

At the very beginning of this short report let me express my innermost pleasure that ECNP Educational Committee has engaged distinguished professor Leucht, expert in systemic reviews and meta-analysis in psychopharmacology, to serve as a research supervisor and a host for ECNP research internship. Of course, I would like to thank ECNP for accepting my application and awarding me 2017 research internship. In particular, I am grateful to professor Stefan Leucht from Technical University of Munich Department of Psychiatry for accepting to be my supervisor and for giving me the opportunity to learn from him and his young colleagues from his extraordinary “multilateral” research team. I had applied for this particular internship under the supervision of world-renowned researcher, in order to acquire skills and knowledge required for serious critical appraisal and practical implementation of systemic reviews of literature and meta-analysis in psychiatry (such as planning/designing protocol, searching and selecting randomized controlled studies, collecting and extracting data, assessing risk of bias, statistical analysis, GRADE etc). It is known that results of systemic reviews and meta-analysis of RCTs are fundamental for evidence-based clinical practice and are incorporated into treatment guidelines. Professor Leucht is an exceptional researcher and psychiatrist who authored or coauthored numerous systemic reviews and network/meta analysis related to crucial psychotropic drugs in psychiatry (with the specific emphasis on schizophrenia). He is one of the editors of Cochrane schizophrenia publishing group and, in his work, applies very strict methodological and ethical standards of the Cochrane organization. I spent my ECNP research internship from 4th of February to 16th of February 2018 at the Department of psychiatry and psychotherapy, Center for evidence-based medicine in psychiatry, Klinikum rechts der Isar, Technical University of Munich. Professor Leucht was my supervisor who has introduced me to the field of evidence-based psychiatry through brief theoretical course and extensive practical training. Just before my arrival to Munich Professor and his international team of young and enthusiastic researchers published important meta-analysis “Antipsychotic drugs for patients with schizophrenia and predominant or prominent negative symptoms: a systematic review and meta-analysis”. Also they have just submitted another paper about the effectiveness of antipsychotics in children and adolescence. Hence, the working atmosphere at professor’s Center was overwhelming. Department of psychiatry and psychotherapy, Klinikum rechts der Isar, Technical University of Munich is housed in a humanized, residential-style building localized in the middle of medical center and sounded with other buildings, small sport terrain, patios with benches and greenery. That is exactly how modern psychiatric hospital should look like- you would never even guess that it is mental health hospital. After spending two weeks there I could claim that it is hospital with ideal balance or combination of inpatient and outpatient treatment and research. I had opportunity not merely to theoretically learn about the very concept and the process of systemic review of RCTs and meta-analysis in psychopharmacotherapy, but also to take active part in conducting it. First I got insight into the process of the preparation of the specific protocol for the prospective systemic review and meta-analysis, that should be registered, in advance, in PROSPERO registry. Protocol has specified the aim of the study, searching strategy, inclusion and exclusion criteria, primary and secondary outcomes - measures that should be extracted, statistical methods that will be applied for the calculation of effect sizes (impact of interventions) etc. Professor and his excellent team submitted the protocol of a new meta-analysis which is addressing the controversy around the actual effect sizes (reduction of psychotic symptoms) of antipsychotics compared to active placebo. After designing and posting protocol publicly on PROSPERO web site, professor Leucht’s team did the systemic search of different databases (from Cochrane to PubMed, EMBASE, databases of regulators and Pharma companies etc) looking for the eligible studies- mainly results of the studies in the form of published papers or study reports, applying predefined, specific search criteria and strategy. After collecting hundreds of abstracts, researchers did double screening of abstracts or summaries of studies for the potential exclusion and inclusion in the systemic review. I was able to observe this process firsthand. The next step was to acquire the full texts of papers (which abstracts were collected), so that thorough screening/analysis could be done, also by two independent researchers. Different databases were searched looking for the full text papers with the results of studies comparing antipsychotics with barbiturates or benzodiazepines as active placebos. The culmination of my internship was my visit to

Bavarian Library where I obtained and scanned full texts of some of the “antique” papers from 1950-ties and 1960-ties that will be included in this meta-analysis. By reading, in detail, full-text papers final decision which studies will be included in the systemic review and meta-analysis could be made. The whole process is done on the basis of registered Protocol, following the rules of Cochrane Handbook for Systematic Reviews of Interventions. Next phase of the research is the extraction of data - outcome measures that will be used for the calculation of the effect sizes. This is being done in parallel with thorough evaluation of the risk of bias of included studies. This process is underway. Final stage in the research would be statistical synthesis of the data, or the meta-analysis itself. The main aim of the meta-analysis would be the calculation of the effect sizes of individual studies, determining their “strength” or “weight” in the analysis and then summing the combined effect size of all studies presenting the direction and magnitude of the effect. There is a statistical software that could be used for all these calculations. For the understanding of the whole process and the concept the book “ Introduction to Meta-Analysis. Michael Borenstein, L. V. Hedges, J. P. T. Higgins and H. R. Rothstein (© 2009 John Wiley & Sons, Ltd.) is indispensable and always ‘at the table’ of professor Leucht’s team.

Professor Stefan Leucht and his young research associates Johannes Schneider-Thoma (in particular), Marc Krause, Irene Bighelli etc. have been great hosts who were always ready to render me a help, not just related to research internship, but also with my everyday life in Munich. I will miss them all and Munich a lot and hope that we will continue cooperation in the future.

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