Commentary

Reading, semantic loss and neural networks in Japanese ALS patients

Julie S. Snowden

Cerebral Function Unit, Manchester Centre for Clinical Neurosciences, Salford Royal NHS Foundation Trust, Salford and Division of Neuroscience and Experimental Psychology, School of Biological Sciences, University of Manchester, UK

A unique characteristic of the Japanese language is its dual writing systems. Whereas *kana* (phonograms) have an invariant and predictable correspondence between the written form and its pronunciation, *kanji* (morphograms) do not. In this issue of *EBioMedicine*, Prof Gen Sobue and colleagues [1] report a study of reading in amyotrophic lateral sclerosis (ALS), in which they focus attention on a subset of *kanji* words referred to as Jukujikun, for which the pronunciation of the whole bears no relationship to that for its constituent parts. The authors offer a striking example. The *kanji* character that means 'snow' is pronounced either "YUKI" or "SETSU", the character for 'collapse' is pronounced "HOH", but when those two characters are combined to designate the meaning 'avalanche' they are pronounced "NADARE". This is intriguing, but why should such apparent linguistic idiosyncrasies be theoretically relevant or of general clinical interest in relation to people with ALS?

There are a number of reasons. Jukujikun represent a particularly pure example of words that cannot be 'sounded out' phonetically from their component parts and therefore have implications for and place constraints on models of reading. Pronunciation depends on semantic context and access to the characters' meaning. The closest, albeit imperfect, parallel in English are exception words such as 'sew' or 'pint', whose pronunciation does not conform to the typical rendition of the letter string: the pronunciation of 'sew' might *a priori* be expected to rhyme with 'few', 'new' and 'pew', and the pronunciation of 'pint' with 'hint', 'mint' and 'tint'. The traditional dual-route model proposes that the reading of exception words requires the involvement of a direct lexical/semantic route, whereby the sound of a word is accessed directly from the whole word form/word meaning. In keeping with the proposed semantic demands, a difficulty reading exception words is a hallmark of semantic dementia, a degenerative disorder of the temporal lobes, in which patients lose understanding of words. Similarly, a study of 10 Japanese patients with semantic dementia showed an association between overall severity of patients' semantic disorder and reading impairment of *kanji,* the strongest relationship being with inconsistent atypical kanji, which includes Jukujikun [2]. Reading performance of Jukujikun therefore represents a potentially sensitive marker of semantic loss.

The particular relevance to ALS stems from the established link between ALS and frontotemporal dementia (FTD), of which semantic dementia is one clinical form. Studies of cognitive change in ALS have hitherto paid most attention to executive functioning, but there is growing awareness that language problems may be a prominent feature [3], with some authors suggesting that language disorder may be even more common than executive impairments [4]. What is clear is that full understanding of the cognitive changes in ALS depends on assessments that address the range of symptoms that are associated with FTD. It is within this context that the study by Sobue and colleagues is especially welcome. Single case reports confirm that ALS may occur in association with word meaning aphasia (semantic dementia) and *kanji* reading impairment [5], although a study of writing in 14 Japanese ALS patients [6] reported *kana* errors to be more common. The study by Sobue and colleagues is the first of which I am aware to investigate *kanji* reading in a very large consecutive cohort of ALS patients. The study demonstrates Jukujikun reading deficits in a high proportion of patients, raising the possibility that semantic deficits may be a more common feature of ALS patients' language disorder than generally recognised. Jukujikun reading performance may constitute an early indicator of semantic processing impairments in ALS.

Kana and *kanji* reading and writing are known to have different neural bases [7,8], reflecting their differential underlying cognitive processing demands. Sobue and colleagues extend previous neuroimaging work by their examination, in a proportion of patients, of the relationship between Jukujikun reading and resting-state functional magnetic resonance imaging network findings, based on voxel-based graph analysis. The authors' identification of a critical role of the right fusiform/lingual gyrus raises tantalizing questions about the role of perception, imagery and visual semantic processing in Jukujikun reading. It also underscores the importance of widespread network abnormalities underpinning cognitive symptoms.

The earliest report of language problems in ALS was published more than a century ago in 1893 by the Japanese author Watanabe [9], many years before non-motor symptoms in ALS began to receive widespread recognition. The paper by Sobue and colleagues in this issue adds to the long line of notable Japanese contributions to clinical neuroscience and to the understanding of language and cognition in ALS.

Author contributions

JS critically reviewed the article by Sobue and colleagues, accessed relevant literature, interpreted findings and wrote the commentary.

Declaration of Competing Interest

Dr. Snowden has nothing to disclose.

References

[1] Ogura A, Watanabe H, Kawabata K, et al. Semantic deficits in ALS related to right lingual/fusiform gyrus network involvement: A case control study. EBioMedicine 2019. https://doi.org/10.1016/j.ebiom.2019.08.022.

[2] Fushimi T, Komori K, Ikeda M, Lambon Ralph MA, Patterson K. The association between semantic dementia and surface dyslexia in Japanese. Neuropsychologia 2009;47:1061–8. https://doi.org/10.1016/j.neuropsychologia.2008.12.030.

[3] Strong MJ, Abrahams S, Goldstein LH, et al. Amyotrophic lateral sclerosis – frontotemporal spectrum disorder (ALS-FTSD): revised diagnostic criteria. Amyotroph Lateral Scler Frontotemporal Degener 2017;18:153–74. https://doi.org/10.1080/21678421.2016.1267768.

[4] Taylor LJ, Brown RG, Tsermentseli S, et al. Is language impairment more common than executive dysfunction in amyotrophic lateral sclerosis? J Neurol Neurosurg Psychiatry 2013;84:494–8. https://doi.org/10.1136/jnnp-2012-303526.

[5] Iroi A, Okuma Y, Fukae J, Fujishima K, Goto K, Mizuno Y. Amyotrophic lateral sclerosis presented with alexia of kanji and word meaning aphasia. Brain Nerve 2002;54:903–7.

[6] Ichikawa H, Hieda S, Ohno H, et al. Kana versus Kanji in amyotrophic lateral sclerosis: a clinicoradiological study of writing errors. Eur Neurol 2010;64:148–55. https://doi.org/10.1159/000317011.

[7] Sakurai Y, Momose T, Iwata M, Sudo Y, Ohtomo K, Kanazawa I. Different cortical activity in reading of Kanji words, Kana words and Kana nonwords. Cogn Brain Res 2000;9:111–5. https://doi.org/10.1016/S09266410(99)00052-X.

[8] Sakurai Y. Kanji (morphogram) and Kana (Phonogram) problem in Japanese Alexia and Agraphia. Front Neurol Neurosci 2019;44:53–63. https://doi.org/10.1159/000494952.

[9] Ichikawa H, Miller MW, Kawamura M. Amyotrophic lateral sclerosis and language dysfunction: kana, kanji and a prescient report in Japanese by Watanabe (1893). Eur Neurol 2011;65:144–9. https://doi.org/10.1159/000324336.