August 30, 2013


To whom it may concern:

The thesis of Mgr. Deborah Kaminska focuses on problems related to anorexia nervosa (AN) and bulimia nervosa (BN). Both diseases are very serious psychiatric disorders that are common in the population, especially among teens, mainly females. These disorders present with episodes of starvation, as well as urges and episodes of overeating and obsessive fears about becoming overweight. Both these disorders are very difficult to treat, often resulting in serious metabolic disturbances as well as ultimately death. Therefore, there is a huge interest to unravel the pathogenesis of these diseases, but this is not an easy task since both diseases are multifactorial and therefore, many angles must be taken to study these disease to come up with novel findings and possible future treatment options. Therefore, the Reviewer very positively values the unique and very difficult approach of Mgr. Deborah Kaminska to study a large population of these patients with either AN or BN. Her use of a molecular biology angle and approach is especially interesting to further study the involvement of serotonin and its receptors in the pathogenesis of these diseases.

Specifically:

1. The present thesis includes two separate studies 75 patients with AN and 127 patients with BN. It was a privilege of Mgr. Deborah Kaminska to work with such a large database of patients, DNA bank and controls. The Reviewer congratulates Mgr. Deborah Kaminska on having such a huge collection of these patients, which is definitely not an easy task.

2. The statistical approaches are very well presented, and they are appropriate.

3. The aims of the study are very clear and the Reviewer likes that both the aims and hypotheses are very logically sequenced and appropriate for the present study.
4. The methodological approaches are excellent; they meet the highest current standards and reflect the outlined aims and hypotheses. As mentioned before, the Reviewer very well appreciates and values that the author learned and correctly used molecular biology methods that was an enormous and difficult task. Learning such methods and using them appropriately is a very difficult task. This required a lot of learning, dedication, and effort.

5. There are 4 basic hypotheses, all clearly defined and written and addressed later in the report.

6. The Reviewer is very pleased to learn how the author used questionnaires to study these patients.

7. The publications reflect the entire study, and they are sufficient to accept this thesis.

8. Results: The results related to serotonin (5HT) are novel and unique, especially those related to the 5-HTR2A polymorphism with BMI and serotonin factors. In 5-HTT LPR polymorphism analysis, unlike in the 5-HT2A, neither allelic nor quantitative association with BMI for the biallelic 5-HTT marker was observed. Results of this study support previous reports of a significant role of the A allele (-1438 A/G, 5-HT2A receptor) as a risk factor for AN. The authors also uniquely concluded that decreased HO-1 expression in the presence of the L/L genotype together with more intensive stress perception in patients could lead to secondary stress, with increasing severity of the symptoms and aggravation of the disease. Further results focusing on relatives of those with AN or BN showed that there is a higher incidence of these disorders among relatives (siblings).

9. The summaries are done extremely well and outlined fairly and modestly.

10. The perspectives are interestingly written; the author's view about exome screening is very positively valued, similar to the correlation of gene expression with metabolic parameters that may play an important role. Metabolomics will become a field of interest in medicine (diagnosis, follow-up, etc.) in the near future. The same applies for proteomics. The Reviewer likes the author's view about future multi-institutional and international studies, consortia, and working groups.

In summary, this is an excellent, exemplary, and very original scientific study/thesis focusing on AN and BN. The thesis represents state-of-the-art approaches, methodologies, applications, results, discussion, and outcomes for clinical practice. The thesis also reflects the enormous work and dedication of the author. The Reviewer does not have any major criticism and comments to such an excellent work.
Without any reservation I fully recommend Mgr. Deborah Kaminska to be awarded a Ph.D. based on the present thesis.

Sincerely,

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