Amino acid and nucleotide profile in plasma, kidney, and liver of mice with Huntington's disease

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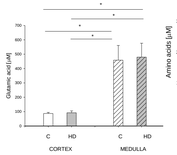
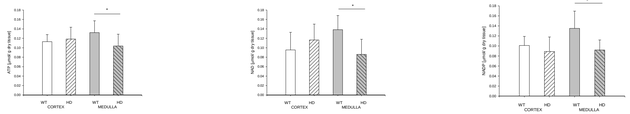
PURPOSE

Huntington disease is autosomal dominant neurodegenerative disorder caused by the mutant protein huntingtin where polyglumine tract is overexpressed. N-acetylglutamate regulates, among others, carbamoylphosphate synthetase, in the urea cycle, so we examined systemic amino acid transformations in the liver and kidney. In addition, since amino acids can be precursors to, among others, NAD, we examined nucleotide transformations and also plasma amino acid levels following administration of nicotinamide riboside.

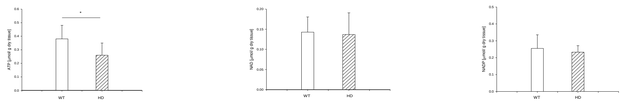
MATERIAL AND METHODS

Eight-month-old R6/1 with developed Huntington's disease model mice and C57BL/J control mice were used for the study. Nucleotides were determined by HPLC. Amino acids were determined by LC-MS TSQ Vantage. Mice were injected 250 mg/kg body mass nicotinamide riboside for four weeks and then amino acid concentrations plasma were studied.

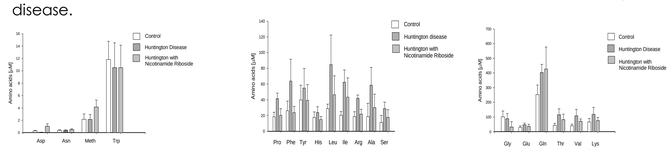




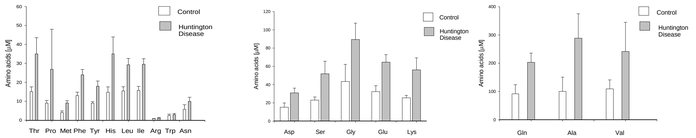
The concentration of ATP, NAD, NADP nucleotides in the kidney divided into cortex and medulla in mice with Huntington's disease.



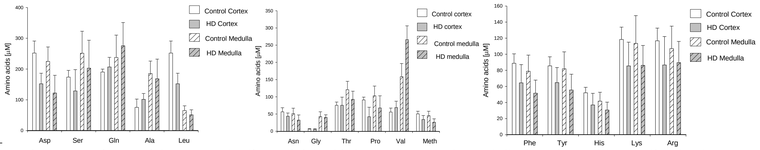
Concentration of ATP, NAD and NADP nucleotides in the liver of mice with Huntington's disease.



Plasma amino acid concentrations following administration of Nicotinamide Riboside in Huntington's Disease Mice.



Liver amino acid concentration in mice with Huntington's disease.



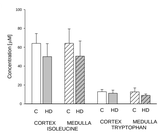
Kidney amino acid concentration divided into cortex and medulla in mice with Huntington's disease

RESULTS

Tryptophan, methionine and asparagine concentrations were unchanged in Huntington's disease model mice plasma. Nicotinamide riboside administration significantly decreased the amino acid concentrations in plasma, only tryptophan remained unchanged while methionine and aspartate increased. Concentrations of arginine and tryptophan in liver, did not change in Huntington's mice. Concentration of glycine, valine and leucine in the kidney differed from the way the other amino acids were changed. ATP levels were lowered in the liver and kidney medulla of mice with Huntington's disease, did not change in kidney cortex. The concentration of NAD and NADP did not change in the liver and kidney cortex, while it was decreased in the kidney medulla of mice with Huntington's disease.

CONCLUSIONS

The lack of changes in the concentration of arginine formed in the urea cycle may indicate the body's defense mechanism against the excessive amount of urea formed. Nicotinamide riboside brought the amino acid profile closer to that of healthy mice. Administering it as a supplement could improve the situation of changes in the amino acid profile of people with Huntington's disease.



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2. Alejandro Lloret, M. Flint Beal. PGC-1a, Sirtuins and PARPs in Huntington's Disease and Other Neurodegenerative Conditions: NAD+ to Rule Them All. Neurochemical Research (2019) 44:2423–2434