PERGAMON

Neuropsychologia 40 (2002) 435–445

NEUROPSYCHOLOGIA

www.elsevier.com/locate/neuropsychologia

Capacity to maintain mental set in dementia

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Received 23 May 2000; received in revised form 8 May 2001; accepted 31 May 2001

Abstract

Two experiments investigating the capacity to sustain mental set in dementia were conducted. Experiment 1 analyzed performance of a non-demented control group (NC), participants with Alzheimer's disease (AD) and participants with ischemic vascular dementia (IVD) on the Boston Revision of the Wechsler Memory Scale Mental Control subtest (MC). On simple tasks there were no between-group differences after controlling for time to completion. On complex tasks, NC participants outperformed both dementia groups and AD participants obtained higher accuracy indices than IVD participants. The IVD group produced a disproportionate number of commission errors regardless of task complexity. The AD group tended to produce more omission errors on more difficult measures of mental set. Individual task performance was divided into three sections—first, middle, and last. IVD participants made fewer and fewer correct responses over all three sections, whereas performance of AD participants leveled off by the middle section with no further decline. Experiment 2 compared letter fluency performance among NC, AD and IVD groups, and participants with dementia secondary to idiopathic Parkinson's disease (PD). For all letter cues, IVD and PD participants generated fewer responses than NC and AD participants. However, IVD and PD participants generated a larger proportion of words than AD and NC participants within the first 15 s. As the task progressed, the output of IVD and PD participants dropped precipitously. These findings indicate that failure to maintain mental set is not a diffuse or general cognitive disability. Rather, failure to maintain mental set in dementia may be best understood within the context of predictable and specific within-task time epochs.

Keywords: Alzheimer's disease; Vascular dementia; Executive functions; Frontal lobe functioning

1. Introduction

The term executive systems functioning has been used to describe a variety of behaviors associated with the frontal lobes such as the ability to selectively inhibit inappropriate responses, form abstract concepts, sustain mental set, and manipulate information in working memory [21,14,27]. Although the deficits in dementia associated with memory and language have been extensively studied e.g. [7,11], impairments in executive systems functions have received less attention. Research conducted in our laboratory has focused on understanding the severity of executive systems deficits in dementia as well as determining the underlying cognitive constructs that may be responsible for these deficits.

For example, drawing from the work of Luria [21] and Goldberg [17], Lamar and colleagues [18] investigated motor perseverative behavior among patients with Alzheimer's disease (AD) and ischemic vascular dementia (IVD). We found that the severity of executive systems impairment, more specifically, the overall volume of perseverative behavior, was greater among IVD as compared to AD participants. An investigation

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0028-3932/01/$ - see front matter
PII: S0028-3932(01)00125-7

into the underlying mechanisms for this distinction revealed that poor regulation of rudimentary motor functions appears to underlie the perseverative behavior in IVD, whereas the perseverative behavior in AD was associated with deficits in the response selection of semantically-related information [18].

In a companion study, Giovannetti and colleagues [16] examined deficits in concept formation among patients with AD and IVD. Deficits in concept formation among participants with IVD were more severe such that these individuals were often unable to maintain mental set. By contrast, AD participants were able to attain mental set, but had difficulty selecting the most salient response. As in the study of Lamar and colleagues [18], deficits in the response selection of semantically-related information contributed to the impairment in concept formation seen in AD.

These studies suggest that patients with subcortical dementia exhibit a more pervasive and greater degree of executive systems impairment, whereas the executive systems problems in AD are less severe and may be more context specific, i.e. associated with degradation of semantic knowledge. These findings are consistent with the theoretical constructs put forth by Luria [21] and Goldberg [17], and suggest that executive function deficits in dementia may be hierarchically arranged in the sense that some deficits are related to higher-level disorders of cognition, while other deficits are related to more rudimentary motor cognitive functions. Moreover, the overall severity of executive systems dysfunction in dementia may depend on the degree of association of patients' lesions involving critical afferent and efferent pathways involving the frontal lobes.

1.1. The concept of mental set

In clinical assessment, the ability to establish and maintain 'mental set' refers to the capacity of patients to understand the nature of the task at hand and to operate within the parameters of that task until the task is completed. Impairment in this domain of cognitive functioning is ubiquitous among neurologic patients, including patients with dementia. We chose the Boston Revision of the Weschler Memory Scale Mental Control subtest [MC; 9] to assess problems patients exhibit in establishing and maintaining mental set for several reasons. First, the MC subtest requires patients to both comprehend and maintain task demands over a specific period of time. Due to the specific nature of each MC task, deviations from task requirements afford the opportunity for qualitative error analysis and may provide some insight into the possible mental derailments that may occur during task completion. Furthermore, it is likely that the production of errors negatively influences the ability to produce correct responses. An investigation of error production and correct responses over time may provide a means by which we can operationally define some of the difficulties patients' experience in either establishing or maintaining mental set. For example, a disproportionate number of errors to correct responses at the beginning of an MC task would imply difficulty attaining an accurate mental set. By contrast, a greater number of errors to correct responses at the end of the task would suggest difficulty maintaining an accurate mental set.

The purpose of Experiment I was to investigate the mechanisms that may underlie impairment in establishing and maintaining mental set on working memory tasks among dementia patients. Thus, we conducted an analysis of errors produced by dementia participants on the MC subtest [9]. On these tasks dementia patients tend to produce both errors of commission and omission. Errors of commission, i.e. the production of an irrelevant response, appear to reflect a substantial loss of mental set and may even imply a certain degree of confabulation or disinhibition. By contrast, errors of omission or failing to identify all target items, sometimes referred to as a 'miss', may reflect less severe impairment in maintaining mental set. Thus, some semblance of mental set is maintained to the extent that patients produce some correct responses while inhibiting erroneous ones. These observations, coupled with our previous research as described above, formed the basis of our hypothesis and predictions.

1.2. Hypotheses and predictions

The hypothesis to be tested in both experiments is that impairment in mental set is not a diffuse or generalized phenomenon. Rather, we believe that failure to maintain mental set in dementia is best understood in terms of differential impairment across task, either in the generation of correct responses or in the production of errors. Based on previous findings of greater executive dysfunction in IVD, our first prediction is that regardless of the demands of the task, between-group analyses will show that IVD participants make more total errors than their AD counterparts. In addition, we predict that within-group analyses will show that the majority of IVD participants' errors will be errors of commission. By contrast, for AD participants, the majority of their errors will be errors of omission.

In an attempt to separate impairment in attaining from maintaining mental set, the proportion of correct responses will be calculated for the beginning, middle, and end of each MC task administered. It is our expectation that IVD participants will be unable to maintain mental set, a more severe indication of executive dysfunction than their AD counterparts, who, we anticipate will remain in set once it is established. Therefore, our second prediction is that IVD partici-

pants will produce a lower portion of correct responses confined to the latter portions of MC tasks. By contrast, for AD patients, we predict the percent of correct responses made as a function of task section will be equal across all three task sections.

2. Methods—Experiment 1

2.1. Participants

All participants with dementia came from the Crozer Chester Medical Center's (CCMC) Alexander Silberman Geriatric Assessment Program. This is a 3-day outpatient dementia evaluation in which a social worker, geriatrician, neurologist, psychiatrist, and neuropsychologist examine all patients. A magnetic resonance imaging (MRI) or computerized tomography (CT) study of the brain and appropriate laboratory studies were obtained on all participants. A clinical diagnosis was determined at an interdisciplinary team conference.

On the basis of this evaluation, 49 patients were diagnosed with probable AD consistent with criteria of the National Institute of Neurological & Communicative Disease and the Alzheimer's disease and Related Disorders Association [NINCDS-ADRDA; 22]. Forty-seven patients were diagnosed with probable or possible IVD using the California Criteria of Chui [8]. In addition to periventricular and deep white matter alterations, all patients diagnosed with probable IVD had evidence of two or more ischemic strokes on the basis of their history, neurological examination, and/or a T1 weighted-MRI study of the brain. Patients diagnosed with possible IVD presented with evidence of a single stroke without a clear documented relationship to the onset of their dementia and/or Binswanger's disease as defined by Chui [8].

AD ($n = 6$) and IVD ($n = 6$) patients with cortical CVAs on MRI scans were excluded. Patients were excluded if there was any family reported history of head injury, substance abuse, epilepsy, or major psychiatric disorders including major depression. Further exclusionary criteria included abnormal findings with respect to B12, folate, or thyroid deficiency obtained from laboratory assays conducted at the time of the evaluation.

Eighteen normal control (NC) participants were also recruited and subjected to identical exclusionary criteria as listed above with the exception of laboratory assays. The NC group consisted of elderly, healthy individuals who were living independently in the community. NC participants were accepted into the study if they obtained a score of 27 or greater on the Mini-Mental State Examination [MMSE; 13] and a score of less than 10 on the Geriatric Depression Scale [GDS; [29]].

2.2. The Boston revision of the WMS mental control subtest [9]

In addition to the three tasks that comprise the standard WMS Mental Control subtest [i.e. counting backward from 20 to 1, reciting the alphabet, and adding serial 3s; [28]], the Boston Revision of the WMS Mental Control (MC) subtest includes four additional tasks: reciting the months of the year forward and backward; an alphabet rhyming task requiring patients to identify letters that rhyme with the word 'key'; and an alphabet visualization task requiring patients to provide all block printed letters that contain curved lines. Participants were allowed to work as long as necessary on these tasks provided they were working meaningfully.

For each of the seven tasks, separate accuracy indices (AcI) were calculated using the following algorithm: $\text{AcI} = [1 - ((\text{false positive} + \text{misses})/\text{number of possible correct})] \times 100$. This algorithm yielded a percentage score such that patients obtaining a score of 100% correctly identified all targets and made no false positive responses or misses. Based on previous factor analytic research [9], we summed performance on four mental control tasks (counting 20 to 1, alphabet, serial 3s, and months forward) to create an overall, automatized working memory index for relatively simple mental operations. The other three MC tasks (months backward, alphabet rhyming, and alphabet visualization) were summed to create an overall, non-automatized working memory index that measures the ability to sustain mental set for more complex, non-automatized mental operations. In addition to the AcIs for automatized and non-automatized MC tasks, the following dependent variables were tallied.

2.2.1. Times to completion

Separate indices for automatized and non-automatized time to completion were compiled.

2.2.2. Errors of omission

The total number of target items omitted from the participant's response were tallied.

2.2.3. Errors of commission

Three types of errors were coded: (1) intrusion errors—responses unrelated to the task at hand (e.g. words instead of letters like 'he' or 'me' for letters of the alphabet that rhyme with the word 'key'); (2) false positive errors—incorrect responses nonetheless within mental set for the task at hand (e.g. 'Z' or 'M' for letters of the alphabet that have curves in them); and (3) perseverations—responses repeated within an individual task.

2.2.4. Section analysis

On all tasks, the total number of correct responses was calculated. All tasks were then divided into three equal sections. Percent correct as well as percent error scores ranging from 0 to 100 were tallied for each section. Thus, for the three alphabet tasks (i.e. reciting the alphabet, alphabet rhyming, and alphabet visualization): section 1 was comprised of the letters A through I; section 2, the letters J through Q; and section 3 the letters R through Z. Tasks requiring participants to provide the months of the year forward and backwards were divided into three sections of four months. For serial 3s, section 1 contained responses 1 through 13; section 2, responses 16 through 25; and section 3, responses 28 through 40. For counting backwards from 20 to 1 the task was divided as follows, section 1 was comprised of the numbers 20 through 14; section 2 the numbers 13 through 8; and section 3 the numbers 7 through 1. Percent correct and percent error scores were approximately inverse for each participant, e.g. a percent correct score of 60% was coupled with a percent error score of 40%; thus, only percent correct scores are reported below.

3. Results

3.1. Participant characteristics

As may be seen in Table 1, the two dementia groups were significantly different from NC participants on age, $F(2, 111) = 5.8$, $P = 0.004$, level of dementia as measured by the MMSE [14] $F(2, 111) = 484.3$, $P = 0.001$, and level of depression as measured with the GDS $F(2, 111) = 5.7$, $P = 0.004$. The IVD group was significantly older than the NC participants but not significantly different from the AD group. As anticipated, both dementia groups' MMSE scores were lower than NC participants but comparable to each other.

Table 1
Experiment 1—demographic and descriptive data

	AD M (S.D.)	IVD M (S.D.)	NC M (S.D.)
Age[a]	77.41 (5.8)	79.02 (6.6)	73.00 (7.0)
Education	12.18 (2.8)	11.17 (2.8)	13.22 (2.9)
MMSE[a]	21.59 (3.9)	20.94 (4.1)	29.22 (1.0)
GDS[a]	5.90 (4.3)	6.32 (4.1)	2.67 (2.5)
Gender			
Male	$n = 21$	$n = 17$	$n = 9$
Female	$n = 28$	$n = 30$	$n = 9$

AD = Alzheimer's disease; IVD = ischemic vascular dementia; NC = normal control; MMSE = mini-mental state examination; GDS = geriatric depression scale.
[a] $P = 0.005$.

Table 2
Indices from the Boston Revision of the WMS Mental Control Subtest

	AD M (S.D.)	IVD M (S.D.)	NC M (S.D.)
Accuracy indices (AcI)			
Automatized[a]	97.70 (4.5)	92.80 (10.2)	98.73 (2.3)[b]
Non-automatized[a]	66.33 (16.7)	46.75 (23.8)	91.14 (10.6)[c]
Time to completion			
Automatized	15.70 (5.7)	23.04 (10.4)[d]	na
Non-automatized	47.13 (22.3)	56.05 (21.2)	na
Omissions			
Automatized	0.53 (1.1)	1.03 (1.72)	na
Non-automatized	2.03 (1.3)	3.25 (2.23)	na
Commissions			
Automatized	0.20 (0.32)	0.58 (0.57)	na
Non-automatized	1.46 (1.1)	2.17 (1.7)	na

AD = Alzheimer's disease; IVD = ischemic vascular dementia; NC = normal control; na = not applicable.
[a] Significant effect of group.
[b] NC = AD > IVD.
[c] NC > AD > IVD.
[d] IVD > AD.

The IVD group scored statistically higher than NC, but not AD participants, on the GDS. Non-parametric statistics confirmed that males and females were equally represented across all study groups, χ^2 (2, $N = 114$) = 1.1, $P = 0.57$.

3.2. Accuracy indices

We conducted a multivariate analysis of variance (MANOVA) on the automatized and non-automatized AcI composite indices by group (significance $P = 0.01$; see Table 2). This analysis yielded significant effects for both automatized ($F[2, 86] = 6.05$, $P = 0.003$), and non-automatized indices ($F[2, 86] = 32.89$, $P = 0.001$). Follow-up analyses revealed no between-group differences for NC and AD participants on the automatized AcI, but both of these groups obtained higher AcIs as compared to participants with IVD (Tukey HSD, $P = 0.01$ for both comparisons). For the non-automatized AcI, the NC group clearly outperformed both groups of dementia patients (Tukey HSD, $P = 0.001$ for both comparisons). In addition, AD participants obtained a higher AcI than IVD participants (Tukey HSD, $P = 0.001$). We also performed separate MANCOVAs controlling for age and GDS. These analyses did not change the results reported above.

With respect to times to completion, separate one-way ANOVAs revealed that time to completion for IVD participants was slower than AD participants for automatized tasks only (automatized: $F[1, 82] = 16.34$, $P = 0.001$). An ANCOVA controlling for time to com-

pletion removed the significant difference between IVD and AD participants' AcI scores for automatized MC tasks, $P = 0.12$.

3.3. Error analyses

Our first prediction was that IVD participants would make more total errors than their AD counterparts regardless of task complexity. Consistent with this prediction, a one-way ANOVA with total errors as the dependent variable and diagnosis as the independent variable collapsed across error type and task revealed that IVD participants made significantly more errors than their AD counterparts ($F[1,64] = 14.04$, $P = 0.001$).

With respect to the within-group analyses of specific error types, as predicted, paired sample t-tests revealed that participants with IVD produced a greater proportion of commission errors when performance was collapsed across task, $t(44) = 3.33$, $P = 0.001$. By contrast, AD participants demonstrated a trend to make more errors of omission, but only during non-automatized tasks, $t(38) = 1.87$, $P = 0.06$.

3.4. Section analyses

Our second prediction was tested with two separate 3 (sections) by 2 (groups) MANOVAs for automatized and non-automatized MC tasks (significance $P = 0.01$). The MANOVA for automatized section data revealed no between-group differences for AD and IVD participants. The non-automatized MANOVA results indicated that IVD participants demonstrated lower percent correct scores than AD participants for the first and third sections of the non-automatized tasks (Tukey HSD, $P = 0.006$; Tukey HSD, $P = 0.007$, respectively; Fig. 1).

4. Discussion—Experiment 1

In Experiment 1, tasks from the Boston Revision of the WMS Mental Control subtest were used to assess the level of impairment demonstrated by patients with dementia in establishing and maintaining mental set. Errors of omission and commission were tallied for all dementia participants. We speculated that errors of omission may reflect a degraded, yet still functional, ability to maintain mental set, while errors of commission may reflect a greater degree of impairment in establishing and maintaining mental set.

Consistent with our first prediction, IVD participants made more total errors than their AD counterparts regardless of task demands. Furthermore, IVD participants made a greater proportion of commission errors across both automatized and nonautomatized tasks, thereby showing not only degraded performance in comparison to both AD and NC participants but also more severe impairment in maintaining mental set. There was a trend for AD participants to make more omission than commission errors, albeit only on the more difficult, non-automatized mental control tests. These results suggest that AD participants are able to function seemingly within normal limits on familiar tasks of mental control. Although AD participants are able to inhibit erroneous responses on more difficult MC tasks, AD appears to compromise the ability to identify all requisite targets. Taken as a whole, these results suggest that the impairment in maintaining mental set among patients with IVD is more pervasive, and impedes their ability not only to select appropriate targets, but also to inhibit erroneous responses.

We also predicted that participants with subcortical neuropathology would exhibit differential impairment in maintaining mental set during the latter portion of mental control tasks. We found that individuals with IVD associated with subcortical periventricular and deep white matter alterations produced fewer correct responses both at the beginning as well as at the end of the more complex MC tasks. Thus, the section analyses revealed that IVD participants had difficulty initially attaining and ultimately maintaining an accurate mental set across more complex MC tasks. AD participants did not appear to have a similar problem with MC subtests. As may be seen by Fig. 1, the AD group displayed some initial difficulty in maintaining mental set from section 1 to section 2, but settled into a level of performance sufficient to complete task requirements. These results suggest that problems with mental set cannot be viewed as a general or non-specific phenomenon in dementia. Rather, depending on the presumed underlying neuropathology, differences in mental set exist not only in terms of overall severity, but also with respect to its natural progression.

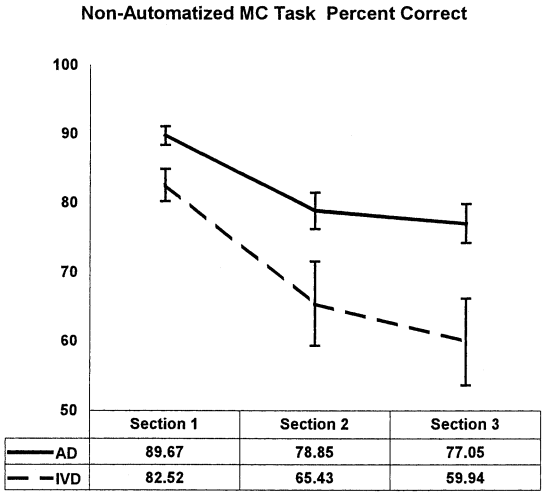


Fig. 1. Experiment 1: non-automatized MC section data.

Executive systems impairment, including failure to maintain mental set, is often investigated in patients with more traditional subcortical dementing disorders such as Parkinson's disease [see [23] for review]. However, the discussion is typically focused on time to completion, rather than differential task performance across within-task time periods or sections. The present findings suggest that cognitive slowing, i.e. time to completion, did not influence performance on the more complex non-automatized MC tasks. Rather, significant between-group differences in the ability to establish and maintain mental set occurred as a function of specific within-task time periods. The results of Experiment 1, therefore, appear to suggest that the pattern with which dementia patients attain and maintain mental set across a task, rather than the time it takes them to complete the task, may provide a better way to conceptualize 'failure to maintain mental set' in dementia.

Experiment 2 was undertaken to tease apart the concepts of mental set among patients with cortical and subcortical dementia using a traditional measure of speeded executive systems performance—letter word list generation. This task was chosen because it controls for time to completion (i.e. 1 min) while allowing for an assessment of task performance across equal within task time periods (i.e. four 15-s intervals). Furthermore, we chose letter word list generation as a task to assess attaining and maintaining mental set because in order to maximize output, one must comprehend task demands, and maintain these task demands to produce a consistent level of performance throughout the entire length of the task.

5. Experiment 2

The purpose of Experiment 2 is to see if the differential impairment in establishing and maintaining mental set observed in Experiment 1 can also be illustrated within other dementia populations and with other neuropsychological tasks. Thus, we studied a group of individuals with dementia secondary to idiopathic Parkinson's disease (PD), as well as patients with IVD or AD, and a non-demented control group (NC). In addition, we analyzed the output produced by patients with dementia on tests of letter word list generation [WLG, 'F,A,S'; 4]. It is well established that patients with dementia produce fewer words than non-demented older adults (NC) on tests of WLG. It has also been observed that demented and cognitively healthy individuals tend to produce the majority of their output early in the course of the task [5]. However, the percent of total output in each of the 15-s within-task time periods has not been extensively investigated in older adults with and without dementia. We believe that an analysis of percentage of total output, rather than raw scores, will allow us to standardize differences in output among different populations. More importantly, an analysis of within-task time epochs may provide specific information regarding the presence of a differential capacity to maintain mental set among our dementia groups, and provide a means to assess exactly when mental set breaks down.

As stated previously, successful performance on tests of word list generation requires individuals to maintain a consistent level of output throughout the entire task. If the reduced output produced by individuals with subcortical dementia is due to some differential impairment in maintaining mental set, it is reasonable to expect the majority of their output to be produced early in the course of the task with a precipitous decline in output later in the task. Thus, as in Experiment 1, we wish to test the hypothesis that failure to maintain mental set in dementia is best understood in terms of differential impairment across test performance, rather than as a diffuse or generalized disability. In Experiment 2 we examine the prediction that participants with subcortical neuropathology, such as IVD and PD, will produce a greater percentage of total output on tests of WLG during the first 15-s time period.

6. Methods—Experiment 2

6.1. Participants

Participants were assigned to one of four groups according to diagnosis. AD and subcortical IVD groups were obtained from the CCMC's Alexander Silberman Geriatric Assessment Program. The AD group included 31 individuals who met the NINCDS-ADRDA criteria for probable AD [22]. The IVD group included 28 individuals diagnosed with probable or possible Ischemic Vascular Dementia using the California criteria of Chui [8]. Twenty individuals with dementia secondary to idiopathic PD were recruited from the CCMC Parkinson's disease and Referral Center. The diagnosis of dementia secondary to PD was made by a neurologist based on the presence of cognitive impairment, the presence of at least three of the four cardinal features of PD—rigidity/postural instability, bradykinesia, resting tremor, and an obvious and sustained response to levodopa or dopamine agonists. All PD patients have been followed for several years at the CCMC Parkinson's Disease and Movement Disorder Clinic. All PD patients were assessed with the Unified Parkinson's Disease Rating Scale and were taking anti-Parkinsonian medication at the time of testing.

Thirty-nine non-demented healthy older (NC) participants were also recruited. Criteria for diagnosis of AD and IVD, as well as inclusion and exclusion for all

Table 3
Experiment 2—demographic and descriptive data

	NC M (S.D.)	AD M (S.D.)	PD M (S.D.)	IVD M (S.D.)
Age	73.84 (6.24)	76.45 (6.28)	75.63 (7.43)	77.53 (6.50)
Education[a]	13.21 (2.75)	12.67 (2.30)	12.50 (3.23)	11.17 (2.70)
MMSE[a]	28.67 (1.10)	22.23 (3.10)	21.80 (3.43)	22.21 (3.96)
Gender				
Male	$n = 14$	$n = 18$	$n = 8$	$n = 11$
Female	$n = 25$	$n = 13$	$n = 12$	$n = 17$

ND = normal control; AD = Alzheimer's disease; PD = Parkinson's disease; IVD = ischemic vascular dementia; MMSE = mini-mental state examination.
[a] $P = 0.05$.

participants for Experiment 2 are identical to those of Experiment 1 (see Section 6 for details). Although the PD participants were taking Parkinsonian medication at the time of testing, they were not taking any other psychoactive medication.

6.2. Materials and procedure

All participants were administered the 'F,A,S' Word List Generation task according to instructions outlined by Benton and Hamsher [4]. Participants were given 1 min to generate words for each letter. Participants were instructed to refrain from providing proper nouns or words that differed with respect to word endings (e.g. fruit, fruits, etc). Responses to each letter were recorded in 15-s intervals.

7. Results

7.1. Participant characteristics

Information regarding demographics and MMSE [13] scores are shown in Table 3. Separate one-way ANOVAs did not reveal significant between-group difference for age ($P = 0.13$) or GDS ($P = 0.46$). However, between-group differences were present for education, $F(3, 114) = 3.15$, $P = 0.028$, and MMSE, $F(3, 78) = 3.5$, $P = 0.019$. The IVD group had fewer years of education than the NC participants. However, when analyzed by a Pearson Product Moment Correlation no significant relationship was found between percent total FAS output and education ($r = 0.18$). As anticipated, all three dementia groups' MMSE scores were lower than NC participants but comparable to each other. Non-parametric statistics confirmed that males and females were equally represented across all groups, χ^2 (3, $N = 118$) = 3.9, $P = 0.27$.

7.2. Proportion of FAS responses

As has been consistently reported by other researchers [see [6] for review] participants with AD generally produced more words than participants with IVD and PD on tests of letters WLG. Table 4 contains a list of raw means and standard deviations, and results of between-group one-way ANOVAs. The proportion of responses produced by section (i.e. correct words generated per quarter/total correct output) was assessed with three separate group (NC, AD, IVD, PD) by section (1–4) MANOVAs for each letter (significance $P = 0.01$). Fig. 2 provides the percent means and illustrates the decline in performance over time for each letter.

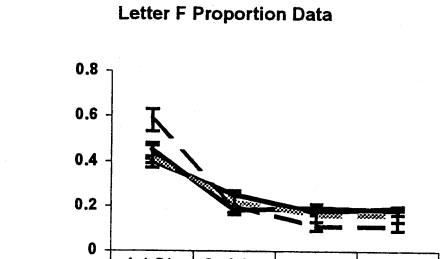
For the letter *F*, the MANOVA yielded a significant effect for the first 15-s time period only ($F[3, 114] = 5.06$, $P = 0.002$) such that participants with IVD generated a larger proportion of responses during the first section as compared to NC participants (Tukey HSD, $P = 0.002$).

The MANOVA for the letter A also yielded a significant effect for the first ($F[3, 112] = 5.82$, $P = 0.001$) 15-s time period such that participants with IVD continued to generate a larger proportion of their responses during the first section as compared to NC participants (Tukey HSD, $P = 0.001$). The MANOVA also revealed

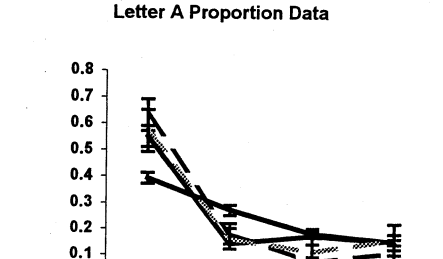
Table 4
Raw FAS output by letter and quarter with summary findings by letter

	NC M (S.D.)	AD M (S.D.)	PD M (S.D.)	IVD M (S.D.)
Letter F—quarter				
1st[a]	6.26 (1.87)	3.83 (1.64)	2.80 (2.23)	3.00 (1.52)
2nd	3.97 (1.68)	1.87 (1.45)	1.60 (1.54)	1.14 (1.27)
3rd	2.79 (1.76)	1.90 (1.37)	1.15 (1.14)	0.79 (1.03)
4th	3.14 (1.72)	1.71 (1.24)	1.20 (1.23)	0.64 (0.68)
Total	16.15 (5.32)	9.32 (3.99)	6.75 (4.13)	5.57 (2.92)
Letter A—quarter				
1st[b]	5.31 (2.08)	3.23 (1.75)	1.95 (1.50)	2.11 (.99)
2nd[b]	3.64 (1.61)	1.07 (1.12)	1.00 (1.49)	0.71 (0.81)
3rd[b]	2.56 (1.48)	1.19 (1.17)	0.70 (1.08)	0.50 (0.84)
4th	2.21 (1.28)	1.10 (1.27)	0.60 (0.75)	0.68 (1.27)
Total	13.72 (4.82)	6.58 (4.02)	4.25 (3.45)	4.00 (2.77)
Letter S—quarter				
1st[c]	5.87 (1.72)	3.68 (1.66)	2.85 (1.60)	2.68 (1.30)
2nd	4.08 (1.98)	2.32 (1.45)	1.25 (1.16)	0.89 (0.92)
3rd	3.36 (1.92)	2.00 (1.34)	0.90 (0.97)	0.86 (1.04)
4th	3.18 (2.19)	1.71 (1.70)	1.00 (1.02)	0.71 (0.98)
Total	16.48 (6.47)	9.71 (4.35)	6.00 (3.71)	5.14 (2.81)

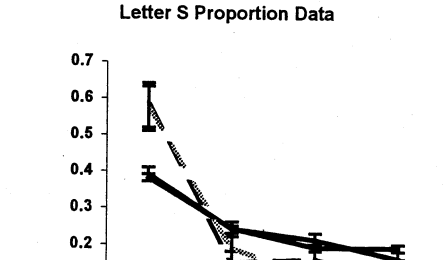
[a] MANOVA: $F(3, 114) = 5.06$, $P = 0.002$ (IVD > NC).
[b] MANOVA: $F(3, 112) = 5.82$, $P = 0.001$ (IVD > NC); $F(3, 112) = 4.42$, $P = 0.006$(ND > AD); $F(3, 112) = 4.17$, $P = 0.008$ (ND > IVD), respectively.
[c] MANOVA: $F(3, 114) = 8.24$, $P = 0.001$ (IVD > NC = AD; PD > NC = AD).



	1st Qtr	2nd Qtr	3rd Qtr	4th Qtr
NC	0.4	0.25	0.17	0.19
AD	0.45	0.18	0.19	0.18
IVD	0.58	0.2	0.11	0.11
PD	0.42	0.22	0.16	0.16



	1st Qtr	2nd Qtr	3rd Qtr	4th Qtr
NC	0.39	0.27	0.18	0.15
AD	0.55	0.14	0.17	0.15
IVD	0.63	0.18	0.07	0.11
PD	0.57	0.16	0.11	0.16



	1st Qtr	2nd Qtr	3rd Qtr	4th Qtr
NC	0.38	0.24	0.19	0.19
AD	0.39	0.24	0.21	0.16
IVD	0.58	0.15	0.16	0.11
PD	0.57	0.19	0.11	0.13

Fig. 2. Experiment 2: proportion data by quarter for each letter 'F', 'A', and 'S'.

significant effects for the second ($F[3, 112] = 4.42$, $P = 0.006$) and third ($F[3, 112] = 4.17$, $P = 0.008$) 15-s time periods. NC participants generated a larger proportion of responses during the second section as compared to AD participants (Tukey HSD, $P = 0.005$) as well as during the third section as compared to IVD participants (Tukey HSD, $P = 0.009$).

For letter S, the MANOVA produced an effect for the first 15-s time period only ($F[3, 114] = 8.25$, $P = 0.001$). During the first section, participants with IVD continued to generate a larger proportion of their responses as compared to NC (Tukey HSD, $P = 0.001$) as well as AD (Tukey HSD, $P = 0.003$) participants. In addition, during the first section, participants with PD also generated a larger proportion of their responses as compared to NC (Tukey HSD, $P = 0.006$) and marginally when compared to AD (Tukey HSD, $P = 0.017$) participants.

We also performed separate MANCOVAs controlling for educational differences noted between groups. These analyses did not change the results reported above for the letters F and S. However, for the letter A, original MANOVA results for the third 15-s time period did not remain significant after controlling for years of education. All other significant effects reported for the letter A remained.

8. Discussion—Experiment 2

It has been consistently demonstrated that patients with subcortical dementia produce fewer responses than patients with AD on tests of letter WLG [12]. These findings are usually interpreted as evidence for greater overall executive systems deficits among subcortical patients. However, consistent with our prediction, we found evidence suggesting that the mechanism that underlies this behavior may revolve around a differential capacity in maintaining mental set across task. Most of the between-group differences that emerged in Experiment 2 were confined to the first 15-s time epoch of the task, where IVD and PD participants tended to produce a disproportionately greater amount of their output. Thus, participants with subcortical dementia do not maintain as consistent a rate of output as do NC participants and participants with AD.

We acknowledge that an alternative way to assess failure to maintain mental set on tasks of letter WLG might be to evaluate for a differential rate in error production. Such an analysis was attempted, however, our participant groups did not produce enough errors to make such an analysis meaningful. Overall, the results from both experiments suggest impairment in mental set is not a general phenomenon, but may be better conceptualized with respect to impairment in specific within-task time periods or sections.

9. General discussion

The data reported in the present investigation corroborate previous findings suggesting that patients with dementia associated with subcortical neuropathology exhibit disproportionate impairment in mental manipu-

lation [1,26]. Our interpretation of these data is also based on the work of Luria [21] and Goldberg [17] who suggested that the severity, as well as the specificity, of executive systems impairment is governed by the degree of association of patients' lesions to the frontal lobes. Thus, on the basis of Luria's theoretical constructs, patient's with dementia associated with subcortical neuropathology can be expected to exhibit pronounced alterations in executive systems functions because their lesions disrupt/ disconnect intimate reciprocal connections between the frontal lobes, basal ganglia, thalamus, and midbrain [2]. This type of anatomical alteration may account for the more severe and pervasive pattern of executive systems dysfunction observed among individuals with subcortical dementia [9,16,18].

By contrast, the executive systems dysfunction we observed among participants with cortical dementia such as AD is less severe. Moreover, both Lamar [18] and Giovannetti [16] found that the perseverations and errors produced on tests of verbal concept formation were highly correlated with measures of semantic knowledge and verbal response selection, domains of cognition that are well known to be affected early in the course of AD. Again, this is consistent with theory derived from the work of Luria [21] and Goldberg [17]. While the neuropathology in AD is located primarily within temporal and temporal-parietal regions, plaques and tangles may be found in the frontal lobes. Furthermore, there are connections from hippocampal regions to the dorsolateral prefrontal cortex. However, disruption of these pathways by plaques and tangles are relatively mild in the early stages of AD. Thus, it follows that executive systems impairment seen early in the course of AD is less severe when compared to their other cognitive deficits. Thus, in dementia it is not the nearness or proximity of particular lesions to frontal cortex that causes the clinical manifestations of executive dysfunction, rather, it is the association or degree of involvement that these lesions have to frontal regions that is of concern for the current theory.

The purpose of the present research was to see if these theoretical constructs might also be useful in explaining problems in maintaining mental set which are common among patients with dementia. Consistent with our predictions, participants with IVD associated with subcortical periventricular and deep white matter alterations produced greater numbers of errors on tests of mental control. In addition, they produced a greater proportion of commission errors signaling more severe executive systems dysfunction than might be suggested by the sole production of errors of omission. They also exhibited a precipitous decline in output on both tests of mental control and letter WLG. Thus, we conclude that impairment in maintaining mental set is not a general or diffuse phenomenon in dementia; rather, it is possible to conceptualize impairment in establishing and maintaining mental set with respect to the behavior produced by patients across specific within-task time periods or sections.

When differences in executive systems operations between groups of patients with cortical versus subcortical dementia are discussed a variety of constructs are often used. One such construct is 'cognitive slowing' [25]; another is working memory [3]. Implicitly, 'cognitive slowing' suggests that a derailment in maintaining mental set may be due to slow or long response latencies. However, in Experiment 1 we did not find particularly robust between-group differences with respect to time to completion, and Experiment 2 controlled for such time related concerns. Thus, our findings of differential impairments in mental set in dementia are not due to response latency but to differences in response patterns. As a result, we believe that it is neither necessary, nor particularly relevant to associate the findings reported above with 'cognitive slowing'.

We acknowledge that the problems described above might be explained within the context of impairment in working memory [3]. Baddeley's model includes a higher-level central executive responsible for the integration and attentional control of information and two temporary information buffers, the articulatory loop and the visuospatial sketchpad. Presumed impairment with both the central executive as well as one or more of the temporary buffers has been used to explain the greater impairment seen among patients with subcortical dementia on working memory tasks [15,19,24]. Our findings also support the idea of greater impairment of executive systems in subcortical dementia. However, it is our belief that our findings related to within-task time periods or sections and our interpretation of neuroanatomical associations offer a more heuristically meaningful explanation regarding the underlying mechanisms of greater executive systems impairment often observed among patients with subcortical dementia.

The 'association model' we have proposed predicts that the strategic location and quantity of lesions in relation to the frontal lobes will govern the severity and type of impairment patients with dementia will exhibit regarding their ability to establish and maintain mental set. We admit that the letter word list generation task, and to some degree, the MC task, rely on verbal retrieval to facilitate performance. However, we do not feel that deficits in retrieval adequately explain our findings. Retrieval deficits seemingly pervade task performance whereas our findings varied depending upon within-task time epochs. More importantly, findings consistent with our association model are documented in our work within the areas of motor perseverative behavior [18] and abstract thinking [16]. In addition, other researchers have demonstrated remarkable sparing of attentional set in AD when compared to subcortical populations on intra- and extra-dimensional set

shifting tasks [26]. Thus, the associative link between frontal involvement and task performance appears evident across various tasks and cannot be fully explained by processes specific to tasks used in the current research.

Indeed, we have found some further support for the association model of executive systems dysfunction in dementia on tests not typically associated with the frontal lobes, i.e. tests of verbal declarative memory. Davis and colleagues [10] undertook an analysis of the intrusions errors and perseverations produced by patients with AD and subcortical IVD on the nine-word version of the California Verbal Learning Test [CVLT; [20]]. Participants with AD and IVD did not differ with respect to their total number of perseverations made on immediate free recall test trials 1–5. However, AD participants not only made more semantically related intrusions, they repeated these intrusion errors across subsequent free recall test trials, as compared to their IVD counterparts who refrained from producing such perseverations. That is, the source of perseverations made by AD participants on immediate free recall test trials was directly derived from their previously produced semantic intrusion errors. Thus, consistent with the constructs discussed above, the perseverations produce by individuals with AD tend to be very specific, and may be understood within context of their greater deficits in semantic knowledge.

We also acknowledge that questions remain regarding the temporal nature of deficits in mental set associated with within-task time periods reported above. Nonetheless, we believe that our research points to a useful theoretical context by which to conceptualize problems in establishing and maintaining mental set in dementia.

Acknowledgements

Portions of these data were presented at the 22nd and 27th Annual Meetings of the International Neuropsychological Society, and the First International Congress on Vascular Dementia. We would like to acknowledge the helpful suggestions of Profession Iversen and two anonymous reviewers throughout the review process for this paper.

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