

 <p>UniSR Università Vita-Salute San Raffaele</p>	<p>APPLICATION TO ACT AS SUPERVISOR AND RESEARCH PROJECT PROPOSAL</p>	<p>MO 20-5 ed. 02 of 16/01/2026 PO 20 Page 5 of 10</p>
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PROJECT

Supervisor: Sara Poletti

Title: Profiling vulnerability and resilience for mental illness following viral infections

Curriculum: NeN

Link to the personal page of the University or relevant hospital site website: <https://research.hsr.it/en/divisions/neuroscience/psychiatry-and-clinical-psychobiology/sara-poletti.html>

Description of the Project (max 3,000 characters including spaces)

Background/gap of knowledge

In the last few decades, the role of infection and inflammation in mental illness (MI) have received much attention, with big data approaches convincingly linking MIs, particularly severe MIs, such as schizophrenia, bipolar disorder (BD) and major depression disorder (MDD), to infections and the immune system (1-3). Different mechanisms have been suggested involving immunological effects (4). Moreover, there is evidence of a worsened outcome of infections in individuals with MI, adding to the burden of MIs (5). Still, viral infection and MI relationships in terms of specific patterns, mechanisms, vulnerability and resilience factors are sparsely studied. Recently, the COVID-19 pandemic provided an unexpected opportunity to observe the association between viral infections and mental and physical health and to investigate the mechanisms through which viral infections lead to MI and severe outcomes in these patients.

Rationale and hypothesis

Despite substantial evidence regarding the association between viral infections and MI, the underlying mechanisms leading to vulnerability and resilience to the long-term mental and physical outcomes following infections are still largely unclear. This study aims to answer the following research questions: (a) does the cumulative history of viral infections increase the risk of developing MI? (b) what are the genetic, epigenetic, neuroanatomical, molecular, immunological, and endocrine mechanisms underlying development of MI after infections? (c) does inflammation mediate or identify a pre-existing vulnerability factor for the association between MI and post-infection mortality and severe outcomes? (d) can we stratify resilient and vulnerable individuals to negative outcomes to infections for an underlying biological and environmental signature?



Objectives and specific aims

- 1) To demonstrate an association between infections, with a particular focus on viral ones, severe MI and post-infection severe outcomes;
- 2) To identify the neurobiological mechanisms in the associations between viral infections and MI (i.e. brain structure and function, inflammation, gene expression)
- 3) To assess the contribution of neurobiological factors (i.e. inflammatory and genetic markers) as risk or resilience indicators modulating the association between infections, mental illness and severe outcome.
- 4) To stratify participants and estimate predictive risk or resilience models of negative outcomes based on individual biological signature
- 5) To identify druggable targets on the basis of gene expression profiles.

Expected outcomes

We expect to demonstrate an association between Infections and mental Illness and to Identify markers of vulnerability and resilience to develop a mental Illness after Infection.

Skills that the student should acquire (max. 600 characters including spaces):

- "Imaging genetics": the use of anatomical or physiological imaging technologies as phenotypic assays to evaluate genetic variation, including gene polymorphisms and gene expression
- MRI analyses to explore structural networks: VBM, subcortical volumes (Freesurfer) and cortical thickness (CAT12), Tract-Based Spatial Statistics (TBSS; FSL) and tractography analysis of WM tracts
- statistical analyses to explore mediation and moderation models and machine learning algorithms to Implement predictive models for the Identification of risk and resilience factors.
- perform bioinformatic analyses to identify druggable targets

References (max. 15)

1. Benros ME, et al. Autoimmune diseases and severe infections as risk factors for schizophrenia: a 30-year population-based register study. Am J Psychiatry. 2011.



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2. Benros ME et al., Autoimmune diseases and severe infections as risk factors for mood disorders: a nationwide study. JAMA Psychiatry 2013. <https://doi.org/10.1001/jamapsychiatry.2013.1111>
3. Köhler-Forsberg O, et al. A Nationwide Study in Denmark of the Association Between Treated Infections and the Subsequent Risk of Treated Mental Disorders in Children and Adolescents. JAMA Psychiatry. 2019. <https://doi.org/10.1001/jamapsychiatry.2018.34285>.
4. Simanek AM, et al. Herpesviruses, inflammatory markers and incident depression in a longitudinal study of Detroit residents. Psychoneuroendocrinology. 2014;.
5. Nemani K, et al. Association of Psychiatric Disorders With Mortality Among Patients With COVID-19. JAMA Psychiatry. 2021.