Behavioral Neurology in Language and Aphasia: From Basic Studies to Clinical Applications

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ABSTRACT

With increasing aging population, cognitive deteriorations due to neuro-degenerative diseases or stroke are so commonly observed that it is thought to be inevitable with aging. For dementia and stroke, a communication disorder due to language deterioration is one of the main problems. Behavioral neurology aims to clarify the relationship between brain function and behavior; language deterioration is one of the main targets, and its clinical applications are really useful for making better understanding of patients.

Language is sequences of sound or characters that carry meanings for communication. From the evolutionary perspective, “language” can be thought about by considering birds and dogs: the basal ganglia and anterior cingulate, and the thalamus and cerebral cortex are thought to provide the neurobiological background, respectively. Humans can use language. The language area is a newly developed brain area in evolution and is mainly localized in the left cerebral hemisphere. Semantic memory has also developed in humans. There are two routes, the superficial and deep routes, with the latter associated with meaning, and three brain areas are involved: the peri-Sylvian area, per-peri-Sylvian area, and right hemisphere. Using these principles, language symptoms of dementia with progressive non-fluent aphasia (PA), semantic dementia (SD), Alzheimer’s disease...
INTRODUCTION

With increasing aging population, cognitive deteriorations due to neuro-degenerative diseases or stroke are so commonly observed in older adults that it is thought to be inevitable with aging. This situation leads us to perform comprehensive approach for the geriatric ward or preventing stroke. For dementia and stroke, a communication disorder due to language deterioration is one of the main problems.

Behavioral neurology aims to clarify the relationship between brain function and human behavior through medical approach to patients with neurodegenerative diseases or stroke. Language deterioration is one of the main targets of behavioral neurology, and its clinical applications are really useful for making better understanding of dementia or stroke patients.

In this review, we will present basic principles and clinical applications of behavioral neurology especially on language deterioration, together with some clinical cases.

BASIC PRINCIPLES

Evolution

From the evolutionary perspective, “language” can be thought about by considering birds, dogs, and humans. Birds can repeat human “words”; however, they clearly cannot understand the language, and can only produce sounds. Neurobiologically, the basal ganglia and anterior cingulate are thought to be associated with this mechanism. Mammals such as dogs can perform “attention-related sound learning”. Thus, a dog can discriminate sounds and show “body language” by shaking its tail. The thalamus and cerebral cortex are thought to provide the neurobiological background. Finally, humans can use “language” The language area is a newly developed brain area in evolution and is mainly localized in the left cerebral hemisphere. Semantic memory has also developed in humans.

Rules of Language

As shown in Figure 1, language, and especially a word, is a sequence of sounds or written characters that carries a meaning. There is a relationship between the sequence and the meaning; for example, the sequence of sounds “A RI GA TO” in Japanese has the meaning of “thank you.” The meaning can also be affected in a pragmatic way; the tone of sounds or a facial expression can demonstrate even an opposite meaning, despite use of the same sequence of sounds. People can say “thank you” to indicate gratitude or with an ironical meaning.

Key words: language, progressive non-fluent aphasia, semantic dementia, Alzheimer’s disease, vascular dementia.

(AD), and vascular dementia (VaD) can be understood. Namely, the symptoms of PA is understood by the dysfunction of peri-Sylvian language area, those of SD and AD by that of peri-peri-Sylvian language area, and those of some VaD cases and AD cases by that of right hemisphere.

Figure 1. Basic principle 2: Rules of language

Dual Route

Language is a process of auditory or visual input for the affecter, and speech or writing output from the effecter, as shown in Figure 2. This process is possible with or without accessing the semantic system. Speaking or reading aloud the sequence of sounds or written characters is possible without knowing the meaning. For example, German language can be easily read aloud according to the regular pronunciation rules; however, it may be difficult to understand. This is equivalent to repetition of human words by a bird.
THREE BRAIN AREAS ASSOCIATED WITH LANGUAGE

Figure 3 illustrates the three brain areas associated with language, with reference to basic principles. The first language area comprises multiple brain regions associated with the sequence of sounds (or written characters) (basic principle 1) and the affecter/effecter (basic principle 2). This area is called the “peri-Sylvian language area,” since it surrounds the Sylvian fissure, and includes the Broca and Wernicke areas, supramarginal and post central sulci, and precentral and postcentral sulci (regions 1-4 in Figure 3). The second language area comprises multiple brain regions associated with meaning (basic principle 1) and the semantic system (basic principle 2). This area surrounds the peri-Sylvian language area, and thus is called the “peri-peri-Sylvian language area”. The area includes the angular gyrus, posterior temporal and anterior temporal lobes, precentral sulcus, and frontal association area (regions 5-9 in Figure 3). The third language area is the right hemisphere (region 10 in Figure 3). This area is associated with the pragmatic system (basic principles 1 and 2).

ASSOCIATION OF THE JAPANESE LANGUAGE WITH THE DUAL ROUTE

Two Different Scripts: Kanji and Kana

There are two kinds of scripts in Japanese writing: Kanji (logogram) and Kana (morphogram). Generally, Kanji words are thought to correspond to irregular words in Western languages, whereas Kana words are considered to be regular words. Regular words have a “regular” rule of pronunciation. As shown in Table 2, Kana characters are learned at home, whereas Kanji characters, which are more complex, are taught at elementary school. The angular gyrus is considered to be associated with character recall for both Kana and Kanji, while the posterior inferior temporal (PIT) lobe is additionally related to Kanji recall.
Reading System

Figure 4 illustrates a schema of a reading system, including three subsystems: letter-by-letter reading, lexical reading without knowing the meaning, and lexical reading with knowledge of the meaning. Reading letter-by-letter (arrow A in Figure 4) is possible independent of the lexicon and semantic systems. Reading of the lexicon is also possible without knowing the meaning (arrow B in Figure 4), or reading can be performed with knowledge of the meaning (arrow C in Figure 4).

In contrast to Taiwanese or Chinese, speakers of Japanese can use a Kanji character to express a sound without a meaning; i.e., “on”-reading of Kanji. For example, “Indonesia” is written as 印度尼支亜 in Kanji, since the respective characters are pronounced as IN-DO-NE-SHI-A. There is no relationship with the respective meanings of each character: stamp-degree-nun-support-“A”.

Table 2. Neuropsychological background of Kanji and Kana

<table>
<thead>
<tr>
<th></th>
<th>Kana</th>
<th>Kanji</th>
</tr>
</thead>
<tbody>
<tr>
<td>Education</td>
<td>Home</td>
<td>School</td>
</tr>
<tr>
<td>Complexity</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Character recall</td>
<td></td>
<td></td>
</tr>
<tr>
<td>“Form” recall</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Writing System

For a writing system, there are also three routes: phoneme-by-phoneme writing, lexical writing without knowing the meaning, and lexical writing with knowledge of the meaning. In Kanji and Kana writing, Kana is used more frequently, but Kanji has more “form” information and semantic information.

Maeshima et al. reported the case of a 61-year-old woman with a left thalamic hemorrhage causing agraphia of Kanji. She had a decrease in the blood flow in the left thalamus as well as in the frontal lobe. The agraphia in this case may be due to the thalamic lesion itself, but the SPECT findings strongly suggest that a secondary cortical lesion may be involved in producing the higher cognitive disorder.

CLINICAL APPLICATIONS

Dysfunction of the Peri-Sylvian Language Area: Progressive Non-fluent Aphasia

Frontotemporal lobar degeneration (FTLD) encompasses a heterogeneous group of clinical syndromes that include frontotemporal dementia (FTD), progressive non-fluent aphasia (PNFA), semantic dementia (SD), etc.

Previous review reported the clinical, neuroimaging, and neuropathologic features of PNFA, a rare neurodegenerative syndrome most notable for its distinct language disturbance. Longitudinal observations of 3 patients revealed progressively telegraphic speech and writing, followed by gradual deterioration of sentence comprehension, and finally, preterminal mutism and dementia. Magnetic Resonance Imaging (MRI) revealed cortical atrophy most pronounced in anterior regions of the left hemisphere. Functional neuroimaging demonstrated reduced cerebral activity most prominently in left frontal and temporal regions.

We present a case of progressive non-fluent aphasia with lacunar infarction as an example of dysfunction in the peri-Sylvian language area. The patient was an 87-year-old, right handed man who had dysarthria, but could communicate with his family. His mother and brother had similar dysarthria.

The patient had suffered a stroke in 1997 and subsequently his dysarthria progressed. He also showed amnesia. Delusion of theft, delirium at night, and aggressiveness were noted in 2001.
He could not communicate well due to dysarthria and dementia. He was admitted to the hospital for further evaluation and rehabilitation.

Neurological examination disclosed no remarkable findings except for dysarthria. He had no buccofacial apraxia. Language skills included relatively good comprehension and good ability at naming daily items. He could repeat a word, but not a sentence. The Mini-Mental State Examination (MMSE) score was 3 and the Cognitive Abilities Screening Instrument (CASI) score was 13, with a perfect score (10/10) on the Figure copying (double pentagon) domain.

An MRI examination disclosed a lacunar infarction in the right basal ganglia region with white matter changes. The frontal and temporal lobes showed atrophic changes. Since the lacunar infarction was not associated with dysarthria, we evaluated the atrophy in detail. The voxel-based specific regional analysis system for AD (VSRAD) images comparing the two hemispheres are shown in Figure 5. The left precentral gyrus had significantly greater atrophic changes compared with the right side. This area is considered to be associated with speech output.

Dysarthria is classified as congenital (functional/organic) or acquired, with the latter class including cerebrovascular diseases, progressive non-fluent aphasia, frontotemporal lobar degeneration, and amyotrophic lateral sclerosis. The clinical course and the location of stroke supported the diagnosis of progressive non-fluent aphasia with lacunar infarction.

Dysfunction of the Peri-Peri-Sylvian Language Area: Semantic Dementia and Alzheimer Aphasia

A clinicopathologic review on FTLD reported that clinical phenotype is often assumed to be a poor predictor of underlying histopathology. They classified pathological material from 79 FTLD brains, blind to clinical diagnosis, according to topography of brain atrophy. There were highly significant relationships to clinical syndrome. Atrophy was predominantly frontal and anterior temporal in FTD, frontal markedly asymmetric peri-sylvian in PNFA, asymmetric bitemporal in SD. The findings demonstrate predictable relationships between clinical phenotype and both topographical distribution of brain atrophy. The findings emphasize the importance of refined delineation of both clinical and pathological phenotype in furthering understanding of FTLD.

We here in present a case of SD and data from patients with Alzheimer’s disease (AD) are discussed as examples of dysfunction of the peri-peri-Sylvian language area.

SD involves brain regions associated with meaning (basic principle 1) and the semantic system (basic principle 2). Areas 6 (posterior temporal lobe), 7 (anterior temporal lobe), and 9 (frontal association area) (Figure 3) are mainly degenerated.

We previously reported a case of SD with multilingualism in a 75-year-old right-handed Taiwanese woman. She had worked as a tailor before her illness, and had been able to speak Taiwanese, Japanese and Chinese fluently until 5 years ago. She gradually had symptoms of profound anomia and word-finding difficulty. Her mother language was Taiwanese and she had learned Japanese as her first symbolized language. Although she had used Chinese for most of her life, she depended on Japanese for writing and reading, such as reading a newspaper and keeping accounts. At the time of examination, she could speak only very simple Taiwanese and Japanese, and she could recognize simple Japanese characters. We speculated that reading and writing in Japanese seemed to have had a greater impact on the semantic system in this case.

It is well known that AD as per the NINCDS-ADRDA diagnostic criteria involves mainly posterior brain regions associated with meaning (basic principle 2), the semantic system (basic principle 3), and the pragmatic system (basic principles 2 and 3). Areas 5 (angular gyrus), 6 (posterior temporal lobe), and 10 (right hemisphere) (Figure 3) are mainly degenerated.
Alzheimer’s speech is referred to as ‘empty’, since patients speak fluently but with abundant pronouns due to word finding difficulties. The Picture Description Task (Figure 6) is useful for evaluation of language function in a narrative fashion. The picture contains 30 basic elements, which are shown as words on the figure (girl, telephone, call, etc.). Three variables can be analyzed: Variable 1: the amount of information conveyed, Variable 2: the number of relevant and irrelevant descriptions, and Variable 3: the efficacy of the description (the ratio of the number of relevant descriptions to the total number of descriptions).

We have found that AD patients show significantly lower scores for Variable 1 and Variable 3, and that regional cerebral blood flows in the occipital lobes and thalamus are correlated with Variable 1. This suggests that visual searching (occipital lobes) and the thalamo-cortical network are part of the neurobiological background.  

The left thalamo-cortical network has been implicated in successful speech separation and identification. Recently, the cortico-striato-thalamo-cortical network has been proposed as a new thalamo-cortical network, in association with syntactic integration of lexical elements in grammatical structure. This caused us to re-analyze our previous data from a syntactic perspective. The Picture Description Task contains 7 verbs: call, smoke, watch, do, have, play, and lie. Among the 14 AD patients, 4 showed decreased blood flow in the thalamus and 5 showed decreased blood flow in the striatum. One patient had decreases in both brain regions and showed impaired syntactic errors, i.e., impaired connections between nouns and verbs (p<0.05 by chi-square test).

In writing disturbance, AD alexia has been thought of as having a surface alexia pattern due to a deteriorated semantic system. That is, the semantic system is damaged. However, our systematic investigation suggested that several patterns may occur, rather than the surface dyslexia pattern alone, with predominance of Kanji errors, as shown in Table 3. 

**Dysfunction of the Right Hemisphere: Vascular Dementia and Alzheimer Disease**

Results from cases of vascular dementia (VaD) as per the diagnosis of NINDS-AIREN and AD are presented as examples of dysfunction of the right hemisphere. It is clinically well known that patients with right hemisphere damage showed overestimation of self-reported physical activities but also manifest communication disability, despite having no apparent language disability. We prepared an original scale, the Daily Communication Assessment Scale, and compared patients with right hemisphere damage to those with left hemisphere damage with similar MMSE scores.

The patients with left hemisphere damage had coarse speech patterns, whereas those with right hemisphere damage showed a “deviant” pattern of language, including limited information, circuitry and

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**Table 3. Alzheimer’s alexia**

<table>
<thead>
<tr>
<th>Task</th>
<th>Items</th>
<th>Sample</th>
<th>AD patients Moderate</th>
<th>AD patients Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reading task</td>
<td>Kana characters</td>
<td>46</td>
<td>えい</td>
<td>○</td>
</tr>
<tr>
<td></td>
<td>Kana transcribed words</td>
<td>122</td>
<td>いえ</td>
<td>○</td>
</tr>
<tr>
<td></td>
<td>Kanji words</td>
<td>122</td>
<td>家</td>
<td>△</td>
</tr>
<tr>
<td>Semantic task</td>
<td>Matching with objects</td>
<td>122</td>
<td></td>
<td>△</td>
</tr>
</tbody>
</table>

The signs ‘O’, ‘X’, and ‘triangle’ mean “OK”, “poor”, “partly OK”.
redundancy, excessive utterance, and disjointed conversation.

We recently reported a 79-year-old patient with chronic severe aphasia. Singing therapy was effective since her right hemisphere was relatively preserved. Interventions 1, 2, and 3 were to practice singing a song that the patient knew, to practice singing a song with a therapist, and to practice saying a greeting using a song with lyrics, respectively. After intervention 1, the patient could sing spontaneously and repeat lyrics. After intervention 2, she could sing with the therapist, and sing spontaneously and repeat lyrics. After intervention 3, she could memorize words with meaning, say the words in context, and use them. These suggest that rehabilitation therapy can still be used in patients with severe cognitive impairment.

We examined 40 AD patients using the Binet-V test and positron emission tomography (PET). The questions on illogical sentences included sentences such as, “A man saw a horse carrying a heavy bag. He felt pity, so he took the bag on his back, and rode on the horse.” Patients were asked to state what is illogical. Illogical pictures in the test (Figure 7) included 1) a girl eating curry and rice with the opposite side of the spoon, 2) a businessman walking with different shoes on his right and left feet, 3) a family holding a barbeque in the garden in the rain, and 4) a boy giving water to a flower garden using a hose, but the opposite end is not connected with the water.

We found that the scores on verbal illogical questions were correlated with regional glucose metabolism in the right angular gyrus and the bilateral temporal and parietal lobes (neurobiologically meaningful findings), and those on illogical pictures were correlated with regional glucose metabolism in the right angular gyrus.

**CONCLUSION**

Language is sequences of sound or characters that carry meanings for communication. There are two routes, the superficial and deep routes, with the latter associated with meaning, and three brain areas are involved: the peri-Sylvian area, per-peri-Sylvian area, and right hemisphere. Using these principles, language symptoms of cases of dementia with progressive non-fluent aphasia, semantic dementia, Alzheimer’s disease, and vascular dementia can be understood.

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**REFERENCES**