

Editorial:

N-acetylaspartic acid monitors oxidative stress

Sankar Surendran

¹ UNT Health Science center, Fort Worth, Texas, USA;
Email: sankar_surendran@yahoo.com; Tel: +1 504 568 5481

N-acetylaspartic acid (NAA) was discovered by Tallan et al., in 1956. It is synthesized from acetyl coenzyme A and aspartate by a mitochondrial enzyme, L-aspartate N-acetyltransferase (Goldstein, 1969). NAA is mainly found in the gray matter of the brain and also present at lower levels in the astroglia, white matter, superior cervical ganglion, splenic nerve, peripheral nervous tissue of spleen, lung, liver, kidney, muscle, ovary, thymus, stomach, heart, adrenal medulla and retina of fishes to mammals (see review, Surendran et al., 2011). Normal level of NAA is important in the maintenance of potential antioxidants. N-acetylaspartic acid level is altered in many diseases including alcoholic brain (Schweinsburg et al., 2001), brain oedema (Demougeot et al., 2001), HIV-related dementia (Meyerhoff et al., 1993; Sacktor et al., 2005), HIV positive alcoholism (Pfefferbaum et al., 2005), Canavan disease (see review, Surendran et al., 2011), Parkinson's disease (Surendran and Rajasankar, 2010), type 2 diabetes (Surendran et al., 2006) and spinocerebellar ataxia type 1 (Oz et al., 2010). Altered levels of NAA changes nitric oxide and potential antioxidant levels to cause disease pathophysiology (Surendran, 2009; Surendran and Rajasankar, 2010), suggesting NAA monitors oxidative stress by regulating antioxidant levels.

Aspartoacylase deacetylates N-acetylaspartic acid into aspartate and acetate (Birnbaum et al., 1952). While aspartoacylase activity is very mild or no activity in normal astrocytes, the activity is increased in inflammatory conditions suggesting aspartoacylase contribution in reactive astrocytes (Surendran, 2007; Surendran et al., 2011). In Table 1, the key message of recently published studies on NAA effect on oxidative stress has been summarized.

Table 1: Studies in N-acetylaspartic acid (NAA) resulting oxidative stress

Key message	Reference
NAA induced nitric oxide toxicity and alters proteins associated with inflammation, transcription and contractility to cause pathophysiology	Surendran, 2009
NAA induced nitric oxide toxicity contribute to neurodegeneration	Surendran, 2008
NAA induced nitric oxide toxicity to cause Canavan disease pathophysiology	Surendran, 2010
Altered levels of nitric oxide cause contractile abnormality	Surendran and Kondapaka, 2005
NAA contributes in Parkinson's disease	Surendran and Rajasankar, 2010
NAA induced oxidative stress to contribute in disease pathophysiology	Surendran and Bhatnagar, 2011
NAA induced nitric oxide toxicity contributes in Canavan disease pathophysiology	Surendran et al., 2011
NAA reduced glucose 6-phosphate dehydrogenase and enhanced protein carbonyl content and superoxide dismutase	Pederzolli et al., 2009
NAA reduced catalase and glutathione peroxidase and induced hydrogen peroxide	Pederzolli et al., 2010

References

- Birnbaum SM, Levintow L, Kingsley RB, Greenstein JP. Specificity of amino acid acylases. *J Biol Chem* 1952;194:455–70.
- Demougeot C, Garnier P, Mossiat C, Bertrand N, Giroud M, Beley A, Marie C. N-Acetylaspartate, a marker of both cellular dysfunction and neuronal loss: its relevance to studies of acute brain injury. *J Neurochem* 2001;77:408-15.
- Goldstein FB. The enzymatic synthesis of N-acetyl-L-aspartic acid by subcellular preparations of rat brain. *J Biol Chem* 1969; 244:4257–60.
- Meyerhoff DJ, MacKay S, Bachman L, Poole N, Dillon WP, Weiner MW, Fein G. Reduced brain N-acetylaspartate suggests neuronal loss in cognitively impaired human immunodeficiency virus-seropositive individuals: in vivo 1H magnetic resonance spectroscopic imaging. *Neurology* 1993;43: 509-15.
- Oz G, Hutter D, Tkác I, Clark HB, Gross MD, Jiang H, Eberly LE, Bushara KO, Gomez CM. Neurochemical alterations in spinocerebellar ataxia type 1 and their correlations with clinical status. *Mov Disord* 2010;25:1253-61.
- Pederzoli CD, Rockenbach FJ, Zanin FR, Henn NT, Romagna EC, Sgaravatti AM, Wyse AT, Wannmacher CM, Wajner M, de Mattos Dutra A, Dutra-Filho CS. Intracerebroventricular administration of N-acetyl-aspartic acid impairs antioxidant defenses and promotes protein oxidation in cerebral cortex of rats. *Metab Brain Dis* 2009;24: 283-98.
- Pederzoli CD, Mescka CP, Magnusson AS, Deckmann KB, de Souza Streck E, Sgaravatti AM, Sgarbi MB, Wyse AT, Wannmacher CM, Wajner M, Dutra-Filho CS. N-acetylaspartic acid impairs enzymatic antioxidant defenses and enhances hydrogen peroxide concentration in rat brain. *Metab Brain Dis* 2010;25:251-9.
- Pfefferbaum A, Adalsteinsson E, Sullivan EV. Cortical NAA deficits in HIV infection without dementia: influence of alcoholism comorbidity. *Neuropsychopharmacology* 2005;30:1392-9.
- Sacktor N, Skolasky RL, Ernst T, Mao X, Selnes O, Pomper MG, Chang L, Zhong K, Shungu DC, Marder K, Shibata D, Schifitto G, Bobo L, Barker PB. A multicenter study of two magnetic resonance spectroscopy techniques in individuals with HIV dementia. *J Magn Reson Imaging* 2005;21:325-33.
- Schweinsburg BC, Taylor MJ, Alhassoon OM, Videen JS, Brown GG, Patterson TL, Berger F, Grant I. Chemical pathology in brain white matter of recently detoxified alcoholics: a 1H magnetic resonance spectroscopy investigation of alcohol-associated frontal lobe injury. *Alcohol Clin Exp Res* 2001;25:924-34.
- Surendran S. Upregulation of aspartoacylase seen in diabetes is due to advanced glycation end-products. *Med Hypotheses* 2007;68:926.
- Surendran S. N-acetyl aspartate induces nitric oxide to result neurodegeneration in Canavan disease. *Biosci Hypotheses* 2008; 1:228-9.
- Surendran S. Upregulation of N-acetyl-aspartic acid alters inflammation, transcription and contractile associated protein levels in the stomach and smooth muscle contractility. *Mol Biol Rep* 2009;36:201-6.

Surendran S. Upregulation of N-acetyl-aspartic acid resulting nitric oxide toxicity induces aspartoacylase mutations and protein interaction to cause pathophysiology seen in Canavan disease. *Med Hypotheses* 2010;75:533-4.

Surendran S, Bhatnagar M. Upregulation of N-acetyl-aspartic acid induces oxidative stress to contribute in disease pathophysiology. *Int J Neurosci* 2011 Feb 25. [Epub ahead of print].

Surendran S, Kondapaka S. Altered expression of neuronal nitric oxide synthase in the duodenum longitudinal muscle-myenteric plexus (LM-MP) of obesity induced diabetes mouse: implications on enteric neurodegeneration. *Biochem Biophys Res Commun* 2005;338:919–22.

Surendran S, Rajasankar S. Parkinson's disease: oxidative stress and therapeutic approaches. *Neurol Sci* 2010;31:531-40.

Surendran S, Matalon R, Tying SK. Upregulation of aspartoacylase activity in the duodenum of obesity induced diabetes mouse: implications on diabetic neuropathy. *Biochem Biophys Res Commun* 2006; 345:973-5.

Surendran S, Kaya N, Ozand P. Canavan disease: molecular pathology, phenotype and therapeutic approaches. In: Surendran S (ed): *Neurochemistry of metabolic diseases: lysosomal storage diseases, phenylketonuria and Canavan disease*. New York: Nova Science Publ. 2011, [in press]. Retrieved on April 14, 2011 from https://www.novapublishers.com/catalog/product_info.php?products_id=21889

Tallan HH, Moore S, Stein WH. N-Acetyl-L-aspartic acid in brain. *J Biol Chem* 1956; 219:257–64.