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Early Detection and Treatment Options for Psychosis in Transition from Childhood to Adolescence: A Review About Three Decades of Psychiatric Clinical Experience

Ralph Meyers

Introduction

While schizophrenia is best known for episodes of psychosis, it is also marked by chronic neurocognitive deficits, such as problems with memory and attention. These neurocognitive symptoms are evident prior to the onset of psychosis in the prodromal phase. The findings suggest that these impairments may serve as early warning signs of schizophrenia, as well as potential targets for intervention that could mitigate the onset of the psychotic disorder and significantly improve cognitive function [1].

Impaired working memory and declarative memory turned out to be the key neurocognitive functions that are impaired in the high-risk, prodromal phase prior to the onset of full-blown psychosis. These findings, as reported by Seidman, are in keeping with the experiences of many people with schizophrenia who report sudden difficulties reading, concentrating, or remembering things in the earliest days of the disorder [1].

Drug abuse will have an important impact on either the first onset or the further development, e.g., the prognosis for treatment outcomes (Fig. 49.1).

R. Meyers (✉)
Socialpsychiatric Center for Child and Adolescent Psychiatry, Dorsten, Germany
e-mail: info@meyers-dorsten.com; Dr.Meyers@gmx.de;
https://www.meyers-dorsten.com

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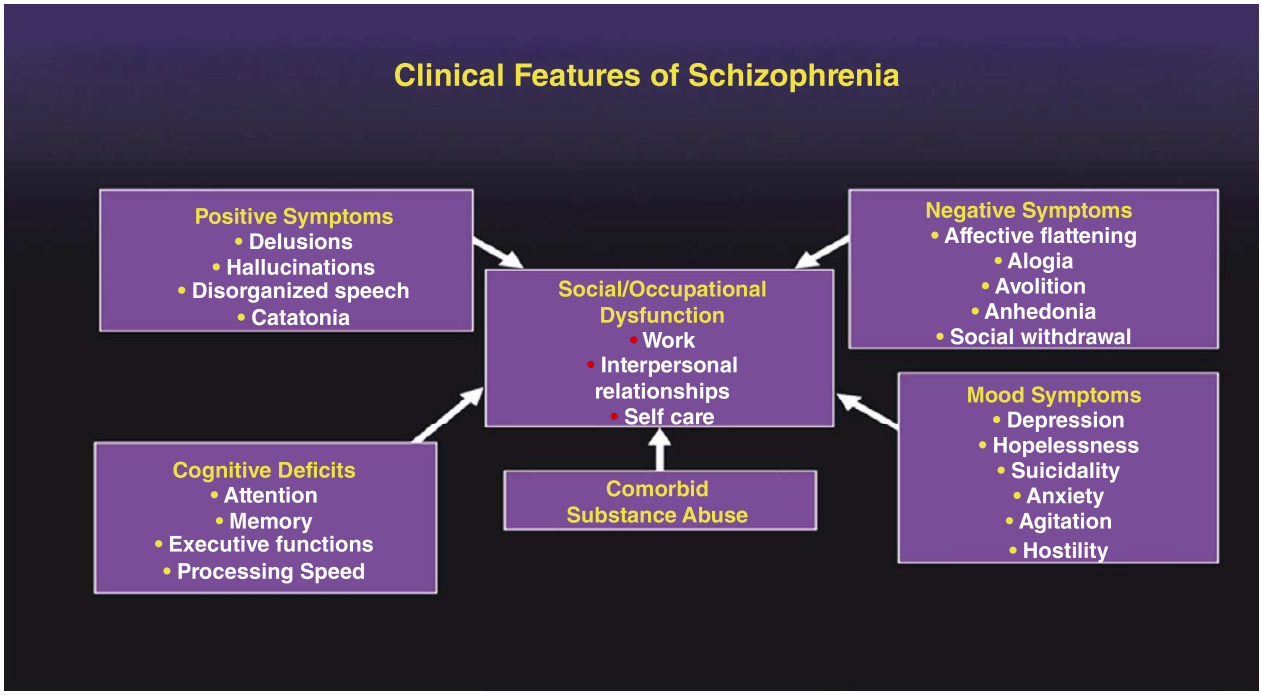

Fig. 49.1 Clinical features of schizophrenia, Best of PSYCH FORUM 2016. Schizophrenia: Preventing Deterioration and Returning to Baseline. Henry A. Nasrallah, MD, Sydney W. Souers Professor, Chair, Department of Psychiatry and Behavioral Neuroscience, Saint Louis University School of Medicine St. Louis, MO. (extract from presentation with authorization by Nasralla) [2]

Early Detection and Treatment Options for Psychosis in Transition from Childhood to Adolescence

As previously mentioned by Seidman, early detection is essential for the later outcome in psychosis. So, in our centre, we focus on a holistic way in anamnesis and diagnosis including neurological, psychiatric, and test psychological assessments for all our patients [1].

Our neurological examination includes motor abilities, checks for persisting preborn reflexes, regarding all kinds of sensory disabilities and hypersensitivities. We also check for generalized internal diseases, and we have a cursory check including the static and orthopaedic state.

Psychiatric evaluation will include the age and mental status and also the cognitive functions, memory, and attention. These have to be objectively measured, and we regularly include the OPATUS CPTa® from age 3 onwards [3–5].

We use a fixed test battery for each developmental stage [3–5]. If there arises the suspicion, there could be a prepsychotic or psychotic disorder behind the symptoms presented, additional examinations and tests will be followed-up.

Quite effective is to check for cognitive basic impairments:

Cognitive Perceptual Basic Disorders [6]

It may be observed more than one of the following 10 basic symptoms within the last 3 months and a first occurrence more than 12 months before:

Thought interference
Compulsive perseveration of contents of consciousness
Urging and chasing thoughts
Mind blocking
Disorder of receptive language
Disorder of discrimination of ideas and perceptions, imagination, and memory ideas
“Subject centrism,” self-relationship tendencies
Derealization
Disorders of visual perception
Acoustic perception disorders

Basic Cognitive Disorders [6]

It may be observed more than two of the following nine basic symptoms within the last 3 months:

Impaired ability to split attention
Thought interference
Urging and chasing thoughts
Mind blocking
Disorder of receptive language
Disorder of expressive language
"Subject centrism," self-relationship tendencies
Disturbance of symbol recognition
Captivation through perceptual details

When suspicion continues, this will be accompanied by a deeper anamnesis, using parents and grandparents reports as well.

Case Report: Anna (Age 12)

Anna reported to our clinic with symptoms of distraction, anxiety, and impulsivity. She was the youngest of four siblings, the others aged 19, 23, and 27 years.

What made her diagnosis a lot easier was that the eldest sister aged 27 and the brothers aged 19 and 23 had been previously diagnosed with psychosis some years ago and were still in treatment. The brother aged 19 had been in our clinic with psychosis, aggravated by substance abuse for nearly 2 years. And, of course, the family had been "forewarned": over the past years, they had all developed into experts to recognize the prodromal symptoms.

Anna then quickly got on neuroleptics and we could prevent an acute phase with hallucinations and more.

Case Report: Arthur (Age 17)

Arthur is Anna's brother, 2 years before the case report mentioned above. When he came to our clinic, he showed a lot of active psychotic symptoms with his first episode like hallucinations, derealization, decline in school performance, depression, and anxiety plus impulsivity.

He was still on cannabis and in the early stage of treatment unwilling to part with this abuse, because, as he put it, THC helped him to control his anxiety and gave him subjectively an increase in attention.

Interventions of his elder siblings helped, to get his consent for neuroleptics and to cease using drugs. He attended a psychotherapy group for young adults at our clinic for several years until his follow-up treatment had to be transferred to an adult psychiatrist.

He managed to achieve his high school grade and afterwards started with training to become a nurse. And gratefully, there was no relapse in all this time and he even started with his own family.

But till today, we regard this outcome special, because it does not represent the long way of clinical persuasion it usually takes to get someone discontinuing substance abuse in the early stages of psychosis (first or even second episode).

In our work, intensive counseling is given to inform our patients that their own management of life will have an important impact on their prognosis. If they are willing to take neuroleptics early on and stop substance abuse, they will face a much better outcome.

At this stage, not only to get a better measurement for mental performance, but also to achieve a good compliance, the application of OPATUS CPTa has proven quite successful.

The results are objective measurements of impulsivity, activity, and volatility, and the graphic test result is easily explained and will show either the decline of former skills or the improvement over time, when treated.

Decline of Mental Performance

Mental decline is observed as rapidly deterioration with each episode, even if treatment is given. This explains why early intervention is essential to prevent the amount of mental decline (Fig. 49.2).

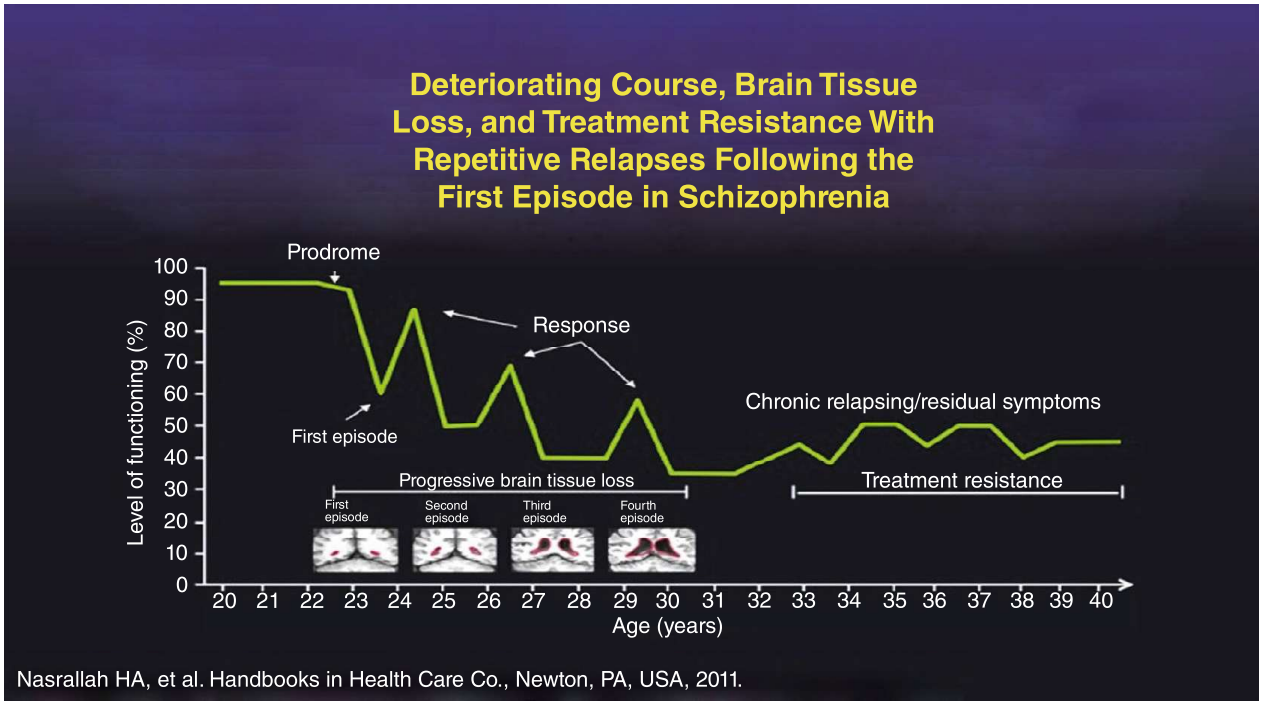

Fig. 49.2 Deteriorating course, brain tissue loss, and treatment resistance with repetitive relapses following the first episode in schizophrenia. (Nasralla et al. [2])

Case Report: George (Age 19)

George was presented by his father with ongoing psychotic derealization, that he tried to dissimulate.

After finishing his exams, he had taken a year abroad in Australia ("work and travel"). In skype and zoom calls, his parents got suspicious of his mental decline and derealization. So, his father decided to fly over and get him home again.

He admitted having tried hallucinogenic mushrooms, LSD, cannabis, ecstasy and legal highs and was not easily persuaded to regard his mental state as declining.

Under the strict control of his parents, it was possible to administer neuroleptics. These medications had an immediate effect in clearing his mind of derealization. It was also possible to improve basic cognitive disorders such as impaired ability to divide attention, thought interference, urgency and pursuit of thoughts, mental blocking, and self-referential tendencies.

However, his attention span was quite affected, as the OPATUS CPTa results shown as follows.

Opatus CPTa in early stage of treatment (3 weeks on aripiprazole 20 mg) (Fig. 49.3). Neurocognitive deficits may be a red flag for psychosis [7]. But there is also the other way round: if you continue to take objective measurements e.g. with a CPTa like the OPATUS test, you may as well show, how the remission is working and how stable this state is.

George recovered fast and wanted to assume personal responsibility again. He then started with study of legal affairs in a town 1.5 h distance to his home town. He was living at a student facility and got involved with drugs again and ceased taking his medication. Four months later, he was presented again with similar symptoms like in his first episode. Starting with aripiprazole again, quickly got him out of the productive phase, but mental decline could be monitored clinically.

However, all our talks about his vulnerability regarding drugs and discontinuation of neuroleptics were not to be held up for long. He was not able to continue with his studies. His father provided him with a training as a commercial clerk at his factory; but in reality, he had to be pushed to rise in the mornings and he was not able to fulfil any difficult task at work.

His situation worsened, when he started using drugs again and discontinued with his medica-

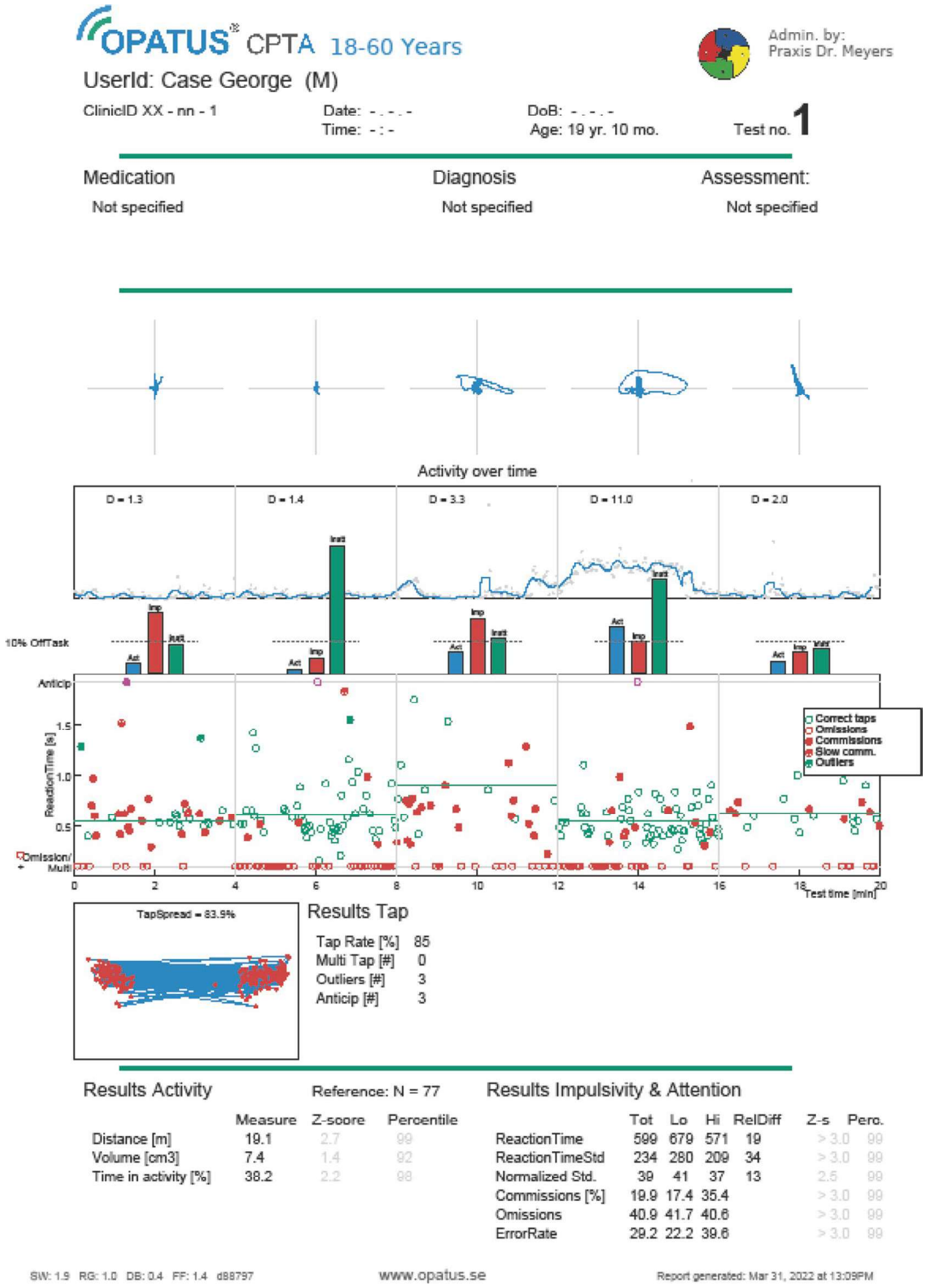

Fig. 49.3 This figure shows George's performance: greens circles are good reactions, red dots represent impulsivity, and red circles stay for omissions. His overall error rate is 29.2%, the blue line in the upper field represents the movement activity, z-scores above 0 are abnormal [4]

tion. He ended with tattoos all over his face, living under guardianship in a therapeutic residential group.

Today, 4 years later, he is willing to maintain drug abstinence and to take his medication. And with intensive support by his family, he is actually studying social work in Spain (his mother has Spanish roots, and the acceptability of his obvious former problems is better than in Germany) and according to his family, he is doing well.

OPATUS CPTa—Objective Measurement for Concentration and Activity [5]

In our clinic, the OPATUS-CPTa test for objective measurement of concentration and activity is an important part of the test packages for all age groups. Its validity has been confirmed in various clinical studies [8–11].

It offers a fast and accurate procedure to support the diagnosis and for progress controls under treatment of ADHD, and it can be used to describe the decline of attention correlating with psychosis as well as shown above.

The OPATUS CPTa is available as an App that runs on Apple devices. It is intended for doctors and scientists in research and therapy. The different versions are adapted for patients from the age of 3 to seniors. Its execution time varies between 8 min for infants, 16 min for children between 6 and 12, and 20 min for older test persons. The complete evaluation including a graphical report is available for professionals.

The test is performed as described below:

The test person holds the iPhone or iPod with both hands. Because the devices can determine their position in space, they pick up the subject's movement pattern. The movement sensor of iPads is less sensitive. They are suitable for presenting the test, but not for conducting it**.** On the screen, either a yellow or blue triangle points up, down, left, or right and becomes visible in rapid succession. The patient has to press on the screen, when two identical targets follow in time. In the adult version that is shown in our example, there are 4 min intervals of low target phases, followed by high target phases and so on.

The upper section shows movement patterns for each of the four 4 min sections. If the device is held calmly in the hand, the picture is quite closed. The more restless the subject is, the more expansive the scribbles become.

The four individual pictures give a first impression of the movement pattern for each 4 min of the test duration; much more meaningful is the graph below. Here, the movement activity is listed as a function of the total time. The blue line shows the real-time deflections, and the red line is somewhat "softer" because it reflects the values averaged over a certain period of time in each case.

The graph with many dots of different colours gives information about the frequency of errors and thus about the concentration ability. This part is divided into 4 min sections.

- Green circles show the correct reactions.
- Red dots show when the respondent made mistakes.
- The green solid lines parallel to the time axis show the average reaction times for each 4 min segment.
- Purple circles stand for random reactions; they are of course not linked to a reaction time and are therefore all displayed at the same height parallel to the time axis.
- Black crosses on the time axis show when the client pressed twice (so-called multitaps); this is also interpreted as a sign of impulsivity.
- Red circles can be seen on the same axis as the black crosses; they indicate the omission errors. This means that there was no response because the client was dreaming or was distracted.

The four small bar charts above the dot diagram give a quick overview of the reaction patterns:

- The blue column reflects the level of restlessness (data from the blue movement lines).

- The red column shows the measure of impulsivity (data from purple circles and black crosses).
- The green column is the measure of inattention (data from the red circles).

Schizophrenia Risk on Heritability up to 80%

In a complete study by Hilker et al. on schizophrenia involving twins to date, researchers estimate that as much as 79% of schizophrenia risk may be explained by genetic factors [12].

Hany et al. say that risk factors include birthing complications, the season of birth, severe maternal malnutrition, maternal influenza in pregnancy, family history, childhood trauma, social isolation, cannabis use, minority ethnicity, and urbanization. Due to its relative complexity and heterogeneity, the etiology and pathophysiological mechanisms are not fully understood. Despite a low prevalence, schizophrenia's global burden of disease is immense. Over half of the patients have significant comorbidities, both psychiatric and medical, making it one of the leading causes of disability worldwide. The diagnosis correlates with a 20% reduction in life expectancy, with up to 40% of deaths attributed to suicide [13].

Schizophrenia is most likely caused by a combination of genetic and environmental factors, most likely interacting in a "two hit" longitudinal trajectory. This means that early factors, such as certain genetic polymorphisms, can cause increased vulnerability of the brain to environmental factors in late adolescence/young adulthood, such as stress or drugs of abuse. This combination might synergize to cause onset of the illness, whereas either of these "hits" by themselves do not have this effect [14].

Schizophrenia risk has often been conceptualized using a model which requires two hits in order to generate the clinical phenotype-the first as an early priming in a genetically predisposed individual and the second a likely environmental insult. Davis et al. sourced the data from PUBMED. They conclude that the development of schizophrenia may be driven by genetic vulnerability interacting with multiple vulnerability factors including lowered prenatal vitamin D exposure, viral infections, smoking intelligence quotient, social cognition cannabis use, social defeat, nutrition, and childhood trauma. They regard it likely that these genetic risks, environmental risks, and vulnerability factors are cumulative and interactive with each other and with critical periods of neurodevelopmental vulnerability. The development of schizophrenia is regarded to be more complex and nuanced than the binary two-hit model originally proposed nearly 30 years ago. Risk appears influenced by a more complex process involving genetic risk interfacing with multiple potentially interacting hits and vulnerability factors occurring at key periods of neurodevelopmental activity, which culminate in the expression of disease state [15].

Psychotic Disorder and Substance Use

It is well known that drug abuse will have an impact on developing the first psychotic episode. The vulnerability depends on heritability and quality as well as dosage of drugs taken.

Not the number of times a drug is used or the dosage, but the personally in most cases unknown risk of heritability will determine, if a psychotic development will start. Sometimes, in our experience, a single use of hallucinogens may be sufficient to start the first episode.

This leads to our next item, the development of substance abuse and connections with clinically relevant needs to treat.

We give an overview, using Canadian and German statistics.

Canadian Hospitalization Trends, 2006–2015

Between 2006 and 2015, the rate of hospitalizations for cannabis-related mental or behavioral disorders in Canada rose from 2.11 to 5.18 per 1,00,000 (Fig. 49.4).

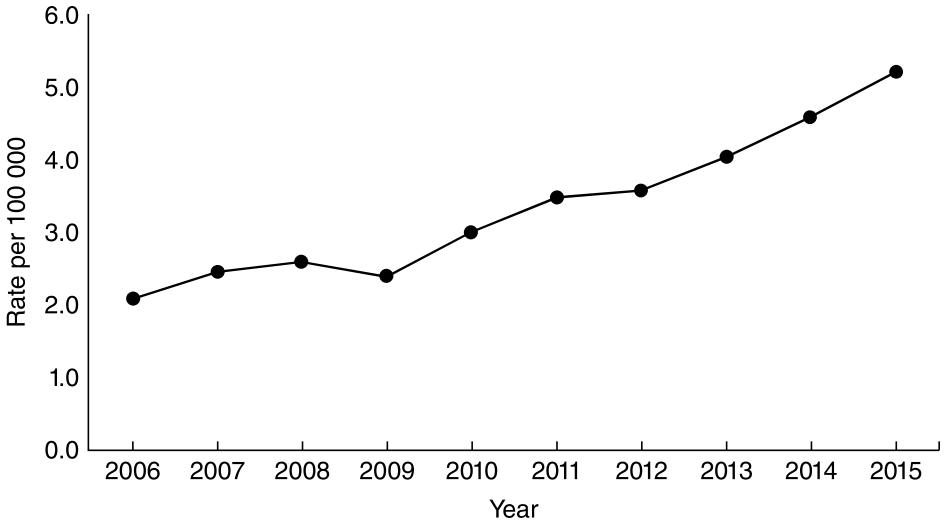

Fig. 49.4 Rate of hospitalizations for cannabis-related mental or behavioral disorder (per 100.000) in Canada (excluding Quebec), 2006–2015. Canadian Institute of Health Information. Hospitalizations were extracted from the Hospital Mental Health Database (HMHDB) for the 10 fiscal years spanning April 2006 to March 2016 (herein referred to as 2006–2015) [16]

Further research is required to investigate the reasons for the increase in hospitalizations for cannabis-related psychotic disorder. The introduction of high-potency cannabinoid products and synthetic cannabinoids into the illicit market is considered as a possible factor in Canada [16].

Incidence of Inpatient Cases with Mental Disorders Due to Use of Cannabinoids in Germany: A Nationwide Evaluation

Quantitative and qualitative changes in cannabinoid use may be associated with changes in the prevalence of cannabinoid-related mental and behavioral disorders and, accordingly, changes the need for medical care.

The study we are presenting here [17] investigated if there are changes in the number of inpatient cases due to cannabinoid-related disorders in Germany. Absolute numbers increased statistically significantly in Germany between 2000 and 2018, and corresponding relative admissions increased considerably (4.8-fold increase when comparing 2000 and 2018). Specifically, absolute numbers with cannabinoid intoxications, dependence syndrome, withdrawal state, psychotic disorders, and residual and late-onset psychotic disorder statistically significantly increased [17].

The Transition from Child and Adolescent Psychiatry to Adult Psychiatry

Working in a clinic for child and adolescent psychiatry, we have to conclude that even if we are able to prevent some outcome of psychosis going chronic, that later on have to be transferred to a clinic for adult psychiatry, if we are able to get an early diagnosis and work with families generating a systemic support net, the willingness and compliance to cease drug abuse, supporting the psychosis to develop into a chronic disorder, is crucial.

In adult psychiatry, an outcome of 50% improvement still is regarded as a positive achievement, like in the early 80 s [18]. And even if specialized residential groups are available, they often deal with patients, that have deteriorated a lot during their history, so the expectations for improvement have to be kept realistically low.

My old professor Hartmut Dziewas described this with the following picture: “Imagine, that your brain is a kind of library, where someone let through

a hefty gush of wind, so that all the books got pushed to the ground, out of their primary order. Your task now, after suffering from a psychotic episode is, to get a new sense into what you want to understand or want to express without direct access to the right book or words". This is what the above-mentioned Benner Program is about [19].

Social cognition was shown as a rate limiting factor for both psychosocial outcome and response to psychosocial intervention in schizophrenia. In a randomized controlled trial, a new cognitive-behavioral group treatment for schizophrenic inpatients (the "Training of Emotional Intelligence", TEI) was tested against the well evaluated "Integrated Psychological Therapy Program" (IPT) of Brenner. Within the framework of Salovey's study, the Training of Emotional Intelligence focussed on three domains of deficits in schizophrenia: emotional perception, emotional understanding, and emotional management. In the randomized controlled trial with 41 DSM-IV schizophrenic inpatients, no differences were found in problem-solving and negative symptoms, both posttreatment and in the 12 months-follow-up. Additionally, there was a better outcome in effect decoding capacity posttreatment and a progress in regulation of negative effects in the follow-up. Emotional role taking behavior and social anxiety returned to the baseline level, perhaps by reasons of no "booster sessions" in the follow-up. Unfortunately, in contrast to our hypotheses, we failed to show treatment-specific effects, which may be due to an underpowered statistical testing. There was only one exception of this: While the Integrated Psychological Therapy Program showed a greater reduction of global psychopathology after treatment, the Training of Emotional Intelligence reduced psychopathology in the follow-up more strongly [20, 21].

Conclusions

- Psychosis prediction is based on clinical criteria in terms of risk symptoms and will be supplemented by a multilevel approach that includes neuropsychological, brain-structural, and brain-functional as well as genetic data and biomarkers.
- Specialized early detection centres should be available for diagnostics to assess the risk of psychosis and should be easily accessible and expanded regionally.
- In psychosis prevention, cognitive behavioral therapy-oriented psychotherapeutic interventions have been established as measures of first choice.
- Second-line drugs are antipsychotics of the second generation, especially if the subjective burden of symptoms is high, in order to prevent severe extrapyramidal side effects and massive weight gain.
- The transition from child and adolescent psychiatry to adult psychiatry should be improved.
- Prevention of drug-related relapses should be improved.
- General knowledge about risks of drugs and their effect on brain function as well as the risk to develop a drug induced psychosis should be improved.
- Systemic therapy might help prevent relapses, because a well-connected family or/and peer group may help to get better results.
- Additional objective measurement tools like OPATUS CPTa may help to indicate the grade of cognitive and concentrative decline as well as improvement under therapy.

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