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Research Article

Reciprocal roots of metabolic syndrome and affective disorder: Temperamental, familial and environmental factors such as climate, geography, migration and changeable life styles

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ABSTRACT

As current classification systems make cross-sectional diagnosis, they do not take into account family history, longitudinal course features and dimensional approach to symptoms. This approach gives precedence to reliability over validity and it isolates psychiatric disorders from their etiologies. In fact, a spectrum model which includes physical diseases is possible. This continuity is also observed in the family history. Comorbidity of affective disorders, Carney syndrome, Multiple Endocrine Neoplasia type I and II, breast and prostate cancers, carcinoid tumors, and vascular diseases may be mediated by metabolic syndrome via the interaction of genetic and environmental factors.

Key words: Affective disorder, physical disease, family history, epigenetic concept

Introduction

Glucocorticoid insulin signaling mechanisms and inflammatory effector systems are intersections pointing to pathophysiological relationships between affective disorders and physical diseases that are susceptible to stress such as metabolic syndrome (MetS) [1]. Although they are not among the diagnostic criteria of MetS, the proinflammatory and prothrombotic states and purinergic dysfunction are considered to be in framework of MetS [2,3].

Susceptibility to stress

The concept "susceptibility to stress" must be highlighted. The susceptibility in question is determined temperamentally. It is biological, hereditary, relatively stable ve heritable. There is a cluster of risk factors that include the presence of the MetS, as well as a more negative prone temperament profile. The temperament types outstanding in our studies were anxious and irritable temperaments. While these temperament types give the mood episode its mixed nature, they also create predisposition to MetS [4]. Temperamental factors were related cross-sectionally to, as well as predicted, the MetS precursors over a 3-year period [5]. Some temperament types were shown to be correlated to MetS constituents [6,7].

Whereas you can be experienced at any stage and domanin of life, childhood trauma is the most crucial structurally and developmentally. Acute stress prompts a response by an inflammatory reaction on the brain, mediated by the autonomous nervous system [8]. On the other hand, chronic stress leads to HPA axis disorders and consequent hypercortisolemia. Therefore, childhood trauma is frequently associated with obesity, diabetes, coronary artery disease, and allergic and autoimmune diseases. Additionally, early menarche and EEG abnormalities are found as the projections of childhood trauma on bipolar disorder [9,10]. At this point abnormal stress response could play a role in the etiology of both a chronic psychiatric disorder and a comorbid medical condition [8]. Herein affective temperament may increase the risk or resilience [11].

Molecular genetic studies showed that, bipolar disorder (BD) shares similar conversions and deletions in the same loci with some general medical conditions [12]. However genetic association can only explain 10% of total variance of clinical co-existence. This outcome, which researchers call "missing heritability", means that interactions with environmental influences absolutely have a role both in etiology and resilience in accordance with epigenetic principles [13].

Missing heritability

Presence of a previous depressive episode (PDE) was found to be the strongest predictor of MetS in first episode mania [1]. As a result, it is worth asking whether depressive episode itself or the psychopharmacological agents used in treatment was the cause of the higher MetS prevalence. According to Vancampfort and colleques, antipsychotic use significantly explained higher MetS prevalence estimates in major depressive disorder (MDD) [14]. In another study, there was some mediating role for tricyclic and non-selective serotonin-reuptake inhibitor antidepressant use but overall, the mediating role of clinical differences were

limited [15]. Margari and colleques, found a positive association between antidepressant drug treatment and triglyceride, and triglyceride/HDL ratio levels and between antipsychotics drugs and the HOMA and Framingham index [16]. In Perugi and colleques's study, duration of pharmacological treatment and age at onset of first major episode were associated with the presence of comorbid MetS [17]. The use of antidepressants and inappropriate use of antipsychotics as antidepressant agents seem to be a risk factor for MetS as well as switch, cycle acceleration and mixed states.

Although its genetic aspects are set forth more clearly in recent years, seasonality is a variable which can also be evaluated in the context of epigenetic principles, and according to our results it is a predictive clinical factor for MetS in first episode mania. Englund and colleques's findings support the relationship between circadian clocks and MetS [18]. Circadian gene variants are related to the risk factors of MetS, as they were associated with hypertension and high fasting blood glucose [19].

MetS was found to be more frequent (94.1% vs 64.3%) in winter type of seasonal affective disorder (SAD) [1]. As an expected data, prevalence of obesity as defined by the World Health Organization (WHO) is relatively low in Asia compared to western countries [20]. Thus, Han and colleques reported that unlike the results from the western countries, summer type of SAD was more frequent than winter type of SAD in China [21]. Levitan stated in 2007 that SAD was independent of latitude difference [22]. In the Turkish study on SAD with the largest sample, Elbi and colleques screened 3229 subjects in eight different regions and found no correlation between latitude and the prevalance of the disorder [23]. Tonetti and colleques made a comparison between Italy and India [24]. They found while winter type of SAD was more frequent in Italy, summer type of SAD was more frequent in India. As they thought the first result was associated with reduced duration and intensity of light in winter, in other words with photoperiodicity, they suggested the second result was associated with climate and heat difference. Guzman and colleques compared African migrant and Afro-American subjects living in Washington and found that while winter type of SAD was similar between two groups, summer type of SAD was more frequent in African migrants [25]. The geographical, climatic, genetic, ethnic and cultural interactions of SAD seem to be worth investigating in the future.

There are not any patients with summer type of SAD in Iceland and England [26]. Although Iceland is in far north, SAD incidence is not higher than England. This can be interpreted both as a result of their tolerance to photoperiodicity due to isolation for more than a thousand years, and also as a result of genetic factors. As a matter of fact, SAD is seen less in migrant Icelanders than other migrant ethnic groups. Writers also underline the importance of weather conditions and living in rural or urban areas. Actually, living in a rural area means exposure to more light than the light exposure of the zone. In our study, all of the summer type of SAD patients were living in urban areas [1]. As an interesting but not unexpected result, all MetS positive subjects with were living in cities and worked in offices without windows. Lighting conditions and their dynamics may serve as a measure for intervention in order to influence the seasonal metabolic signals and in the end to prevent the MetS.

The comorbid diagnoses included anxiety disorders and alcohol and substance use disorders in SAD [1]. The results studies with migrants on SAD provided quite interesting data. A study was conducted among five different migrant groups living in Oslo, and it was found that the winter type of SAD was the least prevalent among Sri Lankan migrants and the most prevalent among Iranian migrants [27]. The winter type of SAD was linked to place of birth, young age, childhood trauma, frequent internal medicine and psychiatry referrals, while the summer type of SAD was linked to place of birth, smoking and alcohol consumption.

Both delayed sleep phase syndrome (DSPS) and SAD may manifest similar delayed circadian phase problems [28]. In our study, DSPS was 26% in SAD and 2% in controls [1]. DSPS or in other words dysfunctional circadian system, may be a compensatory mechanism for energy production that is decreased at cellular level [29]. Thus, mitochondrial calcium stimulated oxidative phosphorylation. Elevated levels of calcium seen in some cases of mania could be a precipitative factor for higher levels of mitochondrial respiration also seen in depression. At this point I want to remind that calcium levels influence the activity of the circadian clock and levels of circadian clock gene outputs. Circadian activity is governed by a tightly self-regulated oscillatory rhythm in the expression of circadian controlled gene. But circadian regulation of interconnected transcriptional feedback loops has proven to be deceptive.

Conclusion

This paper emphasizes the bidirectional relation between mood disorders and general medical conditions, in particular MetS and calls attention to the systemic nature of affective disorders. This may also contribute to the discovery of biological markers, an increase in our diagnostic tools and the development of protective and personalized medicine on the basis of family history especially. At this point, it must be remembered that some non-psychotropic drugs and interventions may be effective in the treatment of affective disorders. Use of allopurinol and tamoxifen were determined as antimanic treatments in guidelines for the treatment of bipolar disorders [4,30]. Also, lithium and sodium valproate inhibit tumor growth in carcinoid tumors [31].

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