

## ORIGINAL ARTICLE

# Assessment of Plasma Amino Acid Dynamics in Response to ACTH Stimulation by Liquid Chromatography Tandem-Mass Spectrometry

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## SUMMARY

**Background:** The adrenocorticotrophic hormone (ACTH) stimulation test is a widely used diagnostic tool to assess the adrenal gland function. Beyond that the ACTH test can be used in stress research to induce a biochemical stress response under standardized conditions. To study the impact of the stress response on protein metabolism, time-course plasma amino acid profiling in healthy individuals was performed with high performance liquid chromatography tandem-mass spectrometry (HPLC-MS/MS).

**Methods:** A set of 39 samples (pre/post 30' and 60' IV-ACTH) from 13 healthy individuals (age range 26 - 58, 3 female and 10 male) was investigated. Plasma amino acids were quantified by LC-MS/MS using the AbsoluteIDQ<sup>®</sup> p180 Kit (Biocrates Life Science, Innsbruck, Austria) including 19 biogenic amino acids, ornithine, and citrulline.

**Results:** Statistically significant decreases were observed for 11 proteinogenic amino acids (alanine, asparagine, isoleucine, leucine, tyrosine, phenylalanine, tryptophan, valine, methionine, aspartate, and threonine). The amino acids alanine, asparagine, and isoleucine showed markedly pronounced relative changes with short-term reduction of median inter-individual plasma concentrations of up to 25%.

**Conclusions:** Amino acid profiling with LC-MS/MS revealed highly dynamic plasma alterations upon application of exogenous corticotropin as a stress model. Our findings provide novel insights into the biochemical stress response and improve our understanding of short-term metabolic consequences. Further studies should elucidate the impact of corticotropin mediated stress responses on amino acid catabolism.

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## Supplementary Table.

Table 1. Statistic ANOVA table.

Metabolite	F-Val	F-pVal	F-pVal(BH)	pVal_T30_T0	pVal_T60_T0	pVal_T60_T30
Ala	2.59E+01	1.03E-06	1.47E-04	4.00E-07	5.02E-04	8.86E-01
Asn	1.49E+01	6.15E-05	4.38E-03	2.13E-03	3.19E-03	1.39E-01
Ile	1.35E+01	1.19E-04	4.38E-03	1.57E-03	4.56E-03	6.70E-01
Leu	1.28E+01	1.65E-04	4.72E-03	3.18E-03	3.82E-03	5.51E-01
Tyr	1.12E+01	3.68E-04	6.68E-03	4.22E-02	3.78E-03	1.99E-02
Phe	1.12E+01	3.74E-04	6.68E-03	2.34E-02	4.84E-03	4.47E-02
Trp	9.94E+00	7.18E-04	1.03E-02	2.24E-02	8.11E-03	7.34E-02
Val	7.92E+00	2.29E-03	2.64E-02	3.20E-02	2.13E-02	1.06E-01
Met	7.53E+00	2.90E-03	2.96E-02	1.54E-02	1.54E-02	4.09E-01
Asp	7.11E+00	3.76E-03	3.36E-02	8.71E-02	8.04E-03	1.33E-01
Thr	6.35E+00	6.13E-03	4.62E-02	1.14E-01	1.52E-02	1.14E-01
Pro	5.83E+00	8.66E-03	6.19E-02	6.39E-02	5.60E-02	1.10E-01
Orn	5.36E+00	1.19E-02	7.75E-02	7.93E-01	1.73E-02	1.73E-02
Arg	4.05E+00	3.04E-02	1.61E-01	5.04E-02	6.07E-01	4.31E-02
His	3.95E+00	3.28E-02	1.62E-01	1.03E-01	1.03E-01	4.05E-01
Ser	2.64E+00	9.17E-02	3.28E-01	1.68E-01	1.68E-01	5.64E-01
Glu	2.20E+00	1.32E-01	3.54E-01	4.68E-01	3.85E-01	1.47E-01
Gly	2.15E+00	1.38E-01	3.54E-01	2.83E-01	2.73E-01	2.83E-01
Lys	1.96E+00	1.62E-01	3.59E-01	2.20E-01	3.09E-01	8.77E-01
Gln	9.23E-01	4.11E-01	5.20E-01	4.96E-01	4.96E-01	9.36E-01
Cit	7.71E-01	4.74E-01	5.61E-01	6.20E-01	6.20E-01	6.20E-01

The table shows the amino acids sorted in ascending order by the overall test statistical significance (F-pVal). The F-value describes the ANOVA test statistic, with corresponding corrected p-value for multiple testing (F-pVal (BH)) and uncorrected p-value (F-pVal). The individual paired *t*-test results, which were also corrected for multiple testing are shown for the comparisons T30 versus T0 (pVal\_T30\_T0), T60 versus T0 (pVal\_T60\_T0), and T60 versus T30 (pVal\_T60\_T30).