Neuroimaging of Discourse Processing in Aging and Alzheimer's Disease

By

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Abstract

Detection of very early stages of Alzheimer's Disease (AD) has been an area of difficulty for researchers due to confounds with age. Prose recall has been suggested as a diagnostically sensitive test of episodic memory declines in AD; however, the process by which this occurs has not been adequately defined. Theories of discourse processing suggest that prose comprehension can be mapped onto distinct patterns of brain activation and that the cognitive mechanisms used for comprehension are dependent on prose content; however, most studies have been limited to healthy adults. In this study we examined healthy young adults, healthy older adults, and adults with AD during comprehension of two different prose genres, expository and narrative. We found significant activation in posterior cingulate cortex for healthy older adults who read expository prose, and significant deactivation in anterior cingulate cortex for AD adults who read narrative prose. These results indicate that aging involves noncompensatory overrecruitment of cognitive control areas for long term memory, and that AD involves attentional deficits. This study further supports the sensitivity of prose comprehension as a diagnostic tool for AD.

Neuroimaging of Discourse Processing in Aging and Alzheimer's Disease

Alzheimer's disease (AD) is the most prevalent type of dementia, affecting nearly 4.5 million people in the United States and accounting for at least 80 percent of cognitive impairment in older adults (Hebert, Scherr, Bienias, Bennett, & Evans, 2003, Evans et al., 1989). AD severely affects quality of life not only for the patient but also their caregivers, putting both populations at risk for depression, anxiety, and insomnia (Teri & Wagner, 1992; Seignourel, Kunik, Snow, Wilson, & Stanley, 2008; McCurry et al., 1999; Ho, Chan, Woo, Chong, & Sham, 2009; Cooper, Balamurali, & Livingston, 2007, Baumgarten et al., 1992). These stressors often lead to institutionalization of AD patients, making availability of long term care an increasing concern in society (Macdonald & Cooper, 2007). In addition to these physical and economic hardships, the emotional aspects of AD are pervasive and devastating.

Despite its widespread prevalence, early detection of AD is difficult and has been an area of difficulty for researchers. Diagnosis is often based on self and collateral reports of daily functioning, which may be subtle and difficult to detect in early stages of the disease (Morris, 1993). Post-mortem examinations remain the only definitive diagnostic measures, and although ante-mortem neuropsychological tests can be conducted, detection is still largely limited to later stages of the disease where greater lesion density has already caused salient cognitive impairment (Berg et al., 1998). Moreover, AD diagnosis is highly correlated with age: while only 3% of adults from the age 65 to 74 are diagnosed with probable AD, this number increases to 18.7% for adults aged 75 to 84, and further increases to a staggering 47.2% for adults over the age of 85 (Evans et al., 1989). These data suggest that age-related cognitive decline may confound disease symptomology, especially at very early stages of the disease. Psychometrically, there is a great amount of overlap of performance scores among adults with no dementia and very mild dementia (Storandt & Hill, 1989). Healthy aging is characterized by cognitive stability over time, while AD is characterized by sharp declines, albeit in later stages of the disease (Rubin et al., 1998); however, due to lack of longitudinal follow-up, distinguishing between baseline individual cognitive ability and disease-related cognitive impairment is difficult. Therefore, absolute measures on psychometric tests may be of limited utility. Though some tests are designed to measure premorbid ability (such as the Vocabulary subtest of the Wechsler Adult Intelligence Scale), these measures may only hold true for a normal adult population, as even mild deterioration in early AD can lead to significant decreases in performance (Albert, 1981; Rubin et al., 1998). Thus, the development of more sensitive ante-mortem tests would be particularly useful in early stage detection of AD and differentiation of the disease state from healthy aging.

Impaired episodic memory is the hallmark of Alzheimer's Disease (American Psychological Association, 2000) and it is closely linked to cognitive decline in AD (Balota & Faust, 2001). Tulving (1985) defines episodic memory as a type of semantic memory that involves remembering events personal to one's life. This type of memory is necessarily correlated to autonoetic consciousness, which allows one to understand past, present, and future events that make up an autobiographical experience. Thus, episodic memory is what allows awareness of oneself across time. Two common types of episodic memory assessments are list-learning and prose. Traditionally, researchers have used list-learning and cued recall tasks to measure episodic memory decline in AD (Buschke, Sliwinski, Kuslansky, & Lipton, 1997; Buschke et al., 1999; Albert, 1981). However, Storandt & Hill (1989) reported that the Logical Memory subtest of the Wechsler Memory Scale, which involves prose recall, is actually more sensitive in differentiating adults with very mild, mild, and no AD. Other studies support this claim, as AD individuals have been shown to have differences in prose recall (Johnson, Storandt, & Balota, 2003; Haut, Demarest, Keefover, & Rankin, 1994) and generation (Ellis, 1996; Kemper et al., 1993; Lyons et al., 1994) compared to healthy older adults. Moreover, a longitudinal study of older adults indicates that declines in performance on the Logical Memory subtest actually precede clinical detection of AD (Rubin et al., 1998). Given these unique deficits in episodic memory specific to the disease state, prose comprehension could potentially be a valuable tool in better understanding the cognitive deficits in AD and aging.

The structure of a story alters its content and subsequently the ability to comprehend it. Johnson et al. (2003) reported that analyzing the Logical Memory subtest story based on its propositional structure, or idea components, is more predictive of AD severity compared to the original scoring instructions that do not account for individual idea units. Similarly, Wolfe (2005) reported that memory for different prose genres can differentially be predicted by distinct linguistic features. The author examined narrative texts (a sequence of causally and temporally related events, with a main protagonist who engages in an action to fulfill a goal) and expository texts (factual information about the basic structure, functioning, or sequence of events commonly learned about in school) and found that narrative prose recall can be predicted by text organization, while expository prose recall can be predicted by degree of semantic association. Preliminary studies from the University of Kansas Neuropsychology and Aging Lab suggest that differences in expository and narrative prose comprehension are diagnostically sensitive tests of AD and aging; older adults have been shown to exhibit more difficulty recalling expository stories, while demented adults exhibit more difficulty recalling narrative stories (Johnson & Wolfe, in preparation). These data indicate that the underlying discourse structure of different story genres is associated with distinct cognitive and neural processes that may go awry in aging and AD.

Neuroimaging research has given support for distinct neural pathways involved in discourse comprehension that map onto different elements of text structure (Mason & Just, 2006). Given that psycholinguistic changes in the form of episodic memory may be used as a diagnostically sensitive test for AD, neuroimaging in tandem with existing cognitive theories could provide useful insight into the processes of aging and AD. Since neuroimaging of prose is still a relatively new field, it is not surprising that populations of older, demented adults have not been studied extensively. The aim of this study is to combine current neuroimaging and psycholinguistics research on prose comprehension to localize patterns of brain activation that differentiate how demented, older, and younger adults understand stories. Making clearer distinctions between the processes of healthy aging and pathological AD would help refine current conceptualizations of the disease, as well as help to formulate diagnostically sensitive techniques to aid in early detection of AD.

Theories of Discourse Processing

In order to use discourse processing to expand on our knowledge of the cognitive processes in aging and AD, it is crucial to gain an understanding of the psycholinguistic theories behind story comprehension. Understanding prose can be divided into three levels of processing. First, at the most shallow level, words in a text must be *disambiguated* and understood as *propositions*. Second, propositions are *integrated* with meaning to form a *textbase* representation. Third, *inference* about that meaning based on prior knowledge occurs, which is further integrated to continuously update the textbase representation. All three processes occur in tandem; however, disambiguation contributes to superficial understanding, while integration and inference are intertwined processes that interact simultaneously to yield a deeper level of understanding.

Proposition Disambiguation

Discourse structure is composed of several linguistic elements such as syntax, grammar, words, and sentences. However, comprehension of meaning requires a representation of semantic relationships that goes beyond words and sentences. This semantic representation is known as a *proposition*, the smallest unit of discourse that represents a single idea (Turner & Greene, 1977). A proposition is composed of words or sets of words that make up word concepts. A word concept can serve either as an argument or a relation; the function of a relation is to connect multiple arguments to form a single idea, the proposition (Turner & Greene, 1977). For example, consider the following proposition:

Betty bought a balloon.

Here, the relational word concept is represented by "bought," which connects the arguments "Betty" and "balloon" to form one idea unit.

Studies on prose generation suggest that AD does not affect this superficial, propositional level of understanding (Ellis, 1996; Lyons et al., 1994; Kemper et al., 1993). If prose generation follows similar patterns to prose recall, then it would be expected that AD-related difficulties with prose comprehension would manifest at deeper levels of understanding, which we now turn to.

Integration

To achieve a deeper level of understanding, the semantic relations between propositions in a text must be examined. *Integration* is involved in two pathways: first, it draws from surface-level input and combines all the disambiguated propositions to form a *textbase* representation, which is an ordered mental representation based on the interrelatedness of all propositions derived from a text. Second, integration also refers to the process of updating this textbase representation based on knowledge derived from long term memory, which is known as *inference*. It should be noted that although integration and inference are separate processes, they are highly dependent on one another in a cycle of generating updated inputs and outputs. A textbase representation rarely provides enough information to generate full meaning from a text; further iterative cycles of integration and inference are usually required to complete comprehension.

Two theories have been proposed to explain the process of integration: a situation model and Structure Building Framework.

Situation model.

Kintsch defines a situation model based on the idea that language acts as a set of instructions to help build a mental representation of situations, which are formed by a combination of linguistic and nonlinguistic cognitive processing (van Dijk & Kintsch, 1983; Zwaan & Radvansky, 1998; Kintsch, 1994, 1998). Situations can be modeled with a general formula: for every clause c_n that is read at time t_n, a current model is formed. This current model is equal to the summation of all previous models formed by reading clauses c_1 to c_{n-1} from time t_1 to t_{n-1}. Thus, models for situations are cumulative collections of knowledge over time. The final model is then stored in long term memory, but not permanently, as new models can still be updated (Zwaan & Radvansky, 1998).

Situation models can often be dependent on schemas and prior knowledge (van Dijk & Kintsch, 1983). Integration of these inferences to modify the textbase representation can provide links between propositions, local elaborations, and larger organization on a text (Kintsch, 1998). For example, consider the following propositions:

Jane could not find the vegetable and the fruit she was looking for. She became upset.

Here, a situation model provides a causal link, since prior knowledge dictates that not being able to find an item commonly leads to being upset. Elaborative links can be formed by a situation model as well:

Jack missed his class because he went to play golf. He told his teacher he was sick.

From these two propositions, a situation model could provide the elaboration, “Jack lied.” Finally, situation models can utilize prior knowledge to apply organization onto a text. For example, in the proposition “Jane goes grocery shopping,” the reader can define episodes often involved in grocery shopping, such as shopping checking out and paying, that contribute to deeper understanding of the story text. Therefore, Kinstch conceptualizes episodic text memory as a combination of two components: a textbase and a situation model, where meaning is partially text-derived and partially knowledge-derived. Integration serves to reconcile these two sources of meaning.

Structure Building Framework.

Gernsbacher (1990) proposes a similar theory of integration known as a Structure Building Framework (SBF). Like the situation model, SBF proposes that mental representations must be built in order to comprehend text. However, unlike the bottom-up approach taken by the situation model, SBF is based on top-down perspective: a foundation is built first, and incoming information is constantly mapped onto that foundation. The foundation is dynamic, changing if incoming information does not match.

SBF was formulated from psycholinguistic theories studying the *advantage of first mention*. This is a phenomenon found when reading a sentence that involves two participants. In a probe recognition task, subjects tend to remember the first name in a sentence faster than the second name. For example, given the following sentence:

Tina beat Lisa in the state tennis match.

One would respond faster to the question, “Did the name Tina appear in the sentence?” compared to “Did the name Lisa appear in the sentence?” because Tina is the first-mentioned participant. This effect does not seem to be attributable to linguistic features such as syntax; rather, it is proposed to be a result of different cognitive mechanisms (Gernsbacher & Hargreaves, 1988).

(Gernsbacher, Hargreaves, & Beeman, 1989) measured accessibility of names in a sentence at different time points. At the earliest time point, they found the advantage of clause recency; that is, the second-mentioned participant was more accessible. 150 ms after the first time point, both the first- and second- mentioned participants were equally accessible. Finally, 1400 ms after the first time point, the advantage of first mention was found. The authors propose that this difference in accessibility can be explained by the SBF: the advantage of clause recency is observed first because the substructure at that point is simply based on the most readily available information – that is, the most recent information presented. The equal accessibility at 150 ms implies that substructures have been developed for both clauses already, but the information for the first clause has not yet been mapped into the previous substructure. Finally, the eventual advantage of first mention indicates that the substructures have been connected and that the first clause is most accessible because it serves as the basis for the whole sentences representation. In summary, the SBF suggests that a structure is laid down first and developed based on incoming information.

Overall, the situation model and SBF are theories that seek to explain the integration of meaning onto text. While situation models are highly additive and cumulative in nature, SBF is a more dynamic structure that involves matching new information against a template. However, both theories are similar in that they suggest that text representation is based on a structure that is built on prior knowledge, a key feature of integration.

Inference

Often a text does not state everything required for understanding. The reader must infer, predicting events or extrapolating when not enough information is explicitly given. This effortful inference-making process utilizes knowledge stored in long term memory to add to the existing textbase representation. Integration is responsible for incorporating relevant inferences to update the textbase representation and form complete understanding from a text.

The exact definitions of inference are currently an area of debate among discourse theorists. Five types of inferences have been defined: superordinate goals, subordinate goals, causal antecedents, causal consequences, and static properties (Graesser, Millis, & Zwaan, 1997). Theorists differ vastly in opinions on how many of these inferences are actually encoded "online" during the process of comprehension. Some argue that all five inferences are encoded, but this position is largely unaccepted because of the overwhelming amount of cognitive resources it would demand (Graesser et al., 1997). Others argue that only causal antecedents would be encoded (McKoon & Ratcliff, 1992). Kintsch defines inference as a controlled, generative process that requires logical deduction, thus arguing that none of the five above inferences are actually encoded "online" (Kintsch, 1998). However, few studies on discourse processing actually use this exact definition of inference. For the purposes of this study, we define inference as an effortful process that requires utilization of prior knowledge stored in long term memory.

Recall that, although inference is a distinct process used to generate predictions or resolve missing information in discourse based on prior knowledge, it occurs in tandem with integration, constantly updating the situation model. Three theories currently exist that describe how inference is used to expand on the text base representation: Construction Integration, Latent Semantic Analysis, and Coarse Coding.

Construction Integration.

A construction integration (CI) model provides a bottom-up approach to discourse processing consistent with the concept of inference. Two phases are involved: in the first, spreading activation leads to construction of several inferences related to the textbase meaning. In the second phase, those inferences with the highest degree of semantic relatedness to the existing textbase meaning are selectively integrated into the textbase meaning. The cycle of construction and integration is continuous, as the textbase representation is constantly being updated from new propositional input. New associative nets are created iteratively until the text base is stabilized and stored in long term memory (Kintsch, 1988; Mason & Just, 2006). It should be noted that this cycle is parallel to the process of forming a textbase representation from propositions: construction of an incoherent textbase is formed from disambiguated propositions, which are then integrated based on semantic relatedness to form a coherent textbase representation. These processes, running in parallel, contribute to a deeper meaning of text. Thus, according to CI, inference is a process that involves updating the textbase representation via an associative network of linguistic input and the individual's prior knowledge base (Mason & Just, 2006).

CI can be utilized as a model to analyze text in a method known as *propositional analysis* (Kintsch & van Dijk, 1978; Kintsch, 1998). Since CI is based on interrelatedness of propositions and inferences, it can be used to predict which propositions will be most likely to be activated by spreading activation, and thus most likely to be recalled. CI defines propositions as nodes in an iterative spreading activation network that can either activate or constrain activation. *Strength values*, which are a function of interconnectedness and activation strength, can be calculated for each proposition, thus developing a hierarchy of propositions in a text (see Kinstch, 1998 for details on calculations). Propositions that are utilized more often in telling a story should have greater strength values, since they have a higher degree of interconnectedness to important story elements. Propositional analysis has been found to be useful in predicting recall and comprehension of prose (Kintsch & van Dijk, 1978; Kintsch, 1994; Zwaan & Radvansky, 1998; Ratcliff & McKoon, 1978).

Latent Semantic Analysis.

Landauer & Dumais (1997) propose a newer model of text analysis known as Latent Semantic Analysis (LSA). LSA is based on the idea that words that occur in the same context are closer in semantic space; by measuring the frequency of co-occurrence of two words, one can estimate the degree of their semantic relatedness. A large database of word meanings in a variety of contexts is used to measure this semantic relatedness (see Landauer & Dumais, 1997 for more details of calculations). In contrast to CI, LSA does not take into account the text structure, possible inferences, or the iterations of spreading activation; it is based purely on stable, semantic relatedness of words to their context. Words that are closer in a semantic network are predicted to be easier to recall; for example, “car” and “brakes” would be expected to have a higher degree of relatedness than “semantic” and “carburetor.”

LSA has been shown to be effective in predicting similarity of meaning. Landauer & Dumais (1997) found that a computer using LSA could perform as well as moderately competent students on the Test of English as a Foreign Language (TOEFL) examination. LSA has also been found to predict comprehensibility of text (Landauer & Dumais, 1997), learning based on text difficulty (Wolfe et al., 1998), and performance on specific genres of text (Wolfe, 2005). The effectiveness of both LSA and CI models of text analysis suggests that prose comprehension involves understanding the basic structure of a text as well as prior knowledge about semantic relationships among words and propositions.

Coarse Coding Model.

Beeman and Chiarello (1998) propose a complementary theory for inference-making that incorporates brain function. They suggest that the right and left hemispheres have differential coding abilities. The right hemisphere is responsible for “coarse coding,” or processing diffusely related concepts. It activates a larger, more nonspecific field for words and therefore takes longer to respond to text. Thus, a process such as inference would be localized to the right hemisphere. The left hemisphere, on the other hand, is responsible for “fine coding” of concepts only very closely related to the text. It is faster and activates smaller, more specific semantic fields, but ultimately is not capable of inference-making.

Evidence for this theory came from studies on visual half field priming by Beeman et al. (1994). In this study, stimuli were presented to only the left visual field/right hemisphere (LVF/RH) or the right visual field/left hemisphere (RVF/LH). The stimuli were target words preceded by two different types of primes: direct primes, which consisted of one word that was highly related to the target word, and summation primes, which consisted of three words loosely related to the target:

Direct prime: scissors; Target: cut

Summation prime: cry, foot, glass; Target: cut

When subjects were asked to name the target word, both the LVF/RH and RVF/LH benefited from the direct prime. However, only the LVF/RH benefited from the summation prime. Moreover, other evidence from similar studies indicate that LVF/RH can be primed over a longer time period with distantly related primes (such as the prime “deer” for the target word “pony”) (Mason & Just, 2006). Consistent with the coarse coding hypothesis, this gives strong evidence that the right hemisphere can activate broader, multiple meanings, over a longer period of time.

Further evidence for coarse coding comes from studies on left- and right- hemisphere damaged patients. Right hemisphere damaged (RHD) patients do not organize discourse recall as well and have difficulty stating the relationships between elements in a story (Hough, 1990). Additionally, RHD patients have difficulty stating the theme of a narrative, suggesting that the processes involved in forming an organized framework for a story are localized to the right hemisphere (Hough, 1990). Moreover, a study using a list recall task found that RHD patients do not cluster words semantically when recalling (Villardita, 1987). These findings are complementary with a CI model of integration and inference, suggesting that right hemisphere damage disrupts the ability to utilize semantic relatedness to build a coherent mental representation of a text.

Summary of Discourse Theories

Taken together, theories on discourse processing define a model for prose comprehension that involves three levels of processing. Surface-level disambiguation of propositions occurs first, and then the semantic relatedness of propositions is integrated to form a textbase representation of the meaning of a text. This textbase representation is constantly being updated via spreading activation based on new incoming propositions and inferences based on knowledge from long term memory. These simultaneous, iterative processes of incorporating new propositions and new inferences continue until a coherent, stable representation of text meaning is formed and stored into long term memory. Both construction integration models and latent semantic analysis can predict prose recall, indicating that prose comprehension involves understanding of text structure and also semantic relatedness between elements of a story.

Neuroimaging Evidence for Discourse Theories

Though language was traditionally conceptualized as being lateralized in the left hemisphere, more recent neuroimaging research has identified a distinct set of bilateral regions in the brain that map onto the three levels of processing involved in story comprehension.

Proposition Disambiguation

Disambiguation of words and propositions has been linked to areas in the left hemisphere traditionally associated with aging. Xu, Kemeny, Park, Frattali, and Braun (2005) used fMRI to test word comprehension and found it to be lateralized to the left hemisphere, particularly in the middle temporal, inferior frontal (Broca's area), lateral premotor, and anterior supplementary motor regions. Similar results were found in a study by Just, Carpenter, Keller, Eddy, and Thulborn (1996) that used a more complex experimental procedure. Subjects were asked to read sets of three superficially similar sentences with different difficulties according to clause type:

No embedded clause: “The reporter attacked the senator and admitted the error”

Subject relative clause: “The reporter that attacked the senator admitted the error”

Object relative clause: “The reporter that the senator attacked admitted the error”

Brain activity was left lateralized and present in the laterosuperior temporal (Wernicke's area) and left inferior frontal areas (Broca's area). However, the authors also noted that amount of activation is positively correlated with text difficulty, suggesting that increased resource allocation is needed for disambiguating harder sentences.

Mazoyer et al. (1993) auditorally presented subjects with single words and stories. The individual words were presented in the subjects' native language (French), but stories were presented either in French or Tamil (a language unfamiliar to all subjects). Moreover, stories in French were either presented as continuous sentences or as disrupted sentences where content words were replaced with pseudowords or semantically unrelated words. Thus, the syntax of these disrupted stories was preserved, while the semantic relatedness was fragmented. Consistent with other studies, PET showed that left inferior frontal gyrus was activated when single words were presented. Bilateral activation of the temporal poles was found when continuous stories in French were presented, but only the left temporal pole was activated when discontinuous stories were presented. This study confirms left lateralization at surface-level disambiguation, but suggests a more complicated pattern of activation involving the right hemisphere when deeper understanding of prose is required.

Integration

An fMRI study by St. George, Kutas, Martinez, and Sereno (1999) give support to the situation model involved in integration of meaning. Subjects were presented with paragraphs with or without a title. The paragraphs were designed such that, without a title, the topic of the paragraph was highly ambiguous. For example, consider the following excerpt from a paragraph:

"This is very rewarding but tends to be quite expensive even if you own all that you need. The outfit does not really matter. One can get seriously injured without proper instruction even if it comes more naturally to some people than others. Some don't like the smell or the lack of

control. So some people are scared to try it even if they've dreamed of it since they were a kid reading about it in books and watching it on television."

The title of this paragraph is "Horse-back riding," but without this title, contextual interpretation of the paragraph is difficult.

Discourse processing was shown to activate bilateral inferior frontal and temporal regions of the brain, indicating that language comprehension is not purely left lateralized. Specifically, greater activation in the left middle and superior temporal regions was observed when a title was present; in contrast, the right homologous regions were more active when a title was not present. Therefore, seemingly small differences in text presentation can lead to vastly different methods of processing a narrative. When a title is presented, a global framework has already been built for the reader, decreasing the need for intense integration. However, the lack of a title requires more cognitive effort on the reader's part to map meaning onto text. These findings suggest that right temporal regions may be responsible for integrating text into a global, coherent representation.

Tomitch, Just, and Newman (2004) presented subjects with three-sentence paragraphs but altered the position of the topic sentence to the first (topic-first condition) or last position (topic-last condition). Brain activity was then measured for each individual sentence. Greater left temporal activation was found for the topic sentence when it was in the topic-last condition, whereas greater right temporal activation was found for the topic sentence regardless of its location. Based on these results, it seems that activation of the topic-last condition may reflect a reorganizing process. Thus, left temporal regions may be responsible for laying the foundation for a basic, syntactical substructure, as suggested in the SBF model (Gernsbacher, 1990). The lack of sensitivity to position in the right temporal region suggests that it may be responsible for using the topic sentence (in the topic-first condition) or shifting the substructure (in the topic-last condition) as a broader mental representation of text is being formed.

A study done by Robertson et al. (2000) provided similar results. Subjects were presented with discourse or disconnected sentences that were formed by using either definite or indefinite articles, respectively:

Discourse sentence: The grandmother sat at the table.

Disconnected sentence: A grandmother sat at a table.

Results suggest that discourse text was associated with greater right frontal activation, compared to disconnected text. Greater left frontal activation was associated with word recognition and syntactic processing. The authors interpret that the right hemisphere involvement indicates mapping of broader, coherent meaning onto the propositionally-derived textbase meaning.

Inference

As stated previously, the exact definition of inference is currently being debated, so several studies on different types of inference exist. A study by Caplan and Dapretto (2001) showed that inference from the textbase representation regarding broader semantic meaning exists and is neurologically distinct from logic-based inferences derived from the surface-level syntax of a sentence. Subjects listened to conversations that required them to make inferences based on reasoning or logic. All subjects were first auditorally presented with a question. In the topic maintenance condition, the question was followed by either an on-topic or off-topic response. In the reasoning condition, the question was followed by either a logical or illogical response. Examples of the stimuli are as follows:

Topic maintenance condition:

Question: “Do you believe in angels?”

Response 1: “Yes, I have my own special angel.” (on-topic)

Response 2: “Yes, I like to go to camp.” (off-topic)

Reasoning condition:

Question: “Do you like having fun?”

Response 1: “Yes, because it makes me happy.”

Response 2: “No, because it makes me happy.”

fMRI showed that, under the reasoning condition, activation was left lateralized to inferior frontal and superior temporal regions (Broca’s and Wernicke’s areas), suggesting that the left hemisphere is involved understanding the organization and logical progression of a sentence. In contrast, in the topic maintenance condition, bilateral activation (with more right hemispheric involvement than left) was found in inferior frontal and superior temporal areas, as well as increased right hemisphere activation in dorsolateral prefrontal cortex. This indicates bilateral, particularly right hemispheric, involvement in integration of information to infer the theme of a sentence. These findings suggest that deeper inference about meaning is a process distinct from inference about the syntax of a sentence.

Mason and Just (2004) studied causal inferences in text. Subjects were given pairs of sentences: an outcome sentence and an antecedent. These sentences varied in the degree of causal relatedness:

Outcome sentence: “The next day his body was covered in bruises.”

Antecedent sentences:

“Joey’s big brother punched him again and again.” (highly related)

“Racing down the hill, Joey fell off his bike.” (moderately related)

“Joey’s crazy mother became furiously angry with him.” (moderately related)

“Joey went to a neighbor’s house to play.” (distantly related)

When reading time and recall for these sentences was tested, interesting results were found. While reading time was negatively correlated with causal relatedness, a U-shaped curve was observed for memory and causal relatedness, such that memory was best for moderately related items and worse for highly related and unrelated items. The authors propose a CI model to explain these results. Since construction of a text base is based on an associative network of relatedness, less related sentences would take longer to process. However, only those textbase representations that underwent inference via repeated, stabilized spreading activation would be stored in long term memory. As a result, memory may have been worse for unrelated sentences because spreading activation could not generate a stable inference about the text meaning. Memory may have been worse for the highly related sentences because there was hardly any need for inference; thus skipping over the process of spreading activation and storage into long term memory.

In the same study, brain activity was found to support the CI model as well. Activation in the left language areas (inferior frontal, inferior and superior temporal, and inferior parietal) showed no change across relatedness, indicating that the same type of syntactic processing took place regardless of causal relatedness. In contrast, the right hemisphere homologues of the language areas were affected by causal relatedness, as activation was greatest in the moderately related condition. This implies that the right hemisphere activation may be related to integration of inferences into memory. Finally, a consistent, slight increase in bilateral activation of dorsolateral prefrontal cortex was found as causal relatedness decreased. Though statistically insignificant, the authors propose that this increase in dorsolateral prefrontal activity may be due to an increased search for inference via spreading activation as relatedness of the sentences decreased. Thus, it is suggested that basic syntax generation is localized to the left hemisphere, inference takes places in dorsolateral prefrontal regions, and this inference is integrated into the text meaning in the right hemisphere. It should be noted that these results are consistent with previously discussed studies on left and right lateralization of discourse processing.

Some studies of inference have focused on how figurative language is understood. Nichelli et al. (1995) had subjects read Aesop's fables and then asked them yes or no questions about changes in font, grammatical errors, semantic features (for example, whether or not a character in the fable shared a specific semantic feature), and morals (for example, whether or not the story shared a similar moral). Thus, the semantic and moral conditions required subjects to infer something about the text, but differed in whether the inference was literal or figurative.

PET scanning showed that bilateral prefrontal cortex was activated in the grammar, semantic, and moral conditions, more evidence that language is not lateralized to just the left hemisphere. Specifically, left inferior parietal and dorsolateral prefrontal cortex were activated during the semantic condition, reflecting the associative, fine coding previously discussed as being left lateralized. In contrast, right inferior frontal and medial temporal regions were activated during the moral condition, suggesting that it is involved in coarse, thematic coding as described by Beeman & Chiarello's (1998) Coarse Coding model.

In another study on literal and figurative inference, Bottini et al. (1994) measured subjects' brain activity during performance of three linguistic tasks. In a metaphor task, subjects had to determine whether a metaphor was plausible or not. Metaphors were new and unconventional, decreasing the likelihood that they had been seen by subjects previous to the experiment:

The investors were squirrels collecting nuts. (plausible)

The investors were trams. (implausible)

In a sentence task, subjects had to decide whether sentences were plausible or not:

The boy used stones as paperweights. (plausible)

The boy used feathers as paperweights. (implausible)

In a lexical decision task, subjects had to indicate whether there was a nonword (for example, "linge") present in a sentence-like string of 8 to 9 words.

PET imaging showed left hemisphere activation for sentence comprehension, specifically in parietal, precuneus, prefrontal, middle/inferior temporal, and temporal pole regions. Metaphor comprehension activated right prefrontal, middle temporal, precuneus, and posterior cingulate areas. This pattern of activation again supports the CI and Coarse Coding models, where left lateralized fine coding is responsible for literal analyses of sentences, while right lateralized coarse coding is responsible for metaphorical analyses. Overall, studies on figurative language suggest that inference is a bilateral process, where easier inferences based on associative processes are processed by left frontal regions, while more difficult, effortful processes occur in the right frontal regions.

Summary of Neuroimaging Data

Neuroimaging studies of discourse processing have shown evidence for networks of brain activation specific to different aspects of prose comprehension. Three patterns of activation can be summarized below:

1. Left temporal activation is observed for automatic, surface-level, linguistic processing in discourse such as syntax and propositions. It lays out a basic structure for subsequent text integration and inference.

2. Right temporal activation is observed for the automatic process of integration of meaning onto a text representation. It is a slower process that utilizes accumulated knowledge over time to yield deeper meaning about a text.
3. Bilateral frontal parietal and precuneus activation is observed for the effortful process of inference-making. Different types of inference-making seem to be lateralized; left frontal/parietal/precuneus regions tend to be involved in fine coding of closely associated semantic meaning, while the right homologous regions seem to use coarse coding to elaborate on broader, figurative semantic meaning.

Discourse Processing and Aging

Research has outlined a set of specific, bilateral areas in the brain that are activated during normal discourse processing. However, there has been speculation that these patterns of prose comprehension may not be consistent across all levels of difficulty and age. For example, it has been found that increased prose difficulty leads to more right hemispheric activation. This phenomenon, termed the *spillover effect*, has been the topic of much recent research in younger and older adults.

The Spillover Effect

Left to right hemispheric spillover is a normal, healthy process that occurs when semantic complexity increases. In a study that was previously discussed, Just et al. (1996) found that, as sentence difficulty increased, the right hemisphere homologues of Wernicke's and Broca's areas were significantly activated. Several other studies have confirmed this phenomenon. Xu et al. (2005) tested subjects' comprehension of words, unconnected sentences, and connected sentences that formed a narrative. Brain activation followed a very consistent pattern. Word comprehension was left lateralized to the middle temporal, inferior frontal, lateral premotor, and anterior supplementary motor areas. Sentence comprehension was still left lateralized to the lateral premotor, inferior frontal, and frontal pole regions. However, narrative comprehension led to bilateral activation of completely different areas such as precuneus, and medial prefrontal regions. Moreover, modulation of brain activity was found as subjects processed narratives; left hemisphere regions were activated first, and areas in the right hemisphere activated as the narrative progressed. This data indicates not only that the right hemisphere may be involved in higher level thinking, but also that as complexity increases, right hemisphere activation increases.

A study by Ferstl, Rinck, and von Cramon (2005) showed similar results. Subjects were given chronological or emotional stories that were made to be consistent or inconsistent upon changing a single word:

> Chronological:
>
> "Today, Markus and Claudia would finally meet again. Markus's train arrived at the station 20 minutes *after/before* Claudia's train…Many people were crowding on the platform. Claudia was already waiting for him when he got off the train with his huge bag." (*after* is consistent, *before* is inconsistent)
>
> Emotional:
>
> "…Sarah's best friend gave her a hug and told her how much fun she was having. Sarah couldn't remember that she had ever been so *happy/sad* before." (*happy* is consistent, *sad* is inconsistent)

In all inconsistent conditions, bilateral activation was found, particularly in the form of increased activation in right anterior frontal areas. Again, this suggests a left to right hemisphere spillover as text difficulty increases.

Reichle and Mason (2006) suggest a computational model to explain left to right spillover based on the limited capacity of working memory. Two assumptions are made in this theory. First, the probability of generating an inference is linearly related to perceived relatedness. Recall that the construction integration model of inference is also based on this idea, and that neuroimaging evidence supports it (Caplan & Dapretto, 2001; Mason & Just, 2004). Second, sentence and inference integration is dependent on some amount of working memory available to allocate to encoding. Given these assumptions, it would make sense that as left hemispheric working memory resources get depleted due to increased cognitive load, incoming information must be passed onto the right hemisphere for continued processing. Therefore, spillover may reflect a type of compensatory neural process utilized for disambiguation of difficult text.

Of note, this theory can also be used to explain the U-shaped relationship between memory and causal relationship found by Mason and Just (2004): distantly related sentences could be too difficult to understand and thus surpass the amount of working memory available to encode them into memory. Highly related sentences would be too easy to understand and, requiring little to no working memory storage at all. Thus, the concept of a limited working memory capacity seems plausible since it can be generalized to many situations.

Aging and Neural Compensation

If left to right hemispheric spillover is a normal cognitive process that exists to compensate for increased text complexity, it is likely that older adults require similar mechanisms to compensate for age-related declines in cognitive resources. Changes in the older adult brain have been theorized by some to be a result of these compensatory mechanisms. The Cognitive Reserve theory of aging (Stern, 2006) states that individual differences in how people cognitively engage in tasks can either lead to a susceptibility or protection to pathology. This theory is in contrast to theory of Brain Reserve Capacity, in which the brain is viewed as a passive construct that is limited by concrete factors such as brain size and synapse density. Once a threshold is reached, pathology arises. Cognitive Reserve, on the other hand, describes the brain as an active construct that copes with neurodegeneration in one of two ways: neural reserve is a preexisting, more efficient neural network; neural compensation is the development of alternate networks. Therefore, it is suggested that neural compensation is a common mechanism to cope with cognitive decline.

A similar theory proposed by Park and Reuter-Lorenz (2009) is known as the Scaffolding Theory of Aging and Cognition (STAC). STAC suggests that the brain is constantly in a dynamic process of learning known as scaffolding. Scaffolding can be a supplementary, complementary, or an altogether alternate method of achieving a cognitive goal. Therefore, many of the cognitive changes observed in older adults may simply be part of this scaffolding process.

Cognitive changes in older adults.

Several types of cognitive decline have been documented in older adults. Logan, Sanders, Snyder, Morris, and Buckner (2002) observed frontal activity of old and young adults on a memory encoding task and found that older adults engaged in two types of inappropriate recruitment. First, they underrecruited areas that were utilized by younger adults. This could either be explained by physical, irreversible atrophy, or ineffective recruitment strategies. Second, older adults nonselectively recruited areas not typically activated by younger adults. This nonselective recruitment was interpreted as a type of compensatory mechanism to overcome the inappropriate underrecruitment.

Another cognitive deficit often found in older adults is known as deactivation (Persson, Lustig, Nelson, & Reuter-Lorenz, 2007). Deactivation refers to the observation that, in normal adults, baseline brain activity decreases when a specific task must be done. Though this may seem counter-intuitive, this deactivation presumably occurs so all cognitive resources can be focused on the task at hand. Therefore, increased task difficulty should lead to increased deactivation. However, Persson et al. (2007) found that, during a verb generating task, older adults had fewer deactivations compared to younger adults. Moreover, when the deactivation did occur, it took much longer, which can be interpreted as a deficit of attention.

Noncompensatory overrecruitment in older adults.

Left to right hemispheric spillover has been suggested as a mechanism in younger, healthy adults to compensate for increased cognitive load due to semantic difficulty. Some studies suggest a mechanism similar to the concept of spillover for compensation in older adults. Unlike the healthy left to right spillover exhibited in younger adults, however, patterns of brain activation found in older adults are not effective, and thus result in a noncompensatory overrecruitment of brain areas.

Evidence for cognitive decline in prose comprehension in older adults supports this idea. Stine-Morrow, Soederberg Miller, Gagne, and Hertzog (2008) showed that different types of prose elicit different cognitive effects. Older and younger adults were presented with text that was either expository, narrative, or composed of single sentences. An immediate recall task showed that older adults could not recall expository text as well as younger adults; moreover, older adults showed different linguistic allocation of resources. It is very likely that this different resource allocation reflects a compensatory mechanism for cognitive decline. However, given the difficulties for memory of expository prose that are still observed in older adults, this mechanism seems to be ineffective. Therefore, in contrast to the normal process of spillover present in younger adults, older adults may utilize a noncompensatory overrecruitment of brain areas when not enough cognitive resources are available. More research should be done in this area to clarify the neural substrates of poor expository text recall in older adults.

Alzheimer's Disease and Attentional Dyscontrol

Like older adults, AD individuals exhibit very specific declines in prose comprehension that could benefit from discourse processing research as well. An Attentional Dyscontrol model has been proposed to explain problems with inhibition in AD individuals (Baddeley, Baddeley, Bucks, & Wilcock, 2001; Balota & Faust, 2001). Experiments on the Stroop task and the Deese, Roediger, and McDermott (DRM) paradigm have been suggested in support of this theory.

The well-known Stroop task measures the degree to which an individual can inhibit an automatic response of reading a color word that is printed in an incongruent ink color (for example, the word "RED" printed in green ink). Spieler, Balota, and Faust (1996) administered the Stroop task to healthy older adults and individuals with AD and found that AD adults showed a disproportionately large Stroop effect compared to healthy older adults. Interestingly, the prolonged reaction time for incongruent trials was approximately the same for AD individuals compared to healthy older adults, but AD individuals displayed significantly more intrusions. This indicates that the cognitive errors specific to AD are not driven by speed of processing, but rather by lack of inhibition.

The DRM paradigm involves inducing false memories for a word based on spreading activation of prime words to a target word. In the task, subjects are presented with a list of words (ex: thread, pin, eye, sewing, sharp, point, prick, thimble, haystack, pain, hurt, injection) that are highly related to a nonpresent target word (ex: needle). Upon free recall, the likelihood of recalling the target word is as large as recalling any other word (Roediger & McDermott, 1995).

Balota et al. (1999) found an age and dementia effect on performance on the DRM paradigm. Participants exhibited a steady decrease in overall veridical memory performance as age and dementia severity increased, accompanied with an age- and disease-specific increase in tendency for false memories – that is, healthy older adults were more susceptible to false memories than younger adults, and demented adults were even more susceptible to false memories compared to healthy older adults. The authors suggest that this is due to a breakdown in the attentional control system rather than a breakdown in the semantic network in AD. For example, the DRM paradigm requires one to discriminate between two sets of activated information: activated semantic association to a nonpresent target word, and activated encoding mechanisms for presented priming words. In a normal attention system, activation for the nonpresent target is inhibited to increase recall for the priming words. The disease-specific increase in false memory rate in AD individuals implies that, similar to the Stroop task, the mechanism for inhibition of automatically activated processes is disrupted in AD, while the actual spreading activation system itself remains relatively intact.

Other priming studies support this idea. For example, Ober, Dronkers, Koss, Delis, and Friedland (1986) found that, although AD individuals produce fewer correct responses and more errors than healthy older adults in verbal fluency tasks, there is no significant difference between the semantic relatedness of the responses produced between groups. However, there is a clear difference in the type of errors produced; increased AD severity was associated with an increased frequency of noncategory responses on a letter fluency task, and decreased access of categories in a semantic retrieval task. These findings suggest that deficits in language production in AD are not due to an inability to activate semantically relevant words, but rather an inability to maintain sustained attention on a task. A study by Balota & Duchek (1991) found similar results. The authors examined the response latency for pronunciation of a homophonic target word that was preceded by two prime words. There were four conditions: concordant (ex: music-organ-piano), discordant (ex: kidney-organ-piano), neutral (ex: ceiling-organ-piano), and unrelated (ex: kidney-ceiling-piano). It was found that healthy older adults had equally longer response latencies for the discordant and unrelated conditions compared to the concordant and neural conditions, indicating an ability to constrain the meaning of the target word effectively. However, AD adults responded faster to the discordant condition compared to the unrelated condition. This suggests retention in the ability to activate multiple meanings for an ambiguous homophone, but an inability to utilize the prime words as a context to constrain the meaning of the target word. Thus, it appears that priming effects that only utilize the spreading activation system is intact in healthy older adults, while priming tasks that involve attentional systems declines in adults with AD. AD individuals seem to be capable of making automatic semantic associations, but have more difficulty with attention-dependent inhibition.

A study by Johnson et al. (2003) further support a theory of attentional dyscontrol in AD. The Logical Memory subtest of the Wechsler Memory Scale was subject to propositional analysis according to Kintsch's (1998) CI model and then administered to young, healthy older, mildly demented, and demented adults. Results indicated that, when compared to young adults, healthy older adults showed deficits in delayed but not immediate recall. Demented adults, on the other hand, showed deficits in immediate recall compared to older adults. Interestingly, the CI model predicted recall equally well across all four participant groups such that more central propositions were associated with higher recall. This suggests that text comprehension and integration are not significantly affected by disease state. Furthermore, there was no evidence of a primacy effect such that propositions that occurred earlier in the prose led to better recall, suggesting that deficits due to AD are not equivalent to the difficulty-dependent (and perhaps age-specific) declines in working memory capacity (Reichle & Mason, 2007).

Attentional dyscontrol is consistent with cognitive theories of working memory. Baddeley (2000) proposes a new model of working memory in which an episodic buffer is added along with the classic visuospatial sketchpad and phonological loop. The episodic buffer is a limited, temporary memory store that is capable of integrating information from multiple sources across time, consistent with Tulving's (1985) definition of episodic memory. Thus, the role of the central executive is to modulate attentional control, consciously retrieving and modifying information from the episodic buffer when necessary. Therefore, deficits in AD can be conceptualized as disruptions in this control system rather than depletion in the episodic buffer's capacity. This is consistent with previously discussed priming studies that suggest that attentional inhibition, rather than semantic integration and activation, is disrupted in AD.

In summary, the implications of these studies on AD and attentional dyscontrol are two-fold. First, there is a clear difference in story recall between younger, healthy older, and demented adults. Second, the difference between healthy older adults and demented adults may primarily be due to deficits in the attentional control system rather than working memory.

Implications for discourse theory.

The clear evidence for cognitive deficits in AD, particularly those involving attentional control systems, may be highly relevant to prose comprehension. For example, if AD individuals have difficulty with attentional processes, they may have difficulties with inferences in narrative text, since inference of meaning requires effort and attention. Again, as with the predictions about prose comprehension in older adults, these hypotheses have not been confirmed by any studies yet. Investigating the relationship between AD and discourse processing could provide insight into the cognitive progression of the disease.

Current Study

Discourse processing can reveal several cognitive deficits in both older adults and individuals with AD, making it a potentially useful tool to study these populations. Evidence from neuroimaging research demonstrates that healthy older adults show bilateral patterns of activation in response to different aspects of a story. Left temporal activation corresponds to automatic syntactical, word, and proposition meaning; right temporal activation corresponds to automatic integration of meaning onto text; and bilateral frontal/parietal/precuneus activation corresponds to effortful inference-making processes. Moreover, brain activation is dependent on the difficulty of a task, such that increased cognitive load leads to a "spillover" of activation from the left to right hemisphere.

Given that aging leads to cognitive decline, it is likely that the older adult brain engages in some type of compensatory mechanism as well. Theories of aging have proposed that the brain is an actively changing system that can generate alternative mechanisms to failing cognitive processes. Since decreased recall for expository text is exhibited in older adults, it is proposed that an ineffective, noncompensatory overrecruitment may occur due to age-related cognitive decline.

Another population of interest is that of AD individuals, who have been shown to have cognitive deficits in episodic memory and attention. In relation to discourse processing, it is proposed that these dementia-specific deficits may manifest in terms of a decreased ability to generate effortful meaning from prose, due to deficits in the attentional control system.

Preliminary studies from this lab on text recall show that older adults have difficulty recalling expository prose compared to younger adults, while demented adults have difficulty recalling narrative prose compared to healthy older adults; that is, a clear age effect and dementia effect can be elicited from comprehension of text (Johnson & Wolfe, in preparation). When the CI and LSA models were applied, it was found the CI model predicted recall of narrative prose across all groups. However, YA recall of expository prose was best predicted by an LSA model while HOA recall was best predicted by a CI model. This may explain the advantage younger adults have in recall: since expository prose is primarily factual and less causal in nature, semantic associations between concepts may help encode information better than relying on text organization.

Given the fMRI evidence from healthy individual studies that show specific patterns of brain activation during prose comprehension, and preliminary evidence that different types of prose can be used to elicit the different cognitive processes by which story comprehension occurs across aging populations, we will investigate determinants of prose comprehension that elicit patterns of brain activation that differentiate young, healthy older, and demented adults. The current study is an extension of these preliminary findings and has two main hypotheses:

1. An age effect will be observed when participants read expository prose. Specifically, we expect increased left to right hemispheric activation, or noncompensatory overrecruitment, due to increased cognitive demand and older adults' ineffective allocation of resources.
2. A dementia effect will be observed when participants read narrative prose. Specifically, we expect decreased frontal/parietal/precuneus activation due to a decreased ability for AD individuals to recruit effortful, attention-demanding processes.

Method

Participants

All participants were right-handed, monolingual, native English-speaking adults. Older adult participants with (n=6) and without dementia (n=10) were recruited from the University of Kansas Alzheimer's Disease Center. The presence or absence and severity of dementia was obtained by a medical clinician trained in AD diagnostic issues using the Clinical Dementia Rating (CDR; Morris, 1993). Inclusion criteria for healthy older adults **(HOA)** consisted of cognitively intact subjects aged 60 and above, characterized by a CDR rating of 0. Inclusion criteria for demented older adults **(AD)** consisted of a CDR rating of 0.5, Very Mild AD. All healthy younger adult **(YA)** participants (n=10) were recruited through local area advertisements and met the same health exclusion criteria as older adult participants.

Design and Procedure

Two types of stories were presented: expository stories, which were didactic and factual in nature, and narrative stories, which involved a protagonist who underwent a sequence of events to fulfill a goal. All stories were adopted from a previous study examining differences between narrative and expository prose comprehension in healthy young adults (Wolfe, 2005). The protocol consisted of 18 sensical stories (9 expository, 9 narrative) and 6 nonsensical, scrambled (3 expository, 3 narrative) stories which lasted for a duration of 60 seconds. Each story was preceded by a 15 second baseline condition consisting of a Korean translation of identical story content. Each story was followed by a 15 second rehearsal condition in which subjects were instructed to recall the story they previously heard, thus producing further semantic elaboration and encoding. Stories were presented binaurally using scanner-safe, noise-attenuating headphones to minimize competing scanner noise.

Imaging and Analysis

Functional data was acquired on a head-only Siemens 3.0 Tesla Allegra MRI scanner as gradient echo blood oxygen level dependent (BOLD) scans in 45 contiguous axial slices (TR=3000ms, TE=30ms, flip angle=90˚, FOV=192mm, 64 x 64 matrix, slice thickness=3mm, in-plane resolution=3x3mm). Prior to functional imaging, high-resolution T1 weighted anatomical images were collected for anatomical localization, Talairach transformation, and coregistration of the functional images (magnetization-prepared rapid gradient echo [MPRAGE]; TR=2300ms, TE=3.05ms, TI= 1100ms flip angle=8˚, FOV=240mm, 267x185 matrix, slice thickness=1mm, in-plane resolution 1.3x0.9mm).

All data analysis was performed on SPM8 (Wellcome Department of Cognitive Neurology, London, UK) running under MATLAB r2010b (The MathWorks, Natick, MA, USA) on Windows XP. Anatomical and functional images were first manually reoriented along the anterior commissure and posterior commissure (AC-PC) line. Functional images were realigned to the first image of the run to account for subject motion. Anatomical and functional data were spatially normalized to a standard Montreal Neurological Institute (MNI) template using parameters generated under the unified segmentation procedure. Functional images were smoothed using a 6mm FWHM Gaussian filter. The experiment was modeled using a boxcar function of Korean Fixation and Sensical Story conditions convolved with a canonical hemodynamic response function. Individual participant motion parameters were entered into the model as regressors of no interest. All conditions required sustained vigilance to stimuli, therefore the contrast of condition effects is designed to capture activity specific to story comprehension. Contrasts of Story conditions (Sensical > Korean) were applied in a second level analysis using a 3x2 ANOVA with group (YA, HOA, AD) as a between-subjects independent variable and contrast (Expository vs. Korean, Narrative vs. Korean) as the within-subjects independent variable. Individual analyses were conducted as 2x2 ANOVAs. We compared HOA vs. YA and HOA vs. AD to test our hypothesis that specific age and dementia effects would be elicited from our paradigm. In SPM, these analyses are equivalent to conducting a second level random-effects analysis using a 1x3 (contrast x group) full factorial model.

A difficulty in neuroimaging of atrophied brains is the partial voluming problem, which occurs when loss of contrast between two adjacent tissue types leads to the presence of multiple tissue types in one voxel. Partial voluming causes further problems when smoothing is applied (which is commonly used in preprocessing to correct for intersubject variability), since non-gray voxels are coded as false positive "activations," leading to overestimation of activation (Momenan, Rawlings, Fong, Knutson, & Hommer, 2004). To ensure our clusters were localized to gray matter, gray matter probability maps were created (see Momenan et al., 2004 for details on calculation) for HOA and AD groups by averaging individual gray matter maps created in the unified segmentation process and creating binary group masks with a lower boundary of $p = .25$. These maps were used as inclusive masks in our second level analyses; any voxel that had a 25% or greater probability of being gray matter was included in analysis, while any voxel that had less than a 25% probability of being gray matter was not included in analysis. Thus, we accounted for the partial voluming problem by using a more conservative analysis. Anatomic localization was then determined using the computerized Talairach Client (Lancaster et al., 1997) within the Wake Forest University (WFU) Pickatlas (Maldjian, Laurienti, Kraft, & Burdette, 2003), and confirmed by visual inspection.

Results

Demographics

The older adult groups were similar in age (two-tailed *t*-test, $t = -1.05$, $p \leq .31$) but not in gender distribution. This is due to an incomplete sample size in our AD group. The 10 YA included 6 men and 4 women who ranged in age from 22 to 29 years ($M = 25.6$, $SD = 2.37$). The 10 HOA (CDR = 0) included 6 men and 4 women who ranged in age from 65 to 83 years (M=73, $SD = 5.46$). The 6 AD adults (CDR = 0.5) included 6 men and 0 women who ranged in age from 61 to 77 years ($M = 70.5$, $SD = 5.61$). All individuals identified their primary race as white, non-Hispanic (N = 26).

Imaging Results

We performed voxel-wise examination of gray matter volumes of all cohorts. To isolate activation during story comprehension, all contrasts involved comparison of stories to their Korean translations. The Korean translated stories provided baseline activation for audition of phonemes lacking semantic content. Examination of activation during Korean trials (significance level $p \leq .001$, cluster threshold k = 5 voxels) shows areas common to YA, HOA, and AD in bilateral superior temporal gyrus (Figure 1). Bilateral superior temporal gyrus is well supported in the literature as a region of primary auditory cortex active during binauaral presentation of word and non-word stimuli (Mazoyer et al., 1993; Caplan & Dapretto, 2001; Friederici, Meyer, & von Cramon, 2000; Binder et al., 2000; O'Leary et al., 1996; Jäncke, Shah, Posse, Grosse-Ryuken, & Müller-Gärtner, 1998, Dhankhar et al., 1997). YA additionally activated superior, medial, and inferior frontal areas (BA 9, BA 47, BA 6, BA 44; Figure 1), which could reflect an attempt to interpret the Korean phonemes. Other studies involving binaural auditory presentation of stimuli report similar frontal activation and interpret this activation as rehearsal, retrieval, or semantic association processes used when listening to unfamiliar speech sounds (Jäncke et al., 1998; Friederici et al., 2000; Binder et al., 2000). Taken together, this evidence suggests that the frontal activation we observed reflects YA tendency to retain information about Korean phonemes on-line or in working memory, while HOA and AD adults do not engage in this process. Thus, our *Story vs. Korean* contrasts resulted in activation, over and above audition of speech sounds, that was specific to comprehension of sensical stories.

Age effect *(HOA vs. YA)*.

Expository stories (vs Korean) were associated with activation in left precentral gyrus in sensorimotor cortex (BA 43, BA 3) and left posterior cingulate (BA 31) (Figure 2, Table 1), $p \leq .0005$ (uncorrected), k = 7 voxels. Narrative *stories (vs Korean)* were associated with activation in left inferior frontal gyrus (BA 47), right superior temporal gyrus (BA 38, 22), middle occipital gyrus (BA 18), left precentral gyrus (BA44), left superior temporal gyrus (BA 22), left superior frontal gyrus (BA6), left superior frontal gyrus (BA6), right superior frontal gyrus (BA 6), and right postcentral gyrus (BA43) (Table 1), $p \leq .005$ (uncorrected), k = 5.

Dementia effect *(HOA vs. AD)*.

Narrative stories (vs Korean) were associated with activation in right superior temporal lobe (BA 41) and right anterior cingulate cortex (BA 25) (Figure 3, Table 2), $p \leq .05$ (uncorrected), k = 5. *Expository stories (vs Korean)* were associated with activation in left parahippocampal gyrus (BA 35) (Table 2), $p \leq .0005$ (uncorrected), k = 7.

Discussion

In this study we examined age and AD specific deficits in comprehension of two types of prose, expository and narrative. Distinct deficits in control networks were apparent in both HOA and AD. Our results were compelling evidence that support our underlying hypotheses although our specific predictions of patterns of brain activation were not supported by the data. We predicted that an age effect would be seen for comprehension of expository prose as increased left to right hemispheric spillover, indicating nonselective overrecruitment in HOA. We predicted that a dementia (AD) effect would be seen for comprehension of narrative prose as decreased frontal/parietal/precuneus activation, indicating a decreased ability for AD adults to use effortful, attentional processes.

Age Effect

When compared to YA, HOA comprehension of expository stories elicited significant activation in left posterior cingulate (Figure 2), left motor cortex, and primary somatosensory cortex.

Posterior cingulate cortex (PCC).

Precuneus and PCC have been linked as a complex involved in comprehension and memory. There is evidence that precuneus-PCC are involved in an episodic memory retrieval process (see Cabeza 2008 or Wagner 2005 for a complete review of all theories). Activation in precuneus-PCC has been correlated to narrative (Xu et al., 2005) and metaphor (Bottini et al., 1994) comprehension, suggesting that these areas are recruited when greater levels of inference from long term memory is required. Other neuroimaging studies on episodic memory support the role of precuneus-PCC in this retrieval process; hearing and retrieving practiced stories activates more precuneus-PCC compared to novel stories (Andreasen et al. 1995; Maguire, Frith, & Morris, 1999), and resting state fMRI studies show similar activation in precuneus-PCC when subjects are asked to answer questions about a previously presented video (Sestieri, Corbetta, Romani, & Shulman, 2011). Other relevant literature shows activation in precuneus-PCC when subjects possess prior knowledge about confusing stories, compared to an absence of prior knowledge (Maguire et al., 1999). This suggests that precuneus-PCC is involved not only in the retrieval process, but also in the integration of information to form a comprehensive representation of prose. It has been proposed that precuneus-PCC may function as an "episodic buffer" (Baddeley, 2000) that temporarily stores retrieved information before it is incorporated on-line (Sestieri et al., 2011; Vilberg & Rugg, 2008). It should be noted that this is consistent with a construction-integration model of prose comprehension (Kintsch & van Dijk, 1978; Kintsch, 1998; Graesser et al., 1997) wherein incoming information from the text and long term memory are selectively and iteratively integrated into the textbase representation, until a stable representation is formed. It is possible that precuneus-PCC areas are involved in control and modulation of integrating long term episodic memories in this process.

Our data indicate that HOA are activating precuneus-PCC over and above what is observed in YA, which is consistent with our hypothesis that HOA may be using inefficient, and therefore noncompensatory, mechanisms in attempt to correct for cognitive decline. As previously discussed, Wolfe (2005) found that recall for expository prose was best predicted by degree of semantic association (LSA model), while recall for narratives was best predicted by text organization (CI model). However, Johnson and Wolfe (in prep) found that HOA recall of expository prose was best predicted by a semantic association model (LSA) rather than text organization. Since the CI model involves integration of long term memories into the textbase representation, the presence of precuneus-PCC activation in HOA supports the hypothesis that HOA may not be using the most efficient mechanism to comprehend expository prose. In a study on sentence comprehension in older adults with poor and good comprehension skills, researchers reported greater PCC activation in poor comprehenders for comprehension of grammatically simple sentences (Grossman et al., 2002). Deficits similar to the difficulties experienced by poor comprehenders could be present in aging, leading HOA to use alternate mechanisms which may not be efficient and ultimately do not improve performance. Thus, our results provide evidence for the role of precuneus-PCC areas in long term episodic memory retrieval and noncompensatory overrecruitment in older adults.

Sensorimotor areas.

Our results indicate significant activation in left postcentral gyrus areas corresponding to areas of sensorimotor cortex (see Figure A1 in appendix). A lateral, inferior area of sensorimotor corresponds to regions controlling the mouth. There is evidence that these specific mouth areas correspond to lip movement, nonvocal laryngeal tasks (Brown, Ngan, & Liotti, 2008) and swallowing (Sörös, Inamoto, & Martin, 2009), suggesting that our older adult participants may have been repeating the stories subvocally as they attempted to encode the stories for future recall. Another more medial, superior area of sensorimotor cortex corresponded to regions controlling the hand and arm. One ecological explanation is that our older adult participants were unable to remain still; it is possible that they were tapping their hands, either inadvertently or as a way to improve concentration on the task. Alternatively, some researchers propose that a somatotopic representation of action words exists in motor cortex, overlapping or adjacent to areas in sensorimotor cortex that correspond to actual movement of a body part involved in the action (Hauk, Johnsrude, & Pulvermüller, 2004; Raposo, Moss, Stamatakis, & Tyler, 2009; Tettamanti et al., 2005). Areas of activation in sensorimotor cortex similar to ours were found when subjects read or listened to action words and sentences involving arm movement (Hauk et al., 2004; Raposo et al., 2009). Therefore, it is possible that our older adult participants detected action words in the presented stories, leading to corresponding somatotopic activations in sensorimotor cortex. However, if these results are truly due to a link between language and the sensorimotor system, it is unclear why only HOA would exhibit greater somatotopic representation of action words compared to YA and AD adults. It is also unclear why HOA would ascribe more “action” content to expository stories compared to narratives; perhaps this could represent another form of compensation HOA engage in to improve story comprehension. Further studies should be done to confirm or expand on these results.

Dementia Effect

When compared to AD adults, HOA comprehension of narrative stories elicited significant activation in right superior temporal lobe and right anterior cingulate cortex (ACC) (Figure 3). In other words, AD adults underrecruited these areas.

Research on ACC suggests it has an evaluative role in cognitive control. Robust ACC activation has been associated with a number of tasks involving response override (such as Stroop, Eriksen flanker, and Simon tasks), undetermined responding (such as stem completion and verb generation tasks), and error detection (such as the error related negativity response in event-related potential (ERP) studies) (Botvinick, Cohen, & Carter, 2004). It is well-established that the Stroop task consistently elicits ACC activation (Kerns et al., 2004; Pardo, Pardo, Janer, & Raichle, 1990; Carter et al., 2000; Barch et al., 2001; Bush et al., 1998), which supports the role of ACC in executive control of attention. In an event-related fMRI study of the Stroop task, Kerns et al. (2004) found less ACC activity during incongruent trials preceded by incongruent trials (incongruent-incongruent), compared to incongruent trials preceded by a congruent trial (congruent-incongruent). Moreover, greater right prefrontal cortex activation was found for trials with more conflict (congruent-incongruent and incongruent-congruent). The authors interpret that ACC not only serves to monitor conflict but also to allocate control to higher level areas that strategically alter attention. Other studies report similar, concurrent activations in prefrontal areas during the Stroop task (Carter et al., 2000) and Eriksen flanker task (Durston et al., 2003). A common fronto-parietal-cingulate-thalamic network common to episodic retrieval and visual attention tasks (Cabeza et al., 2003) has been suggested, where ACC functions to allocate attentional resources during target detection.

One theory, known as the *conflict monitoring theory*, proposes that ACC functions at a broad level as a conflict monitor, signaling adjustments in top-down control areas to reduce conflict in overall performance (Botvinick et al., 2004). Our results suggest that ACC likely serves a role in language processing as well. Studies on discourse and episodic memory, though scant, have reported activation in ACC; Andreason (1995) found increased ACC activation during novel story recall compared to practiced story recall, and Partiot (1996) reported ACC activation when participants were asked to verify whether an event belonged to a particular category. Our data give further support for ACC involvement in discourse processing as we found that HOA recruited more ACC during narrative stories, and thus that AD adults underrecruited ACC areas. This is consistent with our hypothesis that AD involves attentional deficits: AD adults lack the attentional skills necessary to infer and integrate information about narratives, which leads to poorer comprehension and recall of narratives (Johnson and Wolfe, in prep).

However, in contrast to the conflict monitoring theory, we found no concurrent recruitment of areas such as prefrontal cortex, though we did find activations in right temporal lobe (RTL). Since RTL is a higher order processing system that has previously been associated with integration of broader semantic meaning, it is possible ACC modulated RTL activity in our task. It should be noted that RTL activity was also present in the HOA vs YA contrast, concurrent with prefrontal cortex activity. Given that overrecruitment of prefrontal areas has been previously reported as indication of nonselective, noncompensatory overrecruitment in older adults (Logan, Sanders, Snyder, Morris, & Buckner, 2002) and that left to right hemispheric spillover is proposed as another form of compensation, our results suggest that RTL may also be overrecruited in a process controlled by ACC. This gives further evidence that HOA engage in noncompensatory overrecruitment during story comprehension, though to a lesser extent when compared to AD adults than YA.

It is also possible that the lack of PFC activation was due to lack of task difficulty; perhaps listening to stories was not cognitively difficult enough and thus did not elicit higher attentional areas such as prefrontal cortex. We plan to conduct further analyses by comparing scrambled vs. sensical conditions to see if this task is sufficiently difficult to elicit prefrontal activation.

Future Directions

Though not directly related to our hypotheses, we also compared HOA with AD during expository story comprehension, and HOA with YA during narrative story comprehension. We found that HOA activated significantly in left parahippocampal gyrus more than AD adults, when listening to expository stories (see Figure A2 in appendix). This is consistent with literature on AD that reports hippocampal atrophy as a marker of the disease (de Leon, George, Stylopoulos, Smith, & Miller, 1989; Jack et al., 1999; Henneman et al., 2009; Csernansky et al., 2005; Thompson et al., 2007; Morra et al., 2009; Devanand et al., 2007; Stoub, Rogalski, Leurgans, Bennett, & deToledo-Morrell, 2010; Greicius, Srivastava, Reiss, & Menon, 2004).

We also found that HOA had significantly more activation than YA during narrative story comprehension in left inferior prefrontal, bilateral superior temporal, middle occipital gyrus, left precentral gyrus (Broca’s area), bilateral superior frontal, and right postcentral gyrus (see Figure A3 in appendix). These results are consistent with the nonselective overrecruitment we expect in HOA compared to younger adults. Further, the presence of right temporal activations in comparisons with both YA and AD adults for comprehension of narrative stories shows a consistent left to right hemispheric spillover that differentiates aging from the disease process.

We did not find any significant decrease in activation of prefrontal areas for AD adults' comprehension of narrative prose, contrary to our hypothesis. Rather, AD adults seemed to overrecruit prefrontal areas similarly to HOA, given that HOA overrecruited these regions compared to YA but not compared to AD adults. Our prose comprehension task seems to capture functional abilities in HOA and AD, but perhaps our narrative story condition lacks the difficulty that would require greater PFC activation over and above what HOA and AD are already using during passive listening of literal narratives, and thus is unable dissociate between the two groups. Future studies should focus on developing more difficult narratives that involve higher-level attentional and inference processes, or examining a more difficult task such as listening to scrambled stories. Another area for future work could involve replications of the sensorimotor activations we found in HOA comprehension of expository stories, to determine whether these findings are truly related to a somatotopic representation of action sentences or whether they are simply artifacts due to consistent hand movement across healthy older participants. Finally, further investigation on the involvement of hippocampus in expository story comprehension in AD adults is warranted, and could provide further insight into the disease process.

Conclusion

Neuroimaging of story comprehension reveals a distinct pattern of activation in the brain that corresponds to different aspects of the comprehension process in healthy young individuals. However, studies on HOA and AD adults suggest that there may be cognitive deficits specific to the aging and dementia process that may be seen as difficulties with episodic memory. In this study we used a story comprehension paradigm to differentiate YA, HOA, and adults with very mild AD.

PCC areas were activated when HOA read expository stories, indicating that they may be using an inefficient mechanism requiring inference from long term memory to comprehend expository stories. Though this mechanism is efficient for comprehension of narrative stories (CI model), expository stories are best understood by semantic relatedness of words and propositions (LSA model) (Johnson & Wolfe, in prep; Wolfe, 2005). This suggests that age-related cognitive decline is seen as use of noncompensatory overrecruitment of long term episodic memory retrieval areas.

RTL and ACC were underrecruited when AD adults read narrative stories, supporting our hypothesis that AD leads to deficits in the attentional system. ACC is proposed to modulate the amount of resources allocated to higher level attention systems. We interpret decreased ACC activation to mean that AD adults have deficits in their ability to evaluate situations and allocate resources to maximize comprehension. Though we did not find concurrent activation in PFC, a common area associated with activation of ACC, it is possible that the concurrent decrease in RTL activation reflected ACC's modulatory function by recruiting semantic integration areas, or simply that our task was not difficult enough to elicit highly attention-demanding processes.

These results support CI and LSA as psycholinguistic models that can be used to detect differences in HOA and AD at a cognitive level. Activations in RTL, PCC, and ACC reflect the multiple levels of integration inherent to the CI model: while traditional perisylvian language areas (RTL) are involved in integration of broad semantic meaning, extrasylvian areas (PCC, ACC) are involved in integration of long term memories and inferences; integration of all these components is necessary to form a coherent textbase representation. Our results also support that prose comprehension is highly dependent on text elements, and changes in how these elements are processed correspond to specific to age and disease related deficiencies. HOA reliance on an integrative approach to expository story comprehension reflects an inability to use more efficient mechanisms involving semantic association, while AD adults' inability to modulate attentional systems reflects an inability to integrate components of prose. By using CI and LSA as models we were able to interpret differences in the underlying cognitive processes for prose comprehension in YA, HOA, and AD adults. This provides additional support for story comprehension as a potential diagnostic tool for AD.

In summary, we have extended previous work in neuroimaging of psycholinguistics in YA to include HOA and AD adults. Given that our HOA and AD groups are well-characterized, our conclusions presumably reflect true differences between healthy aging and dementia pathology. Using a story comprehension paradigm, we were able to detect subtle cognitive differences between YA, HOA, and adults with very mild AD. This double dissociation of aging and disease state seems to involve 1) inefficient cognitive control mechanisms for long term memory retrieval in HOA 2) deficits in the attentional control system in AD.

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Table 1

Coordinates for significant activation clusters of gray matter for HOA vs. YA contrasts

		Peak MNI Coordinate			
Region	**k**	***x***	***Y***	***z***	***t***
Expository vs. Korean					
L. postcentral gyrus/BA 43	10	-54	-7	19	5.41[a]
L. postcentral gyrus/BA 3	8	-33	-25	49	4.61[a]
L. posterior cingulate/BA 31	9	-3	-37	28	4.48[a]
Narrative vs. Korean					
L. inferior frontal gyrus/BA 47	30	-45	23	-11	4.31[b]
R. superior temporal gyrus/BA 38	12	48	17	-14	4.25[b]
R. superior temporal gyrus/BA 22	with above	51	8	-5	3.33[b]
Middle occipital gyrus/BA 18	19	-27	-82	-11	3.76[b]
L. precentral gyrus/BA 44	5	-51	14	7	3.56[b]
L. superior temporal gyrus/BA 22	18	-6	2	70	3.48[b]
L. superior frontal gyrus/BA 6	with above	-3	17	61	3.35[b]
R. superior frontal gyrus/BA 6	9	3	14	64	3.42[b]
R. postcentral gyrus/BA 43	6	63	-10	16	3.37[b]

[a] significance level $p \leq .0005$ (uncorrected), cluster threshold k = 7 voxels
[b] significance level $p \leq .005$ (uncorrected), cluster threshold k = 5 voxels
Peak voxels associated with significantly activated clusters. Only peak voxels are listed. Region labels are derived from Talairach atlas within the Wake Forest PickAtlas and confirmed with visual inspection on average structural image. Nearest Brodmann's Area designation within 2 mm.

Table 2

Coordinates for significant activation clusters of gray matter for HOA vs. AD contrasts

		Peak MNI Coordinate			
Region	**k**	***x***	***Y***	***z***	***t***
Narrative vs. Korean					
R. superior temporal gyrus/BA 41	27	57	-22	13	2.37[a]
R. anterior cingulate/BA 25	9	3	17	-8	2.19[a]
Expository vs. Korean					
L. parahippocampal gyrus/BA 35	7	-21	-19	-14	4.65[b]

[a] significance level $p \leq .05$ (uncorrected), cluster threshold k = 5 voxels
[b] significance level $p \leq .0005$ (uncorrected), cluster threshold k = 7 voxels
Peak voxels associated with significantly activated clusters. Only peak voxels are listed. Region labels are derived from Talairach atlas within the Wake Forest PickAtlas and confirmed with visual inspection on average structural image. Nearest Brodmann's Area designation within 2mm.

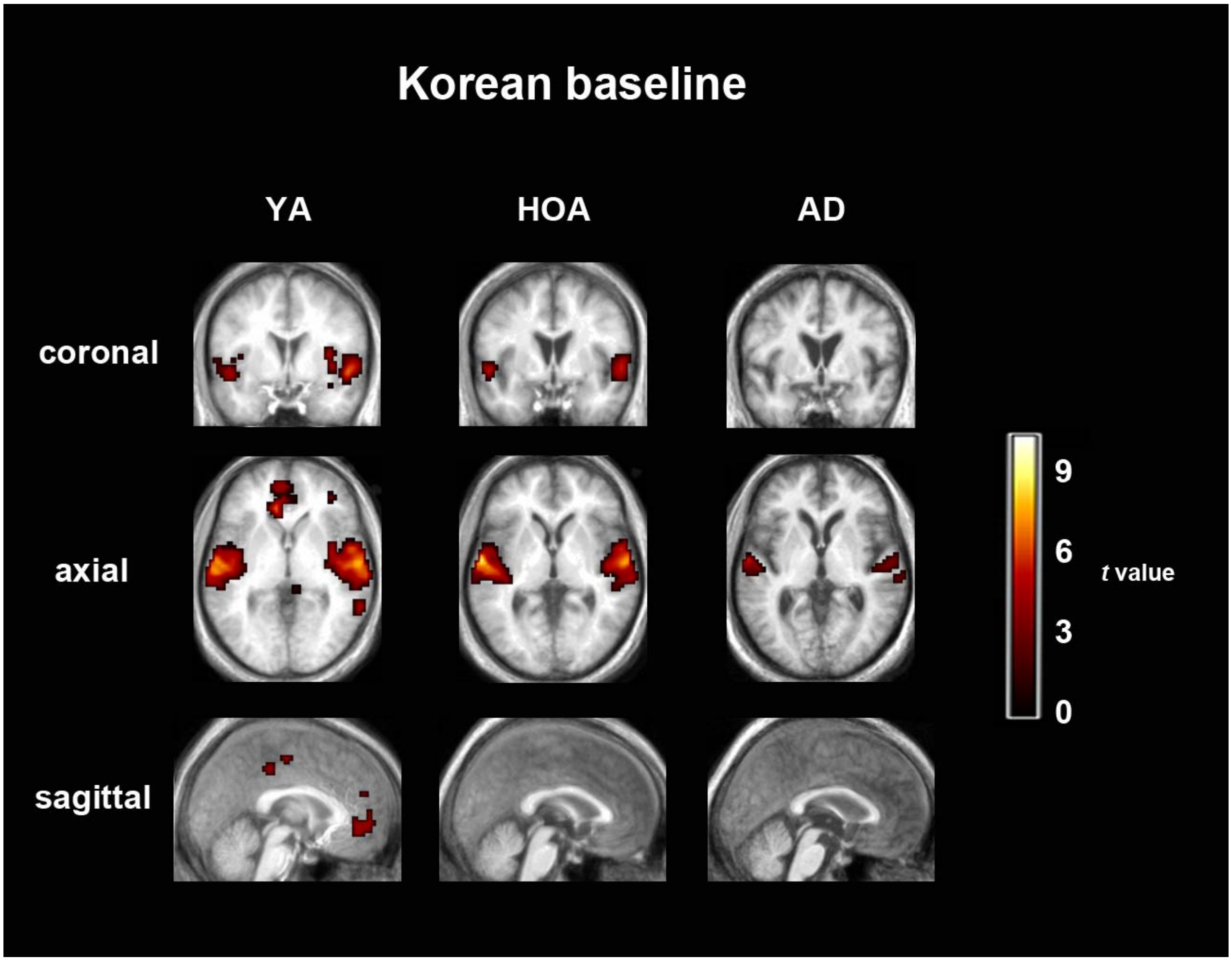

Figure 1. Statistical parametric maps (SPMs) of regions activated during Korean baseline task (*p* ≤ .001 (uncorrected), k = 5) in YA, HOA and AD adults. Thresholded images were transformed into MNI stereotaxic space and converted into *t*-scores, which were projected onto averaged T1-weighted anatomical images of subjects for each group. Images are displayed using neurological convention (left hemisphere is on left). The range of *t*-scores is indicated in the accompanying color table.

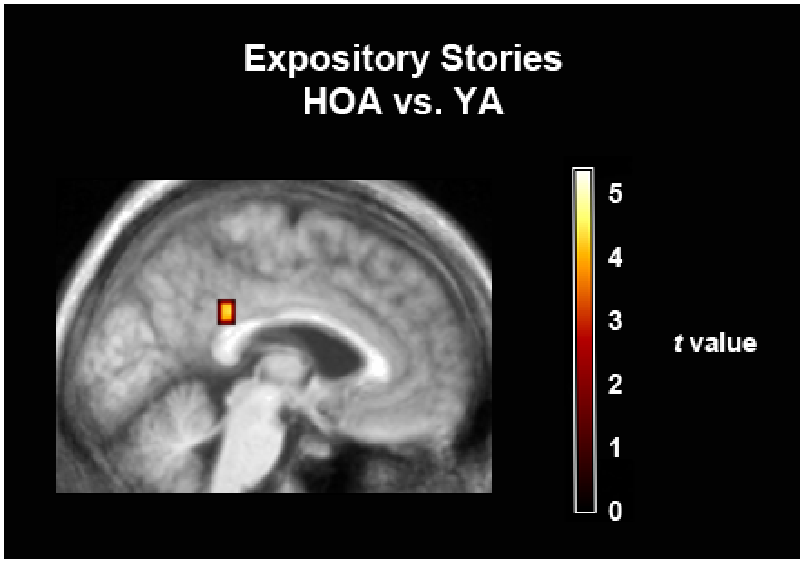

Figure 2. Left posterior cingulate cortex region activation in HOA compared to YA during comprehension of Expository stories, over and above Korean baseline activation ($p \leq .0005$ (uncorrected), $k = 7$). Statistical parametric maps were rendered as described in legend for Fig. 1 and projected onto an average T1-weighted anatomical image for HOA. Images are displayed using neurological convention (left hemisphere is on left). The range of *t*-scores is indicated in the accompanying color table.

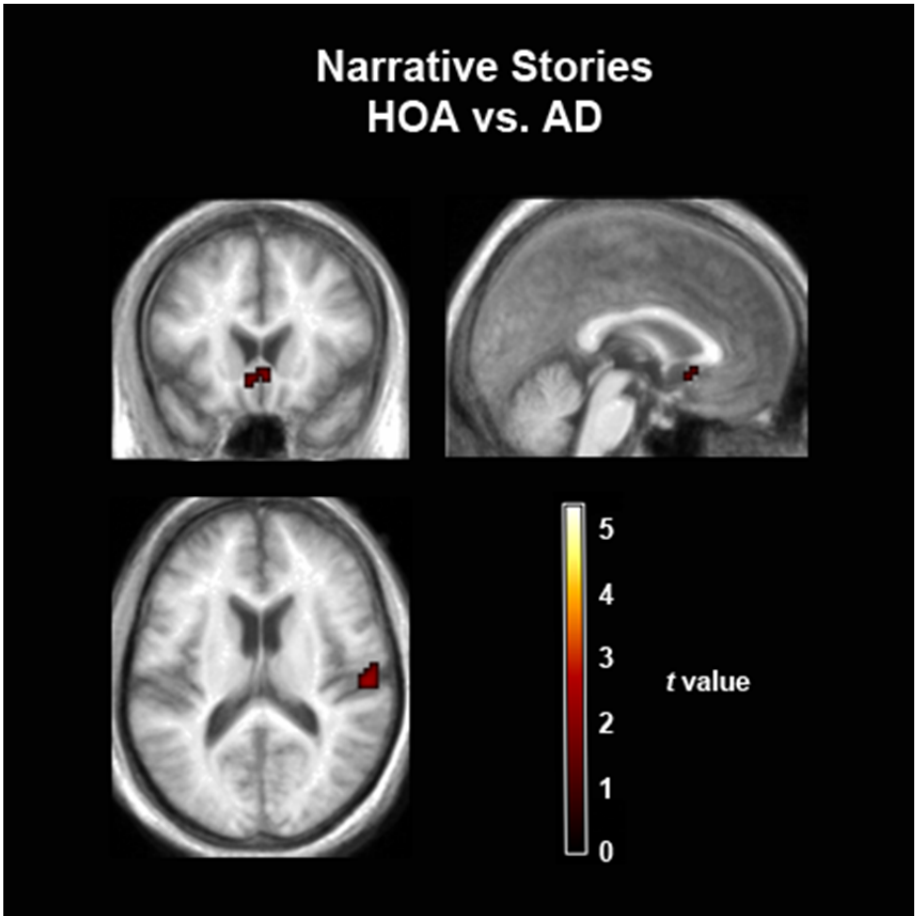

Figure 3. Right anterior cingulate cortex and right superior temporal lobe activation in HOA compared to AD adults during comprehension of Narrative stories, over and above Korean baseline activation (p ≤ .05 (uncorrected), k = 5). Statistical parametric maps were rendered as described in legend for Fig. 1 and projected onto an average T1-weighted anatomical image for HOA. Images are displayed using neurological convention (left hemisphere is on left). The range of *t*-scores is indicated in the accompanying color table.

Appendix
Ancillary Data to Support Future Directions

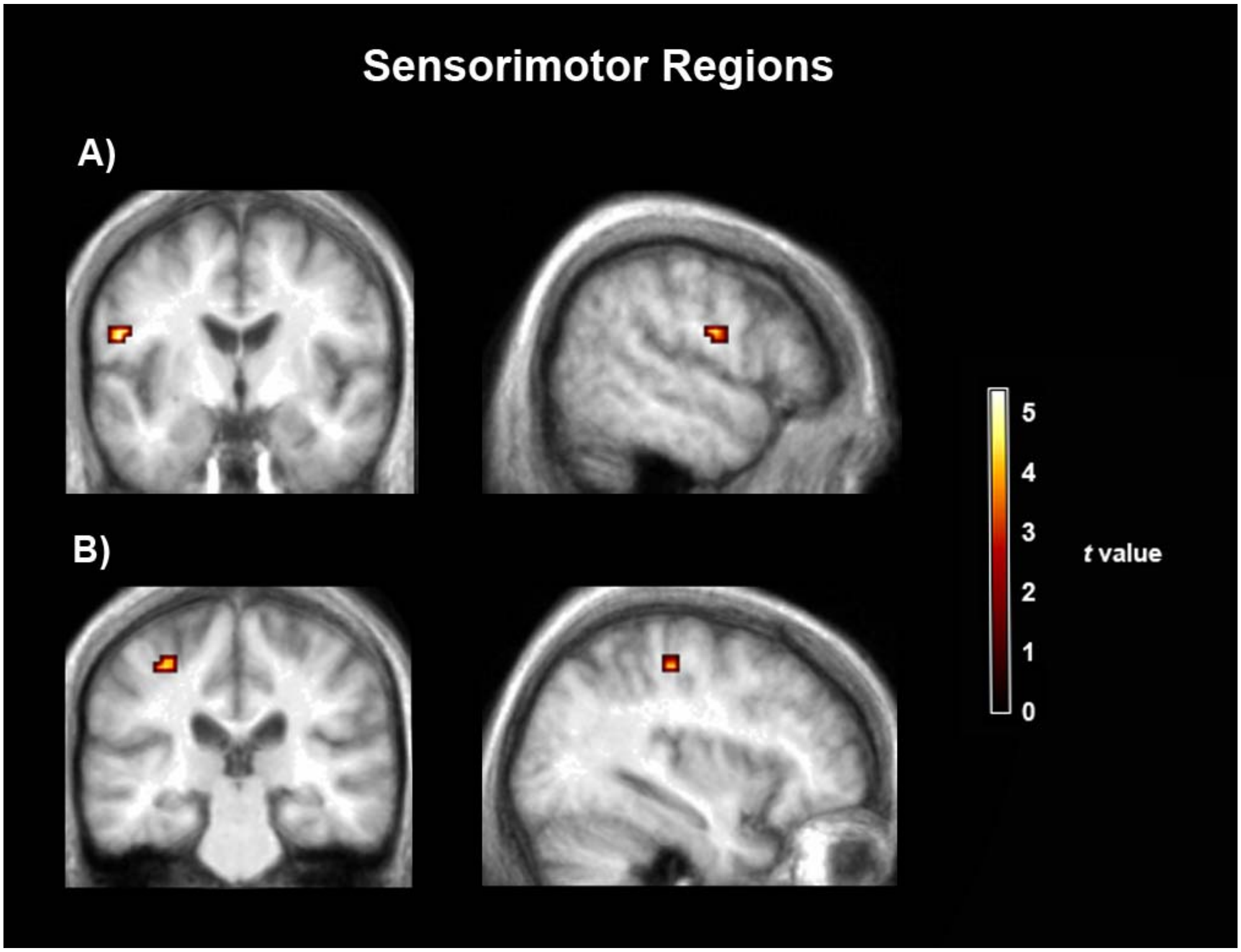

Figure A1. Sensorimotor cortex activations in HOA compared to YA for comprehension of Expository stories, over and above Korean baseline ($p \leq .0005$ (uncorrected), $k = 7$) in a) regions controlling the mouth b) regions controlling the hand/arm. Statistical parametric maps were rendered as described in legend for Fig. 1 and projected onto an average T1-weighted anatomical image for HOA. Images are displayed using neurological convention (left hemisphere is on left). The range of *t*-scores is indicated in the accompanying color table.

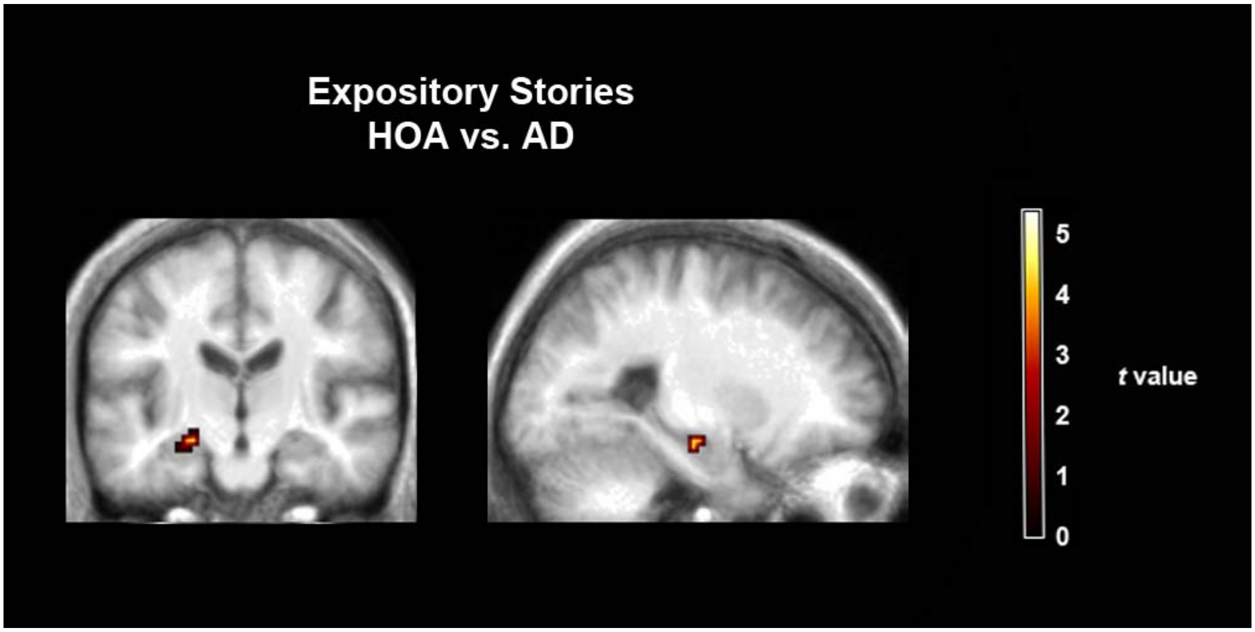

Figure A2. Left parahippocampal gyrus activation in HOA compared to AD adults during comprehension of Expository stories, over and above Korean baseline activation (p ≤ .0005 (uncorrected), k = 7). Statistical parametric maps were rendered as described in legend for Fig. 1 and projected onto an average T1-weighted anatomical image for HOA. Images are displayed using neurological convention (left hemisphere is on left). The range of *t*-scores is indicated in the accompanying color table.

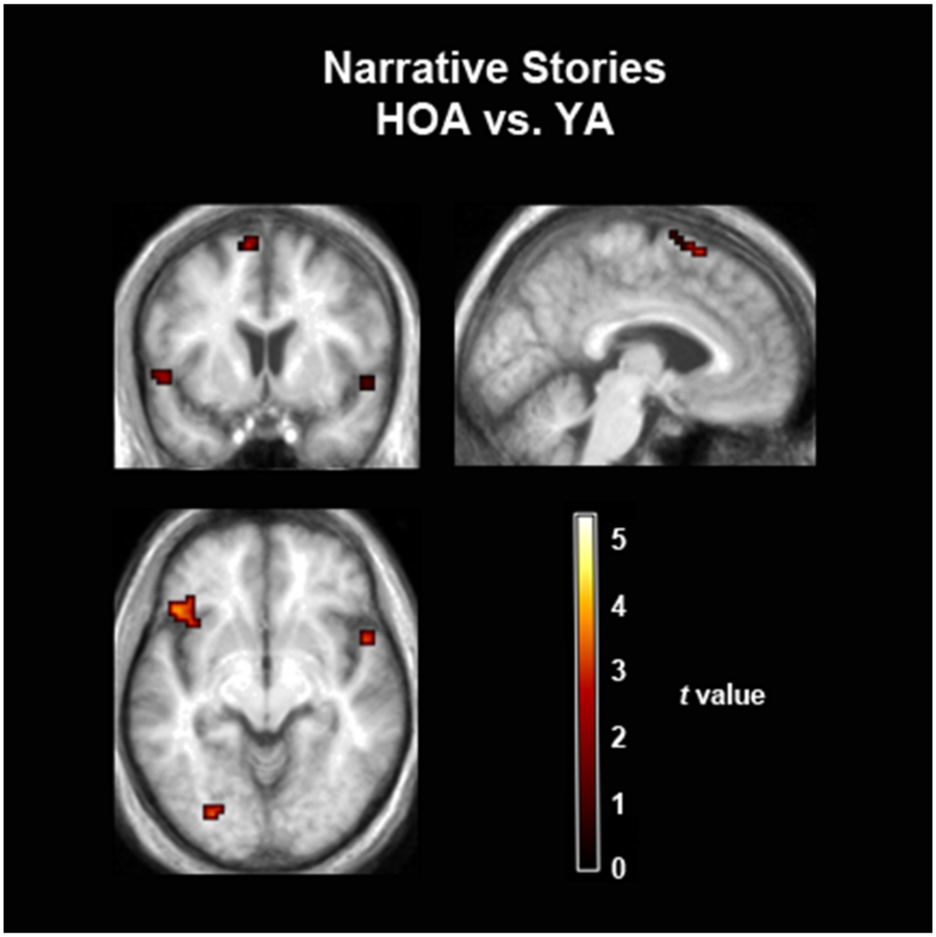

Figure A3. Regions activated in HOA compared to AD adults during comprehension of Narrative stories, over and above Korean baseline activation (p ≤ .005 (uncorrected), k = 5). Statistical parametric maps were rendered as described in legend for Fig. 1 and projected onto an average T1-weighted anatomical image for HOA. Images are displayed using neurological convention (left hemisphere is on left). The range of *t*-scores is indicated in the accompanying color table.