Toxic and autotoxic effects of the cyanobacterial neurotoxin BMAA and its relation to neurodegeneration

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Introduction

The neurotoxic amino acid beta-N-methylamino-L-alanine (BMAA) is produced by cyanobacteria and has been proposed as an environmental trigger of human neurodegeneration (e.g. ALS). We previously detected BMAA in N2-fixing, bloom-forming cyanobacteria in the Baltic Sea (1), and even greater quantities was found in organisms of higher trophic levels (fish, molluscs). However, the connection between BMAA and neurodegenerative diseases remains to be proven. Also, the function for BMAA in cyanobacteria is unknown.

Objectives

➢ To understand the role of BMAA in cyanobacteria with emphasis on N2-fixing cyanobacteria involved in the massive surface blooms occurring in aquatic environments world-wide, here using the N2-fixing cyanobacterium Nostoc sp. PCC 7120 as model.
➢ To investigate the association between the consumption of potentially BMAA amended food and the neurodegenerative disease ALS (amyotrophic lateral sclerosis), by searching for BMAA in samples from ALS patients.

Methods

Consequences of exposing Nostoc sp. 7120 cultures to BMAA was followed at the cellular and physiological level by analyzing the structure/ultrastructure (LM/TEM), N2-fixation (acetylene reduction assay) and growth (OD and chl a). Blood and cerebrospinal fluid (CSF) from ALS-patients and controls was extracted and analysed for BMAA using UPLC-MS/MS.

Conclusions and future perspectives

➢ The rapid inhibition of N2-fixation in Nostoc sp. PCC 7120 at low concentrations, as also evidenced by the massive accumulation of glycogen, suggests that BMAA may be causing oxidative stress and potentially programmed cell death, which in turn may lead to collapse of cyanobacterial blooms (2).
➢ As we identified BMAA in cerebrospinal fluid of a few ALS patients, this opens the possibility that BMAA, potentially administrated via aquatic food items, may be involved in causing human neurodegeneration. This now needs to be further substantiated.

References


Transfer of BMAA through Baltic Sea food webs – a threat to human health?

BMAA at low concentrations (1-5 µM ) rapidly inhibits N2-fixation in Nostoc 7120 and is more potent than most proteinogenic amino acids and other nitrogen sources (at 20 µM)

BMAA induces glycogen accumulation in Nostoc 7120 – illustrating severe nitrogen depletion

24 h control (no BMAA)  24 h treatment 20 µM BMAA

G, glycogen; C, carboxysomes; TH, thylakoid membranes; CP, centroplasm.

Preliminary studies using mass spectrometry show presence of BMAA in cerebrospinal fluid from a few ALS patients as well as in a few controls.

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