

Adjunctive minocycline for major depressive disorder: Characterisation of peripheral immune-inflammatory profile

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Background

Primary treatments for major depressive disorder (MDD) are useful, however shortfalls remain in both remission and recovery [1].

The identification of biological markers that relate to treatment response may improve understanding of the pathophysiology of MDD and assist with this shortfall [2].

Inflammation is now known to play a role in the pathophysiology of MDD, leading to clinical trials of adjunctive treatments that target these pathways [3].

Minocycline has been shown to modify the immune-inflammatory processes, however its effects on the inflammatory profile of participants with MDD are unknown [4].

Aim: This study aims to address a secondary outcome of a clinical trial by assessing inflammatory biomarkers in collected peripheral blood samples.

Methods

This current study is a secondary analysis of peripheral blood samples collected from patients during a randomised placebo-controlled trial evaluating 12 weeks of adjunctive minocycline (200 mg/day) in addition to treatment as usual (ACTRN12612000283875) [5].

Samples were collected from consenting participants at baseline (week 0), and at the end of treatment (week 12).

Of the 71 participants that completed the trial, at least one serum aliquot was available for 47 of the participants. Placebo group $n=24$ (13f/11m), and the minocycline group $n=23$ (13f/10m).

Samples were assessed for an array of 46 inflammatory analytes including cytokines, chemokines and acute-phase reactants using Myriad RBM's InflammationMAP[®]

Composite Z-scores were calculated for detectable immune-inflammatory analytes, and statistical analyses were conducted using SPSS Statistical Package version 25.0 by an investigator blinded to treatment.

Preliminary analysis included generation of descriptives, and subsequent Spearman's nonparametric correlation analysis to assess analyte group profile at baseline and endpoint. Measures of depression (MADRS) and anxiety (HAMA) were included to assess treatment response.

Preliminary Results

	MADRS	HAMA	AAT	A2M	B2M	BDNF	CRP	C3	CCL11	FVII	FRTN	HAPT	ICAM-1	IL-1β	IL-1RA	IL-8	IL12p40	IL-15	IL-18	IL-23	MIP-1β	MMP3	MMP9	MCP1	SCF	RANTES	TIMP1	TNFR2	VCAM-1	VEGF	VDBP	vWF	MINOCYCLINE
MADRS	0.555	0.103	-0.043	0.072	0.317	-0.007	-0.148	-0.083	-0.438	0.082	0.035	0.176	0.219	-0.167	0.214	-0.020	0.049	-0.246	-0.246	-0.208	0.101	0.495	-0.272	-0.290	-0.305	-0.065	0.081	0.208	-0.014	0.176	0.131	MADRS	
HAMA	0.585	-0.234	0.167	-0.015	0.408	-0.310	0.112	-0.364	-0.562	0.224	-0.302	-0.007	0.140	-0.190	-0.008	-0.405	-0.081	0.060	-0.076	0.047	0.088	0.431	-0.556	-0.441	-0.235	-0.330	-0.036	0.257	0.017	0.063	0.110	HAMA	
AAT	0.367	-0.011	0.292	0.449	-0.159	0.180	0.236	-0.036	-0.067	-0.359	0.453	0.118	0.209	0.272	0.030	0.077	0.164	-0.417	-0.258	-0.174	0.245	-0.158	0.010	-0.001	0.274	0.447	0.243	0.070	0.190	0.228	0.166	AAT	
A2M	-0.166	-0.059	0.182	0.468	-0.251	0.102	0.565	-0.518	-0.433	-0.021	0.241	0.268	0.056	-0.096	-0.351	-0.069	-0.252	-0.119	-0.156	-0.367	-0.280	0.083	-0.319	-0.354	0.415	0.585	0.212	0.293	-0.101	-0.003	0.209	A2M	
B2M	0.101	0.116	0.331	0.122	-0.178	0.541	0.207	0.094	-0.054	0.170	0.557	0.537	0.243	0.267	-0.007	0.221	0.593	0.011	0.290	0.084	0.232	0.022	0.150	0.110	0.248	0.706	0.678	0.631	-0.119	0.355	0.607	B2M	
BDNF	0.085	-0.116	0.315	0.025	0.254	-0.155	-0.005	-0.168	-0.107	-0.227	-0.197	-0.315	0.021	-0.236	0.152	-0.044	0.061	-0.326	0.295	0.238	0.039	0.351	0.042	-0.110	0.295	-0.196	0.075	-0.160	0.073	-0.105	0.030	BDNF	
CRP	-0.168	-0.086	0.007	-0.557	-0.055	0.009	0.314	0.127	0.418	-0.086	0.761	0.364	0.407	0.527	-0.531	0.681	0.419	0.063	0.334	-0.074	-0.097	0.053	0.254	0.156	0.171	0.548	0.373	0.255	-0.034	0.635	0.640	CRP	
C3	0.271	-0.160	0.235	-0.286	-0.014	0.189	0.545	-0.383	0.082	0.022	0.254	0.160	0.058	0.130	-0.417	0.319	0.044	0.038	0.029	-0.111	-0.178	0.138	-0.086	0.097	0.324	0.439	0.294	0.146	0.401	0.234	0.427	C3	
CCL11	0.491	0.165	0.328	0.065	0.588	0.450	0.079	0.420	0.396	0.241	0.168	0.000	-0.027	0.131	-0.077	0.322	0.181	0.117	0.241	0.317	0.476	-0.110	0.623	0.421	-0.194	-0.032	0.068	0.083	-0.169	0.241	0.199	CCL11	
FVII	-0.273	-0.262	-0.121	-0.332	-0.022	0.168	0.473	0.636	0.275	0.109	0.331	-0.114	0.160	0.362	0.053	0.600	0.320	0.110	0.378	0.133	0.228	-0.006	0.627	0.708	-0.018	-0.050	0.274	0.064	0.419	0.125	0.349	FVII	
FRTN	-0.488	-0.178	-0.062	-0.318	0.215	-0.072	0.269	-0.196	-0.355	0.034	0.009	0.415	0.193	-0.071	0.561	-0.115	0.464	0.562	0.242	0.511	0.298	0.213	0.249	0.151	-0.339	-0.063	0.285	0.445	0.240	0.116	0.345	FRTN	
HAPT	-0.204	-0.192	-0.074	-0.491	-0.005	0.003	0.715	0.595	0.168	0.601	0.349	0.183	0.725	0.588	-0.193	0.526	0.669	0.077	0.384	-0.044	0.256	0.004	0.476	0.179	0.291	0.649	0.416	0.208	-0.011	0.758	0.668	HAPT	
ICAM-1	-0.084	0.131	-0.171	-0.222	0.349	0.270	0.288	-0.050	0.351	0.229	0.188	0.167	0.019	0.001	-0.214	0.074	0.153	0.277	0.134	0.302	-0.007	0.148	0.073	-0.093	0.022	0.264	0.235	0.355	-0.058	0.194	0.341	ICAM-1	
IL-1β	-0.398	-0.485	0.058	-0.369	0.272	0.580	0.301	0.325	0.320	0.508	0.370	0.362	0.302	0.067	0.057	0.234	0.364	0.646	0.137	0.379	0.070	0.185	0.386	0.359	-0.192	0.273	0.369	0.354	0.198	0.203	0.788	0.716	IL-1β
IL-1RA	0.362	0.244	0.048	-0.324	0.192	0.159	0.597	0.498	0.379	0.390	0.029	0.398	0.442	0.086	-0.077	0.614	0.705	0.272	0.304	0.092	0.111	-0.134	0.238	0.189	-0.063	0.507	0.378	0.074	0.199	0.512	0.504	IL-1RA	
IL-8	0.137	0.376	-0.153	0.202	-0.054	0.101	0.081	-0.178	0.096	0.150	-0.254	0.048	0.407	-0.291	0.640	0.546	0.246	0.028	0.267	0.402	-0.020	-0.004	0.062	-0.513	-0.292	0.178	0.119	0.543	-0.179	-0.202	IL-8		
IL12p40	-0.136	-0.046	-0.503	-0.040	0.027	0.098	-0.161	-0.015	0.048	0.238	-0.237	-0.045	0.388	0.124	-0.044	0.135	0.313	-0.056	0.443	-0.035	0.026	0.280	0.458	0.386	0.241	0.503	0.400	0.127	0.158	0.424	0.639	IL12p40	
IL-15	-0.049	0.069	-0.064	-0.179	0.379	0.285	-0.236	-0.210	0.248	0.194	0.075	-0.268	0.447	0.513	-0.200	-0.015	0.549	0.304	0.322	0.557	0.362	-0.122	0.362	0.367	0.014	0.654	0.902	0.696	0.385	0.633	0.798	IL-15	
IL-18	-0.091	0.457	-0.163	-0.184	0.218	-0.095	0.050	-0.389	0.013	-0.260	0.396	0.026	0.547	0.113	-0.086	-0.048	0.041	0.275	0.096	0.460	0.150	0.185	0.158	-0.608	0.045	0.164	-0.003	0.134	0.058	0.051	IL-18		
IL-23	-0.439	-0.611	0.175	0.065	0.277	0.367	0.035	0.079	0.146	0.289	0.155	-0.080	0.162	0.579	-0.035	-0.252	0.210	0.405	-0.252	0.431	0.464	0.341	0.655	0.454	0.202	0.195	0.387	-0.017	0.041	0.174	0.488	IL-23	
MIP-1β	0.066	0.231	-0.278	0.323	-0.017	-0.152	0.126	0.131	0.197	0.057	-0.127	0.098	0.200	-0.388	0.497	0.418	0.038	-0.479	-0.064	-0.274	0.349	-0.080	0.456	0.379	-0.047	-0.014	0.358	0.116	0.219	0.081	0.208	MIP-1β	
MMP3	-0.286	0.164	-0.103	0.170	-0.043	0.046	-0.252	-0.281	-0.177	-0.062	0.036	-0.248	0.186	0.175	-0.270	0.237	0.343	0.450	0.495	-0.024	-0.230	0.038	0.478	0.586	-0.183	-0.060	0.316	0.084	0.207	0.014	0.140	MMP3	
MMP9	-0.254	-0.111	0.051	0.212	0.194	-0.051	-0.369	-0.128	-0.048	0.122	0.000	-0.084	-0.166	0.215	-0.470	-0.294	0.306	0.345	-0.090	0.502	-0.369	0.152	0.051	-0.278	0.120	-0.001	0.189	0.031	0.366	0.145	0.416	MMP9	
MCP1	0.273	0.366	0.170	0.222	0.241	0.146	0.264	0.179	0.406	0.103	-0.158	0.061	0.217	-0.177	0.466	0.491	-0.033	-0.059	-0.012	0.072	0.235	-0.062	-0.193	0.588	0.235	0.168	0.301	-0.039	0.078	0.239	0.462	MCP1	
SCF	0.255	-0.032	0.194	0.113	0.207	0.640	-0.149	0.391	0.585	0.394	-0.299	0.014	0.238	0.413	0.275	0.220	0.317	0.313	0.145	0.169	0.229	-0.128	0.067	-0.024	0.006	0.452	0.170	0.252	-0.126	0.167	SCF		
RANTES	-0.236	-0.316	-0.222	-0.185	0.006	0.410	0.448	0.212	0.219	0.194	-0.059	0.464	0.355	0.236	0.378	0.209	0.230	-0.225	-0.092	0.112	0.221	-0.316	-0.149	0.076	0.110	0.370	0.132	0.114	-0.202	0.108	0.307	RANTES	
TIMP1	-0.152	-0.073	0.057	-0.073	0.380	0.296	0.273	0.193	0.379	0.289	0.062	0.266	0.422	0.352	0.293	0.227	0.181	-0.086	0.042	0.134	0.044	0.088	-0.007	-0.119	0.347	0.436	0.342	-0.007	0.436	0.576	TIMP1		
TNFR2	0.132	0.212	0.105	-0.009	0.472	0.157	0.201	0.205	0.523	0.160	-0.114	0.152	0.059	0.527	0.419	-0.089	-0.205	0.183	-0.275	0.355	0.046	-0.353	0.106	0.373	0.239	0.616	0.632	0.405	0.171	0.660	TNFR2		
VCAM-1	0.205	0.004	0.203	0.005	0.516	0.191	-0.122	-0.063	0.315	-0.194	0.016	-0.093	0.223	0.063	0.234	-0.151	-0.032	0.044	0.206	-0.185	-0.119	-0.071	-0.166	-0.202	0.239	0.154	0.481	0.483	-0.005	0.178	0.526	VCAM-1	
VEGF	-0.060	-0.205	0.483	0.031	0.241	0.177	0.300	0.278	0.171	0.269	0.201	0.181	-0.005	0.209	0.041	-0.016	-0.244	-0.146	0.150	-0.129	-0.008	-0.123	0.242	0.287	-0.059	0.501	0.222	0.255	-0.013	0.240	VEGF		
VDBP	0.489	0.242	0.268	-0.174	0.141	0.296	0.043	0.290	0.064	-0.138	-0.060	-0.044	-0.043	-0.030	0.046	-0.308	-0.007	-0.169	-0.155	-0.008	-0.116	-0.298	-0.001	-0.096	-0.001	0.101	0.041	0.021	0.172	-0.204	0.657	VDBP	
vWF	0.057	-0.078	0.284	0.031	0.084	-0.017	0.432	0.335	0.211	-0.008	-0.138	0.433	0.119	-0.166	0.227	0.057	-0.125	-0.216	0.027	-0.191	0.225	-0.192	-0.317	0.150	-0.003	0.432	0.162	0.241	0.221	-0.001	0.180	vWF	

	MADRS	HAMA	AAT	A2M	B2M	BDNF	CRP	C3	CCL11	FVII
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