

News Release

Title

Semantic deficits in ALS related to right lingual/fusiform gyrus network involvement

Key Points

○ It has been reported that amyotrophic lateral sclerosis (ALS), which causes symptoms such as motor paralysis and muscle atrophy, can also affect cognitive function.

○ It was revealed that approximately half of ALS patients were impaired in reading Jukujikun, which is a word category similar to exception words.

○ It has been known that Jukujikun and exception words reading are impaired in patients with frontotemporal lobar degeneration (FTLD) as a symptom of semantic deficits.

○ Various similarities have reported between ALS and FTLD, and the Jukujikun reading impairments in ALS may reflect semantic deficits similar to those in FTLD.

○ Besides, using resting-state functional MRI, associated network alterations were identified as a neural basis of this impairment. In this research, instead of focusing on a single brain region, the findings could be obtained by assuming abnormalities in the brain network involving multiple brain regions. Such a perspective is important for understanding various neuropsychological symptoms and useful for the other brain imaging researches

Summary

The clinicopathological continuity between amyotrophic lateral sclerosis (ALS) and frontotemporal lobar degeneration (FTLD) is well known. Although ALS demonstrates language symptoms similar to FTLD, including semantic dementia, word reading impairments in ALS have not been well studied. “Jukujikun” are Kanji-written words with irregular pronunciation comparable to “exception words” and useful for detecting semantic deficits in Japan. We investigated Jukujikun reading impairments and related network changes in ALS. This work was published online in *EBioMedicine* on, Sep. 3, 2019

We enrolled 71 ALS patients and 69 healthy controls (HCs) and examined neuropsychological factors including low frequency Jukujikun reading. We performed resting-state functional magnetic resonance imaging (rsfMRI) with voxel-based graph analysis on a subset of participants who agreed. Low frequency Jukujikun score was decreased in ALS compared with HCs, and 52 percent of ALS had low frequency Jukujikun score of ≤ 5 th percentile of HCs. In the rsfMRI with graph theoretical analysis, ALS with positive Jukujikun deficit showed decreased degree centrality in the right lingual/fusiform gyrus, where connectivities with regions associated with word perception, semantic processing, or speech production were decreased. They also showed increased degree centrality in the left inferior/middle temporal gyrus, associated with increased connectivities involving semantic processing. Dysfunction of the “hub” in the

right lingual/fusiform gyrus can affect semantic deficit in ALS. Considering neuropsychological symptoms as network impairments is vital for understanding various diseases.

Research Background

Approximately 15% of amyotrophic lateral sclerosis (ALS) patients have clinical features similar to frontotemporal lobar degeneration (FTLD). Moreover, 9.1 to 40% of ALS patients can show language impairment, such as exception word reading and production difficulties similar to semantic dementia (SD) and progressive non-fluent aphasia (PNFA). “Jukujikun” is a category of words with irregular pronunciation and is often used to detect semantic impairments in patients with SD in Japan. However, it is not known whether Jukujikun reading impairments exist in ALS patients and what brain networks would be associated with the impairment.

Research Results

Fifty-two percent of ALS patients had low frequency Jukujikun score of ≤ 5 th percentile of HCs. Voxel-based graph theoretical analysis revealed the right fusiform/lingual gyrus as a hub region associated with the impairment. Subsequent seed-based analysis showed decreased connectivity of the right fusiform/lingual gyrus with regions associated with visual word perception, semantic processing, and speech beyond hypothesis-driven study based on local pathology. Besides, left inferior/middle temporal gyrus showed its increased hub function and connectivity with regions associated with semantic processing or phonological processing.

Research Summary and Future Perspective

Approximately half of ALS patients showed low frequency Jukujikun reading impairment. “Hub” dysfunction and decreased network in the right lingual/fusiform gyrus could be crucial for its network basis. The increased network including left inferior/middle temporal gyrus seemed to be an associated alteration, which could be a compensation. Our study revealed semantic deficits in ALS similar to FTLD using Jukujikun reading and its related network alteration using rsfMRI. These findings are expected to lead to elucidations of the pathology of both diseases or developments of new therapies including rehabilitations in the future. Our results suggest that clinical symptoms are not solely derived from one lesion but from network impairment. Voxel-based graph theoretical hub analysis may uncover the network-based impairments of specific cognitive tasks.

Publication

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