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Profiling cognitivemotor interference in a large sample of persons with progressive multiple sclerosis and impaired processing speed: results from the CogEx study

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Profiling cognitive-motor interference in a large sample of persons with progressive Multiple Sclerosis and impaired processing speed – results from the CogEx study.

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Keywords: Multiple sclerosis, progressive, cognitive-motor interference, dual task, gait

Abstract

Background: Performing cognitive-motor dual tasks (DTs) may result in reduced walking speed and cognitive performance. The effect in persons with progressive Multiple Sclerosis (pwPMS) having cognitive dysfunction is unknown.

Objective: To profile DT-performance during walking in cognitively impaired pwPMS and examine DT-performance by disability level.

Methods: Secondary analyses were conducted on baseline data from the CogEx-study. Participants, enrolled with Symbol Digit Modalities Test 1.282 standard deviations below normative value, performed a cognitive single task ([ST], alternating alphabet), motor ST (walking) and DT (both). Outcomes were number of correct answers on the alternating alphabet task, walking speed, and DT-cost (DTC: decline in performance relative to the ST). Outcomes were compared between EDSS subgroups (≤4, 4.5-5.5, ≥6). Spearman correlations were conducted between the DTC_{motor} with clinical measures. Adjusted significance level was 0.01.

Results: Overall, participants (n=307) walked slower and had fewer correct answers on the DT versus ST (both $p<0.001$), with a DTC_{motor} of 15.8% and $DTC_{cognitive}$ of 2.7%. All three subgroups walked slower during the DT versus ST, with DTC_{motor} different from zero (*p's*<0.001). Only the EDSS≥6 group had fewer correct answers on the DT versus ST ($p<0.001$), but the $DTC_{cognitive}$ did not differ from zero for any of the groups ($p\geq0.039$).

Conclusion: Dual tasking substantially affects walking performance in cognitively impaired pwPMS, to a similar degree for EDSS subgroups.

Introduction

Daily life activities often entail the simultaneous performance of cognitive and motor tasks, termed cognitive-motor dual tasking (e.g., walking while talking or while trying to remember a shopping list). In both persons with and without multiple sclerosis (MS) performance of a dual task (DT) during walking commonly results in reduced walking speed [1-4], known as cognitive-motor interference (CMI) [5].

DT walking has been reported to be more closely related to typical walking speed in daily life than single task walking measures in the DT paradigm [6]. The last decade showed a surge in published studies on CMI in persons with MS showing relations of CMI to specific domains of quality of life[7] and possibly to falls[8, 9], although conflicting results have been reported [10, 11]. Further, some studies on CMI in MS have indicated worse cognitive functioning, specified by lower information processing speed measured by the Symbol Digit Modalities Test (SDMT), to be associated with lower DT performance [12, 13]. However, most previous studies included only, or for the majority, persons with a relapsing-remitting form of MS and often in rather small samples. Furthermore, the literature provides conflicting results on the influence of disability level on CMI [12, 14-16] and the bulk of studies on CMI in persons with MS have been conducted in persons with mild- to moderate MS. Notably, persons with progressive MS have generally more severe cognitive and physical impairments [17, 18]. Therefore, it can be speculated that the magnitude of CMI might be greater in persons with a progressive type of MS.

To our knowledge, no study has yet specifically investigated DT performance in persons with progressive MS and cognitive dysfunction. The framework of the CogEx study, being a large multi-national trial in persons with progressive MS having cognitive dysfunction, allows for investigating above-mentioned questions. Specifically, the aim of the current study is to profile DT performance during walking in cognitively impaired persons with progressive MS by examining: 1) the magnitude

of cognitive-motor interference during walking and 2) the relations between the DT performance and clinical measures of cognitive functioning, mobility and patient reported outcomes. The second aim is to examine whether cognitive-motor DT performance depends on the disability level in progressive MS.

Method

Study design

Baseline data from the CogEx-study were analysed (see also the recently published paper of Sandroff et al [19]). The CogEx-study is a double-blinded randomized controlled multicenter intervention study, with a main aim to assess the comparative and combined effects of cognitive rehabilitation and exercise training on impaired processing speed in persons with progressive MS. The study was performed at eleven sites in six different countries (Canada, USA, UK, Denmark, Belgium and Italy). The full protocol has been published [20]. Briefly, participants were randomly assigned to one of four interventions consisting of either cognitive rehabilitation or sham cognitive rehabilitation combined with exercise or sham exercise. The interventions were performed twice per week over a 12-week period and performance assessments were conducted at baseline, after the 12-week intervention and at six month follow-up. The performance assessments were standardized and all tests were conducted in a fixed order at all sites. Additional MRI measures were only taken at selected centers. To ensure similar execution of tests across sites, extensive protocols on the administration of the tests were drafted and an in-person training session to practice the administration of all tasks with all staff involved was arranged prior to the start of the study. In the present study only data from the baseline assessment was included and analysed independent of group allocation.

Participants

Inclusion criteria of the CogEx-study were a diagnosis of primary or secondary progressive MS, age between 25 and 65 years, not wheelchair dependent (Expanded Disability Status Scale [EDSS]<7.0)

and cognitively impaired as defined by a score on the SDMT of 1.282 standard deviation (SD) or more below published population-based normative data of the respective country of the site. Exclusion criteria were high level of current physical activity (Godin Leisure-Time Exercise Questionnaire>23), substance abuse, relapse or use of steroids within the past three months, nervous system disease other than MS, severe mental illness, medical contradiction to exercise, corrected near vision worse than 20/70 (visual acuity test), depression (Beck Depression Inventory≥29) or verbal incomprehensiveness (Token test≥29). For the current analyses, participants were divided in three subgroups using EDSS 4.0 and 6.0 as cut-offs based on the presence of limitations in 500 meter ambulation or daily life activities, and requiring an assistive device for walking, respectively. Therefore, the subgroups were participants labelled with mild (EDSS≤4.0), moderate (EDSS 4.5-5.5) and severe (EDSS≥6.0) disability.

Outcome measures

Descriptive measures of age, sex, body mass index, years of education, highest level of education, type of MS, and disease duration were noted. EDSS scores were provided by the participating centers. We report here on CMI and related parameters, see Feinstein et al (2020) for the full assessment battery [20]. For all tests the version in the native language of the participant was used.

Cognitive-motor interference assessment

Participants performed, in this order, a single cognitive task, a single motor task and a cognitive-motor DT. The single motor task consisted of walking up and down a corridor at preferred speed continuously for 1 minute. The corridor was 15m or 30m depending on the testing facilities. The single cognitive task was performed while seated, and entailed the alternating alphabet task in which participants alternated letters of the alphabet as fast and accurately as possible for 1 minute, starting from the letter L (e.g., L, N, P, etc.). The DT consisted of the alternating alphabet task starting at letter C, while walking at preferred speed up and down the corridor for 1 minute [16]. Participants

were instructed to perform both tasks at their best level and were permitted to use their usual assistive device for both walking tasks. For single and dual walking performance number of meters walked within the minute was recorded, from which walking speed was calculated. For single and dual cognitive performance, the number of correct and total answers on the alphabet task within the minute were recorded. From these measures both the DTC_{motor} and $DTC_{cognitive}$ were calculated with a positive DTC indicating worse performance during the DT relative to the single task (ST) (see formulas).

$$DTC_{motor}\ (\%) = \frac{(single{-}task\ motor\ score){-}(dual{-}task\ motor\ score)}{single{-}task\ motor\ score} * 100$$

$$DTC_{cognition}\ (\%) = \frac{(single{-}task\ cognitive\ score){-}(dual{-}task\ cognitive\ score)}{single{-}task\ cognitive\ score} * 100$$

Additional assessments

The SDMT, the California Verbal Learning Test (CVLT) and the Brief Visuospatial Memory Test (BVMT) were conducted as measures of cognitive functioning [21]. The six minute walking test (6MWT) was performed to establish walking performance [22]. Patient reported outcomes (PROs) included the Multiple Sclerosis Walking Scale-12 (MSWS-12) , Modified Fatigue Impact Scale (MFIS) , Multiple Sclerosis Impact Scale-29 (MSIS-29) , the Perceived Deficits Questionnaire (PDQ) , the Hospital Anxiety and Depression Scale (HADS) and the Functional Assessment of Multiple Sclerosis (FAMS) .

Statistical analysis

The analyses utilized the baseline evaluation of all participants of the CogEx-study who were randomized into the study as of March 2022. Statistical analyses were conducted in SAS v9.4. Missing values were not imputed. A false discovery rate (FDR) correction for all analyses was implemented due to the exploratory nature of these analyses. The FDR resulted in an adjusted significance level of

0.01. Descriptive statistics were used to summarize the participant demographic and clinical characteristics using means ± SD for continuous variables, median [25%, 75%] for ordinal variables, and frequencies (%) for categorical variables.

For the total group and for the three EDSS subgroups, differences between ST and DT performances were evaluated for gait speed and number of correct answers on the alphabet task using dependent t-tests. Further, one-sample t-tests were conducted to evaluate whether the DTC_{motor} and $DTC_{cognitive}$ differed from zero. Differences between EDSS subgroups were evaluated using chi square tests for categorical variables and Analysis of Variance (ANOVAs) with a Tukey-Kramer post-hoc comparison adjustment for continuous variables.

Last, associations between the DTC_{motor} with the $DTC_{cognitive}$, clinical tests and PROs were evaluated using Pearson or Spearman correlation coefficients as appropriate. A correlation above 0.90 was interpreted as very strong, 0.70–0.89 as strong, 0.50–0.69 as moderate, 0.30–0.49 as weak, and ≤0.29 as small [23].

Results

Participants

Table 1 displays the descriptive statistics of the total group and the three disability subgroups. For the present study 307 participants were included. On average, participants were 52.6±7.2 years old with an EDSS score of 6.0 [4.5-6.5]. In total, 75 participants had an EDSS of 4.0 and lower, 70 participants had an EDSS between 4.5 and 5.5 and 162 participants had an EDSS of 6 or greater. As expected, the three disability subgroups differed on outcomes of mobility and perceived mobility (p<0.001 for all). Post-hoc analyses showed that participants in the mild EDSS group had a greater perceived functional status as shown with the FAMS total, a greater number of meters walked during the 6MWT and lower scores on the MSWS-12, MSIS-29 physical subscale and the MFIS, compared to the moderate and severe EDSS groups (p<0.001 for all). The scores on the 6MWT and MSWS-12 also differed between participants in the moderate compared to the severe EDSS group (p≤0.001), but

these two groups showed no differences on the FAMS, MSIS-29 physical and MFIS ($p \geq 0.172$). No significant differences between the subgroups were found on descriptive measures, cognitive performances, or other patient reported outcomes being the HADS, MSIS-29 mental subscale and PDQ. Of the descriptive characteristics (Table 1) 1.1% of the data was missing.

*** Insert Table 1 near here ***

DT performance

DT performance in the total group

Table 2 depicts DT outcomes for the total group and the three EDSS subgroups. The average walking speed declined from 0.77±0.35 m/s during the ST to 0.64±0.31 m/s during the DT ($p<0.001$). The average DTC_{motor} was 15.8±14.4% and differed from zero ($p<0.001$). The average number of correct answers on the alphabet task was higher during the cognitive ST (25.1±10.2) compared to the score during the DT (23.3±9.4, $p<0.001$), but the average $DTC_{cognitive}$ (2.7±32.2%) did not differ from zero ($p=0.143$). In total, 0.5% of the motor data and 1.0% of the cognitive data of the DT outcomes was missing.

*** Insert Table 2 near here ***

DT performance for the EDSS subgroups

For all three subgroups, participants walked slower during the DT compared to the ST ($p<0.001$ for all) and the DTC_{motor} differed from zero ($p<0.001$ for all). Participants with mild disability in the lowest EDSS group had the fastest walking speed and those with severe disability in the highest EDSS group the slowest walking speed, during both the single- and dual walking task ($p<0.001$ for all comparisons between the EDSS subgroups). The DTC_{motor} did not differ between EDSS groups ($p=0.049$). See Figure 1 for a visualisation of the DTCs.

No significant differences between the EDSS groups were found on number of correct answers on the alphabet task (ST: p=0.62 and DT: p=0.40) or on the $DTC_{cognitive}$ (p=0.20). However, the severe EDSS group had a significantly lower number of correct answers on the alphabet task during the DT compared to the ST (p<0.001), what was not the case in the mild or moderate EDSS groups (p=0.119 and p=0.031, respectively). The $DTC_{cognitive}$ did not differ from zero for the mild (p=0.524), moderate (p=0.216) or severe (p=0.039) EDSS group.

*** Insert Figure 1 near here ***

Relation between DTC_{motor} and clinical measures

Table 3 depicts correlations between the DTC_{motor} and the $DTC_{cognitive}$, clinical measures and PROs. For the DTC_{motor}, significant albeit small positive correlations were found with the MFIS and PDQ whereas a negative correlation was observed with the FAMS.

*** Insert Table 3 near here ***

Discussion

To our knowledge, this study was the first to investigate DT performance specifically in persons with progressive MS with cognitive impairment. Participants significantly decreased their gait speed and number of correct answers on an alternating alphabet task during dual compared to single tasking. The effect of the DT on walking did not differ, and on cognitive performance only slightly differed, between participants depending on disability level.

A DTC_{motor} of 15.8% was shown for cognitively impaired persons with progressive MS. Previous studies that examined DT performance in persons with MS using walking while performing the alternating alphabet task as DT paradigm, [16, 24-27] showed broad ranging DTCs of walking

speed (between averages of 8% [26] and 30.2% [25]). However, three of these five studies reported DTCs of walking speed with a similar magnitude (12.5-17.8%) as in the present study. This indicates that the degree of CMI in persons with progressive MS is similar to that in persons with relapsing-remitting MS, as the latter constitute the majority of the participants in the previous studies [2]. The observation that the DTC showed somewhat similar patterns in the present study in persons with progressive MS as have been observed in previous studies in persons with relapsing-remitting MS, fits in the emerging mechanistic-driven framework that the clinical course of MS should not be classified anymore according to fixed phenotypes, but should instead be considered as a continuum with concurrent pathophysiological processes that however may vary across individuals and over time [28]. This similarity in DTCs was not hypothesized as this study reports on a sample selected based on the presence of impaired information processing speed, whereas some studies reported lower information processing speed to be related to greater interference in MS [16, 24, 27]. Methodological differences as for example instructions to prioritize the cognitive task [16] or to walk as fast as possible [27], or the use of an instrumented walkway[25], might have influenced the DTC_{motor} [29]. The inclusion of a control group of persons with relapsing-remitting MS or persons without MS would therefore have been informative. However, a meta-analyses reported no significant differences in degree of motor interference between person with MS and healthy controls (HC) [4]. Further, three of the mentioned studies using an alternating alphabet task, reported no significant differences in DTCs between persons with and without MS, with DTCs for HC ranging between 17.5% and 22.4% [24, 25, 27]. Still, as persons with MS already walk slower in general, a similar DTC might affect daily life to a greater extent. Also, DT walking speed has been reported to be more closely related to typical walking speed in daily life [6], confirming the possible relevance of taking absolute measures of DT walking into account as well.

Literature provides conflicting findings on differences in DTC_{motor} between disability groups. For example, Sosnoff and colleagues reported greater DTC_{motor} in persons with moderate or severe disability, compared to persons with mild disability [14], but others reported no differences [25, 26].

In the present study in cognitively impaired persons with progressive MS, all three EDSS groups showed a significant DTC_{motor}, with no differences between the groups. Additionally, in agreement with previous studies [12, 24, 30], no association was found between the EDSS and the DTC_{motor}. In the cognitive domain of the DT, only participants with severe MS, but not those with mild or moderate MS, had a lower number of correct answers on the alphabet task during the DT compared to the ST. These results might indicate that the DT had a greater effect on cognitive performance in more severely impaired patients which could be explained by the self-prioritization theory of Yogev-Seligmann and colleagues. This theory maintains that (unconscious) prioritization of a task during DT walking depends on someone's ability to respond effectively to a postural threat and estimate potential environmental hazards while taking self-limitations and other factors, like characteristics of the performed task, into the equation [31]. It could be that the walking task is progressively prioritized at the cost of the cognitive task performance, when the risk of postural instability increases by an increase in severity of disability of the patients. Although the average $DTC_{cognitive}$ was not different from zero in this study, similar patterns have previously been reported in the context of increasing complexity of the motor task accompanied by a seemingly increased prioritization of the motor task [29] at the cost of the cognitive task [32]. When measuring DT performance in persons with progressive MS, clinicians should thus be aware of this possible tradeoff between the cognitive and motor performance, and not focus on only motor performance.

Furthermore, no relationship was found between the DTC_{motor} and measures of cognitive functioning. This is in contrast to some previous studies where relations between performance on the SDMT and DT walking performance were reported [12, 13, 15, 33]. However, all participants in the present study were cognitively impaired, decreasing the range of cognitive functioning in the sample which might explain the absence of a relation. Further, in accordance with previous studies, no relationships were found between the DTC_{motor} with perceived walking ability or depression and anxiety scales [12, 13, 30]. Notably, a greater relative decline in walking speed (DTC_{motor}) was related to some extent to higher perceived cognitive dysfunction and impact of fatigue and a lower

perceived quality of life, although the correlations were small. Where contrasting results have been reported regarding associations between DTC and perceived fatigue [15], the high motor and cognitive disability of the present sample might partly explain the presence of an association between the DT interference and the MFIS. Taken together, DT performance was to some extent associated with perceived cognitive deficits and fatigue in daily life. However, DTC did not seem to be associated with objectively measured motor and cognitive capacity in this sample of persons with progressive MS and cognitive deficits.

A strength of the present study is the large sample and the well-defined group, all of whom were cognitively impaired persons with progressive MS providing new and robust information regarding CMI. However, some limitations need to be considered while interpreting the findings. First, there is no control group of either HC, persons with relapsing-remitting MS or persons with MS that are not cognitively impaired. Furthermore, the results are difficult to compare to previous studies as two characteristics of the sample are different from the majority of studies in this field, namely type of MS and degree of cognitive functioning. Second, because of practical issues in this large international multicenter study, neither randomization of the single cognitive, single walking, and cognitive-walking DT, nor of the letters used for the alternating alphabet task, was done. All participants performed the tasks in that fixed order and with fixed letters for the cognitive task, hereby perhaps introducing task-effects by learning, fatigue or difficulty of the start letter [34]. Further, half of the DT measurements were performed on a 15m rather than a 30m walkway, which could have influenced the walking performance by inducing more turning points. However, subjects always performed both the single and dual tasks in the same hallway. Third, it is remarkable that the variability on the $DTC_{cognitive}$ is large. This may be explained by a higher need for familiarization with the cognitive task in some subjects or with low to poor reliability of the $DTC_{cognitive}$ reported in previous studies hampering conclusions based on this measure [35, 36]. Lastly, the inclusion of cognitively impaired participants was based on a validated test of processing speed, as the present study was a secondary analysis of baseline data from the CogEx-study that involved processing speed

as the primary outcome [20]. This was chosen as it is one of the most prevalent and primary cognitive impairments in persons with MS and it can result in problems in other domains of cognitive functioning [20, 37].

The present study showed that a DT particularly affects walking performance in cognitively impaired persons with progressive MS. The degree of interference with walking speed was similar to that previously reported in persons with mild- to moderate disability and - for the majority – relapsing-remitting MS. While it is assumed that previous studies also included cognitively impaired persons with MS, the present study exclusively included cognitively impaired subjects. As such, it could be deduced that the presence of cognitive impairment is not magnifying the DTC. The findings additionally show that the DT interferes to a similar degree in persons with mild, moderate or severe MS.

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Figure legends

Figure 1

Figure 1: Average (±SD) DTC-motor (striped boxes) and DTC-cognitive (filled boxes) for EDSS≤4.0, EDSS 4.5-5.5 and EDSS ≥6.0. Abbreviations: DTC: dual task cost; EDSS: expanded disability status scale. *p-value≤0.01.

Table 1

Table 1 Descriptive characteristics for the total group and the EDSS subgroups

N	Total 307	EDSS ≤ 4.0 75	EDSS 4.5–5.5 70	EDSS ≥ 6 162	*p* value
Age	52.6 ± 7.2	52.5 ± 7.0	50.8 ± 7.7	53.5 ± 6.9	0.034[a]
Sex (% female)	62.2	61.3	54.3	66.0	0.23[b]
BMI	27.3 ± 33.5	29.1 ± 38.8	24.0 ± 4.7	28.0 ± 37.9	0.63[a]
Years of education	13.9 ± 3.3	14.4 ± 3.6	14.5 ± 3.2	13.4 ± 3.1	0.030[a]
Highest level of education (%)					0.13[b]
Primary	8.1	10.7	2.9	9.3	
Secondary	46.9	41.3	42.9	51.2	
College/university	45.0	48.0	54.3	39.5	
EDSS, median	6.0 [4.5,6.5]	3.5 [3.0,4.0]	5.0 [4.5,5.5]	6.3 [6.0,6.5]	–
Disease duration	14.4 ± 9.6	12.5 ± 10.4	14.3 ± 10.0	15.4 ± 9.0	0.10[a]
Type of prog. MS (% primary)	27.0	36.0	20.0	25.9	0.086[b]
Assistive device (%)					–
None	36.2	84.0	58.6	4.3	
Unilateral	28.0	12.0	24.3	37.0	
Bilateral	35.8	4.0	17.1	58.6	
Cognition, mobility and patient-reported outcomes					
SDMT z score	− 2.1 ± 0.76	− 2.0 ± 0.57	− 2.0 ± 0.64	− 2.2 ± 0.86	0.036[a]
CVLT z score	− 1.07 ± 1.2	− 1.2 ± 1.1	− 1.2 ± 1.4	− 0.95 ± 1.2	0.23[a]
BVMT-R z score	− 0.69 ± 1.3	− 0.72 ± 1.2	− 0.65 ± 1.3	− 0.68 ± 1.3	0.95[a]
6MWT total distance (m)	265.7 ± 140.4	398.4 ± 115.8[c]	320.1 ± 106.8[c]	180.3 ± 97.7[c]	< 0.001*[a]
MSWS total	63.4 ± 26.6	39.4 ± 24.5[c]	63.2 ± 24.1[c]	74.6 ± 20.5[c]	< 0.001*[a]
HADS—anxiety	6.5 ± 4.5	6.4 ± 4.6	6.4 ± 4.6	6.6 ± 4.4	0.93[a]
HADS—depression	6.2 ± 4.0	5.3 ± 4.0	6.6 ± 4.2	6.4 ± 3.8	0.071[a]
MSIS-29—physical	57.5 ± 18.4	45.7 ± 16.3[c]	59.0 ± 18.2	62.4 ± 17.0	< 0.001*[a]
MSIS-29—mental	22.4 ± 8.7	20.7 ± 9.1	24.2 ± 8.7	22.4 ± 8.5	0.057[a]
MFIS total	44.2 ± 17.2	35.8 ± 17.1[c]	50.0 ± 16.0	45.7 ± 16.5	< 0.001*[a]
PDQ total	28.5 ± 17.3	24.7 ± 16.5	33.0 ± 17.2	28.3 ± 17.3	0.015[a]
FAMS total	103.3 ± 28.9	118.3 ± 24.1[c]	99.9 ± 30.9	98.2 ± 27.8	< 0.001*[a]

Values presented as Mean ± SD, Median [P25, P75] or column %

BMI body mass index (8); *EDSS* Expanded Disability Status Scale; Disease duration (2); *MS* multiple sclerosis; *SDMT* symbol digit modalities test; *CVLT* California verbal learning test (1); *BVMT* brief visuospatial memory test (5); *6MWT* 6 m walking test (1); *MSWS* Multiple Sclerosis Walking Scale (6); *HADS* Hospital Anxiety and Depression Scale (3); *MSIS-29* Multiple Sclerosis Impact Scale (2); *MFIS* Modified Fatigue Impact Scale (5); *PDQ* Perceived Deficits Questionnaire (3); *FAMS* functional assessment of multiple sclerosis (28)

*Significantly different between EDSS subgroups, p value ≤ 0.01

[a]ANOVA

[b]Pearson's chi-square test

[c]Post hoc comparisons: EDSS group differs significantly from the other two groups

Table 2 Cognitive motor interference in the total group and EDSS subgroups

N	Total 307	EDSS ≤ 4.0 75	EDSS 4.5–5.5 70	EDSS ≥ 6 162	*p* value[a]
Dual task outcomes (mean ± SD)					
ST gait speed	0.77 ± 0.35	1.08 ± 0.26	0.92 ± 0.24	0.56 ± 0.26	< 0.001*
DT gait speed	0.64 ± 0.31	0.94 ± 0.28	0.73 ± 0.22	0.46 ± 0.22	< 0.001*
p value ST vs. DT[b]	< 0.001*	< 0.001*	< 0.001*	< 0.001*	
ST nr. of correct answers	25.1 ± 10.2	25.7 ± 10.2	24.1 ± 10.5	25.2 ± 10.1	0.62
DT nr. of correct answers	23.3 ± 9.4	24.6 ± 9.8	22.6 ± 9.9	23.1 ± 9.1	0.40
p value ST vs. DT[b]	< 0.001*	0.119	0.031	< 0. 001*	
DT cost (motor)	15.8 ± 14.4[c]	13.5 ± 12.6[c]	19.2 ± 15.5[c]	15.4 ± 14.6[c]	0.049
DT cost (cognitive)	2.7 ± 32.2	− 3.0 ± 40.4	4.2 ± 27.9	4.9 ± 29.3	0.20

ST single task; *DT* dual task; nr.: number

*Significantly different between groups or tasks, *p* value ≤ 0.01

[a] *p* values of ANOVA: differences between the three EDSS groups

[b] *p* values of dependent t-tests: differences between ST and DT score per group

[c] Significantly different from zero, *p* value ≤ 0.01

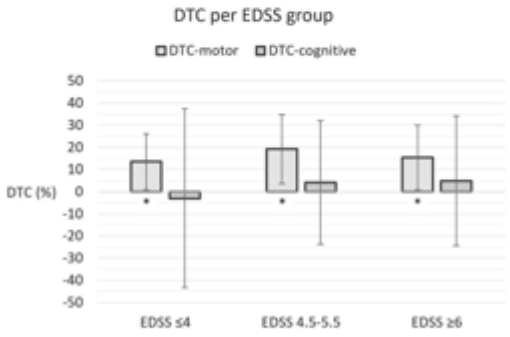

Fig. 1 Average (±SD) DTC-motor (striped boxes) and DTC-cognitive (filled boxes) for EDSS ≤ 4.0, EDSS 4.5–5.5 and EDSS ≥ 6.0. *DTC* dual task cost; *EDSS* Expanded Disability Status Scale. **p* value ≤ 0.01

Table 3 Correlations between DTCs and clinical measures

	DTC_{motor}	
	r	*p* value
$DTC_{cognitive}$	0.05	0.39
EDSS[a]	− 0.02	0.76
SDMT *z* score	0.04	0.54
CVLT *z* score	0.04	0.47
BVMT *z* score	− 0.01	0.84
6MWT	0.03	0.64
MSWS-12	0.01	0.86
MFIS total	0.15	0.01*
PDQ total	0.18	< 0.01*
HADS anxiety	0.11	0.06
HADS depression	0.07	0.23
FAMS total	− 0.16	0.01*

**p* ≤ 0.01

[a] Spearman