Combined cocaine and alcohol chronic administration alters plasma amino acid levels in male and female rats.

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A high percentage of cocaine users combine cocaine with ethanol intake. When used in a combined way, alcohol consumption increases the plasma levels of cocaine and modifies the biotransformation of cocaine, both in rats and in humans. This is of special concern during early stages of life, since combined exposure to both drugs could induce physiological alterations during later stages of development. In a previous work we studied the effects of combined cocaine and alcohol chronic administration on the metabolic profiles of blood plasma of young-adult Wistar rats (51 days old at the beginning of the experiments) by using a Liquid Chromatography-Mass Spectrometry (LC-MS) untargeted metabolomics strategy. From 120 possible metabolites, eleven metabolites were annotated, where eight were unequivocally identified using standards and three were tentatively identified by matching the MS/MS spectra to libraries. The affected metabolic pathways were mainly those related to the metabolism of different amino acids (Sánchez-López et al. 2017). As an extension of that work, in the present study we have analyzed the blood plasma concentration of several amino-acids, in a targeted metabolomic approach, by using capillary electrophoresis (CE-LIF). As in the previous work, male and female Wistar rats received intravenously one of the following four treatments for 21 days: cocaine (15 mg/kg); alcohol (2 g/kg); cocaine+alcohol (15 mg/kg-2 g/kg); and control (saline). Plasma concentrations of eleven amino acids were identified and quantified: Gly, L-Ala, L-Gln, L-Glu, L-Iso, L-Leu, L-Orn, L-Pro, L-Ser, L-Thr, and Tau. A 2x2x2x2 factorial analysis of variance (cocaine*alcohol*age*sex) was performed. The levels for these four factors were presence of cocaine: yes/no; presence of alcohol: yes/no; sex: female/male; and age: young-adult (51 days) / adult (95 days). Cocaine administration significantly increased L-Iso, L-leu, L-Glu and L-Ser values. The presence of alcohol depleted L-Ala and L-ser and increased L-Gln and L-Orn. Females had higher values than males in five amino acids: L-Iso, L-Leu, Gly, Orn, Gln. Fully adult subjects had higher values of L-Iso, L-Leu and L-Gln compared to young adults. In addition, several interactions were observed: cocaine*alcohol for L-Iso, L-Gln, L-Orn and L-Ser, sex*cocaine for L-Pro and alcohol*sex for L-Gln and L-Iso. These data indicate that cocaine chronic cocaine and alcohol exposure, just alone or combined, modifies plasma amino acid patterns, including essential amino acids, and suggest differential effects depending upon sex and age.

Supported by grants from the Ministerio de Ciencia e Innovación (PSI2016-80541-P); Ministerio de Sanidad, Servicios Sociales e Igualdad (Red de Trastornos Adictivos; RTA-RD16/020/0022 del Instituto de Salud Carlos III- and Plan Nacional sobre Drogas, 20161073); Dirección General de Investigación de la Comunidad de Madrid (S-2011/BMD-2308; Programa de Actividades I+D+i CANNAB-CM); and UNED (Plan de Promoción de la Investigación).