Neuroimaging markers of major depressive disorder: orbitomedial prefrontal cortex and beyond

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Knowledge Valorization

Scientific knowledge is neither pursued nor produced in a vacuum as a theoretical or intellectual goal. It is meant to be utilized for societal benefit and progress. The valorization of scientific knowledge, i.e. its utilization in practice should therefore be actively explored and promoted. Scientific knowledge can be put to use in academic settings for research (science and methods) and educational purposes. Outside the university, experts in the public and private sector, institutions, individual consumers and the public in general benefit from the applied knowledge in the form of products and services. The present addendum discusses the valorization possibilities of the knowledge produced during this PhD project.

1. Social & economic relevance of current results

MDD is a debilitating disorder which, according to the World Health Organization, is the leading cause of disability and is projected to be the first overall contributor to the worldwide burden of disease in 2030. MDD affects 350 million people globally and is associated with significant personal, societal and financial costs. These numbers become even more alarming if we take into account all affective disorders which involve episodes of depression as well as somatic conditions to which depressive episodes are secondary. MDD is among the leading causes of death as well, associated with suicide, death due to substance abuse and addiction or due to non-conformity of the patient to therapy in case of somatic disorders. The accurate, timely and effective prevention, diagnosis and treatment of MDD will essentially promote the physical and mental health and well-being of a significant percent of the population and at the same time reduce the economic burden in modern societies. Therefore, the valorization of knowledge towards these goals is very relevant both socially and economically.

In this work, we first extended and validated a new methodological approach to study the functional organization of the human orbitomedial prefrontal cortex. Complex cortical functional organization and connectivity is believed to subserve all higher human affective and cognitive faculties. Subsequently, we used this and other methods to elucidate the role of certain cortical functional fields in MDD and further investigate abnormalities related to affective facial processing. The results of our studies hold promise for the development of applications to diagnose, subtype and treat MDD patients more effectively. These applications will enable clinicians to complement their diagnosis and decision making with neuroimaging/biological evidence about abnormal network function and reactivity. In this way, diagnosis and treatment strategies will become more effective in identifying patients in need of specific treatments. What is more, our results on the existence of network

and reactivity pathology in genetically susceptible individuals might contribute to the development of psycho-prophylactic interventions.

2. Target groups

The results of the current thesis are immediately relevant to other researchers in the field who study functional organization, connectivity and reactivity in MDD disease and vulnerability states. Our results are also relevant to neuroscientists who are interested in parcellation methods and the organization and connectivity of the orbitomedial prefrontal cortex. Further, our results and their implications are of interest to health care professionals who diagnose and treat MDD patients. Most importantly, although not in the immediate future, our results will hopefully become highly relevant for patients, people at risk for depression and their families by contributing to the development of evidence-based diagnosis and treatment methods.

3. Activities & Products

In the context of scientific research, our results give rise to new hypotheses to be tested mainly regarding the function and connectivity of the various cortical fields examined. With regard to the valorization of this knowledge outside of academia, resting state scans could be in the future used as adjunct means of diagnosis and treatment selection. Information on the cortical functional organization and functional connectivity of depressed patients' will assist health care professionals and clinicians in their diagnosis, prognosis and treatment plan. Information on affective processing or BOLD reactivity of specific cortical areas can also be used with the aid of machine learning algorithms to classify patients and at risk individuals. Since at present no single modality of neuroimaging findings sufficiently captures psychiatric pathology, it is also possible that algorithms that take into account both these pieces and other information will be used to classify and subtype depressive pathology. Finally, it is highly likely that soon resting state scans will not only assist in the selection of the best treatment option for individuals out of the existing ones but will also consistently provide new, individualized targets for connectivity-based therapies.

4. Innovation

The results presented in this thesis are innovative in following regards: firstly, we applied an innovative technique to parcellate the cortex into functional fields at the individual level. Although many methodological issues remain to be resolved, this parcellation approach might open the way for the study of cortical organization at the individual level, and many real-life applications in health and disease states. Secondly, we used large samples of depressed patients, healthy controls and people at genetic risk for depression, employing a biomarkers analysis. Our studies are innovative to

the extent that for the first time we show that some of the most well established affective face processing abnormalities and connectivity aberrations are found already at the MDD vulnerable state. Though probably not all, some of these changes are etiologically linked to the development of depressive episodes and might be proven useful for applications in the field of prevention.

5. Schedule & Implementation

The work presented here aimed to advance methods of delineating cortical functional organization based on connectivity and apply them to diseases known to be connectivity disorders and specifically MDD. What is more, we aimed to study and elaborate on brain changes not only in disease states but in vulnerability as well. Although our results will hopefully contribute to practical applications in the fields of prevention, diagnosis and personalized treatment in the future, there remain a number of critical issues to be addressed before the implementation of our knowledge valorization can be scheduled. These issues can be categorized as follows: those that have to do with the methodological aspects of our techniques and those that relate to the approach we have adopted within the psychiatry field. With regard to the methodological aspects, issues such as the establishment of the appropriate threshold for each dataset, cortical region and individual, the improvement of the group clustering/average parcellation solution and the elucidation of the function of each cortical field should be resolved. With regard to using these and other similar methods in clinical practice, issues to be addressed are the establishment of connectivity population norms, subtypes of depression, real-life samples and integration of information from multiple sources such as the connectivity and (re)activity information presented in the third and fourth chapters.