RBC fatty acid profile and sleep conditions in depression patients—a post-hoc analysis

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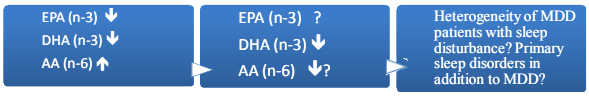
ABSTRACT

Background: Deviation of n-3 and n-6 PUFAs composition may play a role in depression, inflammation, autonomic dysfunction, and cardiovascular disease. However, their functions in sleep need to be further elucidated.

Method: We recruited a total of 122 MDD patients and 120 control subjects in psychiatric out patient clinics. Their severity of depression, sleep conditions and RBC fatty acid compositions were recorded and analyzed.

Results: MDD patients had significantly higher levels of EPA and DHA but lower level of AA. Positive correlation was noted between severity of depression and insomnia; however, a negative correlation was noted between AA level and middle insomnia symptoms.

Discussion: One explanation for patients who had higher level of AA turned out to have better sleep could be that, PGD2, a derivative of AA, is one of the most potent endogeneous sleep-promoting agents. Further studies are warranted to clarify their relationship and underlying mechanisms.



Introduction:

Previous studies suggested abnormal levels of omega-3 and omega-6 polyunsaturated fatty acids (n-3 and n6 PUFAs) may be part of the nexus of depression, inflammation, autonomic dysfunction, sleep disordered breathing and even cardiovascular disease. Among n3-PUFAs, eicosapentaenoic (EPA) and docosahexaenoic acid (DHA), the major bioactive components, are not synthesized in human body and should be obtained directly from the diet, particularly in fatty fish. The main n-3 fatty acid in the brain is DHA, comprising up to 10-20% of total fatty acids in the brain, whereas the n-3 fatty acids α-linolenic acid (ALA), EPA, and docosapentaenoic acid (DPA) comprise only 0.1% of total brain fatty acid composition. DHA is associated with neuronal membrane stability and the functions of serotonin and dopamine transmission, which might connect to the etiology of mood and cognitive manifestations of depression. EPA is important in the balance of the immune and neuronal functions by antagonizing membrane arachidonic acid (AA, an n-6 PUFA) and reducing prostaglandin E2 (PGE2) synthesis.

Animals studies disclosed a high EPA diet could attenuate the sickness behaviors, including anorexia, low activity, and a change in sleep pattern, induced by the high AA diets or the PGE2 treatment; and the sickness behaviors are similar to the somatic symptoms of depressive disorders in human. In human studies on the other hand, RBC-DHA level had been shown to be inversely related to the severity of obstructive sleep apnea (OSA), a sleep breathing disorder. And a link between low DHA status and less mature sleep patterns had been observed in newborns. Sleep disturbance, either insomnia or hypersomnia, is one of the diagnostic criteria of major depressive disorder (MDD). Base on our previous studies, we conducted a post-hoc analysis in an attempt to further elucidate the relationship between MDD, RBC PUFA levels and sleep disturbances.

Method

- 122 MDD out-patients and 120 control subjects collected.
- Depressive symptoms assessed (the 21-item Hamilton Rating Scale for Depression, HRSD, and the 21-item Beck Depression Inventory, BDI). Blood sample collected for analysis of levels of PUFAs. The Hamilton Depression Rating Scale (HDRS) was scored.
- RBC fatty acids assessed by independent-samples *t* test. The categorical data analyzed using $\chi 2$ (chi-squared) test or the Fisher exact test. A correlation analysis done to evaluate the relationship between the levels of fatty acids and sleep disturbances.

Results

	MDD Patients (N=93) N(%)	Controls (N=120) N(%)	P value
Age (y)	39.68±13.58	37.89±11.48	.300
Sex			.195
Male	19(8.9)	35(16.4)	
Female	74(34.6)	85(39.7)	
Smoking			.516
Not everyday	81(37.9)	109(50.9)	
Everyday	12(5.6)	11(5.1)	
Drinking			.996
Not everyday	89(41.6)	116(54.2)	
Everyday	4(1.9)	4(1.9)	

Table 1. No significant difference shown in basic demographic data; MDD patients significantly scored higher in baseline BDI scores (not shown).

	Patients (N=122) M±SD	Controls (N=120) M±SD	t value/p value
C20:4(n-6)	10.02±3.86	13.89±6.43	5.45[a] / <.001
C20:5(n-3)	0.78±.61	1.83±1.18	8.40[a] / <.001
C22:6(n-3)	2.83±2.33	4.32±2.33	4.64[a] / <.001

Note : [a] = Independent t test

Table 2. MDD patients and controls are significantly different in their RBC PUFA levels. MDD patients had significantly higher n-6 PUFA (AA) and lower n3-PUFAs (EPA and DHA) compared to controls.

	Insomnia_Early		Insomnia_Middle		Insomnia_Late	
Variables	Pearson r	p value	Pearson r	p value	Pearson r	p value
C20:4(n-6)	.017	.869	**-.284**	**.006**	-.071	.498
C20:5(n-3)	.134	.199	.039	.714	-.103	.324
C22:6(n-3)	-.002	.987	-.058	.583	-.173	.098

Table 3. Although in the MDD group, patients with more severe MDD also have more intense sleep disturbance (a positive correlation between BDI score and early/middle insomnia; not shown), a negative association was noted significantly between AA level and middle insomnia score in the MDD patients group.

Discussion

Low level of n3-PUFAs had been demonstrated to associate with endothelial dysfunction, more intense sleep disordered breathing such as OSA, and more severe major depressive disorders; supplemental n3-PUFAs treatment had been shown to improve MDD and sleep patterns in human. However, there is lack of literature directly dissecting the relationship between n6-PUFAs, especially AA, and sleep disorder. In our post-hoc analysis, an interesting inverse relationship was noted between AA level and the severity of middle insomnia, implying that at least some of the MDD patients may have more severe depression, but better sleep maintenance at the same time.

One explanation could be, prostaglandin D2 (PGD2), one of the most potent endogenous sleep-promoting agents, and a down-stream product of AA, also increases in MDD patients with higher level of AA. PGD2 had been shown to activate a center of non-rapid eye movement (NREM) sleep regulation in the ventrolateral preoptic area, probably mediated by adenosine signaling, which activation inhibits the histaminergic arousal center in the tuberomammillary nucleus via descending GABAergic and galaninergic projections.

Our study has several limitations. First of all, since it is a post-hoc analysis originally designed to study depressive patients, its measurements on MDD may not directly reflect the exact intensity of sleep disturbance. Also, since we had only measured AA rather than PGD2, whether elevated AA also implies increased PGD2 in the brain is not known Finally, we had only noticed the significant inverse relationship between AA level and middle insomnia but not sleep parameters; all above conditions warrant further larger scale studies using more direct measurements on sleep conditions for elucidation.

Reference
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