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Neuropsychological deficits in patients with myocardial infarction

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Abstract

Myocardial Infarction (MI), commonly known as a Heart Attack, remains a leading cause of death throughout the world. Studies have shown that patients, who had MI, have cognitive impairment affecting attention, problem solving, memory, visuospatial, executive function and even dementia. Since cognition and emotion are integral part of the disease, there are no focused studies addressing this issue in the Indian context. Hence the present study. The objective of the study was to determine the neuropsychological deficits in patients with MI and with MI after cardiac bypass surgery. The sample consisted of 30 patients, 15 MI and 15 MI after CABG. All patients were assessed on. a battery of Neuropsychological tests and Hamilton Rating Scale for depression, The findings revealed impairment in mental speed, sustained attention, Animal Fluency Test, Phonemic Fluency Test, verbal and visual working memory, planning, response inhibition, verbal and visual learning and memory. On comparison with MI patients CABG patients showed significant deficits in Planning.

Keywords: Myocardial Infarction; Coronary Artery Bypass Graft

1. Introduction

A heart attack (myocardial infarction) occurs when an area of heart muscle dies or is permanently damaged because of an inadequate supply of oxygen to that area. WHO estimated that 16.7 million people around the world

die from Cardiovascular Disease each year. This is 29% of all deaths worldwide (International Cardiovascular Disease Statistics Report, 2003). A large number of neuropsychological deficits are seen in patients with Myocardial Infarction. Investigations on individuals with MI indicate neuropsychological deficits involving the areas of attentional processes, memory impairment, motor coordination and disorientation (Barclay, Weiss, Mattis, Bond & Blass, 1998). Causal relationship between MI and cognitive dyfunction remains uncertain.Patients who are at highrisk for MI develop plaques in the arterial wall due to the deposition of fat, cholestrol and other blood products resulting in the obstruction of blood flow to the heart. During heart attack, the plaque will rupture leading to formation of clot resulting in occlusion of the blood vessel. Later these clots enter into arterial circulation and block the flow of the blood to the different parts of the brain . most of these clots to the brain lodge in the middle cerebral artery (MCA) or its branches (Cerebral embolism task force, 1986). MCA gives largest supply to the cerebral hemispheres, accounting for about 75%. It supplies branches to the extencive areas of the cortex, internal nuclear masses and internal capsule. About 20% of these clots go to the posterior circulation (vertebro-basilar and posterior cerebral artery (Caplan, 1994). This will lead to reduced blood flow to the different parts of brain cells resulting in depletion of cells due to hypoxia.

Neuropsychological deficits have been observed in 33% to 83% of CABG patients post surgically, persisting after 12 months in up to 35% of these patients (Barbut & Caplan, 1997). A recent study found that 42% of patients evidenced cognitive deficits 5 years after CABG (Newman et al., 2001). Studies have found postoperative declines in verbal and visual learning and memory, complex attention, information processing speed, and psychomotor speed in up to 70% of patients (Blumenthal et al., 1991; Croughwell et al., 1994; Newman et al., 1994, 1995). The postoperative cognitive changes may result from non-specific effects of surgery or anesthesia.

Myocardial infarction (MI) is frequently complicated by a depressive disorder (Frasure-Smith et al., 1993). Patients with depression after MI probably are doubly at risk for cognitive decline. First, depressive disorder is related to a decline in impaired attention, frontal lobe dysfunction, executive deficits and especially memory impairment (Burt et al., 1995). Psychomotor retardation is also found. Secondly patients with chronic cardiac disease in general perform worse than healthy controls on cognitive tests.

Before a comprehensive rehabilitation strategy can be devised for this growing population of patients, it is important to characterize all aspects of cognitive function, since cognitive function play an important role in day-to-day life.

2. Methods

The study began after obtaining ethical clearance from the NIMHANS ethical committee. and written informed consent from all the patients.

Out of 38 patients, 30 patients, 15 patients with MI and 15 patients after CABG, were selected. Eight patients were rejected since they were not motivated for the assessment and they had a fear that they would be diagnosed as having any mental illness. The age range of 30 and 65, both literate and illiterate and both male and female. All patients were right handed. Details of patients cognitive functions prior to the onset of illness is not known. Patients were included in the CABG group if the duration of surgery was within one month after surgery. Patients were excluded if they had (1) Major physical illnesses such as liver dysfunction, (2) Major psychiatric and neurological disorders, (3) Clinical evidence of mental retardation.

A battery of Neuropsychological Tests (Rao et al., 2004) were selected-Digit Symbol Substitution Test, Digit Vigilance Test, Test of Executive Functions, Phonemic fluency, Category fluency, Verbal N back test, Visual N back test, Tower of London, Wisconsin's card sorting test, Stroop test, Auditory Verbal Learning Test, Complex Figure Text.

2.1. Procedure

After obtaining written informed consent 30 patients, (15 patients with MI and 15 patients after CABG, on cardio-pulmonary bypass) were assessed. Patients were assessed individually in 2-4 sessions. Adequate rest pauses were given to ensure that the patient was not tired. Duration of the assessment was approximately two hours for each patient.

2.2. Data analysis

The data obtained for the variables under study have been subjected to different statistical analysis. The results were analyzed using descriptive statistics such as means and standard deviations on individual tests. Student's "t" test was carried out to find out whether any significant difference was found between the groups. The data obtained was also compared to normative cut off scores, provided in the NIMHANS neuropsychology manual in order to determine the deficits in the respective areas, and then analyzed using 2X2 chi-square test to determine the significant difference between two groups in terms of percent of deficits.

2.3. Results

Mean age of the CABG group was 55 years old and the mean age of the MI group was 54 years old, which indicates that there is no significant age difference between the two samples. Both CABG group and MI group consisted of 11 male patients and 4 female patients. Among 15 patients of the CABG group, 7 patients were college educated and 8 were school educated whereas in MI group 9 were college educated and 6 were school educated. All patients were right handed as assessed by Edinburgh Handedness Inventory. On Hamilton rating scale for depression there were no significant difference. On inspection, one patient in the CABG group and one patient in the MI group had moderate depression and mild depression respectively. This indicates there is no significant comorbidity of depression in MI and CABG patients in the present sample.

2.4. Group differences

T test was conducted to examine the difference between groups with regard to total score obtained on each neuropsychological test. Mean, standard deviation, degrees of freedom and "t" value of various neuropsychological tests across two groups are given in Table 1. Significance level was tested at the .05 level. On Digit vigilance test, mean score of total time for the CABG and MI group are 595.13s and 489.07 s respectively. It was found that the difference between the groups on total time is significant. On Tower of London Test, the mean score of time taken for 5 moves were 55.20 and 41.77 for CABG and MI group respectively. It was found that the mean score of time taken for 5 moves, the difference between the groups was significant. On Auditory Verbal Learning test, the mean scores of long-term percent retention of words were 77.2 and 86.8 and the mean scores of percent of delayed recall were 9.07 and 11.0 for CABG and MI group respectively. It was found that for long-term percent retention and delayed recall of words, the difference of the mean score between the groups was significant. On Complex Figure test, the mean scores of immediate recall of figure were 15.43 and 23.8 and the mean scores of delayed recall were 14.7 and 22.7 for CABG and MI group respectively. A significant difference was found in immediate recall of figure and delayed recall of figure between the groups. It was found that CABG patients had lower scores than MI patients in tests Digit Vigilance, Tower of London, Auditory Verbal Learning and Complex Figure Test indicating that CABG patients were poor in Sustained attention, Planning, Verbal Learning and memory and Visual Learning and memory compared to MI patients.

Table 1. Mean, standard deviation, Degrees of freedom and "t" value of various neuropsychological tests across the groups

Tests	CABG group N = 15		MI group N = 15		df	"t" value
	M	SD	M	SD		
Digit Symbol Substitution	357.5	135.8	284.2	84.0	28	.086
DigitVigilance	595.1	146.4	489.0	32.4	28	.047
Animal Fluency	11.3	2.6	12.4	1.8	28	.184
Phonemic Fluency	7.6	2.9	9.5	2.6	28	.072
Verbal N Back 1	8.3	1.1	8.5	1.3	28	.582
Verbal N Back 2	6.4	1.0	6.4	1.3	28	1.00
Visual N Back 1	7.2	1.4	7.2	1.4	28	1.00
Tower of London 5 moves						
Minimum Moves	2.6	0.7	2.0	0.9	28	.834
Minimum Time	55.2	18.7	41.7	8.7	28	.018
Wisconsin's Card Sorting						
Failure To Maintain Set	0.2	0.5	0.0	0.0	28	0.17
Stroop Effect (seconds)	234	120	179	36	28	0.09
Auditory Verbal Learning						
Long Term Percent Retention	77.2	14.2	86.8	8.5	28	0.03
Delayed Recall	9.07	2.25	11.0	2.54	28	0.03
Complex Figure						
Immediate Recall	15.4	6.4	23.8	6.0	28	.007
Delayed Recall	14.7	6.1	22.7	5.4	28	.001

* Significant at 0.05 level.

2.5. Neuropsychological deficit

To examine the neuropsychological deficit, scores of each patient were compared with gender, age, and education specific norms and the scores falling below 15th percentile of the normative data were treated as deficits. Then chi-square test was conducted to examine the difference between groups with regard to deficits. Significance was tested at the .05 level. Percent of patients with deficits in each group and chi-square value are given in Table 2.

Table 2. Neuropsychological deficits of the groups

Test	Percent of patients with deficit (N = 15)		df	chi-square
	CABG	MI		
Digit Symbol	33	27	1	1.00
Digit Vigilance	27	7	1	.33
Animal fluency	20	13	1	1.00
Phonemic Fluency	40	6	1	.08
Verbal N Back 1	7	7	1	1.00
Verbal N Back 2		13	1	1.00
Visual N Back 1	7	7	1	1.00
Tower of London (TOL) Total Time (5 moves)	9	53	1	.03
Number of moves	7	0	1	1.00
Wisconsin's Card Sorting	0	0	1	NS
Stroop Test	20	27	1	1.00
AVLT-Immediate Recall	20	0	1	.22
AVLTDelayed Recall	26	13	1	1.00
AVLTLong term percent retention	35	7	1	.17
CFT-Immediate Recall	40	20	1	.42
CFT-Delayed Recall	33	7	1	.16

* Significant at 0.05 level.

Deficits were seen in Digit Symbol Substitution Test, which measures mental speed (CABG = 33%, MI = 27%), Digit Vigilance Test, which measures sustained attention (CABG = 27%, MI = 7%), Animal Fluency Test (CABG = 20%, MI = 13%), Phonemic Fluency Test (CABG = 40%, MI = 6%), which measures verbal fluency. Verbal N Back 1 Test (CABG & MI = 7%), verbal N Back 2 Test (CABG& MI = 7%), which measures verbal working memory, Visual N Back 1 Test (CABG&MI = 7%), Visual N Back 2 Test (CABG = 7%, MI = 33%), which measures visual working memory, Tower of London Test (CABG = 93%, MI = 53%, time taken for 5 moves problem), which measures planning, Stroop Test (CABG = 20%, MI = 27%), which measures response inhibition, Auditory Verbal Learning test (CABG = 35%, MI = 7%, long term percent retention), which measures verbal learning and memory and Complex Figure Test (CABG = 40%, MI = 20% for immediate recall, CABG = 33%, MI = 7% for delayed recall), which measures visual learning and memory. On comparison with MI patients CABG patients showed significant deficits in Tower of London which measures Planning.

3. Discussion

The aim of the present study was to examine the neuropsychological deficits in patients with myocardial infarction. The objective of the study was to examine the neuropsychological deficits in patients with myocardial infarction and in patients with MI after cardiac bypass surgery. There was no significant comorbidity of depression in MI and CABG patients in the present sample. Both the groups showed deficits in Digit Symbol Test, which measures mental speed. Mental speed requires coordination of different areas of the brain, mainly frontal and parietal cortices. Hence, on this test deficit shows impairment in frontal and parietal lobe functions in MI and CABG patients.

Digit Vigilance Test measures sustained attention, which refers to the capacity to attend to a task in hand for a required period. Patients in the CABG & MI group have shown deficit, which is not significantly different between the groups. Shaw observed similar findings in 1987 on attentional impairment in postoperative cardiac condition. A right fronto-parietal network mediates sustained attention. Imaging studies have shown that vigilance tasks that require sustained attention activate a network of structures in the right frontal and parietal cortices (Pardo, Fox & Raichle, 1991).

Phonemic fluency refers to the capacity to generate new words in a regulated manner and category fluency (Animal fluency) refers to the capacity to generate words belonging to a category imposed by regulation. Imag-

ing studies show that verbal fluency activates frontal lobes, particularly the prefrontal cortex in the language dominant hemisphere (Elfgren & Risberg, 1998). Lesion studies showed deficits in phonemic fluency following damage to the left frontal lobe (Benton & Hamsher, 1989). Neuro imaging studies have shown temporal lobe involvement in category fluency (Frith, 1991). Patients in MI and CABG group have shown deficits on this test.

Verbal working memory using N-back tasks activated Broca's area and left supplementary motor and premotor areas (Smith & Jonides, 1999). The verbal items appeared to be represented in the left posterior temporal areas, short term storage of phonological information is in the left supramarginal gyrus, the left dorsolateral prefrontal cortex maintains the temporal order and the Broca's area supports articulatory processes (Henson, Burgess & Frith, 2000). There is impairment in CABG and MI patients on this test indicating working memory deficit. The visuo-spatial sketchpad is a buffer responsible for the initial registration of visual material (Baddeley, 1986). Findings showed patients of both the groups have difficulty in visual N Back Test. Activation in the dorsolateral prefrontal cortex reflects manipulation and transformation rather than the storage or retention (Owen, 1998).

Planning is the ability to set goals to monitor performance so as to reach the goals and to make corrections in the course adopted, in order to ensure that the goal is attained (Lezak, 1995). Goal setting involves identifying the final goal, and intermediate goals, which have to be attained in order to achieve the final goal. Planning was tested using the Tower of London test on which the subject had to arrive at the goal state. This was carried out with 2 moves, 3 moves, 4 moves and 5 moves problems. The tests were conducted in a graded manner of increasing task difficulty. On the 5 moves, 93 percent of patients in the surgery group and 53 percent of patients in the MI group have shown deficits in the mean time, which is significantly different between two groups. Patients following CABG were found to solve proportionately fewer problems (7% deficit) in the minimum amount of moves and displayed significantly longer thinking times than patients who have not undergone surgery. This can be attributed to frontal lobe dysfunction. Lesion studies have shown that left frontal lesions are associated with deficits in planning (Shallice, 1982). Performance on the Tower of London correlates with activation in the dorsal prefrontal cortex and additionally the premotor and parietal cortex (Rowe et al., 2001). CABG patients have shown deficit in planning on Maze time test (Sotaniemi, 1986). The planning ability impairment could be attributed to deficit in specific motor functions i.e. slowing or deficit in cognitive speed independent of motor requirement. Another possibility could be attributed to deficits of spatial working memory, thus resulting in an increased difficulty to keep an action plan in memory.

Stroop test measures response inhibition. Response inhibitions refers to the ease with which a perceptual set can be shifted both to conjoin changing demands and by suppressing a habitual response in favour of an unusual one. Patients with bilateral superior medical prefrontal damage showed increased errors and slowness in incongruent condition wherein when the color name had to be read when it was printed in the ink of another color (Stuss, Folden, Levin & Katz, 2001). On the stroop test, cardiac patients were slower and made errors during the interference condition in preoperative as well as post-operative condition (Sotaniemi, 1986; Millar, 2000). The present study corroborates with the previous studies.

Verbal learning and memory is the capacity to learn and remember verbal material and it was tested with the learning and memory of word lists. The right prefrontal lobe is involved to a greater extent in retrieval from episodic memory (Tulving, 1999). Prefrontal cortices are important for the organization of the material, verification of recalled material and formulating heuristic strategies for learning, while the hippocampal structures are important for associations between events discrete in time and space. Lesions in the left temporal lobe disrupt verbal memory and excisions of left hippocampal structures impair verbal memory to a greater extent (Smith-Milner, 1981; Jones-Gotman, 1997). It has been identified that there are 3 subtypes of memory deficit following CABG: memory spared, retrieval deficit and encoding or storage deficit (Kneebone, Luszez & Baker, 2005). MI and CABG patients have shown impairment on this test.

The visuo-constructive ability was tested using the Rey's complex figure test (Meyer's & Meyer's). It is the capacity to construct a design or to translate a visually perceived form into a three dimensional object or a two dimensional figure. Visuo constructive ability requires attention, visuospatial perception, visuomotor coordination, planning, and error correction ability. This ability is a composite function, which is mediated by bilateral parietal structures, predominantly by the right parietal structure. The prefrontal structures also mediate the planning and error correction required for visuo constructive ability (Lezak, 1995). CABG and MI groups have shown deficit in immediate and delayed recall. Findings indicated mild to moderate impaired visual memory skills and suggestive of impairment in right hemisphere functions (Roine, Kajaste & Kaste, 1993). This corroborated with findings of O.A. Selnes (2004) who had tested impairment in visuo-spatial learning and memory in CABG patients.

In conclusion, Deficits were seen in Digit Symbol Substitution Test, which measures ental speed (CABG = 33%, MI = 27%), Digit Vigilance Test, which measures sustained attention (CABG = 27%, MI=7%), Animal Fluency Test (CABG = 20%, MI = 13%), Phonemic Fluency Test (CABG =

40%, MI = 6%), which measures verbal fluency. Verbal N Back 1 Test (CABG & MI = 7%), verbal N Back 2 Test (CABG & MI = 7%), which measures verbal working memory, Visual N Back 1Test (CABG & MI = 7%), Visual N Back 2 Test (CABG = 7%, MI=33%), which measures visual working memory, Tower of London Test (CABG = 93%, MI = 53%, time taken for 5 moves problem), which measures planning, Stroop Test (CABG = 20%, MI = 27%), which measures response inhibition, Auditory Verbal Learning test (CABG = 35%, MI = 7%, long term percent retention), which measures verbal learning and memory and Complex Figure Test (CABG = 40%, MI = 20% for immediate recall, CABG = 33%, MI = 7% for delayed recall), which measures visual learning and memory. On comparison with MI patients CABG patients showed significant deficits in Tower of London which measures Planning.

This is the first study carried out in India, which has explored neuropsychological deficits in Myocardial Infarction. The present study provides evidence of neuropsychological deficits in patients with Myocardial Infarction. Limitations of the study were smaller sample size, female group was not a representative sample, since sample size was small and pre-existing cognitive deficits of patients was not taken into consideration. Further studies can include more patients with MI and CABG and more representative sample of male and female sexes can be included. A detailed study can be carried out for various anesthetic procedures. A similar research can be done on patients with cardiovascular risk factors such as diabetes mellitus and hypertension. Follow up neuropsychological assessment can be carried out.

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References

Alexander, G.E., & Crutcher, M.D. (1990). Functional architecture of basal ganglia circuits: neural substrates of parallel processing. *Trends Neuroscience*, 13.

APA (1994). *Diagnostic and Statistical Manual of Mental Disorders (DSM IV)*. Washington, DC: American Psychiatric Association.

Baddeley, A.D. (1986). *Working Memory*. New York: Oxford University Press.

Barbut, D., & Caplan, L.R. (1997). Brain complications of cardiac surgery. *Current Problems in Cardiology*, 22, 449-480.

Benke, T., Neussl, D., & Aichner, F. (1991). Neuropsychological deficits in asymptomatic carotid artery stenosis. *Acta Neurologica Scandinavica*, 83, 378-381.

Benton, A.L., & Hamsher, K.S. (1989). *Multilingual Aphasia Examination*. New York: Oxford University Press.

Blauth, C.I. (1995). Macroemboli and microemboli during cardiopulmonary bypass. *Annals of Thoracic Surgery*, 59, 1300-1303.

Blumenthal, J.A., Madden, D.J., Burker, E.J., Croughwell, N., Schniebol, S., Smith, R., White, W.D., Hlatky, M., & Reves, J.G. (1991). A preliminary study of the effects of cardiac procedures on cognitive performance. *International Journal of Psychosomatics*, 38, 13-16.

Brækken, S.K., Russell, D., & Brucher, R. (1997). Cerebral microembolic signals during cardiopulmonary bypass surgery. Frequency, time of occurrence, and the association with patient and surgical characteristics. *Stroke*, 28, 1988-1992.

Breteler, M.M.B., Claus, J.J., Grobbee, D.E., & Hofman, A. (1994). Cardiovascular disease and distribution of cognitive function in elderly people: The Rotterdam Study. *British Medical Journal*, 308, 1604-1608.

Breteler, M.M.B., & Van Swieten, J.C. (1994). Cerebral white matter lesions, vascular risk factors, and cognitive function in a population based study: The Rotterdam Study. *Neurology*, 44, 1246-1252.

Caplan, L.R. (1994). Cerebrovascular disease and neurologic manifestations of heart disease. In: Schlant, R.C., & Alexander, R.W. (eds.). *The Heart, Arteries and Veins*. New York: McGraw-Hill, pp. 2141, 2162.

Cerebral Embolism Task Force (1986). Cardiogenic brain embolism. *Archives of Neurology*, 43, 71-83.

Chabot, R.J., Gugino, L.D., Aglio, L.S., Maddi, R., & Cote, W. (1997). QEEG and neuropsychological profiles of patients after undergoing cardiopulmonary bypass surgical procedures. *Clinical Electroencephalography*, 28, 98-105.

Croughwell, N.D., Newman, M.F., Blumenthal, J.A., White, W.D., Lewis, J.B., Frasco, P.E., Smith, L.R., Thyrum, E.A., Hurwitz, B.J., Leone, B.J., Schell, R.M., & Reves, J.G. (1994). Jugular bulb saturation and cognitive

dysfunction after cardiopulmonary bypass. *Annals of Thoracic Surgery*, 58, 1702-1708.

Cummings, J.L. (1993). Frontal-subcortical circuits and human behavior. *Archieves of Neurology*, 50, 873-880.

Djikstra, B.J. (2004). A typical cognitive profile in patients with depression after myocardial infarction. *Journal of Affective Disorders*, 70, 181-190.

Drewe, E.A. (1974). The effect of type and area of brain lesions on Wisconsin's card sorting test performance. *Cortex*, 10, 159-170.

Elfgren, C.I., & Risberg, J. (1998). Lateralised frontal blood flow increases during fluency tasks: Influence of cognitive strategy. *Neuropsychologia*, 36, 505-512.

Frasure-Smith, N., Lesperance, F., & Talajic, M. (1993). Depression following myocardial infarction. Impact on 6-month survival. *Journal of American and Medical Association*, 270, 1819-1825.

Gill, R., & Murkin, J.M. (1996). Neuropsychologic dysfunction after cardiac surgery: What is the problem? *Journal of Cardiothoracic and Vascular Anesthesia*, 10, 91-98.

Goetz Ch.G., & Pappert, E.J. (1999). *Textbook of Clinical Neurology*. Philadephia: W.B. Saunders company.

Grubb, N.R. (1996). Chronic memory impairment after cardiac arrest outside hospital. *British Medical Journal*, 313, 143-146.

Hamilton, M. (1960). A writing scale for depression. *Journal of Neurology Neurosurgery Psychiatry*, 23, 56.

Harrison, M.J.G. (1995). Neurologic complications of coronary artery bypass grafting. Diffuse or focal ischemia. *Annals of Thoracic Surgery*, 59, 1356-1358.

Kannel, W.B., Wolf, P.A., & Verter, J. (1983). Manifestations of coronary disease predisposing to stroke: The Framingham study. *Journal of the American Medical Association*, 250, 2942-2946.

Kneebone, A.C. (2005). A syndromal analysis of neuropsychological outcome following coronary artery bypass graft surgery. *Journal of Neurology Neurosurgery Psychiatry*, 76, 1121-1127.

Lezak, M.D. (1995). *Neuropsychological Assessment (3rd ed)*. New York: Oxford University Press.

Lim, C. (2004). The neurological & cognitive sequelae of cardiac arrest. *Neurology*, 63, 1774-1778.

McLean, R.F., & Wong, B.I. (1996). Normothermic versus hypothermic cardiopulmonary bypass. *Journal of Cardiothoracic and Vascular Anesthesia*, 10, 45-53.

Merrill, E.A. (2001). *Neuropsychology of Cardiovascular Disease*. Mahwah: NJ publication.

Meyers, J., & Meyers, K. (1995). *Rey Complex Figure and Recognition Trial: Professional Manual*. Florida Psychological Assessment Resources.

Millar, K., Asbury, A.J., & Murray, G.D. (2001). Pre-existing cognitive impairment as a factor influencing outcome after cardiac surgery. *British Journal of Anaesthesia*, 86, 63-67.

Milner, B. (1963). Effects of different brain lesions on card sorting. *Archives of Neurology*, 9, 90-100.

Newman, M.F., Croughwell, N.D., Blumenthal, J.A., Lowry, E., White, W.D., & Reves, J.G. (1996). Cardiopulmonary bypass and the central nervous system: Potential for cerebral protection. *Journal of Clinical Anesthesiology*, 8, 53-60.

Newman, M.F., Croughwell, N.D., Blumenthal, J.A., Lowry, E., White, W.D., Spillane, W., Davis, R.D., Glower, D.D., Smith, L.R., Mahanna, E.P., & Reves, J.G. (1995). Predictors of cognitive decline after cardiac operation. *Annals of Thoracic Surgery*, 59, 1326-1330.

Newman, M.F., Kirchner, J.L., Phillips-Bute, B., Gaver, V., Grocott, H., Jones, R.H., Mark, D.B., Reves, J.G., & Blumenthal, J.A. (2001). Longitudinal assessment of neurocognitive function after coronary artery bypass surgery. *New England Journal of Medicine*, 344, 395-402.

Newman, M.F., Kramer, D., Croughwell, N.D., Sanderson, I., Blumenthal, J.A., White, W.D., Smith, L.R., Towner, E.A., & Reves, J.G. (1995). Differential age effects of mean arterial pressure and rewarming on cognitive dysfunction after cardiac surgery. *Anesthesia and Analgesia*, 81, 236-242.

Oldfield, R.C. (1971) The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia*, 9, 97-113.

Osborn, M.J.(1996). Sudden cardiac death: Mechanisms, incidences, and prevention of sudden cardiac death. In: Guliani, E.R., Gersh, B.J., McGoon, M.D., Hayes, D.L., & Shaff, H.V. (eds.). *Mayo Clinic Practice of Cardiology*. St. Louis: Mosby, pp. 862-894.

Owen, A.M. (1990). Planning and spatial working memory following frontal lobe lesions in man. *Neuropsychologia*, 28, 1021-1034.

Peter, D.J. (2006). Symptom dimensions of depression following myocardial infarction and their relationship with somatic health status and cardiovascular prognosis. *American Journal of Psychiatry*, 163, 138-144.

Rabbitt, P. (1997). *Methodology of Frontal and Executive Functions*. East Sussex: Psychological Press.

Rankin, P.K. (2003). Presurgical cognitive deficits in patients receiving CABG. *Journal of International Neuropsychological Society*, 9, 913-924.

Rao, S.L. (2004). *NIMHANS Neuropsychology Battery Manual*. Bangalore: NIMHANS.

Roine, R.O., Kajaste, S., & Kaste, M. (1993). Sequelae of cardiac arrest. *Journal of American Medical Association*, 269, 237-242.

Rokey, R., Rolak, L.A., Harati, Y., Kutka, N., & Verani, M.S. (1984). Coronary artery disease in patients with cerebrovascular disease. *A Prospective Study. Annals of Neurology*, 16, 50-53.

Rueckert, I., & Grafman, J. (1996). Sustained attention deficits in patients with right frontal lesions. *Neuropsychologia*, 36, 953-963.

Schleifer, S.J., Macari-Hinson, M.M., Coyle, D.A., Slater, W.R., Kahn, M., Gorlin, R., & Zucker, H.D. (1989). The nature and course of depression following myocardial infarction. *Archives of Internal Medicine*, 149, 1785-1789.

Schmidt, M. (1996). *Rey Auditory Verbal Learning Test: A Handbook*. Los Angles: Western Psychological Services.

Selnes, O.A., Goldsborough, M.A., Borowicz, L.M., & McKhann, G.M. (1999). Neurobehavioral sequelae of cardiopulmonary bypass. *Lancet*, 353, 1601-1606.

Shallice, T. (1982). Specific impairments of planning. *Philosophical Transactions of Royal Society of London*, 298, 199-209.

Shaw, P.J. (1987). Neurologic morbidity after major surgery. *Stroke*, 18, 700-707.

Smith, E.E., & Jonides, J. (1999). Storage and executive processes in the frontal lobes. *Science*, 283, 1657-1661.

Sotaneimi, K.A. (1986). Long term cerebral outcome after open heart surgery. A five year follow up study. *Stroke*, 3, 410-416.

Sotaniemi, K.A. (1995). Long-term neurologic outcome after cardiac operation. *Annals of Thoracic Surgery*, 59, 1336-1339.

Spreen, O., & Strauss, J. (1998). *A Compendium of Neuropsychological Tests. Administration, Norms and Commentary*. New York: Oxford University Press.

Struss, D.T., & Benson, D.F. (1986). *The Frontal Lobes*. New York: Raven Press.

Vataja, R. (2005). *Depression and Executive Dysfunction after Stroke*. Dissertation discussed by permission of Medical faculty of the University of Helsink, Neurology, Finland.

Vijay, V.G. (2003). *Late Complications of Cardiac Surgery. Cardiac Surgery in the Adult*. New York: Mc. Gray-Hill.

Vingerhoets, G., De Soete, G., & Jannes, C. (1995). Subjective complaints versus neuropsychological test performance after cardiopulmonary bypass. *Journal of Psychosomatic Research*, 139, 843-853.

Volpe, B.T., & Petito, C.K. (1985). Dementia with bilateral medial temporal ischemia. *Neurology*, 35, 1793-1797.

Wade, O.L., & Bishop, J.M. (1962). *Cardiac Output and Regional Blood Flow*. Oxford: Blackwell.

Wechsler, D. (1981). *WAIS-R Manual*. New York: The Psychological Corporation.