

Cerebrolysin

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Cerebrolysin is a mixture of peptides purified from the brains of pigs. It is approved in many European and Asian countries as an intravenous injection for the treatment of stroke, traumatic brain injury, and dementia. It is not, however, approved for use in the United States and a large 2012 trial casts doubts on its usefulness in stroke, except perhaps in severe cases [1]. It appears safe for short-term use (up to 3 years) and results from several clinical trials suggest it might offer small improvements to symptoms of Alzheimer's disease and vascular dementia. It remains unknown if cerebrolysin might prevent dementia or slow cognitive decline.

EVIDENCE AND POTENTIAL BENEFIT FOR BRAIN HEALTH Rated 2/4 based on 2/4 evidence

Many clinical trials have been carried out in people with dementia, but the evidence is limited for healthy adults and no studies have tested whether cerebrolysin can prevent dementia.

<u>Randomized controlled trials</u>: A few small clinical trials have reported that cerebrolysin can improve cognitive function in older people with memory problems and in people with schizophrenia, although the effects are modest. In a double-blind randomized controlled trial in schizophrenia patients in China, cerebrolysin treatment for four weeks improved cognition and memory [10]. In older adults with memory loss, a 30-day treatment with a peptide preparation derived from cerebrolysin (N-PEP-12) improved memory performance but not verbal fluency [11]. The effect size of N-PEP-12 on memory was lower than that of currently approved Alzheimer's medications (e.g., cholinesterase inhibitors).

Other human research: An uncontrolled clinical trial reported that healthy elderly people taking a single oral dose of cerebrolysin solution had better memory performance after the treatment compared to before the treatment, but result could have been caused by the placebo effect [12].

<u>Biology:</u> No clinical studies have tested whether cerebrolysin can prevent dementia but some preclinical research supports the idea. Cerebrolysin protected cultured neurons and brain slices from damage [2; 3; 4], reduced inflammation [5], and promoted the formation of new neural connections (synapses) [6]. In mouse models of Alzheimer's disease, cerebrolysin appears to ameliorate cognitive impairment [7] and reduce pathological markers (e.g., beta-amyloid plaques and hyperphosphorylated tau) [8; 9]. Whether these effects will occur in humans is unknown.

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APOE4 carriers: The evidence is mixed and limited on whether cerebrolysin selectively affects APOE4 carriers versus non-carriers. In a four-month trial in Russia, Alzheimer's patients without an APOE4 allele were about three times more likely to respond to treatment than APOE4 carriers [13]. But another randomized trial reported that in APOE4 carriers, cerebrolysin was more effective at increasing the level of BDNF, a protein that enhances brain cell growth and survival [14]. For more information on what the *APOE* gene allele means for your health, read our <u>APOE4 information page</u>.

For Dementia Patients

Several meta-analyses of numerous randomized controlled trials have suggested that cerebrolysin has an overall beneficial effect on cognitive function and global clinical change in patients with mild-to-moderate Alzheimer's patients [15; 16]. The standard treatment in these trials was a daily intravenous infusion of 30 ml cerebrolysin with durations ranging from four weeks to six months. Because cerebrolysin is prepared from pig brain homogenate, effects may vary depending on the content and concentration of each preparation.

A double-blind randomized controlled study suggested that cerebrolysin may be as effective as donepezil and may have additive benefits when used in combination with donepezil for treating Alzheimer's disease symptoms [17]. A follow-up study concluded that cerebrolysin or the combination of cerebrolysin and donepezil, but not donepezil alone, increased levels of a protein that enhances brain cell growth and survival (i.e., BDNF) in mild-to-moderate Alzheimer's patients [14]. However, these results have not been confirmed yet in larger, randomized, well-controlled trials.

Cerebrolysin may also be effective at treating symptoms of vascular dementia. A large meta-analysis of multiple randomized clinical trials, lasting up to three years, concluded that cerebrolysin treatment improved clinical symptoms compared to placebo or no treatment, with few reported side effects [18]. While the measured improvements were statistically significant, the degree of improvement was small. Additionally, because of the small number of trials and the lack of long-term follow-up, there was insufficient evidence to recommend it for routine treatment of vascular dementia.

A four-month trial from Russia comparing the effectiveness of cerebrolysin treatment to the Exelon[™] patch (i.e., rivastigmine, an acetylcholinesterase inhibitor) reported a 1.7-fold higher response rate to cerebrolysin than Exelon[™]. The clinical effectiveness of cerebrolysin was estimated to be 6.5-fold greater than the Exelon[™] patch [13]. However, this study was published only in Russian so we are unable to critically review it. No other studies appear to have replicated its findings from 2005.

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SAFETY

Rated 3/4

Results from a meta-analysis along with multiple clinical trials suggest that cerebrolysin is safe for use up to three years with few adverse effects that are usually transient and include headaches, weight loss, dizziness, anxiety, agitation, and feeling hot [15; 19]. The rates of adverse events were comparable between people receiving cerebrolysin versus placebo. As with all intravenous medications, the process of injecting cerebrolysin carries some risks. And as cerebrolysin is purified from animal tissue, there is a risk of bacterial, viral, or fungal contamination of the product.

HOW TO USE

Cerebrolysin is not approved in the U.S. for the treatment of any condition. In clinical studies, doses of 30 ml daily, delivered intravenously for four weeks have produced positive results, while higher doses may be less effective [20]. The content and concentration of amino acids may vary by manufacturer and by batch. There is very little information on potential harmful interactions with other medications. Although sometimes sold for use orally (by mouth), peptides such as those in cerebrolysin are typically broken down in the gut without ever reaching the body or brain.

WHAT'S THE FUTURE?

The Cochrane Library summarizes clinical trial results of cerebrolysin in patients with vascular dementia and acute ischemic stroke.

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