Clinical depression predicts persistence of paranoia in clinical high-risk patients to psychosis

Pathways to both occurrence and persistence of paranoia and persecutory ideation have always been a topic of great interest in psychiatry research. Emotions, anxiety and depression in particular, have been in focus of this discussion. Wilhelm Griesinger regarded paranoia as secondary to and always preceded by an affective disorder, while Emil Kraepelin regarded paranoia primarily as an illness of the intellect (*Verstand*) and affective (depressive) mood as a reaction to the paranoid experiences.

Patients with depressive disorders often report paranoid symptoms, while on the other hand, depressive symptoms are prevalent in patients with delusional disorders. Additionally, depressiveness and anxiety have been associated with persecutory ideation. The link between paranoia and emotions in paranoid-prone persons does not appear to be unidirectional but rather to form a vicious circle that should be broken by targeted interventions - preferably before severity of paranoia has reached a delusional degree.

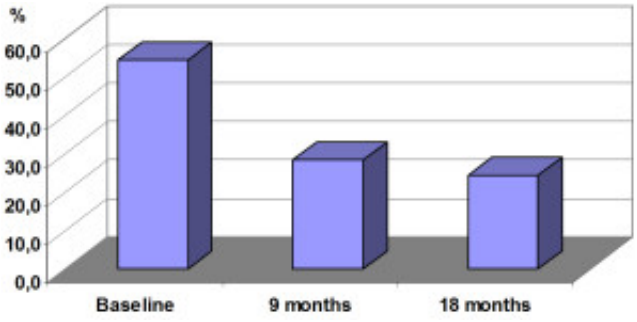

Fig. 1. Paranoid symptoms in clinical high risk patients at baseline and follow-ups

Depressive and anxiety disorders are extremely prevalent co-morbidities in clinical high-risk of psychosis (CHR) patients who also frequently report attenuated, not yet delusional paranoia. Thus, based on data of the European Prediction of Psychosis Study (EPOS), we examined whether 1) there is an association between affective and clinical disorders and affective symptoms, and paranoid symptoms, and whether 2) depression and anxiety predict persistence of paranoid symptoms during follow-up.

EPOS is a naturalistic, prospective follow-up study of 245 CHR patients recruited in six centres: Cologne and Berlin, Germany; Turku, Finland; Amsterdam, the Netherlands; and Birmingham and Manchester, UK. Assessments were carried out at baseline, and at 9-month and 18-month follow-ups. Baseline examination comprised assessment of clinical disorders, paranoid, depressive and anxiety symptoms, childhood adverse experiences and trait suspiciousness. Paranoid symptoms

were assessed also at the follow-up points.

At baseline, 54.3% of CHR patients reported at least moderate paranoid symptoms. At 9- and 18-month follow-ups, the corresponding figures were 28.3% and 24.4% indicating improvement in clinical state. However, at the follow-ups, still a quarter of CHR patients reported paranoid symptoms and had thus to be considered at high clinical risk of developing a psychotic disorder with persecutory delusions (Fig. 1).

In multivariate analyses, depressive and obsessive-compulsive disorders, sexual abuse, anxiety symptoms and trait-suspiciousness predicted occurrence and persistence of paranoid symptoms during the follow-up period when the effects of baseline paranoid symptoms and trait suspiciousness had been controlled. Thus, the major finding was that clinical depression played a central role in persistence and possibly also in occurrence of paranoia. Because of high co-occurrence with depressive disorders, the role of obsessive-compulsive disorder in predicting paranoia possibly lied as an indicator of greater clinical severity of affective disorders.

The associations between affective diagnoses and paranoia may arise from a common neurobiological vulnerability. Generally, patients with depression have lower, while patients with psychosis have elevated and dysregulated, dopaminergic activity of the central nervous system (CNS). E.g. in drug-naive schizophrenia patients, depressiveness was associated with low, but suspiciousness and persecutory ideas with higher CNS dopamine function indicating that CNS dopaminergic tone is one of the factors modulating the relationship between concurrent depressive and paranoid symptoms.

The dopaminergic system is sensitive to various stressors, and repetitive challenge by stressors, such as childhood abuse, sexual abuse in particular, may sensitise the developing dopaminergic system to an increased dopaminergic response to different challenges. In stressful situations, the dysregulated dopaminergic system might thus first manifest as depression (decreased transmission), while in persons with additional internal (e.g. genetic or personality) and/or external vulnerability factors, the dysregulated dopaminergic system may lose its coherence, and increased transmission leads to paranoid interpretations.

In line with previous studies, also anxiousness associated strongly with follow-up paranoid symptoms confirming that paranoid patients commonly suffer from anxiety symptoms, which together with paranoid experiences might greatly disturb their interpersonal relations.

Interventions focused on reducing affective disorders and anxiety may help to reduce severity of paranoid symptoms in CHR patients and possibly prevent their proceeding to delusional level. Antidepressants and cognitive-behavioural therapy have proved to be effective in the treatment of depression, obsessive-compulsive disorder and anxiety, and cognitive-behavioural therapy has recently been recommended as first-choice treatment of CHR states. These interventions may also reduce the paranoid thinking and interpersonal sensitivity often found in CHR patients.

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