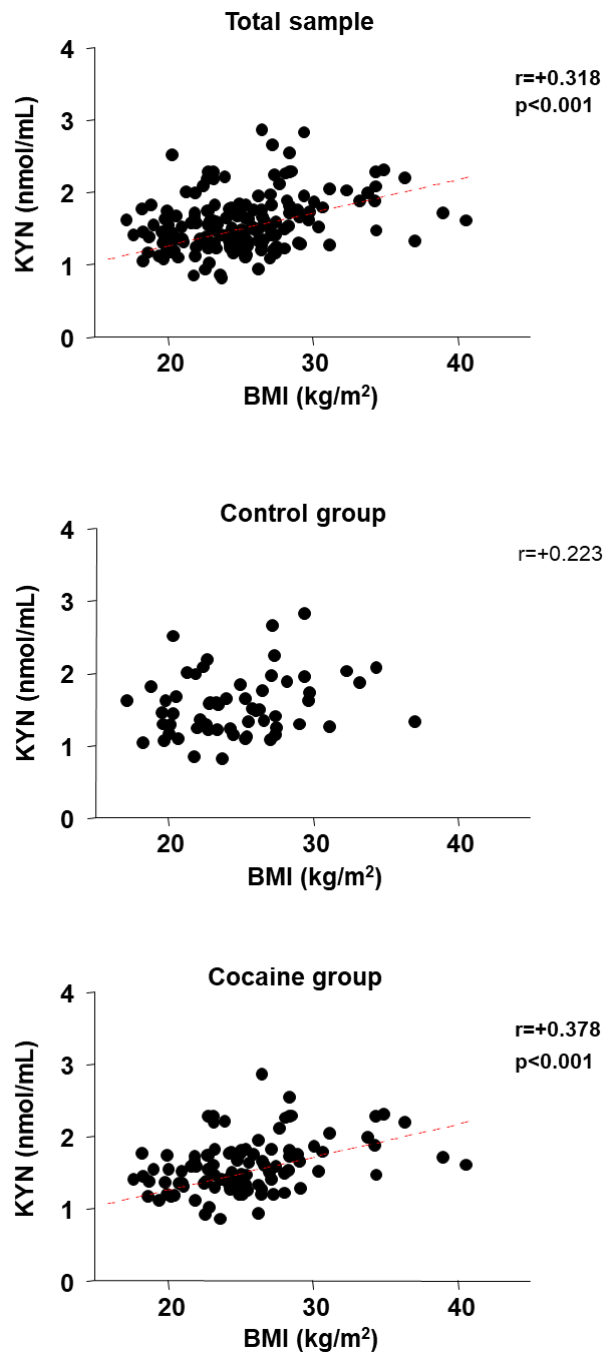


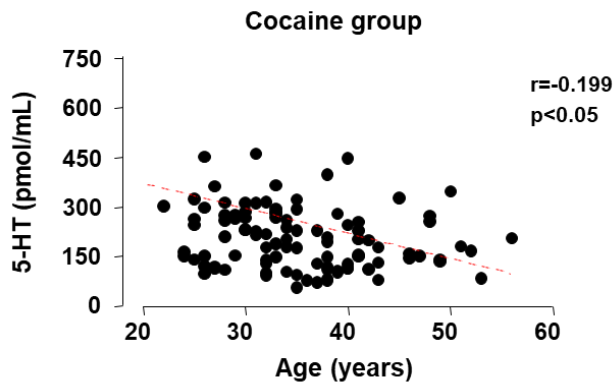
**Serotonin is the main tryptophan metabolite associated with psychiatric comorbidity in abstinent cocaine-addicted patients**

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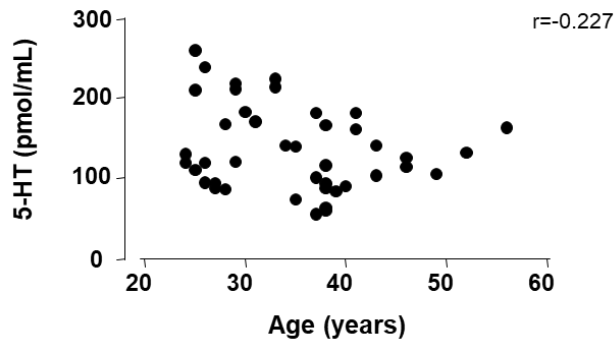
## SUPPLEMENTARY FIGURES



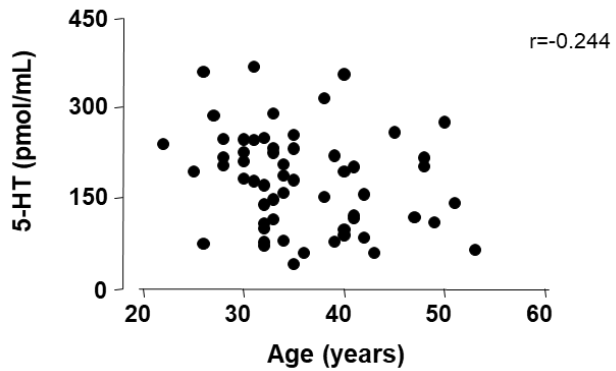
**Figure S1.** Correlation analyses between plasma concentrations of KYN and BMI in abstinent CUD-patients and control subjects. Black dots are individual values. Pearson correlation coefficients ( $r$ ) were calculated for the total sample, the control group and the cocaine group.



**Non-comorbid (mental disorders) subgroup**



**Comorbid (mental disorders) subgroup**



**Figure S2.** Correlation analyses between plasma concentrations of 5-HT and age in abstinent CUD-patients according to diagnosis of comorbid mental disorders. Black dots are individual values. Pearson correlation coefficients ( $r$ ) were calculated for the control group, the non-comorbid subgroup and the comorbid (mental disorders) subgroup.

**Table S1.** Biological and socio-demographic variables

VARIABLE		COCAINE GROUP N=100	CONTROL GROUP N=60	P-value
<b>Age</b> [mean (SD)]	years	35.4 (7.5)	36.4 (10.4)	ns <sup>a</sup>
<b>Body mass index</b> [mean (SD)]	kg/m <sup>2</sup>	25.4 (4.4)	24.6 (4.3)	ns <sup>a</sup>
<b>Sex</b> [N (%)]	Female Male	18 (18.0) 82 (82.0)	30 (50.0) 30 (50.0)	<0.001 <sup>b</sup>
<b>Marital status</b> [N (%)]	Single Married/cohabiting Divorced/separated Widowed	40 (40.0) 37 (37.0) 23 (23.0) 0 (0.0)	29 (48.3) 25 (41.7) 6 (10.0) 0 (0.0)	ns <sup>b</sup>
<b>Education</b> [N (%)]	≤ Primary Secondary Higher	57 (57.0) 32 (32.0) 11 (11.0)	5 (8.3) 25 (41.7) 30 (50.0)	<0.001 <sup>b</sup>
<b>Occupation</b> [N (%)]	Student Employed Unemployed Retired	0 (0.0) 41 (41.0) 58 (58.0) 1 (1.0)	4 (6.7) 52 (86.7) 4 (6.7) 0 (0.0)	<0.001 <sup>b</sup>

(<sup>a</sup>) P-value from Student's t-test.

(<sup>b</sup>) P-value from Fisher's exact test or Chi-square test.

Abbreviations: ns, non-significant

**Table S2.** Ratios of metabolites related to TRP of participants.

RATIO		COCAINE GROUP	CONTROL GROUP	P-value <sup>a</sup>
<b>KYN/TRP</b>	mean (95%CI)	$7.08 \times 10^{-2}$ ( $5.92 \times 10^{-2}$ - $8.47 \times 10^{-2}$ )	$7.60 \times 10^{-2}$ ( $6.22 \times 10^{-2}$ - $9.31 \times 10^{-2}$ )	ns
<b>KA/KYN</b>	mean (95%CI)	$1.49 \times 10^{-2}$ ( $1.36 \times 10^{-2}$ - $1.63 \times 10^{-2}$ )	$1.73 \times 10^{-2}$ ( $1.57 \times 10^{-2}$ - $1.91 \times 10^{-2}$ )	<b>0.022</b>
<b>QA/KYN</b>	mean (95%CI)	11.02 (9.73-12.47)	9.42 (8.47-10.50)	ns
<b>5-HT/TRP</b>	mean (95%CI)	$2.39 \times 10^{-3}$ ( $2.07 \times 10^{-3}$ - $2.81 \times 10^{-3}$ )	$1.94 \times 10^{-3}$ ( $1.70 \times 10^{-3}$ - $2.25 \times 10^{-3}$ )	<b>0.046</b>

(<sup>a</sup>) P-values from ANCOVA (*F* statistics and degrees of freedom are indicated in the text).  
Abbreviations: ns, non-significant

**Table S3.** Ratios of metabolites related to TRP metabolism of abstinent CUD-patients according to comorbid mental disorders.

RATIO		COMORBID MENTAL DISORDERS		P-value <sup>a</sup>
		NON-COMORBID	COMORBID	
<b>KYN/TRP</b>	mean (95%CI)	$8.89 \times 10^{-2}$ ( $6.68 \times 10^{-2}$ - $11.83 \times 10^{-2}$ )	$6.56 \times 10^{-2}$ ( $5.24 \times 10^{-2}$ - $8.22 \times 10^{-2}$ )	0.063
<b>KA/KYN</b>	mean (95%CI)	$1.52 \times 10^{-2}$ ( $1.31 \times 10^{-2}$ - $1.76 \times 10^{-2}$ )	$1.43 \times 10^{-2}$ ( $1.27 \times 10^{-2}$ - $1.61 \times 10^{-2}$ )	0.772
<b>QA/KYN</b>	mean (95%CI)	10.67 (8.63-13.15)	10.45 (8.77-12.46)	0.855
<b>5-HT/TRP</b>	mean (95%CI)	$3.36 \times 10^{-3}$ ( $2.47 \times 10^{-3}$ - $4.56 \times 10^{-3}$ )	$3.06 \times 10^{-3}$ ( $2.40 \times 10^{-3}$ - $3.88 \times 10^{-3}$ )	0.582

(<sup>a</sup>) P-values from ANCOVA (*F* statistics and degrees of freedom are indicated in the text).