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A potential barrier to adherence? Memory for future intentions is impaired in hemodialysis patients

Running head: Memory impairment in HD

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Abstract

Introduction: End-stage renal disease (ESRD) has been associated with a range of cognitive deficits, including impaired retrospective memory and attention. Prospective Memory (PM) is memory for future intentions, such as remembering to take medication on time. PM has not been examined in any ESRD patients, yet the implications upon diet and medication management could have potentially detrimental effects on patient welfare. This is the first study to examine PM in ESRD patients being treated with hemodialysis (HD).

Methods: HD patients (n=18) were compared to age and education-matched controls (n=18) on a boardgame task that emulates a typical week of activities (i.e. grocery shopping, meetings with friends), requiring the participant to remember a series of upcoming tasks. Other measures were also examined, including general cognitive decline, measures of independent living, IQ and mood.

Findings: Patients recalled significantly fewer upcoming events than the control group, suggesting an impairment of PM. No significant relationship was found between PM performance and any other measures, suggesting the difference between groups is likely due to the effects of ESRD, HD treatment or some associated comorbidity.

Discussion: This is the first study to demonstrate a PM deficit in patients undergoing HD treatment. This finding contributes to the current knowledge of the cognitive profile of patients undergoing HD, whilst also highlighting the implications that a PM deficit may have on patient quality of life. The finding may go some way to explaining variances in patients' ability to monitor and adhere to medication and dietary regimes, and ultimately, to live independently. The study also highlights the necessity of viewing treatment for ESRD as a holistic process to maximise patient wellbeing.

Keywords:

Cognition; end-stage renal disease; hemodialysis; memory; impairment

Introduction

The most common form of treatment for end-stage renal disease (ESRD) in the UK is hemodialysis (HD)[1]. Impairments in cognition are widely observed in patients: Murray et al.[2] suggested they are commonly underdiagnosed, finding 87.3% of a 338-patient sample showing some form of mild to severe cognitive impairment. To maintain independence whilst receiving HD, a patient must be able to monitor their own activities accurately (diet and medication), requiring proficient Prospective Memory (PM). PM is memory for future intentions and involves remembering to perform a specific action whilst being involved in an ongoing activity[3], for example, remembering to post a letter when passing the post office or at four o'clock to feed the cat. The distinction between PM and retrospective memory (RM) (e.g. of what one had for dinner last night) has been demonstrated in typical aging[4,5], showing differences in retrospective and PM performance between young and older adults, in brain imaging[6] and in neuropsychological studies[7,8,9,10].

Impairments of RM have been found in ESRD, both in verbal and visual memory[11,12,13], learning[14], and episodic memory[15]. In addition, impairments of the executive functions (inhibition, task switching), shown to be important in PM, have been found in ESRD[15,16,17]. Thus, one might expect an impairment of PM in ESRD, arguably a more important type of memory, especially in day-to-day functioning. The ability to plan and execute delayed future actions has been shown to affect management and rehabilitation within vulnerable adult groups, such as those with neurological disorders[18]. Cohen[19] states that "without an intact PM it is scarcely possible to function independently in an everyday life context" (p. 54). HD patients need to manage their multifaceted treatment schedule, including dietary restrictions, medication regimes and hospital appointments, e.g. remembering to take phosphate binders around meal times[20].

A key distinction in the PM literature is between time-based and event-based tasks[21,22]. Event-based tasks are cued by a situation or event (e.g. remembering to pick up the washing when walking by the dry cleaners) and require monitoring of the external environment. In contrast, time-based tasks are carried out in relation to a specific time, requiring self-monitoring of the situation (e.g. at one o'clock remember to give your mother a ring) and are often more cognitively demanding due to the self-initiation of the task and the lack of an external cue[23]. Only event-based tasks were assessed in this study, since, if performance on these is impaired, it is likely that performance on time-based tasks will also be impaired.

When discussing impairments in HD one must be aware of the oscillations in cognitive performance across the dialysis cycle (e.g. pre vs. post-dialysis performance). Several studies have suggested that cognitive functioning is optimal at 24 hours post-dialysis[24,25,26]. Thus, we tested patients immediately before dialysis, with the aim of maximising any differences between patient and control performance.

We examined PM in HD patients using the Virtual Week (VW) task, developed by Rendell and Craik[27]. The VW task has been shown to be a sensitive marker of PM in older adults[28,29], drug users[30,31], schizophrenia[32,33], multiple sclerosis[34,35], patients following a stroke[36], mild cognitive impairment[37] and dementia[38]. Advantages of the VW task include its high face validity in that it mimics routines of daily life. We predict that patients receiving hemodialysis will perform worse on the VW task compared to an age, sex and education-matched healthy control group.

Materials and Methods

Participants

Eighteen patients (M: 70.9, SD: 11.6) were recruited from the renal unit at the Royal Berkshire Hospital (RBH), Reading, Berkshire. Patients were receiving HD three times per week for 3 to 5 hours per treatment and had been receiving HD for a minimum of 90 days prior to testing, with a Kt/v > 1.4 (see Table 1 for a summary of patient characteristics). Patients were deemed eligible for the study by the treating nephrologist who informed and obtained consent. Comorbid conditions and other relevant medical history were obtained from medical history records. Patients were excluded from the study if they had any prior history of ophthalmological or neurological illness.

Eighteen healthy control participants, with no history of ophthalmological or neurological illness, (M: 70.6 years, SD: 10.9) were recruited from a research volunteer panel maintained by the School of Psychology & CLS at the University of Reading. Control participants were individually matched to the patients on age, sex and education level and tested in the university and reimbursed their travelling expenses.

Stimuli and Materials

The VW is a board game, made up of squares, in which one loop of the board constitutes one 'virtual' day from 7am until 10pm; progression over the squares emulates the progression of time over the course of one day. Participants were told that the memories for each day would be restricted to individual days and information would not need to be remembered over the course of the entire game. To progress, the participant must roll a die, which gives the number of squares they must move. Clocks are present around each square to communicate to the player the approximate time-of-day, aiding in the construction of a virtual day. As a player moves around the board they must pick up 'event-cards' as they pass over 'event-squares'. These 'event-cards' require the player to make a choice about a typical daily activity (e.g. "What would you like for dinner?") and, on occasion, an additional instruction which the player must remember to carry out in the imminent future; a prompt is given later in the day (an event-based task). For example, an 'event-card' in the morning may state that the player must remember "to pay the telephone bill after lunch", later on an 'event-card' will mention lunch (the prompt), requiring the player to report what they are required to do. If the player successfully reports the information, they receive a point for this instruction. Over the course of one day, there are four pieces of event-based information that a player is instructed to remember. The task further aims to emulate a typical day by having additional distractions to minimise the chance of rehearsal: players are required to verbally count the squares and to read instructions aloud. Furthermore, after responding to the 'event-cards', a player is required to roll a certain number on the dice, decided at random by another card selected by the experimenter. In our study, all time-based event cards were removed.

In the auditory RM task, participants listened to a series of 36 words and were required to count and report the number of syllables in each word. During retrieval, they were presented with a series of six category names and had to recall and report any words from the earlier list which belonged in that category (full details provided in Jones et al[39]). Participants also completed the Mini Mental State Examination (MMSE)[40], to screen for moderate to severe cognitive impairment. The Instrumental Activity of Daily Living (IADL)[41], a self-report questionnaire to assess independence. The National Adult Reading Test (NART)[42], a performance-based questionnaire assessing pre-morbid intelligence, and the Bond-Lader Mood Assessment Scale[43], a measure of subjective mood.

Design

A busy dialysis schedule resulted in a 2-day version of the VW (Monday & Tuesday) being conducted. Shortened versions of the VW task have shown to be reliable when compared with the full version of the test; split-half reliabilities were found between .74 and .66[32]. A matched-pairs independent groups design was used. The patient group was tested immediately prior to a weekly dialysis session. To control for time of day effects, matched controls were tested at a similar time. All participants completed the RM task, allowing comparisons between RM and PM.

Procedure

Prior to commencing the study, all procedures were approved by the University Research Ethics Committee and National Health Service (NHS) Research Ethics Committees. Written informed consent was obtained and the nature of the test session was explained. Prior to completing the VW task participants completed the Bond-Lader and MMSE. Testing was conducted in a quiet office on the renal ward. Participants completed one practice round of the game. Throughout the task, no prompts were given by the experimenter and scores were recorded. The task lasted approximately 25-35 minutes. Participants then completed the NART and IADL, were fully debriefed, and follow-up questions answered.

Results

Demographics

Table 2 shows means and standard deviations of participants' age, education level, NART overall IQ, MMSE, IADL and Bond-Lader score, separated by group. Independent t-tests showed no significant differences between patients and healthy controls for age or education level. Differences were found between groups: NART (overall IQ) and MMSE scores were significantly lower in patients than controls. Although scores differed significantly, both patients and controls were within the expected normal range. IADL scores were significantly lower in patients, however the difference may reflect the physical restrictions of treatment, rather than cognitive difficulties, e.g. HD schedule may restrict times for shopping.

Sum of the scores per participant were calculated for each of the three Bond-Lader factors (alertness, calmness and contentedness), and groups compared with independent t-tests. No significant differences were found, suggesting mood states were similar.

Prospective memory performance

Participants completed the VW task; scores are reported as proportion of 'event-based' items correctly recalled. Over the course of the task, any items correctly recalled were labelled as 'correct', whereas items that were recalled incorrectly or simply missed were labelled 'wrong'. PM scores are shown in Figure 1. Performance on Day 1 was compared with that on Day 2, since an improvement on Day 2 could suggest a practice effect, rather than a difference in PM. From the 2 (patient vs control) x 2 (day 1 vs day 2) between-subjects ANOVA, a significant main effect of group was found, $F(1,68) = 8.837$, $p = .004$, confirming the higher PM scores in the control (Figure 1). However, the effect of day was not significant, $F(1,68) = 0.863$, $p = .356$, nor was the interaction between group and day, $F(1,68) = 0.138$, $p = .711$, suggesting no learning effect was taking place. The Kolmogorov-Smirnov test of normality revealed the control data to be normally distributed ($D(18) = 0.161$, $p = .2$), but the patient data were not ($D(18) = 0.241$, $p = .007$), possibly due to a floor effect. However, non-parametric Mann-Whitney tests confirmed the parametric test result, in that the control group median (*0.56*) was significantly higher than that of the patients (*0.38*), {$U = 96.0$, $z = -2.121$, $p = .034$, with a medium to large effect size (Mann- Whitney r for non-parametric data = -.35).

Possible effects of covariates

To investigate whether any additional measures were affecting performance, a between-subjects ANCOVA was conducted. Neither education level, $F(1,29) = 0.025$, $p = .876$, MMSE, $F(1,29) = 0.057$, $p = .813$, NART, $F(1,29) = 2.739$, $p = .109$, or IADL, $F(1,29) = 3.688$, $p = .065$, had significant effects on PM. The effects of age were significant ($F(1,29) = 9.196$, $p = .005$), but there were no significant differences in age between the groups, so this is unable to explain group differences in PM.

Relationship to retrospective memory

The correlation between performance by patients on the RM and the VW in the present study was measured with a Pearson r correlation test; the correlation was significant ($r = 0.49$, $p=0.002$, n= 18).

Discussion

The primary aim of this study was to further our knowledge of the cognitive profile of ESRD patients undergoing HD, by investigating PM. Patients recalled significantly fewer items on the PM task than controls, suggesting that PM may be impaired in this population. Except for age, no significant relationship was found between PM performance and other measures (education, general cognitive decline, independent living or IQ), suggesting the difference is likely because of ESRD, HD treatment or some associated comorbidity. The similarity of mean ages in the patient and control groups shows that this cannot be contributing significantly to the group differences. Thus, this appears to be the first study to identify a PM deficit, a specific impairment of memory for future intentions, in ESRD patients receiving HD.

Patients were tested immediately before HD because studies have suggested that cognitive functioning, including retrospective memory and executive functions, may be less efficient at this time, compared with 24 hr after dialysis[11, 24, 25, 26]. It is also worth noting that Murray et al[44] found that performance was even worse during dialysis than before it, suggesting that, even though their timing may be most convenient for clinical staff, discussion with patients about their illness and treatment before/during dialysis may be less well remembered. It is uncertain to what extent PM would normalise by 24 hr post-dialysis, and this is a possible topic for future research.

Conventionally, the VW task is for seven days to emulate a typical week, however, because of rigid treatment scheduling the present study only assessed two days. To check that participants' scores were not influenced by familiarity with the task, and participants' full comprehension of the task was achieved during the practice day, scores of the two separate days were compared with one another across groups. No significant difference was found between the two days in either group, suggesting that scores on the two days accurately reflected patients' PM performance, in line with earlier studies using shortened versions of the task[32]. Although the shortened version was found to be reliable, it would have been useful to extend the task to more days, allowing firm comparisons to be drawn with other typical and atypical populations. Only event-based PM was examined in this study; however, this does reflect typical everyday task requirements of dialysis patients. If the cognitive demands of event-based tasks are too high for ESRD patients, as the work of McDaniel and Einstein[22] suggests, we would expect to find an even greater impairment in time-based activities in which self-monitoring is a requirement during the task.

Our findings suggest that both retrospective and prospective memory are affected in HD patients, however, due to the naturalistic element of the task it is difficult to unpack how much of the RM deficit is contributing to the PM deficit; a potential for future examination. Irrespective of the underlying mechanisms, a PM deficit has considerable implications for patients' quality of life. PM is essential for dealing with the demands of everyday life, much work has been carried out on the importance of PM across the lifespan and into older adulthood[45,46]. Reliance on PM becomes even more pronounced in individuals with health-related problems, such as ESRD[47]. Restrictions must be adhered to in terms of diet, medication and fluid intake, appointments and HD treatment must be attended[48]; if these are not met, patient wellbeing will certainly be affected. A deficit of PM may go some way to explaining the variance observed in HD patients' ability to monitor and adhere to dietary and medication regimes[49]. Patient quality of life is a strong predictor of mortality and hospitalisation of HD patients[50]. If we aim to maximise patient satisfaction and quality of life, PM is likely to be an area that requires increased focus. Hospitals and healthcare professionals would likely benefit from additional support to ensure that patients are receiving the necessary provision to live independently and maximise wellbeing, i.e. memory aids. Discussions of cognitive impairments highlights the necessity to examine a patient holistically, in terms of their physical treatment, state of mind and cognitive health. Observed in isolation, the impact of a PM deficit may be small, but collectively the result may be the difference between hospitalisation and a patient going home.

There are some limitations to the study which provide an opportunity for future investigation: a more sensitive test than the MMSE may have identified cases of mild cognitive impairment[12]. However, taken together with the NART scores, the MMSE scores suggest that our patients' general cognitive abilities were not grossly impaired. As in most studies of ESRD, our patients had co-morbidities (though hypertension and diabetes were being treated), thus, we cannot rule out some contribution of co-morbidities to the PM results. It may also be worth comparing PM score with biomedical markers or adherence to treatment.

This study provides the first evidence that ESRD patients undergoing HD may have impaired PM, at least for event-based tasks. This finding contributes to the current knowledge of the cognitive profile of these patients, whilst simultaneously highlighting the implications that such a deficit can have for patients and healthcare professionals alike. The impact of a PM deficit on quality of life is known to be significant in clinical populations, especially in which the rate of decline, in terms of independence, is salient. This finding also highlights the importance of a holistic approach to patient care, considering physical and psychological difficulties, to maximise wellbeing.

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Figure Legends

Figure 1. Patients vs. Controls: mean number of items recalled for the patient and control group for Day 1 and Day 2 on the Virtual Week task. Error bars = ±1 S.E.

Table 1. Haemodialysis patients' characteristics

	HD Patients (n = 18)	
Characteristic	**No. of Patients**	**Percentage or Mean ± SD**
Age (years)		
<55	2	11.1
55-64	4	22.2
65-74	4	22.2
75-85	6	33.3
>85	2	11.1
Mean		70.9 ± 11.6
Dialysis Duration (months)		
0-12	1	5.6
13-24	6	33.3
>24	11	61.1
Mean		57.0 ± 68.3
Cause of ESRD		
Type 2 diabetes mellitus	1	5.6
Type 1 diabetes mellitus	1	5.6
Adult polycystic kidney disease	4	22.2
Chronic kidney disease (unknown cause)	3	16.7
Obstructive uropathy	1	5.6
Glomerulonephritis	3	16.7
Vasculitis	2	11.1
Hypertensive/renovascular disease	2	11.1
Surgical loss	1	5.6
Comorbid Conditions		
Peripheral vascular disease	4	22.2
Diabetes	5	27.8
Hypertension	4	22.2
Stroke	3	16.7
Myocardial infarction	1	5.6

Table 2. Demographic information for patient and control groups.

	Group					
	Patient (N = 18)		**Control (N = 18)**			
	Mean	**SD**	**Mean**	**SD**	***t***	***p-value***
Age (years)	70.9	11.6	70.6	10.9	0.103	.918
Education (years)	11.3	2.7	11.7	2.4	-0.518	.608
NART Overall IQ	116.0	6.0	120.5	3.5	-2.736*	.010
MMSE	27.3	1.3	28.6	1.3	-2.928**	.006
IADL	6.4	1.4	7.9	0.2	-4.721***	<.001
Bond-Lader:						
Alertness	25.94	17.08	23.72	14.02	0.425	.673
Calmness	20.17	18.87	19.86	18.48	0.050	.961
Contentedness	21.82	21.31	31.60	19.87	-1.424	.164
M / F	10 / 8	-	10 / 8	-	-	