

**Al collegio docenti del Dottorato in Medicina Molecolare**

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**- Introduction**

My research activity over the past year has primarily focused on investigating mediating factors and possible biomarkers in major depressive disorder evaluating the role of C reactive protein and lifestyle. My study aims to evaluate the association among healthy or unhealthy lifestyle adherence with inflammatory biomarkers and severity of depression focusing on the dimension of anhedonia, hypothesizing CRP, other pro-inflammatory markers, and an impaired glucose metabolism as mediating factors.

**- Materials and Methods**

50 consecutive inpatients admitted to the Psychiatry Unit of Siena University Hospital and diagnosed with Major Depressive Disorder (MDD) or Bipolar Disorder in the depressive phase have been enrolled.

The inclusion criteria included: Age  $\geq 18$ ; Diagnosis of Major Depressive Disorder or Bipolar Disorder in depressive phase; Ability to sign informed consent;

The exclusion criteria included: Pregnancy or breastfeeding; Diagnosis of schizophrenia, schizoaffective disorder, or schizophreniform disorder.

Psychometric assessments included: QueMD: Questionnaire for adherence to the Mediterranean diet; PSQI (Pittsburgh Sleep Quality Index): Questionnaire assessing sleep quality; IPAQ (International Physical Activity Questionnaire): Questionnaire on daily physical activity; BDI (Beck's Depression Inventory): Questionnaire to assess the severity of depressive symptoms; SHAPS (Snaith-Hamilton Pleasure Scale): Questionnaire to assess anhedonia; MADRS (Montgomery-Asberg Depression Rating Scale).

Blood samples were taken to analyze CRP levels.

**- Results**

The initial analyses conducted on the preliminary sample of patients yielded the following results. The correlation analysis between anhedonia and depression revealed a significant association between adherence to the Mediterranean diet and lower levels of anhedonia. Regression analysis indicated an inverse relationship between total SHAPS scores and dietary adherence ( $p < 0.05$ ). Furthermore, adherence to the Mediterranean diet was associated with a significant reduction in CRP levels ( $p = 0.037$ ), suggesting a protective role against inflammation.

Additionally, adherence to the Mediterranean diet was linked to less severe depressive symptoms, with a significant correlation ( $p < 0.05$ ). Patients adhering to the Mediterranean diet had lower mean MADRS scores (17.7) compared to non-adherent individuals (24.6). Grouping patients based on depression severity further confirmed the protective effect of diet adherence, with a p-value of 0.017.

The regression analysis between anhedonia and sleep quality demonstrated a significant correlation between poor sleep quality (PSQI) and worsening anhedonia (SHAPS), with a positive correlation ( $p = 0.038$ ). This finding supports the link between disturbed sleep and higher levels of anhedonia. Moreover, sleep quality was significantly correlated with depression severity ( $p < 0.001$ ). Worse PSQI scores were associated with greater depression severity, suggesting that poor sleep is a critical factor in exacerbating depressive symptoms.

An inverse correlation between physical activity and anhedonia was found in evaluating physical activity: physically active patients had significantly lower levels of anhedonia ( $p = 0.014$ ). Those who engaged in at least a sufficient level of physical activity had a mean SHAPS score of 2.50, compared to 5.88 in inactive patients.

Physical activity also demonstrated a protective effect against depression, with a significant correlation between physical activity levels (IPAQ) and depressive symptoms (BDI), with a p-value of 0.003. Active patients had lower mean BDI scores (18.4) compared to inactive individuals (29.8), with a similar median difference.

No significant correlation was found between physical activity and CRP levels. Expanding the sample size may help reveal results that are more consistent with the literature.

*Abstracts e partecipazione a congressi e corsi: autori, titolo della presentazione, nome e date del congresso*

- x International Society for Affective Disorders (ISAD), Dec 2023, Milan
- x Intravenous trazodone for the treatment of agitation in major depressive disorder patients experiencing a depressive episode with mixed features P. Carmellini, A. Cuomo, S. Pardossi, C. Pierini, M. Pinzi, A. Fagiolini (2024), ECNP, Milan, Sept. 2024; Neuroscience applied (in press).
- x European College of Neuropsychopharmacology Congress (ECNP), Sept. 2024, Milan
- x First Annual Meeting OPADE EU HORIZON Project, June 2024, Salerno
- x First Annual Meeting BIPCOM EU EraPerMed Project, Sept 2024, Barcellona,

*Pubblicazioni scientifiche autori, titolo della pubblicazione, nome e numero della rivista, anno di pubblicazione*

- x P. Carmellini, A. Cuomo, A. Fagiolini. Journal of Affective Disorder Reports (2024). Efficacy of Topiramate in treating obsessive compulsive disorder: A systematic review and meta-analysis. Journal of Affective Disorder Reports.  
<https://doi.org/10.1016/j.jadr.2024.100787>
- x Cuomo, A., Barillà, G., Cattolico, M., Pardossi, S., Mariantoni, E., Koukouna, D.,

- Carmellini, P., & Fagiolini, A. (2024). Perspectives on the impact of vortioxetine on the treatment armamentarium of major depressive disorder. Expert review of neurotherapeutics, 1–12. Advance online publication. <https://doi.org/10.1080/14737175.2024.2333394>
- x Cuomo, A., Barillà, G., Serafini, G., Aguglia, A., Amerio, A., Cattolico, M., Carmellini, P., Spiti, A., & Fagiolini, A. (2023). Drug-drug interactions between COVID-19 therapeutics and psychotropic medications. Expert opinion on drug metabolism & toxicology, 1–12. Advance online publication. <https://doi.org/10.1080/17425255.2023.2288681>
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  - x Corrivetti, G., Monaco, F., Vignapiano, A., Marenga, A., Palm, K., Fernández-Arroyo, S., Frigola-Capell, E., Leen, V., Ibarrola, O., Amil, B., Caruson, M. M., Chiariotti, L., Palacios-Ariza, M. A., Hoekstra, P. J., Chiang, H. Y., Floares, A., Fagiolini, A., & Fasano, A. (2024). Optimizing and Predicting Antidepressant Efficacy in Patients with Major Depressive Disorder Using Multi-Omics Analysis and the Opade AI Prediction Tools. Brain sciences, 14(7), 658. <https://doi.org/10.3390/brainsci14070658>
  - x De Girolamo, G., Andreassen, O. A., Bauer, M., Brambilla, P., Calza, S., Citerà, N., Corcoy, R., Fagiolini, A., Garcia-Argibay, M., Godin, O., Klingler, F., Kobayashi, N. F., Larsson, H., Leboyer, M., Matura, S., Martinelli, A., De la Peña-Arteaga, V., Poli, R., Reif, A., Ritter, P., ... BIPCOM consortium (2024). Medical comorbidities in bipolar disorder (BIPCOM): clinical validation of risk factors and biomarkers to improve prevention and treatment. Study protocol. International journal of bipolar disorders, 12(1), 15. <https://doi.org/10.1186/s40345-024-00337-8>