

The Additive Effects of Type 2 Diabetes Mellitus on Neurobehavioral Functioning of Patients Diagnosed With Myocardial Infarction

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The pathophysiology of Coronary Heart Disease (CHD) predisposes patients to neurobehavioral problems. This study was designed to assess differences in neurobehavioral functioning between patients diagnosed with myocardial infarction (MI) with and without type 2 Diabetes Mellitus (T2DM) and their age, gender, and education-matched community controls. It was proposed that the neurobehavioral functioning of MI patients with T2DM would be different from that of MI patients without T2DM as well as from that of community controls. The Neurobehavioral Functioning Inventory (NFI) (Kreutzer, Seel, & Marwitz, 1999) was administered to MI patients aged between 35 and 55 and the controls. To infer the proposed differences between the groups, Multivariate Analysis of Covariance and Univariate Analysis of Variances was carried out. The results of the study endorse the additive effects of T2DM, as a significant difference was found between the three groups in neurobehavioral functioning, except in communication. MI patients with T2DM scored higher on depression, somatic, memory, aggression and motor subscales compared to MI patients without T2DM and the controls. Moreover, women MI patients scored higher on somatic, memory, aggression and motor deficits; however, no significant gender differences are observed for depression and communication. The study will help direct cardiologists in the formation of realistic goals for MI patients. Future work can scrutinize the additive

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scrutinize the additive effects of T2DM across other types of cardiac conditions, e.g. stable and unstable angina.

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The neurobehavioral sequel of cardiovascular conditions is well-documented and can have a devastating impact on individuals' quality of life. The growing interest in the field of neurobehavior has led investigators and researchers to examine neurobehavioral deficit as related to brain deficits in a wide variety of medical conditions including cardiac diseases (Kang et al., 1991). Diabetes affects the central nervous system, leading to cognitive decline among patients with type 2 diabetes (Gispén & Biessels, 2000). Research endorses a strong association of diabetes with increased risk of dementia, including Alzheimer's disease and vascular dementia (Biessels, De Leeuw, Lindeboom, Barkhof, & Scheltens, 2006). Case-control studies indicated cognitive impairment affecting verbal memory and processing speed, although the results were not found to associate with nonverbal memory and executive functioning (Awad, Gagnon, & Messier, 2004). Not all studies have suggested these cognitive impairments. Differences in methods and study designs such as demographic and diabetic characteristics have made some results inconclusive. Inconsistencies may also be due to differences in the control of confounding factors.

Cardiac dysrhythmias or MI can decrease cardiac output, which may in turn result in decreased cerebral perfusion resulting in disrupted functions like visual perceptual disabilities. Moreover, attention, memory, language and executive control can also be affected (Rockwood, Dobbs, Rule, Howlett, & Black, 1992). Vascular risk factors, such as cardiovascular and cerebrovascular diseases, hypertension, dyslipidemia, and cigarette smoking, as well as psychological distress and lifestyle factors including alcohol consumption, have been suggested to influence cognitive functions. However, the relation between these factors and neurobehavioral functioning has not been examined in detail. Age is also an important demographic factor for cognitive impairment in type 2 diabetes. The characteristics of diminished neurobehavioral functioning in diabetes, resemble the pattern of cognitive decline described in normal aging (Tisserand & Jolles, 2003). Several studies indicated accelerated brain aging caused by diabetes mellitus (Brands et al., 2007), and thus assessing broad neurobehavioral aspects and providing descriptive

evaluations, after controlling for confounding factors such as age, are necessary. Few studies have evaluated the neurobehavioral functions of diabetes in patients with relatively poor glycemic control (Yeung, Fischer, & Dixon, 2009). We performed neurobehavioral tests on hospitalized patients with poorly controlled diabetes and examined the neurobehavioral characteristics of patients with poor glycemic control.

Most research carried out on CHD patients has investigated neurobehavioral functioning in patients with coronary artery bypass graft (CABG) surgery (Daniel & Mark, 2002; Dupuis et al., 1999) and those involved in cardiac rehabilitation programmes (Moser et al., 1999). Patients undergoing cardiac rehabilitation demonstrate worse neurobehavioral performance compared to control subjects, with relative deficits in the domains of memory and verbal fluency (Biessels, Deary, & Ryan, 2008; Moser et al., 1999). Dementia and cognitive decline in type 2 diabetes and prediabetic stages (Biessels, Strachan, Visseren, Kappelle & Whitmer, 2014) and cognitive decline in older people with type 2 diabetes have been endorsed (Feinkohl, Aung, & Keller, 2014). Dupuis et al. (1999) endorsed the fact that patients having undergone CABG, as well as those diagnosed with diabetes mellitus, have an elevated risk of manifesting mild cognitive deficits. Verbal fluency, logical verbal memory, and attention/concentration appear to recover in pre- and post-CABG surgery patients, and no decline in neurobehavioral functioning was found through the battery of tests administered 6 months post-operatively.

Mild cognitive deterioration in areas of attention and memory (working and verbal), processing speed and executive function is observed in older diabetic patients (Awad et al., 2004; Stewart & Liolitsa, 1999; Takeuchi et al., 2012). However, in patients with uncomplicated type 2 diabetes and in mild-to-moderate cases of type 2 Diabetes Mellitus, minimal cognitive impairment differences have been reported between diabetics and an age and gender matched control group in terms of visuospatial attention, constant complex visual attention, attention, mental double tracking, implicit memory, and self-reported memory problems (Asimakopoulou, Hampson, & Morrish, 2002; Nilsson, 2006).

Patients with post-MI status are found to display differences in tests of memory, executive functioning and motor coordination (Barclay, Weiss, Maltis, Bond, & Blass, 1988). The degree of carotid atherosclerosis predicted poorer performance on tests of mental status, verbal and nonverbal fluency and perceptual motor speed (Kaplan, Everson, Koivish, Salonen, & Salonen, 1996). Nielsen and colleagues

(1983) highlighted cognitive deficits in MI patients and in those who have been resuscitated from cardiac arrest. Breteler, Claus, Grobbee, and Hofman (1994) found lower scores on mental status examinations among elderly patients with a history of previous diagnosis of MI. Greater neurobehavioral impairments in medical comorbid conditions, heart failure (HF) and T2DM, have been endorsed (Zuccalà et al., 2005). This increases the risk of congestive heart failure, reinfarction or death. Hyperglycemia is an indicator and correlates with extensive cardiac damage. Dysglycaemia in a patient with AMI unmasks insulin resistance and pancreatic B-Cells dysfunction and identifies subjects with cardiac vascular risk factors. High admission blood glucose level is associated with short-term as well as long-term death according to the AMI index as these patients have more extensive coronary artery disease (Norhammar, Ryden, & Malamberg, 1999).

Mostly, studies have determined the neurobehavioral sequel of precise cardiac problems. However, limited studies have investigated the associated cognitive capacities such as neurobehavioral functioning of cardiac patients, such as those with MI having a comorbid condition, e.g. T2DM. In spite of the large body of research demonstrating that cardiac as well as surgical conditions are related to a decline in cognitive and neurobehavioral functions across diverse domains of performance, numerous imperative questions remain inadequately answered and therefore need additional exploration. It is pertinent for researchers to employ comprehensive neurobehavioral test batteries in order to determine which domains of these functions are affected the most by MI, and in particular, subgroups of MI patients with or without a comorbid condition. Previous studies have mostly investigated neurobehavioral functioning in older patients with CABG surgery (Daniel & Mark, 2002; Dupuis et al., 1999) and in those involved in cardiac rehabilitation programmes (Moser et al., 1999). Limited studies have investigated neurobehavioral functioning in comorbid and multi-morbid conditions of MI like T2DM or T2DM and hypertension, etc.

Despite earlier evidence, it remains unclear whether T2DM and MI have additive effects on neurobehavioral functioning. We examined this possibility in a sample of adults with MI after adjusting for other important demographic variables such as age, gender and education.

Many of the domains of neurobehavioral functioning are reversible; hence it is important to identify differences in the specific domains of neurobehavioral functioning affected in patients diagnosed with MI with and without T2DM. This study will help planning timely

interventions to reverse neurobehavioral damages and improve the quality of life of patients experiencing neurobehavioral problems. Secondly, the results of the study will help in laying grounds for neurobehavioral screening in patients diagnosed with MI that can be included within the routine medical protocol of these patients. This information may be useful for medical staff to realize the significance of conveying health care information in an effective way for the individual patient and may also be useful in the formation of realistic goals for the patient. Differences thus identified within the groups will provide useful information to the cardiologists to target neurobehavioral areas needing compensatory strategies typical of these subgroups.

Objective of the Study

The current study was undertaken with the objective of investigating differences in neurobehavioral functioning between three groups; a) MI cases with diabetes, b) MI cases without diabetes and c) their age-, gender- and education-matched community controls. Furthermore the study explored whether there are gender differences in neurobehavioral functioning in MI patients.

Hypotheses

1. Neurobehavioral functioning of MI patients with T2DM is expected to be lower than that of MI patients without T2DM, which will be lower than that of the controls.
2. There are likely to be gender differences in neurobehavioral functioning across domains of depression, somatic, memory/attention, communication, aggression and motor areas.

Method

Research Design

A retrospective between groups research design was employed for this study.

Sample

The participants of the study ranged in age between 35-55, and were recruited from five hospitals situated in Lahore, where there was a cardiology unit/ward. The participants were recruited in three groups i.e. MI cases with T2DM ($n = 47$; mean age = 52.23; $SD = 2.58$), MI cases without T2DM ($n = 34$; mean age = 47.09; $SD = 3.11$), and community controls ($n = 81$; mean age = 51.38; $SD = 2.89$).

Cases With and Without T2DM. Cases confirming the following study inclusion/exclusion criteria participated in the study.

Inclusion criteria. Cases with myocardial infarction (MI) diagnosed at least 5 years ago, with and without T2DM, with a confirmed diagnosis of an MI based on a summary provided by the cardiologists on the basis of clinical symptoms or changes in electrocardiogram, or elevated concentration of troponin levels, were included in this study.

Exclusion criteria. Cases with the following signs and symptoms were not included in the study: patients with cardiogenic shock or chest pain due to non-cardiac reasons; cases with a significant chronic medical illness like hypertension, and history of stroke, elevated cholesterol, liver disease, hyperthyroidism or hypothyroidism, renal disease, or malignant disease; pregnant women, as well as patients with a prior history of any psychiatric diagnosis or neurological disorder, or those who were currently on any antipsychotic medication. Patients who had a previous history of treatment for heart disease like percutaneous transluminal coronary angioplasty (PTCA) or CABG surgery; patients having more than one episode of MI or any other cardiac condition besides the diagnosis of MI; participants not willing to provide informed consent, as well as those unable to read or write in the Urdu language.

Community Controls. Community-based controls recruited in the study were attendants, visitors or relatives of the cardiac patient, unrelated (not first-degree blood relatives) and having no previous diagnosis of heart disease or history of exertional chest pain, or diabetes.

Community controls were matched on age, gender and education (as these factors can effect neurobehavioral functioning). Exclusion criteria followed for the selection of the community controls were the same as those established for the cases. Community controls were recruited as they comprised the more appropriate control group compared to a hospital control group. Community controls were relatively comparable to representative samples of the community.

Assessment Measures

Demographic/Medical Information. Demographic information was gathered on age, gender, education, marital status, duration since MI, duration since diabetes was diagnosed, and information regarding any neurological, psychological or medical disorder other than MI.

Neurobehavioral Functioning Inventory (NFI) (Kreutzer et al., 1999). The Patient Record Form was employed to assess neurologic disability encountered in daily life. It is a 76-item inventory with a five-point Likert-type scale (from “never” = 1 to “always” = 5). Items are divided among six subscales: Depression, Somatic, Memory/Attention, Communication, Aggression and Motor. The depression subscale measures themes of hopelessness, anhedonia, social isolation and fearfulness (items 7, 13, 19, 25, 31, 37, 43, 49, 59, 65, 67, 70, 72); the somatic subscale measures sleep disturbances, headaches and appetite and digestive difficulties (items 8, 14, 20, 26, 32, 38, 44, 50, 74, 75, 76); the memory/attention subscale assesses problems such as forgetfulness, poor concentration, confusion and disorientation (items 9, 15, 21, 27, 33, 39, 45, 51, 55, 56, 57, 58, 60, 62, 64, 66, 69, 71, 73); the communication subscale assesses problems related to speech initiation, execution and reading/writing difficulties (items 10, 16, 22, 28, 34, 40, 46, 52, 61, 63); the aggression subscale covers items assessing argumentative, physically/verbally abusive and destructive behavior (items 11, 17, 23, 29, 35, 41, 47, 53, 68); and lastly the motor subscale assesses physical weakness and coordination and balance problems (items 12, 18, 24, 30, 36, 42, 48, 54). The everyday living problems highlighted by the *NFI* can be contrasted with performance on neurobehavioral tests. Furthermore, by enabling comparisons to be made between the patients’ and carers’ perspectives, issues relating to self-awareness and insight can be addressed. In this way, the *NFI* helps to focus on the quality-of-life concerns of patients and their families, thus allowing for effective treatment planning and clinical intervention.

The reliability of the scale has been reported to be .97 for the total NFI. Values of alpha exceeding .80 are considered to be good indicators of internal consistency (Crocker & Algina, 1986). The criterion-related validity of NFI is well-documented through correlation analyses, which compared inventory responses to standardized neurobehavioral and personality measures of patient status (Kreutzer, Marwitz, Seel, & Serio, 1996).

Procedure

Institutional approval from the appropriate hospital authorities was sought before conducting the current investigation. Participants who volunteered to participate in the study were asked to sign a written consent form. All participants were briefed about the purpose of the study and guarantees were made about the confidentiality and privacy of their responses. Participants were told that they were free to leave the study any time without providing any reasons, and that this would not incur any prejudice or penalty to them. Before carrying out the research, the NFI (Kreutzer et al., 1999) was translated and the process of validation was carried out. After gathering the detailed demographic and medical information from the study sample, participants were given the Urdu version of the NFI. The questionnaire took approximately 30 minutes to complete. Once the participants had filled out the questionnaire, the researcher thanked and debriefed the participants about the nature of the study. Information thus obtained was analysed using Statistical Package for Social Sciences (SPSS) software (version 20) to test the proposed hypotheses.

Results

Besides descriptive statistics, inferential statistics were run to test the proposed hypotheses. The chi square test was run to find the significance of the difference between three groups: 1) MI patients with T2DM, 2) MI patients without T2DM and 3) age-, gender- and education-matched community control groups on categorical variables. Univariate ANOVAs were run to find differences in continuous medical and/or demographic variables. Multivariate Analysis of Covariance (MANCOVA) and univariate ANOVAs were conducted to find differences among the three groups. Moreover, to infer gender differences in neurobehavioral functioning, a *t*-test was applied. SPSS software program version 20 was used to analyze the data.

Demographic and Medical Differences Between MI Patients With and Without T2DM and Controls

Table 1

Demographic/Medical Information of Sample Presented as Frequency and Percentages (N = 150)

Variable	Cases		Controls n (%)
	With T2DM n (%)	Without T2DM n (%)	
Gender			
Women	28 (59.60)	17 (50.00)	36 (44.40)
Men	19 (40.40)	17 (50.00)	45 (55.60)
Education			
10 or less years	14 (29.78)	13 (38.20)	33 (40.74)
12 to 14 years	22 (46.81)	20 (58.80)	34 (41.98)
16 or more years	11 (23.40)	1 (2.94)	14 (17.28)
Marital status			
Married	46 (97.87)	20 (58.82)	72 (88.89)
Not married	1 (2.13)	13 (38.24)	9 (11.11)
Family history of Diabetes			
Present	42 (89.36)	26 (76.47)	67 (82.72)
Absent	5 (10.64)	8 (23.53)	14 (17.28)
Diagnosed in Parents	47 (100)	20 (58.80)	68 (83.95)
Diagnosed in Siblings	-	14 (41.20)	13 (16.05)
Family history of MI			
Present	32 (68.10)	20 (58.80)	63 (77.80)
Absent	15 (31.90)	14 (41.20)	18 (22.20)
Diagnosed in Parents	45 (95.70)	33 (97.10)	78 (96.30)
Diagnosed in Siblings	2 (4.30)	1 (2.90)	3 (3.70)
Family history of Hypertension			
Present	47 (100)	33 (97.10)	79 (97.50)
Absent	-	1 (2.90)	2 (2.50)
Diagnosed in Parents	34 (72.30)	34 (100)	72 (88.90)
Diagnosed in Siblings	13 (27.70)	-	9 (11.10)
Current Smokers	11 (23.40)	15 (44.10)	30 (37.00)
Non-smokers	36 (76.60)	19 (55.90)	51 (63.00)

The Chi square test (for categorical variables) and univariate ANOVAs (for continuous variables) were computed to find significant differences between MI patients with and without T2DM and the controls on important demographic and medical characteristics. The purpose was to verify invariance between the groups and to identify the characteristics on which the three groups differed, so as to statistically control them in the main analysis. No significant differences were found between groups

for gender ($\chi^2 (2, N = 162) = 2.66, p = .26$), family history of diabetes ($\chi^2 (2, N = 162) = 2.41, p = .30$), and the associated medical condition of hypertension ($\chi^2 (2, N = 162) = 1.28, p = .53$). On the other hand, significant differences were found in marital status ($\chi^2 (2, N = 162) = 23.33, p = <.001$) (marital status is likely to effect NFI scores, e.g. depression and aggression in some cases). Similarly, univariate ANOVAs revealed significant differences on age ($F (2, 159) = 36.29, p = <.001$) and education ($F (2, 159) = 10.48, p = .01$). Marital status, age and education were entered into the main analysis as covariates so as to control their possible effects on neurobehavioral functioning.

Neurobehavioral Functioning of the Groups

MANCOVA was carried out to find the overall significance of differences in study groups on NFI subscales. The result indicated that there was a statistically significant difference between the three groups on composite NFI scores after controlling for the effect of age, marital status and education, $F(6.50) = 1.88, p = .03$; Pilla's = .15 with effect size, partial $\eta^2 = .08$. Further, ANOVAs were carried out to infer the influence of disease status on each of the six NFI subscales separately. All results are statistically significant, however, no significant difference was found among the three groups in communication. Significant differences are established among the groups on depression, somatic, memory, aggression, and motor subscales. Overall, memory is the most affected area of functioning in MI patients both with and without T2DM.

Table 2

Differences Between the MI Cases With T2DM, Without T2DM and Community Controls on Neurobehavioral Functioning

NFI subscale	<u>MI with</u> <u>T2DM</u>		<u>MI without</u> <u>T2DM</u>		<u>Community</u> <u>Controls</u>		F	p
	M	SD	M	SD	M	SD		
Depression	41.25	6.62	32.08	7.52	37.25	8.04	14.56	<.001
Somatic	34.38	4.54	28.97	4.51	32.39	5.32	11.87	<.001
Memory	47.74	9.84	40.02	9.45	44.55	9.41	6.43	.05
Communication	16.56	6.67	17.66	5.95	16.94	6.14	0.27	.75
Aggression	27.80	10.97	23.97	9.42	18.91	5.03	9.21	<.001
Motor	23.40	4.03	16.94	3.59	16.44	5.02	21.08	<.001

Post-hoc Analysis for Differences on NFI Subscales

The Tukey HSD test for post-hoc comparisons (mean differences are reported in Table 3) revealed that depression was significantly greater in cases with T2DM than cases without T2DM and the controls; however

the controls had higher depression than cases without T2DM. Likewise on the somatic subscale, cases with T2DM have a greater mean score than cases without T2DM, although the controls have a greater mean score than cases without T2DM on somatic concerns. Memory is affected in cases with T2DM more than in cases without T2DM, although no significant difference was found between both groups and the controls. On the communication subscale the three groups do not significantly differ. Aggression is higher in cases with T2DM, compared to cases without T2DM who scored higher in aggression than the controls. Finally, a significant difference is observed between cases with T2DM and cases without T2DM, as well as the controls, on the motor subscale; cases with T2DM have a greater mean score compared to cases without T2DM and the controls ($M = 21.44$, $SD = 5.02$). There is no significant difference between cases without T2DM and the controls.

Table 3

Post-hoc Analysis Indicating Precise Differences Between Groups

NFI subscale	Group	Comparison Group	Difference Score
Depression	MI with T2DM	MI without T2DM	9.17**
		Controls	4.00**
	MI without T2DM	Controls	-5.17**
Somatic	MI with T2DM	MI without T2DM	5.41**
		Controls	2.01*
	MI without T2DM	Controls	-3.42**
Memory	MI with T2DM	MI without T2DM	7.72**
		Controls	3.19
	MI without T2DM	Controls	-4.53*
Communication	MI with T2DM	MI without T2DM	-1.10
		Controls	-0.38
	MI without T2DM	Controls	0.72
Aggression	MI with T2DM	MI without T2DM	3.83*
		Controls	8.89**
	MI without T2DM	Controls	5.06**
Motor	MI with T2DM	MI without T2DM	6.46**
		Controls	6.96**
	MI without T2DM	Controls	0.50

* $p < .05$, ** $p < .01$

Gender Differences in Neurobehavioral Functioning

A series of independent sample t -test was conducted to determine gender differences on neurobehavioral functioning. There are significant differences between men and women on all subscales of NFI except for depression. Women have poorer neurobehavioral functioning than men.

Table 4
Gender Difference on Subscales of Neurological Functioning

Variable	Women		Men		<i>t</i> (158)	<i>P</i>	95% CI		Cohen's <i>d</i>
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>			<i>LL</i>	<i>UL</i>	
Depression	38.20	7.06	36.45	9.33	1.35	.18	-.81	4.31	0.21
Somatic	33.19	5.53	30.97	4.71	2.74	.00	.59	3.85	0.43
Memory	46.66	10.65	41.59	8.00	3.39	.00	2.06	8.09	0.53
Com*	17.29	2.84	15.60	3.61	3.30	.00	.68	2.69	0.52
Aggression	27.86	10.64	19.29	5.54	6.15	.00	5.82	11.32	0.97
Motor	22.89	4.70	18.83	4.51	5.53	.00	2.61	5.52	0.87

Note. *Com = communication. CI = confidence interval. *LL* = lower limit. *UL* = upper limit.

Discussion

Consistent with past work, the current study extends these findings by showing that adults with MI and T2DM have greater impairment in neurobehavioral function than those with MI alone. Our study findings suggest significant differences among the three groups on depression, somatic, memory, aggression, and motor subscales. No significant difference was found among the three groups on communication. Our findings suggest that T2DM may be an additional risk factor for neurobehavioral functioning in patients with MI. The current study suggests that MI patients with T2DM have additive impairments in depression, somatic, memory, aggression and motor areas. The past literature is in line with the results of our study; patients with diagnosis of either HF or T2DM exhibit high rates of neurobehavioral and cognitive impairment in these domains (Vogels, Scheltens, Schroeder-Tanka, & Weinstein, 2007). Moreover, elevated fasting glucose in clinically normal adults is associated with reduced performance in executive and neurobehavioral functions (Dahle, Jacobs & Raz, 2009).

Follow-up investigations have shown that HF patients with T2DM demonstrated more impairment in psychomotor speed and speeded tasks of attention, memory and other executive function (Alosco et al., 2012). Our findings are in line with the results of a study conducted on HF patients with T2DM. These patients performed significantly worse than those without T2DM on digit symbol coding, trail making and grooved pegboards with dominant and non-dominant hands (Alosco et al., 2012). Indeed, past research has shown that T2DM (independent of HF) is associated with reduced performance in speeded neurobehavioral measures and psychomotor competence (Yeung et al., 2009). Patients

with T2DM show a cognitive pattern of reduced mental speed and flexibility (Brands, Biessels, de Haan, Kappelle, & Kessels, 2005).

Systematic reviews of the literature on cases diagnosed with T2DM have highlighted deterioration in information-processing speed, verbal memory and executive functioning (Awad et al., 2004; Stewart & Liolitsa, 1999). Nilsson (2006) endorses that in mild-to-moderate cases of T2DM the affected areas are less and not all aspects of cognition are uniformly affected. Moreover, greater neurobehavioral impairments in medical comorbid conditions; HF and T2DM have been proved (Zuccalà et al., 2005).

Alosco et al. (2012) have found that T2DM groups with HF have greater impairment in attention, executive functioning and motor areas. Research carried on patients with cardiac disease has mainly focused on the influence of CABG on cognitive status (Elkins & Johnston, 2004; Newman et al., 2001). Mild to severe neurocognitive decline in CABG patients has been documented (Dupuis et al., 1999). Carotid atherosclerosis predicts worse performance on mental status examination, verbal and nonverbal fluency and perceptual motor speed (Kaplan et al., 1996).

Our study findings suggest that the MI group with T2DM has comparatively greater neurobehavioral deficits in memory, motor and communication areas, and moreover it has higher clinical concerns such as aggression and depression. The additive effects of T2DM have been reported earlier, as studies revealed that patients with T2DM alone also show mild cognitive deterioration in areas of attention and working memory, processing speed, verbal memory, and executive function (Palta, Schneider, Biessels, Touradji, & Hill-Briggs, 2014; Takeuchi et al., 2012). HF and diabetes alone, or as a comorbid medical condition, has found to result in neurobehavioral as well as cognitive impairments with greater impairment observed with a comorbid condition (Alosco et al., 2012).

The existing findings propose that T2DM is a significant contributor to neurobehavioral impairment in patients with MI. Marked impairments in the cognitive abilities in people with type 2 diabetes (Reynolds, Strachan, & Labad, 2010; Yaffe et al., 2012) and early stage type 2 diabetes (Ruis et al., 2009) have been endorsed. Greater neurocognitive deficits in patients with HF with comorbid conditions like T2DM have been documented (Zuccalà et al., 2005). Such findings are probably not unexpected, given the mounting proof for adverse neurocognitive and neurobehavioral outcomes in persons with T2DM.

Poor glycemic control and the resulting cerebral microvascular and macrovascular damage (including reduced endothelial functioning) among patients with T2DM have been shown to be associated with various neurobehavioral impairments (Maggi et al., 2009). Future work is required to elucidate the mechanisms by which MI and T2DM may interact and result in deficits in neurobehavioral domains.

The results of our study highlight the fact that MI patients without T2DM had poor performance on memory, aggression and motor domains compared to the control group. Patients with MI without a comorbid condition present cognitive deficits on tests of memory, executive functioning and motor coordination (Barclay et al., 1988; Nielsen et al., 1983). Furthermore, worse neurobehavioral functioning in patients with a comorbid condition has been reported. Patients with a history of stroke, hypertension, MI, and elevated cholesterol have found to have neurobehavioral decline even in the absence of a comorbid condition (Breteler et al., 1994).

Neurobehavioral impairments have been reported in survivors of sudden cardiac arrest (MI) (Nunes et al., 2003). Seventy-five percent of patients with HF have been found to have cognitive impairment (Vogels et al., 2007) and depression (Koenig, 1998; Pullicino et al., 2008). The prevalence of depression among HF negatively affects the scores on neurobehavioral tests (Havranek, Ware, & Lowes, 1999).

The results of our study revealed that memory was the most affected area of functioning in MI patients both with and without T2DM. Severe to mild neurocognitive deficits have been reported in patients with comorbid and multi-morbid conditions (Alves, Rays, & Fraguas, 2005). Thus, these findings are probably not unexpected given the proof for adverse neurobehavioral outcomes in individuals with MI and comorbid conditions (Alosco et al., 2012).

The results of our study reveal that the controls (compared to MI patients without T2DM) reported greater depression, somatic concerns and memory. These findings are inconsistent with the available evidence at hand. On the whole, the performance of the HF patients compared to that of the controls is worse on tasks associated with psychomotor areas, attention, perceptual speed, cognitive flexibility and visual memory (Almeida & Tamai, 2001; Alves et al., 2005). The probable reason for the disparity in the results of the study is the fact that we did not utilize a longitudinal research design, so it was not possible to assess the pre-existing level of neurobehavioral functioning for the groups. Moreover the sample of MI patients with and without T2DM was recruited from

hospital settings. It is quite possible that patients not reporting to hospitals might have a different pattern of decline in cognitive functioning. Furthermore, Scherrer and colleagues (2011) showed in a study that patients having diabetes with comorbid depression are at greater risk of MI, compared to those with diabetes or depression only. This might explain why MI patients without T2DM had lower levels of depression than those with T2DM and the controls. The patients with T2DM and symptoms of depression might have developed MI afterwards, whereas those without T2DM had lower levels of depression compared to them and the controls, who might have depression only. Even if this is the case, a longitudinal investigation is warranted.

Moreover, research specifying greater neurobehavioral and cognitive impairments in heart disease patients compared to those of the controls has predominantly utilized older patients with a severe condition such as congestive heart failure (Cacciatore et al., 1998; Sauv e, Lewis, Blankenbiller, Rickabaugh, & Pressler, 2009). Most studies have been carried out on a sample of CABG patients (Dupuis et al., 1999) or those with T2DM (Biessels et al., 2008). Evidence of whether the control group differs from the MI group on neurobehavioral functioning is limited and needs further exploration with regard to pre-existing levels of neurobehavioral functioning.

We found no significant differences between MI cases without diabetes and the controls with regard to motor functioning. Most of the earlier findings reported neurocognitive deficits such as memory and cognitive impairments in patients with cardiovascular disease, even in the absence of a comorbid condition (Moser et al., 1999; Newman et al., 2001; Singh-Manoux, Britton, & Marmot, 2003). Silbert, Scott, Evered, Lewis, and Maruff (2007) report pre-existing cognitive impairment in 35% of CABG patients, with the most severe deficits in verbal memory, learning and executive functions. Evidence regarding deterioration in the motor areas of patients with MI has only been reported in a sample of older patients with HF and among those who have undergone CABG (Bruce et al., 2003; Rockwood et al., 1992). We recruited a younger sample of patients with MI, and MI is a less severe condition compared to HF.

Incongruity in our study findings with research evidence at hand can be attributed to multiple causes: first we only took patients with MI aged between 35 and 55 years old, diagnosed five years ago, and having undergone one episode of MI. The severity and duration of cardiovascular disease are determinants of cortical derangements in

middle-aged and older adults with heart disease (Nash, 2007; Tanne et al., 2005). Obesity and other clinical factors such as age at the onset of MI also determine the level of cognitive decline in patients with cardiovascular diseases (Yau et al., 2010; Yaffe et al., 2012).

Evidence regarding the association between the severity and deficits of recall and learning in MI patients exists from studies having utilized a much older sample (Bruce et al., 2003; Rockwood et al., 1992) or from those that recruited a sample of patients who had undergone a severe heart condition like chronic or congestive HF (Cacciatore et al., 1998; Sauvé et al., 2009) or had undergone cardiac rehabilitation (Moser et al., 1999). Second, we inquired about self-reported diabetes from the study participants, as similar prevalence rates in self-reported and actual prevalence of diabetes have been endorsed (Haapanen, Miilunpalo, Pasanen, Oja, & Vuori, 1997; Kehoe, Wu, Leske, & Chylack, 1994). However the contribution of insulin resistance to cognitive decline within MI patients using more precise measures (e.g., HbA1C, oral glucose tolerance testing) should have been undertaken along with an investigation of disease duration. As a result, it is likely that cases in the MI-only and control group of the current study essentially have some degree of insulin resistance, and these processes have lately been linked to cognitive decline (Tan et al., 2011). Therefore they may have not contributed to any significant differences in the MI-only group and the controls with regard to memory and attention deficits.

Moreover, measures used earlier to assess neurobehavioral functioning are varied and quite different to those employed in our study (Newman et al., 2001; Singh-Manoux et al., 2003). Future work is warranted to explicate this and other plausible explanations. Third, pre-existing cognitive levels were not assessed in our study sample. This means that there is a possibility that the control group might have pre-existing memory and attention decline that may be associated with poor existing cognition, resulting in the non-significant difference between MI cases and the controls.

Significant differences between men and women on somatic, memory, aggression, communication and motor deficits areas were found, except on depression. Women had poor neurobehavioral functioning compared to men. The greatest difference was found with aggression. CHD is linked with deterioration in neurobehavioral functioning in both men and women (Singh-Manoux et al., 2008). To the best of the researcher's knowledge, studies do exist on gender differences in clinical etiology and manifestation of patients with MI, however none

of the studies in the past have examined gender differences in neurobehavioral areas in a sample of MI patients. Hence there is no evidence at hand to prove or disprove the existing findings. Generally, women report higher somatic concerns, verbal aggression and communication disturbances under stressful circumstances compared to men (Piccinelli & Wilkinson, 2000); our findings might be attributed to this fact.

Nevertheless, these differences can be attributed to sampling bias as well. The sample of patients was recruited from hospitals. There is also the fact that more women MI patients (59.6%) compared to men (40.4%) in our sample had a comorbid T2DM condition. These medical comorbid conditions have been found to lead to greater deterioration in neurobehavioral as well as cognitive decline (Alosco et al., 2012). Another possibility could be that women MI patients might have had a severe and longer duration of onset of MI or T2DM compared to male patients. Disease severity and length is associated with greater neurobehavioral decline (Singh-Manoux et al, 2008), however, the severity of MI as well as T2DM was not investigated in this study. Emotional disturbance and other factors can affect the neurobehavioral performance of patients with MI and need to be considered in interpreting the results of studies. Although age and education were controlled for in our study, other moderating factors such as existing medical status and use of medication needs to be controlled for, as these factors can affect the neurobehavioral functioning of patients (Blumenthal, Madden, Pierce, Siegel, & Appelbaum, 1993).

Strengths of the Study. Our study can be considered a preliminary study that has investigated neurobehavioral differences among a comparatively younger sample of MI patients aged 35 to 55 years. Moreover, the current study examined a precise subtype of CHD, i.e. MI. It was important to take one specific category as the way in which these CHD etiologies interact with T2DM to result on neurobehavioral/ cognitive decline which may be diverse. Future work can scrutinize the additive effects of T2DM across other types of cardiac conditions e.g. angina.

Limitations. Like our study, most of the studies in this domain are cross-sectional and hardly allow a judgment to be made on whether CHD preceded or was a consequence of poor cognitive functioning (Cacciatore et al., 1998). Another limitation worth mentioning is that we

did not examine the subtype, severity and duration of onset of MI (Singh-Manoux et al., 2008) and T2DM, which may be associated with neurobehavioral function (Hardy & Selkoe, 2002; Okereke et al., 2008; Yaffe et al., 2012). Many controls reported having hypertension, however we did not investigate whether these controls were on medication. This needs to be investigated in detail in future studies, as being on medication can affect the study findings. Time since the first coronary event occurred is linked with the progression of neuro-behavioral decline. Impairments in communication, reasoning, vocabulary, and semantic fluency among those with a longer duration of coronary disease have been documented (Singh-Manoux et al., 2008). Lesser cognitive decline has been reported in the early stage of type 2 diabetes (Ruis et al., 2009).

Finally, the relatively small sample size in the present study did not permit analyses to control for primary variables such as medication status and other variables such as obesity. These points towards undertaking studies with larger samples of MI patients with T2DM so as to clarify differences between MI cases with and without the additive effects of T2DM on neurobehavioral function.

Conclusion. The current study demonstrates that MI patients with T2DM have greater cognitive impairments than MI patients without T2DM. Future work is required to make known the mechanisms by which T2DM exacerbates neurobehavioral and cognitive impairment in young adults with MI. However literature specifying neurobehavioral functioning in comorbid and multi-morbid conditions of MI such as T2DM, T2DM and hypertension etc. is limited, highlighting an important area for future research. In future, we need to recruit more controls per case and more patients without T2DM. The results of the study could have been different depending on the source of the control groups. We were able to attain a high response rate, i.e. 86%, so the best choice of controls was from the community.

Researchers should focus on the identification of a screening instrument that is sensitive to the neurobehavioral profile of MI patients, and at the same time easy to use in a clinical setting. This study provides important understanding of planning assessment of the neurobehavioral functioning of MI patients with or without T2DM needing compensatory strategies. As MI with T2DM is associated with poorer neurobehavioral functioning, a timely assessment of neurobehavioral impairments can be helpful for these patients to identify neurobehavioral decline and to help them manage the deficits, which can help to improve their quality of life.

The study points towards the need to plan neurobehavioral screening that can be included within the routine medical protocol of these patients. Future work can scrutinize the additive effects of T2DM across other types of cardiac conditions, e.g. stable and unstable angina.

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