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# Executive Function, Working Memory, and Medication Adherence Among Older Adults

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**The purpose of this study was to investigate the association between cognitive processes and medication adherence among community-dwelling older adults. Ninety-five participants (*M* = 78 years) completed a battery of cognitive assessments including measures of executive function, working memory, cued recall, and recognition memory. Medication adherence was examined over 8 weeks for one prescribed medicine by use of an electronic medication-monitoring cap. In a simultaneous regression, the composite of executive function and working memory tasks was the only significant predictor ($\beta = .44$, $p < .01$). Findings suggest that assessments of executive function and working memory can be used to identify community-dwelling older adults who may be at risk for failure to take medicines as prescribed.**

OLDER adults comprise the fastest growing segment of our population. Although the percentage of older adults who are healthy has increased, there are a growing number of individuals with chronic illness. Recent studies have addressed the capacity for self-management of chronic conditions among older adults. Self-management often includes taking prescribed medications. It is thought that this activity is governed in part by cognitive processes (Morrell, Park, Kidder & Martin, 1997; Park, Morrell, & Shifren, 1999). Older adults can experience age-related declines in the cognitive processes necessary for medication adherence (Raz, 2000), and therefore they may be at higher risk for neglecting to take medication as prescribed. This risk is accentuated for individuals suffering from chronic disease. Several studies have identified associations between certain chronic illnesses, such as hypertension, and declines in cognitive function (see, e.g., Elias, D'Agostino, Elias, & Wolf, 1995; Swan, Carmelli, & Larue, 1998). Thus, those most in need of adhering to prescribed medicines are also more likely to experience a decline in medication-taking capacity.

The goal of our investigation was to refine our understanding of the relationships between cognitive function and medication adherence among the older adult population. Prefrontal cortex theory (Fuster, 1997; West, 1996) provided the theoretical grounding for predicting the types of cognitive processes that are most important in successful medication adherence. According to this framework, there are two general types of cognitive processes that influence daily function—one that involves executive function and working memory and one that involves memory storage and retrieval (Moscovitch, 1994; see also Raz, 2000).

Adherence is defined as taking a prescribed medication at the appropriate time in the correct amount and manner (e.g., with food). Adhering to medicines requires the recruitment of executive function, because taking medicines consistently involves developing and implementing a plan to adhere; remembering to adhere, which may require time-based (e.g., at 2:00 p.m.) or event-based prospective remembering (e.g., with meals); and remembering whether the medicine was taken as desired (source monitoring). The ability to monitor source, that is to determine if the medication was taken as intended, is likely to become more difficult when the action is repetitive (Einstein, McDaniel, Smith, & Shaw, 1998). Taking medicines for chronic conditions is often repetitive because the same medicine is taken in the same way day after day.

Medication adherence may also involve working memory. For example, a person must keep the intention to take medicines active in working memory while doing other things, such as checking the time, pouring a glass of water, and getting the medicines. Einstein, McDaniel, and colleagues (Einstein, McDaniel, Manzi, Cochran, & Baker, 2000; McDaniel, Einstein, Stout, & Morgan, 2003) pointed out that, after retrieving an intention, individuals often have to delay the action until the conditions are appropriate for performing it. The investigators created conditions in which younger and older adults retrieved intentions but then had to briefly delay (5–30 s) performing the action. They found dramatic memory losses in older adults in as little as 5 s and proposed that maintaining the intention over brief delays is particularly difficult for older adults. This converges with a variety of theoretical views about the proposed function of working memory to keep representations active in the face of distraction (Engle, Tuholski, Laughlin, & Conway, 1999) and to maintain an integrated representation of the task context (Kimberg & Farah, 1993). These results also are consistent with age-associated deficits in inhibitory ability (presumed to be an executive function), which would make older adults highly susceptible to both internal and external distraction over delays (Hasher & Zacks, 1988). If medication adherence involves executive processes and working memory, then adherence should be associated with measures of these processes.

In addition to executive processes and working memory, medication adherence may depend on the encoding and storage of information about the medicine (why is the medicine important, why does the person need to take it) and instructions concerning when and how (e.g., with food) the medicine is to be taken. If this is the case, then the performance on cued recall and recognition tasks should also predict adherence.

Although there is no clear-cut evidence, the literature suggests that adherence is predicted by measures of cognition, especially executive function and working memory (Gray, Mahoney, & Blough, 2001; Morrell et al., 1997; Park et al., 1994). For example, cognitive impairment has been associated with twice the risk of nonadherence in a population-based investigation on antihypertensive drug use in the elderly population (The Rotterdam Study; see Salas et al., 2001). Cognitive processes have been associated with medication adherence among individuals who are HIV positive (Hinkin et al., 2002). In this study, an interaction was found between executive function and regimen complexity on medication adherence, suggesting that as regimen complexity increases, compromised executive function leads to increasing difficulty in adhering to medication. In contrast, Morrell and his colleagues found that neither a measure of working memory nor a vocabulary test was significantly associated with adherence to antihypertensive medication, but the investigators cited some methodological concerns related to these findings. In summary, there is some evidence associating cognition and adherence, particularly with measures that assess executive function.

We designed the present study to extend the literature on older adults' medication adherence in several ways. First, we examined relationships between adherence and measures of executive function or working memory and memory (storage), guided by prefrontal cortex theory and using a more comprehensive battery of executive function measures than in earlier studies. Second, we used a relatively large ($N = 95$) diverse sample of older adults, including elders who would not necessarily come to a university setting to participate in a research project. Third, our targeted sample included individuals who were taking medications commonly prescribed to older adults (e.g., antihypertensives, lipid lowering agents, and antiarthritic agents). Finally, we included variables in the literature shown to influence medication adherence: age, education, financial well-being, illness severity, mental status, depression, and activity (busyness).

## Methods

### Participants

We recruited a community-based sample of 100 older adults (67 years or older). The participants could live in housing for elderly persons but not in assisted living because of the requirement that they self-manage their medications. Participants also needed to be taking daily prescribed medications, including one that they were willing to place in a bottle with a medication-monitoring cap.

### Setting

Because our goal was to assess adherence in as ecologically valid a manner as possible, we recruited individuals from a variety of settings, including community centers, senior nutrition centers, clinics, church meetings, and other community gatherings. Data collection often occurred in the home so that individuals who might feel uncomfortable coming to a university setting were not eliminated from the sample. These recruitment strategies should have the effect of improving the representativeness of the sample.

### Procedure

Initial testing involved a 3-hr session. At the end of this session, we asked participants to place one of their prescribed medications in a provided medication container with a medication-monitoring cap system (MEMS; Aardex, 2002). This cap, which contains a microchip, recorded when the container was opened. We told participants that the bottle would help us count their medications. We informed them that the bottle must be used for each medication-taking event. In those instances in which people were using an organizer, we provided a box that was labeled in a manner consistent with medication organizers and that was divided into seven sections (one for each day of the week). Each section held the medication container, and it could be moved from day to day just as a medication organizer.

We asked participants to use the provided medication container for 8 weeks. At the completion of the 8 weeks, we collected the medication cap. Participants reviewed the medication log from the MEMS, with the investigator providing an opportunity for the participant to clarify medication-taking events recorded as errors of omission or commission. For example, an error of commission (opening the medication container more than prescribed) could occur if the participant were refilling the container. When there were reasons for the opening of the bottle other than taking a pill, we excluded the opening of the container from our analysis.

### Measures

*Demographic variables.*—We asked participants questions about their age, marital status, and financial well-being (1 = not able to make ends meet, 2 = barely make ends meet, 3 = have enough money, 4 = have enough money to do whatever you want; J. Verran, personal communication, October 11, 1999). We also asked them about the number of years of schooling they had completed, and how many days they had been too ill to carry out their routine activities during the past 6 months. We used a 5-point scale, ranging from 0 = none, 1 = a week or less, 2 = more than 1 week but less than 1 month, 3 = 1–3 months, to 4 = 4–6 months, which we took from the Older Americans Resources and Services Questionnaire (Duke University Center for the Study of Aging and Human Development, 1975). We also had participants complete the 30-item Geriatric Depression Scale (GDS; Yesavage, 1982) and the subscale of the Activity Questionnaire (Park, Hertzog, et al., 1999) in order to measure depression and busyness, respectively. Each item of the questionnaire has 5 response alternatives ranging from 1 = never true about self to 5 = always true about self. An example is, "How often are you so busy that you miss your regular meal times?"

*Cognitive function.*—We used the Mini-Mental State Examination (MMSE), an established screening tool for dementia, as a measure of general cognition (Folstein, Folstein, & McHugh, 1975). We also used six additional cognitive tests and subtests. These measures were the Wisconsin Card Sorting Test (WCST; Heaton, Chelune, Talley, Kay, & Curtis, 1993);

the letter–number sequence, digit span backward, mental control, and logical memory from the Wechsler Memory Scale III (WMS III; Wechsler, 1997); and the California Verbal Learning Test (CVLT; Delis, Kramer, Kaplan, & Ober, 1987).

The WCST, developed by Berg (1948) and Grant (Grant & Berg, 1948), assesses abstraction and a person's ability to shift cognitive strategies when given feedback. It is an assessment of executive function. Working memory concerns the cognitive resources that are available to actively hold and process information. Assessments developed to measure working memory usually involve those that increase the amount of to-be-remembered information or ask the individual to perform a storage and processing task simultaneously. Researchers have classified these tasks as simple span or complex span (Turner & Engle, 1989). The simple span tasks emphasize storage, whereas the complex span tasks introduce the manipulation of information (Spreen & Strauss, 1998). The characteristics of the WMS III subscales of letter–number sequence, digit span backward, and mental control include elements of storing and manipulating information.

*Medication adherence.*—We measured adherence with the MEMS (Aardex, 2002). We defined adherence as the percentage of days that the correct number of doses was taken. By examining the percentage of days that correct doses were taken, we identified individuals who opened the bottle more than prescribed one day, but did not open the bottle on another day, as not being adherent on both days. Although electronic monitoring does not ensure that the participant took the correct amount of medication, opening the cap does indicate that the participant remembered to take the medication.

## Results

### *Demographic Variables*

Ninety-five participants completed the 8 weeks of medication monitoring. The mean age was 78 years (67–93 years); 78% were women ($n$ = 74). Sixty-three participants were non-Hispanic White, 23 were of Hispanic heritage, and 9 were African-American. There were missing data for 5 participants; 4 did not complete medication monitoring because they lost the monitoring cap, moved, or died during the monitoring interval, and 1 could not complete the computer version of the WCST. There was no significant difference in mean age and MMSE score between those who completed the assessments and medication monitoring and those who did not, although the small number of participants who did not complete the study makes this comparison speculative.

We monitored the majority of participants ($n$ = 72) for their adherence to antihypertensives, 9 for lipid-lowering agents, and 11 for antiarthritic agents. We monitored the remaining 3 participants for aspirin, thyroid replacement, and quinine sulfate. There were no significant differences between the type of medication and adherence, although the comparison is limited by the small number of participants per group. The monitored medication was taken once per day for 91.6% of the participants, and twice a day for 8.4% of the participants. Mean, standard error, and range are presented in Table 1 for age, education, financial well-being, sick days, depression, busyness, and adherence.

Table 1. Mean, Standard Error, And Range For Demographic And Relevant Variables

| Variable | *M* (*SE*) | Range |
|---|---|---|
| Age, in years | 77.74 (0.6) | 67–93 |
| Education, in years | 12.86 (0.37) | 2–21 |
| Financial well-being | 3.03 (0.08) | 1–4 |
| Sick days | 0.61 (0.09) | 0–3 |
| Depression (GDS) | 5.08 (0.47) | 0–25 |
| Activity subscale (busyness) | 21.41 (0.53) | 10–33 |
| Medication adherence (% of days) | 80.36 (2.58) | 1.8–100 |

*Note*: GDS = Geriatric Depression Scale.

The majority of individuals were usually healthy enough to engage in routine activities over the preceding 6 months; 57 participants reported no ill days and 22 reported between 1 and 7 days. Of the remaining 16 participants, 12 indicated they were ill more than a week but less than a month, and 4 indicated they were too ill to perform normal activities for 1 to 3 months of the previous 6 months.

The GDS is scored as follows: 0–9 is normal, 10–19 indicates mild depression, and 20–30 indicates severe depression (Hickie & Snowdon, 1987). The mean was 5.1 on the GDS, and most individuals in this sample ($n$ = 82) were not depressed (Table 1). Cronbach's alpha for the GDS indicated high internal consistency, $\alpha = 0.86$, in this sample.

The mean score on the Activity Questionnaire subtest for busyness was 21, or 2.3 per item, indicating that most individuals were not busy or considered themselves to be minimally busy. Cronbach's alpha for this subscale was $\alpha = 0.84$.

*Medication adherence.*—The average percentage of days that medications were taken as prescribed was 80.4. Sixty-two percent of the participants in the sample were adherent to medication at least 85% of the time; the remaining 38%, whose adherence fell below 85%, were evenly distributed throughout the lower range (0% to 85%) and a linear function described the relationship.

*The cognitive composites.*—We obtained the executive function–working memory composite score by averaging the $z$ score for each participant on the following performance indicators: from the WCST, categories completed and perseveration raw score, which was reverse scored; from the WMS III, letter–number sequence, mental control, and digit span backward. We obtained the memory composite score by averaging each participant's $z$ score on the total recall score of logical memory from the WMS III, and short-delay cued recall, long-delay cued recall, and recognition from the CVLT.

This procedure for computing the composite is equivalent to the estimation of unit-weighted factor scores. The unit weighting of multivariate constructs has the additional advantage of increasing the stability (and thus interpretability) of results across independent samples (Gorsuch, 1983) as well as overcoming any potential difficulties associated with the estimation of factor scores with missing data and with smaller sample sizes (Figueredo, McKnight, McKnight, & Sidani, 2000).

We provide part–whole correlations in Table 2 for the relationship between the composite scores for executive

Table 2. Part Whole Correlations of Each Scale to the Executive Function and Working Memory and the Memory Composite Scores

| Variable | Correlation to Executive Function and Working Memory Composite Score | Correlation to the Memory Composite Score |
|---|---|---|
| WMS III Letter Number Sequencing | .85** | |
| WMS III Mental Control | .84** | |
| WMS III Digit Span Backward | .85** | |
| WCST Perseverative responses | −.44** | |
| WCST Categories Completed | .64** | |
| CVLT Short Delay Cued Recall | | .95** |
| CVLT Long Delay Cued Recall | | .92** |
| CVLT Recognition measures | | .88** |
| WMS III Logical Memory | | .59** |

*Notes*: WMS III = Wechsler Memory Scale III; WCST = Wisconsin Card Sorting Test; CVLT = California Verbal Learning Test.
**$p < .001$.

function–working memory and memory and the component parts. This procedure is equivalent to a factor structure for unit-weighted factor scales that are theoretically specified, and it is recommended for use with smaller sample sizes for which a formal factor analysis might not be advisable (Figueredo et al., 2000). As one can see, each scale is significantly related to its respective composite score, indicating the convergent validity of the composite.

The correlation matrix of the variables of interest is provided in Table 3. The zero-order correlations reveal that achieved educational level in years, MMSE score, and the composites measuring executive function–working memory and memory were significantly related to medication adherence. No other variables were associated with adherence.

Using hierarchical regression, we entered the variables in the following order: age, MMSE, the composite memory score, achieved educational level, number of sick days in the previous 6 months, financial well-being, GDS, and finally the executive function–working memory composite score. We determined the order first by interest in controlling for the effects of age, MMSE, and memory, and then by interest in establishing the unique contribution of the executive function–working memory composite after all other variables were entered. As indicated in Table 4, performance on the MMSE adds unique variance.

Table 3. Zero Order Correlations

| Variables | Adherence | Age | Ed | Fin | SI | GDS | Busy | MMSE | Execom |
|---|---|---|---|---|---|---|---|---|---|
| Age | −.11 | | | | | | | | |
| Ed | .23* | .15 | | | | | | | |
| Fin | .18 | .20* | .31** | | | | | | |
| SI | .06 | −.13 | .24* | .12 | | | | | |
| GDS | .02 | .10 | −.05 | .14 | .12 | | | | |
| Busy (n = 94) | .13 | −.31** | .02 | −.13 | .06 | .16 | | | |
| MMSE | .21* | .01 | .39** | .29** | .14 | −.08 | .17 | | |
| Exe com | .40** | −.10 | .53** | .27** | .18 | −.02 | .25* | .61** | |
| Mem com | .21* | −.22** | .29** | .10 | .16 | −.13 | .26* | .54** | .54** |

*Notes*: Ed = achieved educational level; Fin = financial well-being; SI = severity of illness; GDS = Geriatric Depression Scale; busy = busyness; MMSE = Mini-Mental State Exam; Exe com = executive function and working memory composite score; Mem com = cued recall and recognition memory composite.
*$p < .05$; **$p < .01$.

Table 4. Hierarchical Regression Predicting Medication Adherence

| Variable | $R^2$ Increments | $F$ Change | Degree of Freedom |
|---|---|---|---|
| Age, in years | .01 | 1.07 | 1,93 |
| MMSE | .04* | 4.40 | 1,92 |
| Memory score | .01 | .818 | 1,91 |
| Education | .03 | 2.71 | 1,90 |
| Illness severity | .00 | .08 | 1,89 |
| Financial well-being | .01 | 1.34 | 1,88 |
| Depression | .01 | .65 | 1,87 |
| Executive Working Memory Score | .09* | 9.28 | 1,86 |
| Total | .20* | 2.68 | 1,86 |

*Note*: MMSE = Mini-Mental State Exam.
*$p < .05$.

The executive function–working memory composite also adds unique variance, although it is entered at the end of the hierarchical regression (increment $R^2 = .09$). We ran an additional regression, entering all variables simultaneously. In this regression, executive function–working memory is the only significant predictor variable ($\beta = .44$, $p < .05$; see Table 5).

## Discussion

Consistent with prefrontal cortex theory, the composite score of executive function and working memory measures was significantly related to adherence. This finding supports the importance of examining executive function and working memory as risk factors for failure to perform everyday activities. This finding is also consistent with a recent study that identifies relationships between lower performance on executive function measures and adherence in an HIV-positive population (Hinkin et al., 2002). Temporal integration, supported by working memory, prospective memory, and control of interference or distractions, enables planning, strategizing, and implementing strategies to support medication adherence.

In contrast, the memory composite score did not predict adherence. In the naturalistic setting, remembering the medication and the instructions may not be the problem, with some exceptions. Memory and comprehension for medication information is likely to be more critical in less educated participants. The adherence study by Murray and his colleagues (2004) demonstrates strong relationships between adherence and a measure of health literacy when the mean education in

Table 5. Simultaneous Regression With All Variables Entered in the Model

| Variable | Standardized β | $t$ |
|---|---|---|
| Age, in years | −.08 | −.76 |
| MMSE | −.08 | −.62 |
| Memory composite | −.00 | −.03 |
| Education | .01 | .11 |
| Illness severity | −.01 | −.14 |
| Financial well-being | .12 | 1.07 |
| Depression | .06 | .60 |
| Executive Working Memory Score | .44* | 3.05 |

*Note*: MMSE = Mini-Mental State Exam.
*$p < .05$; **$p < .01$.

years is 10.8. For individuals in the current investigation, when the task is repetitive, as is medication adherence, it becomes associated with many things in the home environment and is likely to be recalled. However, particularly over a delay, remembering the intention and monitoring the completion of the medication-taking event may become more difficult, leading to the question, "Did I take it this morning or do I just think I took it?"

These findings converge with existing evidence that executive function influences self-care capacity. For example, some researchers have found performance on cognitive assessments to be associated with instrumental activities of daily living (e.g., paying bills, shopping for groceries; see Cahn-Weiner, Boyle, & Malloy, 2002; Grisgby, Kaye, Baxter, Shetterly, & Hamman, 1998). Royall, Palmer, Chiodo, and Polk (2004), using growth curve analysis, demonstrated that a decline in executive function over three assessments in 3 years (interval for testing, $M = 18.2$ months) is associated with functional decline in instrumental activities of daily living among older adults. The Executive Interview, developed to assess executive function, has been found to be more sensitive to cognitive changes associated with changes in instrumental activities of daily living than the MMSE. Consistent with these findings, learning proper inhaler-use technique has been associated with higher scores on the Executive Interview among older adults (Allen, Jain, Ragab, & Malik, 2003). Cognitive assessments, including measures of inductive reasoning, knowledge, and declarative memory, have also been associated with measures designed to simulate everyday tasks (Allaire & Marsiske, 2002; Marsiske & Willis, 1995; Willis, Jay, Diehl, & Marsiske, 1992). Other investigations have associated cognitive assessments with everyday functions (e.g., driving) or with everyday tasks in a home environment (Ball, 1997; Diehl, Willis, & Schaie, 1995).

Medication adherence is an important self-care activity. Unfortunately, low adherence to prescribed medication is pervasive and results in attenuated treatment efficiency (Haynes, McKibbon, & Kanani, 1996). Investigations identifying who is at risk for medication nonadherence have included issues of access, beliefs, living arrangements, and comorbidities (Balkrishnan, 1998). Findings have been inconsistent. In our investigation, when the executive function–working memory composite was in the regression model, we did not find evidence that adherence was related to education, financial well-being, illness severity, mental status depression, or activity level for community-dwelling older adults who were self-managing prescribed medications. Although these variables may generally play a role in medication adherence, they explained less variance in adherence in our sample than the executive function–working memory composite.

An important component of this investigation was its focus on older adults' performance of an everyday activity, using the participant's own medications and extending laboratory findings in an everyday context. Rendell and his colleagues (Rendell & Craik, 2000; Rendell & Thomson, 1999) have demonstrated improvement in prospective tasks in naturalistic settings among older adults compared with young counterparts. In our investigation we found that medication adherence, a prospective memory task, was not significantly associated with age. Focusing on cognitive function rather than chronological age may be a better way to identify who is at risk for failure to self-manage.

Although age effects are found in laboratory environments, there are differences in the context of laboratory investigations versus naturalistic environments. For example, West and colleagues (West, Jakubek, & Wymbs, 2002) suggest that the age-related decline in prospective tasks may result from declines in encoding the intention into memory and the detection of prospective memory cues. However, these processes are less likely to be a limiting factor in routine medication-taking situations, because the information is well learned and there are many associations in the home environment to remind one to take the medication as intended. A more important challenge may be source monitoring: "Did I do it today or do I just think I did it because I've been taking the same medication everyday for the past 2 years?" This confusion becomes particularly relevant in the context of a delay in the execution of the intended action, which often occurs in real life. This explanation is supported by findings concerning the effects of a delay in the execution of a prospective task in a laboratory environment (Einstein et al., 2000).

In conclusion, cognitive function has not been the focus of investigations of medication nonadherence, with the notable exception of Park and colleagues (Morrell et al., 1997; Park & Jones, 1997; Park, Morrell, & Shifren, 1999) and more recent work in an HIV-positive population (Hinkin et al., 2002). When cognitive ability is investigated, the measures have usually been too global to index abilities involved in adherence. For example, the MMSE is not sensitive to executive function, which we show is central to adherence behavior. Thus, there is a need for ecologically valid and reliable measures of self-care capacity, which must include executive function and working memory abilities.

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