

## **First Self-perceived Signs and Symptoms in Emerging Psychosis Compared to Depression**

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**Abstract**

**Aim:** To investigate differences between the early symptoms of schizophrenia and depressive disorders.

**Methods:** Sixty-one individuals with an at-risk mental state (ARMS), 17 of whom later made the transition to psychosis (ARMS-T), 37 patients with a first episode of psychosis (FE) and 16 controls with depressive disorders (DC) were interviewed about first self-perceived signs and symptoms.

**Results:** In ARMS and FE, on average, first self-perceived signs or symptoms had occurred about 5-6 years before the interview.

In ARMS, including ARMS-T, "loss of energy" and "difficulties concentrating" were the most frequently recalled first signs. There was much overlap for the four most frequently mentioned symptoms in the three groups.

As compared to ARMS, DC significantly more often recalled "depression" and "social isolation" as the very first signs of disease.

**Conclusions:** Clinicians should consider the development of self-recalled first signs over time carefully when assessing suspected early prodromal stages of schizophrenia and beginning depressive disorder.

*Keywords:* at risk mental state, depressive disorders, early recognition, psychotic disorders, schizophrenia.

## 1. Introduction

The prodrome of schizophrenia is characterised by unspecific symptoms. Subjects concerned often realise something is “wrong”, years before diagnostic criteria for a psychotic disorder are met. The duration of the prodrome is variable, around 2 - 3.5 years (1).

Self-perceived deficits concerning perception, cognition and stress reactivity have been reported in the prodrome, negative symptoms and depression are also often present (2-6).

Depressive symptoms are often so severe that depression is reported as a comorbid diagnosis (7-9). This indicates an overlap between symptoms of depressive disorders and beginning psychosis, which makes differential diagnosis, especially in early phases, difficult.

There are few studies comparing the earliest phase of the prodrome in schizophrenia with depressive disorders. Using a retrospective interview in patients with a first episode of psychosis (FE) and patients with depression, Häfner et al. compared the presenting initial symptoms in psychosis and major depression. A high degree of overlap in the ten most frequent presenting symptoms was found (10).

The aim of this study is to clarify which early signs may be useful for differentiating an early prodromal stage of psychosis from depression. At-risk mental state (ARMS) individuals, with a focus on the subgroup with later transition to psychosis (ARMS-T), that is with a confirmed prodrome, were compared with patients with depressive disorders (DC) and FE.

## 2. Methods

### 2.1. Subjects

From 3/1/2000 – 29/2/2004 we screened 234 individuals referred to our specialised outpatient clinic for the early recognition of psychosis as they were suspected to be at risk for or in an early stage of psychosis. The screening was conducted within the **FePsy** (**F**rüherkennung von **P**sychosen – early detection of psychosis) study (11), using the Basel Screening Instrument for Psychosis (BSIP) (12), which allows to identify ARMS and FE individuals according to the criteria of Yung et al. (13).

In 38 cases no risk for psychosis was found. One hundred and six were identified as ARMS, 42 refused participation, 64 agreed to participate in the main study, 61 of these could be interviewed with the Basel Interview for Psychosis (see below). Of these 61 ARMS, n=50 could be followed up until 3/1/2007 and 17 made the transition to psychosis.

Thirty-seven of the screened FE from our specialised outpatient clinic were also interviewed, these patients were either still in or recovering from a first psychotic episode.

The other control group consisted of 16 patients with depressive disorders (DC-15: major depression, 1: adjustment disorder/depressive reaction DSM-IV), these were outpatients from our general outpatient clinic remitting from a depressive episode, they had not been referred with suspected psychosis.

All study subjects gave written informed consent and the study was approved by the Ethics Committee of Basel, Switzerland.

Exclusion criteria were age below 18 years, insufficient knowledge of German, IQ <70, psychosis clearly due to organic reasons or substance abuse, or psychotic

symptoms within a clearly diagnosed depressive disorder oder borderline personality disorder (11, 14).

## 2.2. Interview

The Basel Interview for Psychosis is a structured interview covering all aspects of the patient's history which contribute to assessing the risk for psychosis. It was specifically developed for the Basel **FePsy** study (11). All important risk factors and early signs of psychosis, such as prodromal symptoms, overall loss in general functioning, beginning "subthreshold" psychotic symptoms, genetic and other risk factors, drug abuse early indicators such as childhood developmental disturbances, etc. were included. Also already established instruments such as the IRAOS (Instrument for the Retrospective Assessment of Schizophrenia (15)), the SIPS/SOPS (Structured Interview for Prodromal Syndromes/Scale of Prodromal Syndromes (16)), and the BSABS (Bonn Scale for the Assessment of Basic Symptoms (17)) were taken into account.

One section explores when any change in well-being was first noticed and what the very first signs and symptoms were; up to three can be mentioned in response to an open question, and, for this analysis, were then categorised post-hoc.

All interviews were conducted by experienced psychiatrists, after a series of training sessions.

For diagnostic purposes the SCID (Structured Clinical Interview for DSM Disorders) was performed at baseline (18-20).

## 2.3. Statistical Analyses

Statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS 14.0). Sociodemographic differences between groups were examined using the chi-square test, and ANOVA for age. For every symptom, the chi-square test was used for overall group comparison (ARMS/FE/DC) and post hoc for items where a significant difference was found. In an additional analysis, differences between ARMS-T and DC were evaluated with the chi-square test.

### **3. Results**

#### *3.1. Sample Characteristics*

The mean age of the 61 ARMS (36 male, 25 female) was 26.6 years (SD 8.5 years), of the 37 FE (25 male, 12 female) 31.1 years (SD 8.5 years) and of the 16 DC (8 male, 8 female) 27.3 years (SD 5.6 years). The significant difference in mean age between groups ( $F=3.7$ ,  $df=2$ ,  $p=0.026$ ) was only due to the higher age of FE compared to ARMS. There were no significant differences between groups for gender distribution (chi square=1.56,  $df=2$ ,  $p=0.457$ ) or educational level (chi square=6.82,  $df=6$ ,  $p=0.338$ ).

#### *3.2. Duration of Symptoms*

On average, first self-perceived signs or symptoms had occurred about 5-6 years before the interview which was conducted at baseline, at the time of the first contact with our specialised clinic. Mean duration from the very first signs up to the interview was 60.6 (SD 63.9) months for ARMS and 70.5 (SD 86.5) months for FE. The median was 48 months for ARMS and 36 months for FE.

#### *3.3. First Signs and Symptoms*

Table 1 shows the most frequently mentioned first signs and symptoms of ARMS, FE, and DC ranked by frequencies within each group.

"Loss of energy" and "difficulties concentrating" were the most frequently mentioned first signs in ARMS, "depression" and "irritability" the most frequent in FE, and "depression" and "social isolation" the most frequent in DC.

Table 1

### 3.4. SCID-results

A SCID-interview was done at baseline in 68.8% of the ARMS. In 34.1% of these a mood disorder was found, and in 6.8% anxiety disorder.

### 3.5. Group Comparison

There was much overlap in the first self-percieved signs of illness – “depression”, “irritability”, and “social isolation” being mentioned often. In the overall group comparison (ARMS/FE/DC), only two significant differences were found: "depression" and "social isolation" (see Fig 1). In the post hoc analysis for the item "depression", significant differences were found between ARMS and DC, for "social isolation" also between ARMS and DC, as well as between FE and DC.

Figure 1

### 3.6. Subgroup of ARMS-T

We separately analysed those 17 ARMS who went on to develop psychosis (ARMS-T). The two most frequently mentioned first signs also were "loss of energy" (17.6%) and "difficulties concentrating" (17.6%). Also, the overall pattern of first signs

and symptoms was similar to the total ARMS sample: beginning difficulties at school, unusual fears and suspiciousness were frequently reported.

The comparison of 17 ARMS-T with DC again showed significant differences for "depression" ( $p=0.031$ ) and "social isolation" ( $p=0.021$ ).

#### 4. Discussion

There was much overlap in the very first signs over all groups, "depression" (meaning "feeling sad", and not having a clinical diagnosis of depression in this context), "irritability", and "social isolation" are all mentioned amongst the first four signs in each group. The percentage of ARMS individuals with a SCID-diagnosis of mood disorder was, as to be expected, relatively high.

Häfner et al. 1999 reported on the first 10 most frequent earliest signs of schizophrenia, depressive mood emerged before the first positive symptom in about 42% of the patients, and was amongst the first 10 most frequent reported very first signs.

ARMS individuals mainly described "loss of energy" and "difficulties concentrating" as very first signs. Restricting the analyses to those who later made the transition to psychosis, the results remained stable. To our knowledge, this is the first study to investigate early signs and symptoms in ARMS individuals interviewed before the onset of psychosis, that is in a "true" prodromal stage, and perceived themselves when they first noticed a change in wellbeing, in comparison to DC. Although 14.8% of ARMS individuals also mentioned "depression" as one of the first three symptoms, DC significantly more often reported "depression" and "social isolation" as very first signs.

Interestingly, difficulties concentrating and loss of energy were not mentioned frequently by FE as very first signs, but they recalled feeling depressed, irritable,



worried, and socially isolated. Similar results were found in another study on FE patients retrospectively interviewed about the first signs of mental disease (21). The difficulties concentrating and loss of energy mentioned by the ARMS seem to be less important to the FE patients in retrospect and at this later stage. An explanation may be that subtle first signs pale after the experience of acute psychosis, and recall bias is more of a problem.

Self-reported difficulties concentrating may be an indicator of neurocognitive deficits, which are known to be present in ARMS (14, 22, 23) and have also been reported in individuals with a genetic risk for schizophrenia (24). Specific cognitive deficits, combined with certain early symptoms in an integrated model, have been shown to improve prediction of transition to psychosis (14).

The present study furthermore confirms the long delay between first symptoms and help-seeking which has also been found in other studies (for review Riecher-Rössler et al. (1); Barnes et al. (25); O'Callaghan et al. (26)).

As the prodrome can be of long duration, when exploring very first signs of disease, there can be a problem of recall bias. This should be mentioned as a limiting factor. Another limiting factor is the moderate sample size, especially the controls with depression.

## **Conclusion**

Clinicians should consider the development of self recalled first signs over time carefully when assessing a suspected early stage of schizophrenia and depressive disorders in young adults.

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### **Conflict of Interest**

All authors declare not having any conflict of interest that might be interpreted as influencing the content of the manuscript.

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### **Ethical Considerations**

The protocol for the research project has been approved by the Ethics Committee of Basel. It conforms to the provisions of the Declaration of Helsinki. All patients gave informed consent.

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**Table 1.** First self-perceived signs<sup>1</sup> of illness in ARMS, FE and DC – ranking order

ARMS (n=61)			FE (n=37)			DC (n=16)		
1.	loss of energy	18.0%	1.	depression	24.3%	1.	depression	43.8%
2.	difficulties concentrating	16.4%	2.	irritability	13.5%	2.	social isolation	37.5%
3.	depression	14.8%	3.	anxiety	10.8%	3.	nervousness	18.8%
4.	social isolation	14.8%	4.	social isolation	10.8%	4.	irritability	12.5%
5.	sleep disturbance	11.5%	5.	suspiciousness	8.1%	5.	sleep disturbance	12.5%
6.	over-sensitivity	11.5%	6.	over-sensitivity	8.1%	6.	abnormal appetite	12.5%
7.	irritability	9.8%	7.	nervousness	8.1%			
8.	unusual fears	8.2%	8.	difficulties at work/school	8.1%			
			9.	thoughts that others intend harm	8.1%			

<sup>1</sup>Only signs occurring in more than 7% of the individuals are mentioned.

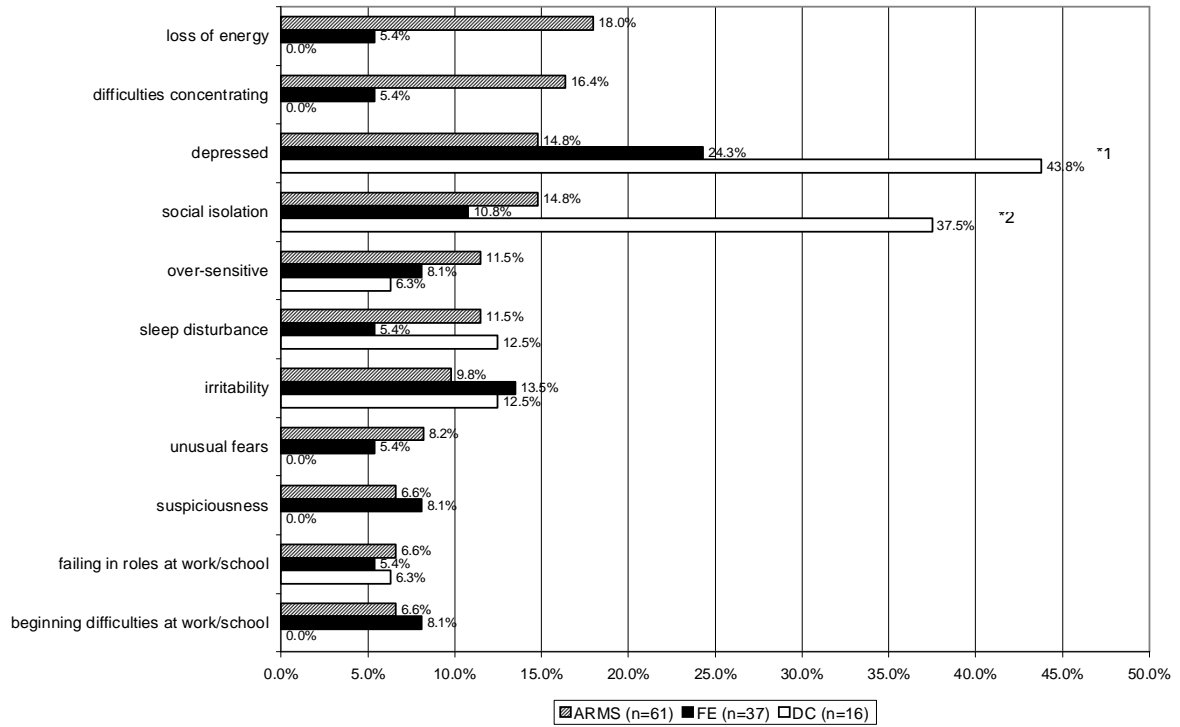
ARMS: At Risk Mental State

FE: First Episode of Psychosis

DC: Controls with Depressive Disorder

**Figure 1**

The most frequent first signs in ARMS compared to the frequencies of the respective signs in FE and DC.



Significant differences (chi-square test):

<sup>\*1</sup>p=0.041

<sup>\*2</sup>p=0.048

ARMS: At Risk Mental State

FE: First Episode of Psychosis

DC: Controls with Depressive Disorder