Brain Neurorehabil. 2024 Jul;17(2):e11
https://doi.org/10.12786/bn.2024.17.e11
pISSN 1976-8753·eISSN 2383-9910

Brain & NeuroRehabilitation

Case Report

Cerebrolysin Concentrate: Therapeutic Potential for Severe Oral Apraxia After Stroke: A Case Report

Hyeonwoo Jeon, Doo Young Kim

Received: Jan 29, 2024
Revised: May 9, 2024
Accepted: Jun 9, 2024
Published online: Jun 17, 2024

Correspondence to
Doo young Kim
Department of Rehabilitation Medicine, International St. Mary's Hospital, The Convergence Institute of Healthcare and Medical Science, Catholic Kwandong University College of Medicine, Incheon 22711, Korea.
Email: kdygeno@gmail.com

HIGHLIGHTS

- Stroke involving the Lt insular cortex is accompanied by severe oral apraxia.
- Cerebrolysin concentrate is effective for severe oral apraxia after stroke.

Brain Neurorehabil. 2024 Jul;17(2):e11
https://doi.org/10.12786/bn.2024.17.e11
pISSN 1976-8753·eISSN 2383-9910

bnr
Brain & NeuroRehabilitation

Case Report

Cerebrolysin Concentrate: Therapeutic Potential for Severe Oral Apraxia After Stroke: A Case Report

Hyeonwoo Jeon [1], **Doo Young Kim** [1,2]

[1]Department of Rehabilitation Medicine, International St. Mary's Hospital, Catholic Kwandong University College of Medicine, Incheon, Korea
[2]The Convergence Institute of Healthcare and Medical Science, Catholic Kwandong University College of Medicine, Incheon, Korea

Received: Jan 29, 2024
Revised: May 9, 2024
Accepted: Jun 9, 2024
Published online: Jun 17, 2024

Correspondence to
Doo young Kim
Department of Rehabilitation Medicine, International St. Mary's Hospital, The Convergence Institute of Healthcare and Medical Science, Catholic Kwandong University College of Medicine, Incheon 22711, Korea.
Email: kdygeno@gmail.com

ORCID iDs
Hyeonwoo Jeon
https://orcid.org/0009-0009-3869-913X
Doo Young Kim
https://orcid.org/0000-0003-1327-5348

Funding
This research was supported by a grant of the Korean Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: RS-2024-00263587).

ABSTRACT

Cerebrolysin concentrate is a medication whose main active ingredient is brain-derived neurotrophic factor. It has been reported to help in the restoration of cognitive function and overall physical function after brain injuries. We present the case of a 72-year-old man with severe oral apraxia due to a left middle cerebral artery ischemic stroke involving the left insular cortex. He was being tube fed due to severe oral apraxia with cognitive decline that made it difficult for him to even imitate simple oral movements. The patient initially had impaired consciousness and cognitive function. He also had limited physical activity due to acute stroke complications, such as hemorrhagic transformation of cerebral infarction, and required bed rest until 23 days after onset. The patient received intravenous cerebrolysin concentrate in addition to intensive rehabilitation therapy from 23 days after onset. After rehabilitation and administration of cerebrolysin concentrate, there was a marked recovery within a short period of time to the point where oral intake of a regular diet was possible, indicating a significant improvement in oral apraxia. It is a notable example of the potential therapeutic effect of cerebrolysin concentrate for post-stroke oral apraxia.

Keywords: Apraxias; Brain-Derived Neurotrophic Factor; Cerebrolysin; Stroke

INTRODUCTION

Stroke remains a significant global health concern affecting millions of individuals, particularly in the elderly population, where it ranks among the leading causes of death and disability [1]. About 60%–80% of all strokes are ischemic strokes, characterized with irreversible changes in brain tissue attributed to ischemia, resulting in subsequent disability for the patient [1,2]. Therefore, in the acute phase, reperfusion strategies involving pharmacological and mechanical interventions are widely used to minimize ischemic damage [2]. Extending the therapeutic approach of neuroprotection and repair, recent clinical studies have also explored strategies to repair brain cells that have already been damaged after stroke [3].

Brain-derived neurotrophic factor (BDNF) is known to improve brain plasticity, contributing to the formation of new neuronal synapses, and thus improving consciousness and cognitive function in degenerative brain disorder such as Alzheimer's disease [4]. Recently, clinical

Conflict of Interest
The authors have no potential conflicts of interest to disclose.

Author Contributions
Conceptualization: Kim DY; Data curation: Jeon H; Formal analysis: Kim DY, Jeon H; Writing - original draft: Jeon H; Writing - review & editing: Kim DY.

studies have reported that BDNF has a positive effect on neuroprotection and neurorecovery of brain cells in the post-stroke rehabilitation phase [5,6].

Cerebrolysin concentrate is a medication whose main active ingredient is BDNF, which belongs to the category of neuropeptide preparations [5,7]. It has been reported to help in the restoration of cognitive function and overall physical function after brain injuries [8-12]. However, to our knowledge, there is no report of this medication in patients with post-stroke oral apraxia. We report a case of a patient with left middle cerebral artery ischemic stroke who had severe cognitive and physical impairment, accompanied by severe oral apraxia, which made oral ingestion of any diets impossible. The patient showed significant functional improvement after receiving cerebrolysin concentrate via intravenous infusion in addition to rehabilitation. In addition to the recovery of cognitive and physical functions, the severe oral apraxia also improved, and within a short period of time, swallowing function improved and he was able to orally ingest his regular diet, which is a notable example of the potential therapeutic effect of cerebrolysin concentrate for post-stroke oral apraxia.

CASE DESCRIPTION

A 72-year-old male patient was found collapsed outside his home and brought to the emergency department, where brain magnetic resonance imaging (MRI) confirmed a left middle cerebral artery infarction. The infarct involved the left basal ganglia, corona radiata, supramarginal gyrus, arcuate fasciculus, primary motor cortex, premotor cortex, and insular cortex (**Fig. 1**). The patient had a history of lumbar spondylosis, spinal stenosis, diabetes, and atrial fibrillation, but was capable of independent ambulation and activities of daily living (ADLs) prior to the stroke. His initial National Institutes of Health Stroke Scale (NIHSS) score was 12 out of 42, and his right upper and lower extremity muscle strength was Medical Research Council (MRC) grade 2. Admitted to the neurology department, the patient received acute stroke care and was transferred to the rehabilitation department 14 days after onset.

On the 15th day after onset, the first day of transfer to the rehabilitation department, he had a decrease in consciousness and underwent a follow-up MRI, which revealed hemorrhagic transformation of the infarcted area. To stabilize his vital signs, the patient had to be placed on bed rest with fluid therapy. It was 23 days after onset when vital signs were stable and rehabilitation could begin in earnest, and we began treatment with cerebrolysin concentrate via intravenous infusion concurrent with rehabilitation. Rehabilitation included 2 hours of physical therapy and 1 hour of occupational therapy each day for 5 days per week, and

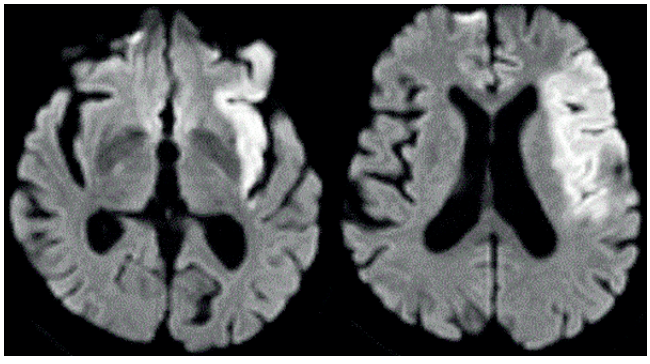

Fig. 1. Brain diffusion-weighted magnetic resonance imaging, involving left insular cortex.

https://doi.org/10.12786/bn.2024.17.e11

Cerebrain® (Daewoong-Bio, Jecheon, Korea) was administered through intravenous infusion for 14 days, with a daily dose of 20 mL diluted in 100 mL normal saline.

The patient's condition prior to cerebrolysin concentrate administration was MRC grade 2 overall muscle strength of the right upper and lower extremity, with a Coma Recovery Scale (CRS) [13] of 7 (Auditory 1, Visual 2, Motor 3, Oromotor/verbal 1, Communication 0, Arousal 0). He was completely dependent on caregivers for ADLs in bed, unable to imitate oral or limb movements, and unable to speak spontaneously. His Berg Balance Scale (BBS) score, which indicates balance ability, was 0, and his modified Barthel index (MBI) score, which indicates performance ADLs, was 0. He had a score of 0 on the Korean version of the French Aphasia Screening Test (K-FAST) [14]. The oral domain score in the Limb and Oral Apraxia Test [15] was 0, and severe oral apraxia necessitated tube feeding (**Table 1**).

On day 5 of cerebrolysin concentrate administration (28 days after onset), the patient's CRS score improved to 13 (Auditory 2, Visual 3, Motor 5, Oromotor/verbal 1, Communication 0, Arousal 2). Motor function improved, allowing him to balance himself in a seated position, and he was able to perform a formal speech assessment. At the completion of 14 days of cerebrolysin concentrate therapy (36 days after onset), his CRS score reached 18 (Auditory

Table 1. Key clinical progressions

Outcomes	23 days after onset (before cerebrolysin administration)	36 days after onset (completion of cerebrolysin administration)	58 days after onset (at discharge)
CRS_Auditory	1	3	4
CRS_Visual	2	4	5
CRS_Motor	3	5	6
CRS_Oromotor/verbal	1	2	3
CRS_Communication	0	2	2
CRS_Arousal	0	2	3
CRS_Total	7	18	23
MMSE	Uncheckable	Uncheckable	7
K-FAST	0	3	4
Upper extremity strength on the paretic side	MRC 2	MRC 3	MRC 3
Lower extremity strength on the paretic side	MRC 2	MRC 3	MRC 3
BBS	0	23	39
MBI	0	29	75
Oral apraxia test (16)			
Verbal command (8)			
Imitate blowing a kiss	0	1	2
Inflate your cheeks like balloons	0	1	2
Bite your lower lip with your upper teethes	0	1	2
Simulate chewing gum	0	1	2
Push your cheek with your tongue	0	0	2
Stick out your tongue	0	1	2
Mimic blowing out a candle	0	1	2
Pretend to sip a drink through a straw	0	0	2
Imitation of gesture (8)			
Smile while showing your teeth	0	0	2
Make your lips round and protrude them forward	0	1	2
Make a ‘tutting’ sound and touch your tongue	0	0	2
Lick spilled milk from your lips	0	0	2
Push your cheek with your tongue	0	0	2
Stick out your tongue	0	1	2
Pretend to blow out a candle	0	1	2
Mimic drinking through a straw	0	0	2

Oral domain of Limb and Oral Apraxia test for Korean, scoring of each item as incorrect (0), partially adequate (1), adequate (2), and correct (3).
CRS, Coma Recovery Scale; MMSE, Mini-Mental State Examination; K-FAST, Korean version of Frenchay Aphasia Screening Test; MRC, Medical Research Council; BBS, Berg Balance Scale; MBI, modified Barthel index.

https://doi.org/10.12786/bn.2024.17.e11

3, Visual 4, Motor 5, Oromotor/verbal 2, Communication 2, Arousal 2) and his right upper and lower extremity muscle strength improved to MRC grade 3. In addition, his BBS was 23, MBI was 29, and K-FAST was 3. His apraxia improved to the status of imitating limb and oral movements, and he demonstrated spooning when asked to "pretend to eat." As he was able to respond to simple commands for oral movements and swallowing, a videofluoroscopic swallowing study (VFSS) was planned.

VFSS was performed 8 days after completion of cerebrolysin concentrate administration (44 days after onset). Moderate premature bolus loss was observed throughout the diet with decreased tongue movement in the oral phase, but there were no notable findings suggestive of oral apraxia such as tongue hesitation or groping. No oropharyngeal residue or aspiration was observed on any of the tested diets. Oral feeding of the regular diet was initiated, and no aspiration was consistently observed after initiation of the diet.

Twelve days after completion of cerebrolysin concentrate administration (48 days after onset), the CRS score recovered to 21, and then patient's consciousness and general cognitive status were assessed with the Mini-Mental State Examination (MMSE). The MMSE at this point was 3 out of 30. The BBS improved to 30, and the K-FAST test was 4.

At 22 days after completion of the cerebrolysin concentrate (58 days after onset), the patient was transferred to a specialized rehabilitation institution for ongoing rehabilitation, with functional scores of CRS 23 (Auditory 4, Visual 5, Motor 6, Oromotor/verbal 3, Communication 2, Arousal 3), BBS 39, MMSE 7, MBI 75, and K-FAST 4. On the Limb and Oral Apraxia Test, the Oral domain scored 24 at discharge, a significant improvement from an initial score of 0.

DISCUSSION

Stroke presents with a variety of neurological symptoms depending on the location and extent of the infarct. Involvement of the left insular cortex can result in oral apraxia, which is closely associated with stroke sequelae such as communication disorder and dysphagia [16]. This region is closely related to Broca's area, which is responsible for language skills, and has shown anatomical links to function, affecting key mechanisms related to oral movements.

Cerebrolysin concentrate, primarily containing BDNF, is a complex of amino acids and peptides predominantly expressed in the brain but also found in muscles, fat, and endothelial cells. It circulates in cerebrospinal fluid and blood, modulated by physical activity [17]. BDNF plays a crucial role in promoting neuroplasticity, contributing significantly to neural recovery and protection [18]. Physical impairment following stroke can negatively affect BDNF expression and regulation, potentially perpetuating a detrimental cycle.

In various animal and in vitro studies, cerebrolysin concentrate has been shown to have a variety of effects on neuroprotection and repair, including reducing neurotoxicity by reducing programmed cell death and free radicals along with modulation of the inflammatory response, and promoting neuroplasticity through increased synapses [18-21]. The mechanism of action of this agent in promoting neuroregeneration involves activation of Sonic Hedgehog signaling pathway. The neural pathway of Sonic Hedgehog is a signaling pathway that transmits information necessary for cell differentiation and plays an important

https://doi.org/10.12786/bn.2024.17.e11

role in the development of animals, including tissues in the brain. The mRNA expression of this signaling pathway is promoted by the administration of cerebrolysin concentrate [22].

Cerebrolysin concentrate has undergone numerous clinical trials, the majority of which have produced positive outcomes in terms of its multimodal and pleiotropic effects [3,8,9]. Intravenous administration of Cerebrolysin concentrate has demonstrated the potential to enhance neurological outcomes in patients with acute ischemic stroke, either alone or in combination with rehabilitations. In a study of the combination of cerebrolysin concentrate and standardized rehabilitation therapy, Chang et al. [8] found that in patients with severe motor impairment due to acute ischemic stroke, the combination therapy provided additional benefits in motor recovery compared to conventional rehabilitation therapy alone. Randomized controlled trials have investigated the enhancement of upper extremity function during rehabilitation after stroke, with more favorable outcomes observed in the group receiving cerebrolysin concentrate alongside rehabilitation [3,9]. Additionally, cerebrolysin concentrate has demonstrated its efficacy in improving levels of consciousness and cognition among stroke patients [12]. In a retrospective observational study conducted by Kim et al. [12], the impact of cerebrolysin concentrate on consciousness in minimally conscious state (MCS) stroke patients was evaluated. The study compared the Coma Recovery Scale-Revised (CRS-R) scores between MCS patients undergoing rehabilitation with and without cerebrolysin concentrate. Significant improvements in subscales representing oromotor and arousal were seen in patients treated with cerebrolysin concentrate [12]. Furthermore, several meta-analyses have consistently confirmed the safety of cerebrolysin concentrate, showing little or no difference in mild or serious side effects compared to the placebo group [23-26]. These findings indicate that it is suitable for use in stroke recovery. Based on this evidence, the European Academy of Neurology and European Federation of Neurorehabilitation Societies, German and South Korea stroke rehabilitation guidelines recommend cerebrolysin concentrate for motor function recovery [27-29]. However, given its mechanism of action, it is expected to have a significant positive effect not only on motor function but also on recovery from other sequelae of stroke.

This case involves a patient with left insular cortex, resulting in severe oral apraxia. Additionally, the left insular cortex is anatomically closely associated with communication disorders (especially apraxia of speech), and previous studies have reported positive effects of cerebrolysin in aphasia [30]. Furthermore, cerebrolysin concentrate, which has shown efficacy in other sequelae of stroke, is presumed to have similar effects in improving apraxia. To our knowledge, there have been no previous studies on the effect of cerebrolysin concentrate on apraxia. This case report is the first to observe improvement in apraxia in stroke patients following cerebrolysin treatment. In this case, despite the initial lesion's size, the functional performance was significantly compromised. Looking at the overall recovery course of the patient in this case, there were remarkable improvements in motor and limb functions, allowing for independent ambulation and self-feeding. Although there was sufficient recovery in oral movement to enable self-feeding, oral apraxia persisted during follow-up assessments. Therefore, it is presumed that the reason for the initially impaired functional performance was apraxia. The patient exhibited severe oral apraxia to an extent where language and limb function assessments were impossible until 23 days after stroke onset. Due to the hemorrhagic transformation of the cerebral infarction, the restriction of physical activity should have been until 23 days after the onset of the stroke. The supplementing BDNF with cerebrolysin concentrate along with rehabilitation is thought to have interrupted the vicious cycle described above and promoted neural recovery and

https://doi.org/10.12786/bn.2024.17.e11

protection. After rehabilitation and administration of cerebrolysin concentrate, there was a marked recovery within a short period of time to the point where oral intake of a regular diet was possible, indicating a significant improvement in oral apraxia. It is a notable example of the potential therapeutic effect of cerebrolysin concentrate for post-stroke oral apraxia.

REFERENCES

1. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, Abraham J, Adair T, Aggarwal R, Ahn SY, Alvarado M, Anderson HR, Anderson LM, Andrews KG, Atkinson C, Baddour LM, Barker-Collo S, Bartels DH, Bell ML, Benjamin EJ, Bennett D, Bhalla K, Bikbov B, Bin Abdulhak A, Birbeck G, Blyth F, Bolliger I, Boufous S, Bucello C, Burch M, Burney P, Carapetis J, Chen H, Chou D, Chugh SS, Coffeng LE, Colan SD, Colquhoun S, Colson KE, Condon J, Connor MD, Cooper LT, Corriere M, Cortinovis M, de Vaccaro KC, Couser W, Cowie BC, Criqui MH, Cross M, Dabhadkar KC, Dahodwala N, De Leo D, Degenhardt L, Delossantos A, Denenberg J, Des Jarlais DC, Dharmaratne SD, Dorsey ER, Driscoll T, Duber H, Ebel B, Erwin PJ, Espindola P, Ezzati M, Feigin V, Flaxman AD, Forouzanfar MH, Fowkes FG, Franklin R, Fransen M, Freeman MK, Gabriel SE, Gakidou E, Gaspari F, Gillum RF, Gonzalez-Medina D, Halasa YA, Haring D, Harrison JE, Havmoeller R, Hay RJ, Hoen B, Hotez PJ, Hoy D, Jacobsen KH, James SL, Jasrasaria R, Jayaraman S, Johns N, Karthikeyan G, Kassebaum N, Keren A, Khoo JP, Knowlton LM, Kobusingye O, Koranteng A, Krishnamurthi R, Lipnick M, Lipshultz SE, Ohno SL, Mabweijano J, MacIntyre MF, Mallinger L, March L, Marks GB, Marks R, Matsumori A, Matzopoulos R, Mayosi BM, McAnulty JH, McDermott MM, McGrath J, Mensah GA, Merriman TR, Michaud C, Miller M, Miller TR, Mock C, Mocumbi AO, Mokdad AA, Moran A, Mulholland K, Nair MN, Naldi L, Narayan KM, Nasseri K, Norman P, O'Donnell M, Omer SB, Ortblad K, Osborne R, Ozgediz D, Pahari B, Pandian JD, Rivero AP, Padilla RP, Perez-Ruiz F, Perico N, Phillips D, Pierce K, Pope CA 3rd, Porrini E, Pourmalek F, Raju M, Ranganathan D, Rehm JT, Rein DB, Remuzzi G, Rivara FP, Roberts T, De León FR, Rosenfeld LC, Rushton L, Sacco RL, Salomon JA, Sampson U, Sanman E, Schwebel DC, Segui-Gomez M, Shepard DS, Singh D, Singleton J, Sliwa K, Smith E, Steer A, Taylor JA, Thomas B, Tleyjeh IM, Towbin JA, Truelsen T, Undurraga EA, Venketasubramanian N, Vijayakumar L, Vos T, Wagner GR, Wang M, Wang W, Watt K, Weinstock MA, Weintraub R, Wilkinson JD, Woolf AD, Wulf S, Yeh PH, Yip P, Zabetian A, Zheng ZJ, Lopez AD, Murray CJ, AlMazroa MA, Memish ZA. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2095-2128. PUBMED | CROSSREF
2. Phipps MS, Cronin CA. Management of acute ischemic stroke. BMJ 2020;368:l6983. PUBMED | CROSSREF
3. Muresanu DF, Heiss WD, Hoemberg V, Bajenaru O, Popescu CD, Vester JC, Rahlfs VW, Doppler E, Meier D, Moessler H, Guekht A. Cerebrolysin and Recovery After Stroke (CARS) A randomized, placebo-controlled, double-blind, multicenter trial. Stroke 2016;47:151-159. PUBMED | CROSSREF
4. Song JH, Yu JT, Tan L. Brain-derived neurotrophic factor in Alzheimer's disease: risk, mechanisms, and therapy. Mol Neurobiol 2015;52:1477-1493. PUBMED | CROSSREF
5. Zhang C, Chopp M, Cui Y, Wang L, Zhang R, Zhang L, Lu M, Szalad A, Doppler E, Hitzl M, Zhang ZG. Cerebrolysin enhances neurogenesis in the ischemic brain and improves functional outcome after stroke. J Neurosci Res 2010;88:3275-3281. PUBMED | CROSSREF
6. Chen CC, Wei ST, Tsaia SC, Chen XX, Cho DY. Cerebrolysin enhances cognitive recovery of mild traumatic brain injury patients: double-blind, placebo-controlled, randomized study. Br J Neurosurg 2013;27:803-807. PUBMED | CROSSREF
7. Mureşanu DF, Livinţ Popa L, Chira D, Dăbală V, Hapca E, Vlad I, Văcăraş V, Popescu BO, Cherecheş R, Strilciuc Ş, Brainin M. Role and impact of cerebrolysin for ischemic stroke care. J Clin Med 2022;11:1273. PUBMED | CROSSREF
8. Chang WH, Lee J, Shin YI, Ko MH, Kim DY, Sohn MK, Kim J, Kim YH. Cerebrolysin combined with rehabilitation enhances motor recovery and prevents neural network degeneration in ischemic stroke patients with severe motor deficits. J Pers Med 2021;11:545. PUBMED | CROSSREF
9. Chang WH, Park CH, Kim DY, Shin YI, Ko MH, Lee A, Jang SY, Kim YH. Cerebrolysin combined with rehabilitation promotes motor recovery in patients with severe motor impairment after stroke. BMC Neurol 2016;16:31. PUBMED | CROSSREF
10. Xue LX, Zhang T, Zhao YW, Geng Z, Chen JJ, Chen H. Efficacy and safety comparison of DL-3-n-butylphthalide and Cerebrolysin: effects on neurological and behavioral outcomes in acute ischemic stroke. Exp Ther Med 2016;11:2015-2020. PUBMED | CROSSREF
11. Stan A, Birle C, Blesneag A, Iancu M. Cerebrolysin and early neurorehabilitation in patients with acute ischemic stroke: a prospective, randomized, placebo-controlled clinical study. J Med Life 2017;10:216-222. PUBMED

12. Kim JY, Kim HJ, Choi HS, Park SY, Kim DY. Effects of cerebrolysin® in patients with minimally conscious state after stroke: an observational retrospective clinical study. Front Neurol 2019;10:803. PUBMED | CROSSREF
13. Han HJ, Kim EJ, Lee HJ, Pyun SB, Joa KL, Jung HY. Validation of Korean version of coma recovery scale-revised (K-CRSR). Ann Rehabil Med 2018;42:536-541. PUBMED | CROSSREF
14. Ha JW, Pyun SB, Lee HY, Hwang YM, Nam K. Reliability and validity analyses of the Korean version of Frenchay Aphasia Screening Test in brain-damaged patients. Commun Sci Disord 2009;14:46-57.
15. Pyun SB, Hwang YM, Jo SY, Ha JW. Reliability and validity of the comprehensive limb and oral apraxia test: standardization and clinical application in Korean patients with stroke. Ann Rehabil Med 2019;43:544-554. PUBMED | CROSSREF
16. Dronkers NF. A new brain region for coordinating speech articulation. Nature 1996;384:159-161. PUBMED | CROSSREF
17. Berchtold NC, Chinn G, Chou M, Kesslak JP, Cotman CW. Exercise primes a molecular memory for brain-derived neurotrophic factor protein induction in the rat hippocampus. Neuroscience 2005;133:853-861. PUBMED | CROSSREF
18. Sharma V, Singh TG, Kaur A, Mannan A, Dhiman S. Brain-derived neurotrophic factor: a novel dynamically regulated therapeutic modulator in neurological disorders. Neurochem Res 2023;48:317-339. PUBMED | CROSSREF
19. Sugita Y, Kondo T, Kanazawa A, Itou T, Mizuno Y. Protective effect of FPF 1070 (cerebrolysin) on delayed neuronal death in the gerbil--detection of hydroxyl radicals with salicylic acid. No To Shinkei 1993;45:325-331. PUBMED
20. Hutter-Paier B, Grygar E, Windisch M. Death of cultured telencephalon neurons induced by glutamate is reduced by the peptide derivative Cerebrolysin.J Neural Transm Suppl 1996;47:267-273. PUBMED | CROSSREF
21. Rockenstein E, Adame A, Mante M, Moessler H, Windisch M, Masliah E. The neuroprotective effects of Cerebrolysin in a transgenic model of Alzheimer's disease are associated with improved behavioral performance. J Neural Transm (Vienna) 2003;110:1313-1327. PUBMED | CROSSREF
22. Zhang L, Chopp M, Meier DH, Winter S, Wang L, Szalad A, Lu M, Wei M, Cui Y, Zhang ZG. Sonic hedgehog signaling pathway mediates cerebrolysin-improved neurological function after stroke. Stroke 2013;44:1965-1972. PUBMED | CROSSREF
23. Bornstein NM, Guekht A, Vester J, Heiss WD, Gusev E, Hömberg V, Rahlfs VW, Bajenaru O, Popescu BO, Muresanu D. Safety and efficacy of Cerebrolysin in early post-stroke recovery: a meta-analysis of nine randomized clinical trials. Neurol Sci 2018;39:629-640. PUBMED | CROSSREF
24. Guekht A, Vester J, Heiss WD, Gusev E, Hoemberg V, Rahlfs VW, Bajenaru O, Popescu BO, Doppler E, Winter S, Moessler H, Muresanu D. Safety and efficacy of Cerebrolysin in motor function recovery after stroke: a meta-analysis of the CARS trials. Neurol Sci 2017;38:1761-1769. PUBMED | CROSSREF
25. Strilciuc S, Vécsei L, Boering D, Pražnikar A, Kaut O, Riederer P, Battistin L. Safety of cerebrolysin for neurorecovery after acute ischemic stroke: a systematic review and meta-analysis of twelve randomized-controlled trials. Pharmaceuticals (Basel) 2021;14:1297. PUBMED | CROSSREF
26. Ziganshina LE, Abakumova T, Hoyle CH. Cerebrolysin for acute ischaemic stroke. Cochrane Database Syst Rev 2020;7:CD007026. PUBMED | CROSSREF
27. Platz T, Fheodoroff K, Mehrholz J. S3 guideline rehabilitation therapy for arm paresis after stroke of the DGNR long version. Greifswald, Germany: Springer; 2020.
28. Beghi E, Binder H, Birle C, Bornstein N, Diserens K, Groppa S, Homberg V, Lisnic V, Pugliatti M, Randall G, Saltuari L, Strilciuc S, Vester J, Muresanu D. European Academy of Neurology and European Federation of Neurorehabilitation Societies guideline on pharmacological support in early motor rehabilitation after acute ischaemic stroke. Eur J Neurol 2021;28:2831-2845. PUBMED | CROSSREF
29. Kim DY, Ryu B, Oh BM, Kim DY, Kim DS, Kim DY, Kim DK, Kim EJ, Lee HY, Choi H, Kim HS, Lee HH, Kim HJ, Oh HM, Seok H, Park J, Park J, Park JG, Kim JM, Lee J, Shin JH, Lee JK, Oh JS, Park KD, Kim KT, Chang MC, Chun MH, Kim MW, Kang MG, Song MK, Choi M, Ko MH, Kim NY, Paik NJ, Jung SH, Yoon SY, Lim SH, Lee SJ, Yoo SD, Lee SH, Yang SN, Park SW, Lee SY, Han SJ, Lee SJ, Bok SK, Ohn SH, Im S, Pyun SB, Hyun SE, Kim SH, Ko SH, Jee S, Kwon S, Kim TW, Chang WH, Chang WK, Yoo WK, Kim YH, Yoo YJ, Kim YW, Shin YI, Park YG, Choi YH, Kim Y; KSNR Stroke CPG Writing Group. Clinical Practice Guideline for Stroke Rehabilitation in Korea-Part 1: rehabilitation for motor function (2022). Brain Neurorehabil 2023;16:e18. PUBMED | CROSSREF
30. Jianu DC, Muresanu DF, Bajenaru O, Popescu BO, Deme SM, Moessler H, Meinzingen SZ, Petrica L. Cerebrolysin adjuvant treatment in Broca's aphasics following first acute ischemic stroke of the left middle cerebral artery. J Med Life 2010;3:297-307. PUBMED