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Experience Sampling Assessment of Mental Health in Patients with Psychosis and First-Degree Relatives

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1. Summary

1.1 Deutsche Zusammenfassung

Hintergrund Mobile Health ist ein Bereich von rasch wachsendem Interesse in der Diagnostik und Intervention bei PatientInnen mit Psychosen sowie in der Forschung zu psychischen Störungen im Allgemeinen. Hierbei handelt es sich um eine Untergruppe von elektronischen Gesundheitssystemen und -technologien, die auf mobilen Geräten angeboten und durchgeführt werden.[1]

Eine dieser Methoden, die Experience Sampling Method (ESM) eignet sich besonders gut für die Erhebung von Gesundheitsdaten bei PatientInnen mit Psychose, da die Daten engmaschig erhoben und somit zeitliche Schwankungen präziser erkannt werden können.[2] Bisherige Forschungen zeigen, dass die ESM gut geeignet ist, um PatientInnen mit Psychose und gesunde Personen zu unterscheiden.[3] Darüber hinaus lassen sich mit der ESM auch subklinische Symptome erfassen.[4-6], was insbesondere vor dem Hintergrund der hohen Heritabilität von psychotischen Erkrankungen relevant ist.[7] Frühere Studien zeigen, dass Verwandte von Individuen mit Psychose häufiger subklinische Symptome aufweisen als gesunde Kontrollpersonen.[8]

Ziele In diesem Projekt wird untersucht, ob die Studiengruppen [1] Personen mit diagnostizierter Psychose, [2] erstgradige Verwandte von Menschen mit diagnostizierter Psychose und [3] gesunde Kontrollpersonen mit Hilfe einer Clusteranalyse auf der Grundlage von ESM-Daten rekonstruiert werden können.

Methodik Es wurden die Daten von initial 82 Personen (Durchschnittsalter: 38,0 $\pm$ 10,3 Jahre) untersucht. Nach Ausschluss von sieben Personen verblieben 75 Personen für die Analyse. Die ProbandInnen wurden anhand von ESM-Fragebögen während eines siebentägigen Studienzeitraums und durch klinische Assessments beurteilt. Zur Analyse der Daten führten wir eine multiple Faktorenanalyse (MFA) durch, um die Variablen in Komponenten zu komprimieren. Danach erfolgten eine Studiengruppenanalyse und eine hierarchische Clusteranalyse.

Ergebnisse Die MFA ergab drei Hauptkomponenten („Allgemeine Psychopathologie“, „Soziale Beziehungen“, „Psychotische Symptome“). Die Cluster stimmten in keiner der Komponenten mit den Studiengruppen überein.

Schlussfolgerung In unserem Projekt war eine Rekonstruktion der Studiengruppen nicht möglich. Dennoch deuten die Ergebnisse darauf hin, dass ESM Personen mit subklinischen Symptomen identifizieren kann. Daher sind weitere Forschungsarbeiten notwendig, um das Potenzial der ESM als Evaluierungsinstrument für den klinischen Einsatz zu untersuchen.

1.2 Abstract

Background Mobile health is an area of rapidly growing interest in diagnostics and intervention for patients with psychosis and in research on mental disorders in general. It is a subgroup of electronic health systems and technologies that are offered and delivered through mobile devices.[1]

One of these methods, the Experience Sampling Method (ESM), is particularly suitable for collecting health data from individuals with psychotic disorders, as the data can be collected in a close-meshed manner, making it easier to detect fluctuations.[2] Research to date shows that ESM is well suited to differentiate between healthy individuals and those with psychotic disorders.[3] In addition, ESM also allows the assessment of subclinical symptoms[4-6], which is particularly relevant against the background of the high heritability of psychosis.[7] Previous studies demonstrate that first-degree relatives of individuals with psychotic disorders show subclinical symptoms more frequently than healthy controls.[8]

Objective The aim of this study is to investigate whether the study groups of [1] individuals with diagnosed psychotic disorders, [2] first-degree relatives of individuals with diagnosed psychotic disorders, and [3] healthy controls can be reconstructed using cluster analysis based on ESM data.

Methods Data from 82 subjects (mean age: 38.0 $\pm$ 10.3 years) were initially examined, after exclusion, data from 75 subjects remained. Subjects were assessed by ESM questionnaires over a seven-day study period and by clinical tests. Data analysis included multiple factor analysis (MFA) to compress variables into principal components, study group analysis and hierarchical cluster analysis.

Results The MFA resulted in three principal components (“General Psychopathology”, “Social Relations”, “Psychotic Symptoms”). The clusters did not align with the study groups in any of the components.

Conclusion In our study it was not possible to reconstruct the study groups. Nevertheless, the results indicate that ESM can identify individuals with subclinical symptoms, which was reflected in poorer performance on clinical tests. Further research is therefore required to explore the potential of ESM as an evaluation instrument in clinical use.

2. Introduction

2.1 Psychosis

Psychosis is a clinical syndrome that can be found in a number of different disorders. To date, there is no uniform definition of the term psychosis.[9,10] The syndrome is characterised by a variety of symptoms, including temporary or permanent mental states in which the affected person is detached from reality. Psychotic disorders represent a heterogeneous group of disorders, of which schizophrenia is the most common subtype.[11]

In the field of psychiatry, two principal classification systems for mental illnesses are in use. The International Classification of Diseases (ICD-10), published by the World Health Organisation (WHO), is primarily utilised in Europe. This encompasses all psychotic disorders, which are classified under codes F20-F29. These include schizophrenia, schizotypal, delusional, and schizoaffective disorders.[11] The WHO has developed a definition of schizophrenia that distinguishes between characteristic and non-characteristic symptoms. Characteristic symptoms are those that are typical and defining of schizophrenia. They include thought insertion and withdrawal, delusional perceptions, hallucinatory voices, and thought broadcasting. Such symptoms are also referred to as positive symptoms.[12] Non-characteristic symptoms are not exclusive to schizophrenia but can serve as an indicator of the severity of the illness. These include persistent hallucinations of any kind, incoherent or irrelevant speech, catatonic behaviour and negative symptoms.[11,13] The latter are defined by a decrease in or loss of normal functioning, such as diminished emotional expression or reduced levels of drive or motivation.[14,15] These symptoms usually appear as temporally persistent traits of the disorder. In order to meet the criteria for a diagnosis of schizophrenia according to the ICD-10, it is necessary to demonstrate the presence of at least one of the characteristic symptoms or two of the non-characteristic symptoms. The symptoms must have been present for a minimum of one month, and the disorder must not have been caused by substance use or an organic brain disease.[16]

Another classification system, the Diagnostic and Statistical Manual of Mental Disorders (DSM-V), published by the American Psychiatric Association (APA), is primarily utilised in the United States. The diagnostic criteria set forth in the DSM-V are largely identical to those outlined in the ICD-10. In addition to a period of at least one month during which symptoms have to be persistent, there must be further limitations in the individual's social or occupational functioning for at least six months.[17]

Psychosis is often associated with other comorbidities. The most common of these is depression, which occurs as a comorbidity in 28.6% of cases of schizophrenia.[18] A correlation in the courses of the illnesses has been observed, with depressive symptoms increasing during acute psychotic episodes and decreasing during the remission of the primary illness.[19] Hartley

et al. (2013) found that the depressive symptoms also influence the severity, content and prognosis of the psychotic symptoms. Depression is therefore proposed as a significant target for therapeutic intervention.[20] Other comorbidities associated with increased risk in psychosis include type 2 diabetes mellitus and metabolic syndrome, due to medication use and an unhealthy lifestyle in terms of diet, exercise and substance use.[21,22] However, this may be facilitated by the fact that individuals with mental disorders generally undergo more screenings and examinations, which increases the detection rate of somatic illnesses.[23] Cannabis use is also particularly prevalent in cases of psychosis, increasing the risk of developing schizophrenia and exacerbating symptoms.[24,25] Additionally, the suicide rate is significantly increased in psychotic disorders due to other risk factors such as depression, hopelessness and insufficient self-control, which also occur in the context of psychosis.[26] The estimated risk of committing suicide in individuals with psychotic disorders ranges from 4 to 13 %.[27,28] Unhealthy lifestyles, substance abuse and elevated suicide rates all contribute to a reduction in life expectancy, with an average loss of 14.5 to 20 years of potential life in individuals with psychotic disorders.[29,30]

2.1.1. Epidemiology

Psychosis is a common disorder with a 12-month prevalence of 4.03 per 1000 persons. The lifetime prevalence amounts to 7.49 per 1000 persons.[31] Considering all psychotic disorders that first occurred in adulthood and were not of an organic cause, the global pooled incidence of these was found to be as high as 26.6 per 100,000 person-years.[32] The age of onset for schizophrenia is particularly high between the ages of 25 and 35 for women and between the ages of 10 and 25 for men.[33] This may be attributed to the fact that young adulthood is an important period of neurodevelopment and an essential phase for personality development.[34] Another peak occurs in postmenopausal women. Here, the alteration im hormonal equilibrium is postulated as a potential etiological factor.[35]

2.1.2. Therapy

The prevailing approach to treating psychotic disorders is a combination of pharmacological and psychotherapeutic interventions. Atypical neuroleptics, such as risperidone or clozapine, are the initial pharmacological intervention.[36] Atypical neuroleptics are preferred to older typical neuroleptics due to their broader spectrum of action and fewer side effects. Atypical neuroleptics are drugs that act mainly on the dopamine system, but also affect serotonin and histamine receptors. It has been demonstrated that these drugs are also effective in the treatment of mood disorders.[37]

In contemporary psychiatry, psychological care in the form of psychoeducation and psychotherapy plays an important role alongside drug treatment.[38] Cognitive Behavioural Therapy (CBT) has been shown to be an effective form of treatment, particularly in reducing the positive symptoms of psychotic illness and leading to a faster recovery into life.[39-41]

2.1.3. Genetic and Environmental Risk Factors

Research has shown that both genetic and environmental factors exert a substantial influence on the pathogenesis of psychosis.[42] A family history of psychotic disorders is regarded as the most significant risk factor.[43] Twin studies have revealed that common gene variants play a pivotal role in the aetiology of psychosis.[44] Research has focused on the gene *Disrupted in Schizophrenia 1* (DISC 1), in which alterations often occur in individuals with psychotic disorders.[45] Furthermore, the importance of genetic predisposition is underscored by the estimated heritability, which defines the amount of variation in a trait that can be attributed to genetic effects[46] and has been found to be as high as 79% in schizophrenia.[7]

However, there are also environmental risk factors that contribute to the manifestation of psychosis.[47] These include childhood abuse and early-life head injury. It has been proposed that all traumatic experiences encountered during childhood may also be involved in the subsequent development of psychosis.[48] Additionally, early psychotic experiences, particularly during adolescence or early adulthood have been found to be a strong risk marker.[5,49] Besides, minority group experience and migration to another country also contribute to an increased risk.[50] Other factors that have been identified as potential contributors to the development of psychosis include residing in an urban setting, particularly in large cities, and advanced paternal age and obstetric complications..[51]

Specifically in adulthood, drug use, especially cannabis, is considered to be the most important environmental risk factor.[24] There is a correlation between the extent of cannabis exposure and the likelihood of developing a psychotic disorder.[52,53] In addition, personality factors and disorders such as borderline personality disorder or schizotypy, have been linked to an increased risk of developing psychosis.[54,55]

2.2 Mobile Health

Mobile Health (mHealth) is an area of rapidly growing interest in diagnostics and interventions for patients with psychosis, as well as in the research of mental disorders in general.[1] The term refers to a subset of Electronic Health (e-Health), which includes systems and technologies that are delivered and performed on electronic devices. mHealth specifically employs the use of smartphones or tablets to record the participants' health-related information, experiences and symptoms in real-time.[56] The fundamental objective of mHealth is to enhance medical care

in all areas, including prevention, diagnostics, therapy, follow-up care and monitoring of patients through the utilisation of mobile technologies.[57] Additionally, the tools are designed to contribute to a responsible approach to one's own health and an increase in patients' health literacy by providing health information.[58]

A challenge for mHealth applications is the handling of sensitive data, which needs to be professionally managed by data security experts.[59] Depending on the approach, patient data is usually collected in the form of questionnaires with scales or as written self-reports. In general, mHealth apps are not regarded as a substitute for psychiatric treatment, but as a supportive adjunct. They are considered to be particularly effacious in the clinical assessment of psychosis, improving illness insight and symptom management[60-62] which have been shown to be frequently impaired in individuals suffering from psychosis.[63,64]

2.2.1. Mobile Health in Psychosis

In the diagnosis and treatment of psychosis, mHealth offers a number of advantages. On the one hand, patients engage in passive self-management, which has frequently been shown to be constrained in individuals with psychotic disorders.[65] This is addressed by involving them in the diagnostic process through mobile formats such as mHealth methods.[66] On the other hand, mHealth provides enhanced flexibility in conducting diagnostics and the potential for personalised treatment.[67] In comparison to conventional diagnostics, mHealth could offer additional opportunities for cost savings[68], for instance by necessitating fewer personnel and resources for diagnostics.[69] There is a notable interest in cost-saving technologies in the context of psychotic disorders, which are perceived as being particularly costly due to their heterogeneity, the high levels of suffering associated with them, and the substantial costs involved in diagnosing, treating and caring for individuals with these disorders.[70] Studies have demonstrated that individuals with mental disorders have comparable smartphone usage rates to the general population[71], which does not impede the applicability of mHealth in this area of research.

However, there are challenges for mHealth in psychosis as well. Critics are apprehensive of the fact that this form of intervention may not be accepted by participants, given that it relies on sensitive data, particularly in the field of mental disorders, where patients' mental health is often stigmatised.[72] On top of that, some individuals with mental disorders have been shown to be fundamentally sceptical about the introduction of new technologies.[73] Additionally, not everyone has access to a smartphone or requisite skills to use the technology. Moreover, research centres need to be equipped with the necessary resources to process data appropriately.[56] Another challenge that must be considered in mHealth and particularly in self-administered questionnaires is the potential for individuals to misestimate their own state of mind, perception, and abilities.[74] This is due to a lack of insight into the illness, which has been

shown to be pronounced in cases of psychosis, as indicated by discrepancies between the results of self-administered questionnaires and those of objectively evaluable diagnostic tests.[75,76] Various manifestations of these discrepancies can be identified in the literature. For example, patients with psychotic disorders have been observed to accurately self-assess positive psychotic, negative psychotic, and depressive symptoms, yet inaccurately assess persecutory delusions.[77] Other studies have identified that the discrepancies primarily pertain to the evaluation of their abilities, including cognitive performance and functional capacity.[74] Overall, psychosis patients appear to overestimate rather than accurately assess or underestimate their own level of functioning and ability.[78]

2.2.2. Experience Sampling Method

One of the mHealth technologies that is gaining increasing interest and importance is the ESM.[79] It is a self-conducted structured diary technique that employs the use of a mobile device to assist in the accurate recording of a person's subjective experiences in their daily life.[80,81] One advantage of the ESM is that it allows for the immediate acquisition of participants' feelings and perceptions eliminating the potential for memory problems and retrospective recall bias that can arise when there is a time lag between the occurrence of the symptoms and their assessment.[82] Additionally, the absence of observation by a supervisor while completing the questionnaire on the mobile phone reduces the likelihood of performance pressure and surveillance influencing the answers provided. Moreover, the ESM captures typical performance rather than optimal performance, as participants are not in a traditional examination situation. Typical performance represents the individual's true ability, which is not distorted by the performance in the situation of a one-time query situation. This generates a more realistic overview of the participant's emotions and symptoms.[83] As a further advantage, the repeated questioning provides a more comprehensive and stable overall picture of the feelings and perceptions assessed in the survey[2], as it allows personalised symptom trajectories to be recorded. This permits the tracking of the distinctive attributes of each participant's data, including symptom correlations, cyclical behaviour patterns, and the capacity to recuperate from setbacks over a defined period.[68] Besides, ESM minimises recall bias, as the precision of immediate assessments is superior to that of alternative methods.[84] Overall, ESM thus increases the ecological validity of studies in comparison to one-time-queries.[85,86]

2.2.3. Psychosis Research using ESM

In the field of mental illness, ESM can be used to discern disparate levels of emotions and symptoms among collectives of individuals. ESM is of particular relevance in the field of

psychosis, as the aggregation of data allows a more nuanced understanding of the behaviour and emotions of study subjects in this heterogeneous disorder.[87]

For instance, Oorschot et al. (2013) found that patients diagnosed with schizophrenia reported more negative and fewer positive emotions in their daily lives than healthy controls.[3] Such findings would not have been possible until the emergence of ESM. Prior to this, emotions had only been recorded in artificially created settings within clinics. The results of the two groups hardly differed from each other. It was only when the subjects were assessed in their everyday lives that the aforementioned differences became evident.[88,89] One way to distinguish between psychosis patients and healthy individuals in ESM studies is that the former show lower levels of positive affect. In addition, patients reported a greater number of unpleasant events and a greater amount of time spent alone than healthy controls, which resulted in an increase in negative affect and higher levels of negative symptoms.[3] Besides, ESM studies have indicated that individuals with psychotic disorders are both significantly more sensitive to stress and more affected by avolition.[90] They also tend to report both increased feelings of generalised numbness and greater rejection of society than healthy controls.[91] The majority of symptoms observed in patients with psychiatric disorders, such as paranoia and hallucinations, demonstrate considerable temporal dynamics and fluctuation in the context of everyday life.[92,93] Due to its longitudinal nature, the ESM has been shown to be an appropriate tool for accurately capturing these symptoms.[90] Clustering analyses are frequently performed on ESM data, as they are able to identify subgroups within a study population.[94-96]

2.2.4. Relatives Research using ESM

The ESM is not only a valid tool for discriminating between patients and healthy individuals, it has also been proven to be effective in detecting subclinical psychotic experiences in the general population and in individuals at clinical high risk (CHR).[4,6,97] Clinical high risk describes the state of a pre-psychotic phase. In this state, attenuated psychotic symptoms are experienced, which, however, do not necessarily progress to psychosis.[98] Despite being subthreshold for the diagnosis of first-episode psychosis, CHR have been found to display symptoms such as suicidal thoughts and neurobiological dysfunction. Furthermore, structural brain changes were detected.[99] In current research, schizotypal traits such as difficulties in forming social relationships, eccentric behaviour or magical thinking are increasingly being observed in relation to the onset of schizophrenia in later life.[100,101]

As mentioned above, hereditary factors contribute to the development of psychotic disorders. This implies that first-degree relatives of individuals with psychotic disorders are at an elevated risk of developing psychosis themselves. In general, relatives have been demonstrated to exhibit greater mental limitations and experience more symptoms than healthy controls. However, at the same time, they do not exceed the threshold for a diagnosis of psychosis. For

example, they have shown premorbid cognitive deficits and reduced general intelligence.[102,103] Fusar-Poli et al. (2012) found that relatives of individuals with psychotic disorders do not only have reduced neurocognitive function, but also impairments in social cognition, defined as the ability to perceive, process and apply information about others.[104] A further finding was that relatives exhibited stronger obsessive-compulsive behaviour than healthy controls, but less than individuals with a diagnosis of a psychotic disorder.[105]

To date, there has been a paucity of research focusing specifically on the clinical characteristics of first-degree relatives of individuals with psychotic disorders in experience sampling studies. Thus far, Myin-Germeys et al. (2005) found in an ESM study that relatives showed subclinical symptoms that fluctuate on a daily basis and intensify during periods of activity-related stress.[8] Using experience sampling, Daemen et al. (2022) showed that relatives had heightened variability in self-esteem. The study demonstrated that this variability was associated with an increased prevalence of psychotic and paranoid experiences. The phenomenon was most pronounced in the group of patients diagnosed with a psychotic disorder, followed by the group of relatives, while the group of healthy controls exhibited significantly lower scores than the other two groups.[106]

2.3 Aims and Hypotheses

The aim of this study is to investigate whether the study groups of [1] individuals with a diagnosed psychotic disorder (IPD), [2] relatives of individuals with psychotic disorders, and [3] healthy controls (HC) can be reconstructed using cluster analysis based on ESM data. Prior research suggests that IPD and HC can be effectively differentiated using ESM data.[3] Cluster analysis enables the identification of subgroups within a study population.[107] Consequently, we assume that the study groups of IPD and HC can be reconstructed in our cluster analysis of the ESM data (hypothesis 1a).

If individuals do not exceed the diagnostic threshold for a specific disorder, they are considered healthy, regardless of the possible presence of subclinical symptoms. As first-degree relatives of IPD often present subclinical symptoms[108], we anticipate that the individuals in the study group of relatives will not be clearly assignable to a specific cluster (hypothesis 1b).

As reported in the literature, HC and IPD groups differ not only in the ESM data but also in the results of clinical test results.[109] We expect that the scores obtained by the group of first-degree relatives on clinical tests would fall between those of the HC and the IPD groups (hypothesis 2).

3. Material and Methods

3.1 Recruitment and Data Acquisition

The data on which the present thesis is based on was collected by the Institute of Psychiatry, Psychology and Neuroscience (IoPPN) of the King's College London.

The patient group was recruited via the Consent for Consent c4c initiative, NHS Foundation Trusts OXLEAS, NELFT and SEPT in collaboration with the Mental Health Research Network, South London and Maudsley NHS Foundation Trust and other research projects within the IoPPN. Relatives were recruited through the mental health charities Mind and Rethink and through patients. Control subjects were recruited via IoPPN online recruitment circulars, as well as through online platforms, including Gumtree and Callforparticipants. Approval for all procedures was granted by the London Harrow Research Ethics Commitee.[110]

3.2 Study Sample

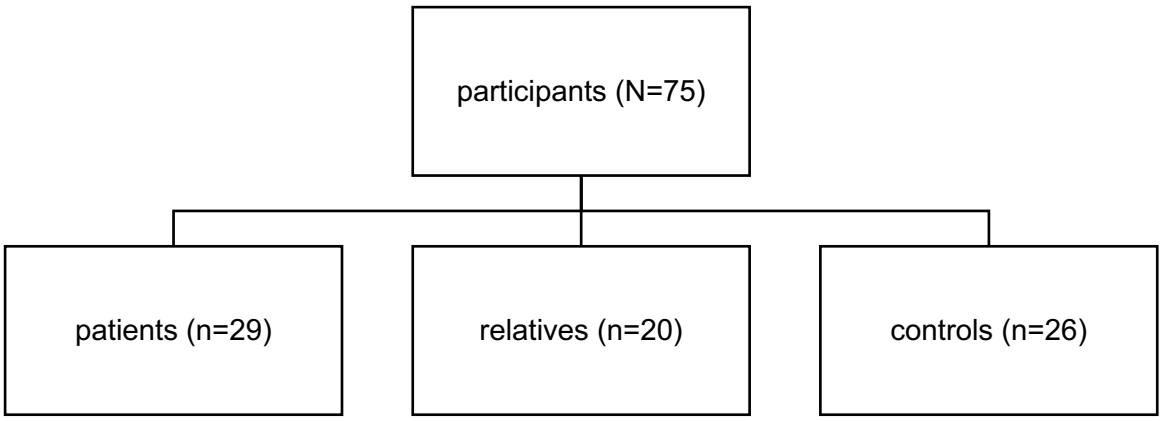
A total of 82 participants, with an age range of 19 to 63 years, were recruited for the study. The following criteria had to be met for inclusion: The minimum age was set at 18 years, with a maximum of 65 years, and the estimated IQ had to be above 70. Furthermore, participants were required to demonstrate sufficient proficiency in English to ensure comprehension of the questionnaires and assessments. An additional inclusion criterion for the IPD study group was a diagnosis of non-affective psychosis according to ICD-10[111] and a stable medication regimen for a minimum of 6 weeks prior to enrolment.

Individuals with a history of neurological disease or diagnosed alcohol or drug dependence within six months prior to the commencement of the study were excluded from participation.

Following the exclusion of participants who provided less than one-third of the requested data, the number of participants was reduced to 75. The participants were divided into three study groups as outlined below: 29 participants were IPD diagnosed with chronic non-affective psychosis, 20 participants were first-degree-relatives of individuals with the above-mentioned diagnosis and 26 participants were healthy controls with no family history of psychosis. The participating IPD and relatives had no familial relation to each other.

Figure 1

Study Group Distribution



Of the 75 participants 46 were male (61.3%) and 29 were female (38.7%). A more comprehensive overview of the demographic and descriptive variables of the study population is provided in Table 1.

Table 1

Demographic and Clinical Data

	HC (n=26)	Relatives (n=20)	IPD (n=29)
Gender	17 m (67.1%) 9 f (32.9%)	6 m (30.3%) 14 f (69.7%)	23 m (74.9%) 6 f (25.1%)
Education(in %)			
None/Primary	-	5	17.3
Secondary	27	-	31
College	23	30	34.5
University	50	55	17.2
Living status (%)			
Alone	31	20	69
Family/Partner	46	60	31
Other	23	20	-
Age	36.2 (8.1)	37.2 (14.7)	39.1 (9.9)
PANSS_G	-	-	1.71 (.35)
PANSS_N	-	-	2.17 (.83)
PANSS_P	-	-	1.86 (.60)

Note. m = male, f = female, PANSS = Positive and Negative Syndrome Scale, PANSS_G = General Scale, PANSS_N = Negative Scale, PANSS_P = Positive Scale

3.3 Material

3.3.1. Psychometric Instruments

The Positive and Negative Syndrome Scale (PANSS)[112], a 30-item questionnaire, is a well-established assessment tool for schizophrenia. The symptoms are divided into three scales: the positive scale, which covers positive symptoms such as delusion and hallucinations, the negative scale, which measures the prevalence of negative symptoms; and the global scale, which includes questions about general psychopathology.[112] All items are recorded on an Likert Scale of 1-7 with 1 indicating that the symptom is absent and 7 indicating that the symptom is extreme. Consequently, the minimum score is 30 and the maximum score 210.[113] The PANSS has shown to be particularly sensitive in detecting severe courses of schizophrenia.[114] In this study, only IPD were assessed with the PANSS. The Community Assessment of Psychic Experience (CAPE) is a tool used to assess the frequency and distress

associated with psychotic experiences in the general population. It comprises three scales with a total of 42 items. These scales represent the positive (pos), negative (neg), and depressive (dep) symptomatology in psychosis.[115] Each item is rated on a 1-4 scale. Subsequently, weighted frequency and distress scores are calculated for each scale by summing the item scores and dividing by the number of items completed. A higher value indicates a greater frequency or level of distress associated with psychotic experiences.[116]

The Green et al. Paranoid Thought Scale is a psychometric instrument designed to quantify paranoid thoughts.[117] It comprises two sections, which assess ideas of persecution (Part A) and ideas of reference (Part B). Each of the two scales consists of 16 items.[118] Scores range from 16 to 80, with the following cut-off values: A score of 16-23 is considered to be within the normal range, while a score of 24-34 is regarded as elevated. A score of 35-44 is considered to indicate a moderate level of severity, while a score of 45-59 is indicative of a severe level. A score of 60 or above signifies the presence of very severe paranoid thoughts.[119]

Additionally, an eye movement test was performed. Peak velocity, latency, and accuracy in pro- and antisaccades, as well as predictive saccade tasks are tested using a videonystagmograph.

3.3.2. ESM Questionnaire

Following the completion of the demographic and clinical assessments, the participants were provided with an iPod containing the ESM application or were given the option of downloading it to their smartphone. Over the seven-day study period, a query was performed ten times a day resulting in approximately 70 reports per study participant. To obtain an unbiased estimate of the daily and weekly progression, IPD were alerted pseudo-randomly between 8 a.m. and 10:30 p.m. Questionnaire completion was to be conducted as soon as possible, or directly following an activity that could not be interrupted.

The basic structure of the ESM questionnaire consisted of 30 items including questions about the participants' present social company, emotional state and psychotic symptoms.

The current affective state was determined by questions on positive (*e.g.* '*I feel content, …relaxed*') and negative affect (*e.g.* '*I feel low, …irritated, …tense*'), as well as perception (e.g. '*I feel dependable, …trusted, …that I can trust others*'). Acute psychotic symptoms were assessed with items such as '*visual hallucinations*', '*auditory hallucinations*'. In this questionnaire, items were rated on a Likert scale (1-7), with 1 indicating 'not at all' and 7 indicating 'very'.[120]

3.4 Statistical Analysis

The initial step involved the pre-processing of the data. Secondly, a study group analysis was performed, in which the characteristics of the sample were evaluated. Subsequently, a multiple

factor analysis (MFA) was carried out to evaluate the ESM data, followed by a cluster analysis. Finally, the clusters were compared with respect to the clinical questionnaires and tests described above. The following sections explain the theoretical framework of the statistical analyses (see Figure 5).

3.4.1. Pre-Processing and Study Group Analysis

In the first step the data was checked for missing values. Seven participants, who had answered less than a third of the total beeps were excluded. To deal with missing data, we imputed the missing values with the mean value of the respective rows.

As the next part of the statistical analysis, we performed a study group analysis. This involved both demographic data and clinical data from the assessments, as well as the ESM questionnaires.

The analysis itself was done by running a mixed-model approach. First, a linear mixed-effect model was fitted to the data. Mixed models represent an extension of linear models. They combine both fixed and random effects into a unified approach and have the advantage of being unbiased in the case of missing data.[121,122] Fixed effects influence variables that are constant across individuals, whereas random effects influence unpredictable variables that may vary across individuals.[123]

Second, an analysis-of-variance was calculated to assess the effect of the independent variables *daynumber*, *studygroup* and *participant id* on the dependent variable *component score*. Pairwise t-tests were employed to characterise significant main or interaction effects.

The significance level was set for $p \leq .05$ with False Discovery Rate (FDR) correction for multiple comparisons.[124] In order to conduct a paired t-test, it is essential that the subjects are independent, the data follows a normal distribution, and the sample is randomly selected. Additionally, the variances for the two independent groups must be equal..[125]

3.4.2. Multiple Factor Analysis

The subsequent phase involved the implementation of an MFA. An MFA represents a further development of a principal component analysis (PCA). A standard PCA is a multivariate statistical technique that aims to represent as much of the observed variance across all variables as possible in a smaller number of principal components. The objective, therefore, is to enhance the clarity of the data through the process of data reduction.[126,127]

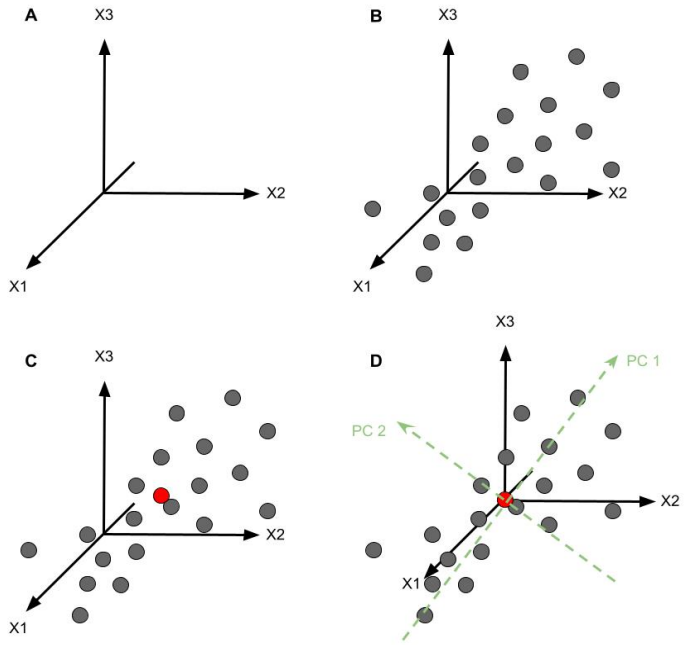
Following the scaling of the variables, mean centering was performed. To achieve this, the mean value of each variable is calculated for all data points, which then allows for the computation of a new centre point. In a Cartesian coordinate system, this implies that the zero point of the coordinate system shifts to the previously calculated centre point.[128] To obtain the

first principal component, a line is drawn through the point swarm that best approximates its multidimensional shape. Thus, the line reflects the largest source of variation within the data. Each data point can then be projected onto this line to obtain a coordinate value.

The next step is to create a second line that is orthogonal to the first and intersects the centre point. It represents the second principal component. In this manner, the description of the variance in the data is improved as much as possible.

Figure 2

Schematic Representation of Mean-Centering



Note. A: The multidimensional space is represented by a coordinate system. B: All data points are plotted on the coordinate system. C: The centre of the data points is determined. D: The coordinate system is realigned based on the centre point and the lines for principal components 1 and 2 are added. Figure based on Sartorius AG (2020).[129]

As previously stated, an MFA is an extension of a PCA and is specifically designed to deal with multiple data tables generated by measures over multiple time points. Each data table represents a time point, in this case a study day.

The fundamental aim of an MFA is similar to that of a PCA, in that the variables of interest are compressed into principal components, which are ranked according to their explanation of variance in the data. In an MFA, this is achieved by running each of the pre-generated data tables through a PCA individually, and at the end merging these data tables back into one.[130]

The factor loading, which is a measure that describes the contribution of each variable to a specific component, can be used to derive the importance of a variable for a component. Factor loadings are expressed as values between -1.0 and +1.0, indicating the positive or negative direction in which a variable influences a component. A value of +1.0 would indicate that all

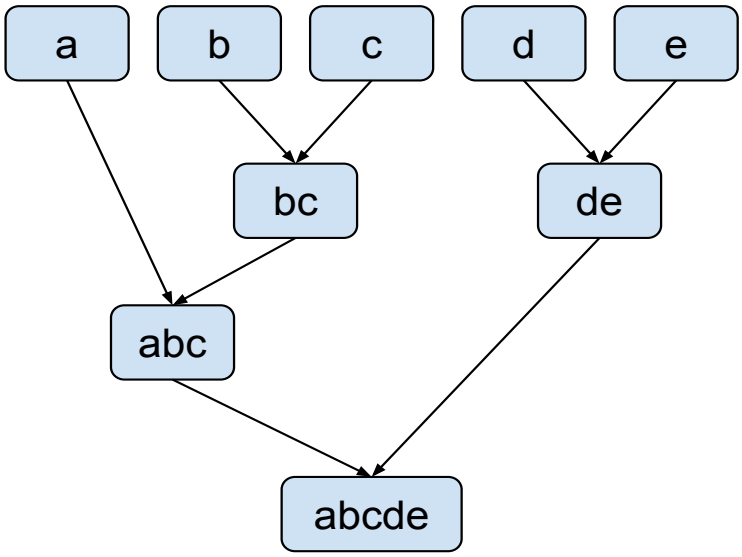
information pertaining to a variable is also present within the component. As a result, each variable can be assigned to a specific component based on its largest contribution and components can therefore be interpreted as the sum of their contributing individual items.[130]
The results of an MFA can be effectively presented in a scree plot, which can be used to determine the number of principal components that the items of the ESM questionnaires should be reduced to. The elbow method selects principal components up to the elbow of the plot, at which point the slope between components begins to change most significantly.[131] As items were answered across a seven-day time period, items from different days may load on different dimensions. In instances where not all sub-items would load onto the same dimension, the item was assigned to the dimension on which the majority of the sub-items loaded.

3.4.3. Cluster Analysis

The next part focuses on the cluster analysis itself, which used the results of the MFA as a basis for identifying distinct clusters. Clusters are defined as a set of data objects that are similar to objects within the same cluster, but different from objects in other clusters.[132] Clustering is one of the methods of unsupervised machine learning. Here, machine learning algorithms are used to identify hidden patterns or groups of data in unlabelled data sets.[133] One of the advantages over supervised machine learning is that it does not require human intervention to perform the analysis, as it does not necessitate labelled input. Thus, unsupervised machine learning allows the algorithm to learn and optimise itself.[134] Prior to commencing the cluster analysis, the data were scaled.
The cluster analysis itself was carried out according to the method of agglomerative hierarchical clustering. Here, each data point is initially considered as its own cluster. Then the two closest clusters are identified using Ward's method. Ward's method calculates the distance by identifying the pair of clusters that have the lowest variance when merged. The variance is determined using the sum of squares.[135] Generated distance measures can be visualised by a heatmap.[136] Heatmaps are useful for representing relationships, in this case the similarities between participants' trajectories, within large data sets.[137] As a quality control measure for the heatmap results, we performed a similarity check: For each component, we checked the trajectories of two participants who were shown to be very similar and two participants who were shown to be very dissimilar.
Subsequently, the two closest clusters are merged and this process is repeated until only one large cluster remains.[138]

Figure 3

Schematic Representation of Hierarchical Clustering



Note. This figure exemplifies hierarchical clustering. Starting, each data point (a, b, c, d, e) is considered a single cluster. In the following, the closest clusters are merged until all data points are in one cluster.

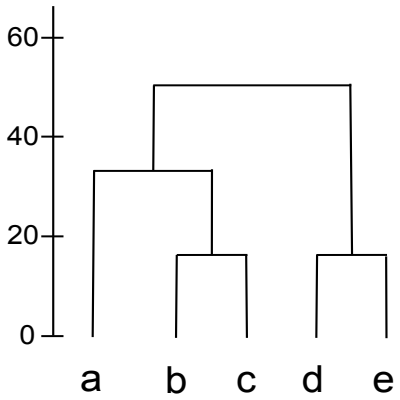
In order to cluster the data, we performed hierarchical clustering using RStudio's 'clusterboot' function from the ‘fpc’ package.[139] We performed 50 runs of clustering to assess the stability of the clusters over different subsets of the data. For each of the 50 iterations, 50 % of the data set was randomly selected.

To identify the optimal number of clusters in the current data we used the Jaccard coefficient[140], which can determine the similarities between clusters. The mean over these similarities, the Jaccard index, represents the stability of the cluster solutions for each possible number of clusters. A Jaccard index value of less than 0.6 is indicative of an unstable cluster. A value between 0.6 and 0.75 is indicative of the detection of a pattern within the data. A cluster with an index between 0.75 and 0.85 is deemed stable while a stability score above 0.85 indicates that a cluster is highly stable.[141,142] We set the range from 2 to 6 clusters in which we sought the best cluster solution.

To facilitate visual inspection of various cluster solutions, a dendrogram is created, which illustrates the hierarchical relationship between the objects, in this case the clusters. The observations are plotted on the x-axis, whereas the Ward’s distance measure is displayed on the y-axis. In this case, a high distance measure indicates that the clusters are dissimilar at this level of the scale.[143]

Figure 4

Exemplary Schematic Representation of a Dendrogram

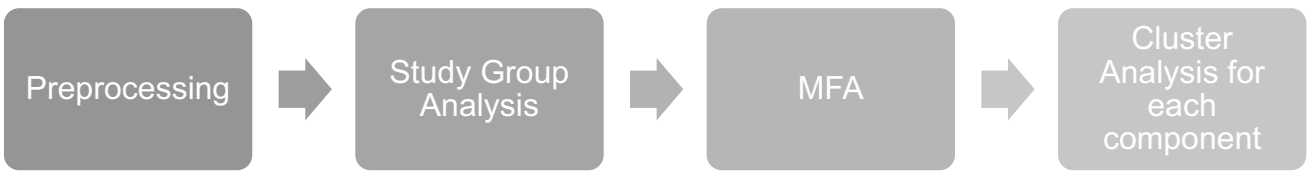


3.4.4. Cluster Characterisation

In a following step, we characterised the clusters based on demographic and clinical variables to determine whether any distinctive features could be identified that distinguished the clusters from one another. Thus, it was possible to ascertain whether certain tendencies observed in clinical tests were associated with abnormalities in the ESM survey. Both the demographic questionnaire and the clinical assessments served as the basis for this analysis. For this purpose, we employed chi-square tests of independence for categorical variables and Analysis of Variance (ANOVA) for continuous variables. Chi-square tests assume that the observations are independent. The assumptions for ANOVA are also the independence of the observations, plus a normal distribution, the homogeneity of variances, and the absence of significant outliers.[144]

Figure 5

Flowchart of Statistical Analyses



4. Results

4.1 Study Group Analysis

The assumptions for the statistical tests were met. Significant differences in the composition of the study groups were found regarding the ethnicity of the participants. In the HC group, over 50 % of the participants were of white ethnicity and about a quarter were of Asian origin. While participants of white ethnicity dominated the group of relatives (40%) there was a substantial number of participants of black ethnicity (25%). In the group of IPD, more than half of the participants were of black ethnicity, $X^2(10, N = 75) = 25.80$, $p = .0004$. Furthermore, there were significant differences regarding the living status. IPD live alone or with their family significantly more often than the other study groups, who mainly live with their partners, $X^2(4, N = 75) = 16.69$, $p = .002$. In addition, IPD held lower levels of educational qualifications, $X^2(10, N = 75) = 22.51$, $p = .01$.

On the positive scale of the CAPE, IPD reported significantly more frequent psychic experiences than HC ($p < .005$, 95% CI [-0.63, -0.11]) and relatives ($p < .005$, 95% CI [-0.69, -0.15]). Their psychic experiences were also shown to be more distressing than those of HC ($p < .05$, 95% CI [-0.49, -0.05]).

Regarding the negative scale, IPD also reported significantly more distressing experiences than HC ($p < .01$, 95% CI [-0.58, -0.07]).

On the eye movement test, IPD performed significantly worse than the relatives ($p < .005$, 95% CI [1.35, 8.79]) and HC ($p < .0001$, 95% CI [3.31, 10.02]).

Table 2

Clinical Results for Study Groups

	HC	Relatives	IPD
CAPE_pos_frequency	1.43 (0.3)	1.45 (0.3)	1.89 (0.6)
CAPE_pos_distress	2.09 (0.2)	2.19 (0.2)	2.37 (0.5)
CAPE_neg_frequency	1.74 (0.4)	1.77 (0.5)	2.05 (0.6)
CAPE_neg_distress	1.94 (0.3)	2.06 (0.3)	2.32 (0.5)
CAPE_dep_frequency	1.85 (0.4)	1.90 (0.6)	2.07 (0.6)
CAPE_dep_distress	2.52 (0.4)	2.68 (0.5)	2.68 (0.5)
GPTS_reference	26.1 (11.2)	26.3 (11.2)	31.7 (14.9)
GPTS_persecution	21.7 (7.5)	23.2 (13.6)	31.6 (18.4)
Eye Movement	28.0 (3.5)	26.2 (5.1)	20.8 (6.2)

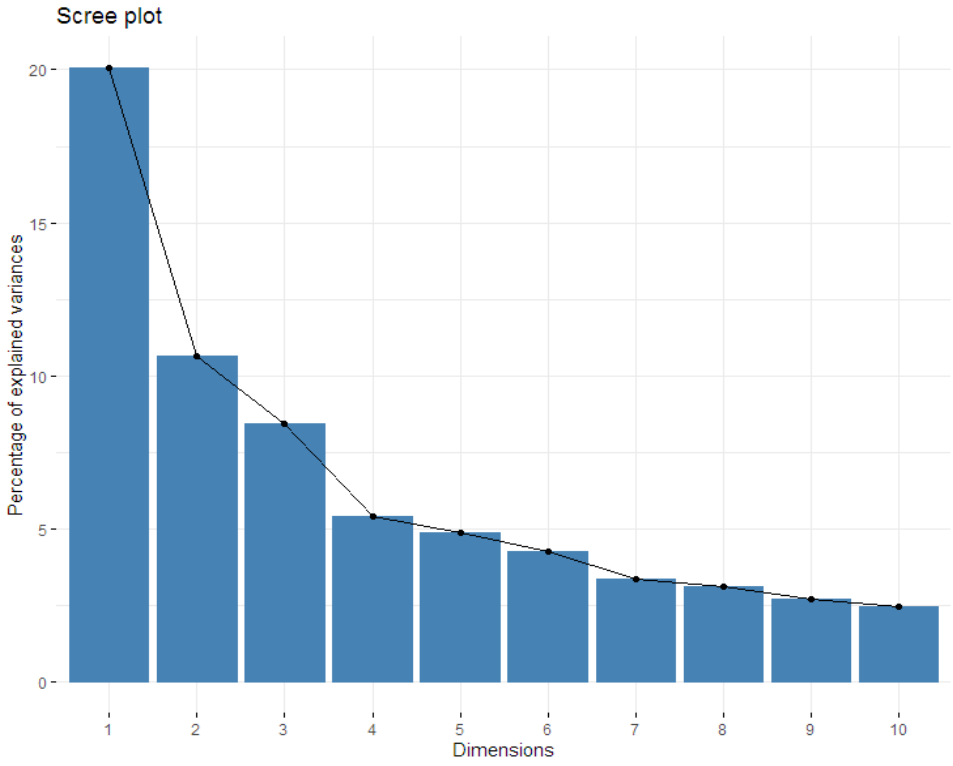
Note. The values are given as Mean (Standard Deviation).

4.2 Preprocessing and Multiple Factor Analysis

Based on the elbow method we were able to determine three components as the most meaningful solution. The results showed that component I explains 20.07 % of the variability in the data, component II 10.67 %, and component III 8.44 %.

Figure 6

Explained Variance Percentage for Different Dimensions



Note. This figure explains how much variance of the data is explained by the first ten dimensions in percent. The elbow of the plot is located at the height of 3 dimensions. y-axis: Percentage of explained variance; x-axis: Dimensions 1 to 10.

Based on the loadings, it was now possible to determine which items from the ESM questionnaire could best be assigned to which of the three components.

A positive loading, as observed with the item “irritated”, indicates that a high score on the item in the questionnaire is associated with a high score on the corresponding component I. For the variables with negative loadings, the MFA resulted in a negative loading for the respective component. This means, for example, that a high score on the item “cheerful” was associated with a low score on the scale of component I. If a participant was rarely cheerful, they would have higher scores in component I.

Therefore, all items that exhibited a negative loading on the components were recoded by reversing the Likert scale values, which ranged from 1-7. This ensured a consistent handling of all variables in subsequent steps of the analysis.

Items pertaining to Component I included, among others: *I feel irritated*, *I feel suspicious*, *I feel threatened*, *I am not cheerful* and *I am not relaxed*. Component II contained items relating to social relationships, for example: *I feel accepted* or *I like others*. Component III included items such as: *I have auditory hallucinations* and *I have visual hallucinations*, which ask about psychotic symptoms. In accordance with the corresponding items, we labelled the components [I] "General Psychopathology", [II] "Social Relations", and [III] "Psychotic Symptoms". A comprehensive overview of the item allocation can be found in the table below.

Table 3

Assignment of the Items to the Components

General Psychopathology	Social Relations	Psychotic Symptoms
cheerful**,** irritated, relaxed**,** content**,** low, tense, like myself**,** suspicious, safe**,** disliked, harm, unreal, ruminating, threatened, prefer being alone, excluded, lonely, concentrated, tired	I feel accepted, I like others, I feel close to others, I feel dependable, I can trust others, Others trust me, I prefer company	auditory hallucinations, visual hallucinations, I enjoy being alone, I am alone by choice, I feel motivated

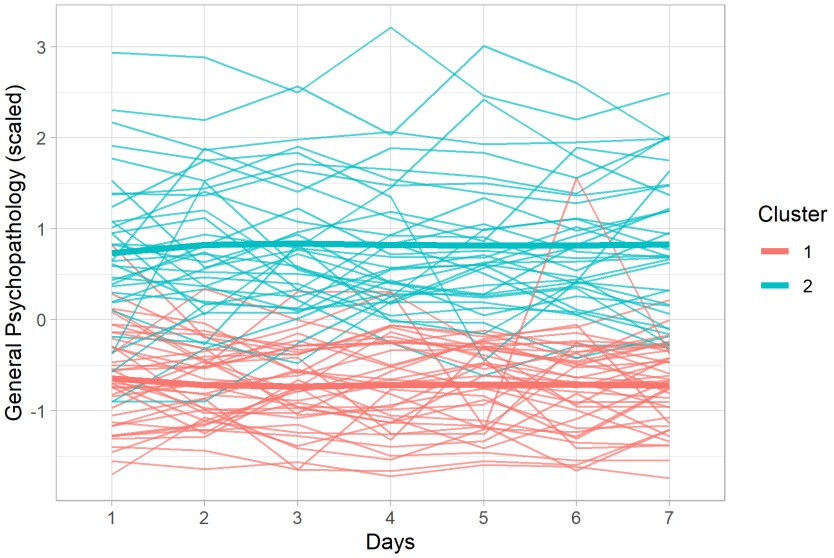
4.3 Component “General Psychopathology“

4.3.1. Cluster Analysis

For the component “General Psychopathology”, two clusters provided the most stable solution with Jaccard indices of [1] *0.83* [2] *0.*76. The cluster solution is shown in Figure 7.

Figure 7

Cluster Solution for "General Psychopathology"



Note. The plot shows the scores of the two generated clusters for the component "General Psychopathology" from the ESM questionnaire. x-axis: Days of the study period. y-axis: Averaged scaled component values for the component "General Psychopathology".

The two clusters each comprise individuals from all three study groups. The distribution presents a heterogeneous picture. It is noteworthy that the lower-scoring cluster contains a greater proportion of HC, while relatives and IPD are represented in roughly equal proportions in both clusters. See Appendix A for similarity checks. For a visual representation of the cluster solution using the heat map and the dendrogram, see Figures B1 and B2 in the Appendix.

Table 4

Cluster Solution for Component "General Psychopathology"

	Study Group		
Cluster	HC	Relatives	IPD
1	17	10	13
2	9	10	16

4.3.2. Cluster Characterisation

No significant differences were observed in the demographic variables, including education, gender, nationality, or occupation, between the two clusters. The findings of the clinical assessments conducted for the "General Psychopathology" component are presented in Table 5.

Table 5

Clinical Results for Clusters in "General Psychopathology"

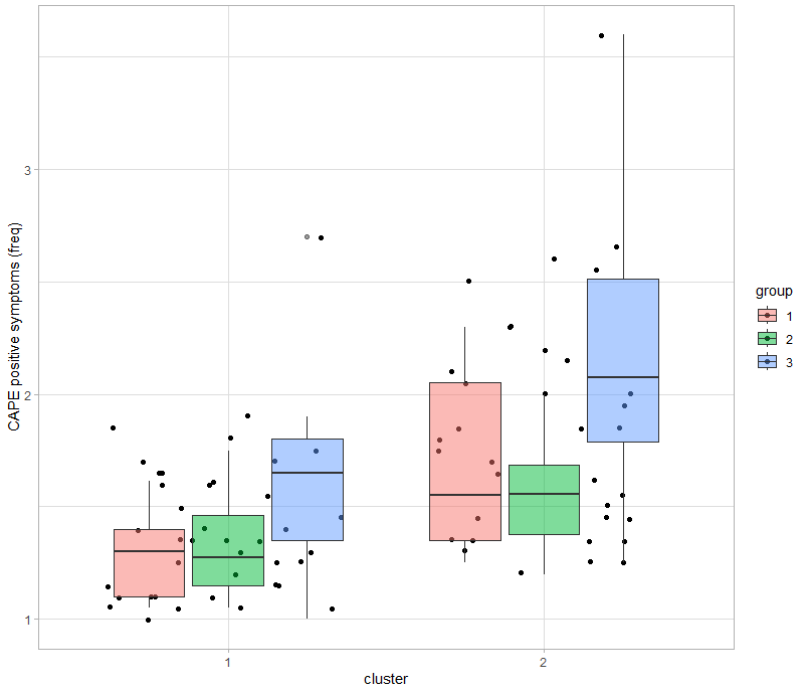
	Cluster 1	Cluster 2
CAPE_pos_frequency	1.41 (0.3)	1.85 (0.5)
CAPE_pos_distress	2.15 (0.2)	2.31 (0.5)
CAPE_neg_frequency	1.67 (0.4)	2.1 (0.5)
CAPE_neg_distress	1.97 (0.4)	2.28 (0.4)
CAPE_dep_frequency	1.75 (0.4)	2.19 (0.6)
CAPE_dep_distress	2.50 (0.4)	2.77 (0.5)
GPTS_reference	22.43 (7.1)	35.04 (14.7)
GPTS_persecution	19.4 (6.0)	33.46 (17.9)
PANSS_general	24.18 (4.0)	29.43 (6.2)
PANSS_positive	10.82 (2.1)	14.53 (4.8)
PANSS_negative	13.45 (6.3)	16.40 (5.8)
Eye Movement	26.2 (4.4)	23.2 (7.0)

Note. The values are given as Mean (Standard Deviation).

Here, the participants in cluster 2 demonstrated significantly higher scores on four distinct subscales of the CAPE. They reported experiencing psychic phenomena to a greater extent than participants in cluster 1, with a greater frequency of positive symptoms ($p < .0001$, 95% CI [-0.57, -0.20]).

Figure 8

Results of the CAPE Positive Frequency Scale for "General Psychopathology"

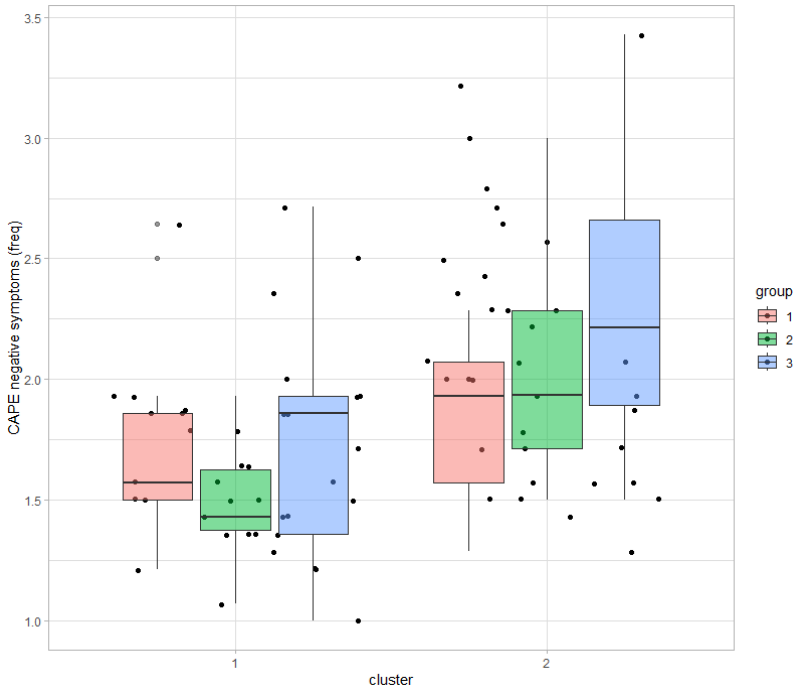


Note. Median lines, standard deviation and individual results are visualised. Group 1: HC, Group 2: Relatives, Group 3: IPD. x-axis: Clusters from component "General Psychopathology" divided into study groups; y-axis: Weighted sum scores on the positive frequency scale of CAPE.

Furthermore, cluster 2 also exhibited a higher frequency of negative symptoms associated with psychic experiences ($p < .0005$, 95% CI [-0.62, -0.19]).

Figure 9

Scores of the CAPE Negative Frequency Scale for "General Psychopathology"

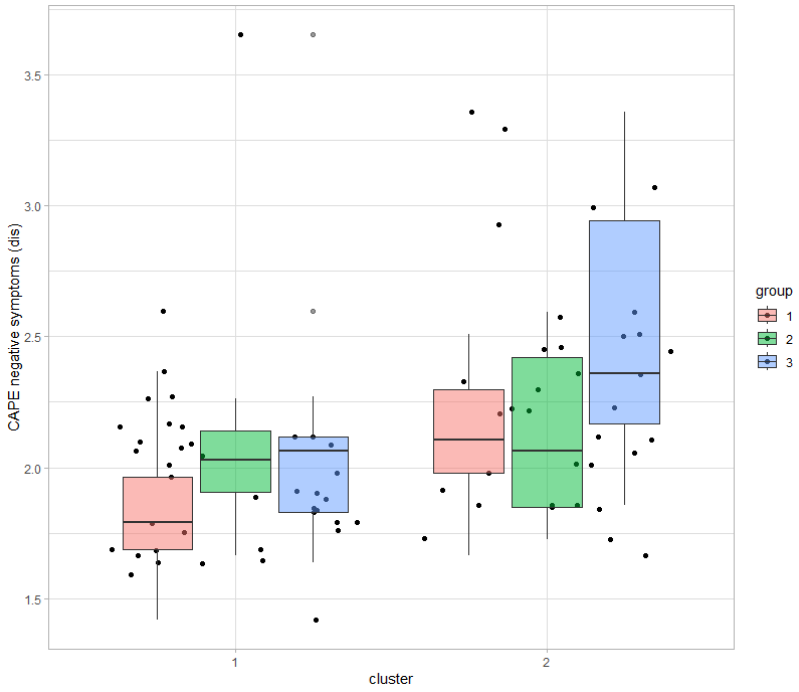


Note. Median lines, standard deviation and individual results are visualised. Group 1: HC, Group 2: Relatives, Group 3: IPD. x-axis: Clusters from component "General Psychopathology" divided into study groups; y-axis: Weighted sum scores on the negative frequency scale of CAPE.

Additionally, cluster 2 demonstrated significantly elevated scores on the Negative Distress Scale in comparison to cluster 1. (p < .001, 95% CI [-0.43, -0.07]).

Figure 10

Scores of the CAPE Negative Distress Scale for "General Psychopathology"

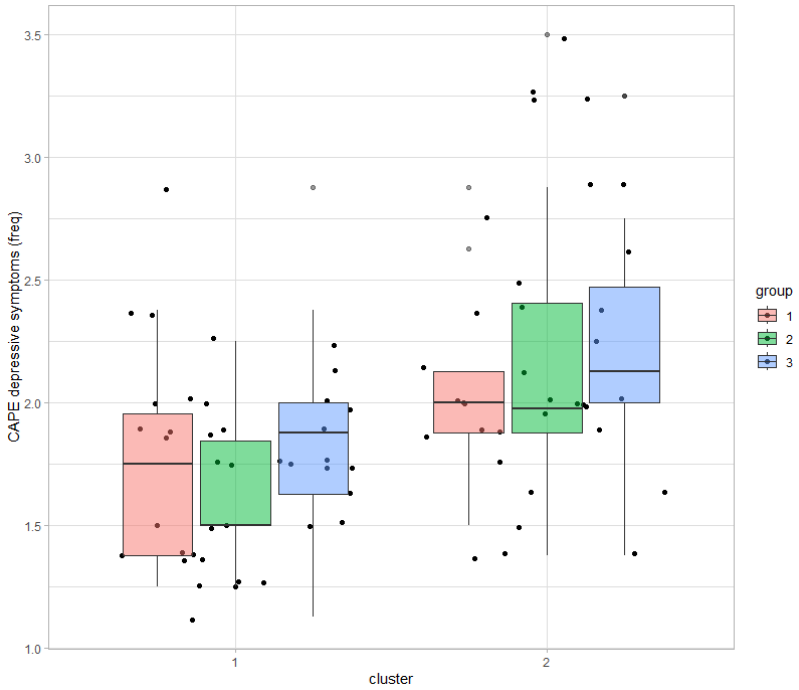


Note. Median lines, standard deviation and individual results are visualised. Group 1: HC, Group 2: Relatives, Group 3: IPD. x-axis: Clusters from component "General Psychopathology" divided into study groups; y-axis: Weighted sum scores on the negative distress scale of CAPE.

A significant difference was also observed between clusters 1 and 2 on the CAPE Depressive Frequency Scale, with cluster 2 reporting significantly higher scores than cluster 1 ($p < .0005$, 95% CI [-0.66, -0.20]).

Figure 11

Scores of the CAPE Depressive Frequency Scale for "General Psychopathology"

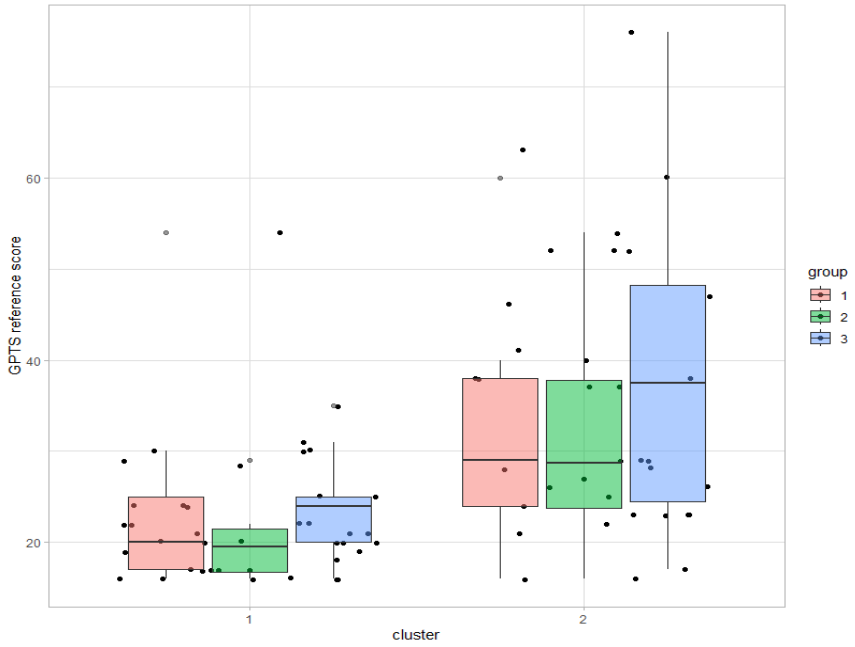


Note. Median lines, standard deviation and individual results are visualised. Group 1: HC, Group 2: Relatives, Group 3: IPD. x-axis: Clusters from component "General Psychopathology" divided into study groups; y-axis: Weighted sum scores on the depressive frequency scale of CAPE.

To quantify paranoid thoughts, a comparison was made between the mean scores of the clusters in the two scales of the GPTS. It was found that, in the scale referring to ideas of reference, cluster 2 demonstrated significantly higher scores than cluster 1 ($p < .0001$, 95% CI [-17.5, -6.71]).

Figure 12

Results of the GPTS Ideas of Reference Scale for "General Psychopathology"

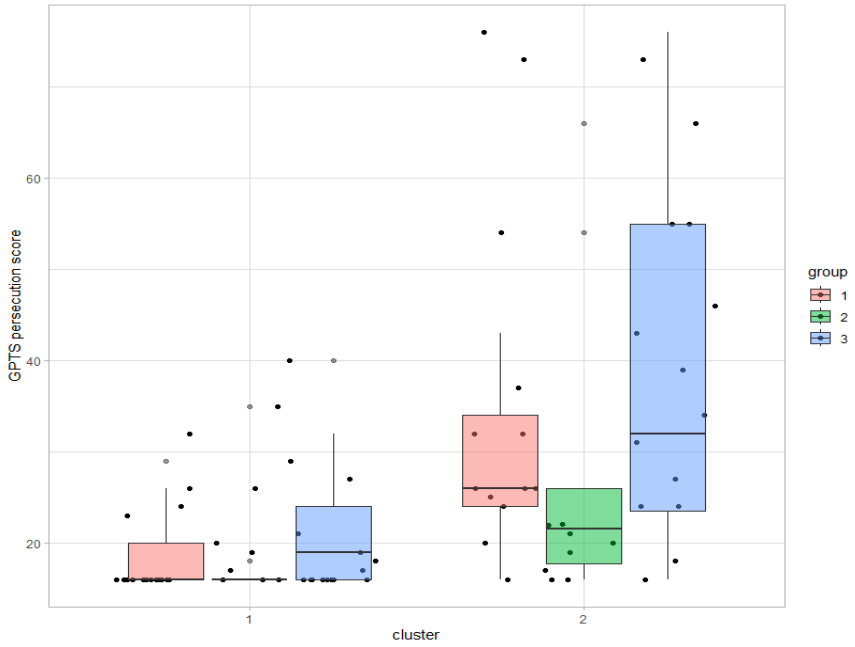


Note. Median lines, standard deviation and individual results are visualised. Group 1: HC, Group 2: Relatives, Group 3: IPD. x-axis: Clusters from component "General Psychopathology" divided into study groups; y-axis: Scores on the GPTS Ideas of Reference Scale

With respect to ideas of persecution, participants from cluster 2 exhibited significantly higher scores than those from cluster 1 (p = .0001, 95% CI [-18.6, -6.58]).

Figure 13

Scores of GPTS Ideas of Persecution Scale for "General Psychopathology"

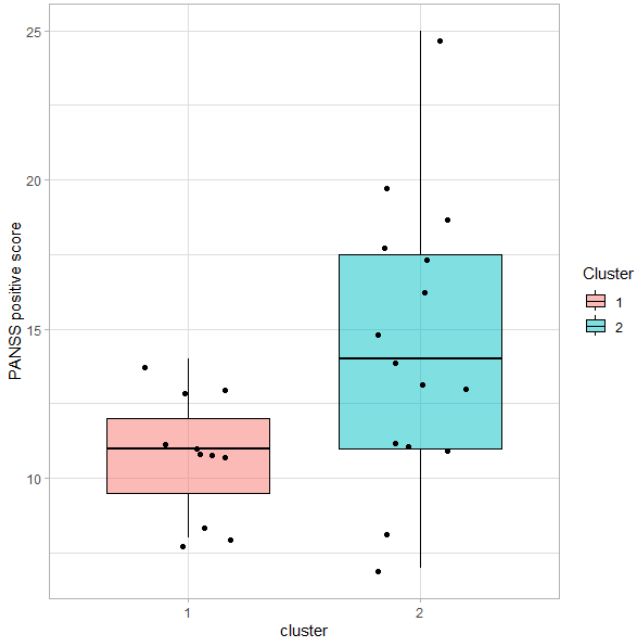


Note. Median lines, standard deviation and individual results are visualised. Group 1: HC, Group 2: Relatives, Group 3: IPD. x-axis: Clusters from component "General Psychopathology" divided into study groups; y-axis: Scores on the GPTS Ideas of Persecution Scale

The PANSS test, in which only IPD were tested, revealed that the IPD of cluster 2 exhibited significantly elevated symptom severity across both the positive ($p < .05$, 95% CI [-9.45, -1.04]) and general scales ($p < .05$, 95% CI [-6.61, -0.82]).

Figure 14

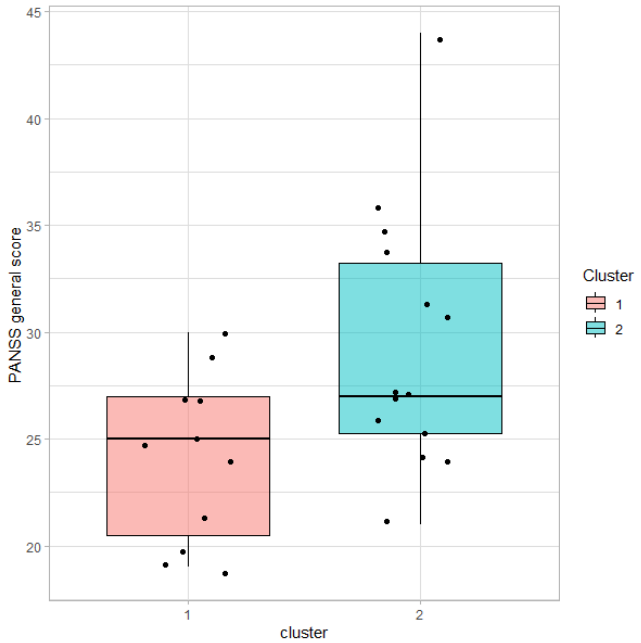
Results of the PANSS Positive Scale for the Component "General Psychopathology"



Note. Median lines and standard deviation are visualised. x-axis: Clusters from component "General Psychopathology"; y-axis: Scores on the PANSS Positive Scale

Figure 15

Results of the PANSS General Scale for "General Psychopathology"



Note. Median lines and standard deviation are visualised. x-axis: Clusters from component "General Psychopathology"; y-axis: Scores on the PANSS General Scale

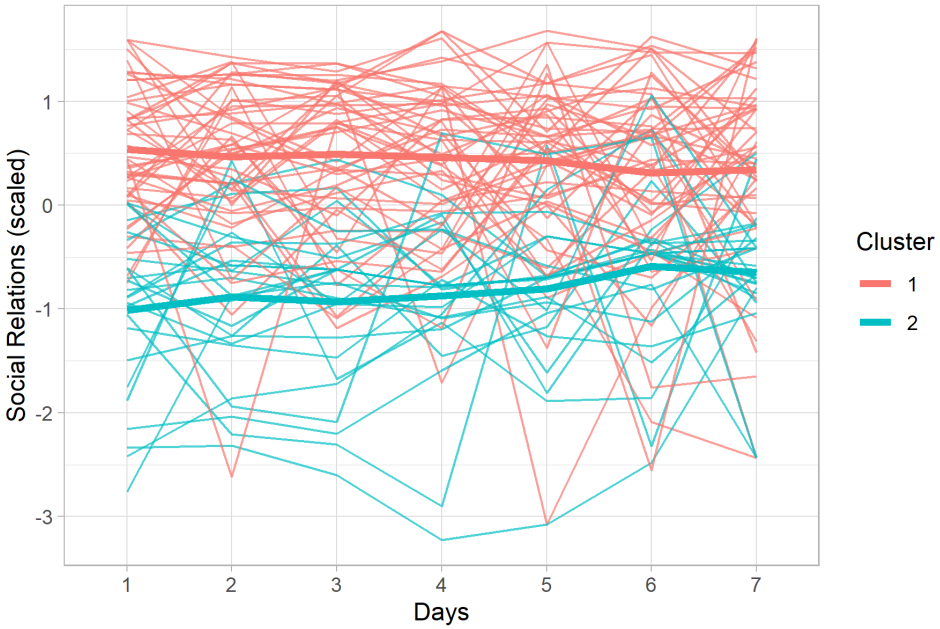
4.4 Component “Social Relations“

4.4.1. Cluster Analysis

A 2-cluster-solution was identified as most stable with Jaccard indices of [1] *0.85* and [2] *0.78* and is illustrated in the figure below.

Figure 16

Cluster Solution for “Social Relations”



Note. The plot shows the scores of the two generated clusters for the component “Social Relations” from the ESM questionnaire. x-axis: Days of the study period. y-axis: Averaged scaled component values for the component “Social Relations”.

As illustrated in the figure, cluster 1 exhibited consistently elevated values on the component scale throughout the study period. The majority of relatives are included in this cluster, which also contains a greater number of IPD than cluster 2.

Table 6

Division among Study Groups for “Social Relations”

	Study Group		
Cluster	HC	Relatives	IPD
1	16	15	18
2	10	5	11

4.4.2. Cluster Characterisation

There were no significant differences between the two clusters after FDR correction for either demographic or clinical data regarding the component “Social Relations”. Table 7 contains the results of the clinical assessments.

Table 7

Clinical Results for Clusters in Component “Social Relations”

	Cluster 1	Cluster 2
CAPE_pos_frequency	1.63 (0.5)	1.58 (0.4)
CAPE_pos_distress	2.26 (0.4)	2.15 (0.3)
CAPE_neg_frequency	1.89 (0.5)	1.84 (0.5)
CAPE_neg_distress	2.14 (0.4)	2.08 (0.4)
CAPE_dep_frequency	2.02 (0.6)	1.82 (0.4)
CAPE_dep_distress	2.71 (0.5)	2.46 (0.4)
GPTS_reference	29.11 (13.8)	26.81 (11.0)
GPTS_persecution	25.86 (14.4)	26.19 (15.5)
PANSS_general	26.57 (4.8)	27.82 (7.1)
PANSS_positive	12.87 (3.4)	13.09 (5.4)
PANSS_negative	15.07 (6.9)	15.27 (4.9)
Eye Movement	24.68 (6.2)	24.88 (5.5)

Note. The values are given as Mean (Standard Deviation).

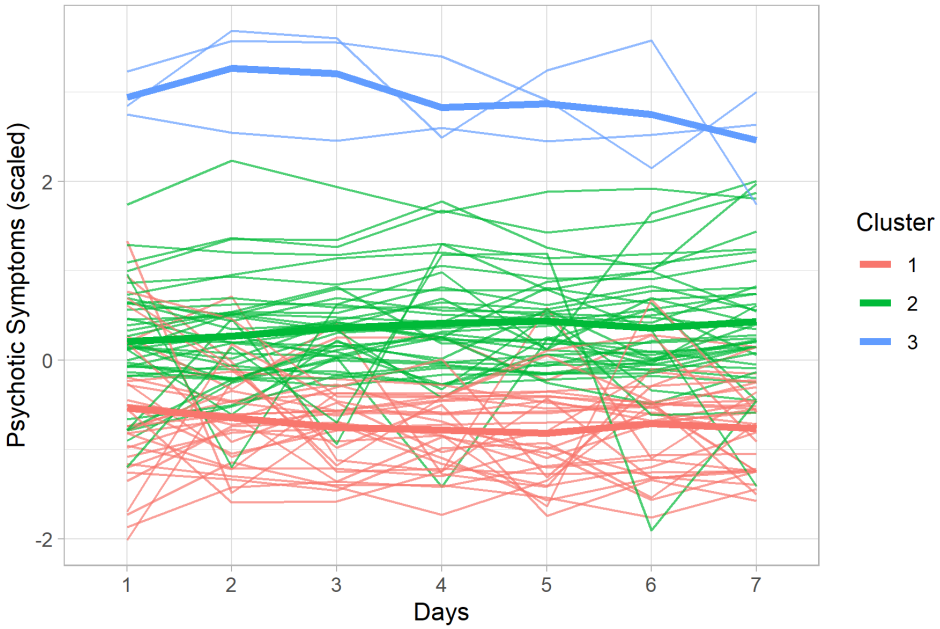
4.5 Component “Psychotic Symptoms“

4.5.1. Cluster Analysis

A 3-cluster solution was identified as most stable for the third component. This produced Jaccard indices of [1] *0.76*, [2] *0.70* and [3] *0.49*.

Figure 17

Cluster Solution for the Component "Psychotic Symptoms"



Note. The plot shows the scores of the two generated clusters for the component "Psychotic Symptoms" from the ESM questionnaire. x-axis: Days of the study period. y-axis: Averaged scaled component values for the component "Psychotic Symptoms".

The highest scoring cluster 3 consisted of three IPD only. Clusters 1 and 2 displayed a heterogenous composition, as displayed in the table below.

Table 8

Division among Study Groups for "Psychotic Symptoms"

	Study Group		
Cluster	HC	Relatives	IPD
1	10	11	11
2	16	9	15
3	0	0	3

4.5.2. Cluster Characterisation

Prior to correction, significant results were observed in both scales of the GPTS, as well as the Eye Movement Test. However, following the implementation of the FDR correction, no results for individual variables for this component remained significant.

The results of the clinical assessments for the clusters of the component "Psychotic

Symptoms” are shown in Table 9.

Table 9

Clinical Results for Clusters in Component “Psychotic Symptoms”

	Cluster 1	Cluster 2	Cluster 3
CAPE_pos_frequency	1.49 (0.3)	1.67 (0.6)	2.25 (0.5)
CAPE_pos_distress	2.23 (0.2)	2.20 (0.4)	2.49 (0.3)
CAPE_neg_frequency	1.82 (0.5)	1.90 (0.6)	2.00 (0.6)
CAPE_neg_distress	2.09 (0.4)	2.13 (0.5)	2.29 (0.1)
CAPE_dep_frequency	2.00 (0.5)	1.93 (0.6)	1.79 (0.4)
CAPE_dep_distress	2.63 (0.5)	2.65 (0.5)	2.23 (0.2)
GPTS_reference	25.36 (9.4)	29.32 (14.2)	46.33 (14.7)
GPTS_persecution	23.06 (11.5)	26.62 (15.3)	48.33 (21.7)
PANSS_general	24.33 (3.7)	29.29 (6.6)	24.50 (0.7)
PANSS_positive	10.67 (2.9)	14.13 (4.7)	14.5 (2.1)
PANSS_negative	13.78 (6.44)	15.80 (6.1)	16.5 (6.4)
Eye Movement	25.67 (5.2)	24.58 (6.1)	14.50 (6.4)

Note. The values are given as Mean (Standard Deviation).

5. Discussion

The aim of this thesis was to examine whether the study groups of patients diagnosed with a psychotic disorder, healthy controls, and first-degree relatives of individuals with a psychotic disorder could be reconstructed by performing cluster analysis on ESM data. The MFA resulted in three components within which the clusters did not align with the study groups.

For Component I ("General Psychopathology"), two clusters gave the most stable solution in the cluster analysis. The component contained items that described a variety of mental states. A high score on this component scale indicated a state associated with an increased prevalence of psychopathological characteristics, such as feeling hated or disliked by others, over the course of the ESM period. The analysis for the component, revealed that participants in cluster 2 reported a significantly higher frequency and level of distress associated with psychic experiences as measured by the CAPE. They also demonstrated significantly higher scores in both scales of the GPTS. The findings revealed that both clusters exhibited a comparable number of IPD and relatives. However, cluster 1 demonstrated a higher prevalence of HC, which could account for the diminished psychotic experiences and lower

scores on the "General Psychopathology" Scale of this cluster. In conclusion, it was not feasible to ascertain a definitive allocation of the study groups to the cluster for component I.

Similarly, for component II ("Social Relations"), two clusters provided the most stable solution. On this component scale, higher ESM ratings may be interpreted as indicative of good social relations in the lives of the participants. The social relations were evaluated through the use of items such as "I like others" or "I feel accepted". The cluster analysis of the "Social Relations" component yielded no significant results among the two clusters that emerged from the ESM query. This indicates that both clusters reported similar rates of social interaction and a similar level of satisfaction with their social relationships. The clusters again showed a heterogenous distribution with respect to the study groups, although it could be observed that a greater proportion of relatives and IPD were represented in the higher-scoring cluster, which would indicate better social relations. As it has previously been shown that people with mental health symptoms generally have poorer social relationships, these results are not what one might expect.[145] A potential explanation for our results is that social relationships can only be measured with limited accuracy, when using scaled items. In addition, individuals with psychotic disorders are known to make extensive use of social media[146], which can contribute to a reduction in the feeling of isolation without human contact.[147] Moreover, the questionnaire may also capture social contact with caregivers of IPD, which does not reflect the individuals' integration into society or other external social interactions.

Three clusters offered the most stable solution for component III ("Psychotic Symptoms"). The items within this component describe psychotic symptoms such as hallucinations. A higher rating on the component scale indicates a greater severity of symptoms as recorded in the ESM questionnaire. The composition of clusters 1 and 2 was once again heterogenous, while cluster 3 consisted of only three individuals, all with a diagnosed psychotic disorder. This may be indicative of the elevated scores observed in cluster 3 with respect to this component, potentially reflecting the presence of acute symptoms during the study period. However, the validity of this finding may be limited by the small number of individuals in the cluster.

In conclusion, it can be stated that the study groups of IPD and HC could not be reconstructed as they did not align with the clusters that emerged after the analysis of the ESM data. This refutes hypothesis 1a. The present result may be influenced by the fact that psychosis is a heterogeneous disorder, with symptomatology expressed differently in each individual. This indicates the potential for interindividual differences, whereby two individuals diagnosed with the same psychotic disorder may exhibit disparate symptom expressions.[148] It is important to recognise that differences are observed not only between individuals, but also within an

individual. This applies both to the symptoms themselves and to their temporal dynamics.[92] An example of intra-individual variation within a single individual are hallucinations as they are episodic rather than continuous.[92] The above reasons imply that individuals with psychotic disorders cannot easily be classified into a homogeneous subgroup. The inability to clearly assign people with psychosis to a single group may also impede the ability to distinguish them from other groups, for example, because symptoms of IPD do not manifest during the ESM period of data collection.

Although we were not able to confirm the correspondence between the study groups and the ESM clusters, it is notable that the resulting clusters align closely with the performances in the clinical assessments. Individuals in the clusters who reported high ratings in components I and III and low ratings in component II showed higher frequency of psychic experiences (CAPE) and more ideas of reference and persecution (GPTS). It should be emphasised that IPD are not inherently represented in the poor clusters. Rather, the composition of these clusters is very heterogeneous with respect to the study groups. Thus, ESM appears to be an appropriate method for identifying individuals with poor performance and severe symptoms. However, in this instance, it is unable to reconstruct the study groups.

A potential explanation for the discrepancy between study groups and cluster assignments is the categorical diagnostic system employed in psychiatry, namely the DSM[17] or the ICD.[11] The diagnostic system necessitates that a specific number of criteria be fulfilled before a diagnosis, such as paranoid schizophrenia, can be rendered. If a person meets only some of the criteria a diagnosis cannot be made. It is therefore possible that the HC group included individuals who also experienced some form of psychopathology in their daily lives without being dignosed. This is in line with findings that delusions and hallucinations are common subclinical symptoms in the general population.[97,149]

The concept of categorical diagnostics is a long-standing challenge and has been the subject of criticism for many years, for example, for not taking into account subclinical symptoms.[150] In our study, we also identified individuals who exhibited symptoms recorded by ESM, despite not having a diagnosis of a psychotic disorder, thus undermining this point of criticism. The main criticism of the categorical diagnostic system is that it fails to adequately reflect the high heterogeneity observed in psychosis.[151] This results in a reduction in the effectiveness of clinical interventions, as the same treatment is imposed on individuals with highly heterogeneous symptoms.[152,153] Additionally, Morey et al. (2020) have reported that the diagnostic validity of the categorical system is limited.[154] Furthermore, there is criticism that a classification based solely on symptoms alone is imprecise and inconsistent due to potential temporal fluctuations.[152,155] This is where the advantage of ESM becomes evident, as it is particularly adept at recording temporal dynamics due to the close-meshed query.[92] It is argued

that the categories in classification systems, such as the ICD and DSM, do not accurately represent the underlying psychopathology of such discrete disorders.[156]
An alternative diagnostic system is the dimensional diagnostic approach.[157] It focuses on the dimensional nature of clinical phenotypes in psychiatric diagnoses.[158,159] Regarding psychotic diseases, it is assumed that the phenotypes can be depicted on a continuum that covers the full range of psychotic symptoms, including subclinical symptoms. This enables each individual to be categorised on this continuum and the heterogeneity of the disorders to be more accurately represented.[160] In addition, the approach facilitates interdisciplinary collaboration by considering multiple dimensions of the illness, utilising both physiological and psychological measures. ESM could also help here as part of a continuous diagnostic system, as it enables highly individualised and precise recording of symptoms in real environments, which can lead to personalised diagnostics and intervention in the long term.[161]

The data revealed the presence of mixed clusters across all three components. These results confirm hypothesis 1b, as the relatives could not be clearly assigned to a particular subgroup. This may be explained by the presence of subclinical psychotic symptoms in the healthy population. Also, relatives are at an inherently higher genetic risk of developing psychosis and attenuated symptoms[45], which may also contribute to the mixed distribution.

The study group analysis revealed that the highest proportions of IPD were from ethnic minorities. This is consistent with the findings that ethnic minority background is considered a risk factor for developing psychosis.[50] Furthermore, our analysis confirmed previous research findings that individuals with psychotic disorders are more likely to live alone[162] and have lower educational attainment on average.[163] In addition, IPD reported the most psychotic symptoms and experiences on the CAPE and on the GPTS (Ideas of Reference Scale). Furthermore, they exhibited the poorest performance on the eye movement test, which is also in line with previous studies.[117,164-166] Regarding the results of these clinical tests, the group of relatives obtained ratings that fell between HC and IPD, thereby confirming hypothesis 2. On average, they performed better than IPD, but worse than HC. This can be well explained within the framework of heritability and the associated preload of first-degree relatives.

It is important to acknowledge the potential limitations of this project. The relatively small sample size (N=75) has the effect of reducing the stability and interpretability of individual clusters in the statistical analyses. Future studies should pursue further work of this kind with larger sample sizes.
Secondly, it is noticeable that at first glance not all items fit well with the respective component. To illustrate, it may not be immediately obvious that high concentration is related to increased

general psychopathology, as there was a positive correlation between the 'concentration' item and the component scale. However, a possible explanation for the positive correlation could be that participants are reporting their current state when completing the questionnaires and are concentrating on answering the questions. The assignment of the item "motivated" to component III (“Psychotic Symptoms”) is also open to question at first sight, as psychosis is often associated with a disturbance of drive. However, it is plausible that the allocation is based on the fact that IPD may have exhibited positive symptoms during the survey. The presence of positive symptomatology is typically characterised by an increase in drive ("motivated") and exuberance.[167]

Thirdly, when determining the cluster solutions, we identified the most stable cluster solution in each case using the Jaccard indices. Stability values for the clusters of components I and II were above 0.75, which is the lower limit for a stable cluster solution. For values between 0.6 and 0.75, a recognisable pattern emerges from the data. Scores below 0.6 are considered unstable. It is important to note that the reliability of the results may be compromised by the reduced stability observed in some clusters, as outlined in Component III. In particular, Cluster 3 exhibited a Jaccard index of only 0.49, which may have an impact on the overall reliability of the results. This may be attributed to the fact that component III is the least significant of the three components. It explained 8.44% of the data, while components I and II explained 20.07% and 10.67% of the data, respectively. In view of these results, it may be advisable to discuss the selection of two components instead of three. It is also important to note that the ESM data are self-reported. It has been demonstrated that IPD may be less inclined to report their symptoms during the acute phase of the illness.[87] They tend to assess their own positive and negative symptoms correctly, but exhibit a tendency to assess persecutory delusions incorrectly.[77]

6. Conclusion

The ESM is a reliable and valid measurement tool for the assessment of psychopathological symptoms in everyday life. In the present study, we employed cluster analysis to examine ESM data from individuals diagnosed with psychotic disorders, first-degree relatives of individuals diagnosed with psychotic disorders and a control group of healthy controls. The application of MFA yielded three principal components, with component I and II producing two clusters, and component III comprising three clusters. The results demonstrated that it was not feasible to recreate the study groups using the clustering method. Nevertheless, it was demonstrated that ESM may be a valuable tool for identifying both overt and subclinical symptoms, in the general population, irrespective of diagnostic systems. Further research is required to ascertain the potential of ESM as an evaluation instrument in clinical practice, for example by using a larger sample, a longer study period or an alternative cluster method.

7. Literature

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8. Appendix

8.1 Appendix A

Figure A1

High Similarity for Component "General Psychopathology"

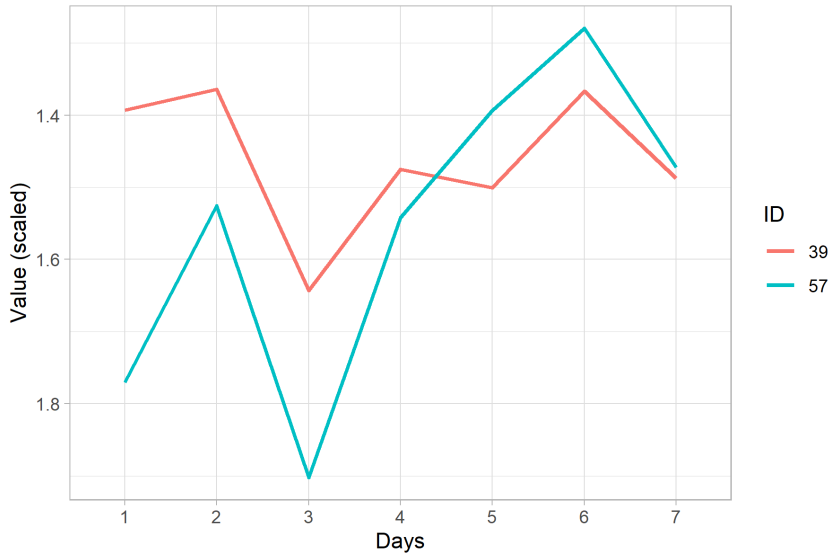


Figure A2

Low Similarity for Component "General Psychopathology"

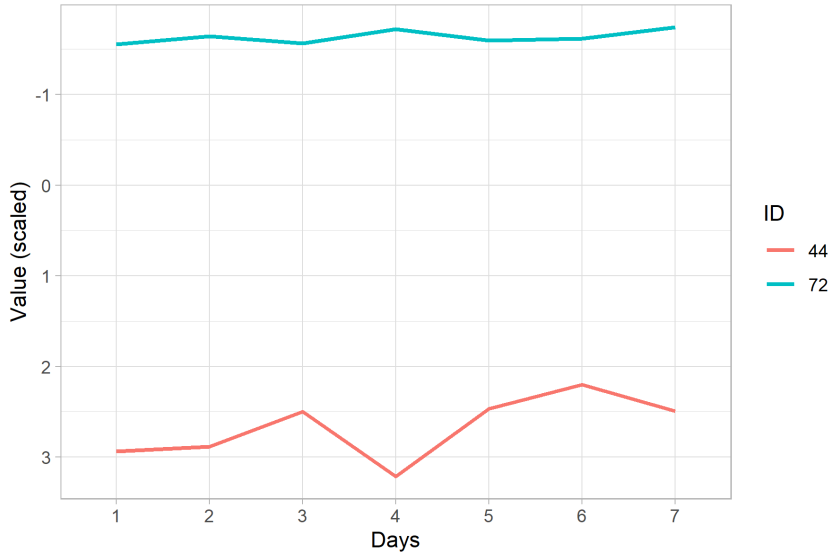


Figure A3

High Similarity for Component „Social Relations"

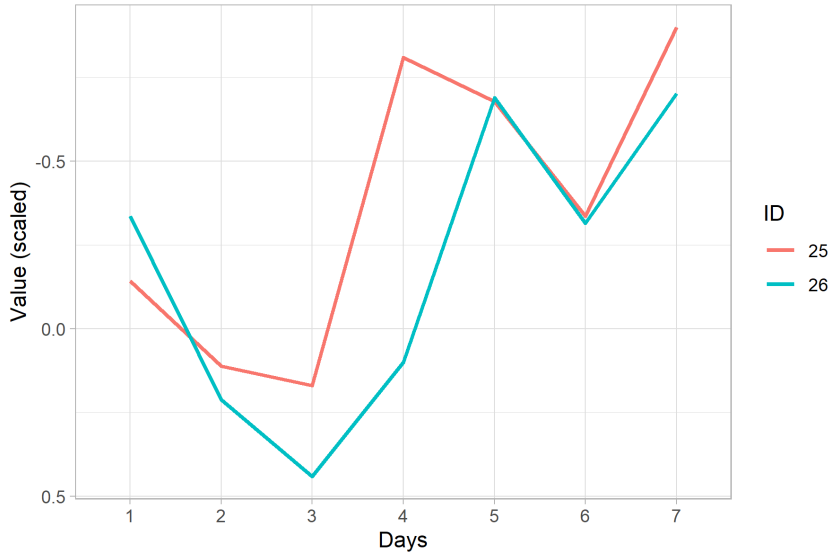


Figure A4

Low Similarity for Component „Social Relations"

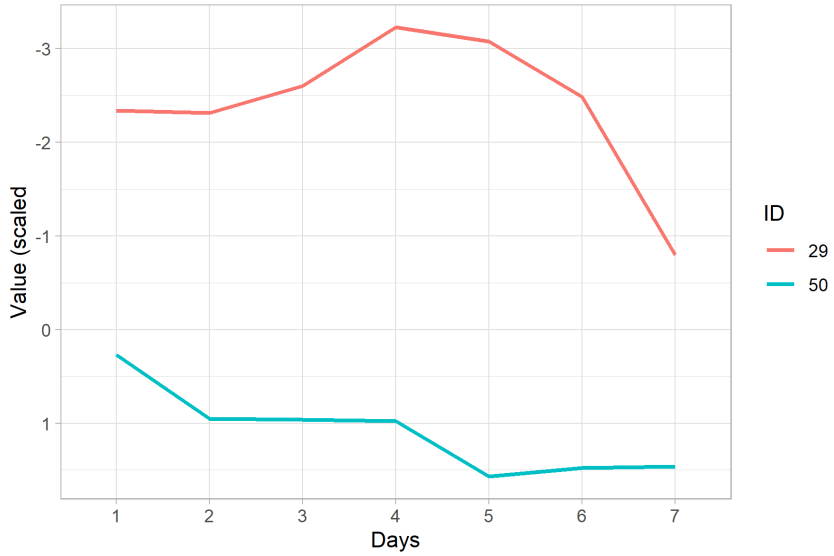


Figure A5

High Similarity for Component "Psychotic Symptoms"

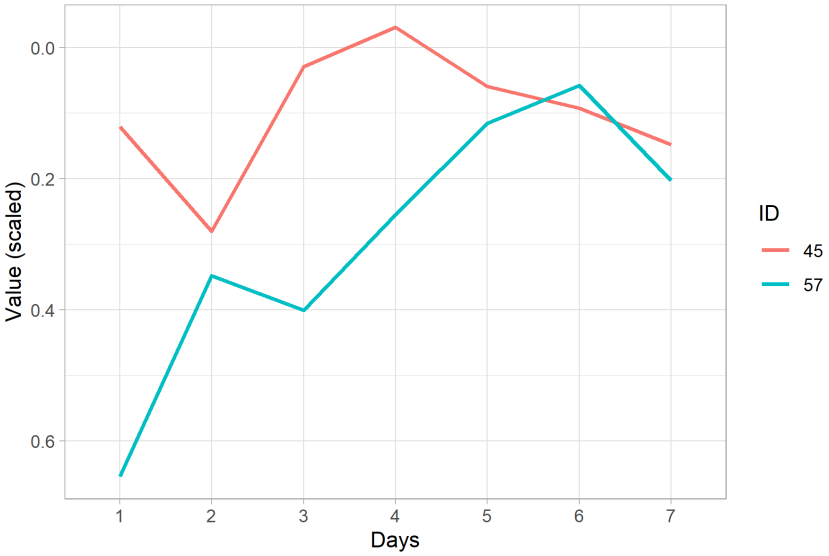
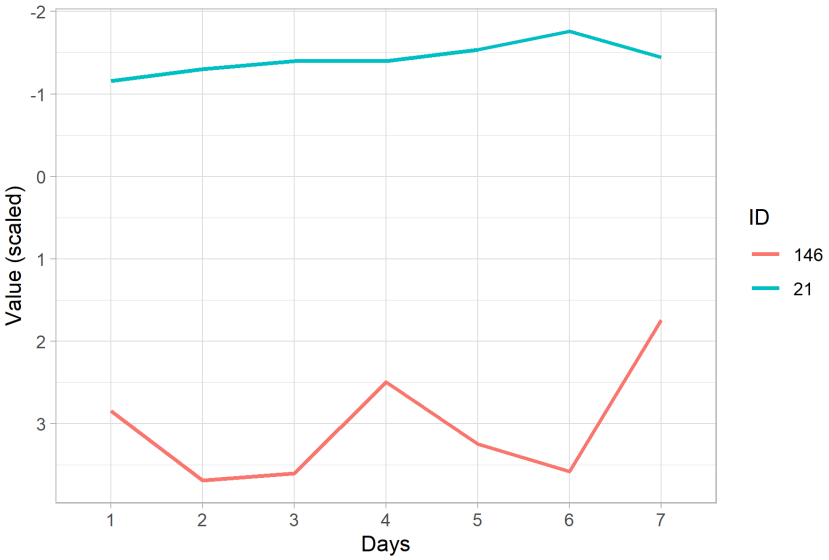


Figure A6

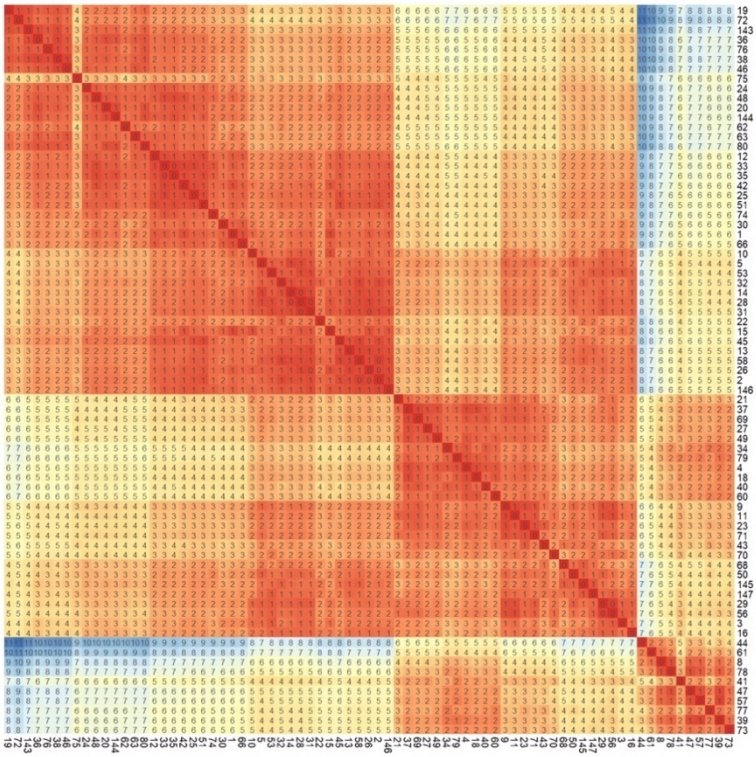
Low Similarity for Component "Psychotic Symptoms"



8.2 Appendix B

Figure B1

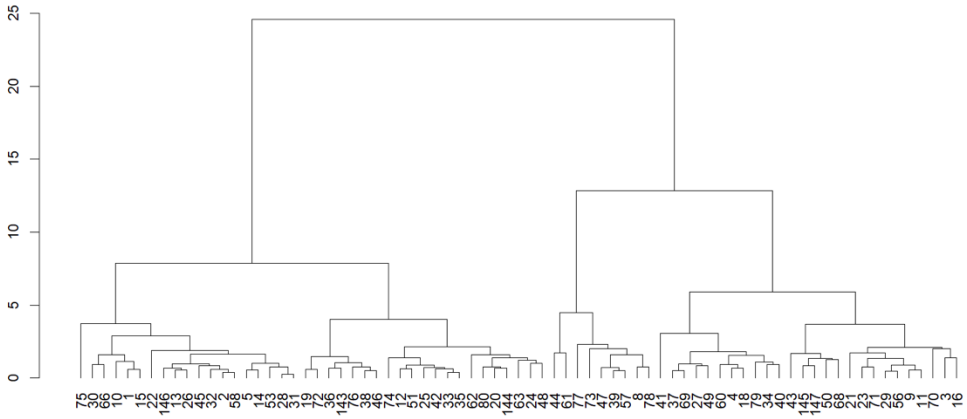
Heatmap of Dimension "General Psychopathology"



Note. Heatmap for Component "General Psychopathology". x-axis and y- axis: Participants´ IDs. The further the intersecting field is located in the red colour spectrum the more similar are the trajectories of the ESM results of the participants.

Figure B2

Dendrogram for Component "General Psychopathology"



Note. The dendrogram shows the sequence of merges in hierarchical clustering. At the lowest level, all participants are viewed as individual clusters. x-axis: Participants' IDs; y-axis: Measure of closeness of the clusters.

Figure B3

Heatmap of Component "Social Relations"

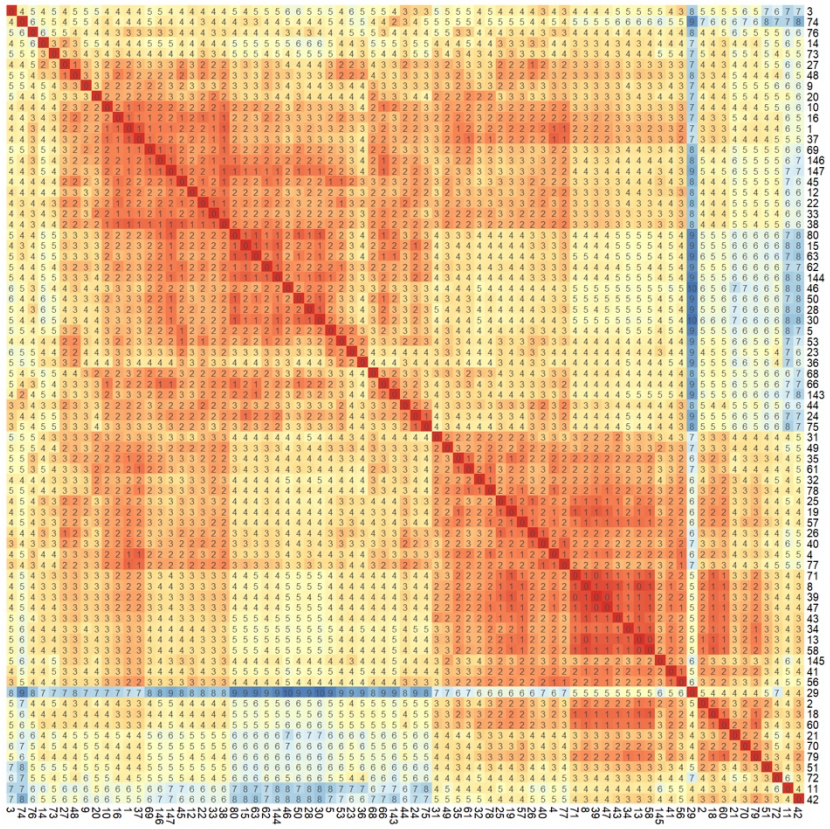


Figure B4

Dendrogram of Component "Social Relations"

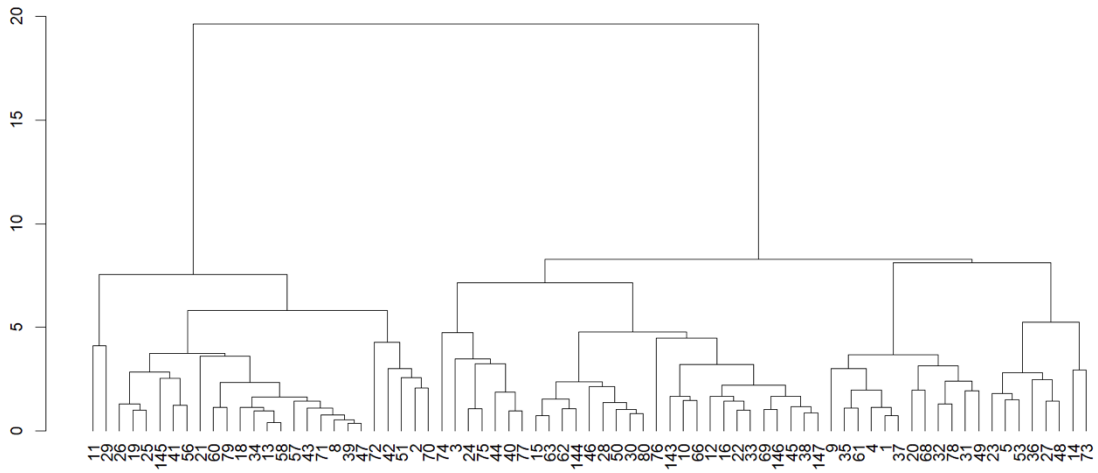


Figure B5

Heatmap of Component “Psychotic Symptoms”

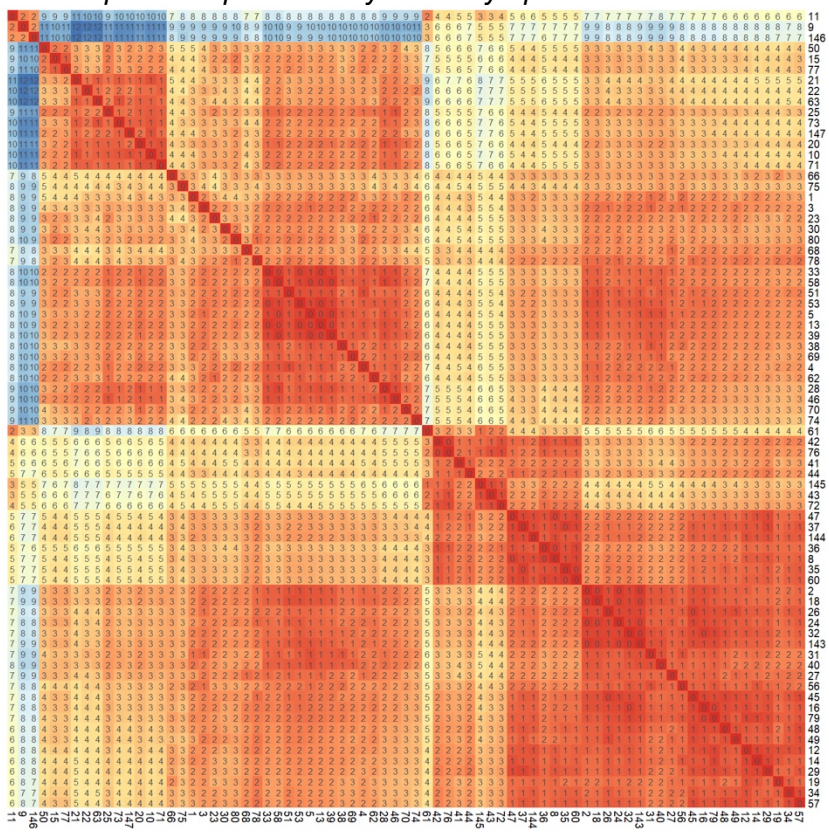
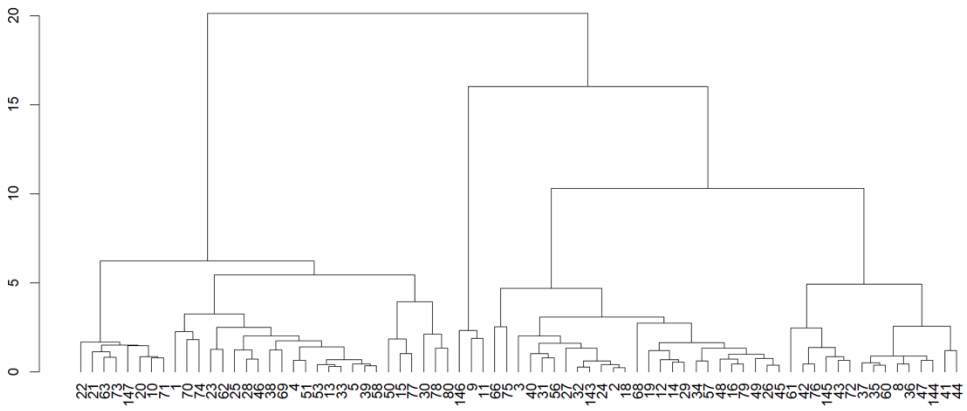


Figure B6

Dendrogram of Component “Psychotic Symptoms”



8.3 List of Figures

8.4 List of Tables