International Journal of Gerontology 15 (2021) 174–176
https://doi.org/10.6890/IJGE.202104_15(2).0017

International Journal of Gerontology

journal homepage: http://www.sgecm.org.tw/ijge/

Case Report

Possibility of Cognitive Improvement in Severe Dementia: A Case Series Assessed by Cognitive Test for Severe Dementia

Hiroyuki Tanaka [a *], Yuma Nagata [a,b], Daiki Ishimaru [a,b], Yasuhiro Ogawa [a,c], Keita Fukuhara [a,d], Takashi Nishikawa [a,d]

[a] *Graduate School of Comprehensive Rehabilitation, Osaka Prefecture University, Osaka, Japan,* [b] *Department of Psychiatry, Osaka University Graduate School of Medicine, Osaka, Japan,* [c] *Department of Occupational Therapy, Morinomiya University of Medical Sciences Faculty of Health Sciences, Morinomiya, Japan,* [d] *Division of Occupational Therapy, Department of Rehabilitation, Faculty of Health Sciences, Naragakuen University, Nara, Japan*

ARTICLE INFO

Accepted 28 September 2020

Keywords:
dementia,
cognitive test,
cognitive function

SUMMARY

Improvements in the cognitive function of patients with severe dementia may be overlooked if the tests being used have low sensitivity. The Cognitive Test for Severe Dementia (CTSD) that we previously developed is sensitive to such changes. Here, we report four severe dementia subjects whose cognitive function improved, assessed by CTSD as "Minimal Detectable Change" after one year of daily clinical intervention. Comparably, their Mini-Mental State Examination scores remained unchanged. With the use of a test tailor-made for severe dementia such as the CTSD, it is also possible to appreciate the effects of daily clinical treatment and rehabilitation better and in greater detail. "Clinically significant cognitive improvement can be quantified by devising interventions and outcome measures, even in severe stage dementia".

1. Introduction

It is important to assess cognitive function using the appropriate assessment scales.[1] Traditional scales such as the Mini-Mental State Examination (MMSE)[2] or Alzheimer Disease Assessment Scale (ADAS)[3] have proved inadequate in detecting severe cognitive impairment and decline, tending to show floor effects in patients with severe dementia.[4] Further, the lack of a reliable assessment tool has also made it difficult to monitor the effectiveness of treatment in severe dementia. To solve this problem, we previously developed the Cognitive Test for Severe Dementia (CTSD), which is sensitive enough to detect treatment efficacy.[5]

The CTSD has been evaluated as valid and reliable.[5] In our previous study, we found cognitive improvement in four subjects with severe dementia who exceeded the Minimal Detectable Change (MDC) (over 4 points)[6] among 40 subjects assessed for long-term changes for twelve months after baseline assessment. Although MMSE was measured simultaneously, none of the subjects exceeded MDC of MMSE (over 3 points).[7] In other words, by using a specialized test such as CTSD for severe dementia, it is possible to detect improvements that are overlooked during clinical studies. Herein, we discuss four cases of severe dementia wherein cognitive improvement was appreciated due to the excellent sensitivity of the CTSD in a daily clinical setting.

2. Cases

This case series study is a continuation of our previous study,[5,6] spanning the period from April 2015 to March 2017.

We conducted a single-center observational study at three time-points (baseline [the day a patient started rehabilitation] and after 6 and 12 months from baseline) in a rural recuperation hospital at Hyogo prefecture, Japan. Almost all patients had dementia of varying severity and etiology, with approximately half having severe disease. Major neurocognitive disorders were assessed and classified using the Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-5). Most patients in this hospital would undergo rehabilitation interventions (physiotherapy, occupational therapy, and speech therapy) at least twice a week.

2.1. Identifying four cases that showed improved cognitive function

At baseline, 161 severe dementia patients were assessed using Clinical Dementia Rating (CDR). We excluded 121 who were discharged, relocated, or died. The remaining 40 who could be followed up over 12 months were divided into three groups based on their MDC scores. The first group (n = 19) had worsened cognitive function, exceeding MDC of CTSD. The second group (n = 17) maintained their cognitive function, with no change in the MDC. The third group (n = 4), which was the focus of this study, only contained the patients diagnosed with vascular dementia (VaD) and had improved scores, exceeding the MDC. They showed no improvement in MMSE scores, and their MMSE MDC was 3 points.[9] Therefore, CTSD demonstrated greater sensitivity than MMSE for severe dementia.

2.2. Ethical considerations

This study was approved by the ethics committee of Osaka Pre-

* Corresponding author. Osaka Prefecture University Graduate School of Comprehensive Rehabilitation, 3-7-30 Habikino, Habikino-City, Osaka 5838555, Japan.
E-mail address: hytanaka@rehab.osakafu-u.ac.jp (H. Tanaka)

fecture University (2017-207). Written informed consent was obtained from a family member of each participant.

2.3. Description of individual cases

2.3.1. Medical histories of cases

Case 1: An 84-year-old woman with cerebrovascular dementia post right thalamic hemorrhage. Baseline assessment was performed 1085 days after hospital admission. She was prescribed warfarin, amlodipine, and brotizolam. Her MMSE score was 1, and CTSD was 13. She was bedridden, needed complete assistance in activities of daily living (ADLs), and was fed via gastrostomy.

Case 2: An 82-year-old man had cerebrovascular dementia post right putaminal hemorrhage. He also had cerebral infarction ten years earlier. Baseline assessment was performed 849 days after admission. He was prescribed aspirin, amlodipine, and brotizolam. MMSE score was 4; CTSD was 9. Gastrostomy was used for feeding, and he was fully assisted and bed ridden during the day.

Case 3: A 96-year-old woman had mixed multi-infarct dementia with Alzheimer's Disease (AD). She also had cerebral infarction and subarachnoid hemorrhage five years earlier and AD diagnosis seven years earlier. Baseline assessment was performed 1376 days after admission. She was prescribed aspirin and amlodipine. MMSE score was 1, and CTSD was 6. She was bedridden with restraints, needed full assistance, and was fed by gastrostomy.

Case 4: An 87-year-old woman had cerebrovascular dementia post multiple cerebral infarctions one year earlier. Baseline assessment was performed 336 days after admission. She was prescribed warfarin, amlodipine, and brotizolam. MMSE score was 11, and CTSD was 23. She was bedridden, needed full assistance, but could consume food orally.

For all four patients, baseline assessment was performed 911.5 $\pm$ 440.1 (range: 336–1376) days after admission. All cases were prescribed physiotherapy and/or occupational and/or speech therapy for 20 minutes, four to six times a week.

One year later, the four subjects carried out more physical activities with a therapist, and getting out of bed and oral feeding became possible. During the study period, there were no significant morbidities or changes in medication. There were no major changes in medications.

2.3.2. Assessment scales

Table 1 shows the results of baseline assessment scales. Cognitive function was assessed by MMSE and CTSD. The ability to carry out ADLs was assessed using the Physical Self-Maintenance Scale (PSMS), which showed the need for complete assistance in all activities. The scores on feeding items among Cases 1, 2, and 3 all improved 1 point from baseline. The behavioral and psychological symptoms of dementia (BPSD) were assessed using the Neuro Psychiatric Inventory-Nursing Home version (NPI-NH); it showed lower neuropsychiatric symptoms in all cases except for case 3. Case 3 had severe neuropsychiatric symptoms at baseline, and this score was reduced from 33 to 17 points one year after. Nutritional status was assessed using Mini-Nutritional Assessment-Short Form (MNA-SF), which showed malnutrition in all cases. Comorbidities, assessed using the Charlson Comorbidity Index (CCI), were high to very high in all cases due to cerebrovascular disorders and dementia. The MNA-SF and CCI scores were unchanged after one year.

2.3.3. Summary of cognitive improvement among the four cases

Figure 1 shows the cognitive improvement scores after one year as measured on MMSE and CTSD for each case. **Case 1**: 1 to 2 points (1-point increase) and 13 to 19 points (6-point increase); **Case 2**: 4 points to 2 points (2-point decrease) and 9 to 16 points (7-point increase); **Case 3**: 1 to 2 points (1-point increase) and 6 to 10 points (4-point increase); **Case 4**: 11 to 11 (unchanged) and 23 to 27 points (4-point increase) (Figure 1).

3. Discussion

Improvement in cognitive function in severe dementia has not yet been reported since the current cognitive tests are insufficient for severe disease. To our knowledge, this is the first study to report that cognitive function improvement is possible in four severe VaD cases, as assessed by CTSD.

We believe that this is mainly due to the superior sensitivity of the CTSD. First, regarding its sensitivity, the CTSD can measure a wide range of cognitive domains and functionsin a short time, tailored to the attentional resources of less severe dementia, and capture cognitive changes in more detail than existing cognitive tests.[5,6] The present report proved that CTSD detected not only cognitive decline but also detailed improvement.

Second, also interesting was that the clinical profiles of each of the present cases were similar. They were all diagnosed with cerebrovascular dementia, continued pharmacotherapy for cerebrovascular disease, and improved daily mobility and eating performance (except Case 4), shifting from gastrostomy to oral feeding. These cases did not receive any novel therapeutic interventions but experienced cognitive improvement. Indeed, previous studies have shown that cerebrovascular pharmacological intervention,[8] an increase in physical activity,[9] and improving abilities to masticate and eat orally[10] improve cognitive function. Hence, using a test specifically for severe dementia, such as the CTSD, may also provide more detailed insight into the effects of routine treatment and rehabilitation that may have been previously masked.

Recently, therapeutic applications of Transcranial Magnetic Stimulation (TMS) for cortical plasticity in AD have also been reported.[11] Related studies have investigated cortical plasticity and neuropsychological tests,[12] and it has been reported that cortical plasticity is strongly associated with reduced cognitive impairment.[13] Patients with severe dementia have a low possibility of improving cognitively, and thus, are redirected to end-of-life care and generally excluded from clinical studies aimed at improving cognition. Com-

Table 1
Baseline assessment of the cases.

Case	Age	Type	Sex	Age	Date of hospitalization	MMSE	CTSD	PSMS	NPINH	MNASF	CCI
1	84 y	VaD	Female	84	1085	1/30	13/30	12/30	3/144	8/14	4/37
2	82 y	VaD	Male	82	849	4/30	9/30	10/30	1/144	7/14	3/37
3	96 y	Mixed	Female	96	1376	1/30	6/30	8/30	33/144	7/14	5/37
4	87 y	VaD	Female	87	156	11/30	23/30	14/30	3/144	8/14	6/37

MMSE = Mini Mental State Examination, CTSD = Cognitive Test for Severe Dementia, PSMS = Physical Self-Maintenance Scale (PSMS), NPI-NH = Neuro Psychiatric Inventory-Nursing Home version, MNA-SF = Mini Nutritional Assessment-Short form(MNA-SF), CCI = Charlson Comorbidity Index.

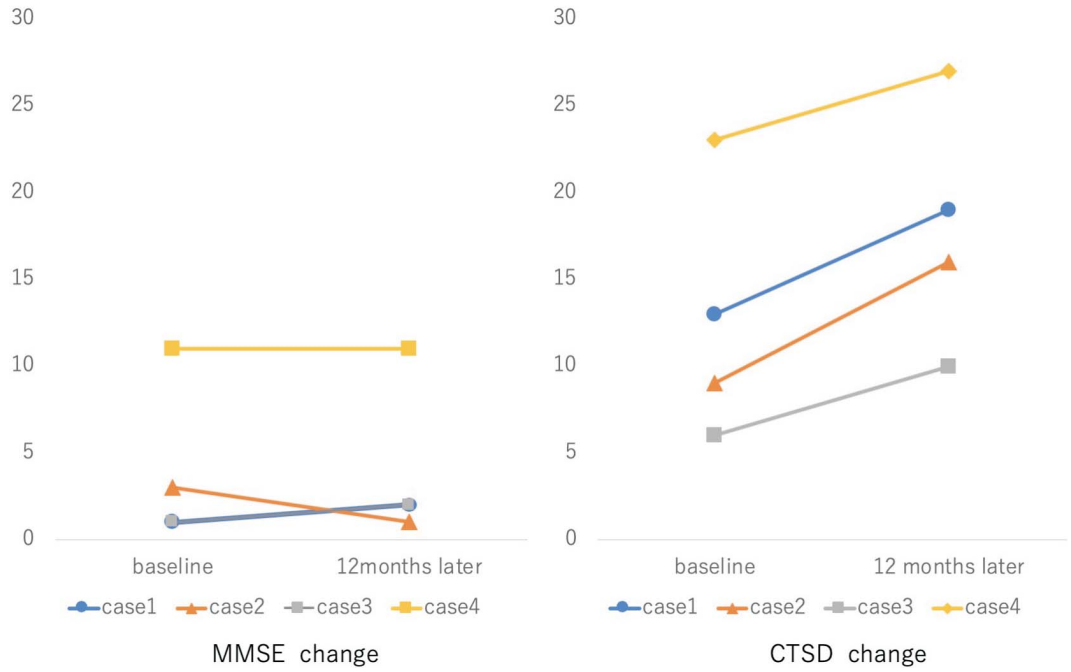

Figure 1. Changes of the MMSE and CTSD scores over a 12-month period. The MMSE scores remained unchanged while the CTSD scores improved by 6, 7, 4 and 4 points for cases 1–4 respectively. Abbreviations: MMSE = Mini-mental State Examination; CTSD = Cognitive Test for Severe Dementia.

bining the use of TMS with tests such as CTSD as an outcome measuremay broaden the range of disease severity to be covered.

4. Conclusion

Clinically significant cognitive improvement can be quantified by devising interventions and outcome measures, even in severe dementia.

Funding

This work was supported by JSPS KAKENHI Grant-in-Aid for Scientific Research (C) 19K11421.

Conflict of interest

The authors declare no conflicts of interest.

References

1. Vellas B, Gauthier S, Allain H, et al. Consensus statement on dementia of Alzheimer type in the severe stage. *J Nutr Health Aging*. 2005;9(5):330–338.
2. Folestein MF, Folstein SE, McHugh PR. “Mini-mental state”. A practical method for grading the cognitive state of patients for the clinician. *J Psychiat Res*. 1975;12(3):189–198.
3. Mohs RC, Rosen WG, Davis KL. The Alzheimer’s disease assessment scale: an instrument for assessing treatment efficacy. *Psychopharmacol Bull*. 1983;19(3):448–450.
4. Herrmann N, Gauthier S, Lysy PG. Clinical practice guidelines for severe Alzheimer’s disease. *Alzheimers Dement*. 2007;3(4):385–397.
5. Tanaka H, Nagata Y, Uematsu M, et al. Development of the cognitive test for severe dementia. *Dement Geriatr Cogn Disord.* 2015;40(1–2):94–106.
6. Tanaka H, Nagata Y, Ishimaru D, et al. Clinical utility of the cognitive test for severe dementia: Factor analysis, minimal detectable change, and longitudinal changes. *Dement Geriatr Cogn Dis Extra*. 2018;8(2):214–225.
7. Feeney J, Savva GM, O’Regan C, et al. Measurement error, reliability, and minimum detectable change in the Mini-Mental State Examination, Montreal Cognitive Assessment, and color trials test among community living middle-aged and older adults. *J Alzheimers Dis*. 2016;53(3):1107–1114.
8. Douiri A, McKevitt C, Emmett ES, et al. Long-term effects of secondary prevention on cognitive function in stroke patients. *Circulation.* 2013; 128(12): 1341–1348.
9. Forbes D, Thiessen EJ, Blake CM, et al. Exercise programs for people with dementia. *Cochrane Database Syst Rev.* 2013;12:CD006489.
10. Tada A, Miura H. Association between mastication and cognitive status: A systematic review. *Arch Gerontol Geriatr.* 2017;70:44–53.
11. Koch G, Esposito Z, Kusayanagi H, et al. CSF Tau levels influence cortical plasticity in Alzheimer’s disease patients. *J Alzheimers Dis*. 2011;26(1): 181–186.
12. Lorenzo F, Motta C, Bonni S, et al. LTP-like cortical plasticity is associated with verbal memory impairment in Alzheimer’s disease patients. *Brain Stimul*. 2019;12(1):148–151.
13. Motta C, Lorenzo F, Ponzo V, et al. Transical magnetic stimulation predicts cognitive decline in paitents with Alzheimer’s disease. *J Neurol Neurosurg Psychiatry.* 2018;89(12):1237–1242.