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Factors Associated With Adherence to Medication Regimens by Older Primary Care Patients: The Steel Valley Seniors Survey

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Abstract

Objectives/Background—To explore associations between two specific cognitive domains and aspects of medication management among older primary care patients.

Methods—A sample of patients aged 65+ years drawn from several small-town primary care practices was carefully characterized with cognitive testing and use of prescription medications. Two primary outcome variables were examined: (a) self reports of setting up schedules to manage their own medication, and (b) overall research assessment of adherence to prescribed medications. Predictor variables included scores on a test of verbal memory (Hopkins Verbal Learning Test, HVLT) and a test of executive functions (Part B of the Trailmaking test) presence of prescription insurance, number of medications, and dosing frequency, adjusting for age, sex, and education. Multiple logistic regression and generalized estimating equation models were used for multivariable analyses.

Results—Higher scores on the verbal memory test and having prescription insurance were independently associated with successfully setting up a medication schedule, after adjusting for covariates. Higher scores on the test of working memory and a lower number of prescription drugs were associated with the participant being assessed as adherent to medications.

Conclusions—Independent cognitive processes are associated with the ability to set up a medication schedule and overall adherence to prescriptions. Better verbal memory functioning was strongly and independently associated with study participants setting up their own medication schedules, while better executive functioning was strongly and independently associated with being fully adherent to prescription instructions. Deficits in either cognitive ability could result in medication errors.

Keywords

Medication adherence; elderly; cognition

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Introduction

The dramatic increase in the number of medications prescribed by US physicians is due in large part to the aging of the US population. Older adults are prescribed on average two to five prescription medications^{1,2} with more medications prescribed for those reporting more than one chronic illness.³ Incorrect use of medications among the elderly is therefore a growing public health concern. Its potential consequences include recurrence of illness, increased morbidity with poorer clinical outcomes, and increased healthcare cost.^{4,5} The degree to which older adults are able to independently manage multiple medications and remain adherent to their prescribers' instructions, depends in part on sensory motor functions, psychosocial factors such as personal and cultural beliefs related to medication taking as well as cognitive abilities such as memory and problem solving skills.⁶

Medication management and adherence is a complex cognitive activity requiring more than basic abilities such as reading and telling the time. It also entails higher order cognitive functions such as the ability to encode and store in memory, and later retrieve, complex verbal information, and the ability to hold and manipulate multiple bits of information in memory at one time.⁷

These two functions may be related to separate aspects of medication management. For example, setting up one's own medication schedule may depend on successful encoding, storage, and retrieval of verbal information typically printed on the label, such as when to take a given medication and how much to take. In contrast, tracking whether or not one has taken a particular medication may be more dependent on executive processes, specifically aspects of working memory, e.g. whether the given dose of the given medication has already been taken on a given day. Deficits in executive abilities have been shown to be associated with poor medication adherence in younger patients with HIV infection,⁸ older patients with schizophrenia⁹ and community-dwelling elderly.¹⁰

Both memory and executive deficits increase in prevalence with aging and impairments in these domains may represent very early signs of dementia.^{11,12} Regardless of etiology, cognitive deficits can interfere with older adults' ability to independently carry out daily functions such as the ability to understand and carry out physicians' instructions for taking prescribed medications, an activity that is critical to health and autonomy in today's society.

Since most older adults receive medical care solely from their primary care physicians, we focused our clinical epidemiology study of cognitive impairment and dementia on a sample of older primary care patients in a small-town area of Pennsylvania.^{13,14} We have previously reported that as dementia severity increased, so did the discrepancy between inadvertent non-adherence as documented by the physicians in medical records, and as observed during standard research assessments. Those findings suggested that cognitive impairment incrementally reduces the consistency and reliability of patients' self-reports to physicians, and thus compromises providers' ability to monitor and enhance adherence.

Recognizing factors that are associated with adherence would help prescribers and pharmacists identify patients who need closer monitoring and assistance. For the present study, we examined factors associated with older primary care patients' adherence to medication regimens. We hypothesized that medication adherence would be associated with performance on tests of executive abilities, specifically working memory, and that the ability to set up and manage a medication schedule would be more related to performance on tests of verbal memory as well as other factors related to dosing.

Methods

Study site and sample

The Steel Valley Seniors Survey was conducted in the McKeesport area, an economically depressed region of Southwestern Pennsylvania including several contiguous and historically linked small towns. Fifteen primary care (family practice and internal medicine) physicians, in seven private office practices, provided researchers with access to their patients and medical records, contingent on patients' consent. Trained research nurses with previous home health or hospice experience collected data. All new or returning patients aged 65 or older, living within the study area and visiting participating physicians from 1999-2001, were eligible to participate.

Recruitment and Initial Screening

The University of Pittsburgh Institutional Review Board approved all study procedures. In the physician's offices, patients provided written informed consent and basic demographic and contact information, and were screened with the Mini-Mental State Examination (MMSE). ¹⁵ Patients also gave permission for review of medical records and home contact for additional assessment.

Detailed in-home assessment

Patients with research MMSE scores < 25 were invited to undergo a more detailed in-home assessment. The same assessment was offered to a randomly selected comparison patient subgroup with MMSE scores \geq 25, each of whom had visited the same physician within the same month as a low-scoring patient. To ensure independent assessments, different research nurses conducted the MMSE screening in the office and the assessment at home on the same patient.

The in-home assessment consisted of a semi-structured interview, a brief general physical and neurological evaluation, an assessment of medications and adherence, and a neuropsychological assessment, as reported previously.¹³ As the adherence information was used in completing the Clinical Dementia Rating (CDR)¹⁶, we did not use the CDR in the present analyses.

Medication adherence and management—Participants' medications were examined by direct inspection of prescription vials during the home visit. Participants were asked how often they took their medications, what they believed each medication was for, whether they had forgotten to take medications (and if so, how often), whether they took them as prescribed, reasons for deliberately not taking as prescribed, whether anyone helped them manage their medications, and whether the participant had a system for managing medications (and if so, what type of system (e.g. checklist, calendar, reminders, multi-compartment pillbox)). We also asked whether they were responsible for setting up their own medication schedules. Based on this information, the general state of the medications, and participants' knowledge of and familiarity with their own medications, research nurses rendered a global judgment of the level of prescription adherence. Participants were classified as non-adherent if they failed to keep up with any medication, took less than one-half of the prescribed doses as prescribed, or did not take one medication as directed even if adherent with the other medications. They were classified as adherent if they missed doses or took too much medication more than twice weekly but tried to keep up, or if they took all medications regularly as prescribed. Participants also reported whether they had prescription insurance and where they usually purchased their prescription drugs.

Research data were obtained directly from home visit participants. Data from other informants, when available, were coded separately and not used in the current analyses.

Neuropsychological Assessment—Patients underwent a detailed neuropsychological assessment consisting of a brief battery tapping the cognitive domains typically affected in dementia, as reported previously.¹⁷ To test hypotheses related to memory and executive functioning, we chose the following tests:

- 1. *The Hopkins Verbal Learning Test (HVLT)* is a 12-item word list learning test with three trials of learning, a 20-minute delayed recall, and forced choice recognition. ¹⁸ We used the sum of 3 learning trials as a measure of verbal learning and memory, which we hypothesized would be a key factor in remembering verbal (oral or written) instructions for medication management and adherence. Higher scores reflect better performance on this test.
- 2. *Trailmaking B* (Part B of the Trailmaking Test) measures executive functions (working memory, set-shifting and mental flexibility) in addition to attention, processing speed, and visual search.¹⁹ Subjects were given up to 240 seconds to complete the task. Trail making scores were calculated as number of correct connections divided by time (seconds) to complete, as the distribution is less skewed than when using time alone; thus, higher scores indicate better performance.

Statistical Analysis

For descriptive purposes, means and standard deviations were reported for continuous variables and frequencies and percentages were reported for categorical variables. Where the distribution of a variable was extremely skewed, we categorized it at natural break-points.

For participants who reported regularly taking at least one prescription drug, two main outcome variables were investigated: (a) the overall research assessment of medication adherence (yes/ no, as described above), and (b) self-report of being responsible for setting up a schedule to manage one's own medication (yes/no). The main explanatory variable for predicting medication adherence was the executive function test (Trailmaking Test B). The main explanatory variable for predicting the self-management of medication schedule was the memory test Hopkins Verbal Learning Test (HVLT). For each outcome, we used both univariable and multivariable stepwise regression models to assess the relationship between the outcome and primary explanatory variable.

Since both the HVLT and Trailmaking B scores had skewed distributions, we categorized them into three groups; scores less than the tenth percentile (which we treated as the reference group), scores between the 10th and 50th percentiles, and scores greater than the 50th percentile. Other covariates included in the multivariable models were the total number of medications being taken (five or more vs. less than five), frequency of dosing (four or more vs. one to three times a day), age (in years), sex, and education (less than high school graduate or high school graduate or above).

For the models not including the effect of frequency of dosing as a covariate, we used a logistic regression technique. For the models including the frequency of dosing, we used a population-average model with generalized estimating equation (GEE) to adjust for the cluster effect because each individual may take multiple medications. Individuals with data missing on the main outcome or predictor variables were excluded from the analysis. There was no *a priori* reason to believe that missingness was related to the adherence in this group of individuals. All statistical results were obtained using SAS 8.0. Sensitivity analyses using ISNI²⁰ indicated that the results of the logistic regression models were not affected by excluding data from subjects with missing data.

Results

The analytical sample (n=343) had a mean (SD) age of 77.52 (6.71) years; 238 (69.38%) were women, and 227 (66.18%) had high school or greater education. We excluded from the models six respondents (1.75% of the sample) who were taking no prescription drugs. The mean (SD) number of drugs was 4.25 (2.65); 130 respondents (37.9%) were taking five or more drugs.

Of those taking one or more prescription drugs, 237 (70.32%) had a dosing frequency of once a day, 89 (20.64%) were taking medications twice a day, 19 (5.65%) three times a day, and 11 (3.39%) four or more times a day.

Two hundred fifty seven respondents (75%) reported having a system to keep track of their own medication; the characteristics of those who did and did not report having such a system are shown in Table 1. Among those who reported using a system, 63 (23.5%) reported using a multi-compartment pillbox, 64 (23.97%) reported using a single-compartment pillbox, 20 (7.5%) reported using a checklist, 5 (1.87%) used a calendar, 33 (12.26%) laid out their pills at mealtimes, 69 (25.56%) laid out their whole day's medications in the morning, and 92 (34.2%) placed their medications in a location that would remind them to take them at the appropriate time. Sixteen individuals (5.75%) who reported taking their medication completely under someone else's supervision were excluded from the models; 45(16.7%) who stated that someone else helped them manage their medications were included in the models

One hundred forty two study respondents (approximately 79% of the study respondents) reported forgetting a dose less than once a week, 27(15.17%) forgot once or twice a week, and 9 (5.06%) forgot their medications more than twice a week. Among those taking one or more prescription drugs, in the research assessment of overall adherence(compliance), 245 (71.01%) took all their medications regularly as prescribed, 63 (18.26%) missed doses or took too much medication more than twice weekly but tried to keep up with medications, for a total of 308 89.28%) whom we classified as adherent. We classified as non-adherent 23 (6.67%) who did not take at least one medication as directed by physician, 12 (3.48%) who took less than one-half of the prescribed dose as prescribed, and 2 (0.58%) who failed to keep up with any medications. Characteristics of these two groups are shown in Table 2.

As seen in Table 3, having better memory (higher scores on the Hopkins Verbal Learning Test) was significantly associated with participants setting up their own medication schedules, both in univariable analyses and after adjusting for demographics and other potential confounders. Having prescription insurance was associated in the univariable model but lost statistical significance after adjusting for covariates.

As seen in Table 4, having better executive function (higher scores on Trailmaking Test B) and a lower total number of prescription drugs (less than 5) were associated with participants being assessed as adherent, in both univariable and multivariable analyses. A lower dosing frequency (less than four times a day) was associated with adherence in the univariable analysis but not after adjusting for covariates.

Discussion

Setting up a medication schedule involves the interplay of patient beliefs about their illness, prospective and retrospective memory, working memory, and long-term memory.^{21,22}. Taking one's medications correctly requires the recruitment of verbal memory to set up a system for managing medications and executive control functions to develop and implement a plan to take medications.¹⁰, 23

In order to adhere to their physicians' instructions for taking prescription and non-prescription drug regimens, many older adults develop medication management strategies that reduce the cognitive effort required to remember to take medications. The strategies may be as simple as laying medications out daily or as complex as using a calendar or pillbox to track medication usage. Adherence rates, particularly among the oldest-old, improve when medication aids are employed²⁴ thus at least partially offsetting the impact of memory loss on adherence. Gould *et al*²³ found that older adults' beliefs (self-efficacy or metamemory) and anxiety about their own cognitive functioning were strong predictors of adherence; specifically, low self-efficacy led individuals to adopt external strategies and high memory anxiety led them to employ internal strategies to help themselves remain adherent. Branin²⁵ found that older adults reported greater use of internal memory strategies and a preference for event-based (for example, taking medications with meals or at bedtime) over time-based prescription medication instructions. Depression and memory anxiety were significant predictors of type of medication adherence strategies used among the elderly, while health status and social support were not.

Our study participants employed a variety of external memory strategies to help them remember to take their medications. Almost one-half of them reported using a pillbox (either a single compartment or multi-compartment pillbox) to help them keep track of their medications. One in three of our seniors (34.2%) placed medications in a location that would remind them to take medication; one in four (25.56%) laid out medications early in the morning; and nearly one in eight (12.26%) laid out medication at mealtimes.

In our sample, 75% of those taking at least one prescription medication reported setting up their own medication schedules. Doing so was strongly associated with participants' performance on the Hopkins Verbal Learning Test (HVLT) that assesses verbal learning and delayed recall, but was not associated with overall adherence. We did not assess metamemory or internal strategies in our study.

Developing a strategy to manage medications is an indicator of the patient's intention to follow prescription instructions. However, executing the plan and adhering to the prescriber's instructions is only partly a function of the strategies the individual uses. In our study subjects, higher Trailmaking Test B scores were associated with better overall adherence, suggesting that executive function, not verbal memory, underlies the ability to adhere to prescribed medication regimens.

Executive function has previously been shown to correlate with instrumental activities of daily living requiring goal directed activities, such as paying bills and managing money, preparing meals and shopping for groceries, using the telephone, and managing medications.^{26, 27} A decline in executive function is associated with a corresponding functional decline in instrumental activities of daily living in older adults.²⁸

Insel *et al*⁹ studied executive function and working memory as predictors of medication adherence in 95 community-dwelling adults. Adherence was monitored for eight weeks using a medication monitoring cap system (MEMS). The composite of executive function and working memory tasks was the only significant predictor of adherence. In contrast, Morrell and colleagues²⁹ reported that neither a measure of working memory nor a vocabulary test was significantly associated with adherence to antihypertensive medication.

Our study has both strengths and limitations. Our study sample was recruited from a representative population of older small-town primary care patients whom we assessed in their homes. In this context, our well-trained experienced nurses were able to reliably assess the extent to which participants were taking their medications as prescribed. However, we did not have objective measures of adherence such as electronic bottle caps as are typically employed

in experimental studies of adherence. Further, we were limited to participant's self-reports of the strategies they employed to enhance their own adherence, however, as noted by Gould et al²², self-reports are routinely used by patients and providers and are of significant theoretical and practical importance independently of their objective accuracy. We note these were community-dwelling elderly who were visiting their own physicians at the time of recruitment and were presumably giving their prescribers information no more accurate than that obtained by us in a standardized manner. We did exclude from our analytic models those individuals who were taking their medication under others' supervision. In this epidemiological study, we did not include measures of metacognition, such as self-efficacy and memory anxiety, often used in experimental psychology studies. We did however include standard and robust neuropsychological measures of verbal learning/ memory and executive functioning that can easily be incorporated into primary care settings.

Conclusions

In a sample of older adults recruited from several small-town primary care practices for a clinical epidemiology study, we found that better verbal memory functioning was strongly and independently associated with study participants setting up their own medication schedules, while better executive functioning was strongly and independently associated with being fully adherent to prescription instructions. These associations remained statistically significant even after adjustment for the effects of number of medications and dosing frequency as well as age, sex, and education. Overall adherence was also associated with taking a lower total number of drugs but not to dosing frequency. Unexpectedly, neither number of medications nor dosing frequency was associated with participants setting up schedules. Having insurance for prescription medication was associated with participants setting up their schedules but only in the univariate analyses; we speculate that insurance here was a surrogate for socioeconomic status including education. It has been well-established that poorer cognitive functioning is associated with worse adherence.^{30,31} However, to our knowledge, there have been few previous attempts to deconstruct cognitive functioning and identify specific cognitive domains associated with aspects of adherence in a representative community sample of older primary care patients. Our findings may assist primary care providers and pharmacists in assessing older patients for potential difficulty with medication adherence, thus potentially lowering the many risks associated with non-adherence in the elderly.

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Table 1

Setting up own medication schedule (among those taking at least one prescription drug)*

Characteristics	Setting up own schedule	Not setting up own schedule
N	257 (75%)	86 (25%)
Age: (mean (SD)	77.07 (6.48)	78.87 (7.24)
Sex: % female	180 (70.04 %)	58 (67.44 %)
Education: % > high school	172 (66.93 %)	55 (63.95 %)
Number of Rx drugs: mean (SD)	4.30 (2.56)	4.10 (2.91)
$\% \ge 5 \text{ Rx drugs}$	98 (38.13 %)	32 (37.21 %)
Dosing frequency $\% \ge 4$ times/day	34 (3.10 %)	14 (4.20 %)
Adherence: % fully adherent	231 (89.88 %)	87.21 %
% with prescription insurance	220 (86.96 %)	63 (75 %)
HVLT mean (SD)	20.00 (5.50)	16.75 (6.88)
Trails B (mean(SD))	0.18 (0.09)	0.17 (0.10)

* For the univariate analyses, the sample size across the different variables varies slightly from 337 to 343, depending on data missing on given variables.

Table 2 Adherence (among those taking at least one prescription drug)*

Characteristics	Fully adherent	Not fully adherent
Ν	308 (89.28)	37 (10.72)
Age: (mean (SD)	77.41 (6.66)	78.54 (6.99)
Sex: % female	214 (69.48 %)	26 (70.27 %)
Education: % > high school	208 (67.53 %)	21 (56.76 %)
Number of Rx drugs: mean (SD)	4.18 (2.65)	4.76 (2.69)
$\% \ge 5 \text{ Rx drugs}$	110 (35.71 %)	21 (56.76 %)
Dosing frequency $\% \ge 4$ times/day	36 (2.85 %)	12 (6.86 %)
% setting up own schedule	232 (75.49 %)	26 (70.27 %)
% having a system	248 (80.52%)	24 (64.86%)
% with prescription insurance	256 (84.21 %)	28 (80.00 %)
HVLT mean (SD)	19.39 (5.85)	17.25 (7.28)
Trails B (mean(SD))	0.18 (0.096)	0.14 (0.101)

* For the univariate analyses, the sample size across the different variables varies slightly from 316 to 345, depending on data missing on given variables

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Table 3 Factors associated with setting up own medication schedule *

EXPLANATORY VARIABLES	CATEGORIES	A	SSOCIATION WI	TH SETTIN	G UP OWN	ASSOCIATION WITH SETTING UP OWN MEDICATION SCHEDULE	HEDULE
			Univariate Analyses	Ises		Multivariate Analyses ²	lyses ²
		Г	Linear Regression or GEE	r GEE		GEE	
		OR	95% CI	Ρ	OR	95% CI	Ρ
Hopkins Verbal Learning Test	10th - 50th%ile vs. <10th %ile	2.86	(1.21, 6.78)	0.16	5.02	(2.22, 11.33)	<0.0001
Hopkins Verbal Learning Test	> 50th % ile vs. <10th % ile	3.44	(1.48, 7.98)	0.02	6.52	(2.76, 15.42)	<0.0001
Trailmaking Test B	10th - 50th % ile vs. <10th % ile	2.52	(1.07, 5.98)	0.06	2		
Trailmaking Test B	>50th % ile * vs. <10th % ile	1.89	(0.83, 4.31)	0.56		n/a	
Number of Rx meds	>5 vs. ≤5	1.81	(0.68, 2.06)	0.56	1.04	(0.61, 1.78)	0.88
Dosing frequency	\geq 4 vs. < 4 times per day	0.99	(0.99, 1.00)	0.68	66.0	(0.98, 1.00)	0.49
Prescription drug insurance	Present vs. absent	2.18	(1.13, 4.21)	0.02	1.91	(0.97, 3.75)	0.06
Age	Years (continuous)	0.98	(0.94, 1.02)	0.30	0.99	(0.96, 1.04)	0.99
Sex	Male vs. Female	0.82	(0.47, 1.44)	0.49	0.81	(0.45, 1.44)	0.47
Education	\geq hs grad vs. < hs grad	1.19	(0.69, 2.07)	0.52	06.0	(0.49, 1.65)	0.74

* Excluding individuals who took their medication under others' supervision. ISingle logistic regression or GEE model (Dosing frequency \ge 4 vs < 4) to calculate these estimates.

²GEE model used to calculate these estimates.

Table 4 Factors associated with overall assessment of adherence *

EXPLANATORY VARIABLES	CATEGORIES		ASSOCIA	HIIW NOIT	OVERALL	ASSOCIATION WITH OVERALL ADHERENCE	
			Univariable analyses	yses		Multivariable analyses	yses
			Linear Regression or GEE	r GEE		GEE	
		OR	95% CI	d	NO	95% CI	Р
Hopkins Verbal Learning Test	10^{th} - $50^{th}\%$ ile vs. ${<}10^{th}$ %ile	2.73	(0.92, 8.12)	0.19			
	$>50^{th}$ %ile vs. <10 th %ile	2.56	(0.91, 7.21)	0.25		n/a	
Trailmaking Test B	10^{th} - 50^{th} % ile vs. < 10^{th} ile	2.81	(1.06, 7.49)	0.38	3.25	(1.13, 9.33)	0.03
	$>50^{th}$ %ile [*] vs. <10 th %ile	4.02	(1.47, 10.97)	0.03	4.38	(1.22,15.68)	0.02
Number of prescription drugs	> 5 vs. ≤ 5	0.38	(0.18, 0.77)	800.0	0.45	(0.21, 0.95)	0.04
Dosing frequency / day	≥ 4 vs. <4	66.0	(0.99, 1.00)	0.005	66'0	(0.98, 1.00)	0.08
Prescription drug insurance	Present vs. absent	1.22	(0.48, 3.11)	89.0		n/a	
Age	Years (continuous)	0.99	(0.94, 1.05)	0.87	1.02	(0.95, 1.09)	0.60
Sex	Male vs. Female	0.92	(0.43, 1.96)	0.83	0.91	(0.41, 2.00)	0.81
Education	\geq hs grad vs. < hs grad	1.43	(0.69, 2.95)	0.33	06.0	(0.39, 2.00)	0.81

 $^{\ast}_{\rm Excluding individuals who took their medication under others' supervision.$