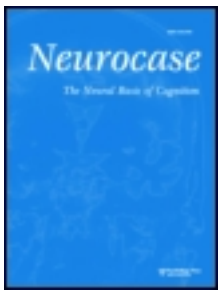

Neurocase: The Neural Basis of Cognition
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/nncs20

Sign language aphasia from a neurodegenerative disease

Adam D. Falchook [a b], Rachel I. Mayberry [c], Howard Poizner [d], David Brandon Burtis [a b], Leilani Doty [a] & Kenneth M. Heilman [a b]

[a] Cognitive and Memory Disorder Clinics, Department of Neurology and Center for Neuropsychological Studies, University of Florida, Gainesville, FL, USA

[b] Malcom Randall Veterans Affairs Medical Center, Gainesville, FL, USA

[c] Department of Linguistics, University of California, San Diego, CA, USA

[d] Institute for Neural Computation La Jolla, California, United States and Department of Cognitive Science and Program in Neurosciences, University of California, San Diego, CA, USA

Version of record first published: 24 Jul 2012.

To cite this article: Adam D. Falchook , Rachel I. Mayberry , Howard Poizner , David Brandon Burtis , Leilani Doty & Kenneth M. Heilman (2012): Sign language aphasia from a neurodegenerative disease, Neurocase: The Neural Basis of Cognition, DOI:10.1080/13554794.2012.690427

To link to this article: http://dx.doi.org/10.1080/13554794.2012.690427

NEUROCASE
2012, i*First*, 1–11

Psychology Press
Taylor & Francis Group

Sign language aphasia from a neurodegenerative disease

Adam D. Falchook[1,2], Rachel I. Mayberry[3], Howard Poizner[4], David Brandon Burtis[1,2], Leilani Doty[1], and Kenneth M. Heilman[1,2]

[1]Cognitive and Memory Disorder Clinics, Department of Neurology and Center for Neuropsychological Studies, University of Florida, Gainesville, FL, USA
[2]Malcom Randall Veterans Affairs Medical Center, Gainesville, FL, USA
[3]Department of Linguistics, University of California, San Diego, CA, USA
[4]Institute for Neural Computation La Jolla, California, United States and Department of Cognitive Science and Program in Neurosciences, University of California, San Diego, CA, USA

While Alois Alzheimer recognized the effects of the disease he described on speech and language in his original description of the disease in 1907, the effects of Alzheimer's disease (AD) on language in deaf signers has not previously been reported. We evaluated a 55-year-old right-handed congenitally deaf woman with a 2-year history of progressive memory loss and a deterioration of her ability to communicate in American Sign Language, which she learned at the age of eight. Examination revealed that she had impaired episodic memory as well as marked impairments in the production and comprehension of fingerspelling and grammatically complex sentences. She also had signs of anomia as well as an ideomotor apraxia and visual-spatial dysfunction. This report illustrates the challenges in evaluation of a patient for the presence of degenerative dementia when the person is deaf from birth, uses sign language, and has a late age of primary language acquisition. Although our patient could neither speak nor hear, in many respects her cognitive disorders mirror those of patients with AD who had normally learned to speak.

Keywords: Sign language aphasia; Alzheimer's disease; Verbal memory; Age of acquisition; Neurolinguistics.

In American Sign Language (ASL), thoughts are expressed by movements of the hands in space (and sometimes accompanied by movements of the face, head, or trunk) and comprehended by the visual, temporal, and spatial analysis of movements and postures. Although the precise neural pathways responsible for all the stages of sign language processing are currently not well understood, and visual-spatial analysis is required in sign language, it is the left hemisphere that is essential for comprehension of both signed and spoken language (Damasio, Bellugi, Damasio, Poizner, & Van Gilder, 1986; Hickok, Love-Geffen, & Klima, 2002; Poizner, Klima, & Bellugi, 1987). As reported by Poizner, Kaplan, Bellugi, and Padden (1984), the pattern of visual-spatial deficiencies in deaf signers

Address correspondence to Adam D. Falchook, MD, Department of Neurology, University of Florida, College of Medicine, McKnight Brain Institute (L3-100), 100 South Newell Drive, P.O. Box 100236, Gainesville, FL 32610-0236, USA. (E-mail: Adam.Falchook@neurology.ufl.edu).

Partial support for this clinical and research activity is from the Florida Department of Elder Affairs, Alzheimer's Disease Initiative program. Dr Heilman receives research funding from the Department of Veterans Affairs Office of Research and Development. Dr Poizner receives research funding from NSF grant #SBE-0542013 (UCSD). Dr Burtis receives research funding from NIDCD/NIH grant # 1T32DC008768-01. This research was not funded by any other specific grants from any funding agency, commercial, or not-for profit sectors. There are no conflicts of interest.

 http://dx.doi.org/10.1080/13554794.2012.690427

with left hemisphere damage is parallel to that of hearing individuals with damage to the left hemisphere. Poizner, Bellugi, and Iragui (1984) also studied left hemisphere damaged deaf signers for the presence of an ideomotor apraxia as well as sign language aphasia and found that impairments in the production of ASL were dissociable from impairments in the production of transitive gestures (pantomimes). Thus, the motor and visual-spatial skills required to produce and comprehend ASL appear to be specific to the linguistic nature of the task and not necessarily affected by neurological disease that impairs nonlinguistic motor and visual-spatial skills.

Although there are many similarities in the means by which the brain mediates speech and ASL, there are also ways that ASL is different from spoken language beyond the different input and output channels (visual-gestural or auditory-spoken). While the syntax in English is conveyed by function words and the sequence of individual words, in ASL the syntax is often conveyed by the spatial position of the hands and by modifications to individual signs. As a result, English (spoken and written) has a different grammar than ASL and may be more akin to a second language in deaf signers, depending on the methods of instruction and ages of acquisition for ASL and written English. In ASL, some lexical items (words) can be conveyed by individual signs, while other lexical items do not have signs and must be fingerspelled. As compared to the ability to produce and comprehend signs in the context of their spatial locations, the ability to produce and comprehend fingerspelled words may utilize different neural systems that may be more closely related to reading and writing.

In most reported cases of sign language aphasia, changes in signing resulted from cerebral infarction, a focal process that impairs certain cognitive processes while leaving others preserved as determined by the location of the lesion. Brentari, Poizner, and Kegl (1995) studied sign language ability in two deaf signers with Parkinson disease, a neurodegenerative condition known to affect the speed and deftness of movement (Quencer et al., 2007). It was demonstrated that Parkinson disease affects the handshape and movement of articulators, phonetic alterations that are consistent with the known motor deficits that occur with Parkinson disease. We are not aware of any previous reports of the changes in sign language associated with the cognitive impairments caused by Alzheimer's disease (AD), the most common neurodegenerative type of dementia.

AD is characterized by impairments of episodic memory (amnesia), language (most often word finding), ideomotor apraxia, and visual-spatial dysfunction caused by temporoparietal degeneration. It remains unknown, however, how AD alters communication, memory, and praxis in deaf signers. We expect that AD will cause language impairments in sign language that are similar to those well described in spoken language, with difficulties in naming, repetition, and comprehension (Cummings, Benson, Hill, & Read, 1985; Gorno-Tempini et al., 2008). Impairments of reading comprehension and writing have also been reported in AD (Cummings, Houlihan, & Hill, 1986; Luzzatti, Laiacona, & Agazzi, 2003), and it is possible that these impairments could affect fingerspelling, an aspect of communication unique to sign languages. Fingerspelling could also be adversely affected by the reduced working memory span associated with AD (Baddeley, 1992). The clinical hallmark of AD is an impairment of episodic memory, both verbal and spatial (Moss, Albert, Butters, & Payne, 1986). As the temporal sequence of hand movements and the spatial position of the hands are essential to communication in sign language, it is possible that the loss of episodic memory with AD could impair the ability to communicate by sign language in a manner distinct from the effects of this disease on spoken language.

A thorough understanding of the changes in sign language that result from AD is essential for early recognition, diagnosis, and treatment of AD in deaf signers. While the mental status exam is an essential part of the neurological evaluation, there are many difficulties inherent in attempting to directly "translate" standard neuropsychological tests into sign language, and the similarities and differences between signed and spoken languages must be thoroughly considered. It is not known how the heterogeneity in the age of sign language acquisition among deaf signers may influence changes in language that occur in the course of neurodegenerative diseases such as AD. Recently, we had the opportunity to gain insight into these issues by evaluating a congenitally deaf woman who appears to have a degenerative dementia.

CASE DESCRIPTION

First clinic visit

Our patient is a 55-year-old right-handed woman seen in our clinic for memory problems that

began 1.5 years prior to her first visit. She was accompanied by her husband who is also deaf, and both use ASL as their primary form of communication. The patient's husband of 4 years noticed that his wife has had progressive difficulty comprehending him and has sign finding difficulty. He reported that changes in her ability to communicate in sign language were new. When they dated for 3 years and during the first couple of years of the marriage, her communication (ASL) was clear, accurate, and quick. She has been repeating herself at times and sometimes forgets things that he told her. Recently she was not able to learn how to use their universal remote control, and she had been losing her car keys. She uses a computer but they reported that her spelling has been getting worse. Her previous occupational history includes employment at a bank where she worked at a computer, helped customers with bank statements, and handled money. She was then employed at a facility for mentally ill deaf children, where she dispensed scheduled medicines and helped organize and supervise children during daily activities such as going to the store. She then worked in the stock room of a retail store, folding and replenishing clothing on the floor. As her husband reports, she began having problems with memory and left this job 1.5 years ago to become a full-time homemaker, although she denied that she stopped working because of cognitive problems. She has been able to continue cooking for herself and her husband, although she recently had difficulty using a microwave to cook rice.

Our patient was born deaf to two hearing parents, but she had a deaf aunt. She has four children from a previous marriage; one is deaf, two are hard of hearing, and one has normal hearing. The patient learned sign language between the ages of 8 and 9 while attending a school for the deaf in Queens, NY. Prior to attending this school, she attended an oral school where sign language was strictly forbidden. She reported not understanding anything at the oral school and begged her mother to send her to another school where, as mentioned before, she learned sign language between the ages of 8 and 9. She was more fully immersed in this language at the age of 17 when she lived in a dormitory with other deaf students who signed. She did not learn how to speak. She had difficulty reading in school and never read books. She also did not take algebra or other advanced math classes. She did, however, graduate from high school. She then raised four children and worked in a bank, a group home, and a clothing store.

Our patient has a history of valvular heart disease treated with a tricuspid annuloplasty ring and an aneurysm of the pancreaticoduodenal artery which ruptured in 2006 necessitating surgical treatment. She takes warfarin 5.5 mg daily and simvastatin 20 mg. She had previously been prescribed memantine, which she stopped due to nausea. She reported that she sleeps well and denied feeling depressed. She denied any additional neurological or psychiatric symptoms and has no history of alcohol or tobacco abuse. Her father and other members of his family had memory disorders, and he died in his 50s. However, the patient's 81-year-old mother and the patient's two hearing brothers have no history of dementia.

Our patient's general examination was normal except for the presence of finger clubbing. Her heart rate and rhythm were regular with no audible murmurs, rubs, or gallops, and no carotid bruits. On neurological examination she was awake, alert, and fully cooperative. For the most part, she communicated in sign language and since we (ADF, DBB, LD, KMH) are not competent in ASL we required the assistance of an interpreter. These sessions were videotaped for later analysis of her signing (RIM, HP). A summary of selected neuropsychological test results is presented in Table 1 at the end of the results section. During her evaluation it was apparent that she had difficulty telling a story. Her signed sentences were short and simple, lacking any complex syntax. Consistent with her simple expressive language, she only used one question word: WHAT, and she did not use WHO, HOW, WHEN, or IF. She also had serious problems with sign comprehension that were greater for multi-clause sentences as compared to single clause sentences, and she had particular difficulty understanding pronouns including interrogative pronouns. For example, when testing buccofacial praxis she could not understand the difference between *me* and *you*, and she had great difficulty in understanding that she was to perform the action.

Her comprehension and production of fingerspelling were markedly impaired. These impairments were worse than her comprehension and expression of signs, which were also impaired. She would only spell the first 2–3 letters of a word, even when trying to repeat a fingerspelled model. For example, when copying the fingerspelled word V-A-L-V-E, she spelled V-A-L, then stopped and tapped in the air with the extended index finger of the letter "L." She then tried to copy a second

TABLE 1
Summary of selected neuropsychological test results

Test[1]	*Visit 1*	*Visit 2*	*Visit 3*
Folstein MMSE	15/30	18/30	NA
Hopkins Verbal Learning Test	Form 1 Part A: 7 (0+1+3+3, across four trials) Part B: free recall 0, discrimination index 4	NA[2]	Adapted from forms 1, 4, and 6 to avoid inclusion of fingerspelled words Part A: 14 (2+5+7) Part B: free recall 4, discrimination index 5
Boston Naming Test	14/30 (odd numbered pages)	6/15 (short form)	8/20 (even numbered pages, stopped after page 40)
Phonemic fluency (F,A,S)	20 words total	NA	NA
Semantic fluency	6 animals	11 animals	3 fruits and vegetables, 8 animals
Digit span (letters)	4 forwards, 2 backwards	NA	NA

[1]Critical differences between English and ASL significantly limit direct "translation" of these tests into ASL and thus preclude comparing the patient's scores with the test norms (see results and discussion sections for further appraisal of these issues). Note that performance on many of these tests was significantly limited by the patient's impaired fingerspelling ability.
[2]Not administered.

model, and got one more letter, V-A-L-V and stopped; she then tapped in the air again, this time simultaneously with the extended index and middle fingers of the last letter used, "V." However, in her spontaneous signing she could sometimes correctly produce fingerspelled words consisting of 5–6 letters.

She demonstrated no semantic paraphasic errors (incorrect substitutions of semantically related signs) in her signs. Signs have sublexical structure that includes the hand shape, type of movement of the hand in space, and place of articulation in peripersonal space or on the body where the sign is produced. There are a limited number of elements in each formational class, and what is termed "phonemic paraphasic errors" in signs consists of incorrect substitution of elements within a formational class. Our patient did not demonstrate any phonemic paraphasic errors in her signing.

Our patient's naming in ASL was also impaired. On the odd numbered pages of the Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1983), she named 14 of 30 pictures correctly. She had difficulty repeating (imitating) signed sentences but appeared to be able to repeat signs for single words, sometimes changing the sign into her dialect rather than that of the interpreter. She had difficulty repeating individual letters and would sometimes misread one letter as another. At times, when asked to repeat a series of letters she would convert these letters into a word. For example when asked to repeat the letters F V N, she fingerspelled FUN. When asked to repeat the letters G A R, she fingerspelled D R, and then produced the sign DOCTOR. Digit span (using letters B, C, D, F, G, K, L, N, S) was four forwards and two backwards (Bavelier et al., 2008).

When writing, she could produce well-formed letters, but one spelling error was noted when she wrote a short sentence. She could not perform simple calculations (for 4+3 she answered 6, for 6–2 she answered 5). There was no right–left confusion. The patient could not name (fingerspell) the index finger, but the significance of this is unclear as the sign for index finger in ASL is to point to the index finger (which she was able to do). In contrast, her husband was able to fingerspell the word for index finger.

The patient was impaired at pantomiming some transitive gestures (ideomotor apraxia). When asked to pantomime, the patient often produced classifier signs. These are ASL signs in which the shape of the hand performing the motion is used as the sign itself. Her ideomotor limb and buccofacial praxis both improved when the patient was asked to imitate gestures. She could also imitate meaningless gestures. On the Brief Apraxia Screening Test from the Florida Apraxia Battery (Rothi et al., 1992), the patient had at least 6 errors on 24 trials. Graphesthesia was intact bilaterally. On the Folstein Mini Mental Status Exam (MMSE) (Folstein, Folstein, & McHugh, 1975), she had a score of 15/30 with 9/10 points for orientation, 2/3 registration, 0/3 delayed recall, and an inability to perform serial 7s. She could name a pen and watch and follow 2 parts of the 3-step command.

She could not follow a written command, copy intersecting pentagons, or repeat "No ifs, ands, or buts." The significance of this last finding is unclear as this English idiom does not occur in ASL. In addition, she had no evidence of neglect or simultanagnosia, and her behavior and affect were appropriate.

On Part A of the Hopkins Verbal Learning Test (HVLT), Form 1 (Brandt, 1991), administered in fingerspelling, she recalled 0 words on the first trial, 1 word on the second trial, and 3 words on the third trial (and 3 words on a fourth trial administered because we were unsure if she understood the instructions during the first trial). On Part B she had a free recall of 0. With recognition she had a discrimination index of 4. On a controlled oral word association test (Benton & Hamsher, 1976) with 1 minute per letter she sign-named a total of 20 words beginning with F, A, and S (7+5+8). On a category fluency test she sign-named six animals in 1 minute. For hearing individuals who speak English, it is normal to name approximately 35 words total with the letters F, A, and S when given 1 minute per letter (with variation due to demographic characteristics such as age, gender, and level of education) (Loonstra, Tarlow, & Sellers, 2001). It is normal to name 19–20 animals in 1 minute, also with variation due to demographic characteristics (Gladsjo et al., 1999). However, these tests do not have standardized normal values for deaf signing populations, and our patient's late age of ASL acquisition could also have influenced her performance.

Neurological examination was normal except for deafness and a mild action tremor more noticeable with the left hand than the right. Her B12, folate, and thyroid function tests were within normal limits, and a treponemal antibody test was non-reactive. An MRI of the brain showed minimal asymmetrical atrophy of the left anterior temporal lobe present on two sagittal slices. However, the patient's head was slightly tilted in the scanner, and on coronal reconstruction of the images no asymmetrical temporal atrophy was present. There was no significant mesial temporal atrophy. There was no significant leukoaraiosis or evidence of infarcts or mass lesions.

Second clinic visit

When our patient returned to clinic 2 months later, the patient's husband reported that the patient's memory had declined. She would often forget what she just saw on TV; she lost things more often, and she continued to have difficulty cooking – for example she seemed not to know which pan to use, a sign of conceptual apraxia (Ochipa, Rothi, & Heilman, 1992). She had increased difficulty reading and her husband reported that she would often ask him what each word meant. She also developed increased difficulty understanding her husband when he signed to her. He reported sometimes having difficulty understanding her when she would sign to him.

On repeat cognitive testing, she had a Folstein MMSE score of 18 with 7/10 points for orientation. She was unable to perform serial 7s, repeat the English idiom "No ifs, ands, or buts," follow all 3 steps of the multistep command, or copy the intersecting pentagons. She registered 2/3 words initially, and she registered all 3 words after several further attempts. She recalled all three words after a brief delay of a few minutes. After completing the Folstein MMSE, we asked her to recall the 3 words again, and she could not recall any at that time. On a category fluency test she sign-named 11 animals in 1 minute, and on the short form of the Boston Naming Test she sign-named 6 of 15 pictures. She could not fingerspell the name of the index finger and she had right–left confusion and impaired calculations. She could write a sentence, although with one spelling error and nonstandard grammar. We advised her to stop taking hydroxyzine for itching and to avoid anticholinergic medications. A PET scan was obtained, which on our review showed left temporoparietal hypometabolism. We reviewed the images with a neuroradiologist from our institution who identified hypometabolism bilaterally in the parietal and anterior temporal lobes greater on the left side than the right.

Third clinic visit

Two months after the second clinic visit, our patient's husband reported that her ability to communicate had continued to decline. He stated that she has difficulty finding the correct signs and that her signs did not appear to be correct. He equated her signs to a foreign language.

On examination, as in the past, the patient had difficulty understanding the instructions, and these instructions had to be repeated several times by the interpreter for most of the neuropsychological

tests. The interpreter also stated that she could understand why the patient's husband said he had difficulty understanding her signs. We began with a version of the HVLT composed of words from Forms 1, 4, and 6 that had ASL signs and did not have to be fingerspelled. The semantic categories included animals (Form 1), clothing (Form 4) and building items (Form 6). On Part A, trials 1–3, she recalled 2, 5, and 7 words, which was improved from her previous visit. After a 20-minute delay, her free recall was 4. On recognition testing, she recognized 9 of 12 true positives and identified 4 of 12 false positives. When asked to sign-name as many fruits and vegetables as she could think of in 1 minute, she signed 3 fruits in 30 seconds but then lost set and sign-named milk, cereal and butter while perseverating on the latter two. Her husband helped her understand the task, and once she understood we tried a test of animal fluency. She was able to sign-name 8 animals in 1 minute. On the Boston Naming Test, odd numbered pages, she was able to sign-name the first 8 pictures but none of the next 12 and we stopped after item 40 for a total of 20 attempted. Of those pictures that she could not sign-name, she appeared to recognize at least some of them but either told us she did not know their names, misspelled "camel" and "pretzel" (finger-spelled "camle" and "prez"), made the gesture (for throwing a dart) but could not name it, and named some pictures with semantically related words (she called a globe a "world," called a rhinoceros a "hippopotamus," and called an igloo an "ice house"). These semantically related words would be considered typical for an ASL signer with limited fingerspelling ability.

The patient had particular difficulty repeating all the signs of a simple sentence. While our patient may have never attained full proficiency with written English grammar, in this case she was being asked to repeat sentences that were signed in ASL. Thus, we stated, "The boy went to the store." The interpreter signed this, and told us that, when converting this to the syntax of ASL, it translates as "BOY GO TO STORE," but the patient signed "BOY GO THERE." Similarly, when we asked the patient to repeat "point to the light before you point to the door," the interpreter signed "LIGHT POINT BEFORE DOOR POINT," and the patient signed "LIGHT POINT . . . DOOR POINT." When we asked the patient to repeat "the girl holding the flower is hitting the boy," the patient did not include "FLOWER" in her signing. However, when we asked the patient to repeat single signs, she was consistently able to do this correctly. With the help of the interpreter, we discussed with the patient and her husband how her neurological disease had impaired her ability to communicate by ASL, and we prescribed a cholinesterase inhibitor.

DISCUSSION

Determining cognitive impairment can be particularly challenging in deaf signers due to heterogeneity in etiology of deafness, age of acquisition of sign language, literacy skills, and premorbid cognitive abilities. Our patient learned ASL in school between the ages of 8 and 9. The proficiency with which she learned ASL at age 8 is unclear as her first full ASL immersion was only at age 17 when she lived in a dormitory with other deaf students who signed. Her ASL skills may never have developed to the level of someone exposed to ASL since birth, and comprehension difficulties are a hallmark of late sign language learning (Morford, 2003). Her late sign language acquisition may also be reflected in her academic difficulties in school (Mayberry, Lock, & Kazmi, 2002). However, as she has a deaf husband and raised deaf children, it is reasonable to assume that she attained a functional level of ASL proficiency. Her husband of 4 years reported that changes in her ability to communicate in sign language were new and not present when they first met 7 years earlier. In the absence of comparable neuropsychological and language assessments from before and after disease onset, we have limited ability to reach specific conclusions regarding our patient's current neurological impairments in relation to her premorbid language ability. Nevertheless, there is a significant amount of research that reports the effects of late age of primary language acquisition on linguistic ability and brain organization for language processing. Consideration of how these effects could potentially influence performance on neurological tests and the clinical manifestations of AD in deaf signers have important implications for patient care and future research, and as such, these issues will be included in our discussion.

The characteristics of our patient's present language impairments include difficulty with comprehension of syntax and pronouns, impaired repetition and naming, and a tendency to produce short simple sentences. Her most marked language impairment is in her ability to produce and comprehend fingerspelled words. We believe that our patient's history and the results of our

evaluation are most consistent with a diagnosis of AD. In the following discussion, we consider three ways in which the neuropsychological and pathophysiological changes that occur in the course of AD may relate to the impairments in our patient's ability to communicate in ASL and how in many respects, her cognitive disorders mirror those of patients with AD who had normally learned to speak. While her husband described continued decline in her ability to communicate at each clinic visit, her cognitive and sign language abilities, though clearly impaired, appeared relatively stable as assessed by performance on neuropsychological tests during this time. This suggests that clinical tests to assess language and cognitive skills in English may not be sensitive to declines in sign language ability even when they are translated into ASL. We end by considering the unique assessment and diagnostic challenges posed by deaf signers with AD.

Temporal-parietal language processing: effects of AD and late age of primary language acquisition

Our patient's impaired language comprehension was most evident for multi-clause sentences and for comprehension of pronouns. The sentences that she produced were short and simple. These types of language impairments are in part consistent with those of late language learners (Ferjan Ramirez, Lieberman, & Mayberry, in press; Mayberry et al., 2002; Morford, 2003). Mayberry, Chen, Witcher, and Klein (2011) studied how the age of acquisition for ASL in a congenitally deaf population affected the neurological correlates for judgment of the grammatical and phonemic information conveyed by hand positions in ASL. The study utilized a behavioral paradigm and fMRI. Grammatical judgments showed bilateral hemispheric activation greatest in the left inferior frontal gyrus (anterior activation), while phonemic judgments showed increased activation in the inferior temporal, parietal, and occipital regions (posterior activation). However, with later acquisition of ASL, there was decreased activation of anterior regions (including the left perisylvian region) and increased activation of posterior regions (left lingual gyrus and left middle occipital gyrus) for both grammatical and phonemic judgments in ASL. Mayberry et al. (2011) noted that these results suggest a shallower level of linguistic processing for ASL by deaf signers who learn the language later in life, since syntactic processing (which normally requires more anterior activation) is essential to extract meaning from linguistic material. It is presently unknown how healthy aging or neurological diseases that selectively affect distinct neuroanatomical systems interact with sign language processing related to late acquisition. It is possible that the effects of a temporal-parietal degenerative condition, such as AD, will have effects on language and particularly on the syntactic processing of late learners of ASL because they rely on more posterior cortical regions for processing of syntax relative to early ASL learners. A similar situation is observed in hearing-speaking individuals, where the effects of age of acquisition are apparent in the language impairments that occur during the course of AD (Forbes-McKay, Ellis, Shanks, & Venneri, 2005; Kremin et al., 2001).

The overlay of language impairment due to AD on reduced premorbid language ability was also observed in our patient's literacy skills. When deaf signers learn to read and write English at a later age, English may be more akin to a second language (Morford, Wilkinson, Villwok, Piañr, & Kroll, 2011). An fMRI study by Waters et al. (2007) showed that signed, fingerspelled, and printed words all activated a left frontal temporal network including portions of the left inferior temporal and mid-fusiform gyri in congenitally deaf signers exposed to British Sign Language from birth. Our patient was able to write well formed letters when writing a sentence. Although some of her spelling and grammar were incorrect, one interpreter noted that her grammar was consistent with that used in ASL. This suggests that the patient may have never attained full proficiency with written English. Similarly, on some visits, the patient could read and follow a written command while other times she could not. Moreover, the patient's husband reported that at home she often had difficulty reading words and would ask him for help. This change suggests that, regardless of our patient's baseline abilities to read and write in English, there has been additional functional decline in her literacy skills that parallel her decline in fingerspelling ability. Unlike signs, fingerspelled words are a direct representation of English print and thus limited by the strength of one's graphemic-lexical representations for those words. Although our patient never achieved full proficiency with written English, her reported history indicates that her reading abilities, along with her loss of the ability to produce and comprehend fingerspelled words, has been degraded by her neurological disease.

Our patient did have constructional apraxia, and her difficulty in copying intersecting pentagons is not likely to be due to her premorbid abilities given the well documented superior visual-spatial skills in people who use a sign language (Cattani, Clibbens, & Perfect, 2007). Poizner, Kaplan, et al. (1984) reported that the linguistic visual-spatial skills necessary for production and comprehension of sign language are dissociable from the nonlinguistic visual-spatial impairments that occur after right hemisphere damage in hearing and deaf individuals. However, in a disease such as AD, it is possible that the parietal lobe degeneration that leads to nonlinguistic visuospatial impairments could also lead to impairments in the visual-spatial analysis of ASL, especially in late learners of ASL. Poizner, Bellugi, et al. (1984) also found language production and transitive gesture production (pantomime) to be dissociable in left hemisphere damaged deaf signers. Our patient did show evidence of ideomotor apraxia that is consistent with parietal lobe dysfunction, but previous studies of the relation between aphasia and apraxia in ASL suggest that our patient's apraxic errors in pantomime production may be dissociable from her errors in production of ASL.

Disruption of the phonological loop in AD: potential effects on fingerspelling

During testing of working memory, the patient had marked difficulty with recognition and repetition of fingerspelled letters. When attempting to repeat series of fingerspelled letters, she would sometimes change them into an actual word (F V N became F U N). There are two routes for sentence repetition (Coslett, Roeltgen, Gonzalez Rothi, & Heilman, 1987). Words can be repeated either directly by a phonological route without semantic-conceptual processing to determine meaning (e.g., repeating a nonword) or by a lexical-semantic route in which a person comprehends the word and then reconstructs it in order to repeat it, a process that is defective in patients with deep dysphasia (Katz & Goodglass, 1990). The phonological route includes Heschl's gyrus, Wernicke's area, the arcuate fasciculus, Broca's area and its connections to motor cortex. Patients with damage to this phonological loop in the perisylvian region of the dominant hemisphere have impaired repetition with particular difficulty repeating nonwords, since in the latter case it is not possible to repeat by the lexical-semantic route. When attempting to repeat nonwords, or grammatically incorrect sentences, a person with deep dysphasia with an inability to repeat by the direct route may spontaneously convert the nonword to a real word, or correct the grammatical error in the sentence as she or he attempts to repeat by the lexical-semantic route.

Our patient's difficulty in repeating meaningless strings of fingerspelled letters and her tendency to convert these to actual words may reflect damage to the phonological loop. In an fMRI study, Bavelier et al. (2008) found that the left perisylvian (and prefrontal) regions that mediate auditory verbal working memory span in hearing individuals mediate working memory for fingerspelled letters in deaf signers who had been exposed to ASL since birth. This is another example in which the linguistic properties rather than the input and output channels of ASL (visual-gestural) determine the neural systems associated with ASL. Damage to the phonological loop may also underlie our patient's impaired repetition of sentences. The repetition section of the Folstein MMSE is particularly problematic when being translated into ASL. Due to grammatical differences between English and ASL, a study by Dean, Feldman, Morere, and Morton (2009) found that only 21.4% of healthy older deaf signers could repeat the English idiom "No ifs, ands, or buts." This is an example of differences between English and ASL that prevents direct word for word translation. However, our patient also was unable to repeat other sentences as described earlier. Aphasia caused by dysfunction of the phonological loop is classically referred to as conduction aphasia.

There are two other cardinal features of conduction aphasia that were *not* present in our patient, fluent speech with spontaneous phonemic paraphasic errors and intact comprehension (Benson et al., 1973). However, patients with logopenic progressive aphasia (Gorno-Tempini et al., 2008) typically have impaired sentence comprehension. Hearing patients with this condition also have impaired repetition and naming, decreased fluency, and impaired letter span that parallel our patient's deficits. This disorder is often caused by the pathological changes associated with AD.

Working memory impairment in AD: manifestations in sign language

Our patient had impaired comprehension of ASL that was greater than would be expected from disconnection of posterior and anterior regions of

the phonological loop. In ASL, comprehension of the grammatical construction of a sentence can be determined by word order in some sentences and by inflectional morphology (modifications to the individual signs that alter their syntactic relationship to other signs) in other sentences. Newman, Supalla, Hauser, Newport, and Bavelier (2010) used fMRI to study sentence comprehension in deaf signers exposed to ASL since birth. They found that sentence comprehension that is reliant on inflectional morphology was associated with greater activation of the bilateral medial temporal gyri/superior temporal sulci, anterior temporal regions, left inferior frontal gyrus pars triangularis, bilateral inferior frontal gyrus pars orbitalis, left hemisphere supplementary motor area, and bilateral cerebellum. Comprehension of sentences determined solely by word order was associated with increased activation of areas also associated with working memory, the bilateral dorsolateral prefrontal cortex, and also with the right inferior frontal gyrus pars triangularis and left angular gyrus. Thus, our patient's alterations in comprehension may result from two mechanisms. Our patient may have a shift away from the more typical anterior language areas and toward activation of more posterior cortical regions as occurs in deaf signers with a later age of acquisition for ASL (Mayberry et al., 2011), and effects from this shift could be accentuated by the temporal-parietal degeneration associated with AD. Our patient's AD may have also led to an impairment of her working memory. Baddeley (1992) described three components of the working memory system: (i) a central executive system that directs attentional focus, (ii) a phonological loop for encoding and rehearsal of verbal material, and (iii) a visual-spatial sketch pad for manipulation of visual images. He noted that the central executive component is particularly susceptible to dysfunction in AD.

Warrington and Shallice (1969) described a hearing-speaking man with a history of trauma to the left parietal lobe and a resultant inability to repeat verbal material. This was associated with a profound impairment of auditory verbal short-term memory (working memory). Perhaps the visual-spatial aspects of ASL, including the use of space to convey grammatical information, increase the demands on working memory for ASL comprehension. In ASL, the space in which each individual word is signed in a sentence is essential to the meaning of the sentence, and an impairment of working memory may lead to difficulty in the spatial organization of present and planned future signs with respect to previous signs and the intended meaning of the sentence.

Our patient had evidence of spatial dislocation errors in her signing. For example, she correctly used the signing space to set up FATHER as a grammatical referent in a given spatial location. She then signed HIS at that location, which is also grammatically correct. However, she then signed AUNT at the same location she just signed HIS, instead of returning to canonical sign space where AUNT should have been signed. It is possible that impaired working memory for the words that she had previously produced in the sentence led her to perseverate the sign space for the following word. Our patient had difficulty understanding the difference between "me" and "you," and understanding that she was to pantomime the requested actions during the praxis testing. These difficulties may represent examples of spatial problems related to impaired working memory that caused her to either misread the location or not spatially transform the sign. Impaired comprehension of grammar is often associated with impaired ability to construct grammatically complex sentences and this may have contributed to our patient's tendency to produce short and simple sentences.

Fingerspelled words may be particularly susceptible to the effects of working memory. Warrington and Shallice (1969) noted in the landmark case descriptions of conduction aphasia that spelling and writing abilities were the second most common linguistic skills to be impaired (after repetition). The hearing-speaking patient described by Warrington and Shallice (1969) had an impairment of spelling that was greater than his impairment of reading. These impairments of spelling and writing in conduction aphasia may be related to the associated impairments of repetition and working memory which limit the ability to arrange and hold the individual letters of a word in working memory during formation of the motor program to spell aloud or write the word. It is possible that our patient's poor working memory system may be limiting her comprehension and production of fingerspelled words, particularly for those fingerspelled words that match or exceed her working memory span. Fingerspelling may load the memory system in ways that signs do not. Bavelier et al. (2008) found that in lifelong deaf signers, working memory for sequences of fingerspelled letters is mediated not only by the left perisylvian region, consistent with the role of the phonological loop, but also by prefrontal regions that are associated with verbal working memory in hearing individuals. Impaired

fingerspelling comprehension and expression may be an early marker of language and working memory impairments in signers with neurological disease, and assessment of fingerspelling may be a sensitive measure for impaired working memory in deaf signers with potential cognitive dysfunction. While our patient did not display phonemic paraphasic errors in her articulation of signs, perhaps her inability to fingerspell represents an aspect of the sequencing deficit that is manifest as phonological paraphasic errors in hearing-speaking patients with conduction aphasia.

The evaluation of neurodegenerative disease in deaf signers: diagnostic considerations and directions for future research

Our patient appeared to have an impairment of episodic memory. However, as noted earlier, some words on traditional list learning memory tests do not have specific signs and in this case were fingerspelled. As our patient had particular impairment of fingerspelling, this likely added to her difficulty encoding and retrieving the test words during our initial administration of the Hopkins Verbal Learning Test. Our patient also appeared to have an impairment of semantics. Category fluency, a common measure to assess semantically related word generation, was reduced. While this suggests impairment of semantic network activation, our patient's difficulty in naming to confrontation appeared to be an anomia rather than an agnosia because she could recognize and describe some of the pictures that she could not name. The interpretation of her performance on the test of phonemic fluency is less clear. She was likely using orthography to guide her on this task and was observed to make the hand shape for the letter (such as "a") and to then hold and move it around to help retrieve English words that begin with this letter. The common phonemic property of spoken words beginning with a certain letter is not expected to be present in the signs for these same words. This is yet another example of the difficulties in attempting to directly translate neuropsychological tests designed for an English speaking population into sign language. Overall, our patient's history of gradually progressive memory loss with associated impairments of language comprehension, apraxia, and visual-spatial dysfunction is most consistent with a diagnosis of AD, a diagnosis supported by the findings on the PET scan.

To summarize, this report illustrates several important issues in the neurological evaluation of deaf signers. There is often heterogeneity in age of language acquisition in deaf signers that is greater than that seen in populations that communicate by spoken languages, and these differences in language acquisition among deaf signers can have different effects on performance of signing, fingerspelling, and written language. Dissociable effects of neurological disease on these distinct linguistic elements are often lost with direct translation of standardized neuropsychological tests that do not take into account, for example, differences between signs and fingerspelling for different items on a naming or verbal learning test. We combined three semantic categories from different forms of the HVLT such that all target items had signs in ASL and none of the items had to be fingerspelled. Naming tests should also include separate assessments for target words with ASL signs and words that must be fingerspelled. ASL has a distinct system of grammar, and this also prevents direct word for word translation of English language tests into ASL. Our patient's most notable impairment on examination was a loss of ability to produce and comprehend fingerspelled words. The temporal sequencing and working memory requirements of fingerspelling may make this task particularly sensitive to language and/or left hemisphere dysfunction in deaf signers. As the number of aging deaf signers increases in proportion with the general population, these issues will become more common in clinical practice and merit urgent solutions.

Original manuscript received 25 September 2011
Revised manuscript accepted 1 April 2012
First published online 23 July 2012

REFERENCES

Alzheimer, A. (1907). Über eine eigenartige Erkrankung der Hirnrinde [About a peculiar disease of the cerebral cortex]. *Allgemeine Zeitschrift fur Psychiatrie und Psychisch-Gerichtlich Medizin*, *64*, 146–148.

Baddeley, A. (1992). Working memory. *Science*, *255*, 556–559.

Bavelier, D., Newman, A. J., Mukherjee, M., Hauser, P., Kemeny, S., Braun, A., & Boutla, M. (2008). Encoding, rehearsal, and recall in signers and speakers: Shared network but differential engagement. *Cerebral Cortex*, *18*, 2263–2274.

Benson, D. F., Sheremata, W. A., Bouchard, R., Segarra, J. M., Price, D., & Geschwind, N. (1973). Conduction aphasia. A clinicopathological study. *Archives of Neurology*, *28*, 339–346.

Benton, A. L., & Hamsher, K. (1976). *Multilingual aphasia examination* (2nd ed.). Iowa City, IA: AJA Associates.

Brandt, J. (1991). The Hopkins Verbal Learning Test: Development of a new memory test with six equivalent forms. *Clinical Neuropsychology*, *5*, 125–142.

Brentari, D., Poizner, H., & Kegl, J. (1995). Aphasic and parkinsonian signing: Differences in phonological disruption. *Brain and Language*, *48*, 69–105.

Cattani, A., Clibbens, J., & Perfect, T. J. (2007). Visual memory for shapes in deaf signers and nonsigners and in hearing signers and nonsigners: Atypical lateralization and enhancement. *Neuropsychology*, *21*, 114–121.

Coslett, H. B., Roeltgen, D. P., Gonzalez Rothi, L., & Heilman, K. M. (1987). Transcortical sensory aphasia: Evidence for subtypes. *Brain and Language*, *32*, 362–378.

Cummings, J. L., Benson, F., Hill, M. A., & Read, S. (1985). Aphasia in dementia of the Alzheimer type. *Neurology*, *35*, 394–397.

Cummings, J. L., Houlihan, J. P., & Hill, M. A. (1986). The pattern of reading deterioration in dementia of the Alzheimer type: Observations and implications. *Brain and Language*, *29*, 315–323.

Damasio, A., Bellugi, U., Damasio, H., Poizner, H., & Van Gilder, J. (1986). Sign language aphasia during left-hemisphere Amytal injection. *Nature*, *322*, 363–365.

Dean, P. M., Feldman, D. M., Morere, D., & Morton, D. (2009). Clinical evaluation of the mini-mental state exam with culturally deaf senior citizens. *Archives of Clinical Neuropsychology*, *24*, 753–760.

Ferjan Ramirez, N., Lieberman, A. M., & Mayberry, R. I. (in press). The initial stages of language acquisition begun in adolescence: When late looks early. *Journal of Child Language*.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). 'Mini-mental state'. A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, *12*, 189–198.

Forbes-McKay, K. E., Ellis, A. W., Shanks, M. F., & Venneri, A. (2005). The age of acquisition of words produced in a semantic fluency task can reliably differentiate normal from pathological age related cognitive decline. *Neuropsychologia*, *43*, 1625–1632.

Gladsjo, J. A., Schuman, C. C., Evans, J. D., Peavy, G. M., Miller, S. W., & Heaton, R. K. (1999). Norms for letter and category fluency: Demographic corrections for age, education, and ethnicity. *Assessment*, *6*, 147–178.

Gorno-Tempini, M. L., Brambati, S. M., Ginex, V., Ogar, J., Dronkers, N. F., Marcone, A., . . . & Miller, B. L. (2008). The logopenic/phonological variant of primary progressive aphasia. *Neurology*, *71*, 1227–1234.

Hickok, G., Love-Geffen, T., & Klima, E. S. (2002). Role of the left hemisphere in sign language comprehension. *Brain and Language*, *82*, 167–178.

Kaplan, E., Goodglass, H., & Weintraub, S. (1983). *The Boston naming test* (2nd ed.). Philadelphia, PA: Lea & Febiger.

Katz, R. B., & Goodglass, H. (1990). Deep dysphasia: Analysis of a rare form of repetition disorder. *Brain and Language*, *39*, 153–185.

Kremin, H., Perrier, D., De Wilde, M., Dordain, M., Le Bayon, A., Gatignol, P., . . . & Arabia, C. (2001). Factors predicting success in picture naming in Alzheimer's disease and primary progressive aphasia. *Brain and Cognition*, *46*, 180–183.

Loonstra, A. S., Tarlow, A. R., & Sellers, A. H. (2001). COWAT metanorms across age, education, and gender. *Applied Neuropsychology*, *8*, 161–166.

Luzzatti, C., Laiacona, M., & Agazzi, D. (2003). Multiple patterns of writing disorders in dementia of the Alzheimer type and their evolution. *Neuropsychologia*, *41*, 759–772.

Mayberry, R. I., Lock, E., & Kazmi, H. (2002). Linguistic ability and early language exposure. *Nature*, *417*, 38.

Mayberry, R. I., Chen, J.-K., Witcher, P., & Klein, D. (2011). Age of acquisition effects on the functional organization of language in the adult brain. *Brain and Language*, *119*, 16–29.

Morford, J. P. (2003). Grammatical development in adolescent first-language learners. *Linguistics*, *41*, 681–721.

Morford, J. P., Wilkinson, E., Villwock, A., Piñar, P., & Kroll, J. F. (2011). When deaf signers read English: Do written words activate their sign translations? *Cognition*, *118*, 286–292.

Moss, M. B., Albert, M. S., Butters, N., & Payne, M. (1986). Differential patterns of memory loss among patients with Alzheimer's disease, Huntington's disease, and alcoholic Korsakoff's syndrome. *Archives of Neurology*, *43*, 239–246.

Newman, A. J., Supalla, T., Hauser, P., Newport, E. L., & Bavelier, D. (2010). Dissociating neural subsystems for grammar by contrasting word order and inflection. *Proceedings of the National Academy of Science USA*, *107*, 7539–7544.

Ochipa, C., Rothi, L. J., & Heilman, K. M. (1992). Conceptual apraxia in Alzheimer's disease. *Brain*, *115*, 1061–1071.

Poizner, H., Bellugi, U., & Iragui, V. (1984). Apraxia and aphasia for a visual-gestural language. *American Journal of Physiology*, *246*, R868–883.

Poizner, H., Kaplan, E., Bellugi, U., & Padden, C. A. (1984). Visual-spatial processing in deaf brain-damaged signers. *Brain and Cognition*, *3*, 281–306.

Poizner, H., Klima, E. S., & Bellugi, U. (1987). *What the hands reveal about the brain*. Cambridge, MA: MIT Press/Bradford Books.

Quencer, K., Okun, M. S., Crucian, G., Fernandez, H. H., Skidmore, F., & Heilman, K. M. (2007). Limb-kinetic apraxia in Parkinson disease. *Neurology*, *68*, 150–151.

Rothi, L. J. G., Raymer, A. M., Ochipa, C., Maher, L. M., Greenwald, M. L., & Heilman, K. M. (1992). *Florida Apraxia Battery, experimental edition*. Gainesville, FL: University of Florida College of Medicine.

Warrington, E. K., & Shallice, T. (1969). The selective impairment of auditory verbal short-term memory. *Brain*, *92*, 885–896.

Waters, D., Campbell, R., Capek, C. M., Woll, B., David, A. S., McGuire, P., . . . & MacSweeney, M. (2007). Fingerspelling, signed language, text and picture processing in deaf native signers: The role of the mid-fusiform gyrus. *NeuroImage*, *35*,1287–1302.