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EDITORIAL

# Mood disorders in the light of genes, comorbidity and contemporary treatment

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Affective disorders like depression rank worldwide among the most disabling in terms of WHO global burden of disease, are socioeconomically relevant, severe and prevalent. Due to persisting cognitive symptoms, these diseases lead to enormous social disabilities and they dramatically increase the risk of suicide. A genetic influence and the serotonin transporter (5HTT) play a major role in the pathophysiology of mood disorders and suicidal behavior. Pinto et al. [1] investigated the effect of genomic imprinting of the four 5HTT genetic markers and expression of 5HTT alleles in lymphocytes of suicide attempters and 312 nuclear families with at least one member affected by bipolar disorder. Allele 2651T was transmitted more often to bipolar patients, but the authors did not find differential gene expression between bipolar suicide attempters and non-attempters, which does not support a role for allelic expression of 5HTT in suicidal behavior.

Due to the high risk of suicide and social disabilities despite antidepressant medication, add-on therapy entailing fewer side effects should be investigated. Tajalizadekhoob et al. [2] applied fish oil capsules containing polyunsaturated fatty acids (PUFAs) in elderly patients with mild to moderate depression as add-on therapy during a period of six months. Treatment with PUFAs showed significant effects compared to placebo and may be beneficial in depressed elderly patients who are at greater risk for cardiovascular diseases. In fact, major depression is associated with increased volumes of visceral fat and high prevalence of the metabolic syndrome, leading to coronary artery disease. Greggersen et al. [3] investigated visceral fat content in young depressed women with and without comorbid borderline personality disorder. They found a significant increase in visceral fat content in major depression, but no additional effects of borderline personality disorder, which does not seem to be an additive risk factor for the metabolic syndrome.

Sleep disturbances are common in both depressed and alcohol-dependent patients, including decreased slow wave sleeps (SWS). Brower et al. [4] compared power spectral analysis of polysomnography recordings in men with alcohol dependence compared to subjects with major depression. Both groups showed blunted slow wave activities: men with major depression showed the least slow wave activities in the first non-REM period, whereas men with alcohol dependence had the slowest slow wave activity decay rate. New treatment approaches should selectively improve these different components of sleep homeostasis. In a study by Cordes et al. [5], antidepressant therapy with clomipramine has shown to induce a significant increase in serum prolactin levels in women, but not in men with major depression, indicating effects of clomipramine on the central monoaminergic system. In line with a glutamate hypothesis of depression, the N-methyl-D-aspartate (NMDA) receptor antagonist ketamine has been shown to be therapeutically effective in unipolar and bipolar depression. In a retrospective chart analysis of Kranaster et al. [6], effects of ketamine as anesthetic during electroconvulsive therapy (ECT) in patients with therapy-resistant depression have been compared to anesthesia with the barbiturate thiopental. Interestingly, the ketamine group

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needed fewer ECT sessions and had lower HAMD and higher MMSE scores after treatment, pointing toward synergistic effects of ECT and ketamine as well as fewer cognitive side effects. The tolerability was good aside from more comedication for blood pressure control in the ketamine group.

Kebir and Joober [7] reviewed results from genetic studies investigating associations between susceptibility genes for attention-deficit hyperactivity disorder (ADHD) and neuropsychological traits relevant for the disorder. The most consistent result was the association between the DRD4 gene and high reaction time variability, whereas many findings of association with other genes need replication. Furthermore, Fasmer et al. report a higher prevalence of migraine in ADHD [8], pointing to a comorbidity between ADHD and migraine.

In order to improve compliance and enhance therapeutic alliance, patients should at least trust in their treating psychiatrists. Minamisawa et al. [9] investigated this issue in 504 outpatients of a psychiatric clinic using a self-report questionnaire. The trust in psychiatrists was higher with longer treatment duration and a longer than 10 years expertise of psychiatrists, but also dependent on diagnosis, since F4 patients showed lesser trust in their psychiatrists than F3 patients. Altogether, we should continue to develop better treatment strategies for psychiatric diseases, entailing fewer side effects to achieve better response to treatment and to improve the patient's trust in our efforts.



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