Workshop FePsy Jubilee-Symposium 25.09.2014

Training: "Basel Screening-Interview für Psychosen"

Dr. med. Jacqueline Aston

Was ist die Prodromalphase einer schizophrenen Psychose?

- Frühphase einer sich entwickelnden Erkrankung aus dem schizophrenen Formkreis
- Anhaltende Veränderungen ohne ersichtlichen Grund vor allem:
  - Veränderungen des Wesens
  - Veränderungen der Gefühle
  - Veränderungen der Leistungsfähigkeit
  - Veränderungen im sozialen Bereich
  - Veränderungen der Wahrnehmung

Warum ist die Früherkennung wichtig?

- Schizophrene Psychosen gehören zu den folgenschwersten Erkrankungen mit hoher Mortalität und Chronifizierungsneigung.
- Früherkennung und Frühbehandlung verbessern die Prognose
- Ca. 30% der nach BSIP als Risikopatienten eingestuften Patienten, entwickeln eine manifeste Psychose im Beobachtungszeitraum von 3 Jahren
- Klinische Ziele der Früherkennung: Verhinderung der Transition zur Psychose, Minimierung der Zeit zwischen Ausbruch und Behandlung der Psychose, Verhinderung von Spätfolgen der Erkrankung (dadurch Einsparungen im Gesundheitssystem); Verbesserung der Lebensqualität durch therapeutische Unterstützung; Coping Skills entwickeln und Ressourcen stärken

Wie kann man ein mögliches Psychoserisiko identifizieren?

- Selbst-screening durch betroffene Personen: „Self-screen Prodrom"
- Risikocheckliste
- Screening mit Hilfe des BSIP

Wie ist der BSIP anzuwenden?

- Strukturiertes klinisches Interview
- Erhebung von möglichen Frühwarnzeichen (Risikoalter, Psychopathologie, Potentielle Prodromi, Unspezifische Anzeichen, (Prä-)psychotische/attenuierte Symptome, Knick in der Lebenslinie, Drogen Psychiatrische Vorerkrankungen/ psychische Auffälligkeiten in der Kindheit, Psychiatrische Erkrankungen in der Familie, Zuweisung mit Psychose Verdacht)
- Beurteilung des Risikos anhand von internationalen Richtlinien

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Training: "Neuropsychologisches Assessment bei fraglichen Prodromal-Status"

Dr. phil. Martina Papmeyer, Dr. phil. Erich Studerus

Cognitive deficits form a prominent feature in psychosis. It has been well-documented that subtle neuropsychological impairments are already evident in individuals with an at-risk mental state (ARMS) for psychosis years before the actual onset of disease. Accordingly, assessment of neurocognitive function in ARMS individuals can help to detect more accurately if a patient is likely experiencing the prodromal phase of psychosis. This workshop aims at providing state of the art information on neuropsychological assessment in ARMS individuals.

In detail, workshop participants will be informed about the neuropsychological domains commonly impaired during the prodromal stage and learn about specific neuropsychological tasks found to be predictive for transition to psychosis. The neuropsychological test battery used in the FePsy study will be presented. Moreover, the administration and evaluation of several neuropsychological tasks important for the assessment of the prodromal stage will be shown. With the help of case reports, the interpretation of neuropsychological reports will be illustrated. Finally, the workshop closes with discussions focusing on future perspectives as well as current limitations that need to be addressed.

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Training: "Differentialdiagnostische Probleme in der Früherkennung"

PD Dr. med. Andor Simon, Dr. med. Anna Walter

Symptome, denen wir in einer beginnenden Psychose begegnen, sind nicht immer spezifisch für eine solche. Nicht selten sind sie Ausdruck einer anderen zugrundeliegenden psychischen Störung, oder - gerade in der Adoleszenz – transitorisch. Die Abklärung einer beginnenden Psychose beschränkt sich daher nie auf die ausschliessliche Erhebung psychose-typischer Symptome.

Ausgehend von einer Serie von kurzen, einleitenden Fallvignetten wollen wir in einer offenen und interaktiven Diskussion gemeinsam mit Ihnen verschiedene Diagnosespektren besprechen, auf welchen psychotische Symptome jeweils mit nicht-psychotischen Symptomen vorkommen und somit psychotische und nicht-psychotische Störungen überlappen können.

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Training: "Früherkennung von ersten Zeichen der Psychose"

PD Dr. phil. Frauke Schultze-Lutter

Kognitive und perzeptive Basissymptome haben sich wiederholt als prädiktiv für eine spätere Psychose gezeigt und bilden die Grundlage der zwei teils überlappenden Basissymptomkriterien, COPER (cognitive-perceptive basic symptoms) und COGDIS (cognitive disturbances). Im Gegensatz zu den attenuierten und transienten psychotischen Symptomen der ultra-high risk Kriterien erfassen diese Basissymptome Störungen in Denk- und Wahrnehmungsprozessen und nicht -inhalten und werden vollständig von den Betroffenen selbst als Abweichungen von der 'normalen' Informationsverarbeitung wahrgenommen. Doch trotz dieser Selbstwahrnehmung werden sie oftmals nicht spontan berichtet oder verbergen sich hinter eher allgemeinen Klagen über Konzentrationsprobleme oder Probleme beim Denken. Ihre Erfassung und Abgrenzung gegenüber weniger prädiktiven kognitiven Beschwerden bedarf daher genauen Nachfragens in einem semi-strukturierten klinischen Interview, dem Schizophrenia Proneness Instrument, Adult (SPI-A) or Child and Youth version (SPI-CY).

Der Workshop soll anhand von Beispielen eine praxisnahe Einführung in die Erhebung der 14 für COPER und COGDIS relevanten Basissymptome gemäss der SPI-A/SPI-CY geben.

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Training: "Früherkennung von Psychosen: Hilfreiche oder stigmatisierende Erfahrung?"

Martina Uttinger

Hintergrund:

Psychose- und Schizophreniepatienten sind bis heute die am meisten von Stigmatisierung betroffene psychiatrische Patientengruppe. Die Früherkennung von Psychosen versucht unter anderem, möglicher Stigmatisierung entgegenzuwirken, indem sie Betroffene möglichst früh unterstützt und behandelt, um schwerwiegende negative Konsequenzen einer Psychose abzumildern, und nach Möglichkeit zu vermeiden. Dennoch findet sich potentielle Stigmatisierung von Patienten unter den meist geäusserten Kritikpunkten an der Früherkennung.

Zielsetzung des Workshops:

Im Workshop geht es in einem ersten Teil darum, gemeinsam ein Verständnis von Stigma und seiner Rolle in der Früherkennung von Psychosen zu erarbeiten, welches anschliessend durch Erkenntnisse aus der Literatur ergänzt wird. Wir gehen dabei auf verschiedene Aspekte von Stigma ein, welche für die Früherkennung relevant sind.

Der zweite Teil des Workshops widmet sich möglichen Interventionen und Strategien im Umgang mit Stigma im klinischen Alltag in der Früherkennung. Auch in diesem Teil steht die Diskussion mit den Teilnehmern im Vordergrund, welche eingeladen sind, sowohl Fachwissen wie auch berufliche oder persönliche Erfahrung zum Thema einzubringen.

Begleitet wird der Workshop von einem Patienten der Fepsy-Sprechstunde, sowie einer Angehörigen, welche die Diskussion in Bezug auf Relevanz und Machbarkeit aus subjektiver Sicht der Betroffenen mitverfolgen, und sich dazu einbringen werden.

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Training: "MRI, EEG and laboratory in early detection and differential diagnosis"

Dr. phil. Renata Smieskova, M.Sc. Avinash Ramyead, M.Sc. Sarah Ittig

MRI measurement, an integral part of clinical examination, consists of clinical sequences, necessary for neuroradiological findings, and of research sequences. The clinical sequences are used for exclusion of individuals with structural brain abnormalities. Since 2008 until 2014, we scanned 226 individuals with 13 of them having the incidental findings (5.7%). The majority of them were born anomalies. During the workshop there will be presented some abnormal MRI scans with short description of their individual symptoms. Unfortunately, individual MRI scans cannot be used for individual diagnosis of psychosis or prediction of the disease development yet. All used research sequences have been group-vice evaluated and the procedure and acquired results will be shortly presented. Currently, we are collecting the follow-up scans to evaluate changes during the development to psychosis or during the progression of the disease.

Electroencephalography (EEG) is routinely used in the diagnosis of patients exhibiting schizophrenia-like symptoms to exclude organic brain diseases such as limbic encephalitis or epilepsy. EEG has so far been used in clinical research to assess 1) event-related potentials and 2) to quantify the surface power of spontaneous neuronal oscillations at different frequency bands during rest. After a brief introduction of EEG, we will demonstrate how clinical resting-state EEGs could be analysed and used for the prediction of psychosis in prodromal patients. Currently, we are investigating whether low frequency bands, measured by high density EEG recordings, could be involved in 1) the shielding of the working memory against external distractors and also 2) contribute to self-monitoring mechanisms in patients with emerging psychosis.

To determine prolactin-value among other blood parameters is also of high relevancy in prodromal phase of psychosis. Prolactin, a polypeptide hormone secreted from the anterior pituitary, is released in response to psychosocial stress. The main regulatory mechanism acting on prolactin is the inhibition of prolactin synthesis by dopamine. It can be suggested that stress induces hyperprolactinemia and that the increase of dopamine in psychosis is, at least in part, a regulatory mechanism to down-regulate prolactin. There will be presented one casuistic of patient suffering from prodromal psychotic symptoms, which could be related to her elevated prolactin-values.

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"Früherkennung von Psychosen: State of the Art und Zukunftsausblick"

Prof. Dr. med. Joachim Klosterkötter

In modern medicine, vigorous efforts are being made in the prediction and prevention of diseases. Mental disorders are suitable candidates for the application of this program. The currently known neurobiological and psychosocial risk indicators for schizophrenia do not have a predictive power sufficient for selective prevention in asymptomatic patients at risk. However, once predictive basic and later pre-psychotic high risk symptoms of psychosis develop into the five-year initial prodrome, the impending outbreak of the disease can be predicted with high accuracy. Research findings suggest a differential strategy of indicated prevention with cognitive behavioral therapy in early initial prodromal states and low dosage atypical antipsychotics in late initial prodromal states. The most important future tasks are the improvement of the predictive power by risk enrichment and stratification, as well as the confirmation of the existing and the development of new prevention strategies, with a stronger focus on the etiology of the disorder. In addition, the prediction and prevention approach would benefit from the inclusion of risk symptoms in the DSM-5 criteria.

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"Preventive Strategies in Emerging Mental Disorders in Young People: Clinical Staging and Translational Research"

Prof. Dr. med. Patrick McGorry

A key goal in psychiatry is to build new diagnostic, therapeutic and translational tools and capacity to reduce the impact of emerging mental disorders in young people on survival, distress, quality of life and productivity. Young people bear the major burden of onset for mental disorders with 75% of such illnesses appearing before age 25 years. This can only be done within a novel non-stigmatising interface between young people and clinical care in mental health such as that recently created by headspace in Australia and increasingly in some other developed nations. We must also develop new terminology enabling early clinical phenotypes of mental disorders to be defined in a normalizing and health-promoting way that will promote trust and confidence. A transdiagnostic strategy is critical, transcending existing subthreshold risk syndromes, with new "pluripotential" criteria capturing clinical high risk for multiple syndromes. This strategy seeks to solve problems with specificity, power and reduce false positives. Secondly, we must focus on novel therapeutics. This starts with the development and evaluation of novel forms of psychosocial intervention for early stage illness. A complementary strategy needs to focus upon candidate biomarkers as therapeutic probes within a reverse translation strategy moving towards biosignatures or profiles of emerging disorder. Relationships between response and baseline levels of and changes in biomarkers may create a pathway to personalised/stratified medicine. Finally translation of existing expertise and systematic reform of clinical practice and cultures of care is something that is achievable with the present state of knowledge yet is poorly implemented.

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"First signs of emerging psychosis"

PD Dr. phil. Frauke Schultze-Lutter

The majority of first-episode psychoses are preceded by a prodromal phase that is several years on average, frequently leads to some decline in psychosocial functioning and offers the opportunity for an early detection within the framework of an indicated prevention. To this, two approaches are currently mainly followed. The ultra-high risk (UHR) criteria were explicitly developed to predict first-episode psychosis within 12 months, and indeed the majority of conversions in clinical UHR samples seem to occur within the first 12 months of initial assessment. Their main criterion, the attenuated psychotic symptoms (APS) criterion, captures symptoms that resemble positive symptoms of psychosis (i.e., delusions, hallucinations and formal thought disorders) with the exception that some level of insight is still maintained and that frequently compromise functioning already. In contrast, the basic symptom criteria try to catch patients at increased risk of psychoses at the earliest possible time, i.e., ideally when only first subtle disturbances in information processing have developed that are experienced with full insight and do not yet overload the person's coping abilities and thus have not yet resulted in any functional decline. First results from retrospective and prospective studies not only support this view but indicate that the combination of both approaches might be a most favorable way to increase sensitivity and earliness of risk detection as well as to establish a change sensitive risk stratification approach.

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"Psychosis high-risk states in adolescents"

PD Dr. med. Andor Simon

Most mental states and disorders emerge in adolescence or young adulthood. Individuals in these age groups undergo multitudinous changes in behaviour, develop diversity of contextual thinking, and experience frequent emotional turmoil. Within this developmental context, mental phenomena may either occur only transiently, or they may evolve into actual mental health disorders in more vulnerable and predisposed individuals.

This presentation reviews five groups of symptoms and clinical features that are frequently reported by individuals with suspected psychosis risk states, yet share strong commonalities with other mental disorders and conditions and thus form diagnostic spectra: isolated hallucinations; unusual bodily perceptions, hypochondriatic fears and cenesthetic psychotic symptoms; depersonalization; obsessive-compulsive, overvalued and delusional ideas; and autism spectrum disorders. Also, the role of brief psychotic episodes will be discussed.

Results are based on findings from over 600 individuals that were so far assessed in the Bruderholz Early Psychosis Outpatient Service for Adolescents and Young Adults since its establishment in 2002.

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"The psychosis high risk state – is it valid?"

Dr. med. Paolo Fusar-Poli

Prodromal features of the schizophrenia syndrome have been described for a century, and work in the past two decades has produced a substantial literature based on these features to identify individuals at increased risk for developing a psychotic disorder. Sometimes conceptualized as a "risk state" and sometimes as early manifestations of a "disorder," the work has been conducted with several related but different constructs. Early in the preparation of the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) public comment was sought on the proposal to create a new disorder termed attenuated psychosis syndrome (APS), and a range of issues emerged that generated interesting and important controversies. In this talk, these criticisms are fully discussed, the APS concept is explicated; data relating to reliability, validity, and treatment are updated; the heterogeneity of APS is considered; and alternative views of the construct are presented with an emphasis on developmental pattern with timing for primary and secondary prevention and early treatment. Areas of future research are identified, and a potential roadmap for inclusion in DSM-5.1 is traced.

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"Psychosis early detection: Helpful or stigmatizing experience for those concerned"

M.Sc. Martina Uttinger

Despite the large scientific debate concerning potential stigma associated with early detection of psychosis and identifying an at-risk mental state (ARMS) for psychosis, studies examining this topic from the subjective perspective of patients are rare.

Therefore we conducted a study that investigates the question if ARMS individuals experience any stigma – and if so what kind of – and if early detection centres are contributing to it in any form or if the support offered is rather experienced as relieving and helpful.

Results from qualitative interviews with ARMS individuals currently enrolled in the follow–up assessments of the prospective Basel Früherkennung von Psychosen (FePsy; English: Early Detection of Psychosis) study are presented and illustrated with examples of patient statements.

Further implications resulting from the study results concerning future research and treatment of ARMS individuals in early detection services are discussed.

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"Connectivity abnormalities in emerging psychosis"

Dr. sc. nat. André Schmidt

It has been proposed that brain changes in psychosis may not only refer to local brain abnormalities, but to dysfunctional integration of task-related brain regions. Thus, recent investigations have focused attention on functional brain interactions, with experimental imaging studies supporting the disconnection hypothesis of schizophrenia. These studies have revealed a wide spectrum of brain connectivity abnormalities mainly in chronic patients, particularly for connections integrating the prefrontal cortex. However, brain changes in psychosis evolve along a dynamic trajectory, emerging before psychosis onset and proceeding with ongoing illness. For example, evidence from neuroimaging studies showed that different stages of psychosis are associated with distinct functional alterations of local brain regions during working memory and reward prediction tasks. But as yet it still remains unclear whether these local effects have arisen from changes in the underlying connectivity to other brain regions involved during the task. We therefore explored whether dysconnectivity among specific brain regions activated during working memory processing and reward prediction predates the onset of psychosis. In addition, we also tested for the impact of antipsychotic treatment in patients with first-episode psychosis and whether the connection strengths were related to the severity of psychotic symptoms. Our findings suggest that the vulnerability to psychosis is associated with a progressive failure of functional integration of brain regions involved in working memory and reward prediction. Moreover, these abnormal connection strengths were reversed after antipsychotic medication, suggesting a normalizing effect. These studies together emphasize that such model-based assays may help us to classify the psychosis continuum based on the extent of dysconnectivity and might also serve to assess the efficacy of pharmacological treatments.

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"Neurocognition and fine motor functioning in the prediction of psychosis"

Dr. phil. Erich Studerus

Neurocognitive and motor functioning deficits are core features of schizophrenia. They are not only present in patients with schizophrenic psychoses, but also in individuals with an at-risk mental state (ARMS) for psychosis. Meta-analyses indicate that ARMS individuals with later transition to psychosis have more severe deficits than those without transition in almost all domains. Accordingly, it has been demonstrated that neurocognitive measures can be exploited to improve the prediction of psychosis. However, while several studies have assessed neurocognitive deficits in ARMS individuals, most of them did not cover motor functioning. Furthermore, the existing studies mostly relied on the Finger Tapping Test, which only assesses motor speed, but not other important domains of motor functioning, such as dexterity. The Basel early detection of psychosis (FePsy) study is the only study that has investigated a wide range of different dimensions of fine motor functioning in ARMS individuals using standardized computerized test battery. Thus, the aim of this talk is to present and discuss the newest findings from the FePsy study regarding the specific pattern of neurocognitive and fine motor functioning deficits in ARMS individuals. Our results indicate that ARMS individuals with later transition to psychosis show important differences in some but not all domains of cognitive and fine motor functioning compared to those without transition. Furthermore, we show that cognitive and fine motor functioning measures can improve the prediction of psychosis when included in a multivariable prediction model. However, we also demonstrate that great care must be taken when developing a multivariable prediction model from a large number of measures from different domains, as improper variable selection and lack of internal cross-validation can lead to highly overoptimistic predictive performance measures and severely hamper the generalizability of the model.

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"Neurophysiological Predictors of Psychosis"

Prof. Dr. med. Stephan Ruhrmann

The available models for risk estimation are mainly based on psychopathological and functional predictor variables. The associated mean 36-month transition rate is about 30%, yet varies considerably across centers. These differences may in part be due to environmental differences, as has been suggested by incidences of psychosis in epidemiological samples. However, the time between the onset of a prodromal phase and the inclusion into a follow-up sample may also be different. In particular, the determination of this temporal dimension of risk by clinical means is limited. Neurobiological variables may be useful to overcome this limitation. Thereby, findings of a diminished neurocognitive performance already in the at-risk state as well as the high predictive validity of the "substrate-close" cognitive basic symptoms suggest a promising role for measures of information processing. Electroencephalographic parameters, particularly event related potentials (ERP), provide the advantage of studying such processing real-time. Meanwhile, predictive models have been reported for MMN, P300 and EEG parameter, including models enabling a stratification of risk with regard to magnitude as well as time. Thereby, the strongest evidence can currently be demonstrated for the MMN as its predictive value has been shown in two independent studies. As previous approaches to narrow already the inclusion criteria led to a tremendous loss of sensitivity, such variables should be part of a multistep-step procedure combining highly sensitive risk detection by clinical criteria (ultra-high risk criteria and/or basic symptom criteria) with subsequent individualized risk estimation by a prognostic index.

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"Non-pharmacological substances for early intervention"

Prof. Dr. med. Phillipe Conus

The first treatment trials conducted in UHR patients were based either on atypical antipsychotic medication, psychological interventions or a combination of both. For many reasons including side effects, the prescription of atypical antipsychotic in patients who have not yet crossed the threshold for psychosis diagnosis is however questionable. In addition, it is likely that the mechanisms at stake during this phase of the illness are different from those happening later. Among the various alternative treatment possibilities that were recently explored, 3 main avenues will be discussed in this talk.

First, based on the hypothesis that emerging psychosis may be linked to an increased apoptotic process, the concept of neuro-protection has received a lot of attention. Administration of Poly-Unsaturated-Fatty-Acids (PUFA) has been trialed in this context, initially in first episode psychosis patients and then in UHR subjects, with one trial suggesting an important reduction of symptoms and of rate of transition to psychosis, which was maintained after 12 months. Second, based on the hypothesis that NMDA hypoactivity may be one of the mechanisms involved in psychotic disorders, some groups have conducted preliminary trials based on the administration of glycine, an amino acid neurotransmitter that act on the glycine/D-serine modulatory site on the NMDA receptor as a full co-agonist with glutamate. Two preliminary short term trials were conducted in UHR patients and showed promising results of an impact on positive, negative and cognitive symptoms. However, recent negative results in larger samples of schizophrenia patients came to question this strategy. Finally, based on the observation, in chronic schizophrenia patients, of a deficit of glutathione, a potent antioxidant, a large body of work has been conducted to explore the possible effect of N-acetyl-cysteine, a precursor of glutathione, on symptoms in various disorders, including schizophrenia. While a trial in chronic schizophrenia patients showed an impact on negative symptoms and side effects, recent work seems to confirm that redox-dysregulation may be a central phenomenon in the development of psychosis, which opens new avenues for the development of new and more benign treatments for the early phase of psychosis.

Although these developments are promising, the limited evidence based knowledge on the mechanisms involved in the development of psychoses is a major limiting factor in this domain of research, and an important effort should therefore be put in the study of the basic neurobiological mechanisms at stake during the early phases of these disorders.

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"Psychological methods of early Intervention in emerging psychosis"

Prof. Dr. med. Andreas Bechdolf

Recent meta-analyses in almost 1.500 cases confirmed that criteria based on sub-threshold levels of psychotic symptoms (ultra high-risk criteria) or self-perceived cognitive deficits (basic symptoms) have been found to predict psychosis onset within 12 months in 20-30 % of the cases in large cohorts of help-seeking clients. These findings have provided the opportunity to deliver indicated prevention strategies to people at-risk in order to reduce or prevent the devastating effects of schizophrenia. Ninet randomized controlled trials (RCTs) including more than 1000 participants in the at-risk population have been completed so far. They have included evaluations of low dose risperidone and cognitive behavioural therapy (CBT) combined, CBT or an integrated psychological intervention alone, olanzapine and omega-3 fatty acids. The results of the treatment phase indicated advantages on a descriptive level or significant results in favour of the respective experimental condition in terms of transition to psychosis. Three independent meta-analyses confirmed these findings. However, at present the results for psychosocial and antipsychotic treatment are equivocal. Because of advantages regarding the risk/benefit ratio of psychosocial interventions, we argue psychosocial intervnetions should serve as first line treatment for people at risk and antipsychotics should be used as a second line treatment. However, due to a number of methodological limitations the empirical evidence of the superiority of psychological interventions or antipsychotics to unspecific control conditions in the at-risk population is preliminary. Therefore there is a need for methodological sound collaborative large scale RCT involving CBT and antipsychotics as preventive strategies. Such trials are on the way at present.