Abstract – BENEFRI Workshop 2017

Emotional Dysregulation in Psychosis – Perception of Threat

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Background:
Around 0.5 – 1 % of the population is affected by psychosis during their lifetime and present a variety of clinical symptoms, despite identical diagnosis. To uncover the underlying pathophysiological processes of psychosis we use a system-specific approach. The Bern Psychopathology Scale (BPS) identifies three different disturbed symptom dimensions: affect, language & motor function. Several emotional processes are affected in persons at risk with psychosis. The dimension of affect includes various symptoms like delusion of threat, tension, psychotic anxiety, suspiciousness, aggressiveness or social avoidance. Further, a core impairment in psychosis has been found to be the perception of emotional information from faces.

Methods:
We investigate neural activation patterns using Magnetic Resonance Imaging (MRI) and Electroencephalography (EEG) in four different subjects groups: patients with psychosis, clinical high-risk patients with psychosis, 1st-degree relatives with psychosis and healthy controls. Additionally, we conduct clinical interviews, assess emotional intelligence and social anxiety questionnaires, test emotion recognition and examine heart-rate-variability (HRV). During EEG and MRI examination, a self-developed face perception task with faces varying in gender, aesthetic, head movement and gaze direction will be presented.

Hypotheses:
We hypothesize, that the psychopathology of psychosis in the dimension of affect increases as a function of increasing psychosis vulnerability. Further, the brain activation in the regions of interest (limbic-, reward system & face processing areas) during the face perception task differ between groups. Additionally, the physiological parameter HRV is negatively correlated with brain activation in the limbic system in all groups.

Aim:
Studying the neurophysiological correlates underlying psychotic symptom dimensions appears a promising approach to increase our understanding of the pathophysiological processes underlying the aetiology of psychoses and considered key to improve diagnosis and treatment options.

Abstract:" Lost in Associations during Psychosis"
Francilia Zengaffinen (BENEFRI Workshop 2017)

Background Psychoses are aetiologically complex disorders that affect about 0.5 − 1% of the population during their lifetime [1]. Psychosis patients with identical diagnoses can vary greatly with regard to their clinical presentation. Psychotic symptoms can include delusions, hallucinations, disorganized speech, formal thought disorder, catatonic behavior and negative symptoms [2]. According to Strik and Dierks, psychotic symptoms represent disturbances in higher-order brain functions [3]. As such, they can be grouped according to their dysfunction in one or more of the three following neural brain circuitries: language, affect, motor function. Dysfunction of the neural language brain circuitry appear to be related to disturbances in expressive speech, formal thought disorders or delusions [3]. Previous research has shown that psychosis patients do not predominantly activate the left hemisphere during language tasks in comparison to healthy controls [4, 5]. Furthermore, previous EEG studies have shown that there are differences in brain activity patterns during a language priming task, specifically with regard to the N400 waveform [6].

Research Questions Is the language brain circuitry disturbed only in psychosis, or do already first degree relatives and clinical high-risk individuals show some extend of aberrancy? Also, do all of the psychosis patients show to some part a disruption in the language circuitry or is it predominantly the patients with language and thought disturbances?

Methods The subject will complete a lexical decision task during a EEG and fMRI measurement. The lexical priming task has two subtasks, which either a category or a relation of word pairs. The stimuli are category, related or unrelated word pairs. With this task the disturbances in language in psychosis will be examined. Additionally, 120 subjects will be examined to study the whole spectrum from health to psychosis with four different subject groups (healthy controls, first degree relatives of psychosis patients, clinical high-risk individuals and psychosis patients).

Expected Results The underlying language brain circuitry presents with hyperactivation and structural brain abnormalities in relation to the strength of the disturbances. With EEG we expect, that the disturbed neural activation patterns of the language system are specific to patients with language and thought impairments. Furthermore, we assume that with the progression of the disorder the performance in the EEG, fMRI and neuropsychological testing will be significantly poorer. Also the clinical and familial high-risk individuals show some extent of language dysfunction in all the language tasks (fMRI, EEG and neuropsychological testing). Moreover, looking at specific group results, we assume to find that not all psychotic patients show a disturbance in the language system.

References:

[1] McGrath, J., Saha, S., Welham, J., El Saadi, O., MacCauley, C., & Chant, D. (2004). A systematic review of the incidence of schizophrenia: the distribution of rates and the influence of sex, urbanicity, migrant status and methodology. *BMC medicine*, *2*(1), 1-22.
[2] Wheeler, A. L., & Voineskos, A. N. (2014). A review of structural neuroimaging in schizophrenia: from connectivity to connectomics. *Frontiers in human neuroscience*, *8* (653), 1-18.
[3] Strik, W., & Dierks, T. (2008). Neurophysiological mechanisms of psychotic symptoms. *European archives of psychiatry and clinical neuroscience*, *258*(5), 66-70.
[4] Dollfus, S., Razafimandimby, A., Delamillieure, P., Brazo, P., Joliot, M., Mazoyer, B., & Tzourio-Mazoyer, N. (2005). Atypical hemispheric specialization for language in right-handed schizophrenia patients. *Biological psychiatry*, *57*(9), 1020-1028.
[5] Bleich-Cohen, M., Sharon, H., Weizman, R., Poyurovsky, M., Faragian, S., & Hendler, T. (2012). Diminished language lateralization in schizophrenia corresponds to impaired inter-hemispheric functional connectivity. *Schizophrenia research*, *134*(2), 131-136.
[6] Kostova, M., Passerieux, C., Laurent, J. P., & Hardy-Baylé, M. C. (2005). N400 anomalies in schizophrenia are correlated with the severity of formal thought disorder. *Schizophrenia Research*, *78*(2), 285-291.

Epithelial Growth Factor Receptor Expression influences 5-ALA induced Glioblastoma Fluorescence

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Background:
The extent of 5-aminolevulinic acid (5-ALA) guided tumor resection has a determining impact in glioma surgery. Although the intensity of the 5-ALA induced fluorescence has been described to vary in confirmed glioma, the detection method is currently subjective and non-quantitative. We correlated 5-ALA induced fluorescence with the quantitative expression of Epithelial Growth Factor Receptor (EGFR) in different glioblastoma (GBM) cell lines.
Methods:
To elucidate the role of EGFR in the metabolism of 5-ALA in (U87MG and BS153), we analyzed the activation of EGFR by its primary ligand EGF, and its downstream effect on Heme oxygenase-1 (HO-1), a key enzyme regulating the metabolism of Protoporphyrin IX (PpIX), the fluorescent metabolite of 5-ALA. Effects of direct pharmacological inhibition by Tin(IV)-Protoporphyrin (SnPP) or gene knockdown by small interfering RNA on HO-1 enzyme were analyzed in respect to 5-ALA induced fluorescence.
Results:
A significant difference in 5-ALA induced fluorescence was obtained in U87MG compared to BS153 cell lines, correlating with the different quantitative EGFR expression. Treatment of U87MG cells with EGF was able to promote HO-1 transcription and expression in a concentration-dependent manner, leading to a reduced cellular fluorescence. This effect could be reversed by EGFR-specific siRNA treatment. Reducing HO-1 activity by SnPP or HO-1-specific siRNA significantly enhanced fluorescence, independently of EGFR quantitative expression.
Conclusion and Future Perspective:
EGF-induced HO-1 protein expression was identified as negative regulator of 5-ALA induced fluorescence, thus dependent of EGFR expression. These findings justify the clinical observation of different intensities of 5-ALA induced fluorescence in glioblastoma surgery.
To further confirm our finding we would retrospectively ivestigate, in biopsies of patient who had recived 5-ALA before operation, the correlation between EGFR expression and PpIX fluorescence.
Moreover, we will to develop, in addition to the ongoing xenograft animal model of U87MG, a xenograft model of BS153 to evaluate ex-vivo, following the in vivo administration of 5-ALA, the different expression in PpIX fluorescence and its correlation with the EGFR expression.