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Psychosocial Correlates of Medication Adherence among HIV-Positive, Cognitively Impaired Individuals

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Abstract

Although cognitive impairment has been shown to adversely affect antiviral medication adherence, a subset of cognitively impaired adults nonetheless are able to adequately adhere to their medication regimen. However, little is known about factors that serve as buffers against suboptimal adherence among the cognitively impaired. This study consisted of 160 HIV-positive, cognitively impaired adults (Global Deficit Score = 0.50) whose medication adherence was monitored over 6-months using an electronic monitoring device (MEMS caps). Logistic regressions were run to determine psychosocial variables associated with medication adherence. Higher self-efficacy and treatment related support, a stable medication regimen, stable stress levels, and absence of current stimulant use were predictive of optimal adherence. A distinct array of psychosocial factors was found that buffer against the adverse effects of cognitive impairment on medication adherence. Assessment and interventions targeting these factors may improve adherence rates among cognitively impaired adults.

Keywords

Cognitively Impaired; Medication Adherence; HIV; Stress; Stimulant Use

Introduction

Combined antiretroviral therapy (cART) can suppress HIV replication, thereby reducing morbidity and improving quality of life, but it requires strict adherence (Bangsberg et al., 2000; Casado et al., 1999; Gifford et al., 2000; Paterson et al., 2000). Cognitive impairment has repeatedly been shown to adversely affect adherence (Becker, Thames, Woo, Castellon, & Hinkin, 2011; Ettenhofer, Foley, Castellon, & Hinkin, 2010; Ezeabogu, Copenhaver, & Potrepka, 2012; Hinkin et al., 2002; Hinkin et al., 2004; Panos et al., 2013). For example, Hinkin et al. (2004) found that HIV+ individuals with cognitive dysfunction were 2.5 times

more likely to be poor adherers to their antiretroviral therapy regimen. More in-depth study has revealed that higher order cognitive processes (e.g., executive functioning, learning/memory, and prospective memory) appear most strongly related to adherence (Becker et al., 2011; Ettenhofer et al., 2010; Woods et al., 2009; Woods et al., 2008). In addition, cognitive impairment has a reciprocal relationship with adherence, such that poor adherence can exacerbate cognitive dysfunction which can then in turn further worsen adherence (Ettenhofer et al., 2010).

Based on previous findings, researchers have suggested tailoring intervention programs to boost medication adherence rates for the cognitively impaired population (e.g., Becker et al., 2011; Ezeabogu et al., 2012), and a number of potentially useful interventions have been suggested, such as reducing medication regimen complexity (Hinkin et al., 2002), continually monitoring for changes in cognitive functioning (Becker et al., 2011; Lovejoy & Suhr, 2009), and the use of memory prompting devices (Andrade et al., 2005; Becker et al., 2011). However, little attention has been focused on identifying psychosocial variables that may act as a buffer and attenuate the adverse effects of cognitive impairment on medication adherence.

A number of psychosocial factors have been associated with medication adherence to antiretroviral therapy. Younger age (Levine et al., 2005), ethnic minority status (Simoni et al., 2012; Thames et al., 2012), and lower education or health literacy (Golin et al., 2002) have all appeared to be associated with lower medication adherence. Current substance use and/or abuse/dependence (Arnsten et al., 2002; Hinkin et al., 2004; Malta, Strathdee, Magnanini, & Bastos, 2008; Tucker et al., 2004) has a well-documented deleterious impact on medication adherence. Particularly, active stimulant use adversely affects medication adherence (Gruber, Sorensen, & Haug, 2007; Hinkin et al., 2007; Meade, Conn, Skalski, & Safren, 2011). Hinkin et al. (2007) found that individuals who screened positive for stimulant use (i.e., cocaine or methamphetamine) during the course of a six-month study were 7-times more likely to evidence medication adherence failure compared to those who did not screen positive for any illicit substance use during the course of the study. Other psychosocial factors that have been linked to better adherence include greater self-efficacy (Chesney et al., 2000; Smith, Rublein, Marcus, Penick Brock, & Chesney, 2003), increased social support (Burgoyne, 2005), and greater treatment specific support (Golin et al., 2006; Gruber et al., 2007).

The goal of the current study was to focus on a population known to be a great risk for poor medication adherence – patients with neurocognitive impairment – and to identify unique psychosocial factors that may serve to buffer the adverse effects of cognitive impairment on medication adherence. The current study evaluates the influence of several key psychosocial variables in predicting optimal medication adherence among cognitively impaired HIV-positive individuals.

Method

Participants

Participants were drawn from a larger prospective (six-month) study assessing factors associated with medication adherence to combined antiretroviral therapy (cART; $N = 276$). Participants from this larger study were recruited from community agencies and medical centers in Los Angeles that serve a demographically diverse clientele. They also met the following inclusion criteria: (1) were at least 18 years of age; (2) prescribed cART; (3) self-administered their own medication; and (4) were willing to utilize an electronic monitoring device (MEMS caps) that tracks medication adherence. All participants were individually provided written and verbal information about the study before consenting to participate and were financially compensated for their time. The study was approved by both the UCLA and West Los Angeles Veterans Administration Healthcare Center institutional review boards.

Participants in the larger study underwent neuropsychological testing at baseline and medication adherence was subsequently tracked over the course of the next six-months (details provided below). Of the 276 participants who presented at baseline from the larger study, medication adherence data was available for a total of 251 participants. From this remaining sample, participants for the current study were retained based on whether they met criteria for global cognitive impairment at baseline. To determine this, all participants from the larger study completed a comprehensive neuropsychological test battery administered by trained psychometrists who were supervised by a board-certified neuropsychologist (C.H.H.). The battery included tests of information processing speed (i.e., WAIS-III Digit Symbol and Symbol Search subtests, and Trail Making Part A), learning and memory (i.e., CVLT-II Total Learning and Delayed Free Recall, and BVMT-R Total Learning and Delayed Recall), attention (i.e., WAIS-III Digit Span and Letter-Number Sequencing, and PASAT Trial 1), executive functioning (i.e., Trail Making Part B, Stroop Interference, and WCST-64 Perseverative Errors), verbal fluency (i.e., COWAT), and motor skills (i.e., Grooved Pegboard). Test scores were converted to demographically adjusted t -scores ($M = 50$; $SD = 10$) using published normative data to minimize the influence of age, education, gender, and ethnicity. Deficit scores were then calculated using an established algorithm (see Heaton, Miller, Taylor, & Grant, 2004) that assigned an impairment rating to t -scores as follows: $t > 39 = 0$; $39 \geq t \geq 35 = 1$; $34 \geq t \geq 30 = 2$; $29 \geq t \geq 25 = 3$; $24 \geq t \geq 20 = 4$; $t < 20 = 5$. Deficit scores for each neuropsychological test were then averaged into one score to reflect a Global Deficit Score (GDS). Given that a GDS of ≥ 0.50 has been shown to produce an optimal balance between sensitivity and specificity in classifying cognitive impairment (Carey et al., 2004), and that this cut-score has been directly shown to be effective in assessing the relationship between cognition and medication adherence (Hinkin et al., 2004), GDS ≥ 0.50 served as the cognitive classification cut-off in the current study. From that initial cohort of 276 participants, 160 were classified as “cognitively impaired” and were thus retained in the current study (see Table 1 for demographic and clinical characteristics).

Procedure

Participants in the current study were administered psychosocial questionnaires and urine toxicology screening at baseline. At the study midpoint (three months post-baseline) participants were administered a questionnaire assessing recent life changes. Medication adherence was monitored throughout the six-month study.

Psychosocial factors—Self-efficacy (i.e., participants' confidence in their ability to take their medication) was measured using a self-efficacy question from a widely-used adherence questionnaire developed by the AIDS Clinical Trials Group form (ACTG; Chesney et al., 2000). This question asks participants how confident they were that they would be able to take all or most of their medication as directed. A 4-point Likert response scale (0 = "Not at all sure" – 3 = "Extremely sure") was used, with higher scores indicating greater self-efficacy.

The Adherence Determinants Questionnaire (ADQ; DiMatteo et al., 1993) is a 38-item self-report measure of adherence that assesses 7 key adherence constructs with a 5-point Likert scale: (1) interpersonal aspects, (2) benefits/costs of adhering; (3) perceived severity of disease; (4) perceived susceptibility; (5) subjective norms; (6) intentions to adhere; and (7) treatment-related support.

Recent life changes (RLC) were assessed at month three with a 6-item, Yes/No questionnaire. Participants endorsed if they experienced each of the following: medication regimen changes, health status changes, living situation changes, a new relationship, a new break-up, or a perceived increased stress.

Drug use—At baseline, participants provided a urine specimen to screen for the following illicit substances: amphetamines, barbiturates, benzodiazepines, cocaine metabolites, methadone, opiates, phencyclidine, and propoxyphene. Individuals were characterized as stimulant users if they screened positive for amphetamine and/or cocaine metabolites.

Medication adherence—Medication adherence was measured using the Medication Event Monitoring System (MEMS cap; Aprex, Union City, CA), an electronic monitoring device that records the times and dates of bottle openings. Participants were instructed to take their medications as prescribed, to open the bottle only when taking their medications, and not to "pocket dose" (i.e., removing additional medications for later use). Participants returned monthly, during which time medication adherence data was downloaded and calculated as the ratio of bottle opening to prescribed dosages X 100. Using overall average adherence rates over the course of the six-month study, participants were then classified into adherence groups based on previous literature (e.g., Martin et al., 2008) that suggested negative clinical outcomes were associated with adherence levels of less than 90%. Thus, participants in the current study were classified as optimal adherers (i.e., those who took 90% of doses) and sub-optimal adherers (i.e., those who took < 90% of doses).

Statistical analyses—Cross-sectional analyses were conducted to determine baseline factors that distinguish (and predict) medication adherence. A series of logistic regressions were conducted, using each of the psychosocial variables as independent variables and

determining their predictive validity in determining adherence outcomes (optimal adherence vs. suboptimal adherence). In addition, as the current study aimed at examining future medication adherence and the RLC was administered at month three, analyses with these variables were rerun with adherence classifications defined by the adherence rate spanning the final three months of the study for confirmation. Finally, logistic regression models were also conducted to examine the combined impact of psychosocial variables in the prediction of medication adherence group.

Results

Of the cognitively impaired individuals, 36 (22.5%) were classified as good adherers and 124 (77.5%) were poor adherers over the full course of the 6-month study. Adherence groups did not differ according to demographic information (see Table 1). However, the good adherers were less likely to use stimulants than were the poor adherers ($p = .01$).

Each of the psychosocial variables was placed in separate logistic regressions to determine their predictive validity in distinguishing adherence groups. In order to control for the effects of stimulant use, each regression also included stimulant use as a predictor (see Table 2). Results of the logistic regressions revealed that higher self-efficacy ($B = 0.63$, $S.E. = 0.25$, Wald = 6.25, $p = .01$), fewer treatment barriers ($B = 0.18$, $S.E. = 0.07$, Wald = 6.12, $p = .04$), and a stable stress level ($B = 1.78$, $S.E. = 0.50$, Wald = 12.70, $p < .001$) were predictors of optimal medication adherence over the 6-month period.

As the RLC was collected at the study midpoint, analyses including RLC variables were confirmed with an adherence classification that only utilized the rate of adherence over the last three months of the study (23.2% with optimal adherence; 76.8% with suboptimal adherence; see Table 2). The adherence classification using the total study duration correlated strongly with the classification using data that only spanned the second half of the study ($r_s = .90$, $p < .001$). Using revised adherence classifications, a stable stress level continued to predict optimum adherence ($B = 1.99$, $S.E. = 0.55$, Wald = 13.34, $p < .001$), but medication regimen changes emerged as a significant predictor of future adherence classification ($B = 2.12$, $S.E. = 1.06$, Wald = 4.01, $p = .045$). The other RLC items were nonsignificant ($p > .05$).

Finally, a logistic regression was used to examine the concomitant predictive value of the above discussed psychosocial variables in classifying good vs. poor total adherence, χ^2 (4, $N=132$) = 32.08, $p < .001$, $R^2 = .31$. Self efficacy ($B = 0.65$, $S.E. = .27$, Wald = 5.58, $p = .02$) and perceived increases in stress ($B = 1.62$, $S.E. = .51$, Wald = 9.81, $p < .01$) contributed significantly to this model. Stimulant use ($p = .08$) and treatment related support ($p = .09$) emerged as significant trends, but were not predictive of adherence in this model.

Results were repeated using adherence classifications based on the second half of the study and included all the previous variables as well as medication regimen changes, χ^2 (5, $N=132$) = 38.59, $p < .001$, $R^2 = .39$. Here, stimulant use ($\beta = 1.91$, Wald = 6.19, $p = .01$), changes in medication regimen ($\beta = 2.35$, Wald = 4.39, $p = .04$), and perceived increases in stress ($\beta = 1.91$, Wald = 11.12, $p = .001$) contributed significantly. Self-efficacy ($p = .07$),

and treatment related support ($p = .37$) did not emerge as significantly predictive in this model.

Discussion

The purpose of the current study was to identify protective factors associated with optimal adherence among HIV-positive individuals with cognitive impairment. Results indicated that nearly a fourth of the participants maintained an optimal level of medication adherence (90% of their prescribed dosages) despite being cognitively impaired. Several variables were found to serve as protective factors among the cognitively impaired participants. Cognitively impaired subjects who were not stimulant users demonstrated significantly higher medication adherence rates than did those who were active users. In contrast, individuals who were both cognitively impaired and current stimulant users were at particular risk for poor adherence. Only 10.5% of cognitively impaired stimulant users were able to adequately adhere to their medication regimen. When controlling for stimulant use, several psychosocial variables were shown to be associated with good adherence despite the presence of cognitive impairment. Among those variables that predicted good adherence were perceived stability in levels of stress, stability in medication regimen, and self-efficacy. Perceived treatment support also functioned as protective factors, though its impact was reduced when all predictors were simultaneously analyzed using logistic regression.

Results suggest that treatment specific variables such as a supportive treatment environment and a stable medication regimen may improve medication adherence for cognitively impaired individuals. In addition to this population being especially susceptible to poor adherence due to regimen complexity (Hinkin et al., 2002), this study demonstrates that they are also sensitive to alterations in their medication regimen. Similar findings have highlighted the potential relevance of switching medication regimens on adherence within a heterogeneous sample (Miller et al., 2002), but to our knowledge, this variable has not been examined within a sample of exclusively cognitively impaired individuals. The current study demonstrated that cognitively impaired individuals may be especially reliant on external, treatment related support to bolster their compliance. Specifically, this study examined their perceptions of supports available for and absence of barriers to adherence (see DiMatteo et al., 1993). Generally, HIV-positive patients who consistently adhered to their medication perceived greater social support (Burgoyne, 2005), but little attention has previously examined the role of social support on the functional capabilities of cognitively impaired HIV-positive individuals (Gorman, Foley, Ettenhofer, Hinkin, & van Gorp, 2009).

Perceived stress level stability served as a protective factor, supporting previous research on the detrimental impact of increased stress on treatment adherence (e.g., French, Tesoriero, & Agins, 2011; Gebo, Keruly, & Moore, 2003; Leserman, Ironson, O'Cleirigh, Fordiani, & Balbin, 2008; Mugavero et al., 2009) by highlighting its specific importance within a cognitively impaired sample. As increased stress has related to cognitive dysfunction among HIV patients (Pukay-Martin, Cristiani, Saveanu, & Bornstein, 2003), this population may be particularly susceptible to the adverse consequences of increased life stressors on treatment adherence. Clinicians treating cognitively impaired individuals may benefit from being

attuned to increases in perceived stress levels as a warning sign of potential future lapses in medication adherence.

Self-efficacy, a generalized belief in one's ability to achieve target goals, appears to play an important role in helping patients maintain adequate adherence rates despite cognitive impairment. In part, higher levels of self-efficacy may help individuals overcome barriers and endure the demands of antiretroviral medication regimen (DiIorio et al., 2009). While the relationship between self-efficacy and HIV medication adherence has been documented in more heterogeneous samples of HIV-patients (Deschamps et al., 2004; DiIorio et al., 2009), to our knowledge research has yet to focus on the influence of self-efficacy on adherence strictly among cognitively impaired individuals. Higher rates of self-efficacy have previously related to improved treatment outcomes (e.g., greater functional independence) for some neurocognitive disorders (e.g., stroke patients; Hellström, Lindmark, Wahlberg, & Fugl-Meyer, 2003), but little, if any, research has examined the role of self-efficacy among treatment outcomes for patients with HIV Associated Neurocognitive Disorders. Future research may also want to focus on interventions aimed at bolstering self-efficacy of cognitively impaired patients in order to improve adherence for this at-risk population.

Consistent with previous findings (e.g., Gruber et al., 2007; Hinkin et al., 2007; Meade et al., 2011), current stimulant use is strongly predictive of poor medication adherence. As cognitive functioning only partially mediates the relationship between stimulant use and adherence, examining psychosocial variables (e.g., disruptions in routine, environmental instability) may assist in further understanding this relationship (Meade et al., 2011). Further, individuals with sustained recovery from longstanding stimulant dependence have demonstrated similar adherence rates and neuropsychological functioning relative to drug naïve individuals, suggesting that drug-induced, neurocognitive impairments and medication non-adherence are reversible (Meade et al., 2011). The present findings support incorporating stimulant use treatment, when appropriate, into intervention programs that specifically target optimization of medication adherence for cognitively impaired individuals.

As specific treatment recommendations have been made for other at-risk populations (see Thompson et al., 2012), the current results set the stage for possible recommendations that are specific for individuals with cognitive impairment. Identifying a subset of psychosocial variables that can impact medication adherence is crucial for intervention programs that seek to treat specific at risk populations due to the benefits of a multidisciplinary approach (Rajabiun, Coleman, & Drainoni, 2011; Stirratt & Gordon, 2007). Despite the role of cognitive impairment as a risk factor for poor adherence (Becker et al., 2011; Ettenhofer et al., 2010; Ezeabogu et al., 2012; Hinkin et al., 2002; Hinkin et al., 2004), little research has focused on how social workers or case managers may specifically assist this population. The results of this study warrant future research into the utility of improving a cognitively impaired patient's ability to cope with life stressors within intervention programs for treatment adherence. Furthermore, in light of the role self-efficacy serves in buffering the relationship between cognitive impairment and adherence, there may be clinical utility in encouraging a cognitively impaired patient to identify psychosocial factors that may impact their treatment adherence and to take steps towards managing these factors. Though the

current study does not directly examine psychosocial variables in the context of specific treatment interventions, the current results may provide clinicians and future researchers with direction for designing intervention techniques.

Several limitations bear mention. In order to examine the role of psychosocial variables in addition to other known risk factors for treatment noncompliance, active stimulant use served as a controlling variable during many of the main analyses. Future studies that extract cognitively impaired participants from a larger pool of subjects may exclude substance abusing participants from their final sample in order to more purely gauge the impact of psychosocial variables and confirm the current results. Such individuals were retained in the current study to increase power and generalizability. Further, recent life changes were assessed through individual, unweighted items that gauged if the life change occurred or not. This simple assessment approach may be useful in some clinical settings where time and resources are limited, but more sophisticated instruments may provide more nuanced information within future studies. Future attention may also focus on the relationship between adherence and the quality of family / social support for this population, which was not fully assessed within the current study. Additionally, previous research employing MEMS cap data have suggested that this technique may underestimate actual adherence rates to some extent (Lui et al., 2001; Panos et al., 2013), especially for individuals with poor cognitive functioning (Levine et al., 2006). The current study sought to control for potential underestimates by directly instructing participants against pocket-dosing medication (i.e., removing medication from the bottle to take at a later time) and through repeated follow-up appointments to encourage MEMS bottle use. Despite these steps, reliance upon electronic monitoring devices likely still results in an under-estimate of actual adherence rates. These limitations notwithstanding, the current study provides useful insights for social workers and case managers who are designing and implementing services to promote treatment adherence for cognitively impaired, HIV-positive individuals.

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Participant Demographic Information in Means, Standard Deviations, and Percentages for the Overall Sample and According to Adherence Status for the Cognitively Impaired Subset

Table 1

	MEMS		90% ($n = 36$)		MEMS < 90% ($n = 124$)		Comparison of MEMS Groups	
	M	or %	SD	M	or %	SD	t or χ^2	d or ϕ
Age (years)	44.08		7.85	41.91		6.93	1.61	.29
Education (years)	12.72		2.48	12.62		2.07	0.26	.04
Global <i>t</i> -score from cognitive testing	39.29		4.29	39.36		3.75	-0.11	.02
Gender (% Male)	83.3			80.6			0.13	.03
Ethnicity (%) ^a							0.26	.04
Caucasian	8.3			11.3				
African American	55.6			77.4				
Hispanic	33.3			9.7				
American Indian	0.0			0.8				
Other	2.8			0.8				
Recent CD4 count	527.71		397.45	425.36		296.40	1.64	.30
Nadir CD4 count	217.09		211.28	203.52		193.76	0.35	.07
Meets AIDS criteria based on opportunistic infection or CD4 < 200 (%)	64.7			65.3			0.00	.01
Stimulant use (%)	17.6			41.5			6.53 *	.20

Note. MEMS = Medication Event Monitoring System; 90% indicated good medication adherence and < 90% indicated poor adherence. Stimulant Use = Positive toxicology screen for cocaine and/or methamphetamine metabolites.

^a χ^2 analysis examined proportions of Caucasian vs. Minority participants.

* $p < .05$.

Table 2
Significant Psychosocial Variables Predicting Adherence Classifications, Controlling for Stimulant Use

Variable	MEMS > 90%		MEMS < 90%		B	S.E.	Wald
	M or %	SD	M or %	SD			
<u>AIDs Clinical Trials Group Form</u>							
Self efficacy	2.50	0.71	2.18	0.77	0.63*	.25	6.25
<u>Adherence Determinants Questionnaire</u>							
Interpersonal care	33.32	4.54	31.19	5.62	-0.07	.04	3.06
Perceived utility	33.91	5.11	32.09	5.80	-0.06	.04	2.30
Perceived severity	12.52	2.95	12.00	2.77	-0.06	.07	0.76
Perceived susceptibility	12.03	3.33	11.79	3.15	-0.01	.06	0.04
Subjective norms	44.82	19.09	39.80	20.96	-0.01	.01	1.37
Intentions	17.71	3.26	16.78	3.11	-0.08	.07	1.21
Treatment related barriers	8.53	2.60	10.05	2.70	0.18*	.07	6.12
<u>Recent Life Changes Scale^d</u>							
Change in medication	3.13		19.05		2.12*	1.06	4.01
Change in health status	25.00		41.34		0.60	0.47	1.60
Change in living situation	9.38		20.95		0.71	0.67	1.11
New relationship	6.25		10.58		1.55	1.08	2.08
Break up	3.13		9.62		1.31	1.08	1.46
Perceived increased stress	18.75		56.19		1.99	0.55	13.34

Note. MEMS = Medication Event Monitoring System; 90% indicated good medication adherence and < 90% indicated poor adherence.

^a Analyses utilized adherence classifications that spanned the final three study months.

* $p < .05$.

** $p < .001$.