Research Program Applicant Input Form

The Katz-Forbes Foundation™

"Moving money from the greedy, directly to the needy"

Jane Q. Student, B.S. — *First Name, Middle Initial, Last Name*

123-45-6789 — *Social Security Number*

Storage vs. Access: A functional study of semantic impairments in Semantic Dementia and Stroke Aphasia

Project Title (Use upper and lower case) (no more than 120 characters)

School of Behavioral and Brain Sciences — *Department*

Communication Disorders — *Division*

University of Texas at Dallas — *Institution*

Callier Center for Communication Disorders — *Address Line 1*

1966 Inwood Road. — *Address Line 2*

Dallas, TX 75235 — *City, State, Zip Code*

(817) 891-9524 — *Work Phone (include Area Code and Extension or Pager Number if Appropriate)*

Fax Number (include Area Code)

Internet Address

Citizenship*	Visa*	Academic Position*	Career Stage	Tenure?	Tenure Year	Patent
IN	F1				N	

1st Degree	Month/Year	Field of 1st Degree	2nd Degree	Month/Year	Field of 2nd Degree
BS	09		MS		11

The following information is requested for program evaluation purposes. Data will be reported in aggregate statistical form only.

Indicate percent of time spent on:

5 % *Administration*

40 % *Patient Care*

10 % *Research*

0 % *Teaching*

45 % *Other* — Coursework — *Please specify:*

Are you a post-graduate trainee? Yes ____ No x

PROJECT SUMMARY

1. *Name of award program for which application is being made:*

The Katz-Forbes Foundation

2. *Dates of proposed award:*	*From:*	May 2011	*through:*	May 2013
3. *Name of applicant (first, middle initial, last name, degree(s)):*	Jane Q. Student, B.S.			
4. *Applicant's current institution:*	University of Texas at Dallas			

5. Institution where work will be done:	University of Texas at Dallas
6. Name of sponsor (if applicable):	Dr. William F. Katz
7. Sponsor's institution (if applicable):	University of Texas at Dallas

8. Project title (limit to 120 characters or less):

Storage vs. Access: A functional study of semantic impairments in Semantic Dementia and Stroke Aphasia

9. Project summary (must be completed on this page):

Impairments of semantic memory are debilitating and can occur in a range of disorders, including semantic dementia (SD) and stroke aphasia (SA). Although the two groups display similar patterns of semantic deficits, these deficits are hypothesized to be qualitatively different. Moreover, the location of lesions in both groups differ, despite the presence of similar deficits; SD is characterized by atrophy of the anterior temporal lobes while poor comprehension in SA is associated with temporal–parietal infarcts. Previous studies have suggested that the anterior temporal lobes form a store of amodal semantic knowledge which is degraded in SD. In contrast, comprehension impaired SA patients have an impairment of the executive processes that direct and control semantic activation in a task-appropriate fashion. These studies suggest that there might be some important differences between the comprehension deficits accompanying SD and SA. Although a few studies have compared verbal and non-verbal semantic tasks separately in SD and SA, there have been almost no direct comparisons of these groups using the same semantic tasks.

The present investigation addresses these limitations by directly comparing 10 comprehension-impaired SD patients and 10 patients with transcortical sensory aphasia (TSA) on a common battery of both verbal and nonverbal semantic tests. The primary aim of the study is to examine the hypothesis that bilateral atrophy of the ATL in SD produces a gradual degradation of core semantic representations, while a deficit of cognitive control produces multimodal semantic impairments in patients with TSA following damage to the cortical regions in and around the temporo-parietal areas. More specifically, the study aims to examine the strength of three phenomena that have been argued to distinguish between 'storage' and 'access' deficits, namely frequency/familiarity effects, consistency between different semantic tests and the effect of cues on semantic retrieval.

Based on the data obtained, the study proposes to address the inconsistencies between the dementia and aphasiology literatures with respect to semantic impairments, and to elucidate the specific contributions of the different brain regions to semantic cognition.

Amount Requested	$57,200	$51,720	**Total = $108,920**
	Year 1	Year 2	

PROPOSED PROJECT BUDGET

1. *Salary and Fringe Benefits (if appropriate)*					2011/12	2012/13		
Personnel (itemize)	Degree	Role on Project	% Effort on Project		$ Amount Year 1	$ Amount Year 2		
Speech Pathologist	M.S	Principle Investigator/Clinician	40%	Salary Fringe	$22,000	$23,320		
Neuro-psychologist	Ph.D	Testing and Analysis	30%	Salary fringe	$15,000	$15,600		
Assistant	B.S	Subject Supervisor	20%	Salary Fringe	$8,000	$8,480		
Statistician	Ph.D.	Consultant	10%		$2,000	$2,120		
2. Subtotal of Salary and Fringe Benefits					$47,000	$49,520		
3. Equipment (itemize)								
Computer/Printer					$2,500			
Digital Sound Recorder					$500			
Test Material					$6,000			
				Subtotal:	$9,000			
4. Supplies (Itemize)								
Printer Paper					$100	$100		
Office Supplies					$100	$100		
5. Other Expenses (Itemize)								
Travel costs, Gasoline					$1000	$1000		
6. Subtotal of Lines 3 through 5					$10,200	$2,200		
7. Indirect Costs (If allowed by KF funding component: see instructions for additional Information.)								
								Total =

8. Total Costs	$57,200	$51,720	$	$108,920

Aims of Research Program

Semantic memory allows us to comprehend a multitude of different stimuli, such as words, pictures, objects, environmental sounds and faces. It also allows us to express knowledge

in a wide variety of domains, both verbal (e.g. naming and verbal definitions) and non-verbal (e.g. drawing and object use). Impairments of semantic memory are extremely debilitating and can occur in a range of disorders, including semantic dementia (SD) and stroke aphasia (SA). Different neuropsychological populations implicate diverse cortical regions in semantic memory; semantic dementia (SD) is characterized by atrophy of the anterior temporal lobes while poor comprehension in stroke aphasia is associated with temporal–parietal infarcts. Although both of these conditions provide insights into the neural organization of semantic memory, the two groups of patients tend have been studied by different researchers: they have almost never been directly compared using the same semantic tasks and are typically discussed in separate literatures that highlight different brain regions as being critical for semantic memory. Some previous studies have suggested that the anterior temporal lobes form a store of amodal semantic knowledge which is degraded in SD. In contrast, comprehension impaired stroke aphasic patients with left inferior frontal and temporoparietal lesions have an impairment of the executive processes that direct and control semantic activation in a task-appropriate fashion. These studies suggest that there might be some important differences between the comprehension deficits accompanying SD and stroke aphasia. It is difficult to draw firm conclusions about potential differences from the current literature because it is dominated by single case studies that employed different semantic tasks. The present investigation addressed these limitations by directly comparing 10 comprehension-impaired SD patients and 10 stroke aphasic cases on a common battery of both verbal and nonverbal semantic tests. The primary aim of the study is to examine the hypothesis that bilateral atrophy of the ATL in SD produces a gradual degradation of core semantic representations, while a deficit of cognitive control produces multimodal semantic impairments in patients with stroke aphasia following damage to the cortical regions in and around the temporo-parietal areas. More specifically, the study aims to examine the strength of three phenomena that have been argued to distinguish between ‘storage’ and ‘access’ deficits, namely frequency/familiarity effects, consistency between different semantic tests and the effect of cues on semantic retrieval.

It proposes to investigate the following questions:

1. What are the differences observed in the semantic impairments of patients with stroke aphasia (TSA) and semantic dementia (SD) and what are the variables that affect them?
2. Based on the data obtained, what can we conclude about the representation of semantic cognition in the brain?

Thus, by directly comparing SA and SD patients on the same semantic test battery, the present study proposes to establish if there are qualitative differences between the groups and investigate the hypothesis that patients with SD suffer from a gradual degradation of core semantic representations, whilst the semantic impairment in SA reflects poor cognitive control.

Background and Significance of Research

Semantic cognition refers to the processes and representations that underlie our understanding and use of the meanings of words, pictures, objects, sounds, faces and events (Rogers et al.,
2004; Jefferies and Ralph, 2006). It plays a critical role in many everyday activities, not only in the verbal domain, but also in a range of non-verbal situations, such as knowing how objects are used (Bozeat et al., 2000; 2002). Impairments of semantic cognition are highly debilitating and can arise in a range of disorders including semantic dementia (SD) and stroke induced aphasia (SA). However, the qualitative nature of the impairments is dependent on which component of semantic cognition is affected in a particular patient group.

Various models and theories have been put forth to explain the nature of the semantic impairments seen in patients with dementia as well as aphasia. The present study is designed to investigate a recent model of semantic cognition, which suggests that patients with SD suffer from a gradual degradation of semantic information, whereas patients with SA have an impairment of the executive processes that direct and control semantic activation in a task-appropriate fashion. (Ralph et al, 2006). This model, which also serves as the working hypothesis for the present study has been elaborated further.

Semantic cognition requires two interacting elements. The first is a set of amodal semantic representations that are formed through the distillation of information arising in various association areas specific to particular input or output modalities. The anterior temporal lobes are strongly connected to all the cortical association areas and are thus a prime location for this type of amodal data reduction. A second factor that underpins semantic cognition is semantic control. Although, we know many different things about objects, the aspects that are relevant for a particular task or context vary. Therefore there has to be flexibility in the information being activated by the underlying amodal concept to produce task-appropriate behavior. For example, we know many things about pianos including the manner in which notes are extracted from the instrument and the fact that they are heavy. Semantic control is required if task appropriate behavior is going to follow; thus actions related to fine-motor movements need to be to the fore when playing a piano whilst these will be irrelevant when moving across a room (Saffran, 2000). Thus, it follows that the semantic framework in the brain incorporates both amodal semantic representations and semantic control.

It is hypothesized that when the anterior temporal lobes are damaged in patients with SD, the core semantic representations themselves become degraded. Due to the amodal nature of these semantic representations, the degraded knowledge is apparent in all tasks and leads to high correlations and item consistency across different types and modalities of semantic tasks. In contrast, abilities in all other domains, such as phonology, visual processing and decision-making remain largely preserved. This is also considered to be the reason that the positive effects of cueing are not observed in this particular group of patients.

An integration of recent evidence suggests that patients with SD demonstrate the following behavioral profile:

- Patients with SD have a highly specific impairment of semantic memory: they fail diverse semantic tasks even though other aspects of cognition and language, such as phonology, visual processing and decision-making remain intact (Snowden et al., 1989; Hodges et al., 1992).
- They show poor comprehension of items presented in every modality, including spoken and written words, pictures, environmental sounds, smells and touch (Bozeat et al.,2000).
- The marked semantic deficit is also apparent in production tasks, such as picture naming (Ralph et al., 1998, 2001), verbal definitions, object drawing and object use (Bozeat et al., 2002).
- In all of these tasks, performance on highly familiar items (e.g. horse) is better preserved than less frequently encountered stimuli (e.g. zebra; Bozeat et al., 2000).
- SD patients show very high correlations between their scores on different semantic tasks and strong item-specific consistency across modalities, suggesting that the anterior temporal lobes underpin a single store of amodal semantic knowledge (Bozeat et al., 2000; Rogers et al., 2004).

Comprehension impairments are also frequently observed in stroke aphasia typically alongside other language deficits; in particular, they occur in Wernicke's aphasia, TSA and global aphasia. Stroke patients with TSA are of particular interest because their aphasia profile is at least superficially similar to that observed in SD. Within the aphasiology literature, SD is considered to be a variety of TSA (Berthier, 2000). TSA is defined as comprehension impairment in the context of fluent speech and good repetition. The behavioral similarity of stroke induced TSA and SD is unclear, however, because stroke TSA and SD patients have not been systematically compared using the same semantic tasks. There is a richer literature on non-verbal comprehension in stroke aphasia in general and Wernicke's aphasia in particular. This has revealed that poor verbal comprehension can be accompanied by impairment on a variety of nonlanguage semantic tasks. Stroke aphasia can, therefore, lead to multimodal semantic deficits even though the anterior temporal lobes remain intact.

Based on the working hypothesis, while SD patients suffer from degraded semantic representations, the semantic impairment in stroke aphasia seems to result from deregulated semantic cognition. The deficit in these patients is multimodal because all tasks, irrespective of which sensory/verbal modalities are involved, require at least some degree of semantic control. They demonstrate similar levels of semantic performance across different versions of the same semantic task because the semantic control requirements are held constant. However, this consistency drops away when comparing across different tasks because the semantic control requirements change; although the aphasic patients may be able to regulate the activation of information appropriate for one task (e.g. naming), they may be unable to reshape the information required for another test/ situation even though the same concept is being tapped. The positive effects

of cueing would seem to follow naturally in that this external source of constraint helps by reducing the amount of self-generated semantic control required in the task. Finally, performance on semantic association tests can be predicted if the ease of selecting the correct association and rejecting irrelevant factors are taken into account. These ratings presumably reflect the difficulty of controlling the semantic representations appropriately.

Need for present study:

Separate neuropsychological literatures (centred on SD, TSA and Wernicke's aphasia) implicate a widely distributed set of brain areas in semantic cognition, such as the anterior temporal cortex bilaterally (in SD) and the left posterior temporal/inferior parietal cortex (in TSA). Neuropsychological studies that compare semantically impaired patients with lesions in each of these regions can enable us to draw further conclusions about their specific roles in semantic processing. Although a few studies have compared verbal and non-verbal semantic tasks separately in SD and TSA, there have been almost no direct comparisons of these groups using the same semantic tasks. As elaborated earlier, past studies have suggested that the anterior temporal lobes form a store of amodal semantic knowledge which is degraded in SD. In contrast, comprehension impaired stroke aphasic patients with left inferior frontal and temporoparietal lesions have an impairment of the executive processes that direct and control semantic activation in a task-appropriate fashion. These studies suggest that there might be some important differences between the comprehension deficits accompanying SD and stroke aphasia. It is difficult to draw firm conclusions about potential differences from the current literature because it is dominated by single case studies that employed different semantic tasks. The present investigation addresses these limitations by directly comparing 10 comprehension-impaired SD patients and 10 stroke aphasic cases on a common battery of verbal and nonverbal semantic tests. The study proposes to examine the strength of three phenomena that have been argued to distinguish between 'storage' and 'access' deficits, namely frequency/familiarity effects, consistency between different semantic tests and the effect of phonemic cues on semantic retrieval. From a more wide-ranging perspective, it proposes to address the inconsistencies between the dementia and aphasiology literatures, and to elucidate the specific contributions of the different brain regions to semantic cognition.

Questions to be investigated:

1. What are the differences observed in the semantic impairments of patients with stroke aphasia (TSA) and semantic dementia (SD) and what are the variables that affect them?
2. Based on the data obtained, what can we conclude about the representation of semantic cognition in the brain?

Specific Predictions:

1. Patients with SD will demonstrate greater familiarity effects than the stroke aphasic cases across all tasks.
2. Patients with SD will demonstrate consistent errors for the same items across different semantic tasks, while the SA patients will not demonstrate this consistency effect
3. All SA will demonstrate a significant improvement with phonemic cueing, whereas cueing effects will not be positive in patients with SD.

Contemplated Method of Approach to the Problem

Participants:

10 patients with semantic dementia (SD) and 10 patients with stroke aphasia (SA) will be recruited for the study.

Participant criteria:

- *SD Group*

  All patients must fulfill all of the published criteria for SD (Hodges et al., 1992): presence of word-finding difficulties in the context of fluent speech, presence of impaired semantic knowledge and single word comprehension; with phonology, syntax, visual-spatial abilities and day-to-day memory being relatively well preserved.

  MRI should reveal focal bilateral atrophy of the inferior and lateral aspects of the anterior temporal lobes in every case.

- *SA Group*

  All participants should have a diagnosis of Transcortical Sensory Aphasia (TSA) All participants must be relatively equivalent in terms of selection criteria. Onset of stroke at least 12 months prior to participation in the study is a must, in order to avoid minimize treatment effects attributable to spontaneous recovery. They must demonstrate failure on both picture and word tests of semantic association on initial screening to be eligible for the study. In line with the literature on semantic impairment in stroke aphasia, all of the participants must have left temporoparietal lesions, as identified on MRI scans.

The level of impairment on verbal and non-verbal semantic tasks will be matched to ensure equivalence for the two groups.

Assessment:

A. General Neuropsychology Tests

Both groups will initially be evaluated using a range of general neuropsychological assessments, such as forwards and backwards digit span (Wechsler, 1987), the Visual Object and Space Perception (VOSP) battery (Warrington and James, 1991) and the Coloured Progressive Matrices test of non-verbal reasoning (Raven, 1962).

The SA group will be given additional tests of attention and executive skill such as the Wisconsin Card Sort test (WCST; Milner, 1964; Stuss et al., 2000), the Brixton Spatial Rule Attainment task (Burgess and Shallice, 1996) and the Elevator Counting subtests with and

without distraction from the Test of Everyday Attention (Robertson et al., 1994).

B. Semantic Memory Tests

Semantic memory will be assessed in both groups using a combination of standard tests as well as supplementary assessments. Standard tests include the pyramids and palm trees test (PPT), in which subjects decide which of two items is more associated with a target—e.g. pyramid with pine tree or palm tree (Howard and Patterson, 1992) and the concrete and abstract word synonym test (Warrington et al., 1998)

A battery of verbal and non verbal semantic tests will be used to assess semantic knowledge of subjects a across different input and output modalities and types of semantic judgement. This is adapted from a series of tests used earlier by (Bozeat et al., 2000). Concept familiarity ratings for these items are available from a previous study (Garrard et al., 2001). For all the tasks, patient responses to probes will serve as the primary dependent measure in the study.

1. Semantic Association Task:

(i) Camel and cactus test (CCT; Bozeat et al., 2000): This is a test of semantic association similar to the PPT (Howard and Patterson, 1992). Subjects must decide which of four semantically related items is most associated with a stimulus: e.g. does camel go with cactus, tree, sunflower or rose. There are two versions: in one, the probe and choices are coloured pictures; in the other,they are presented as written words that are also read aloud by the examiner.

(ii) Spoken word–picture matching: Subjects will match spoken names to pictures. There will be semantically related foils alongside the target picture in each trial.

(iii) Spoken picture naming: Subjects will be asked to name each item presented as a picture.

2. Environmental Sounds Task

This test contains recorded sounds from six categories: domestic/foreign animals, human sounds, household items, vehicles and musical instruments. There are three conditions: matching sounds to pictures, sounds to written words and spoken words to pictures. On each trial, the target is presented with 10 within-category distractors. Familiarity ratings for these concepts and sounds were obtained by Bozeat et al. (2000).

3. Phonemic Cueing Task

The effect of phonemic cues on picture naming will be assessed using the Boston Naming Test (Kaplan et al., 1983). Patients will be asked to name the 60 test items and will be given the prescribed phonemic cue for any they are unable to name (typically the first two phonemes of the word).

Experimental Problems

First and foremost, it may be difficult to locate sufficient number of patients with isolated semantic dementia and/or a isolated transcortical sensory aphasia for the study. Many of the participants might have a number of associated neurological lesions/deficits, which can act as confounds in the study. Since the stimuli will be presented via different input modalities and require responses via a number of output modalities, it is essential to ensure that the performance for all subjects is equivalent across all of them and none of these modalities are impaired. This can interfere with the results of the study as well. Additionally, there is no control group for the study as the semantic tasks have not been tested on neurologically healthy individuals. Furthermore, SD is degenerative in nature. Hence, patient performance may vary from one session to the next. This would affect intersession reliability and validity of findings. Follow up would also be difficult with these patients. Finally, all the semantic tasks measure performance and not accuracy. No online measures of testing are included in this study.

Ethical Aspects of Proposed Research

The proposed research study is involves minimal risk to all the participants involved. It does not involve physical manipulation of human subjects. There is no treatment involved; hence there is no question about morality of withholding treatment. Payment for participation in study will be low enough to prevent perception of compulsory participation. All patients will sign a form of informed consent prior to testing and test sessions will be divided to prevent fatigue and for ease of testing. Before consenting, all the patients will receive a thorough explanation of the nature of the study as well as detailed information about the tasks involved. At any point during the study, the patients have the right to withdraw consent. Finally, all personal information will remain strictly confidential and any published data will identify the subjects by a designated number (e.g., Subject 1, Subject 2) only. This method of identification ensures confidentiality and respects the privacy of the individuals involved in the study.

References

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