

# Acute Effect of Hemodialysis on Cognition in Patient of End Stage Renal Disease

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## Abstract

**Aim:** To assess effect of hemodialysis on cognitive control.

**Introduction:** Studies till date have not confirmed the immediate effect of hemodialysis on cognitive function. Cognitive control consists of core cognitive functions such as working memory and inhibition. In several studies it was observed that patients performed worse than healthy control in terms of fluency, working memory, inhibitory control, cognitive flexibility, and decision-making. This study was specifically designed to observe the effect of hemodialysis on learning and memory (Cognitive Control) in fifty ambulatory male subjects of end stage renal disease undergoing twice a week hemodialysis of age more than 21 years.

**Material and Method** Subjects on hemodialysis for more than 2 months up to a year were only included. They were instructed about methodology of Stroop color Word Test, Backward digit span Test and Ray Auditory Verbal learning Test. Following instruction on methodology they were given five practice sessions. They were then tested before and after hemodialysis.

**Result:** Post hemodialysis, the reaction time for Stroop color condition, Stroop word condition and Stroop color word condition was less and this was found to be statistically significant when compared to pre-hemodialysis. This indicates an improvement in executive control acutely after dialysis.

If we look at backward digit span test and RAVLT total score, delayed recall and average recall no significant change was seen. The RAVLT immediate recall time changed significantly after hemodialysis.

**Conclusion:** There is acute effect of hemodialysis on executive function (cognitive control) domain of cognition.

**Keywords:** Hemodialysis, cognitive control, Stroop Color Word Test.

## Introduction

Better longevity of the patient of End renal disease has seen a recent upsurge in the prevalence mainly due to the recent advances in the treatment modality like peritoneal dialysis and hemodialysis and tremendous

growth in the health care infrastructure. Parallel to this increase in the longevity a number of researches related to the impairment in the cognitive abilities has seen an upward graph in the recent years. Multifaceted impairment in the cognitive decline primarily in the domain of executive functions, short term memory and cognitive control.

Studies have explored cognitive functions in ESRD-HD patients by using a comprehensive test battery encompassing the domains of updating (fluency, working memory, and reasoning), inhibitory control, cognitive flexibility, planning and decision-making.

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In several studies it was observed that patients performed worse than healthy control in terms of fluency, working memory, inhibitory control, cognitive flexibility, and decision-making.

Literatures till date give a conflicting view of the immediate effect of hemodialysis on cognitive function.

In case of verbal fluency, Harciarek et al.<sup>1</sup> found a reduced rate of word production of in a task of phonological fluency, while Post et al.<sup>2</sup>, using the *Fluency-Controlled Oral Word Association Test (COWAT)*, showed a reduced performance in phonological and semantic verbal fluency. While studying working memory, Anwar et al. and Costa et al. observed lower performance by ESRD-HD patients in comparison to healthy controls.<sup>3,4</sup> Some earlier studies also demonstrated impaired inhibitory control in ESRD-HD patients.<sup>5,2</sup> However, with respect to cognitive flexibility, Anwar et al.<sup>3</sup> and Post et al.<sup>2</sup> observed in ESRD-HD patients on the Trail Making Test B, a reduced performance. Evaluating reasoning, Pereira et al. in another study reported significant deteriorations in non-verbal fluency reasoning by ESRD-HD patients.<sup>6</sup>

Cognitive control encompasses core cognitive process like inhibition, working memory and cognitive flexibility. Key elements like selection, scheduling and coordinated programming process are needed for cognitive control that is brought about by target oriented, self-regulatory operations of brain<sup>11</sup>.

We undertook this study to add to the existing literature our finding on the acute effect of haemodialysis on one particular area of cognitive function i.e. cognitive control that has been quite neglected by the researchers.

## Material and Method

This study was performed as a before-after analytical research in patients on maintenance hemodialysis older than 20 years of age, in dialysis unit of department of Nephrology; IGIMS Patna. Only patients who were on maintenance hemodialysis for more than 2 months and less than one year were included in the study.

The study population consisted of 50 ambulatory male patients with ESRD (GFR < 15 mL/m undergoing maintenance hemodialysis twice a week. The causes of ESRD were diabetes mellitus type II (20%), arterial hypertension (35%), glomerulonephritis (30%), and cystic kidney disease (15%).

### Inclusion criteria:

- (a) Age above 20 years
- (b) MMSE score more than 28
- (c) Stable clinical and functional state
- (d) Education level; Matriculation and above

### Exclusion criteria

- (a) Cardiovascular disorders
- (b) Known lung disease, such as asthma or COPD
- (c) Neuromuscular disorders and neuropsychiatric disorder
- (d) Being a past or active smoker
- (e) Malnutrition (BMI < 18).
- (f) Patients showing any sign and symptoms of uremic encephalopathy

The study had the prior approval of the institute ethics committee. All subjects gave informed signed consent.

**Hemodialysis:** All the included patients in the study were on hemodialysis two times per week in the morning shifts. Dialysis was done using Dialog<sup>+</sup> B BRAUN Melsungen AG, Germany machines. The patients included were kept on a strict maintenance regime. The water was treated by a reverse-osmosis de-ionizing system.

The Dialyzers were multiple-use, 1.3 m<sup>2</sup> surface area high-flux synthetic hollow fiber polynephron (Nipro Corporation, Japan) with bicarbonate-based dialysate (Glucose 1 mmol/L, Na<sup>+</sup> 140 mEq/L, HCO<sub>3</sub><sup>-</sup> 32 mEq/L, K<sup>+</sup> 2.0 mEq/L, Ca<sup>2+</sup> 1.25 mmol/L, Mg<sup>2+</sup> 0.5 mEq/L). The prescribed duration was 3 h with a blood flow rate of 250-350 ml/min and dialysate flow rate of 500 ml/min. Spirometry was performed twice for the eligible patients who consented to participate in the study; before the hemodialysis session and immediately after it.

**Cognitive Function Testing:** They were instructed on methodology of Stroop colour Word Test, Ray Auditory Verbal Test and Backward digit span. Following instruction on methodology they were given five practice sessions. Any query about the test was answered.

**Stroop Colour Word Test<sup>15</sup>:** Vitoria version of Stroop Colour Word Test was used. It consists of three

21.5X14 cm cards, each containing six rows of four items (Helvetica, 28 point in rows which are placed one centimeter apart. In Part D (Dots), the subject is instructed to name as quickly as possible the colour of 24 dots printed in blue, green, red, or yellow ink. Each color is used six times, and the four colors are arranged in a pseudorandom order within the array, each color appearing once in each row. Part W (Words) is similar to Part D, except that the dots are replaced by common words, printed in lowercase letters. The subject is required to name the colors in which the stimuli are printed and to disregard their verbal content. Part C (Colors) is similar to Parts D and W, but here the colored stimuli are the color names “blue, green, red, and yellow” printed in lowercase so that the print color never corresponds to the color name. This latter task thus requires the individual to inhibit an automatic reading response and to produce a more effortful color naming response. The time difference between part C and Part W is known as interference effect or Stroop effect.

**The Rey Auditory Verbal learning Test (RAVLT)<sup>15</sup>** : RAVLT assessed verbal memory and learning. Participants were read a list of 15 common words five times. Immediately after each time, they were asked to recapitulate as many words as possible. After completion of the fifth trial, an interference list was presented following which subject had to spontaneously recall the original words. Finally, participants were required to spontaneously recall the original words after a 20-minute delay. Scores were calculated as the total number of words recalled (1) across the five trials

(total acquisition); (2) after the interference list (recall after interference); (3) on the fifth trial minus after the interference (loss after interference); and (4) after the delay (long delay free recall).

**Backwards Digit Span test<sup>15</sup>**: In a standard Backwards Digit Span test, the length of the number-string increases by 1 and continues until participants fail two consecutive attempts at reciting strings of a given length—generating a score in relation to the maximum string-length successfully recited. Participants attempted to recite nine number-strings which were 3-11 digits in length, increasing with order.

**Statistical analysis:** All data are expressed as mean  $\pm$  standard deviation (SD). The analysis was performed using SPSS 17. Statistical significance was accepted at  $P < 0.05$ . Comparisons among after hemodialysis and before hemodialysis were performed by two tailed paired t test.

## Result

After a session of Hemodialysis, the reaction time for Stroop color condition, Stroop word condition and Stroop color word condition were decreased and this was found to be statistically significant when compared to Pre hemodialysis.

In case of backward digit span test and RAVLT total score, delayed recall and average recall no significant change was observed. The immediate recall time changed significantly after Hemodialysis.

**Table1: Comparison of before–hemodialysis and after-hemodialysis Neuropsychological tests score**

Neuropsychological Test	Pre Haemodialysis Score (Mean $\pm$ SD)	Post Haemodialysis Score (Mean $\pm$ SD)	p-Value
RAVLT-Total Score	42.91 $\pm$ 10.07	41.84 $\pm$ 10.28	>0.05
RAVLT-Average Score	8.18 $\pm$ 2.02	8.25 $\pm$ 2.06	>0.05
RAVLT-Immediate Recall	8.68 $\pm$ 2.86	8.05 $\pm$ 2.18	<0.01
RAVLT-Delayed Recall	9.35 $\pm$ 3.17	9.73 $\pm$ 2.13	>0.05
Backward digit span test	4.51 (1.04)	4.39 (1.18)	>0.05
Stroop color condition (time in second)	19.87 $\pm$ 5.9	14.82 $\pm$ 3.2	<0.001
Stroop word condition (time in second)	25.68 $\pm$ 5.2	18.5.4 $\pm$ 2.6	<0.001
Stroop color-word condition (time in second)	38.56 $\pm$ 8.3	27.80 $\pm$ 3.6	<0.001
Stroop Interference (time in second)	16.82 $\pm$ 7.1	11.57 $\pm$ 3.2	<0.001

All results are expressed as Mean  $\pm$  standard deviation,  $p < 0.05$  is considered significant

## Discussion

Post hemodialysis, the reaction time for Stroop color condition, Stroop word condition and Stroop color word condition was less and this was found to be statistically significant when compared to pre-hemodialysis. This indicates an improvement in executive control acutely after dialysis.

If we look at backward digit span test and RAVLT total score, delayed recall and average recall no significant change was seen. The RAVLT immediate recall time changed significantly after hemodialysis.

Tests for cognitive function are of two major classes, neuropsychological and neurophysiological. In our study we have focused on the neuropsychological testing but similar studies with event related potential (ERP) must be evaluated.

Tilki HE, Akpolat T, Tunalı G, Kara A & Onar MK in their study documented the presence of electrophysiological and psychometric test abnormalities in chronic renal failure patients, and showed that continuous ambulatory peritoneal dialysis (CAPD) patients may have better outcomes as compared to HD patients.<sup>8</sup>

Earlier studies evaluating MMS scores and P300 latency in uraemia were focused on HD patients. There are only a few studies assessing P300 latency and with dissimilar study designs. Gallai et al. demonstrated improvements in P300 latency after dialysis in 20 patients undergoing HD treatment.<sup>9</sup>

Abnormal P300 and visual evoked potential latencies were found in 22 patients (13 were maintained on long term hemodialysis and 9 were being given only a low-protein diet) in a study by Cohen et al.<sup>10</sup>

Tennyson et al. evaluated long-latency event-related potentials and the Symbol Digit Modalities Test in 10 hemodialysis patients. Significant increases in N200 and P300 amplitude were observed after dialysis treatment in these 10 patients. In their study, ERP component latency and the Symbol Digit Modalities Test were not affected by dialysis. Control groups were not used.<sup>11</sup>

Evers et al. investigated visually evoked ERPs in 33 neurologically asymptomatic patients before and after they underwent hemodialysis. They compared the data with those of age-matched healthy subjects.

Before hemodialysis, the patients' P300 latency was significantly prolonged as compared with that of the control group. After hemodialysis, P300 latency of the patients decreased, this was statistically significant.<sup>12</sup>

This study evaluated in some detail cognitive outcomes in psychometric testing of ESRD patients on maintenance hemodialysis. The neuropsychological tests consisted of tests measuring learning ability, working memory, executive function and cognitive control. The post-hemodialysis testing had poorer performance only on some of these parameters than the pre-hemodialysis scores. Between the pre-hemodialysis and post-hemodialysis studies it should be noted that Stroop word condition, Stroop color condition, Stroop word-color condition and Stroop interference test all showed significant improvement in performance. This stressed the beneficial effect of hemodialysis on executive functions and cognitive control domains of the subject. There was an insignificant increase in performance in RAVLT-average score and RAVLT-delayed recall. A slight improvement was seen in backward digit span test but was not significant. The backward digit span assesses working memory.

There was no significant change in RAVLT-total, RAVLT-average, RAVLT-delayed recall scores. RAVLT-immediate recall scores differed significantly in the post hemodialysis test. The RAVLT is a measure of learning ability. It requires learning and memorizing function over a longer time. The available alertness of dialysis patients lasts to keep up with the short-term memory functions but immediate recall is still affected. Higher brain actions are involved, which are apparently reduced in patients on HD. Patients on hemodialysis are more likely able to memorize, concentrate and manage situations a day after dialysis. Lower cognitive function is a major hinderance as it impairs self-management, and follow a complicated pharmacologic time-table. Errors in medication and diet due to decreased cognitive performance can have deleterious consequences. As pointed out by Elias et al., the measures of everyday cognitive abilities relevant to patient understanding of the disease and treatments should be outlined, studied and implemented.<sup>13</sup>

Harciarek et al.<sup>1</sup> and Lux et al.<sup>14</sup> are two studies similar to ours but both had a sample size smaller than ours. Lux et al. had only 12 subjects and Harciarek et al had 20. In contrast to our study both the studies show an increase in cognitive performance in namely executive

functions, psychomotor performance and learning and memory. One of the major limitations of our study was testing of only a few domains of cognition.

### Conclusion

There is acute effect of hemodialysis on executive function (cognitive control) domain of cognition.

**Conflict of Interest:** None

**Ethical Clearance:** Taken

**Source of Funding:** Self

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