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ScienceDirect
Brain and Cognition 62 (2006) 250–260
Brain and Cognition
www.elsevier.com/locate/b&c

Quantifier comprehension in corticobasal degeneration ☆

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Accepted 23 June 2006
Available online 1 September 2006

Abstract

In this study, we investigated patients with focal neurodegenerative diseases to examine a formal linguistic distinction between classes of generalized quantifiers, like "some X" and "less than half of X." Our model of quantifier comprehension proposes that number knowledge is required to understand both first-order and higher-order quantifiers. The present results demonstrate that corticobasal degeneration (CBD) patients, who have number knowledge impairments but little evidence for a deficit understanding other aspects of language, are impaired in their comprehension of quantifiers relative to healthy seniors, Alzheimer's disease (AD) and frontotemporal dementia (FTD) patients [$F(3,77) = 4.98$; $p < .005$]. Moreover, our model attempts to honor a distinction in complexity between classes of quantifiers such that working memory is required to comprehend higher-order quantifiers. Our results support this distinction by demonstrating that FTD and AD patients, who have working memory limitations, have greater difficulty understanding higher-order quantifiers relative to first-order quantifiers [$F(1,77) = 124.29$; $p < .001$]. An important implication of these findings is that the meaning of generalized quantifiers appears to involve two dissociable components, number knowledge and working memory, which are supported by distinct brain regions.

Keywords: Number; Comprehension; Corticobasal degeneration; Frontotemporal dementia; Alzheimer's disease

1. Introduction

Quantifiers are noun phrases like "some pirates" and "less than half of the buccaneers" that are commonly used in daily language. The semantics of quantifiers are well-defined by linguists (Frege, 2000), yet little is known about their neural representation. Unlike traditionally studied semantic categories of objects like "animals" and "tools," quantifiers have very broad exposure and are quite frequent. In this study, we investigated quantifier comprehension in patients with focal neurodegenerative disease.

A quantifier can be defined as a noun phrase containing a determiner and a noun that functionally asserts some property from a set and assigns it a truth-value (Barwise & Cooper, 1981). Linguists and logicians have demonstrated that quantifiers and number knowledge are systematically related (Barwise & Cooper, 1981; Keenan & Stavi, 1986; van Benthem, 1986). This relationship exists for quantifiers containing a numeric determiner and those with a logical determiner. On the one hand, there are *first-order quantifiers* like those in (1):

1a. At least three treasures
1b. Some pirates

Comprehending phrases containing a numerical determiner, like "at least three" in 1a, requires the assertion that the states of "one treasure," "two treasures," and "three treasures" are TRUE before the phrase "at least three treasures" can be assigned a TRUE value. Likewise, the comprehension of phrases with logical determiners like "some pirates drink rum" requires the objects "pirates" and

☆ This work was supported in part by the US Public Health Service (NS44266, AG15116, and AG17586). Corey McMillan is now at PPLS, University of Edinburgh.
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doi:10.1016/j.bandc.2006.06.005

"rum-drinkers" specified by the noun phrases to be queried, and for at least one instance satisfying the intersection of these objects to be assigned a TRUE value. From a formal linguistic approach, van Benthem (1986) has demonstrated that a simple computing device—a finite-state automaton—can be used to simulate first-order quantifiers based on knowledge of numeric states. For example, logical determiners like "some" can be reinterpreted as "at least one." Our model of first-order quantifier comprehension, based on the work of linguists and logicians, thus posits that determining the numerical content of a set is fundamental to understanding quantifiers. Given the linguistic relation of number processing and quantifiers, the core theoretical focus of this paper is to establish neuropsychological evidence of the relationship between numbers and quantifier comprehension.

Preliminary support for this model comes from a recent fMRI study investigating quantifier comprehension in healthy adults (McMillan, Clark, Moore, DeVita, & Grossman, 2005). This study demonstrated right inferior parietal cortex recruitment during comprehension of first-order quantifiers. Inferior parietal cortex is also recruited in fMRI studies by healthy adults while performing simple number processing tasks (Burbaud, Degreze, Lafon, & Franconi, 1996; Cohen, Dehaene, Chochon, Lehericy, & Naccache, 2001; Kazui, Kitagaki, & Mori, 2000; Le Clec'H et al., 2000; Pinel, Dehaene, Riviere, & Le Bihan, 2001; Rueckert et al., 1996; Simon, Mangin, Cohen, Le Bihan, & Dehaene, 2002; Stanescu-Cosson et al., 2000). Given the overlapping inferior parietal activation in both the quantifier study and neuroimaging investigations of number processing, these findings can be taken as preliminary support for the involvement of number knowledge in first-order quantifier comprehension.

The present study seeks to provide additional evidence for this relation between number knowledge and quantifier meaning by studying patients with focal neurodegenerative diseases. In particular, we examine quantifier comprehension in patients with corticobasal degeneration (CBD) who have impaired number comprehension but little evidence for lexical comprehension difficulty. CBD typically presents with clinical features such as apraxia, cortical sensory loss, and naming difficulty (Grimes, Lang, & Bergeron, 1999; Litvan et al., 1997; Murray et al., (submitted for publication)). Neuroimaging studies (Brooks, 2000; Grisoli, Fetoni, Savoiardo, Girotti, & Bruzzone, 1995; Grossman et al., 2004; Halpern et al., 2004b; Savoiardo, Grisoli, & Girotti, 2000) and pathological observations (Murray et al., (submitted for publication)) associate these clinical features with disease involving at least parietal cortex. While acalculia is mentioned in the initial description of CBD (Rebeiz, Kolodny, & Richardson, 1968), number processing deficits have been demonstrated only recently (Halpern et al., 2003, 2004a, 2004b). Evidence that this impairment in CBD is specific for numbers rather than a non-specific semantic memory deficit comes from a double dissociation of number difficulty in CBD relative to a deficit on a measure requiring object knowledge in patients with semantic dementia who have disease centered in the ventral temporal lobe (Cappelletti, Butterworth, & Kopelman, 2001; Halpern et al., 2004b). If our hypothesis associating quantifiers with number knowledge is correct, we would expect difficulty understanding quantifiers in CBD despite otherwise preserved lexical comprehension.

This paper also seeks to investigate the nature of the number knowledge impairment during quantifier comprehension in CBD. In the previously reported fMRI study of quantifier comprehension, McMillan et al., 2005 observed right-lateralized cortical activation. This suggests the contribution of non-verbal number concepts to quantifier comprehension. However, Dehaene's (1997) 'triple-code" model of number posits two number processing systems: There is a non-verbal analog representational system for number meaning that represents approximate amounts, and a precise number system that depends on linguistic representations in order to distinguish between very similar amounts such as "5" and "6." Evidence to support this account comes from a meta-analysis showing inferior parietal activation of the left hemisphere during the performance of tasks requiring precise number, but intraparietal sulcus activation during tasks assessing approximate number knowledge (Dehaene, Piazza, Pinel, & Cohen, 2003). To assess the Dehaene model of number knowledge in CBD, we constructed our materials so that we could examine limitations of verbally mediated precise number compared to a deficit that depends on approximate number in the quantifier comprehension impairments of CBD.

We also consider a second class of quantifiers. In addition to first-order quantifiers like those in (1), there are also *higher-order quantifiers*, as exemplified in (2):

2a. More than half of the buccaneers
2b. Even number of parrots

These quantifiers depend in part on number knowledge, like first-order quantifiers, but they also involve comparing the relative size of sets. For example, to assign a truth-value to the sentence "More than half of the buccaneers get seasick," the number of buccaneers who get seasick must be identified, this amount must be maintained in working memory while the number equivalent to half of all buccaneers is determined, and then the two values must be compared. The determiner in 2b is different from the one in 2a, but it also involves a comparison. For example, the number of parrots in the set must be queried, stored, and then compared with the set of all even real numbers. While all of the quantifiers in (1) and (2) require determining the numerical content of a set, higher-order quantifiers like those in (2) additionally depend in part on comparative judgments using working memory in a way that the quantifiers in (1) do not. From a formal linguistic perspective, the additional computational resources needed for higher-order quantifiers can not be computed using the simple computational device based on knowledge of number states that is adequate for simulating first-order quantifiers (van Benthem, 1986). Instead, a more complex computing device is needed that is equipped with a working memory mechanism—a pushdown automaton.

Another goal of this paper is to provide neuropsychological evidence for the hypothesized differences between first-order and higher-order quantifier comprehension. Specifically, we aim to demonstrate that the differences in the formal computational machinery needed to simulate different classes of quantifiers would also be reflected in the performance of patients with different distributions of disease. Our model of higher-order quantifier comprehension thus requires a working memory component to maintain the numerical content of a target subset in an active mental state, and the capacity to compare this with a reference number such as half of the entire set or an even number.

Neuroimaging investigations of healthy adults indicate that inferior frontal cortex and adjacent dorsolateral prefrontal cortex are recruited during performance of working memory tasks (Cohen et al., 1997; Smith & Jonides, 1999). Preliminary evidence consistent with a role for working memory during higher-order quantifier comprehension comes from the neuroimaging investigation showing inferior frontal and dorsolateral prefrontal activation, in addition to inferior parietal activation, during the comprehension of higher-order quantifiers (McMillan et al., 2005).

We can obtain converging evidence to support our model by investigating higher-order quantifier comprehension in patients that have working memory limitations. Thus, we examined quantifier comprehension in patients with frontotemporal dementia (FTD). These patients have disease that often includes the dorsolateral and inferior portions of frontal cortex (Forman et al., 2006; Grossman et al., 2004; Rosen et al., 2005). These areas are associated with working memory limitations in FTD (Jagust, Reed, Seab, Kramer, & Budinger, 1989; Kramer, Jurik, & Sha, 2003; Libon et al., (submitted for publication); Pachana, Boone, Miller, Cummings, & Berman, 1996). An fMRI activation study shows limited frontal activation during performance of a working memory measure in FTD (Rombouts et al., 2003). FTD patients have difficulty understanding sentences with a working memory component, and this deficit is associated with limited inferior frontal activation in an fMRI study of FTD (Cooke et al., 2003). Brain disease in these cortical regions has not been reported to affect number knowledge per se, although resource-demanding calculations involving multiple computational steps such as division are compromised in FTD (Halpern et al., 2003). Based on the computational complexity and working memory demands associated with higher-order quantifiers, we hypothesized that FTD patients would have difficulty with higher-order quantifier comprehension. However, FTD patients were expected to demonstrate only a modest impairment for first-order quantifiers since these terms are thought to depend less on working memory.

We also investigated quantifier comprehension in patients with Alzheimer's disease (AD). These patients have limitations in multiple cognitive domains, including both number calculations (Halpern et al., 2003) and working memory (Baddeley, Bressi, Della Sella, Logie, & Spinnler, 1991). Neuropathologic studies (Arnold, Hyman, Flory, Damasio, & van Hoesen, 1991) and neuroimaging investigations (Grossman et al., 2004) suggest that disease in AD involves parietal and frontal cortex. Based on these findings, we predicted that AD patients would share some features of quantifier comprehension difficulty seen in CBD and FTD. Specifically, we predicted that patients with AD would have difficulty understanding higher-order quantifiers relative to first-order quantifiers due to their working memory limitations, but they might also have some difficulty with first-order quantifiers.

2. Methods

2.1. Subjects

Sixteen CBD patients, 23 FTD patients, 25 AD patients, and 17 age- and education-matched healthy controls participated in the experiment. The patients were mildly to moderately demented, according to the Mini-Mental State Exam (MMSE) (Folstein, Folstein, & McHugh, 1975), and patient groups were matched in their dementia severity. Demographic information and MMSE score means are provided in Table 1. All subjects were right-handed native speakers of English, except for one AD patient who had been a fluent English speaker throughout adulthood, but whose native language was Dutch. Due to the task demands of discriminating between colored objects, all participants were screened for color-blindness. None of the subjects were taking sedating medications at the time of testing, although most individ-

Table 1
Mean (standard deviation) of participant group demographic and clinical features

	Corticobasal degeneration	Frontotemporal dementia	Alzheimer's disease	Healthy seniors
N	16	23	25	17
Age (years)	66.3 (7.7)	69.8 (8.3)	73.2 (8.3)	71.9 (7.0)
Education (years)	14.6 (2.8)	14.8 (2.5)	13.9 (2.4)	16.6 (2.1)
MMSE (max = 30)	20.23 (7.25)	23.37 (5.07)	22.5 (4.12)	—
Dot magnitude comparison (% correct)	61.17 (29.21)	93.12 (9.06)	98.30 (9.06)	—
Reverse digit span (sequence completed correctly)	3.19 (1.11)	1.83 (1.15)	2.04 (1.24)	—
Sentence comprehension (max = 12)	7.93 (1.83)	8.86 (2.5)	8.48 (2.66)	—

uals were taking acetylcholinesterase inhibitors and several individuals were taking a mild anti-depressant or an atypical neuroleptic agent (quetiapine). All subjects were volunteers participating in accordance with an informed consent procedure approved by the University of Pennsylvania Institutional Review Board.

CBD patients were given a clinical diagnosis based on reports in the literature, including our autopsy series (Forman et al., 2002, 2006; Grimes et al., 1999; Litvan et al., 1997; Murray et al., (submitted for publication); Rinne, Lee, Thompson, & Marsden, 1994). These patients had a progressive neurodegenerative syndrome that included apraxia, cortical sensory loss, naming difficulty, and/or evidence for an extrapyramidal disorder (e.g., myoclonus, gait difficulty, rigidity) without a resting tremor. One CBD patient had been excluded from the analysis due to a very low MMSE score.

The diagnosis of AD was based on NINCDS-ADRDA criteria (McKhann et al., 1984). This included a progressive anterograde memory deficit early in the disease process, associated with naming and language difficulty, visual impairment, and/or an executive deficit.

FTD patients were diagnosed according to published criteria (McKhann et al., 2001; Brun, Englund, Gustafson, Neary, & Snowden, 1994). This included progressive aphasia, executive difficulty, and/or a disorder of behavior and social comportment, but proportionately less severe anterograde memory difficulty.

We excluded patients with other causes of dementia such as vascular disease or hydrocephalus, psychiatric disorders such as primary depression or psychosis, medical illnesses or metabolic conditions that may have resulted in encephalopathy, infectious diseases that may have resulted in progressive intellectual decline, and/or other medical conditions that may have an impact on cognitive performance.

2.2. Materials

Subjects were presented with 120 grammatically simple written propositions containing a quantifier (e.g. “some of the cars are red”) that probed a color feature of a familiar object (e.g. balls, flowers, cars, dresses, dinosaurs) in a visual stimulus array. Twenty instances of six different quantifiers were each presented by computer in randomly-ordered trials: half were first-order (all X, some X, at least 3X) and half were higher-order (less than half X, odd number of X, even number of X). The quantifiers selected for this experiment not only allow us to make class distinctions between first-order and higher-order quantifiers, but also distinctions about determiners within each class of quantifiers. For example, within the first-order quantifiers “at least 3X” contains a numeric determiner and “some X” contains a logical determiner. Likewise, for the higher-order quantifiers, “less than half X” is hypothesized to require the identification of “half” within the set while “even number of X” requires a parity comparison of the known set of all even real numbers. The objects in an array were randomly distributed on the computer screen, and the target color property mentioned in the stimulus sentence was randomly distributed over these objects. All of the stimuli were designed to be unambiguously TRUE or FALSE (e.g. for an 8-object array and a stimulus sentence containing “less than half of X,” we never presented an array composed of exactly half of the target objects).

Each trial involved two consecutive events. In the first event, the subject was presented with a proposition for 2500 ms; in the second event, the subject was presented with the proposition and a stimulus array for as long as it took to make a decision. Subjects were asked to decide if the proposition accurately described the stimulus array. They responded by pushing a green colored key on the keyboard if the proposition was true and a red colored key if the proposition was false. Half of each type of item was true and half false. Debriefing following the experiment revealed that none of the participants was aware that the stimulus arrays consisted of eight objects.

The variety of quantifiers allowed the number of target items in the array to be manipulated in order to test various models of number knowledge. First, we examined the role of verbal mediation (precise vs. approximate). A precise judgment thus was required when the number of target items was as close as possible to the criterion for validating or falsifying the proposition (e.g. 3 of 8 objects in the stimulus array displayed the target color mentioned in the proposition “less than half”), while an approximate judgment was when the number of criterial stimuli was far from the threshold criterion (e.g. 1 of 8 objects displayed the target color mentioned in the proposition “less than half”). This is based on the hypothesis that the distinction between adjacent cardinalities on a mental number line (e.g. “5” vs “6”) requires verbal mediation, while cardinalities that are more distant from each other can be estimated without the need for verbal mediation (Dehaene, 1997). Second, we assessed magnitude estimation (small vs. large target arrays). Smaller sets of objects may be enumerated in a manner that involves subitizing (e.g. enumerating a small group of objects using a process such as deconstructing the arrays of objects into a familiar visuospatial pattern), while larger arrays of objects require counting (Mandler & Shebo, 1982; Peterson & Simon, 2000). Therefore, we also manipulated the cardinality of the target arrays in the quantifier stimuli, including either a smaller (<4) number of target items or a larger (>4) number of target items. The criterion of smaller and larger target arrays for this experimental manipulation was based on research suggesting numbers less than four are subitized and numbers greater than four are counted (Mandler & Shebo, 1982).

All stimuli were counterbalanced and pseudo-randomly distributed throughout the experiment, and equally divided into four runs. A Macintosh G3 computer was used to run PsyScope 1.2.5 presentation software (Cohen, MacWhinney, Flatt, & Provost, 1993) in order to present the stimuli and record behavioral accuracy and latency. In this paper, we only report measurements of accuracy.

We administered three additional measures:

2.2.1. Dot magnitude comparison

Since the motivation of this paper is to evaluate the relative contribution of number knowledge in quantifier comprehension, we also assessed basic numeric abilities. We presented patients with 36 pairs of boxes containing arrays of 1 cm diameter filled black circles or "dots." Each array consisted of a set of 1 to 9 dots, where the pairs of arrays differed by a smaller or larger number of dots (Halpern et al., 2004b). Patients were asked which dot array of each pair contained a greater number of dots. We report percent accuracy in correctly identifying the larger array.

2.2.2. Reverse digit span

Since we were interested in assessing the role of working memory in higher-order quantifier comprehension, we administered a task requiring working memory. Reverse digit span (Wechsler, 1987) requires patients to report a sequence of digits in a sequence reversing the order of presentation. We report the longest sequence that is correctly reversed.

2.2.3. Sentence comprehension

Given the linguistic nature of the quantifier judgment task, we assessed sentence comprehension in the patients to rule out that any observed quantifier comprehension impairments could be due to an overall language comprehension deficit. Patients were presented with 12 semantically unconstrained sentences containing a transitive verb and a center-embedded clause. Each sentence was presented twice orally and then followed by a simple probe question. We report the total number of probe questions correctly answered.

3. Results

We found that quantifier comprehension is most impaired in CBD, and these patients showed unique difficulty understanding first-order quantifiers. A mixed-model analysis of variance (ANOVA) assessed quantifier comprehension with Group as a between-subjects factor and Quantifier Class as a repeated measures within-subject factor. We observed a main effect for Group [$F(1,3) = 11.45$; $p < .001$]. As summarized in Fig. 1, all patient groups performed worse than healthy seniors on overall quantifier comprehension. Moreover, CBD patients (72% correct) were significantly worse than FTD [83% correct; $t(37) = 2.61$; $p < .05$] and AD [82% correct; $t(39) = 2.89$; $p < .01$], emphasizing the distinct comprehension deficit for quantifiers in CBD. Our analysis also yielded a significant main effect for Quantifier Class [$F(1,77) = 124.29$; $p < .001$], whereby all groups are more impaired on higher-order quantifier comprehension than first-order quantifier comprehension. Most importantly

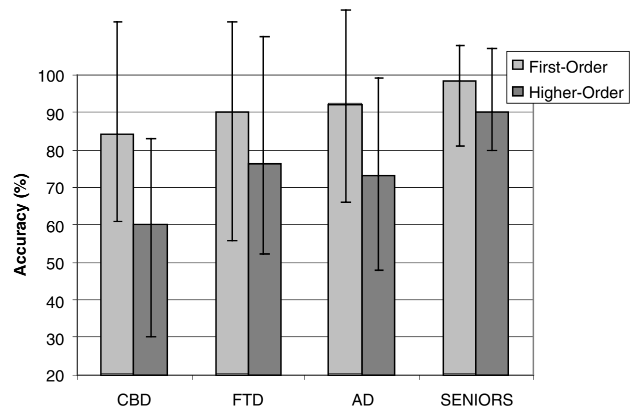

Fig. 1. Mean (standard deviation) accuracy for first-order and higher-order quantifier comprehension in corticobasal degeneration, frontotemporal dementia, Alzheimer's disease, and healthy seniors. *Note.* CBD, corticobasal degeneration; FTD, frontotemporal dementia; AD, Alzheimer's disease.

we observed a significant interaction effect of Group X Quantifier Class [$F(3,77) = 4.98$; $p < .005$]. This was due to the relative deficit of CBD patients for first-order quantifiers, where CBD patients were significantly more impaired than AD patients [$t(39) = 2.54$; $p < .05$]. For higher-order quantifiers, CBD patients were more impaired than both AD [$t(39) = 2.53$; $p < .05$] and FTD [$t(37) = 2.78$; $p < .01$] patients.

This analysis confirmed our hypothesis that CBD patients are significantly impaired in their comprehension of quantifiers, and that their understanding of first-order quantifiers is particularly impaired. In an effort to demonstrate that this impairment is due to number knowledge limitations in CBD patients, we also assessed number knowledge in all the patients groups using a dot magnitude comparison task. Table 1 shows that CBD patients are significantly more impaired on the dot magnitude comparison task than FTD patients [$t(22) = 3.48$; $p < .005$] and AD patients [$t(22) = 4.18$; $p < .001$]. Moreover, dot magnitude comparison is correlated with first-order quantifier comprehension in CBD ($r = .53$, $p < .05$). This is consistent with the hypothesized role of number knowledge in quantifier comprehension.

We also found in our primary analysis that all groups are more impaired on higher-order quantifier than first-order quantifier comprehension, hypothesized to be due to working memory requirements during comprehension of higher-order quantifiers. To further assess the relative contributions of working memory in quantifier comprehension we evaluated reverse digit span scores. Table 1 shows that CBD patients were less impaired than FTD patients [$t(3.68)$; $p < .001$] and AD patients [$t(39) = 3.00$; $p < .005$]. A correlation of reverse digit span with quantifier comprehension revealed that reverse digit span correlates with higher-order quantifier comprehension for all patient groups (CBD, $r = .64$, $p < .01$; AD, $r = .63$, $p < .001$; FTD, $r = .47$, $p < .05$), but there was no correlation with first-order quantifier comprehension.

We also assessed the role of language comprehension abilities using sentence comprehension. As summarized in Table 1, there was no difference between patient groups for sentence comprehension accuracy. This finding of no difference between groups on a test of language comprehension suggests that our findings of selective quantifier comprehension impairments are a result of the hypothesized role of number knowledge and working memory and not a language comprehension impairment. There was no correlation between quantifier comprehension and sentence comprehension accuracy.

In order to test the nature of number knowledge in quantifier comprehension in greater detail, we examined subsets of quantifiers and stimulus arrays. To explore whether a precise, verbally mediated sense of number or an approximate, non-verbal sense of number is differentially compromised in CBD patients' poor quantifier comprehension, we assessed performance on the subset of trials in which the quantity of target items either allowed an approximate judgment (48 items) or required a precise judgment (48 items). Items for this analysis were collapsed across quantifier class. We excluded judgments of stimuli containing "all X" and "some X" from the analysis since these quantifiers do not support the "precise" and "approximate" criteria. A mixed-model ANOVA, with Patient Group as a between-subjects factor and Judgment Type (precise/approximate) as a repeated-measures within-subject factor, revealed a significant main effect for Group [$F(1,3) = 8.86$; $p < .001$]. As summarized in Table 2, all patient groups performed worse than healthy seniors (at least $p < .005$; according to t-tests), and CBD patients were more impaired than both AD patients [$t(39) = 2.88$; $p < .01$] and FTD patients [$t(37) = 2.12$; $p < .05$]. We did not observe a significant main effect for Judgment Type [$F(1,77) < 1.00$; ns] or a Group X Judgment Type interaction effect [$F(3,77) < 1.00$; ns]. While CBD patients are more impaired than other patients groups and healthy controls, these results suggest quantifier comprehension is not differentially related to a verbally mediated sense of precise number.

Table 2
Mean percent accuracy for analyses investigating the nature of number knowledge during quantifier comprehension

Patient Group	CBD	FTD	AD	SEN
Analysis				
Judgment Type				
Approximate	67.0	79.4	81.6	92.9
Precise	65.7	81.3	82.0	92.7
Array magnitude				
Small	59.6	76.4	75.2	90.2
Large	55.8	75.7	70.5	90.0
Determiner				
"At least 3X"	84.5	93.3	93.4	97.8
"All X" + "Some X"	83.4	88.9	90.4	96.8

Note. CBD, corticobasal degeneration; FTD, frontotemporal dementia; AD, Alzheimer's disease; SEN, healthy senior controls.

We also assessed the role of object set magnitude by analyzing trials with higher-order quantifiers containing a small number of target items (36 arrays with 1–3 target items) compared to a large number of target items (36 arrays containing 5–8). Items with a first-order quantifier were excluded from this analysis to minimize several potential confounds. For example, splitting items into small and large for "at least 3" also corresponds to the truth-value of the proposition, since small items are FALSE and large items are TRUE. The stimulus items containing "all" and "some" were excluded since some object arrays contain zero target items. We found a significant main effect for Group [$F(1,3) = 11.73$; $p < .001$]. As summarized in Table 2, patient groups were less accurate than healthy seniors (at least $p < .005$; according to t-tests), and CBD patients were more impaired than AD patients [$t(39) = 2.55$; $p < .05$] and FTD patients [$t(37) = 2.88$; $p < .01$]. However, the analysis did not reveal a significant main effect for Size [$F(1,77) = 3.57$; ns] or a Group X Size interaction effect [$F(3,77) = 1.15$; ns]. We therefore did not find evidence that the size of the object set influences the quantifier comprehension deficit in CBD.

To examine whether CBD patients are impaired only because of the presence of a number in the quantifier phrase we also tested for a difference between first-order quantifiers that contain a numeric determiner (24 items containing "at least 3") and therefore an explicit number, or a logical determiner (48 items containing "all" or "some") which does not include an explicit number. We excluded higher-order quantifiers from this evaluation because of the confound of numeric determiners with quantifier order. This analysis revealed a significant main effect for Group [$F(1,3) = 6.85$; $p < .001$]. As summarized in Table 2, all patient groups were worse than healthy seniors (at least $p < .01$; according to t-tests), and CBD patients were more impaired on quantifier comprehension than AD patients [$t(39) = 2.27$; $p < .05$]. This analysis also revealed a main effect for the Presence/Absence of an explicit number [$F(1,77) = 4.27$; $p < .05$], in which quantifier comprehension was better in propositions that contain a logical determiner without an explicit number. However, we did not find a significant interaction effect for a Group × Presence/Absence of a number. Thus, we did not find evidence that the absence or presence of an explicit number in the quantifier probe differentially influences quantifier comprehension in CBD.

4. Discussion

Previous research suggests that CBD patients have impaired number processing with minimal evidence for lexical comprehension difficulty (Halpern et al., 2003, 2004a, 2004b). We sought to determine whether this deficit in numbers also contributes to a deficit understanding quantifiers. The major finding of the current study is that non-aphasic patients with CBD are significantly impaired in their comprehension of quantifiers. This is demonstrated by their poor overall quantifier comprehension relative to FTD, AD, and healthy seniors, and their impairment for first-order quantifiers relative to AD. Evidence consistent with the hypothesized role of number knowledge in quantifier comprehension comes from the number processing deficit in CBD patients, despite little verbal comprehension impairment. We also found impaired quantifier comprehension in FTD, AD and CBD patients for higher-order quantifiers. FTD and AD patients have working memory limitations, but do not have the number impairments seen in CBD. This constellation of observations is consistent with the claim that the quantifier comprehension deficit in FTD and AD is due in part to difficulty with the working memory component of higher-order quantifiers. Taken together, these findings suggest that two components contribute to quantifier comprehension: number knowledge and working memory. We discuss in turn below the comprehension of first-order quantifiers and higher-order quantifiers in each group of patients.

4.1. Poor comprehension of quantifiers in CBD

Performance on a variety of number tasks has shown a significant impairment in many individual CBD patients, including magnitude comparisons of pairs of single-digit Arabic numerals or small dot arrays, simple addition of two Arabic numerals or two small arrays of dots, and simple calculations involving subtraction, multiplication, and division (Halpern et al., 2003, 2004a, 2004b). Difficulty on tasks requiring number knowledge was dissociated from performance on a task requiring object knowledge (Halpern et al., 2004b). It is in this context that we found a deficit for understanding first-order quantifiers like "Some cars are red" in CBD. Indeed, these patients were significantly more impaired than patients with AD at understanding first-order quantifiers.

Converging evidence for the association of quantifier comprehension with number knowledge comes from an examination of the anatomic distribution of disease in CBD. These patients have cortical atrophy most prominently in parietal cortex (Brooks, 2000; Grisoli et al., 1995; Grossman et al., 2004; Halpern et al., 2004b; Savoiardo et al., 2000). Parietal cortex has been shown to contribute to number knowledge on a variety of calculation and number comparison tasks in healthy young adults (Burbaud et al., 1996; Cohen et al., 2001; Kazui et al., 2000; Le Le Clec'H et al., 2000; Pinel et al., 2001; Rueckert et al., 1996; Simon et al., 2002; Stanescu-Cosson et al., 2000).

Perhaps the strongest evidence comes from an fMRI study demonstrating right inferior parietal activation during the comprehension of both first-order and higher-order quantifiers identical to those used in the present study (McMillan et al., 2005). Moreover, a structural MRI analysis has demonstrated that right parietal cortex is significantly compromised in CBD, and that atrophy in this region contributes to difficulty with number knowledge, including magnitude comparison and simple addition (Halpern et al., 2004b). Taken together, these findings are consistent with our hypothesis that quantifier comprehension depends at least in part on a numerosity component, and that the deficit understanding quantifiers in CBD is due in part to their difficulty with number knowledge.

We performed several analyses to help determine whether a particular model of number representation is compromised in CBD. For example, Dehaene (1997) hypothesizes a non-verbal analog representational system for number meaning that represents approximate amounts, and a precise number system that depends on a linguistic representation that is necessary to distinguish between very similar amounts such as "5" and "6." Some evidence has been cited to support this account. For example, a meta-analysis has shown that peri-Sylvian language regions in the left hemisphere are activated by healthy subjects during the performance of tasks requiring precise number (Dehaene et al., 2003). However, one should keep in mind that the angular gyrus is not typically considered part of the core left hemisphere language system (Gelman & Butterworth, 2005), and that the angular gyrus is often activated bilaterally on measures of precise number knowledge (Stanescu-Cosson et al., 2000) Moreover, patients with profound aphasia are not that impaired on measures requiring calculation and precise number (Cappelletti et al., 2001; Halpern et al., 2004b; Varley, Klessinger, Romanowski, & Siegal, 2005). Previous assessments of CBD show that number knowledge difficulty is not due to a language impairment or a deficit for object knowledge (Halpern et al., 2004b; Halpern et al., 2004a). The distinction between an analog number system and the verbally mediated representation of precise number is said to be more evident for larger numbers (Dehaene, 1997), so we also examined judgments where the target set was relatively small (less than 4) or larger (greater than 4). This also corresponds to the distinction between cardinalities in the range of subitizing compared to counting (Mandler & Shebo, 1982; Peterson & Simon, 2000). Again, we found no difference in CBD patients' performance as a function of target set size. Regardless of the nature of the number representations that contribute to quantifier comprehension, our observations are consistent with the important contribution of a degraded sense of number to impaired quantifier comprehension in CBD.

Other possible accounts for CBD patients' impairment with quantifier comprehension seem less likely. There are reports of visuospatial difficulty in CBD (Graham, Zeman, Young, Patterson, & Hodges, 1999; Soliveri, Monza, & Paridi, 1999), but this does not appear to explain fully their performance on measures of number knowledge. For example, in a dot counting study, CBD patients were equally impaired on this task when counting systematically arranged dots or randomly placed dots (Halpern et al., 2003). Manipulation of the spatial properties of dots—such as changing their spatial extent—did not impact magnitude judgments or addition of dots (Halpern et al., 2004a).

We also do not think that an impairment understanding quantifiers in CBD can be attributed to an aphasia. Some reports describe aphasia in CBD (Graham, Bak, Patterson, & Hodges, 2003; Ikeda, Akiyama, & Iritani, 1996; Riley et al., 1990), although a detailed assessment of semantic memory in 25 CBD patients found a mild deficit in only 8% of these individuals (Grossman et al., (submitted for publication)). The CBD participants in the present study were not aphasic relative to the FTD and AD participants. Several case studies have dissociated number knowledge and aphasia (Cappelletti et al., 2001; Rossor, Warrington, & Cipolotti, 1995; Thioux et al., 1998; Varley et al., 2005; Warrington, 1982), making it less likely that aphasia can account for our findings.

4.2. Impaired comprehension of quantifiers in FTD and AD

Another finding of this investigation is the impairment of higher-order quantifier comprehension. Executive resources such as working memory appear to contribute to higher-order quantifier comprehension. Both AD patients and FTD patients were significantly less accurate for higher-order quantifier relative to first-order quantifier comprehension. Since patients with FTD and AD have working memory limitations (Cherry, Buckwalter, & Henderson, 1996; Mendez et al., 1996; Morris, 1994; Pachana et al., 1996; Razani, Boone, Miller, Lee, & Sherman, 2001), it is possible that their higher-order quantifier deficit is associated with difficulty maintaining number properties in mind during the comparisons required for higher-order comprehension. Converging evidence for the role of working memory in the comprehension of higher-order quantifiers in FTD and AD comes from neuroanatomic studies showing frontal cortex disease in these patients (Arnold et al., 1991; Forman et al., 2006; Grossman et al., 2004; Rosen et al., 2005). These areas have been shown to contribute to working memory in functional neuroimaging studies of healthy adults (Braver et al., 1997; Garavan, Ross, Li, & Stein, 2000; Smith et al., 2001; Sylvester et al., 2003) and in patients with focal insult involving frontal cortex (Muller, Machado, & Knight, 2002; Thompson-Schill et al., 1999). The idea that working memory contributes to the comprehension of higher-order quantifiers receives additional support from a neuroimaging investigation that demonstrated inferior frontal and dorsolateral prefrontal cortex activation during comprehension of higher-order quantifiers in healthy adults (McMillan et al., 2005). On the other hand, we find that FTD and AD patients have relatively modest difficulty with number knowledge in the range of the single digits probed for these quantifiers (Halpern et al., 2003). Perhaps this is sufficient to account for the deficit with first-order quantifiers in these patients, although they are less impaired than CBD patients with first-order quantifiers. Difficulty understanding higher-order quantifiers in FTD and AD nevertheless is consistent with the hypothesized role of working memory in the comprehension of these quantifiers.

CBD patients were impaired for higher-order quantifiers as well. The fact that they had greater difficulty with higher-order quantifiers than their own performance with first-order quantifiers suggests that an additional component beyond number knowledge may be contributing to their deficit. It is possible that this impairment with higher-order quantifiers is related to the resource demands associated with the overwhelming difficulty of judging these stimuli for these patients. Alternately, CBD patients may have compromised frontal lobe functioning, based on histopathologic studies examining the neuroanatomic distribution of disease (Forman et al., 2002; Murray et al., (submitted for publication)). Additional work is needed to determine the basis for difficulty with higher-order quantifiers in CBD.

Two working memory components appear to contribute to higher-order quantifier comprehension: (a) the process of maintaining one number quantity in an active mental state while identifying another number quantity; and (b) the process of comparing these numbers in order to evaluate the truth-value of the proposition. In the present investigation, it is not possible to determine whether one or both components of working memory are impaired during higher-order quantifier comprehension in these patients. Both components depend on cortical areas affected by disease in FTD, AD, and possibly CBD. Some fMRI studies have attempted to dissociate the neuroanatomic basis for these components. For example, working memory appears to be associated more closely with inferior frontal cortex independent of task difficulty (Barch, Braver, Nystrom, Forman, & Cohen, 1997; Braver et al., 1997), while the switching component required for the comparative process may be associated more closely with dorsolateral prefrontal cortex (MacDonald, Cohen, Stenger, & Carter, 2000; Sylvester et al., 2003). Other work is not as consistent with a dissociation between resource components such as these, suggesting that a single executive mechanism underlying both components that recruits both frontal regions in proportion to task difficulty (Prabhakaran, Narayanan, Zhao, & Gabrieli, 2000). Additional work is needed to resolve this issue.

It is less likely that difficulty with higher-order quantifier comprehension in FTD and AD can be accounted for by impairments in other cognitive domains. Both AD and FTD patient groups may have language comprehension difficulty (Cummings, Benson, Hill, & Read, 1985; Grossman et al., 1996; Hodges & Patterson, 1996), for example, but these impairments do not account for the selective difficulty in the comprehension of higher-order quantifiers relative to first-order quantifiers. There are no spatial properties of the arrays that can serve as a basis for greater difficulty with higher-order quantifiers compared to first-order quantifiers. Beyond the computational complexity of the class of quantifiers, both propositions have the same linguistic properties. Specifically, propositions and stimulus arrays were counterbalanced to repeat all of the linguistics material (e.g. "balls are red"), except the experimental manipulation of the determiner in each quantifier condition.

Healthy seniors also showed greater difficulty with higher-order quantifiers compared to their own performance with first-order quantifiers, although their difficulty was not as great as in patients with FTD or AD. The age-associated impairment with higher-order quantifiers may be related to the working memory limitations often seen in healthy aging (Myerson, Emery, White, & Hale, 2003; Salthouse, 1994), a change associated with limited frontal activation during fMRI studies of performance on working memory tasks (Rypma & D'Esposito, 2000; Smith et al., 2001).

5. Conclusion

In this study, we investigated patients with focal neurodegenerative diseases to examine a formal linguistic distinction between classes of quantifiers. Our model proposes that number knowledge is required to understand both first-order and higher-order quantifiers. The present results demonstrate that CBD patients, who have number knowledge impairments but little evidence for a deficit understanding other aspects of language, are impaired in their comprehension of quantifiers. Quantifiers appear to be reliably impaired in CBD because of the dependence of quantifier meaning on number knowledge, and the deficit for numbers in CBD. Moreover, our model attempts to honor a distinction in complexity between classes of quantifiers such that working memory is required to comprehend higher-order quantifiers. Our results also support this distinction by demonstrating that FTD and AD patients, who have working memory limitations, have greater difficulty understanding higher-order quantifiers relative to first-order quantifiers. An important entailment of these findings is that the meaning of certain words like quantifiers involves two dissociable components. Moreover, this semantic structure appears to be honored by the distinct brain regions that apparently underlie these components. The findings of the present study, together with the fMRI study using the same materials (McMillan et al., 2005), suggests a neural architecture for semantic memory that appears to depend in part on the functional integrity of a large-scale neural network involving both of these components.

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