

Sex difference in peripheral inflammatory biomarkers in drug-naïve patients with major depression in young adulthood

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Table S1. Results of baseline in inflammatory biomarkers

Biomarkers	Total population				Male				Female			
	Control		MDD		Control		MDD		Control		MDD	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
TNF- α (pg/ml)	9.868	6.384	9.316	5.295	24.36	25.86	10.38	5.798	8.327	5.794	26.25	36.96
Cortisol (ng/ml)	43.06	10.92	42.68	12.20	45.54	10.27	43.53	13.43	39.93	11.30	42.03	11.64
Adiponectin (ng/ml)	8026	3999	7692	4020	7194	3998	7024	3923	8795	3920	8261	4087
CCL1 (pg/ml)	467.1	510.4	381.5	475.5	471.1	459.2	262.6	386.3	240.6	402.2	289.9	413.3
CCL2 (pg/ml)	25.98	20.94	23.02	28.05	31.61	22.80	27.68	32.11	15.30	8.335	10.30	7.066

Table S2. Correlation of depression index scores and inflammatory biomarkers

Inflammatory		Indexes of depressive symptoms							
biomarkers		BDI	STAI-X-1	HAMD-17	BIS	RSE	BHS	KSSI	RAS
IL-1β	r	0.3376	0.5005	0.2556	0.1309	-0.3755	0.4497	0.2275	-0.3303
	p	0.0007***	<0.0001****	0.0111*	0.2189	0.0005***	<0.0001****	0.0547	0.0046**
	95% CI	0.1492, 0.5024	0.3041, 0.6561	0.06013, 0.4321	-0.07841, 0.3291	-0.5479, -0.1725	0.1222, 0.5109	-0.004495, 0.4362	-0.5221, -0.1068
IL-6	r	0.1681	0.2805	0.1407	0.1872	-0.2352	0.2656	0.2884	-0.2772
	p	0.0981	0.0162*	0.1669	0.0773	0.0334*	0.0159*	0.0133*	0.0176*
	95% CI	-0.03144, 0.3547	0.05383, 0.4796	-0.05941, 0.3300	-0.02078, 0.3796	-0.4303, -0.01914	0.05154, 0.4564	0.06246, 0.4863	-0.4769, -0.05023
CRP	r	0.1565	0.02614	0.2068	-0.06233	-0.04811	0.02740	-0.08822	0.04820
	p	0.1279	0.8299	0.0432*	0.5640	0.6717	0.8093	0.4677	0.6920
	95% CI	-0.04550, 0.3461	-0.2102, 0.2596	0.006558, 0.3911	-0.2683, 0.1491	-0.2651, 0.1735	-0.1935, 0.2457	-0.3167, 0.1499	-0.1890, 0.2801
IL-17	r	0.2368	0.1728	0.2218	0.1777	0.1566	0.2073	0.1727	-0.2711
	p	0.0189*	0.1438	0.0282*	0.1298	0.1574	0.0600	0.1441	0.0204*
	95% CI	0.04025, 0.4158	-0.05970, 0.3875	0.02441, 0.4026	-0.3602, 0.06119	-0.3602, 0.06119	-0.008824, 0.4049	-0.05982, 0.3874	-0.4718, -0.04368
TNF-α	r	0.1128	0.07512	-0.1592	0.1095	0.02227	-0.07740	-0.1395	-0.03842
	p	0.3386	0.5821	0.1611	0.3041	0.8569	0.5304	0.2922	0.7727
	95% CI	-0.1188, 0.3328	-0.1916, 0.3315	-0.3674, 0.06423	-0.05297, 0.3904	-0.2174, 0.2594	-0.3102, 0.1641	-0.3820, 0.1210	-0.2917, 0.2199
Cortisol	r	0.01793	-0.1866	0.02334	0.1093	-0.06521	0.1426	0.02642	0.06072
	p	0.8594	0.1277	0.8177	0.2997	0.5556	0.1957	0.8232	0.6073
	95% CI	-0.1792, 0.2136	-0.2498, 0.2071	-0.1739, 0.2188	-0.09777, 0.3073	-0.2758, 0.1514	-0.07412, 0.3464	-0.2034, 0.2534	-0.1702, 0.2853
Adiponectin	r	0.01455	-0.04795	0.03657	-0.05070	-0.03754	0.03394	0.1627	-0.009076
	p	0.8857	0.6850	0.7179	0.6313	0.7346	0.7592	0.1661	0.9388
	95% CI	-0.1824, 0.2104	-0.2735, 0.1826	-0.1611, 0.2314	-0.2529, 0.1558	-0.2500, 0.1783	-0.1818, 0.2466	-0.06843, 0.3772	-0.2371, 0.2199
CCL1	r	-0.003289	0.04097	-0.03231	0.01168	-0.04715	0.05294	0.1755	-0.05959
	p	0.9741	0.7289	0.7496	0.9120	0.6702	0.6324	0.1347	0.6140

	-0.1996,	-0.1894,	-0.2273,	-0.1937,	-0.2590,	-0.1634,	-0.05524,	-0.2843,
95% CI	0.1933	0.2670	0.1652	0.2160	0.1690	0.2644	0.3885	0.1713
r	-0.03186	-0.1866	-0.01424	-0.1595	0.2303	-0.1429	-0.09173	0.1873
CCL2	<i>p</i>	0.7630	0.1277	0.8928	0.1448	0.0423*	0.2119	0.4569
	95% CI	-0.2352,	-0.4069,	-0.2185,	-0.3604,	0.008085,	-0.3543,	-0.3231,
		0.1741	0.05434	0.1912	0.05557	0.4308	0.08226	0.1500
								0.4076

Table S3. Correlation of depressive scores and inflammatory biomarkers in male group

Inflammatory biomarkers	Indexes of depressive symptoms								
	BDI	STAI-X-1	HAMD-17	BIS	RSE	BHS	KSSI	RAS	
	r	0.2444	0.4809	0.2125	0.3024	-0.3432	0.4318	0.3124	-0.4247
IL-1β	p	0.1057	0.0062**	0.1611	0.0650	0.0404*	0.0085**	0.0870	0.0173*
	95% CI	-0.05306, 0.5019	0.1525, 0.7137	-0.08650, 0.4764	-0.01926, 0.5673	-0.6038, -0.01649	0.1203, 0.6659	-0.04721, 0.6004	-0.6772, -0.08269
	r	0.09509	0.2964	-0.01284	0.1217	0.2685	0.3270	0.3019	-0.2167
IL-6	p	0.5249	0.0940	0.9317	0.4545	0.1032	0.0283*	0.0877	0.2259
	95% CI	-0.1975, 0.3722	-0.05231, 0.5807	-0.2990, 0.2754	-0.1974, 0.4174	-0.05612, 0.5417	0.03694, 0.5662	-0.04629, 0.5847	-0.5213, 0.1369
	r	0.1545	0.09208	0.1410	-0.1058	-0.08821	0.05216	-0.04851	-0.1351
CRP	p	0.3109	0.6222	0.3555	0.5271	0.6089	0.7626	0.7955	0.4688
	95% CI	-0.1457, 0.4287	-0.2712, 0.4324	-0.1592, 0.4173	-0.4117, 0.2214	-0.4051, 0.2476	-0.2813, 0.3744	-0.3961, 0.3113	-0.4671, 0.2303
	r	0.5033	0.4233	0.4880	0.2250	-0.4448	0.4919	0.3513	-0.5412
IL-17	p	0.0005***	0.0141	0.0008***	0.1685	0.0058**	0.0020**	0.0487*	0.0014*
	95% CI	0.07291, 0.5856	0.1382, 0.7000	0.05273, 0.5721	-0.09744, 0.5047	-0.672, -0.1411	0.1997, 0.7037	0.002837, 0.6236	-0.7487, -0.2372
	r	0.06040	0.08432	-0.06521	-0.08602	0.01444	0.02736	0.07944	0.04398
TNF-α	p	0.7225	0.6953	0.7014	0.6513	0.9407	0.8880	0.7121	0.8383
	95% CI	-0.2690, 0.3771	-0.3304, 0.4718	-0.3812, 0.2645	-0.4330, 0.2831	-0.3540, 0.3790	-0.3427, 0.3900	-0.3348, 0.4679	-0.3660, 0.4397
	r	-0.1435	-0.09113	-0.09080	-0.04554	-0.07459	0.03552	0.3019	-0.2167
Cortisol	p	0.3359	0.6140	0.5438	0.7802	0.6563	0.8416	0.0877	0.2259
	95% CI	-0.4137, 0.1499	-0.4213, 0.2604	-0.3684, 0.2017	-0.3521, 0.2699	-0.3852, 0.2512	-0.2893, 0.3495	-0.04629, 0.5847	-0.5213, 0.1369
	r	0.009301	-0.09972	0.01211	0.002145	0.008912	0.01358	0.2471	0.1183
Adiponectin	p	0.9505	0.5808	0.9356	0.9895	0.9577	0.9355	0.1657	0.5121
	95% CI	-0.2787, 0.2957	-0.4284, 0.2523	-0.2761, 0.2983	-0.3096, 0.3135	-0.3117, 0.3277	-0.3074, 0.3318	-0.1052, 0.5443	-0.2346, 0.4437
	r	-0.1102	-0.1341	-0.2122	-0.2997	0.03847	-0.09459	0.06505	0.2083
CCL1	p	0.4609	0.4567	0.1521	0.0603	0.8186	-0.4021, 0.2321	-0.2847, 0.3995	-0.1454, 0.5148
	95% CI	-0.3751, 0.2075	-0.4565, 0.2193	-0.4707, 0.07981	-0.5591, 0.01314	-0.2848, 0.3539	-0.4021, 0.2321	-0.2847, 0.3995	-0.1454, 0.5148
	r	-0.1509	-0.2443	-0.1143	-0.1332	0.2778	-0.2400	-0.2376	0.2881
CCL2	p	0.3464	0.1933	0.4653	0.4320	0.1061	0.1649	0.2062	0.1226
	95% CI	-0.4382, 0.1644	-0.5557, 0.1273	-0.4010, 0.1927	-0.4384, 0.1995	-0.06114, 0.5594	-0.5309, 0.1014	-0.5508, 0.1343	-0.08051, 0.5874

Table S4. Correlation of depressive scores and inflammatory biomarkers in female group

Inflammatory biomarkers	Indexes of depressive symptoms								
	BDI	STAI-X-1	HAMD-17	BIS	RSE	BHS	KSSI	RAS	
	r	0.3757	0.4714	0.3008	0.2235	-0.5629	0.4633	0.4718	-0.5568
IL-1β	p	0.0056**	0.0019**	0.0286*	0.1112	<0.0001****	0.0012**	0.0018**	0.0002***
	95% CI	0.1173, 0.5865	0.1914, 0.6804	0.03313, 0.5282	-0.05265, 0.4679	-0.7334, -0.3258	0.1999, 0.6643	0.1920, 0.6807	-0.7381, -0.3006
	r	0.2365	0.2652	0.2578	0.2178	-0.3319	0.3270	0.2762	-0.3247
IL-6	p	0.0982	0.0981	0.0678	0.1287	0.0297*	0.0283*	0.0844	0.0409*
	95% CI	0.03058, 0.5304	-0.05052, 0.5328	-0.01922, 0.4981	-0.06453, 0.4678	-0.5750, -0.03496	0.03694, 0.5662	-0.03867, 0.5412	-0.5778, -0.01462
	r	0.2351	0.06551	0.2596	-0.1058	-0.06448	0.08959	-0.06686	0.09525
CRP	p	0.0935	0.6880	0.0631	0.5271	0.6739	0.5584	0.6819	0.5588
	95% CI	-0.04051, 0.4774	-0.2512, 0.3696	-0.01441, 0.4973	-0.4117, 0.2214	-0.3514, 0.2335	-0.2095, 0.3734	-0.3707, 0.2499	-0.2229, 0.3951
	r	0.04092	0.1315	0.04571	0.01107	0.1279	-0.05875	-0.01130	-0.06777
IL-17	p	0.7711	0.2640	0.7452	0.9379	0.3970	0.6981	0.9441	0.6737
	95% CI	-0.2320, 0.3079	-0.2873, 0.3279	-0.2275, 0.3122	-0.2627, 0.2832	-0.1687, 0.4033	-0.3433, 0.2356	-0.3179, 0.2975	-0.3678, 0.2451
	r	0.3043	0.2403	0.2486	0.1921	-0.2832	0.2935	0.2522	-0.2518
TNF-α	p	0.0446*	0.1710	0.1037	0.2172	0.0849	0.0737	0.1502	0.1508
	95% CI	0.008054, 0.5514	-0.1066, 0.5351	-0.05223, 0.5080	-0.1150, 0.4656	-0.5529, 0.04023	-0.02896, 0.5607	-0.09407, 0.5440	-0.5437, 0.09447
	r	0.1718	0.05319	0.1304	0.2293	-0.07560	0.2395	0.04086	-0.02205
Cortisol	p	0.2188	0.7412	0.3519	0.1021	0.6175	0.1089	0.7998	0.8912
	95% CI	-0.1034, 0.4225	-0.2588, 0.3551	-0.1450, 0.3871	-0.04662, 0.4726	-0.3581, 0.2196	-0.05469, 0.4954	-0.2703, 0.3443	-0.3275, 0.2876
	r	0.01797	-0.03279	0.05301	-0.1083	-0.05177	0.2395	0.1065	-0.01918
Adiponectin	p	0.8984	0.8387	0.7062	0.4448	0.7326	0.1089	0.5076	0.9052
	95% CI	-0.2536, 0.2869	-0.3371, 0.2777	-0.2205, 0.3188	-0.3703, 0.1697	-0.3371, 0.2422	-0.2254, 0.3528	-0.2081, 0.4011	-0.3250, 0.2903
	r	0.1018	0.1633	0.1012	0.2054	-0.1397	0.1615	0.2209	-0.3078
CCL1	p	0.4682	0.3075	0.4707	0.1441	0.3545	0.2837	0.1652	0.0503
	95% CI	-0.1733, 0.3622	-0.1520, 0.4485	-0.1739, 0.3617	-0.07160, 0.4530	-0.4133, 0.1571	-0.1352, 0.4316	-0.09320, 0.4949	-0.5623, -8.998
	r	0.1018	-0.1906	-0.03903	-0.1439	0.2238	-0.1348	-0.009729	0.1065
CCL2	p	0.4682	0.2450	0.7857	0.3187	0.1442	0.3831	0.9531	0.5187
	95% CI	-0.3436, 0.2049	-0.3113, 0.2392	-0.4061, 0.1401	-0.07835, 0.4883	-0.4151, 0.1689	-0.4147, 0.2091	-0.3243, 0.3068	-0.2163, 0.4084

Supplementary figures

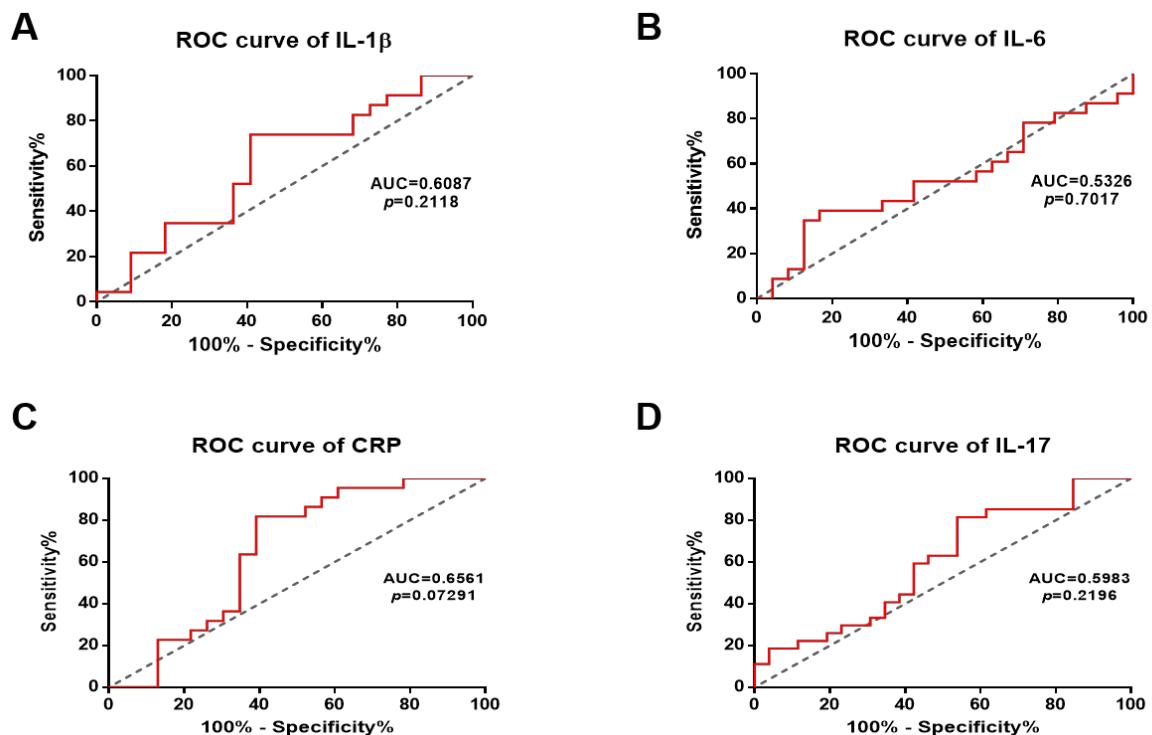


Fig. S1. The results of receiver operating characteristic (ROC) analysis for inflammatory biomarkers in young adulthood. (A-C) ROC curves of IL-1 β , IL-6, and CRP in male group. (D) IL-17 in female group. Male (HC; n=24, MDD; n=23) and female (HC; n=26, MDD; n=27).