Prediction of affective and anxiety disorders in adult men on the basis of steroid profiling

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Background

Affective disorders (depressions, AF) and anxiety disorders (AN) affect almost ¼ population during the lifespan Besides structural and functional changes the pathologies manifests as biochemical immunological and psychoneuroendocrinological alterations with high impact on both HPA and HPG axes and consequently on steroid metabolome in the CNS and periphery. The peripheral steroidogenesis substantially influence the steroid metabolome in the CNS despite the local production of a part of the substances in the CNS tissues. CRH participates in the pathophysiology of mental disorders and, at the same time, may regulate androgen synthesis in adrenal *zona reticularis*. However, the relevance of CRH as predictor is low due to its low stability in the human body as well as in the samples of body fluids. In our previous studies, we found the pregnancy steroids (the formation of which is stimulated by placental CRH) as good predictors of the onset of labor.

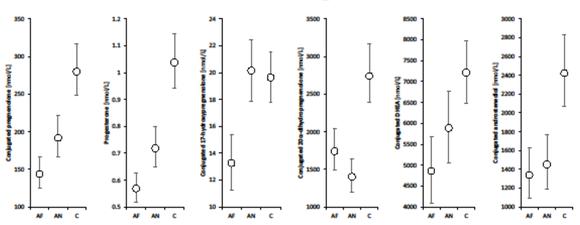
Objective

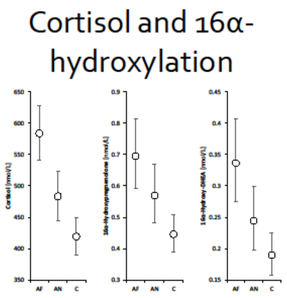
We, assume that alterations in the production of adrenal sulfated Δ^5 steroids (primarily synthesized in adrenal *zona reticularis*) might predict the presence of the aforementioned neuropathologies, which are also affected by CRH.

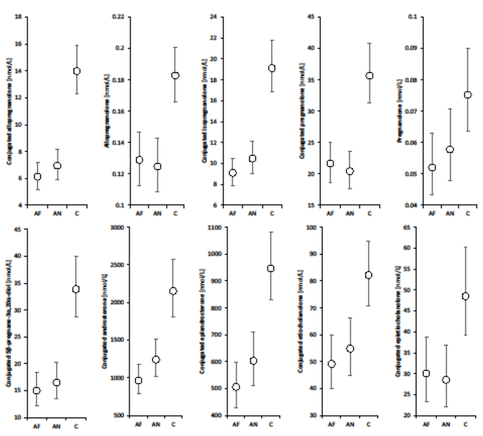
Method

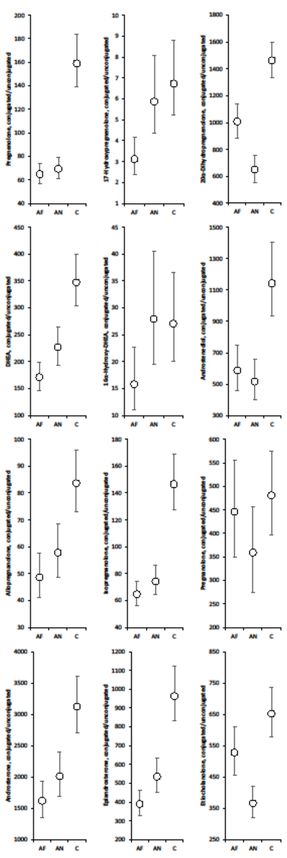
Profiling of circulating steroids in the groups of adult men with affective disorders (AF, n=20), anxiety disorders (AN, n=20) and in the group of age- and gender-corresponding controls (C, n=30) with the use of multicomponent GC-MS method for most steroids and immunoanalysis for additional ones.

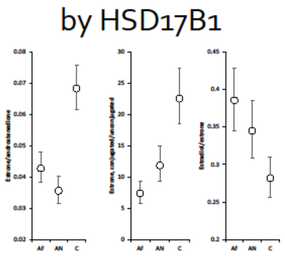
The results were analyzed by three independent statistical methods such as one-way ANOVA, ROC curves and multivariate regression with reduction of dimensionality (OPLS method). Prior further statistical processing, the original continuous variables were transformed by power transformations to attain constant variance and data symmetry. The dependent dichotomous variable (presence vs. absence of pathology) underwent logistic transformation to obtain the values within the interval 0 and 1.

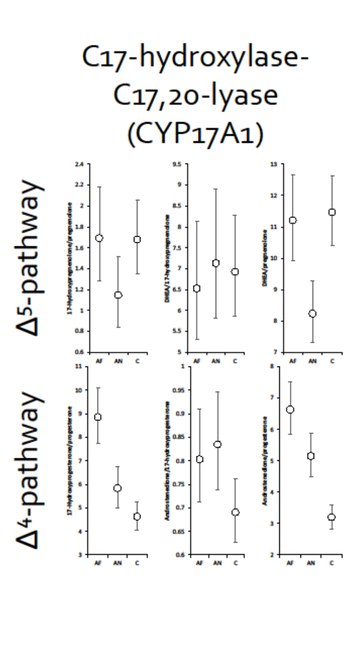












Results

Discrimination of AF-group from controls by OPLS method was absolute as in the case of AN-group from controls (sensitivity = 1.000 (0.839, 1.000), specificity = 1.000 (0.887, 1.000) , shown as estimates with 95%onfidence intervals). Relatively good predictivity was found also for discrimination between D-group from A-group (seniitivity = 0.850 (0.640, 0.948), specificity = 0.900 (0.699, 0.972)).

Men with affective disorders (vs. controls) vs. circulating steroids and other parameters, as evaluated by OPLS model

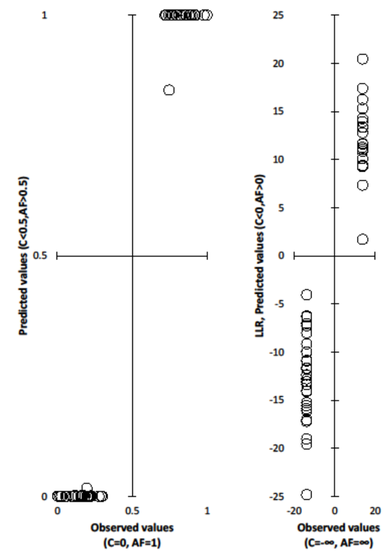
		Predictive component		
	Variable	Component loading	t-statistic	R[a]
Relevant predictors (matrix X)	LH	0.162	2.83	0.397 *
	SHBG	0.112	2.58	0.274 *
	Pregnenolone sulfate	-0.237	-6.28	-0.577 **
	17-Hydroxypregnenolone sulfate	-0.199	-3.34	-0.501 **
	20α-Dihydropregnenolone sulfate	-0.164	-2.47	-0.399 *
	16α-Hydroxypregnenolone	0.166	2.04	0.407 *
	DHEAS	-0.168	-4.14	-0.409 **
	16α-Hydroxy-DHEA	0.163	2.17	0.398 *
	Conjugated androstenediol	-0.204	-3.32	-0.497 **
	Progesterone	-0.260	-4.79	-0.635 **
	Androstenedione	0.128	1.92	0.314 *
	5α-Dihydrotestosterone	-0.152	-2.25	-0.370 *
	Allopregnanolone	-0.162	-2.82	-0.394 *
	Allopregnanolone sulfate	-0.273	-7.27	-0.664 **
	Isopregnanolone sulfate	-0.253	-7.39	-0.616 **
	Pregnanolone	-0.140	-3.12	-0.339 **
	Pregnanolone sulfate	-0.181	-8.63	-0.440 **
	Conjugated 5α-pregnane-3β,20α-diol	-0.173	-5.27	-0.422 **
	Conjugated 5β-pregnane-3β,20α-diol	-0.363	-12.92	-0.885 **
	Conjugated androsterone	-0.216	-4.91	-0.529 **
	Conjugated epiandrosterone	-0.215	-4.30	-0.525 **
	Conjugated etiocholanolone	-0.167	-3.48	-0.407 **
	Conjugated 5α-androstane-3α,17β-diol	-0.099	-2.51	-0.244 *
	Conjugated 5β-androstane-3α,17β-diol	-0.264	-6.14	-0.644 **
	Cortisol	0.174	2.27	0.425 *
(matrix Y)	AF men (vs. controls)	1.000	15.44	0.944 **
Explained variability		89.1% (75.7% after cross-validation)		

[a] *R...Component loadings expressed as a correlation coefficients with predictive component, *p<0.05, **p<0.01*

Men with anxiety disorder (vs. controls) vs. circulating steroids and other parameters, as evaluated by OPLS model

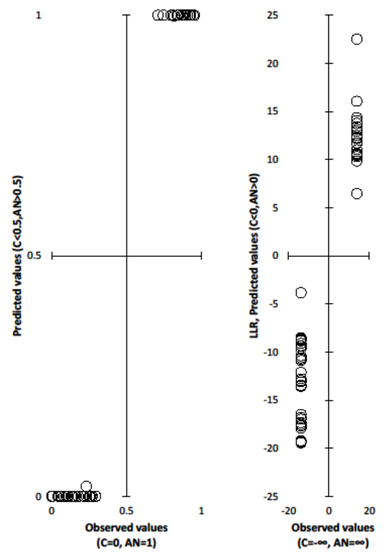
		Predictive component		
	Variable	Component loading	t-statistic	R[a]
Relevant predictors (matrix X)	LH	0.168	3.77	0.382 **
	Pregnenolone	0.193	4.96	0.438 **
	Pregnenolone sulfate	-0.178	-3.72	-0.405 **
	20α-Dihydropregnenolone	0.131	2.20	0.298 *
	20α-Dihydropregnenolone sulfate	-0.257	-6.23	-0.585 **
	DHEAS	-0.099	-1.61	-0.225
	7β-Hydroxy-DHEA	0.185	3.29	0.422 **
	Conjugated androstenediol	-0.199	-4.50	-0.452 **
	5-Androstene-3β,7α,17β-triol	0.077	2.20	0.175 *
	5-Androstene-3β,7β,17β-triol	0.237	6.68	0.540 **
	Progesterone	-0.172	-2.94	-0.390 *
	Allopregnanolone	-0.112	-2.27	-0.255 *
	Allopregnanolone sulfate	-0.264	-9.27	-0.601 **
	Isopregnanolone sulfate	-0.270	-6.07	-0.614 **
	Pregnanolone sulfate	-0.243	-6.06	-0.553 **
	Conjugated 5β-pregnane-3α,20α-diol	-0.206	-5.58	-0.469 **
	Conjugated 5β-pregnane-3β,20α-diol	-0.399	-15.51	-0.907 **
	Conjugated androsterone	-0.200	-3.81	-0.454 **
	Conjugated epiandrosterone	-0.197	-3.71	-0.448 **
	Conjugated etiocholanolone	-0.165	-4.06	-0.374 **
	Conjugated epietiocholanolone	-0.151	-2.43	-0.343 *
	Conjugated 5α-androstane-3β,17β-diol	-0.319	-9.65	-0.726 **
(matrix Y)	AN men (vs. controls)	0.707	23.69	0.959 **
Explained variability		92% (85.6% after cross-validation)		

[a] *R...Component loadings expressed as a correlation coefficients with predictive component, *p<0.05, **p<0.01*



	R+	R-
T+	20	0
T-	0	30

Sensitivity = 1.000 (0.839, 1.000)
Specificity = 1.000 (0.887, 1.000)



	R+	R-
T+	20	0
T-	0	30

Sensitivity = 1 (0.839, 1)
Specificity = 1 (0.887, 1)

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