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人社院心智意識與腦科學研究博士學位學程 Matteo Martino 助理教授學術分享：躁鬱症潛在的神經生物學變化

我的學術訓練和研究經驗以精神醫學和神經科學方面為主，除在義大利熱那亞大學（University of Genoa）醫學院專攻精神醫學，取得神經科學博士學位外；還取得義大利比薩大學（University of Pisa）情緒障礙的診斷和治療碩士學位，以及荷蘭馬斯垂克大學（Maastricht University）情感神經科學碩士。

我以客座研究員身分在各個國際研究中心進行過多次培訓與研究工作，包括：加拿大渥太華大學（University of Ottawa）心腦造影和神經倫理學，美國紐約西奈山伊坎醫學院（Icahn School of Medicine at Mount Sinai），臺灣臺北醫學大學大腦與意識研究中心，以及中國成都四川大學心理衛生中心和精神醫學實驗室，然後，我在西奈山伊坎醫學院擔任博士後研究員。最後我加入臺北醫學大學心智意識與腦科學研究所擔任助理教授。

我的長期研究興趣專注於大腦功能與行為和現象學模式之間關係的理解，以及主要精神疾病（尤其是躁鬱症）心理病理學和病理生理學的研究，這些研究領域可輔助精神神經科學，因為對大腦生理更進一步的了解是研究大腦變化的基礎，同時研究精神疾病的神經生物學對理解大腦的運作方式可提供有價值的資訊。在這方面，躁鬱症特別有相關性，躁鬱症是一種主要的精神疾病，以焦躁不安和抑鬱寡歡狀態為特徵，在各種心理病理學領域（包括心理測驗、情感和思想）呈現出相反的變化模式。因此，躁鬱症可以代表一種獨特的模型，用以研究行為和現象學模式變化與大腦功能變化的相關性，另一方面，對精神疾病的病理生理學機轉之理解，例如躁鬱症，可呈現這些讓人嚴重衰退的疾病所使用的特定診斷工具和有效療法是關鍵步驟。【右圖：人社院心智意識與腦科學研究博士學位學程 Matteo Martino 助理教授】

在過去幾年中，我與同事 Paola Magioncalda 緊密合作，進行了一系列的研究，使用各種神經造影和實驗室技術研究躁鬱症潛在的神經生物學變化，研究顯示躁症及鬱症與大腦內部活動功能性結構明顯的改變有關，這種大腦內部活動呈現出一種神經元的活動，是由大腦自動產生，設定自環境輸入及輸出環境的處理程序；有關躁鬱交錯的症狀，我們的研究顯示，大腦內部活動功能性重組發生於躁鬱症之躁症與鬱症二者間大型網絡的失衡（Martino、Magioncalda 等，《美國國家科學院院刊》，2016 年；Russo、Martino、Magioncalda 等，《思覺失調症期刊》，2020 年），進一步的結果顯示，這種網絡失衡與皮下皮質耦合和神經傳導信號的明顯改變有關（Martino、Magioncalda 等，《思覺失調症期刊》；Conio、Martino、Magioncalda 等，《分子精神醫學》期刊，2020 年）。

綜合以上所述，這些數據顯示，大腦內部活動相對於環境的調整過度或調整不足，可能導致與躁症及鬱症相關的行為/現象學改變，另一方面，我們研究這種功能性大腦改變的潛在結構性大腦基礎，並檢測到大腦白質異常與躁鬱症患者的免疫炎症變化有關（Magioncalda、Martino 等，《大腦，行為和免疫》期刊，2018 年）。最後，根據之前所有研究成果，我們提出一個大腦功能和行為/現象學模式之間關係的工作模式，並將其應用在躁鬱症上面（Martino & Magioncalda，《分子精神醫學》期刊，2021 年）。

未來的計畫將著重於應用實驗工作來測試與改善我們的工作模式，尤其是研究免疫炎症變化與結構性的大腦變化、神經傳導信號改變、大腦內部活動的重組，以及精神病理學，期對於躁鬱症和其他主要精神疾病的大腦功能及其變化的潛在影響有更佳的了解。（Martino & Magioncalda，《分子精神醫學》期刊，2021 年）（文/Matteo Martino，人文暨社會科學院心智意識與腦科學研究博士學位學程助理教授）【左圖：Matteo Martino 助理教授（中）與學生合影】

My academic training and research experience have provided me with a background in psychiatry and neuroscience. After graduating from medical school and specializing in psychiatry (University of Genoa, Italy), I obtained my PhD degree in neuroscience (University of Genoa, Italy) and two postgraduate master degrees, one on clinics and treatment of mood disorders (University of Pisa, Italy) and the other on affective neuroscience (Maastricht University, Netherlands).

I also spent several periods of training and research work at various international research centers as visiting researcher, including the Mind Brain Imaging and Neuroethics (University of Ottawa, Canada), Icahn School of Medicine at Mount Sinai (New York, U.S.), Research Center for Brain and Consciousness (Taipei Medical University, Taiwan), and Mental Health Centre and Psychiatric Laboratory (Sichuan University, Chengdu, China). Then, I worked at the Icahn School of Medicine at

Mount Sinai (New York, U.S.) as a postdoctoral fellow. Finally, I joined the Graduate Institute of Mind Brain and Consciousness at the Taipei Medical University as an assistant professor.

My long term research interests are focused on the understanding of the relationship of brain functioning with behavioral and phenomenological patterns, as well as the investigation of the psychopathology and pathophysiology of major psychiatric disorders, bipolar disorder especially. These research areas are complementary in psychiatric neuroscience, since a better understanding of brain physiology is fundamental for the study of brain alterations, while the investigation of the neurobiology of psychiatric disorders may provide valuable insights for a better comprehension of how the brain works. In this regard, bipolar disorder can be of particular relevance. Bipolar disorder is a major psychiatric disorder characterized by manic and depressive states that show opposite patterns of alterations across various psychopathological domains, including psychomotricity, affectivity, and thought. Thus, bipolar disorder can represent a unique model to investigate how changes in behavioral and phenomenological patterns are related to changes in brain functioning. On the other hand, a mechanistic understanding of the pathophysiology of psychiatric disorders, such as bipolar disorder, represents a crucial step for implementing specific diagnostic tools and effective therapies for these severe and debilitating illnesses.

In the last years I, in strict collaboration with my colleague Dr. Paola Magioncalda, conducted a series of research studies to investigate the potential neurobiological alterations underlying bipolar disorder, using various neuroimaging and laboratory techniques. Our research work showed that mania and depression are related to distinct changes in the functional architecture of intrinsic brain activity. Such intrinsic brain activity represents the neuronal activity that is spontaneously produced by the brain and sets the baseline processing of inputs and outputs from and to the environment. Our findings suggested that a functional reconfiguration of intrinsic brain activity occurs in bipolar disorder with opposite dysbalancing between large-scale networks in mania and depression, underlying the opposite manic-depressive symptomatology (Martino, Magioncalda, et al., PNAS, 2016; Russo, Martino, Magioncalda, et al., Schizophrenia Bulletin, 2020). Further results suggested that such network dysbalancing is associated with distinct changes in the subcortical-cortical coupling and neurotransmitter signaling (Martino, Magioncalda, et al., Schizophrenia Bulletin; Conio, Martino, Magioncalda et al., Molecular Psychiatry, 2020).

Taken together, these data suggest that a relative over-tuning or de-tuning of intrinsic brain activity to the environment may result in the opposite behavioral/phenomenological changes associated with mania and depression. On the other hand, we investigated potential structural brain underpinnings of such functional brain changes and detected abnormalities in the brain's white matter that correlated with immune-inflammatory alterations in patients with bipolar disorder (Magioncalda, Martino, et al., Brain, Behavior, and Immunity, 2018). Finally, based on all our prior work, we recently proposed a working model of the relationship between brain functioning and behavioral/phenomenological patterns and applied it to bipolar disorder (Martino and Magioncalda, Molecular Psychiatry, 2021).

My future plans regard the implementation of experimental work to test and improve our working model, especially investigating the specific relationships between immune-inflammatory changes, structural brain alterations, changes in neurotransmitter signaling, reconfigurations of intrinsic brain activity, and psychopathology, with potential implications for a better understanding of brain functioning and its alterations in bipolar illness and other major psychiatric disorders.