitting, risk comprehension

Received 17 July 2018
Accepted 9 August 2018

European Journal of Neurology 2019, **26:** 106–112

doi:10.1111/ene.13778

Background and purpose: People with multiple sclerosis (MS) have to face important decisions with regard to their medical treatment. The aim of this study was to evaluate whether a targeted cognitive training reduces framing effects and thus improves medical judgments.
Methods: This was a randomized, double-blind, cross-over study enrolling patients with relapsing-remitting MS and healthy controls (HCs). Participants were randomly assigned to training order A (first week, numerical training; second week, control training) or B (reverse order). The primary endpoint was changed in a framing task score (framing effect). In the framing task, participants evaluated the success of fictive medications on a 7-point scale. Medications were described in either positive or negative terms.
Results: A total of 37 patients and 73 HCs performed either training order A (n = 56) or B (n = 54). The framing effect decreased after the numerical training regardless of training order. No such decrease was found after the control training. Mean change in framing effect was -0.3 ± 0.8 after the numerical training and 0.03 ± 0.6 after the control training. This specific effect of training type was comparable between groups.
Conclusion: Judgments of medical information improve in both patients with relapsing-remitting MS and HCs after a targeted numerical training. Thus, a specific cognitive intervention may help patients making informed decisions.

Introduction

Risk understanding is essential for participating in health care and making informed decisions. Health-related information contains complex numerical concepts such as probabilities, fractions or percentages (e.g. 1 out of 6, ¾ or 20%; hereafter, ratio concepts) [1], which are challenging for many people [2,3]. Poor ratio processing is often associated with poor decision making [1] and stronger framing effects [4]. The term *framing effect* means that the way that information is presented influences individuals' preferences and decisions [5]. Neurological patients with cognitive impairments show stronger framing effects than cognitively preserved people [6], which could bias their medical decisions.

People with multiple sclerosis (MS) have to face important decisions regarding their medical treatment. Thus, intact risk understanding is crucial. Promising disease-modifying therapies for MS, especially those used for treatment escalation (e.g. natalizumab), offer substantial benefits but are also associated with potentially serious, even life-threatening side-effects [7,8]. As compared with their treating physicians, patients perceive MS as more disabling and are willing to accept higher risks of treatment side-effects [9]. Patients with MS also show some difficulties in advantageous decision making [10,11]. In this study, we examined whether a targeted numerical training reduces framing effects and thus improves the evaluation of medical information in patients with MS and healthy controls (HCs). We hypothesized that focusing attention on numerical information should lead to reduced framing

Correspondence: L. Zamarian, Medical University of Innsbruck, Anichstrasse 35, 6020 Innsbruck, Austria (tel.: +43 51250423661; e-mail:laura.zamarian@i-med.ac.at).
*These authors have contributed equally to the paper.

effects. However, a control (non-numerical) training should not lead to performance changes. Lower framing effects after training might indicate a lower influence of the information frame and higher reliance on analytical information processing.

Methods

Participants

We recruited 174 participants: 70 patients with a confirmed diagnosis of relapsing-remitting MS (RRMS) [12] and 104 HCs. Exclusion criteria were: history of a major medical, psychiatric or neurological disorder other than RRMS and substance abuse or steroid treatment for MS relapse within 6 weeks prior to evaluation. We also excluded patients with current major depressive episodes or an Expanded Disability Status Scale (EDSS) [13] score >4. All participants had an estimated verbal intelligence quotient of at least 85. The study was approved by the ethics committee of the Medical University of Innsbruck (ethical approval number: UN2013-0056, 332/4.5). Informed consent was obtained from all individuals before participation.

Procedure

Of the 174 participants, 37 patients with RRMS and 73 HCs agreed to participate in the training study (we report here the data of these 110 participants). The remaining participants performed a neuropsychological baseline assessment and scored comparably to the participants of the training study. A schematization of the study procedure is given in Fig. 1. At baseline (T1), participants performed a neuropsychological assessment, ratio-processing tasks and a framing task. Subsequently, they received an envelope with training material, training order and written instructions. Training material and procedure were additionally explained by a laboratory employee. Training order was placed in an extra sealed envelope that could only be seen by the participant. We used a double-blind, controlled, cross-over design with participants being randomly assigned to training order A (first week, numerical training; second week, control training) or B (reverse order). All personnel were masked to treatment assignment. Participants were not informed about the differences between interventions or the expected results. After T1, participants performed 2 weeks of training, each followed by a short examination [first follow-up (T2), second follow-up (T3); parallel task versions were used in counterbalanced order].

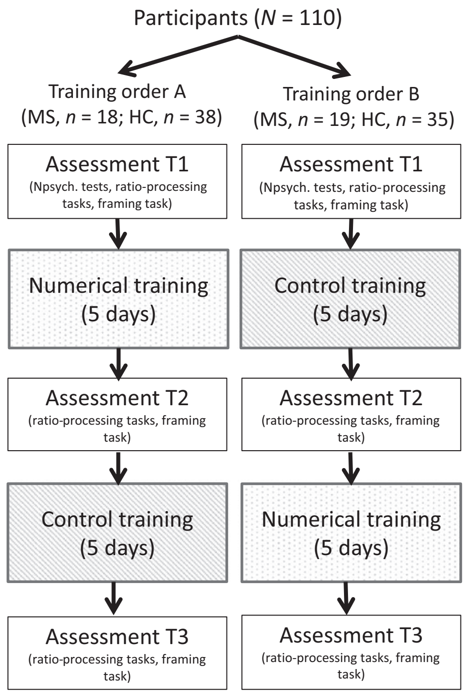

Figure 1 Schematization of study procedure. HC, healthy control; MS, multiple sclerosis. T1, baseline; T2, first follow-up; T3, second follow-up.

Training compliance and results were checked at the end of T3 by L.Z. The majority of participants judged the two trainings as comparably difficult.

Neuropsychological background assessment

Tests assessed logical reasoning, response inhibition, verbal attention span, verbal working memory and mental complex calculation (see Appendix S1, online only). Participants also responded to a questionnaire on anxiety and depression symptoms. Additionally, they performed two ratio-processing tasks in which they were, for example, required to convert percentages or compare proportions. The percentage of total correct answers in both tasks was submitted to analysis.

Framing task

This task contained 20 statements about the success of fictive medications [6]. Participants were informed that medications were used for the treatment of mild diseases like a common cold and were asked to evaluate them on a 7-point color-based scale from negative (left side, red colored) to positive (right side, green colored). Answers were recorded by the examiner by associating a number to each point (from 1, left-most point to 7, right-most point). Medications were described using either positive (e.g. effective in 84% of cases) or negative (e.g. ineffective in 16% of cases) terms. Performance on the framing task (framing effect) was measured as the difference between scores given to positively framed items ($n = 10$) and negatively framed items ($n = 10$). A score difference above zero indicates that positively framed items are evaluated more positively than negatively framed items. We also computed a measure of changes in performance over time specific to the numerical training as 'Framing effect at T1 minus framing effect at T2' for the participants assigned to training order A and 'Framing effect at T2 minus framing effect at T3' for the participants assigned to training order B. This measure was used in the correlation analysis.

Numerical training

In the first two sessions, participants had to link percentages and frequencies to pictographs and to convert frequencies to percentages and vice versa. In the third session, they performed comparison tasks with symbolic (frequencies, percentages) and non-symbolic (pictographs) representations. In the fourth session, tasks required the comparison of decimals and fractions and the conversion of decimals into fractions and vice versa. In the last session, participants had to compute discounted prices (see Appendix S1, online only).

Control training

In each of five sessions, participants received one page of text to read [14], followed by eight multiple-choice questions to probe text comprehension. Texts contained either no numerical information or integers (e.g. 34) but no ratio numbers.

Statistics

Groups were compared by chi-square test (gender), independent-sample *t*-tests (age, education) and MANOVA (neuropsychological tests). A mixed ANOVA with session (T1, T2, T3), training order (A, B) and group (RRMS, HCs) as factors was performed on the percentage of correct answers in ratio-processing tasks. Performance on the framing task was investigated by submitting score differences (framing effect) to a mixed ANOVA with session, training order and group as factors. A Pearson correlation analysis was carried out between the framing effect at T1, changes in framing effects over time specific to the numerical training and demographical/neuropsychological variables. Demographical/neuropsychological variables showing a significant correlation with the framing effect at T1 or the changes in performance over time specific to the numerical training were then entered into a stepwise regression analysis as predictors of interest. Correlation and regression analyses were performed on the whole sample. An additional Spearman rank-order correlation analysis was carried out for the patient group between framing effects at each time point, clinical variables (disease duration, EDSS score) and measures of fatigue (Fatigue Severity Scale [15], currently perceived fatigue). Significance was set at $\alpha = 0.05$.

Results

Characteristics at T1 are given in Table 1. Groups had comparable age and education. There were more female participants in the patient group than in the control group.[1]

Neuropsychological background performance

Descriptive statistics and results of the MANOVA are presented in Table 2. Mean scores of both groups were in the average range of standardized norms in all tests. Groups did not differ in tests of response inhibition, verbal attention span, verbal working memory and mental complex calculation. However, patients scored lower than controls in logical reasoning. Patients also obtained higher (mild) depression scores than controls, whereas groups did not differ in anxiety scores.

Ratio-processing tasks

There was a significant main effect of group ($F_{1,106} = 5.49$, $P = 0.021$, $d = -0.45$, moderate effect size), with patients scoring lower than controls (mean $\pm$ SD: RRMS, 78.0 $\pm$ 19.6% correct answers; HCs, 85.9 $\pm$ 14.9% correct answers). The main effect of session was also significant ($F_{2,212} = 15.30$, $P < 0.001$). *Post hoc* contrasts indicated that accuracy increased from T1 to T2 ($P < 0.001$) and remained stable between T2 and T3 ($P = 0.537$). The mean accuracy in ratio-processing tasks was 79.4 $\pm$ 21.4% at T1, 84.8 $\pm$ 16.7% at T2 and 85.5 $\pm$ 17.0% at T3. Other results were not significant (all $P > 0.1$). The number of participants who responded at ceiling (100% correct answers) was 18 (16.4%) at T1, 19 (17.3%) at T2 and 28 (25.4%) at T3.

Framing task

There was a significant main effect of group ($F_{1,106} = 4.20$, $P = 0.043$, $d = 0.46$, moderate effect

[1]Gender showed no significant influence on performance.

Table 1 Characteristics of patients with multiple sclerosis (MS) and healthy controls (HCs)

	Patients with MS (n = 37)	HCs (n = 73)	Cohen's d	t-value	P-value
Female[a]	27 (73.0)	39 (53.4)	n.a.	n.a.	0.048[b]
Age at T1 (years)[c]	43.30 (10.55)	38.96 (14.30)	0.34	t_{108} = 1.63	0.105[d]
Education at T1 (years)[c]	12.97 (3.02)	13.71 (2.44)	−0.27	t_{108} = −1.38	0.169[d]
EDSS score[e]	2.0 (0–4)	n.a.			
Disease duration (years)[c]	10.39 (7.74)	n.a.			
Current DMT at T1					
Fingolimod[a]	6 (16.2)	n.a.			
Glatiramer acetate[a]	6 (16.2)	n.a.			
Interferon beta-1a i.m.[a]	5 (13.5)	n.a.			
Natalizumab[a]	4 (10.8)	n.a.			
Interferon beta-1a s.c.[a]	3 (8.1)	n.a.			
Other[a]	3 (8.1)	n.a.			
None[a]	10 (27.1)	n.a.			
FSS score[c]	4.45 (1.43)	n.a.			
Currently perceived fatigue (from 0, no fatigue to 10, extreme fatigue)[c]	2.35 (2.08)	n.a.			

DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; FSS, Fatigue Severity Scale; i.m., intramuscular; n.a., not applicable; s.c., subcutaneous; T1, baseline; [a]n (%); [b]Chi-square test; [c]Mean (SD); [d]Independent-sample t-test; [e]Median (range).

Table 2 Scores in neuropsychological background tests of patients with multiple sclerosis (MS) and healthy controls (HCs)

	Max. score	Patients with MS (n = 37) Mean	HCs (n = 73) Mean	Cohen's d	F-value	P-value
Overall MANOVA					$F_{8,101}$ = 2.11	0.041
Logical reasoning (test score)	25	16.8 (3.4)	18.2 (3.3)	−0.41	$F_{1,108}$ = 4.25	0.042
Response inhibition time (ms)		425.0 (82.3)	408.1 (62.9)	0.23	$F_{1,108}$ = 1.44	0.234
Response inhibition (errors)		1.2 (2.0)	0.8 (1.2)	0.25	$F_{1,108}$ = 1.83	0.179
Verbal attention span (test score)	12	8.0 (2.0)	8.0 (1.7)	−0.01	$F_{1,108}$ = 0.00	0.942
Verbal working memory (test score)	12	6.7 (2.2)	6.9 (2.0)	−0.08	$F_{1,108}$ = 0.18	0.674
Mental complex calculation (test score)	16	15.1 (1.0)	15.2 (1.2)	−0.04	$F_{1,108}$ = 0.04	0.851
Anxiety score	21	5.0 (3.6)	4.2 (2.8)	0.26	$F_{1,108}$ = 1.84	0.178
Depression score	21	3.5 (3.3)	2.4 (2.3)	0.39	$F_{1,108}$ = 4.23	0.042

Data are given as Mean (SD).

size), with patients showing overall stronger framing effects than controls (RRMS, 1.0 ± 1.0; HCs, 0.6 ± 0.7). The main effect of session was also significant ($F_{2,212}$ = 4.21, P = 0.016). *Post hoc* contrasts indicated that the framing effect was smaller at T3 (0.6 ± 0.9) than at T1 (0.9 ± 0.9; P = 0.009) and T2 (0.8 ± 1.0; P = 0.043). The contrast T1 vs. T2 was not significant (P = 0.244). There was also a significant interaction between session and training order ($F_{2,212}$ = 3.79, P = 0.024; Fig. 2). *Post hoc* comparisons demonstrated that, regardless of the training order, the framing effect decreased after 1 week of numerical training (both $P < 0.05$). No such decrease was found after 1 week of control training (both $P > 0.1$). Mean change in framing effect was −0.3 ± 0.8 after the numerical training and 0.03 ± 0.6 after the control training. Other results were not significant (all $P > 0.1$).

Healthy controls without training

In order to assess possible test–retest effects, we recruited an additional 25 healthy individuals (age, 41.7 ± 21.2 years; education, 13.8 ± 2.2 years). This new group of HCs performed the three assessments at weekly intervals but received no training in between. Performance on framing and ratio-processing tasks was separately analyzed by means of repeated-measures ANOVA with session as between-subject factor. Results showed no performance changes over time in any measure (Table S1, online only; all $P > 0.1$), even when individuals performing at ceiling (first assessment) were excluded.

Correlation analysis

A stronger framing effect at T1 was associated with older age, lower education and lower scores in logical reasoning, verbal working memory, mental complex calculation and ratio processing. A reduction in framing effects following the numerical training was more evident for those persons who showed a stronger framing effect at T1. Other results were not significant (Table 3 for *r*- and *P*-values). The association of framing effect at T1 with education, logical reasoning, ratio processing and changes in framing effects over time remained significant after Bonferroni correction ($\alpha = 0.0024$).

No significant correlations were found for the patient group between framing effect at any time point, disease duration, EDSS score, Fatigue Severity Scale and perceived fatigue (Table 4).

Regression analysis

A stepwise regression analysis was conducted to evaluate whether logical reasoning, verbal working memory, mental complex calculation, ratio processing, age and education could predict the framing effect at T1. We found a significant model ($F_{1,108} = 22.94$, $P < 0.001$), with 'logical reasoning' entering into the regression equation and being significantly correlated with the dependent variable. The multiple correlation coefficient was 0.18, indicating that approximately 16.8% of variance in the framing effect could be accounted for by performance on the logical reasoning test. Other variables were removed.

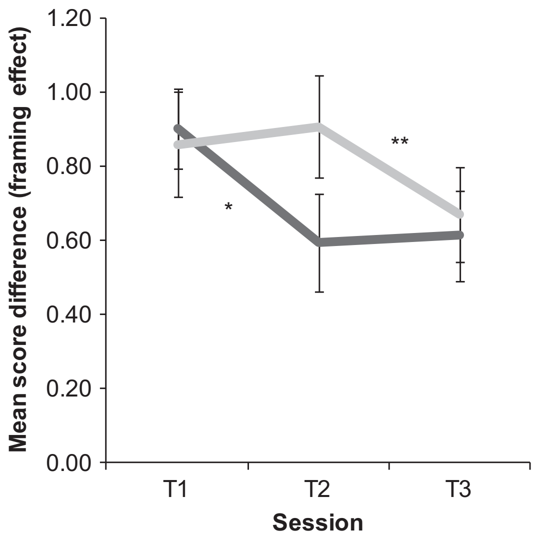

Figure 2 Performance on the framing task of patients with multiple sclerosis and healthy controls. T1, baseline; T2, first follow-up; T3, second follow-up. Error bars are standard errors of the mean. $*P < 0.05$; $**P < 0.01$. Gray line, control training/numerical training; black line, numerical training/control training.

Discussion

This study shows for the first time that a targeted cognitive training improves the evaluation of medical information in both patients with RRMS and HCs. In a controlled cross-over design, patients with RRMS and HCs underwent both a numerical training and a control (non-numerical) training. Participants were tested on a framing task before training and after each training week. Both patients with RRMS and HCs showed a significant effect of training type. Indeed, the framing effect decreased after 1 week of numerical training, whereas performance did not change following 1 week of control training. This finding cannot be explained by test–retest effects, as a second group of HCs, who performed the three assessments but no training in between, did not show any significant change over time. Regardless of the training type, patients were influenced more strongly than HCs by the information frame, which suggests particular caution in the communication of medical information to patients with MS. In a neuropsychological assessment, patients demonstrated minor alterations in logical reasoning, ratio processing and depression scores, whereas they performed comparably to HCs in tests of verbal attention span, verbal working memory, mental calculation, response inhibition and anxiety (for similar results see [10]).

The framing effect of the whole sample correlated with both demographic variables and cognitive scores, with stronger framing effects being associated with

Table 3 Coefficients of a Pearson correlation analysis on the whole sample ($n = 110$)

	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)
(1)	0.405 (<0.001)*	0.226 (0.018)*	−0.328 (<0.001)*	−0.419 (<0.001)*	−0.094 (0.330)*	−0.120 (0.212)*	−0.280 (0.003)*	−0.244 (0.010)*	−0.381 (<0.001)*	0.043 (0.656)*	−0.022 (0.819)*
(2)	—	−0.037 (0.703)*	−0.137 (0.154)*	−0.121 (0.207)*	0.028 (0.775)*	−0.070 (0.469)*	−0.126 (0.189)*	−0.094 (0.329)*	−0.034 (0.723)*	0.004 (0.969)*	0.019 (0.846)*

(1) Framing effect at baseline (difference score); (2) changes in framing effect over time specific to the numerical training; (3) age (years); (4) education (years); (5) logical reasoning (correct answers); (6) response inhibition (reaction times in ms); (7) verbal attention span (test score); (8) verbal working memory (test score); (9) mental complex calculation (correct answers); (10) ratio processing (correct answers); (11) anxiety (test score); (12) depression (test score); *r-value (P-value).

Table 4 Coefficients of a Spearman rank-order correlation analysis performed for the patient group (n = 37)

	(4)	(5)	(6)	(7)
(1)	−0.143 (0.399)*	0.084 (0.621)*	0.219 (0.193)*	0.244 (0.145)*
(2)	−0.221 (0.188)*	0.052 (0.758)*	0.188 (0.266)*	0.201 (0.234)*
(3)	−0.117 (0.491)*	−0.025 (0.881)*	0.111 (0.514)*	0.100 (0.556)*

(1) Framing effect at baseline (difference score); (2) framing effect at first follow-up (difference score); (3) framing effect at second follow-up (difference score); (4) disease duration (years); (5) Expanded Disability Status Scale; (6) Fatigue Severity Scale; (7) currently perceived fatigue; *r-value (P-value).

older age, lower education and lower performance in logical reasoning, working memory, mental calculation and ratio processing. However, only logical reasoning emerged as a significant predictor of variance in the framing task. In a recent study with patients with mild cognitive impairment [16], we showed that numerical training and training of executive functions have differential effects on performance in ratio processing. Only the numerical training proved to be effective. The effects of the two training types on decision making were less clear-cut. A future study might investigate the relative efficacy on medical judgments and framing effects of executive functions training (in particular, logical reasoning) in comparison to numerical training.

Evaluation of different options is a precondition for informed decision making. Previous studies with healthy individuals have shown that explicit reasoning about options, probabilities and consequences [17] as well as explicit advice about advantageous options [18] improves decision making under risk. Our results show that (i) training alters the way that medical information is evaluated; (ii) patients with RRMS and HCs can profit from cognitive training; and (iii) the type of training has specific effects. One might speculate that understanding and processing of ratio concepts improved through the numerical training. This might have led to a better understanding of the numerical information (percentages) presented in the framing task and thus to lower framing effects. However, other factors might also have played a relevant role. It has been shown that framing effects tend to diminish when people are encouraged to use analytical information processing instead of heuristic processing [19]. Reflective processing also moderates the effect of misleading information in decision making under risk [20].

Although these results are very promising, we should acknowledge some limitations. We investigated short-term effects of cognitive training. Other studies reported long-term effects and transfer to daily life activities [21]. Whether this also applies to improvements in medical judgments following a numerical training needs to be assessed. Also, we do not yet know whether the number of sessions plays a role and whether booster sessions are required at regular intervals. Furthermore, we did not find differences with regard to the effects of cognitive training between patients with RRMS and HCs. This finding might be due to the relatively small sample size masking potential differences. Moreover, our patient sample was cognitively well preserved. Future studies might include a larger patient sample with higher degree of disability and different MS forms.

Information seeking and understanding of numerical information are essential for good decision making in medical situations. It is possible that framing effects are lower after the numerical training because participants pay more attention to numbers, accept numbers as a useful information source and rely on numerical information more than on other information [22]. In the light of these findings, we suggest that a targeted cognitive training may enhance the evaluation of new information and may reduce framing effects. This in turn should favor informed decision making in the health context. This study adds to previous investigations on risk understanding in patients with MS [23–25].

Acknowledgements

We thank all patients and controls for their participation in the study. Support was received from Medical University of Innsbruck (MUI-START 2014-05-001).

Disclosure of conflicts of interest

The authors declare no financial or other conflicts of interest.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Neuropsychological background assessment.

Table S1. Performance on the framing and ratio-processing tasks of healthy individuals (n = 25) repeating the three assessments without training.

References

1. Reyna VF, Nelson WL, Han PK, Dieckmann NF. How numeracy influences risk comprehension and medical decision making. *Psychol Bull* 2009; **135:** 943–973.
2. Delazer M, Kemmler G, Benke T. Health numeracy and cognitive decline in advanced age. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn* 2013; **20:** 639–659.
3. Pertl M-T, Benke T, Zamarian L, *et al*. Do patients with mild cognitive impairment understand numerical health information? *J Alzheimers Dis JAD* 2014; **40:** 531–540.
4. Peters E, Västfjäll D, Slovic P, Mertz CK, Mazzocco K, Dickert S. Numeracy and decision making. *Psychol Sci* 2006; **17:** 407–413.
5. Tversky A, Kahneman D. The framing of decisions and the psychology of choice. *Science* 1981; **211:** 453–458.
6. Zamarian L, Benke T, Buchler M, Wenter J, Delazer M. Information about medications may cause misunderstanding in older adults with cognitive impairment. *J Neurol Sci* 2010; **298:** 46–51.
7. Hutchinson M. Natalizumab: a new treatment for relapsing remitting multiple sclerosis. *Ther Clin Risk Manag* 2007; **3:** 259–268.
8. Gupta S, Weinstock-Guttman B. Natalizumab for multiple sclerosis: appraising risk versus benefit, a seemingly demanding tango. *Expert Opin Biol Ther* 2014; **14:** 115–126.
9. Heesen C, Kleiter I, Nguyen F, *et al*. Risk perception in natalizumab-treated multiple sclerosis patients and their neurologists. *Mult Scler Houndmills Basingstoke Engl* 2010; **16:** 1507–1512.
10. Muhlert N, Sethi V, Cipolotti L, *et al*. The grey matter correlates of impaired decision-making in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2015; **86:** 530–536.
11. Simioni S, Schluep M, Bault N, *et al*. Multiple sclerosis decreases explicit counterfactual processing and risk taking in decision making. *PLoS ONE* 2012; **7:** e50718.
12. Polman CH, Reingold SC, Banwell B, *et al*. Diagnostic criteria for multiple sclerosis: 2010 Revisions to the McDonald criteria. *Ann Neurol* 2011; **69:** 292–302.
13. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology* 1983; **33:** 1444–1452.
14. Claros-Salinas D. *Texte Verstehen. Materialien für Diagnostik und Therapie. [Text Comprehension. Material for Diagnostic and Therapy.]* Vol. 3. Dortmund, Germany: Borgmann Publishing, 1993.
15. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. *Arch Neurol* 1989; **46:** 1121–1123.
16. Burgio F, Delazer M, Meneghello F, Pertl M-T, Semenza C, Zamarian L. Cognitive training improves ratio processing and decision making in patients with mild cognitive impairment. *J Alzheimers Dis* 2018; **64:** 1213–1226.
17. Pertl M-T, Zamarian L, Delazer M. Reasoning and mathematical skills contribute to normatively superior decision making under risk: evidence from the game of dice task. *Cogn Process* 2017; **18:** 249–260.
18. Schiebener J, Wegmann E, Pawlikowski M, Brand M. Supporting decisions under risk: explicit advice differentially affects people according to their working memory performance and executive functioning. *Neurosci Decis Mak* 2013; **1:** 9–18.
19. Kim S, Goldstein D, Hasher L, Zacks RT. Framing effects in younger and older adults. *J Gerontol B Psychol Sci Soc Sci* 2005; **60:** 215–218.
20. Schiebener J, Wegmann E, Pawlikowski M, Brand M. Anchor effects in decision making can be reduced by the interaction between goal monitoring and the level of the decision maker's executive functions. *Cogn Process* 2012; **13:** 321–332.
21. Rebok GW, Ball K, Guey LT, *et al*. Ten-year effects of the advanced cognitive training for independent and vital elderly cognitive training trial on cognition and everyday functioning in older adults. *J Am Geriatr Soc* 2014; **62:** 16–24.
22. Lipkus IM, Peters E. Understanding the role of numeracy in health: proposed theoretical framework and practical insights. *Health Educ Behav Off Publ Soc Public Health Educ* 2009; **36:** 1065–1081.
23. Bruce JM, Jarmolowicz DP, Lynch S, *et al*. How patients with multiple sclerosis weigh treatment risks and benefits. *Health Psychol Off J Div Health Psychol Am Psychol Assoc* 2018; **37:** 680–690.
24. Jarmolowicz DP, Bruce AS, Glusman M, *et al*. On how patients with multiple sclerosis weigh side effect severity and treatment efficacy when making treatment decisions. *Exp Clin Psychopharmacol* 2017; **25:** 479–484.
25. Wilson L, Loucks A, Bui C, *et al*. Patient centered decision making: use of conjoint analysis to determine risk-benefit trade-offs for preference sensitive treatment choices. *J Neurol Sci* 2014; **344:** 80–87.