Arginine

Arginine is an α-aminoacid.

The L-form is one of the 20 most common natural amino acids. At the level of molecular genetics, in the structure of the messenger ribonucleic acid mRNA, CGU, CGC, CGA, CGG, AGA, and AGG, are the triplets of nucleotide bases or codons that code for arginine during protein synthesis. In mammals, arginine is classified as a semiessential or conditionally essential amino acid, depending on the developmental stage and health status of the individual.

Preterm infants are unable to synthesize or create arginine internally, making the amino acid nutritionally essential for them.

Arginine was first isolated from a lupin seedling extract in 1886 by the Swiss chemist Ernst Schultze.

In general, most healthy people do not need to supplement with arginine because the body usually produces sufficient amounts.

Arginine, serves as a substrate for nitric oxide (NO) production by nitric oxide synthase (NOS) and a precursor for various metabolites including ornithine, creatine, polyamines, and agmatine. Arginase competes with nitric oxide synthase for substrate arginine to produce orthinine and urea. There is contradictory evidence in the literature on the role of nitric oxide in the pathophysiology of traumatic brain injury (TBI). These contradictory perspectives are likely due to different NOS isoforms - endothelial (eNOS), inducible (iNOS) and neuronal (nNOS) which are expressed in the central nervous system. Of these, the role of nNOS in acute injury remains less clear.

A study of Madan et al., aimed to employ a genetic approach by overexpressing arginase isoforms specifically in neurons using a Thy-1 promoter to manipulate cell autonomous NO production in the context of TBI. The hypothesis was that increased arginase would divert arginine from pathological NO production. We generated 2 mouse lines that overexpress arginase I (a cytoplasmic enzyme) or arginase II (a mitochondrial enzyme) in neurons of FVB mice. We found that two-weeks after induction of controlled cortical injury, overexpressing arginase I but not arginase II in neurons significantly reduced contusion size and contusion index compared to wild-type (WT) mice. This study establishes enhanced neuronal arginase levels as a strategy to affect the course of TBI and provides support for the potential role of neuronal NO production in this condition [1)].

Poly-arginine and arginine-rich cell-penetrating peptides (CPPs), are highly neuroprotective, with efficacy increasing with increasing arginine content, have the capacity to reduce glutamic acid-induced neuronal calcium influx and require heparan sulfate preotoglycan-mediated endocytosis to induce a neuroprotective effect. Furthermore, neuroprotection could be induced with immediate peptide treatment or treatment up to 2 to 4 hours before glutamic acid excitotoxicity or OGD, and with poly-arginine-9 (R9) when administered intravenously after stroke onset in a rat model. In contrast, the JNKI-1 peptide when fused to the (non-arginine) kFGF CPP, which does not rely on endocytosis for uptake, was not neuroprotective in the glutamic acid model; the kFGF peptide was also ineffective. Similarly, positively charged poly-lysine-10 (K10) and R9 fused to the negatively charged poly-glutamic acid-9 (E9) peptide (R9/E9) displayed minimal neuroprotection after

excitotoxicity. These results indicate that peptide positive charge and arginine residues are critical for neuroprotection, and have led us to hypothesize that peptide-induced endocytic internalization of ion channels is a potential mechanism of action. The findings also question the mode of action of different neuroprotective peptides fused to arginine-rich CPPs [2].

1)
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2)
MacDougall G, Anderton RS, Edwards AB, Knuckey NW, Meloni BP. The Neuroprotective Peptide Poly-Arginine-12 (R12) Reduces Cell Surface Levels of NMDA NR2B Receptor Subunit in Cortical Neurons; Investigation into the Involvement of Endocytic Mechanisms. J Mol Neurosci. 2016 Nov 20. [Epub ahead of print] PubMed PMID: 27866326.