

# Association between Manual Dexterity and Domain Specific Cognition in Subjects with Diabetic Polyneuropathy

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## ABSTRACT

**Introduction:** Type 2 Diabetes is a global concern resulting from longstanding hyperglycaemia. One of its major complication is diabetic polyneuropathy (DPN). This study aimed to understand if any relationship exists between manual dexterity and domains of cognition in DPN patients. **Objectives:** To assess manual dexterity and domain specific cognition and to evaluate the association between manual dexterity measure and domain specific cognition score in subjects with DPN. **Methods:** 64 subjects both male and female (35-75 years) diagnosed with DPN were included. Nine Hole Peg Test for assessing manual dexterity and Montreal Cognitive assessment for assessing domain specific cognition are used as outcome measures. **Results:** A statistically significant but weak correlation between dexterity and Forward Digit Span ( $r=0.310$ ) ( $p=0.013$ ) was found. Delayed recall domain ( $r=-0.97$ ) ( $p=0.44$ ) showed inverse correlation with dominant hand dexterity. Statistically significant but weak correlation was found between non-dominant hand dexterity and the domains of Forward Digit Span ( $r=0.33$ ) ( $p=0.007$ ), Backward Digit Span ( $r=0.266$ ) ( $p=0.034$ ), and Sentence Repetition ( $r=0.243$ ) ( $p=0.053$ ). Majority of patients demonstrated intact cognition in Naming Domain (76.6%) (N=49), Forward Digit Span (64.1%) (N=41), Backward Digit Span (75%) (N=48), Abstraction Domain (98.4%) (N=63) and Orientation Domain (64.1%) (N=41). **Conclusions:** The results imply that all domains of cognition are not affected. There was no significant association between manual dexterity of dominant and non-dominant hand indicating that dexterity may be independent of cognitive domain in patients with DPN.

**Keywords:** Cognition; Diabetic Mellitus; DPN; Hand Dexterity; Hand function

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## INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic abnormalities characterized by hyperglycemia and occurs as a result of irregularities in insulin production, insulin action, or both. India is placed second in the list of highest diabetics in the world accounting for about 77 million of the country's population. In terms of age, individuals aged between 50 and 70 years account for the highest prevalence of diabetes in India. It has been projected that by the year 2045, 152.8 million individuals will be affected with diabetes and most likely around 49.8 million additional individuals will have impaired glucose tolerance. Type 2 DM (T2DM) accounts for around 90–95% of all types of diabetes and consists of individuals who have insulin resistance and usually have relative (not absolute) insulin deficiency. The most common complication seen in diabetic patients is diabetic peripheral neuropathy (DPN). The patient may present with pain, tingling sensation, hypersensitivity, elevated thermal sensory threshold, and elevated tactile sensory threshold if small fibers are involved. Patient may have reduced vibration and position sense and also reduced motor function when large fibers are involved.<sup>[1,2]</sup> Epidemiological studies conducted across various regions in India reported that the prevalence of DPN varied from 10.5% to 32.2%.<sup>[3]</sup> T2DM has been directly linked to the dysfunction of the central nervous system, especially cognitive impairment. When compared to healthy controls, individuals with T2DM are at about 60% greater risk for the development of dementia.<sup>[4]</sup> There is an association between diabetes and cognitive performance, mainly in the domains of memory, concentration, psychomotor speed, and executive function.<sup>[5]</sup> Executive function consists of cognitive processes of attention, working memory, planning, judgment, task flexibility, and is a strong predictor of the level of hand motor function.<sup>[6]</sup> Hand

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evaluation must be considered in the routine assessment of diabetic patients as it can affect activities of daily living and reduce the quality of life of the individual.<sup>[7]</sup> Hand dexterity is strongly associated with executive functions and can be used as measurable motor indicator for identifying individuals at higher risk in impairment of the same.<sup>[8]</sup> Significant differences are seen in motor impairments individuals with cognitive impairment.<sup>[9]</sup> Most clinicians thus do not have a sufficient understanding of how cognition might affect manipulation performance and various daily tasks in patients with DPN.<sup>[10]</sup> Thus, this study aimed to evaluate the association between manual dexterity and cognitive performance to provide evidence of the motor risk factors associated with cognitive decline in patients with DPN.

## METHODOLOGY

### Sample

The cross-sectional study was carried out in the outpatient department of the College Of Physiotherapy, Dayananda Sagar University, Bangalore, India. The sample size was kept at 64, as calculated using G\*Power 3.0.10 software with the following specifications: Statistical Test: Point-biserial model, Tail: One Allowable  $\alpha$  (Alpha) error: 0.05, Power ( $1-\beta$  err prob): 0.80. The participants aged between 35 and 75 years with a minimum lower primary education were eligible to participate. Patients with glycated hemoglobin (A1c) level below 4.0%, diabetic retinopathy any underlying disease such as stroke, spinal muscular atrophy, Parkinson's, Alzheimer's, motor neuron diseases, orthopedic disorders of the upper limb and use of antiepileptic medications, neurotropic agents, or psychotropic agents were excluded to avoid interference with the cognitive tests. Informed consent was taken after explaining the participants about the purpose, benefits, risks, and related details of the procedure. The demographic details of the sample including age, gender duration of DM, BMI, formal education, level of physical activity, HbA1C% and upper limb dominance were represented in Table 1.

### Procedure

Ethical approval (reference number IEC/IRBNo:DSU/MPT/2020/005) was obtained from the Institutional Ethical Committee, College of Physiotherapy, Dayananda Sagar University Bangalore. After recruitment, participants were evaluated for manual dexterity and domain specific cognition using 9HPT<sup>[11]</sup> and Montreal Cognitive Assessment<sup>[12]</sup> test, respectively.

### Outcome Measures

#### Montreal cognitive assessment

Domain specific cognition was evaluated using montreal cognitive assessment test (MoCA). The patients were asked their preference of language in taking the MoCA which was made available to the patient in English and the local language. The questionnaire consists of different domain specific questions to be filled, namely, visuospatial/executive, naming, memory, attention, language, abstraction, delayed recall, and orientation. After completion of the MoCA questionnaire, the patients' hand dominance was noted.<sup>[12]</sup>

#### 9-Hole Peg test (9-HPT)

Hand dexterity was measured using 9-HPT. The test board was positioned according to the patient's dominance. That is, if the patient was right-handed, the pegs were placed on the right and vice versa. The 9-HPT was first measured for the dominant hand and then for the non-dominant hand. The scores were noted. The 9HPT was designed in accordance to the dimensions prescribed by Mathiowetz et al.<sup>[11]</sup>

### Statistical Analysis

The data were collected and documented, graphs were generated using Microsoft Excel 2010. SPSS software (version 18) was used

for the statistical analysis. Descriptive and inferential statistics were applied. Descriptive data were represented in numbers and percentages. Inferential statistics was analyzed using Pearson's correlation for evaluating the correlation between manual dexterity and domains of cognition in patients with DPN. Statistical significance ( $P$ ) value was set at  $P \leq 0.05$ .

## RESULTS

In Table 2, primarily affected domains are visuospatial and the mild delayed recall domain with 95.3 % ( $n = 61$ ) and 89.1% ( $n = 57$ ) affection, respectively. The manual dexterity of dominant hand is  $19.60 \pm 2.95$  and non-dominant hand is  $21.83 \pm 3.08$ . A total MOCA score of  $26.65 \pm 2.04$  depicts mild cognitive impairment (MCI) in 81.3% and mild dementia in 9.4% of the participants. Tables 3 and 4 represents the results of Correlations between upper limb dominance and domains of cognition.

## DISCUSSION

The purpose of the study was to find the association between manual dexterity and distinct domains of cognition in DPN patients. This is also one of the few studies that was aimed at exploring the relationship between the domains of cognition and manual dexterity in DPN patients. The previous researches have highlighted the significance of exploring complex cognitive domains in relation to hand dexterity in patients with DPN. Our study has attempted to examine this aspect, which we consider would lead toward planning specific rehabilitation protocols in patients with DPN.<sup>[8]</sup>

The visuospatial working memory (VSWM) is a short-term memory buffer that stores object locations so that an individual can

**Table 1:** Distribution of study sample (demographic details)

Characteristic	Total participants (n=64)
Age	54.1±9.4
Gender	Male (33) Female (31)
Duration of DM	10.34±6.65
BMI	27.31±4.14
Formal education	Below 10 <sup>th</sup> – n=40 10 <sup>th</sup> –12 <sup>th</sup> – n=9 Higher than 12 <sup>th</sup> – n=15
Level of physical activity	No physical activity: n=13 30 min of physical activity: n=44 60 min physical activity: n=7
HbA1C %	Normal: 5 (<5.7%) Prediabetic: 28 (5.8–6.4%) Diabetic: 31 (>6.5%)
Dominant upper limb	Right dominant n=64 Left dominant n=0

Data presented as number or mean±SD. SD: Standard deviation, DM: Diabetes mellitus, BMI: Body mass index, HbA1C: Glycated hemoglobin

**Table 2:** Domains of cognition

Specific domains	Percentage affected
Visuospatial domain	95.3 (n=61)
Naming domain	23.4 (n=15)
Attention domain	35.9 (n=23)
Language domain	76.6 (n=49)
Abstraction domain	1.6 (n=1)
Delayed recall domain	89.1 (n=57)
Orientation domain	35.9 (23)

Data presented as percentage of affected participants in specific domains

**Table 3:** Correlations between dominant dexterity and domains of cognition

Visuospatial domain	Naming domain	Forward digit span (attention domain)	Backward digit span (attention domain)	Vigilance (attention domain)	Administration (attention domain)	Sentence repetition (language domain)	Verbal fluency (language domain)	Abstraction domain	Delayed recall domain	Orientation domain	Total MoCa
Pearson correlation (r)	0.025	0.310*	0.128	0.032	0.022	0.085	0.174	0.108	-0.097	0.112	0.219
Significant (two-tailed)	0.848	0.013	0.314	0.804	0.864	0.503	0.169	0.397	0.448	0.377	0.082
0.755											
n=64	64	64	64	64	64	64	64	64	64	64	64

MoCA: Montreal cognitive assessment test, There was a statistically significant positive but weak correlation between dexterity and forward digit span. Although there is a statistical significance noted, it may not be independently associated with manual dexterity ( $r=0.310$ ) ( $P=0.013$ ). There seems to be a weak but positive correlation between hand dexterity and backward digit span ( $r=0.12$ ) ( $P=0.314$ ). Total MoCa Score ( $r=0.219$ ) ( $P=0.08$ ) and dominant hand dexterity correlation were analyzed, there was found a positive but weak relationship yet not significant ( $P>0.05$ ) between overall cognition and dexterity of the dominant hand; \* mark indicates that the correlation is significant at the 0.05 level.

**Table 4:** Correlations between non-dominant dexterity and domains of cognition

Visuospatial domain	Naming domain	Forward digit span (attention domain)	Backward digit span (attention domain)	Vigilance (attention domain)	Administration (attention domain)	Sentence repetition (language domain)	Verbal fluency (language domain)	Abstraction domain	Delayed recall domain	Orientation domain	Total MoCa
Pearson correlation (r)	0.012	0.336*	0.266*	0.066	0.045	0.243	0.090	0.091	0.063	0.131	0.152
Significant (two-tailed)	0.924	0.007	0.034	0.605	0.722	0.053	0.480	0.474	0.623	0.303	0.231
0.970											
n=64	64	64	64	64	64	64	64	64	64	64	64

MoCA: Montreal cognitive assessment test, Statistically significant but weak, positive correlation was found between non-dominant hand dexterity and the domains of forward digit span ( $r=0.33$ ) ( $P=0.007$ ) backward digit span ( $r=0.266$ ) ( $P=0.034$ ). Total MoCA score ( $r=0.152$ ) ( $P=0.23$ ) which were statistically not significant ( $P>0.05$ ). A very weak negative correlation was found between visuospatial domain ( $r=-0.005$ ) ( $P=0.9$ ) and hand dexterity definitely not statistically significant ( $P>0.05$ ); \* mark indicates that the correlation is significant at the 0.05 level.

remember what the eye visualizes. This, in turn, helps in planning goal-directed actions despite continuous visual disruptions such as blinks and eye movements.<sup>[13,14]</sup> Furthermore, VSWM is critical to many daily tasks and has been demonstrated as a good predictor of fluid intelligence, navigation, and safe driving if impaired, it can severely impact patients' quality of life.<sup>[15-17]</sup> We observed that DPN was associated with the lowest cognitive scores in visuospatial domain (95.3%) ( $n = 61$ ), which is in line with other recent studies.<sup>[11]</sup> It has been reported that the severity of DPN can worsen the VSWM in these patients. Visuospatial domain plays a significant role in hand function and is expected to be positively associated with hand dexterity.<sup>[13-17,18]</sup> Our study results are contradictory to the previous research findings which demonstrates a weak inverse relationship between dominant hand dexterity ( $R = -0.40$ ) ( $P = 0.755$ ) and non-dominant hand dexterity ( $r = -0.005$ ) ( $P = 0.9$ ) indicating that as dexterity scores increase, the Visuospatial domain score will be reduced. In line with the previous study findings, the T2DM participants of our study have reduced verbal fluency 76.6% ( $n = 49$ ).<sup>[19-23]</sup> This implies that an individual with a serious deficit in lexical access and executive control abilities or both will perform poorly in these tasks.<sup>[24]</sup> However, the differences between male and female patients with respect to their performance in the Verbal fluency tasks was not analyzed in our study; hence, we abstain from any comments in this regard. Verbal fluency domain seemed to have weak and negligible association with manual dexterity (dominant hand dexterity [ $r = 0.17$ ] non-dominant hand dexterity [ $r = 0.090$ ]) thus indicating no possible influence of the verbal

fluency domain on motor task (hand dexterity) in DPN subjects. Further, it was noted that age, gender, and education could influence verbal fluency.<sup>[25-27]</sup> Delayed recall domain was impaired in 89.1% ( $n = 57$ ) of the enrolled DPN patients. In addition, 81.3% ( $n = 52$ ) subjects reportedly had MCI and 9.4% ( $n = 6$ ) had dementia, possibly suggesting that DPN patients may be at risk of developing dementia and Alzheimer's disease. The previous literatures have reported that diabetic subjects with MCI are at a high risk for developing dementia, supporting the findings of the present study and have reported over 46% of them developing dementia within 3 years following acquiring T2DM, when compared to 3% of an age-matched non-diabetic population.<sup>[28]</sup> Delayed recall ( $r = -0.97$ ) ( $P = 0.44$ ) was associated with a strong inverse correlation with dominant hand dexterity and very weak positive correlation with non-dominant hand dexterity ( $r = 0.063$ ) ( $P = 0.62$ ) which may suggest that there may be no possible influence of delayed recall domain on hand dexterity function.

Most DPN patients in our study displayed intact cognition in naming domain (76.6%) ( $n = 49$ ), forward digit span (64.1%) ( $n = 41$ ), backward digit span (75%) ( $n = 48$ ), abstraction domain (98.4%) ( $n = 63$ ), and orientation domain (64.1%) ( $n = 41$ ) which is contradictory to the previous studies, which have reported that T2DM subjects have poor scores in almost all domains.<sup>[5,29,30]</sup> Furthermore, we presume that the intact scores may be attributed to the fact that the most of the DPN subjects recruited for this study reported controlled HbA1c% which might have contributed to the preservation of cognitive function. The other cognitive domains that were found to be intact, namely,

vigilance ( $n=32$ ), administration ( $n=30$ ) (Attention domain), sentence repetition ( $n=30$ ), and verbal fluency ( $n=15$ ) (Language domain) had weak positive association with dominant and non-dominant hand dexterity. This may imply that these domains may possibly not influence the dexterity (Motor) performance of the individual. While the previous researchers have focused on assessing global cognition in DPN subjects, it has not been established as to which domain could mostly be contributing to the global cognitive impairment in DPN subjects. All 64 DPN patients in our study had reduced global cognition scores demonstrating cognitive impairment, which resonates with earlier research articles. Furthermore, in our study on assessment of the individual domains, we observed impairment in certain domains such as visuospatial domain ( $n=61$ ), verbal fluency ( $n=49$ ), and delayed recall domain ( $n=57$ ) while, domains such as orientation ( $n=41$ ), abstraction ( $n=63$ ), backward digit span ( $n=48$ ), forward digit span ( $n=41$ ), and naming domain ( $n=49$ ), were mostly intact.<sup>[5,29,31]</sup>

With this, we would state that the majority of the domains (Abstraction, backward digit span, and forward digit span) possibly contributing to the performance of the upper limb manual dexterity are intact and only the visuospatial domain (possibly associated with manual dexterity) is affected in our study population. This could be the reason for a weaker correlation between manual dexterity and global cognition in our study.

## CONCLUSION

We would like to state that in our study, a weaker correlation exists between manual dexterity and global cognition and there appears to be no significant association between manual dexterity of dominant and non-dominant hand with the domains of cognition. Specific domains of cognition influence manual dexterity. Any disease process affecting these domains would contribute to a compromised dexterity. However, in our study, we found that those domains possibly contributing to the upper extremity dexterity performance were intact. We do not rule out the possibility that this may be proven otherwise when a larger sample will be analyzed.

## Strength of the Study

This is one of the few studies that has focused on the upper limb motor performance in patients with DPN.

The study was successful in exploring the relationship between the domains of cognition and manual dexterity in DPN patients.

## Limitations and Future Recommendations

This study had a very small sample size which reduces the generalizability of the results to the DPN population. A larger sample size may be recommended in the future studies.

Level of physical activity, diet, occupation, alcoholism, smoking, etc. could also impact cognition. This study did not analyze the dexterity and cognitive scores based on the above factors due to the smaller sample size.

All patients in our study were right hand dominant ( $n=64$ ). The future studies may explore the association between dominance and manual dexterity in the right and left dominant DPN patients.

Gender differences were not considered in this study which otherwise would have helped in understanding gender-specific

performance in dexterity and cognition. Gender-based analysis may be recommended.

The severity of DPN in our study population was not considered which possibly might have had influenced the results. Classification of DPN patients based on severity would have helped in understanding the relationship between severe DPN and scores of dexterity and cognition.

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