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ABSTRACT

Objectives: To assess: 1) the effect of task (single and dual-task), time (discharge and 4-months) and their interaction for mobility, 2) task prioritization during dual-task testing and 3) the association between cognition on change in mobility between discharge from rehabilitation and 4-months follow-up.

Design: Prospective cohort study

Setting: Rehabilitation hospital

Interventions: Not applicable

Main Outcome Measures: Gait velocity and L Test of *Functional Mobility*, single and dual-task (serial subtractions by threes), were the primary outcomes. Montreal Cognitive Assessment (MoCA) and Trail Making Test quantified cognition *as secondary outcomes*. Repeated measures analysis of variance evaluated the effects of task (single-task and dual-task) and time (discharge and 4-months follow-up) and their interaction on each outcome. A performance-resource operating characteristic graph evaluated gait and cognitive task prioritization. Multivariable linear regression evaluated the association between cognition and change in mobility over time.

Results: 22 people with lower extremity amputations participated (60.7 ±6.5 years, 59% male). No significant interactions between task and time were found (all $p > .121$) for L Test and gait velocity. The L Test single-task ($p = .001$) and dual-task ($p = .004$) improved over time. Gait velocity improved over time for both single-task and dual-task ($p < .001$). Dual-task performance was slower than single-task at each time point. The Trail Making Test B was independently

associated with the change in dual-task L Test ($p=.012$), and single-task ($p=.003$) and dual-task ($p=.006$) gait velocity at follow-up.

Conclusions: Gait velocity and L Test single and dual-task improved over time. *No significant interactions indicated* the cognitive task did not differentially affect performance over time.

Lower executive function scores at discharge were independently associated with lower gains in all gait velocity and dual-task L Test outcomes at follow-up.

Key Words: amputation, cognition, outcome measures, rehabilitation

Abbreviations:

ABC- Activities specific Balance Confidence Scale

CRR- Correct response rate

DM- Diabetes Mellitus

DTC-Dual Task Cost

DTC_{cog}- Dual-Task Cognition Cost

DTC_{gait}- Dual-Task Gait Cost

LLA- Lower limb amputation

MoCA- Montreal Cognitive Assessment

TMT- Trail Making Test

PVD- Peripheral Vascular Disease

INTRODUCTION

In Canada, 87% of amputations are attributed to diabetic complications that occur in a predominately older adult (> 65 years) population.¹ A recent Canadian study found the age-adjusted incidence rates for lower limb amputation (LLA) have decreased, but the absolute number of new LLAs has increased due to the increasing older population.² The combination of diabetes and predominance of older adults places this patient group at a high risk of developing cognitive dysfunction³, particularly in the areas of problem-solving, reasoning and concentration.⁴ Impairment in cognition affects balance⁵ and functional mobility⁶ for LLAs using a prosthesis. While a prosthesis may assist with mobility, the process of learning to use a prosthesis can be cognitively challenging.⁷

The inter-relationship between cognition and gait can be assessed observing people walking while they simultaneously perform another task; the dual-task paradigm.⁸ The difference in performance between single and dual-task conditions is a measure of an individual's ability to allocate attentional resources between the two simultaneous tasks.⁸ When attentional resources are overloaded, performance on one or both tasks may deteriorate.⁹ This is referred to as the dual-task cost (DTC).⁸ Dual-task testing is relevant as many daily activities require the simultaneous performance of two or more tasks - often cognitive and motor tasks in combination.¹⁰

Recovery of functional mobility and improvement of activity levels are major rehabilitation goals following LLA.¹¹ Mobility with a prosthesis has been found to significantly improve until around 6 months after discharge from rehabilitation when performance plateaus.¹² Ongoing gait difficulties are a concern as this is related to an increased falls risk.¹³ The relationship between cognition and gait is not well understood, though 40.9% of established

ambulators with a prosthesis report a need to concentrate on each step they take.¹⁴ Measures of functional mobility are important in providing information about post-rehabilitation mobility trajectories and independence that are linked to quality of life.¹⁵

Impaired global cognitive function is associated with lower mobility scores in LLAs after an inpatient prosthetic rehabilitation program.^{6,16,17} New and established prosthetic ambulators have demonstrated similar performance and task prioritization under dual-task conditions.¹⁸ Specifically, both gait and cognitive task performance deteriorate in dual-task testing, but the majority of people prioritized the gait task for a posture-first strategy.¹⁸ While cross-sectional findings provide insight about mobility and cognition there has been no prospective investigation directly quantifying the cognitive-motor inter-relationship over time in LLAs.

Therefore, the study objectives were: 1) to assess the effect of task (single and dual-task), time (discharge and 4-months) and their interaction for L Test of *Functional Mobility* and gait velocity, 2) to assess task prioritization during dual-task testing, and 3) to investigate the association between cognitive function on change in mobility between discharge from rehabilitation and 4-months follow-up for patients with unilateral trans-femoral or trans-tibial amputations. It was hypothesized performance will improve on all mobility tests at follow-up and lower cognitive scores will be associated with lower *change in* mobility after discharge.

METHODS

Study Design

This was a prospective cohort study of consecutive admissions to the regional inpatient amputee rehabilitation program at Parkwood Institute in London, Ontario, Canada. Data were collected between April 2016 and September 2017. This study was approved by Health Sciences

Research Ethics Boards at the University of Western Ontario and by the Clinical Resources Impact Committee of Lawson Health Research Institute in London, Ontario, Canada.

Participants

Admission criteria for the inpatient amputee rehabilitation program were: age 18 years of age or older, had identifiable rehabilitation goals, was medically stable, and was mentally and physically ready to enter the comprehensive rehabilitation program. Individuals admitted to the inpatient amputee rehabilitation program are admitted from home after the incision has healed. Study eligibility criteria were: 50 years of age or older, first major unilateral lower limb amputation (trans-tibial or trans-femoral), able to walk at least 10m without the assistance of another person (mobility aid use permitted), and a functional use of the English language. Participants who had any prior neurological disorder or physical problem that limited their walking ability were excluded from the study. All participants provided written informed consent.

Data collection

The following demographic and medical information were obtained: age, sex, height, weight, BMI (kg/m^2), years of education, type and level of amputation, amputation etiology and falls history. Global cognition was measured at admission to rehabilitation using the Montreal Cognitive Assessment (MoCA)¹⁹ and the Trail Making Test (TMT) was performed 48 hours prior to discharge. Balance confidence was measured within 48 hours of discharge with the Activities-specific Balance Confidence Scale (ABC).²⁰ The single and dual-task L Test of Functional Mobility, single and dual-task gait velocity, and a single-task cognitive assessment were administered at discharge and 4-months follow-up. (Described in outcome measures below) Assessments were completed in the same order for all participants, with a 5 minute rest provided

between each of the mobility assessments. The return assessment occurred at their regularly scheduled medical visit 4-months after discharge.

Outcome Measures

Cognition: Cognitive function was evaluated using the MoCA and the Trail Making Test (TMT). The MoCA has a maximum score of 30, with scores ≤ 25 indicative of mild impairment in cognition.¹⁹ The TMT has two parts, Part A (TMT-A) assesses visual attention and cognitive speed skills whereas Part B (TMT-B) evaluates higher-order cognitive skills such as working memory and task-shifting/attention, considered a measure of executive functioning.²¹ Results are reported as the time required to complete the task to the nearest 100th of a second; a longer completion time indicates greater impairment.

Single-Task Cognitive Assessment: The cognitive task of serial subtractions by threes, starting at 100, was performed in a seated position prior to the mobility tests. Time to complete 18 subtractions was recorded to the nearest 100th of a second with a stop watch. The responses and number of correct responses given were recorded.²²

L Test of Functional Mobility: The L Test of Functional Mobility (L Test) assesses functional mobility in the LLA population. As per standard instruction, participants began from a sitting position, and upon the word “go” rose to standing and walked three meters, turned 90°, walked seven meters, turned 180°, and walked along the same L-shaped path to return to a seated position.²³ The test was performed at their usual comfortable pace. A dual-task version of the L Test using serial subtractions by threes was also performed according to the protocol described in Hunter et al. 2017.²² L Test times were recorded to the nearest 100th of a second with a stop watch and cognitive responses were recorded. Individuals were given no instructions on task prioritization. The minimum detectable change (MDC) for the single-task L Test is MDC=3.19

sec and for the dual-task L Test is MDC=3.76 sec for trans-tibial amputation of vascular etiology.²²

Gait Velocity: Gait velocity was measured using the GAITRite® System, an instrumented walkway measuring 6 meters by 0.64 meters. A one-meter distance before and after the boundaries of the walkway was used to account for acceleration and deceleration, which was not incorporated into the collected data. Gait velocity at usual comfortable pace was measured in centimeters per second, making larger velocity scores indicative of better physical functioning. Gait testing was performed as a single and dual-task protocol, where the dual-task protocol used serial subtractions by threes as described previously. Responses on the secondary cognitive task were recorded. No instructions on task prioritization were given. The MDC of 0.04 to 0.06 m/s was used to evaluate velocity scores.²⁴

Statistical Analysis

Descriptive statistics using means and SDs or frequency and percentages were calculated to describe the demographic and clinical characteristics of the sample. To address objective 1, the effect of single and dual-task performance on mobility (L Test and gait velocity), changes in gait measures over time (discharge and follow-up) and the interaction of these two factors (task and time) we conducted repeated measures analyses of variance (ANOVA-RM). Cohen's d effect size (ES) quantified the magnitude of the difference in the paired comparisons. Benchmark values for ES to estimate the magnitude of the effect and classified were: trivial (<0.20), small (<0.20 to <0.50), moderate (<0.50 to <0.80) or large (<0.80).²⁵

To evaluate task prioritization, a performance-resource operating characteristic (POC) graph was created by plotting dual-task cost for cognitive task (DTC_{cog}) on the x-axis versus dual-task gait cost (DTC_{gait}) on the y-axis for L Test and gait velocity.⁸ The dual-task cost is the

ratio of change in gait or cognitive performance on the dual-task test relative to the single-task condition.^{21,26,27} The DTC_{gait} was calculated as:

$$DTC_{gait} = \frac{(single\text{-}task\ test - dual\text{-}task\ test)}{single\text{-}task\ test} \times 100\%$$

Cognitive performance was determined by first calculating the correct response rate (CRR) for the single-task cognitive test and dual-task tests (L Test and gait velocity) as: (*Response rate per second X percent correct*).²⁸ CRR accounts for speed and accuracy of responses given.²⁸

DTC_{cog} was calculated as:

$$DTC_{cog} = (-1) \frac{(CRR_{serial\text{-}subtractions:seated} - CRR_{serial\text{-}subtractions:walk})}{CRR_{serial\text{-}subtractions:seated}} \times 100\%$$

The interpretation of the dual-task cost value is the same for both DTC_{gait} and DTC_{cog} . A negative value indicates poorer performance under dual-task conditions (i.e., longer walking time under the dual-task condition). A positive value indicates better performance under dual-task conditions (i.e., shorter walking time). In the POC curve, performance will fall into one of four quadrants: (1) upper left – improvement of gait with worsening of cognitive task, (2) upper right – improvement of gait with improvement of cognitive task, (3) lower left – worsening of gait with worsening of cognitive task, (4) lower right – worsening of gait with improvement of cognitive task. Performance that falls on the axes at 0% DTC for gait and cognition indicates no change in performance between single- and dual-task conditions.¹⁸ A diagonal line through quadrants two and three indicates a 1:1 trade off during dual-task performance; to the left of this line gait is prioritized and to the right the cognitive task is prioritized.⁸

To address the third objective, multivariable linear regression modeling evaluated the association of cognition (MoCA, TMT-A, TMT-B scores) on the change in mobility between discharge and 4-months after discharge. The dependent variable was the 4-months mobility

score. Regression modelling was adjusted on baseline mobility score, age, Activity-specific Balance Confidence score and etiology of amputation. Statistical significance was set at $p < .05$. Data were analyzed using SPSS (Version 25.0; SPSS Inc, Chicago IL).

RESULTS

Demographics

Thirty individuals were enrolled in the study, 22 completed all mobility assessments. Follow-up assessments were incomplete for the following reasons: non-ambulatory (2), deceased (1), stopped wearing the prosthesis (1), testing problems (2), lost to follow-up (1), and unable to return due to family emergency (1). Overall, the 22 participants had a mean age of 60.7 ± 6.5 years and 59% were male. (Table 1)

Mobility Changes

L Test

The interaction between task x time was not statistically significant, indicating the cognitive task did not differentially affect performance between baseline and 4-months. The main effects were statistically significant for task ($p < .001$) and time ($p = .001$). (Table 2) Single-task L Test scores demonstrated that time to complete the test was shorter at 4-months follow-up. The single-task L Test improved for 20 (90.9%) people and this improvement exceeded the MDC value for 17 (81%). Dual-task L Test scores also demonstrated the time to complete the test improved over time. The dual-task L Test improved for 20 (90.9%) participants between discharge and 4-months follow-up. The improvement for 17 (85%) exceeded the MDC value. Performance on the dual-task L Test was statistically significantly slower than the single-task condition at each time point.

Gait Velocity

The interaction between task x time was not statistically significant, indicating the cognitive task did not differentially affect performance between discharge and 4-months. The main effects of task ($p=.009$) and time ($p=.002$) were statistically significant. (Table 3) Single-task and dual-task velocity improved over time with people walking at a faster pace at 4-months. These changes in the dual-task testing exceeded the MDC values for 19 (87%) individuals. Performance on the dual-task test resulted in a statistically significantly slower gait velocity than the single-task condition at each time point.

Performance Operating Characteristic (POC)

In the L Test, the gait and cognitive tasks were negatively impacted by dual-task testing at both time points. While both tasks deteriorated in the dual-task testing, the trade-off between the tasks indicated the majority of the participants prioritized the gait task over the cognitive task at discharge and 4-months follow-up. Visual inspection would support a stable prioritization of tasks at both time points.

For gait velocity, in contrast to the L Test results, there was a prioritization of the cognitive task over gait performance at discharge and the 4-months follow-up. Visually, there was an increase in the prioritization of the cognitive task at 4-months. (Figure 1 and 2)

Association of cognition with mobility function 4-months after discharge

TMT-B was associated with the change in single-task ($p=.003$) and dual-task ($p=.006$) gait velocity, and dual-task L Test ($p=.012$). (Table 4) Increased time to complete the TMT-B, representing greater cognitive impairment, was associated with requiring more time to complete the L Test and slower velocity. Specifically, we found that for every 1 second increase in TMT-B scores, the change in single-task and dual-task gait velocity was reduced by 1.12cm/s and 0.88 cm/sec, respectively.

DISCUSSION

This study has demonstrated that mobility, both the single and dual-task tests, significantly increased between discharge and 4-months after prosthetic rehabilitation. Importantly, the cognitive task did not appear to differentially impact performance over time. Lower cognitive function scores on the Trail Making Test B, which combines visual scanning, motor speed and alternating attention/working memory, were associated with lower functional gains 4-months after discharge from rehabilitation. This study provides novel information on the cognitive-motor inter-relationship after discharge from prosthetic rehabilitation.

Our study supports previous findings of a connection between functional mobility and cognition.^{4,5} Importantly, the recent review by Morgan et al.²⁹ highlighted the limited existing literature on dual-task testing in amputees and the lack of prospective studies evaluating change over time. Our study adds novel information with direct quantification of the cognitive-motor inter-relationship over time. Understanding the role of cognition in the initial months after the rehabilitation process is important, as Coffey et al.⁴ found cognitive deficits result in significant difficulties in learning how to use a prosthesis and in regaining mobility and independence in activities of daily living following LLA. O'Neill and Evans⁶ found executive function, using a test of verbal fluency, was associated with less extensive use of the prosthesis 6-months after discharge from rehabilitation. Our study builds upon the existing research, demonstrating the TMT-B at discharge is associated with dual-task L Test and, single and dual-task gait velocity at 4-months after discharge. Our study supports the need for research into the evaluation of cognitive and physical exercises during rehabilitation, a treatment that has been suggested for other cognitively-impaired populations.³⁰

Another novel finding was the evaluation of gait and cognitive task prioritization during the dual-task testing over time. We found gait performance was prioritized for the L Test and gait velocity at discharge and remained the salient task for the L Test, a more complex activity, at 4-months. In those with functional limitations (e.g., a walking impairment), greater attentional demand is needed when walking to accommodate for a less stable system and therefore gait is expected to be prioritized over competing tasks, called a posture-first strategy.¹⁰ Cognitive demands also vary with task complexity, such that walking in a complex path requires greater cognitive resources than a straight path.³¹ This study's findings are consistent with the posture-first strategy being used at both time points for the more complex task, the L Test, as the gait task was prioritized over the cognitive task.

In our study though mobility improved over time, the cognitive demands of ambulating with a prosthesis did not change. Our findings are consistent with the results of Frengopoulos et al.¹⁸ who found the cognitive demands during walking were similar between new and experienced trans-tibial amputees using a prosthesis. Conversely, Geurts et al.³² found the cognitive load in static balance positions improved with rehabilitation and suggested this was due to central neural adaptation of the new postural requirements. Yet, even years after successful completion of prosthetic rehabilitation, 40.9% of LLAs report having to concentrate on every step they take when ambulating with their prosthesis.¹⁴ Gait is a more complex activity than static balance, requiring greater cognitive resources to successfully adapt walking patterns to avoid or negotiate obstacles, changing direction and planning a path. A limb amputation leads to changes in muscle activity, joint mobility and sensory input to the brain that may not be fully compensated with learning new movement patterns to walk with a prosthesis resulting in fixed greater cognitive demands.^{7,33} An exciting area of emerging research in cognitive-motor effects

is the role of the prosthesis. Morgan et al.³⁴ found a concurrent cognitive task resulted in a similar response to the cognitive demands between age and sex-matched controls and persons with trans-femoral amputations using a prosthesis with a microprocessor knee.

Limitations

This study has several limitations that should be considered. Twenty-seven percent of the sample was not able to contribute mobility data at follow-up and therefore the study may not have been powered enough to find associations. To offset the small sample size, we calculated effect sizes to indicate the magnitude of the effects and compared results to established minimum different change scores. We were also not able to stratify the group to explore interesting clinical features, such as level of amputation. Future studies should employ short and long-term follow-ups to better examine long-term change in functioning. In terms of strengths, all people who met the inclusion criteria during the study time frame were enrolled and therefore this study is representative of the patient population seen at this institution. Valid and reliable measures for the assessment of the cognitive-motor inter-relationship were used and we directly evaluated task prioritization during dual-task testing.

CONCLUSIONS

People with LLAs demonstrated significant improvements in single-task and dual-task gait velocity and L Test after discharge. Lower scores on measures of cognitive function were associated with smaller gains in functional mobility after discharge, though ninety percent of the sample demonstrated gains that were in excess of the minimal detectable change for both gait velocity and L Test. Prospective studies over a longer duration with a larger sample are warranted to monitor ongoing changes between cognition and mobility, along with risk for adverse events such as falls.

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Table 1. Demographic and clinical characteristics of a cohort of adults with lower limb amputation at discharge from prosthetic rehabilitation. (n=22)

Characteristic	Mean±SD or frequency (%)
Age (years)	60.7±6.5
Sex (n, % males)	13 (59.0%)
Height (cm)	173.4±11.1
Weight (kg)	88.7±23.7
Body Mass Index (kg/m ²)	29.3±6.6
Years of Education	13.0±2.0
Activities-specific Balance Confidence Scale (%)	67.7±14.7
Montreal Cognitive Assessment score	26.1±2.5
Level of amputation is trans-tibial	19 (86.4%)
Primary Etiology of Amputation:	
-Diabetes Mellitus	15 (68.2%)
-Peripheral Vascular Disease	2 (9.1%)
-Diabetes Mellitus and Peripheral Vascular Disease	1 (4.6%)
-Cancer	1 (4.6%)
-Other	3 (13.6%)

Note: SD, standard deviation.

Table 2. Evaluation of task, time and their interaction in L Test between discharge from inpatient prosthetic rehabilitation and 4-months follow-up for a cohort of lower limb amputees. (n=22)

Task	Time (mean±SD)		Paired comparison and ES for time	Overall Repeated Measures ANOVA
	Discharge	4-months Follow-up		
Single-task test (seconds)	74.96 (50.68)	52.40 (38.53)	p=.001, ES=0.50	task p<.001 time p=.001 task x time p=.552
Dual-task test (seconds)	93.90 (73.80)	60.54 (42.99)	p=.004, ES=0.55	
Paired comparison and ES for task	p=.023, ES=0.29	p=.001, ES=0.19		

ES, Cohen's d effect size for the magnitude of the difference in the paired comparisons. Benchmark values for ES the magnitude of the effect were: trivial (<0.20), small (<0.20 to <0.50), moderate (<0.50 to <0.80) or large (<0.80).²⁸

Table 3. Evaluation of task, time and their interaction in gait velocity between discharge from inpatient prosthetic rehabilitation and 4-months follow-up for a cohort of lower limb amputees.

(n=22)

Task	Time (mean±SD)		Paired comparison and ES for time	Overall Repeated Measures ANOVA
	Discharge	4-months Follow-up		
Single-task test (cm/s)	54.89 (26.53)	71.86 (25.81)	p<.001, ES=0.64	task p<.002 time p=.009 task x time p=.121
Dual-task test (cm/s)	44.97 (24.68)	62.28 (28.62)	p<.001, ES=0.64	
Paired comparison and ES for task	p=.003, ES=0.38	p=.017, ES=0.35		

ES, Cohen's d effect size for the magnitude of the difference in the paired comparisons. Benchmark values for ES of the magnitude of the effect were: trivial (<0.20), small (<0.20 to <0.50), moderate (<0.50 to <0.80) or large (<0.80).²⁸

Table 4. Results of multivariable linear regression modelling for the association of Montreal Cognitive Assessment and Trail Making Tests A and B scores at discharge on measures of mobility at 4 months after discharge from inpatient prosthetic rehabilitation.

Cognitive Test	Outcome	Unadjusted Unstandardized β (95% CI)	P value	Adjusted Unstandardized β (95% CI)*	P- value
Montreal Cognitive Assessment	L Test –Single- Task	-0.03 (-0.05, 0.004)	.087	0.01 (-0.04, 0.07)	.569
	L Test- Dual- Task	-0.03 (-0.05, 0.002)	.035	-0.005 (-0.05, 0.04)	.809
	Gait Velocity – Single-Task	0.05 (0.01, 0.09)	.015	0.04 (-0.06, 0.13)	.420
	Gait Velocity – Dual-Task	0.06 (0.03, 0.09)	.001	0.06 (-0.01, 0.14)	.099
Trail Making Test – Part A	L Test - Single- Task	0.21 (0.03, 0.40)	.026	0.21 (-0.13, 0.54)	.212
	L Test - Dual- Task	0.18 (0.01, 0.35)	.044	0.16 (-0.13, 0.45)	.248
	Gait Velocity – Single-Task	-0.33 (-0.59, - 0.07)	.016	-0.23 (-0.65, 0.19)	.266
	Gait Velocity – Dual-Task	-0.26 (-0.50, - 0.02)	.036	-0.15 (-0.53, 0.22)	.397

Trail Making Test – Part B	L Test - Single- Task	0.49 (0.17, 0.81)	.005	0.58 (-0.03, 1.19)	.060
	L Test - Dual- Task	0.47 (0.19, 0.74)	.002	0.64 (0.16, 1.12)	.012
	Gait Velocity – Single-Task	-0.99 (-1.35, - 0.64)	.000	-1.12 (-1.80, - 0.45)	.003
	Gait Velocity – Dual-Task	-0.91 (-1.32, - 0.49)	.000	-0.88 (-1.47, - 0.29)	.006

Note: β = standardized regression coefficient; CI = confidence interval; *, variables adjusted for in the regression modeling were baseline mobility score, age, Activity-specific Balance Confidence score and etiology of amputation.

Figure Legends

Figure 1. Performance-resource operating characteristic (POC) graph for cognition-gait interaction in the dual-task L Test.

Figure 2. Performance-resource operating characteristic (POC) graph for cognition-gait interaction in the gait velocity.

Figure 1. Performance-resource operating characteristic (POC) graph for cognition-gait interaction in the dual-task L Test.

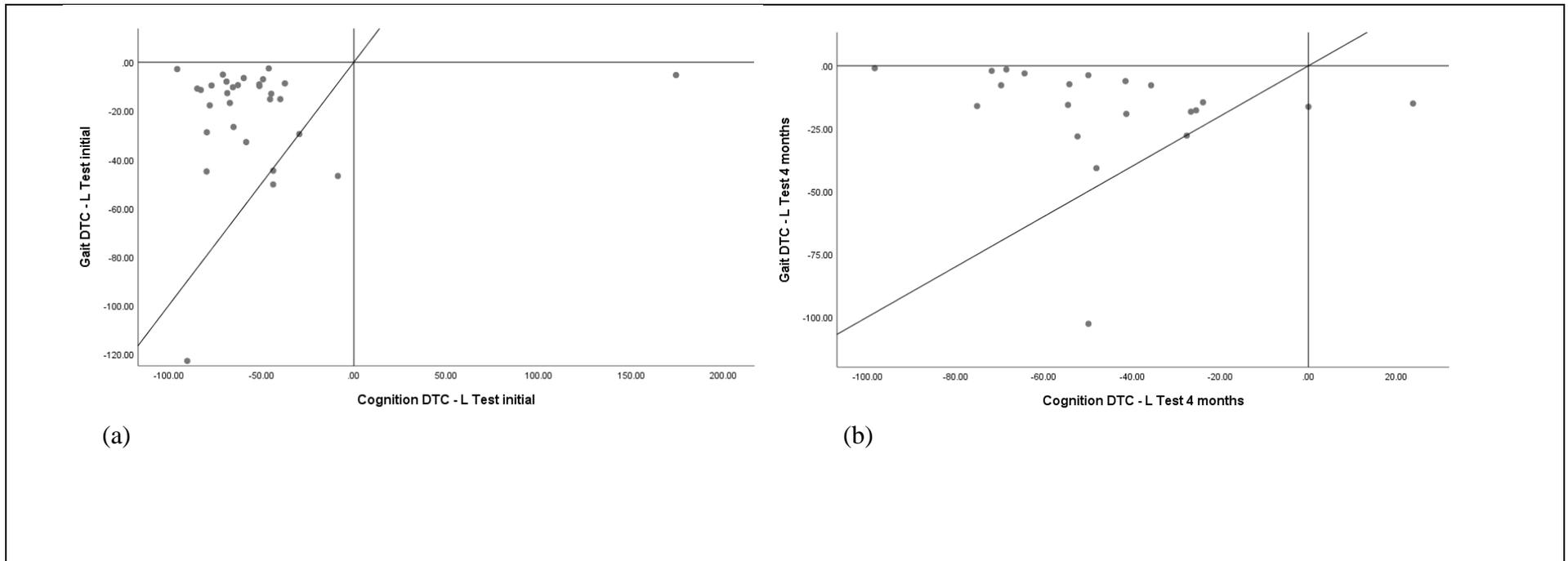


Figure 2. Performance-resource operating characteristic (POC) graph for cognition-gait interaction in the gait velocity.

