Published in final edited form as:

J Neurol Phys Ther. 2014 April ; 38(2): 104–110. doi:10.1097/NPT.0000000000000032.

ADULTS WITH DIABETIC PERIPHERAL NEUROPATHY EXHIBIT IMPAIRMENTS IN MULTI-TASKING AND OTHER EXECUTIVE FUNCTIONS

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Abstract

BACKGROUND AND PURPOSE—Diabetic peripheral neuropathy (DPN) contributes to functional impairment, and there is growing evidence that neuropsychological factors also influence physical function. We compared cognitive and executive function in adults with DPN to an age-matched comparison group, and examined the relationships between DPN, executive function, and physical function.

METHODS—Twenty subjects with DPN and 20 comparison subjects were assessed. DPN was quantified via the Michigan Neuropathy Screening Instrument and nerve conduction velocity testing. Subjects were administered Beck's Depression Inventory, the Mini Mental Status Examination, and the Timed Up and Go test (TUG). Each participant also completed a battery of 7 executive function tasks, including the Cognitive Timed Up and Go test (cTUG), in which a concurrent mental subtraction task was added to the standard TUG test.

RESULTS—The DPN group demonstrated poorer letter fluency (34.2 ± 11.6 vs. 46.2 ± 12.2 words, $p=0.001$), category fluency (47.0 ± 8.1 vs. 56.3 ± 8.5 words, $p=0.003$), and Rey Osterrieth scores (25.9 ± 4.3 vs. 31.7 ± 2.4 points, $p<0.001$), and took longer to complete both the TUG (10.3 ± 2.8 vs.

Disclosures

The authors have nothing to disclose.

Presentations

Portions of this data have been presented in poster form at the American Diabetes Association 72nd Scientific Sessions (Abstract #2012-A-4460-Diabetes; published online at <http://scientificsessions.diabetes.org>).

5.9±1.0 seconds, $p<0.001$) and cTUG (13.0±5.8 vs. 6.9±1.6 seconds, $p<0.001$). Poorer global cognitive performance and greater depression symptoms were significantly related to each other ($r=-0.46$, $p=0.04$) and to slower TUG times ($r=-0.53$, $p=0.02$ and 0.54 , $p=0.02$, respectively).

DISCUSSION AND CONCLUSIONS—Verbal, visuospatial, and multi-tasking measures of executive function may be impaired in adults with DPN. Future research should examine how these and other cognitive and psychological factors, such as depression, affect physical function in this population.

INTRODUCTION

Current estimates suggest that diabetes affects at least 25.8 million individuals in the United States and, with aging, will likely affect over one-quarter of the adult population.¹ Of the many complications related to diabetes, diabetic peripheral neuropathy (DPN) is among the most common, occurring in up to 60% of adult patients.¹ Resulting from peripheral nerve degeneration and impaired neural regeneration, DPN typically manifests as symmetrical pain and/or loss of sensation in the distal extremities.² This is of substantial concern, as DPN is associated with impaired balance, gait abnormalities, and an increased risk for lower extremity amputation.^{3,4}

While its destructive effects on peripheral nerve function are well established, there is also evidence that diabetes damages central nervous system structures underlying important cognitive functions.⁵ In particular, adults with diabetes appear to demonstrate deficits in executive function; the broadly defined set of processes responsible for planning, coordinating, sequencing, and monitoring cognitive operations.⁶⁻⁹ Such diabetes-related executive impairments are especially interesting in light of studies highlighting the complex interplay between cognitive processes and functional motor skills.

Much of the research related to the association between cognitive and motor functions centers on the ability to multi-task in order to perform simultaneous activities. However, other executive processes, such as attention, task shifting, working memory, verbal fluency and organization, and visuospatial organization, may also link cognitive and physical function. Several investigations have found that executive function contributes to gait in individuals with diabetes. Brach et al¹⁰ examined walking speed in a sample of 558 older adults, finding it to be significantly slower in those with diabetes. Interestingly, scores on the Trail Making Test, a common measure of executive function, explained a greater portion of this relationship than lower extremity vibratory perception, a measure of DPN. Likewise, executive measures involving dual-task performance (e.g. walking while performing serial mental subtraction) have been shown to impair gait in individuals with diabetes, both with and without DPN.¹¹

Although it is clear that DPN contributes to the elevated fall risk and functional impairments experienced by those with diabetes, almost nothing is known about executive abilities in those with DPN and how these factors interact to influence physical function. The purpose of this study was to examine whether adults with DPN exhibited changes suggestive of executive dysfunction, and to explore the relationships between measures of neuropsychological function, peripheral neuropathy, and functional ability.

METHODS

Study Design and Sample

This cross-sectional study was conducted in collaboration with a larger investigation of fall risk assessment in individuals with DPN. Institutional approval for both studies was granted by the human subjects committee of the University of Kansas Medical Center.

A total of 20 individuals with DPN and 20 individuals without diabetes (ages 40–65 years) were recruited for the study. Diagnosis of DPN was confirmed via administration of the Michigan Neuropathy Screening Instrument (MNSI) and nerve conduction studies of the tibial and peroneal nerves. If screening and/or nerve conduction testing raised questions about the presence of DPN, a collaborating neurologist was consulted to determine the presence or absence of the condition. Exclusion criteria included the following: 1) major medical depression, 2) musculoskeletal problems limiting ambulation, 3) open wounds on the feet, 4) inability to ambulate independently, 5) uncorrectable visual deficits, 6) central nervous system pathology or dementia, and 7) untreated vestibular disorder and/or postural hypotension.

Procedures

After signing an institutionally-approved consent form, data regarding age, height, and weight were recorded for each participant. Those with DPN were then administered the MNSI, and glycosylated hemoglobin (HbA1c) and nerve conduction testing were completed. Finally, all participants completed measures assessing depression symptoms and global cognitive function, followed by the TUG, cTUG, and a battery of executive function tests administered in a standardized order.

All cognitive testing was conducted by the same investigator in a quiet laboratory setting to minimize distraction. Nerve conduction assessment was conducted by a research technician in the Department of Neurology at the University of Kansas Medical Center.

Measures

The following assessments were obtained from participants with DPN:

1. The Michigan Neuropathy Screening Instrument (MNSI) symptom questionnaire was used to assess self-reported symptoms of DPN via yes/no response to 15 items, reflecting the frequency and severity of neuropathic symptoms. A higher score on a scale of 0–13 indicated greater neuropathic symptoms.¹²
2. The MNSI physical exam score was used to assess foot appearance, vibration sense, reflexes, and monofilament sensation. A score of 2 or more on a scale of 0–10 suggested the presence of peripheral neuropathy.¹²
3. Nerve conduction studies were used to assess nerve conduction velocity, amplitude, and latency of the right lower extremity peroneal and tibial nerves.

The following assessments were obtained from all study participants in both the DPN and comparison groups:

1. Beck's Depression Inventory-II was used to quantify self-reported symptoms of depression. This measure is scored on a 21-item, 63-point scale, with scores of 19 or less indicating minimal symptoms of depression, 20–28 moderate symptoms, and 29 severe symptoms.¹³
2. The Mini-Mental Status Examination (MMSE) was used to assess global cognitive function. This 30-point instrument broadly reflected orientation, memory, concentration, and praxis, with scores of < 24 indicating severe cognitive impairment.¹⁴
3. The Timed Up and Go test (TUG) was used to assess functional mobility.¹⁵ Participants stood from a chair and walked 3 m, turned, returned to the chair, and sat down. The TUG was performed twice, and the average time in seconds recorded. This value also represented single-task walking time for analyses of multi-tasking ability.
4. The Cognitive Timed Up and Go Test (cTUG) was used to assess multi-tasking during functional mobility.¹⁵ Participants performed the standard TUG with a simultaneous cognitive task in which they serially subtracted 3's from a random number between 80 and 100. The cTUG was performed twice, and the average time to complete the walking task and the rate of correctly reported digits per second of walking time were recorded. A single-task trial of the cognitive task was then performed while the subject was seated. The time allowed for this single-task cognitive trial was equivalent to the participant's average cTUG time.
5. The Rey Osterrieth Complex Figure was used to assess visuospatial organization. Participants were given a copy of an asymmetrical geometric figure and asked to draw the figure as accurately as possible without the use of a straight edge. Each drawing was scored by the same examiner on a standardized 36-point scale, with higher scores indicating greater accuracy.¹⁶
6. Letter and Category Fluency were used to assess verbal fluency and organization.¹⁶ Participants were given a letter of the alphabet (F, A, S) or category (animals, vegetables, articles of clothing) and allowed 1 minute to verbally provide as many words as possible (excluding proper nouns) beginning with that letter or falling within that category. The total number of words provided for the 3 letters and 3 categories represented letter fluency and category fluency, respectively.
7. Forward and reverse digit span were used to assess attention and working memory, respectively.¹⁶ Participants were read a series of digits and asked to immediately repeat the digits back in the same or reverse order. The number of correctly reported digits, ranging from 0–8 (forward) and 0–7 (reverse), was recorded.
8. The Trail Making Test was used to assess task shifting ability.¹⁷ In part A of the test, participants drew a line connecting series of letters or numbers in order as quickly as possible (e.g. A-B-C; 1-2-3 etc). In part B of the test participants drew a line connecting numbers and letters in an alternating fashion (e.g. 1-A-2-B etc.). A percent difference score between the two conditions was calculated by taking the

difference between the times required to complete parts A and B, divided by the time required to complete part A.

Statistical Analysis

Data analysis was conducted using SPSS 16.0 for Windows (Chicago, IL). In order to examine multi-tasking performance on the cTUG a percent change, or dual-task cost, from the single-task condition to the dual-task condition was calculated for both walking time and rate of cognitive task performance via the following formula:

$$\text{Dual-task Cost} = \frac{(\text{Dual-task performance} - \text{Single-task performance})}{\text{Single-task performance}} \times 100$$

Descriptive statistics were then calculated for each measure, and mean differences were assessed via 2-tailed t-tests. Pearson-product-moment correlations examined the relationships between variables. An alpha level of 0.05 was used to assess the significance of all findings.

RESULTS

Sample Characteristics

Participant characteristics are illustrated in Table 1. Twenty people with DPN (8 female; age 58.4 ± 6.2 years) and 20 without diabetes (14 female; age 54.9 ± 6.1 years) participated in the study. Differences in age between the two groups were not significant ($p=0.08$). Glycemic control in those with DPN was fair (HbA1c $7.2 \pm 1.4\%$; range 5.6–11.0). Subjects with DPN demonstrated greater BMI (37.0 ± 8.4 vs. 24.8 ± 4.1 kg/m², $p<0.001$); as well as higher levels of depression (Beck's Depression Inventory 11.3 ± 6.5 vs. 1.6 ± 1.8 , $p<0.001$) and lower global cognitive scores (MMSE 27.8 ± 2.0 vs. 29.5 ± 0.8 , $p=0.001$).

Peripheral Neuropathy Measures

The results of DPN screening and tibial and peroneal nerve conduction testing are given in Table 2. One subject declined to undergo nerve conduction testing. In the remaining sample of 19 participants, MNSI-subjective (mean score 3.1 ± 2.0), MNSI-physical (mean score 5.9 ± 2.6), and nerve conduction measures (peroneal nerve conduction velocity 40.9 ± 5.1 m/s; tibial nerve conduction velocity 38.9 ± 4.3 m/s) were consistent with the presence of neuropathy.

Timed Up and Go Performance

The results of the TUG are illustrated in Figure 1. On average, the DPN group required more time to complete the TUG than the comparison group (10.3 ± 2.8 vs. 5.9 ± 1.0 seconds, $p<0.001$).

Cognitive Timed Up and Go Performance

The results of the cTUG are illustrated in Figures 1 and 2. Those with DPN required more time to complete the cTUG than comparison subjects (13.0 ± 5.8 vs. 6.9 ± 1.6 seconds,

$p < 0.001$). The added cognitive task slowed walking time in both the DPN ($+2.7 \pm 3.4$ seconds, $p = 0.002$) and comparison groups ($+1.0 \pm 0.9$ seconds, $p < 0.001$). However, percent changes from single- to dual-task conditions (e.g. dual-task cost) for walking speed were not different between the groups ($p = 0.45$).

The rate at which subjects performed the cognitive task also declined under dual-task conditions in both groups (DPN: -0.12 ± 0.12 digits/second, $p < 0.001$; CN: -0.17 ± 0.22 digits/second, $p = 0.003$). However, there were no between-group differences in either single- or dual-task cognitive performance ($p = 0.11$ and 0.14 , respectively) or in the dual-task cost for the cognitive task ($p = 0.53$).

In order to explore whether subjects with DPN prioritized the two cTUG tasks differently than comparison subjects, we examined the patterns of individual dual-task costs for the walking and cognitive tasks (Figure 3). This was done by plotting each participant's single-task performance against their dual-task performance for both walking speed (A) and rate of cognitive task performance (B). Thus the distance the point fell from a line representing no change in performance from single- to dual-task conditions (e.g. a dual-task cost of 0%) reflected the dual-task cost for that particular task.

This analysis revealed that comparison subjects exhibited an average dual-task cost in walking speed of $17.0 \pm 14.6\%$, with a similar but more variable cost to the cognitive task of $17.5 \pm 28.5\%$. In contrast, subjects with DPN exhibited large and highly variable dual-task costs in both walking speed and cognitive task performance (22.1 ± 26.1 and $23.0 \pm 26.7\%$, respectively).

Executive Function Measures

The results of the remaining executive function measures are illustrated in Table 2. The DPN group performed worse on the Rey Osterrieth Complex Figure (25.9 ± 4.3 vs. 31.7 ± 2.4 points, $p < 0.001$) and measures of letter (34.2 ± 11.6 vs. 46.2 ± 12.2 words, $p = 0.003$) and category fluency (47.0 ± 8.1 vs. 56.3 ± 8.5 words, $p = 0.001$). No between-group differences were observed on forward digit span ($p = 0.535$), reverse digit span ($p = 0.655$), or Trail Making Test ($p = 0.077$).

Relationships between Neuropsychological Function, DPN Measures, and TUG Performance

For 19 subjects with DPN, relationships between age, BMI, HbA1c, depression, signs and symptoms of DPN, and neuropsychological function were examined using Pearson-product moment correlation coefficients. Selected correlations from this data are presented in Table 3. Surprisingly, older age was associated with a lower MNSI physical score ($r = -0.57$, $p = 0.009$), and higher scores on this instrument (e.g. more signs of DPN) were associated with better category fluency scores ($r = 0.45$, $p = 0.05$).

No other measure of DPN was significantly related to any neuropsychological test or to the TUG. Of the remaining variables only depression, BMI, and MMSE scores were associated with cognitive function or TUG performance. Greater symptoms of depression were related to poorer performance on the MMSE ($r = -0.46$, $p = 0.04$) and TUG ($r = 0.54$, $p = 0.02$), while

poorer MMSE score was related to slower TUG time ($r=-0.53$, $p=0.02$). Paradoxically, higher BMI was associated with a better score on the Rey Osterrieth Complex Figure test ($r=0.47$, $p=0.04$).

DISCUSSION

Our study provides preliminary evidence suggesting that individuals with DPN exhibit disturbances in aspects of executive function. Other researchers have reported similar findings of neuropsychological dysfunction in those with diabetes. For example, Yeung et al⁸ reported that older adults with type 2 diabetes performed significantly worse on several executive measures than those without diabetes. Notably, these differences persisted after dividing the subjects into young-old (53–70 years) and old-old (71–90 years) sub-groups, suggesting that the deficits were due to diabetic status rather than age. Likewise, Thabit et al¹⁸ found that nearly half of their sample of 50 older adults with type 2 diabetes demonstrated significant executive impairments, particularly in verbal fluency, on a standardized measure of executive function.

While our data are broadly consistent with such studies, it is important to note that we did not establish the educational level of our subjects. It is possible that some of the deficits we observed, particularly with regard to verbal fluency, reflect differences in education between the groups. However, we also observed differences on a measure less likely to be influenced by educational level. Specifically, we found that those with DPN performed significantly worse on the Rey Osterrieth Complex Figure, an untimed test of visuospatial organization in which the participant simply copies an asymmetrical geometric figure and is scored according to the accuracy of their reproduction.

Although our neuropsychological findings are interesting, their impact on everyday function remains unclear. We did not observe relationships between measures of executive function and the TUG; however others have reported that poor performance on executive measures containing visuospatial and verbal executive components negatively influences diabetes care¹⁹ and disease self-management.¹⁸ Further research is clearly needed to examine whether visuospatial, verbal, and/or other measures of executive function can be specifically linked to functional outcomes such as gait or ADL performance in this and other populations.

Our analysis of TUG performance revealed that the DPN group walked significantly slower than the comparison group. They also took longer to complete the walking portion of the cTUG, with the added cognitive task slowing walking speed by 22%. This is consistent with reported declines of 25% and 22% under similar dual-task walking conditions in subjects with diabetes with and without DPN, respectively¹¹; although the “dual-task cost” in walking speed for our subjects with DPN was not statistically greater than the 17% decline we observed in comparison subjects.

In comparison to published literature, the average cTUG time for our comparison group (6.9 seconds) was well below the average TUG time reported by Bohannon²⁰ for individuals aged 60–69 years (8.1 seconds). In contrast, the average cTUG time for those in the DPN

group was comparable to the reported average TUG time of individuals aged 80–99 years²⁰. The average cTUG time for those in the DPN group also exceeded the fall risk cut-off score of 12 seconds proposed for community-dwelling adults aged 65–85 years.²¹ The fact that the mean age of our DPN sample was only 58 appears to highlight the potential functional implications of multi-tasking in this population.

One possible explanation for the decline in cTUG walking performance is that participants focused their attention on the cognitive task at the expense of walking speed. This does not appear to have been the case in our study, as cognitive task performance also declined significantly in both groups; although the 26% decline in cognitive performance exhibited by the DPN group was not statistically different than the 19% decline observed in the comparison group.

The fact that we did not observe differences in the dual-task costs of walking or cognitive performance between the groups may result from the large degree of variability elicited by these tasks. This may have occurred because, while we instructed participants to “walk as quickly and safely as possible,” we did not explicitly instruct them to prioritize either the walking or cognitive task during the cTUG. The substantially greater degree of variability in cognitive versus walking task performance exhibited by comparison subjects suggests that this group more often opted to sacrifice cognitive task performance in order to protect walking speed. This was in rather stark contrast to those in the DPN group, who seemed unable to consistently protect either task. We observed that participants who performed worst on the TUG appeared least likely to protect walking performance under the dual-task conditions of the cTUG. This was particularly notable in the DPN group and is alarming, as it indicates that individuals already at risk for falling may fail to self-protect walking and/or balance when multi-tasking – potentially placing them at even greater fall risk.

In order to more clearly characterize multi-tasking performance, future research may benefit from dual-task measures that do not require mathematical ability and account for both gait speed and stability, such as the Walking and Remembering Test.²² Likewise, studies that directly influence and/or manipulate task priority may improve understanding of how attention is allocated under dual-task conditions and help explain whether and/or why different populations fail to protect function and safety while multi-tasking.

Because little research has explored the relationships between central and peripheral nervous system function in those with DPN, and it is unclear how these measures may be associated with functional ability in this population, we explored the correlations among measures of neuropsychological function, DPN, and the TUG. Interestingly this analysis indicated that depression and cognitive function were associated with each other, and were the only variables significantly related to slower TUG performance. This is consistent with other studies that have linked depression to cognitive dysfunction in those with diabetes²³ and associated both factors with gait¹⁰ and functional deficits.²⁴

Despite the fact that the prevalence of depression in those with diabetes is nearly twice as high as the non-diabetic population²⁵ such relationships remain largely unrecognized. This is perhaps because conventional wisdom suggests that somatosensory and proprioceptive

deficits resulting from DPN are the primary mediators of functional impairments. Although exploratory, our findings suggest that the factors underlying fall risk and disability in those with DPN are much more numerous, diverse, and subtle than traditionally thought.

Our analysis also indicated an association between higher BMI and better visuospatial performance on the Rey Osterrieth Complex Figure. Although counter-intuitive, there is a large body of recent evidence supporting a so-called “obesity paradox,” in which obesity and/or higher BMI provide some degree of protective benefit in terms of cognitive functions, including attention and visuospatial function²⁶, and lower the risk of mortality in those with diabetes.^{2,27,28} Clearly, no conclusions on such matters can be drawn from our very small sample. However, our findings join those of others in cautioning that the factors positively and/or negatively influencing cognitive function in complex diseases such as diabetes may not be as straightforward as conventional wisdom would suggest.

Limitations

We acknowledge that there are a number of factors limiting interpretation of our data. In addition to the small sample size, first and foremost is the fact that we did not establish the education level of our subjects. This factor undoubtedly may have influenced performance on some cognitive measures, particularly those involving verbal fluency and/or mathematical ability. However, we also observed deficits in measures, such as the Rey Osterrieth Complex Figure, that would not seem to be heavily influenced by education, and the fact that the groups did not perform differently on the mathematical component of the cTUG suggests that education level may not have substantially influenced this measure. Other variables such as sex, duration of diabetes, and the presence and number of other comorbidities may have also influenced our results.

Another limitation, inherent to our study, is the difficulty in assessing complex cognitive abilities such as executive function. This is a topic of much debate within the neuropsychological community, and a standardized approach has yet to be determined.²⁹ Our assessment battery is consistent with current recommendations that executive function be analyzed via multiple measures assessing specific aspects of the executive construct; as opposed to simply relying on one or two measures to globally represent executive function.

Finally, we performed multiple correlations to explore the relationships between demographic factors, measures of neuropsychological function and DPN, and the TUG. Due to the small size and novel nature of our investigation, we did not correct for these multiple analyses. While this unquestionably limits our interpretation, the significant correlation coefficients we observed were relatively strong and provide interesting avenues for further research. The findings of our study should be regarded with caution, and certainly causal relationships cannot be inferred between any of the variables we examined. It is not clear that differences in cognitive function resulted directly from diabetes or depression. Nor can it be said that cognitive deficits, depression, or any other variable caused gait dysfunction. However, we feel that our data do emphasize the complex and multi-factorial relationships between neuropsychological and physiological factors and physical function in those with diabetes and DPN.

CONCLUSIONS

Our investigation suggests that adults with DPN exhibit disturbances in visuospatial, verbal, and multi-tasking aspects of executive function. Further, our data support the view that gait dysfunction, fall risk, and disability in those with diabetes may not be solely a consequence of DPN and/or musculoskeletal impairment. It is critical that clinicians recognize the potential influence of cognitive and psychological function on physical abilities in patients with DPN so that gait dysfunction, fall risk, and disability can be effectively identified and treated in this high risk patient population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding: This work was supported in part by the Kansas Partners in Progress and in part by Frontiers: The Heartland Institute for Clinical and Translational Research (University of Kansas Medical Center's CTSA; UL1RR033179). The contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH.

We wish to acknowledge Dr. Mamatha Pasnoor (University of Kansas Medical Center) and Dr. Patricia Pohl (The Sage Colleges) for their guidance and consultation. We also wish to thank Laura Herbelin (University of Kansas Medical Center) for data collection assistance, and Mary Beth Fisher (North Kansas City Hospital) and Kim Wernel (University of Kansas Medical Center) for assistance with participant recruitment.

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Figure 1. Walking Speed on the Timed Up and Go and Cognitive Timed Up and Go Tests
Walking speed on the Timed Up and Go (TUG; white bars) and Cognitive Timed Up and Go tests (cTUG; black bars). The cTUG test involved the addition of a simultaneous cognitive task to the standard TUG test. * Significant between-group difference at $p < 0.05$. ‡ Significant within-group difference at $p < 0.05$.

Figure 2. Cognitive Task Performance Under Single- and Dual-task Conditions

Changes in the rate of cognitive task performance under single- (white bars) and dual-task conditions (black bars). Under single-task conditions, participants serially subtracted 3's from a random number between 80 and 100 while seated. Under dual-task conditions, participants completed the same cognitive task while simultaneously performing the TUG test (e.g. the cTUG). The time allowed for the cognitive task under single- and dual-task conditions was equivalent. ‡ Significant within-group difference at $p < 0.05$.

Figure 3. Dual-task Effect on Walking (A) and Cognitive (B) Performance

Effect of dual-task performance on walking speed (A) and cognitive task (B) performance. The solid diagonal line represents identical task performance in single- and dual-task conditions (e.g. no change in performance, or dual-task cost, from single- to dual-task conditions). In A, the dual-task conditions of the cTUG generally increased walking time from the single-task TUG. Thus points falling above the diagonal line reflect poorer walking performance under dual-task conditions (e.g. a greater dual-task cost); whereas points below the line reflect improved walking performance under dual-task conditions. Dashed lines indicate proposed TUG fall-risk cut-off of 12 seconds for adults 65–85 years.²¹ In B, dual-task conditions generally decreased the rate of performance of the cognitive task. Thus points falling below the diagonal line reflect poorer cognitive task performance under dual-task conditions; whereas points falling above the line reflect improved cognitive performance under dual-task conditions.

Table 1

Participant Characteristics

	DPN (n=20)	Comparison (n=20)	P-value
Age	58.4 ± 6.2	54.9 ± 6.1	0.080
BMI	37.0 ± 8.4*	24.8 ± 4.1	< 0.001
BDI	11.3 ± 6.5*	1.6 ± 1.8	< 0.001
MMSE	27.8 ± 2.0*	29.5 ± 0.8	0.001
HbA1c	7.2 ± 1.4	NA	NA

Key: DPN, diabetic peripheral neuropathy; BMI, body mass index; BDI, Beck's Depression Inventory; MMSE, Mini-Mental Status Examination; NA, not applicable. Data are mean ± SD.

* Significant between-group difference at $p < 0.05$.

Table 2

Results of Peripheral Neuropathy (n=19) and Executive Assessments (n=20)

	DPN	Comparison	P-value
MNSI – subjective (score out of 13)	3.1 ± 2.0	NA	NA
MNSI – physical (score out of 10)	5.9 ± 2.6	NA	NA
Peroneal nerve conduction velocity (m/s)	40.9 ± 5.1	NA	NA
Tibial nerve conduction velocity (m/s)	38.9 ± 4.3	NA	NA
Rey-Osterrieth complex figure (score out of 36)	25.9 ± 4.3 *	31.7 ± 2.4	< 0.001
Letter fluency (words)	34.2 ± 11.6 *	46.2 ± 12.2	0.003
Category fluency (words)	47.0 ± 8.1 *	56.3 ± 8.5	0.001
Forward digit span (digits)	10.1 ± 1.9	10.5 ± 2.6	0.535
Reverse digit span (digits)	6.3 ± 2.3	6.0 ± 1.9	0.655
Trail Making Test Change (% difference)	32.1 ± 43.0	12.7 ± 21.0	0.077

Key: DPN, diabetic peripheral neuropathy; MNSI, Michigan Neuropathy Screening Instrument; NA, not applicable. Data are mean ± SD.

* Significant between-group difference at $p < 0.05$.

Table 3
Selected Correlations Between Measures of Neuropsychological Function, Nerve Function, and the TUG Test in Subjects with DPN

	MMSE	ROCF	LF	CF	TUG
BDI	-0.46*	-0.03	0.12	0.20	0.54*
MNSI-S	-0.25	-0.03	-0.25	0.22	0.19
MNSI-P	0.14	0.30	0.06	0.45	-0.07
PNCV	-0.09	-0.25	0.03	-0.02	0.04
TNCV	0.17	-0.15	-0.04	0.03	-0.25
TUG	-0.53*	-0.19	-0.28	-0.08	--

Key: BMI, body mass index; BDI, Beck's Depression Inventory; MNSI-S, Michigan Neuropathy Screening Instrument – subjective; MNSI-P, Michigan Neuropathy Screening Instrument – physical; PNCV, peroneal nerve conduction velocity; TNCV, tibial nerve conduction velocity; TUG, Timed Up and Go; MMSE, Mini-Mental Status Examination; ROCF, Rey-Osterrieth Complex Figure; LF, Letter fluency; CF, Category fluency.

* Significant at p<0.05.