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Perspectives of neurobiological research in schizophrenia

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ABSTRACT

The relevance of neurobiologically oriented schizophrenia research has not yet received its deserved perception. A focus on key clinical features of schizophrenia such as cognitive dysfunction or their systematic study will lead to a better understanding of the pathophysiology of schizophrenia. However, it is believed that only paralleling human and animal studies will eventually improve the understanding of the molecular pathways, consequently leading to the symptom dimensions known in schizophrenia.

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1. Historical considerations

The Department of Psychiatry and Psychotherapy of the University of Munich has a longstanding tradition of neurobiologically based research on psychotic disorders, especially schizophrenia. Emil Kraepelin has chaired the department between 1903 and 1922 and succeeded in bringing together outstanding professionals in the field to perform research on schizophrenia, formerly named 'dementia praecox', by applying different methods and approaches. Primarily performed by researchers such as Alois Alzheimer and Franz Nissl and strongly assisted by Emil Kraepelin himself this group was able to comprise research on classification up to systematic investigations of neurobiological correlates. 100 years later the neurobiological basis of schizophrenia is still not well understood and the prognosis of this group of disorders is as yet not very favourable despite the introduction of antipsychotics more than 60 years ago.

A 15-year follow-up study (Möller et al., 2011) on patients with first-episode psychoses was able to demonstrate that 57% of patients with schizophrenia revealed a chronic course with persisting residual symptoms, with a GAF score ≤60% in the last 2 years before follow-up. In comparison, only 5% in patients with affective psychoses and only 15% in patients with schizoaffective psychoses demonstrated this unfavourable chronic outcome (see Fig. 1).

The crucial question here is what modern neurobiologically based research has the ability to accomplish measurable progress in the pathophysiology of schizophrenia in order to develop better treatment options for patients. In the last 3 years the Department of Psychiatry and Psychotherapy of the University of Munich was able to bring together a number of working groups which combine clinical and basic scientific expertise for a joint research approach on schizophrenia. It is obvious that a systematic line of research, starting from the genetic and non-genetic risk factors up to the behavioural level should allow the strengthening of our current knowledge on the pathophysiology of schizophrenia (see Fig. 2).

Furthermore, it is assumed that this line of methods used in humans should be paralleled by a line of research methods based

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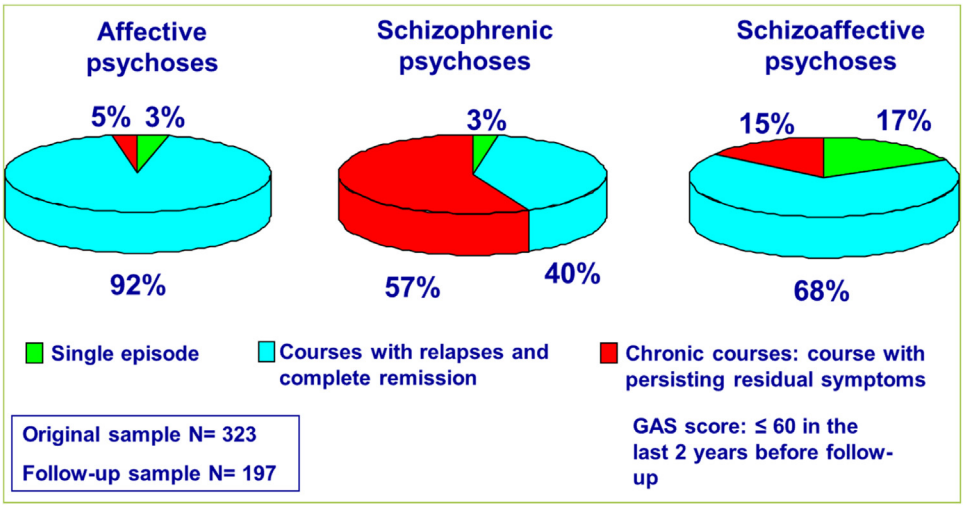

Fig. 1. Munich 15-year follow-up study (MUFUSSAD): global outcome of first-admitted schizophrenic, affective and schizoaffective inpatients (ICD-10) (modified according to (Möller et al., 2011)).

on animal models mimicking the human disease schizophrenia from the risk factors to behavioural changes (Falkai et al., 2015).

The ambition of this article is to try and develop a conceptual framework of the pathophysiology of schizophrenia from aetiological factors via brain mechanisms to the behavioural domains of the illness.

2. What is the clinical phenotype central to the disease process?

Schizophrenia is characterised by a complex phenotype including positive as well as negative symptoms. There is good evidence that especially the negative symptoms which include cognitive dysfunction form the core, lead to an unfavourable social

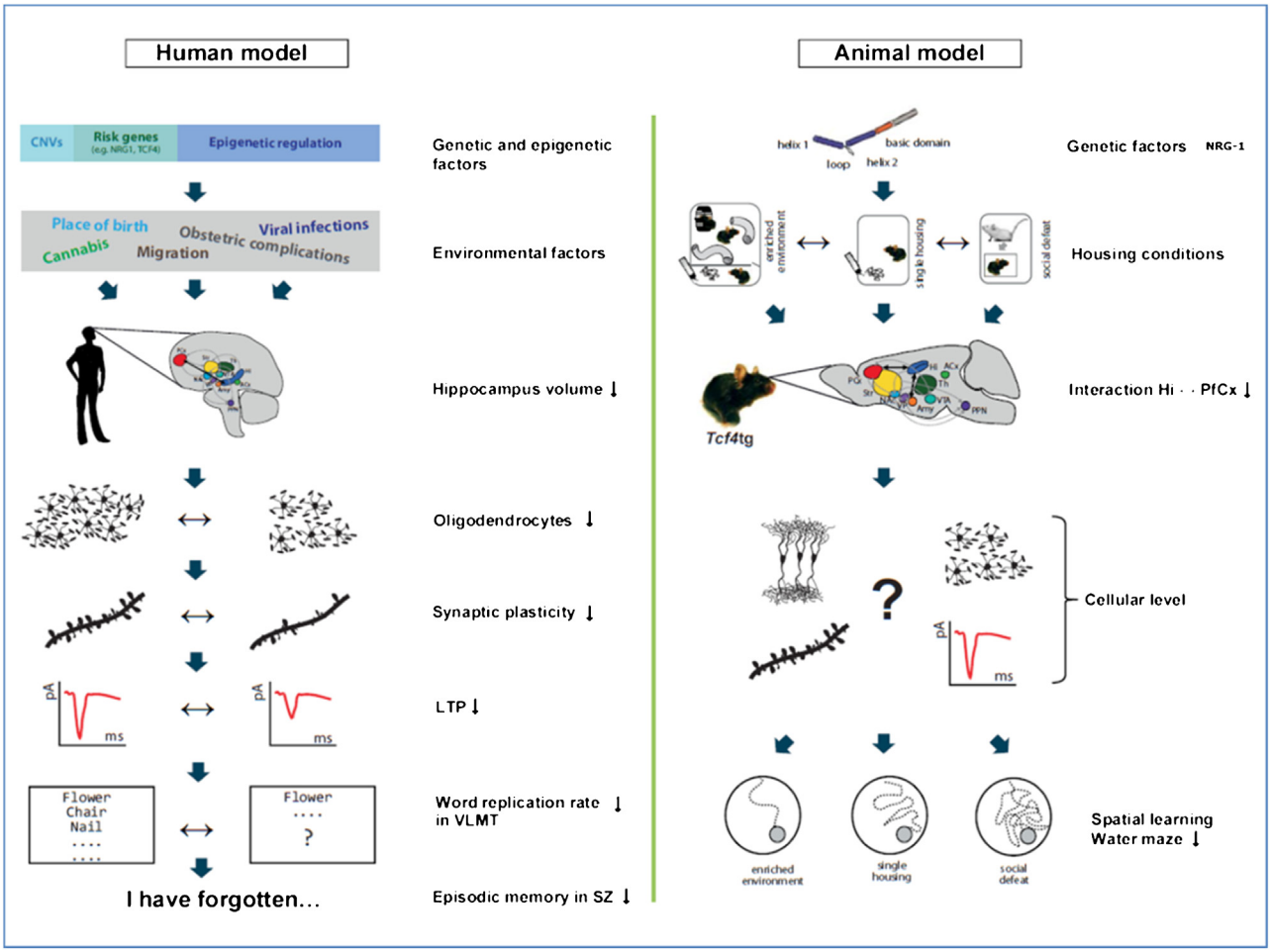

Fig. 2. Pathophysiology of schizophrenia: human and animal model needed (modified according to (Falkai et al., 2015)).
Scheme designed by M.M. Brzózka.