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Reduced Expression of Emotion: A Red Flag Signalling Conversion to Psychosis in Clinical High Risk for Psychosis (CHR-P) Populations

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Objective: In this hypothesis-testing study, which is based on findings from a previous atheoretical machine-learning study, we test the predictive power of baseline "reduced expression of emotion" for psychosis.
Method: Study participants (N = 96, mean age 16.55 years) were recruited from the Prevention of Psychosis Study in Rogaland, Norway. The Structured Interview for Prodromal Syndromes (SIPS) was conducted 13 times over two years. Reduced expression of emotion was added to positive symptoms at baseline (P1–

Jone Bjornestad, PhD is a clinical psychologist holding a professor position at the University of Stavanger. Bjornestad has a researcher position at TIPS – Network for Clinical Research in Psychosis at Stavanger University hospital and a similar position at the District General Hospital of Førde. His research interest includes psychosis, ultra-high risk, early intervention, social media, substance use and social interaction. *Tore Tjora, PhD* is a clinical psychologist holding an associate professor position at the University of Stavanger. His main research interest are epidemiology, statistics and tobacco. *Johannes H. Langeveld, PhD* is a specialist in clinical psychology holding a professor II position at the University of Stavanger. His research includes psychosis, ultra-high-risk states, family work, early intervention and risk of violence in psychosis. *Inge Joa, PhD* is a researcher at TIPS – Network for Clinical Research in Psychosis at Stavanger University hospital and holds an associate professor II position at the University of Stavanger. His research includes psychosis, ultra-high risk states, early intervention and information campaigns targeting vulnerable groups. *Jan Olav Johannessen, PhD, MD,* is a psychiatrist and researcher at TIPS – Network for Clinical Research in Psychosis at Stavanger University hospital and holds a professor II position at the University of Stavanger. He is one of the founders of TIPS and has worked with psychosis and ultra-high-risk states for decades, including early intervention and information campaigns. *Michelle Friedman-Yakoobian, PhD* is the clinic director of the Center for Early Detection, Assessment and Response to Risk Clinic for youth ages 12-30 who are showing signs of clinical high risk for psychosis. She is an Assistant Professor at Beth Israel Deaconess Medical Center at Harvard University. Her program of research has focused on the development and implementation of effective psychosocial interventions for individuals experiencing psychosis (or signs of risk) and their families. *Wenche ten Velden Hegelstad, PhD* is a specialist in clinical psychology holding an associate professor II position at the University of Stavanger. She is a principal investigator (PI) at TIPS – Network for Clinical Research in Psychosis at Stavanger University hospital. Her research mainly focuses on psychosis and ultra-high risk states, including early intervention and information campaigns.

Address correspondence to Jone Bjornestad, Department of Social Studies, Faculty of Social Sciences, University of Stavanger, PO Box 8600 FORUS, 4036 Stavanger, Norway. E-mail: jone.r.bjornestad@uis.no

P5) as a predictor of psychosis onset over a two-year period using logistic regression.
Results: Participants with a score above zero on expression of emotion had over eight times the odds of conversion (OR = 8.69, $p < .001$). Data indicated a significant dose–response association. A model including reduced expression of emotion at baseline together with the positive symptoms of the SIPS rendered the latter statistically insignificant.
Conclusions: The study findings confirm findings from the previous machine-learning study, indicating that observing reduced expression of emotion may serve two purposes: first, it may add predictive value to psychosis conversion, and second, it is readily observable. This may facilitate detection of those most at risk within the clinical high risk of psychosis population, as well as those at clinical high risk. A next step could be including this symptom within current high-risk criteria. Future research should consolidate these findings.

Only between four and nine percent of individuals presenting to mental health care with first episode psychosis (FEP) were detected by clinical high risk for psychosis (CHR-P) services prior to psychosis onset (Ajnakina et al., 2019; Birchwood et al., 2013; Fusar-Poli et al., 2017; Joa et al., 2021). In spite of oftentimes extensive early detection efforts, this remains a challenge, and research continues to run into the prevention paradox that most FEP cases will come from populations that are not identified in CHR-P services. CHR-P risk assessment has been criticized as being too narrowly focused on attenuated or brief positive symptoms and not accounting satisfactorily for social factors (Ajnakina et al., 2019; Anglin et al., 2020; McGorry et al., 2018; Moritz et al., 2019; van Os et al., 2021). It is well known that diminished social functioning is associated both premorbidly with psychosis and with CHR-P (Addington et al., 2008; Monte et al., 2008; Rabinowitz et al., 2002; De Wit et al., 2014). CHR-P onset usually coincides with adolescence (Cannon et al., 2008; Raballo et al., 2020), when relationship formation is increasingly normatively based (Blakemore, 2018). Arguably, norm-breaking expressive behaviors during this time may lead to diminished social interaction and, ultimately, to social exclusion (Becker, 1963; Bjornestad et al., 2020; Blakemore, 2018; Bornstein, 1989). Social anhedonia, avolition, blunting of affect, and social withdrawal can be considered such norm-breaking behaviors and are typical of negative symptoms. These do not form part of CHR-P criteria.

As such, CHR-P criteria as currently identified, which do not consider negative symptoms, appears to be problematic. It may delay and obstruct case detection by CHR-P services. However, negative symptoms have low specificity (Chang et al., 2020; Devoe et al., 2017). They can easily be confused with heartbreak, depression, substance use behavior and other phenomena typically associated with adolescence. Furthermore, research has predominantly been based on sum score analyses of composite symptom constructs, preventing a thorough examination of specific negative symptoms and negative symptom profiles in CHR-P (Gupta et al., 2021).

In a recent longitudinal CHR-P study (Bjornestad et al., 2021) we aimed to accommodate the challenge of low specificity by using an explorative machine-learning approach, employing data from an intensive long-term follow-up with frequent assessments. In this way, it was possible to establish the relative contribution of specific predictors and their timing. Two-hundred and forty-seven specific symptom scores, derived from the Structured Interview for Prodromal Syndromes (SIPS) (Miller et al., 1999), from 13 separate assessments over a two-year course, were simultaneously entered into a machine-leaning model

as single and equally weighted predictors. This approach identified an elevated score on the specific negative symptom of "expression of emotion" (N3) at study inclusion as the superior predictor of conversion to psychosis. A reduced expression of emotion in the SIPS is defined as flat and constricted in respect of emotional responsiveness, modulation of feelings (e.g., monotone speech), communication gestures (e.g., dull appearance), spontaneity, communication initiative and flow, interpersonal distancing, and verbal and non-verbal communication (McGlashan et al., 2001). A score of one or higher on this symptom was present in 16 out of 19 (84.2%) converters, while only three (5.7%) of the participants with a null score later converted to psychosis. Of note, the presence of this symptom, even at levels that are considered to be in the minimal, subclinical range (1 or 2), still contributed to risk for conversion in this model. By deriving a predictor variable from this information, we use the same sample as for the machine-learning study to test the predictive value of "expression of emotion" (N3) at study inclusion when controlled for specific positive symptoms.

HYPOTHESES

H0: A baseline score above zero on item N3 will not yield superior predictive value for psychosis onset compared with any baseline positive item score.

H1: A baseline score above zero on item N3 will yield superior predictive value for psychosis onset compared with any baseline positive item score.

MATERIALS AND METHODS

Sample and Recruitment

This study is based on data from the ongoing Prevention of Psychosis Study (POP) (Joa et al., 2015), a naturalistic longitudinal CHR-P study in Rogaland County, Norway. The POP study included a population-based cohort (approximately 300,000 inhabitants fulfilling the age criteria for inclusion) of CHR-P individuals from August 2012 to December 2018. Participants were recruited through intensified case detection within secondary mental-health clinical services and in the general population. Detailed descriptions of the intensified case detection, including awareness campaigns and a no-threshold referral telephone and recruitment and treatment package, have been published elsewhere (Joa et al., 2021). In addition to baseline assessment, participants were offered 12 structured follow-up assessments over a two-year period. In the first year, they were also offered psychotherapy, family psychoeducational groups, and unsaturated fatty acids. Anti-anxiety agents and antidepressants were available if indicated, and antipsychotic medication could be offered if the participant either entered the study with any SIPS positive symptom score of 5 or if any positive SIPS symptom score(s) moved from 3 or 4 to 5 (Joa et al., 2021). All participants provided written informed consent, and POP was approved by the Regional Committee for Medical Research Ethics Health Region West, Norway (2009/949).

In the present study, 141 participants were eligible for inclusion, and 104 of these gave informed consent. Of those, eight (7.4%) were excluded due to missing data on the main output variable: conversion to psychosis over a two-year follow-up (detailed below). Thus, 96 participants were included in the baseline descriptive statistics (Table 1) and in the statistical models (Tables 2 and 3). These models constitute a second step of a three-step investigation of items predictive of psychosis transition. The first step, an a-theoretical machine learning exploration has previously been published (Bjornestad et al., 2021). In the current study, we use the same data set to test the hypothesis derived from these analyses using conventional statistical methods (see also "statistical analyses"). Due to variations in

TABLE 1. The Distribution of Converted to Psychosis across Age, Gender, N3 and Other Key Predictors at Baseline

		Converted to psychosis			
Continuous variables		**No**	**Yes**	**N**	**Difference**
Age, in years	Mean (SD) n	17.0 (3.06) 77	16.5 (2.98) 19	96	p = .49
		Converted to psychosis			
Categorical variables		No	Yes	N	Difference
Gender	Male	84.1%	15.9%	44	p = .38*
	Female	76.9%	23.1%	52	
N3 Expression of Emotion	= 0	93.6%	6.4%	47	p < .001**
	> 0	62.8%	37.2%	43	
P1 Unusual Thought Content/Delusional Ideas	0– 3	75.0%	25.0%	56	p = .15**
	4– 6	86.1%	13.9%	36	
P2 Suspiciousness/Persecutory Ideas	0– 3	81.3%	18.8%	64	p = .55*
	4– 6	75.9%	24.1%	29	
P3 Grandiosity Perceptual	0– 3	79.4%	20.7%	92	p = .80**
	4– 6	100%	0%	1	
P4 Abnormalities/Hallucinations	0– 3	82.1%	17.9%	28	p = .46**
	4– 6	78.5%	21.5%	65	
P5 Disorganized Communication	0– 3	78.7%	21.4%	89	p = .39**
	4– 6	100.0%	0.0%	4	

* Chi-square
** One-sided Fisher's exact

missing data on each follow-up, the sample size is detailed in each of the tables and figures. Participants converting to psychosis were excluded from the study at the time of conversion and offered inclusion in the Early Treatment and Intervention in Psychosis-2 (TIPS 2) study (Joa et al., 2008). As only baseline predictors were used in this study, conversion to psychosis did not cause attrition. However, attrition analysis on the same sample (Bjornestad et al., 2021) revealed no significant association between attrition and age, gender, or SIPS subscales at baseline. Thus, attrition appears to be random, which in this study is important with regard to the longitudinally designed outcome variable: conversion to psychosis.

CHR-P Inclusion and Exclusion Criteria

Individuals included in the POP study met the following criteria: living in the catchment area; aged 13–65 years; meeting diagnostic criteria for CHR-P based on the Structured Interview for Prodromal Syndromes (SIPS) (Miller et al., 1999); symptoms that were not better accounted for by an Axis I, Axis II, or substance use disorder, based on the SCID I interview (First et al., 1995), with the exception of schizotypal personality disorder (the presence of any of these disorders in itself was not an automatic reason for exclusion); understanding and speaking one of the Scandinavian languages; and being able to provide informed consent. Participants under the age of 16 years also had to have consent from parents or guardians.

Individuals were excluded based on the following criteria: meeting current or lifetime criteria for any psychotic disorder; currently using any antipsychotic medication; use of antipsychotic medication (regardless of dosage) for more than four weeks in their lifetime; known neurological or endocrine disorders related to CHR-P symptoms; and low intellectual ability.

Measures

The SIPS is a 19-item semi-structured interview targeting experiences of attenuated symptoms and other indicators of psychosis risk (Miller et al., 1999). The SIPS subscales include positive (five items), negative (six items), disorganisational (four items), and general/affective (four items) symptoms (see Supplementary material for details on SIPS symptoms). Only the positive symptom scale defines psychosis risk. The SIPS identifies three clinical high-risk syndromes: the Attenuated Positive Symptoms (APS) syndrome, the Brief Limited Intermittent Psychotic Symptoms (BLIPS) syndrome, and the Genetic Risk and/or the Deterioration (GRD) syndrome (Yung & McGorry, 1996). Symptom severity (item scores) are rated on a Likert scale and determined based on interviewers' observations and/or interviewee self-report. In the POP study, SIPS interviews were administered 13 times over two years. Only baseline predictors and psychosis conversion across all waves were used in this study.

Procedure

Psychiatric nurses trained in interviewing for psychosis spectrum disorders conducted the SIPS interviews. Trained clinical researchers conducted the Structured Clinical Interview for the DSM-IV (SCID) for the purpose of diagnosis (First et al., 1995). Consensus on the CHR-P state was reached during weekly diagnostic meetings. The reliability of the SCID in the research group was satisfactory at kappa = .90 in 2012 (Weibell et al., 2013). Regular reliability trainings were undertaken to avoid drift.

Predictors

On the basis of the previously described decision-tree study (Bjornestad et al., 2021), the sample was split between participants scoring zero and participants scoring above zero on baseline reduced expression of emotion (N3). Although this entailed including scores that are considered to be subthreshold for clinical significance on this item, the machine-learning study (Bjornestad et al., 2021) found that zero was a more suitable cutoff. Hence, baseline reduced expression of emotion was operationalized as a single dichotomous variable based on the cutoff from the machine-learning study: (0 = a score of zero on baseline N3, 1 = a score above zero on baseline N3). N3 was also used to make a categorical variable (0 = zero at baseline N3, 1 = 1 or 2 at baseline N3, 2 = 3 through 6 on baseline N3), which was used in a dose–response analysis (Table 3).

Age and gender were reported at inclusion and were included in the descriptive statistics (Table 1). As only the positive symptom items are used to define psychosis risk (detailed below), only these five SIPS items were included in the analysis (Miller et al., 1999). All five positive SIPS items were operationalized as dichotomous variables (0 = scores of 0 through 3, and 1 = scores of 4 through 6), which were used in the ANOVA analyses (Table 1). As not all of the positive symptoms at baseline were part of the decision-tree model, we chose to use the common cutoff for clinical significance (score above 3) by dichotomizing all the positive symptoms. In the logistic regression model (Table 2), P1 through P5 full-item scores were used.

Outcome Measure – Psychosis Conversion

Conversion to psychosis was defined as scoring 6 or above on one or more of the items P1–P5 (in the SIPS), indicating a "severe and psychotic" level of intensity of symptoms. Conversion to psychosis was operationalized as a single dichotomous variable (0 = not converted, 1 = converted).

TABLE 2. Associations between Conversion to Psychosis and Positive Symptoms and N3, in Odds Ratios

	Model 1: all positive symptoms and N3, n = 89			Model 2: only significant from model 1, n = 90		
	Odds ratio	p	95% Conf. interval	Odds ratio	p	95% Conf. interval
N3	9.72	0.001	2.45– 38.53	8.69	0.001	2.31– 32.63
P1	0.80	0.240	0.55– 1.16			
P2	1.02	0.924	0.71– 1.45			
P3	1.02	0.964	0.51– 2.04			
P4	1.38	0.145	0.89– 2.14			
P5	1.12	0.612	0.73– 1.71			

TABLE 3. Dose–response Associations between Level of Symptoms on N3 and Conversion to Psychosis

N3 scores	Odds ratio for conversion	p	95% Conf. interval
0	Reference	-	-
1– 2	8.00	0.004	1.52– 42.23
3– 6	9.17	0.001	1.94– 43.26
		χ^2	p
Test of homogeneity (equal odds)		12.73	0.002
Score test for trend of odds		11.40	0.001

Statistical Analyses

Statistical analyses were performed in STATA, version 15.1. First, a two-way analysis of variance (ANOVA) was performed, examining the distribution of gender, age group, N3 and positive symptoms across the dichotomous conversion variable (Table 1). Differences between groups (converted/non-converted) were estimated using chi-square tests when all cells were above five; for the remaining cells we used Fisher's exact test (detailed in Table 1). Second, logistic regression analyses with conversion to psychosis as the outcome were performed. These were performed stepwise, first including all predictors (dichotomous N3 and five continuous positive items) (Table 2, left column) and then including only significant predictors (dichotomous N3) (Table 2, right column). Finally, a dose–response analysis was performed of the association between different levels of N3 and conversion to psychosis (Table 3).

RESULTS

Of the 96 participants, 19 (19.8%) converted to psychosis (Table 1). Background analyses indicated no significant association between conversion to psychosis and age or gender (Table 1). 37.2% of participants with an N3 score above zero at baseline converted to psychosis during the two-year follow up ($\chi 2 = 12.81$, df = 1, $p < .001$). Of the participants scoring zero, only 6.4% converted to psychosis during the two-year follow-up ($\chi 2 = 12.81$, df = 1, $p < .001$). None of the positive symptoms (P1–P5) were associated with conversion to psychosis (Table 1).

The logistic regression model also showed that none of the positive symptoms were associated with conversion to psychosis (Table 2, left column). Hence, these were omitted from the final model (Table 2, right column). Participants with an N3 score above zero had over eight times the odds of conversion to psychosis (OR = 8.69, 95% CI = 2.31– 32.63, $p < .001$).

There was a significant dose–response association between N3 scores and conversion to psychosis (Table 3). With an N3 score at baseline of zero as reference, participants with scores of 1 or 2 had eight times the chance of conversion to psychosis (OR = 8.00, 95% CI = 1.52–42.23, $p < .05$). Participants with an N3 score of 3 to 6 had over nine times the chance of conversion to psychosis (OR =

9.17, 95% CI = 1.94– 43.26, $p < .05$). The test of homogeneity ($\chi^2 = 12.73$, $p < .05$) indicates that the odds of conversion to psychosis differ by level of N3 symptoms (Table 3). The test for trend ($\chi^2 = 11.40$, $p < .05$) indicates a significant increase in odds for psychosis conversion with increasing levels of symptoms on N3 (Table 3).

DISCUSSION

The main finding of this study is that reduced expression of emotion at study inclusion statistically predicted conversion to psychosis in a CHR-P sample, whereas positive symptoms lost their predictive power when combined with this symptom. Furthermore, a score on this single item yielded odds of conversion that were over eight times higher. A score above three was associated with over nine times the odds. This indicates a dose–response association of severity of this symptom with conversion risk. The findings are in line with those from a previous machine-learning study (Bjornestad et al., 2021).

Reduced Expression of Emotion as Vulnerability to Adverse Outcomes

Across cultures, relationship formation is grounded in norms of acceptability and based on reciprocity and prosocial emotional expressions. Most individuals will react with discomfort, avoidance or social exclusion when confronted with emotional expressions that depart from the ruling social norms (Becker, 1963; Ekman, 1993; Ekman & Friesen, 1982; Ekman et al., 1987; Ekman & Keltner, 1997). Social participation is an arena for the practice and development of core human capacities such as self-agency (Bandura, 1982; Frith, 2014; Jeannerod, 2009) and mentalization (Fonagy & Bateman, 2006). Reduced expression of emotion could lead to a negative capability feedback (Schunk et al., 1987): it may remind the individual of their social skill limitations and their decreased agency (Frith, 2014) and social motivation (Lee et al., 2019) and it may negatively affect their future social involvement.

Furthermore, reduced expression of emotion in CHR-P may be an early precursor of negative symptoms. There are similarities between it and the symptom profiles seen in the development of more severe and insidious psychotic disorders such as schizophrenia (Bortolon et al., 2015; Earls et al., 2016), which are characterized by negative symptoms and poorer social functioning. These are well-known poor prognostic factors (Marder & Galderisi, 2017; Piskulic et al., 2012). Recent research in CHR-P on difficulties with recognition of facial emotion aligns with this notion, suggesting a specific deficit in the structural encoding of faces rather than a general perceptual deficit (Osborne et al., 2021). As in psychosis, social challenges in CHR-P are the long-term vulnerability factors connected to adverse social and psychological outcomes (Addington et al., 2017; Addington et al., 2019; Webb et al., 2015; De Wit et al., 2014).

Our finding indicates that reduced expression of emotion may serve as an addition to the current criteria defining CHR-P, adding specificity and predictive power to both the "psychosis risk calculator" prediction framework (Cannon et al., 2016) and the CHR-P criteria. It may serve as a red flag, signaling an increased risk of psychosis in those identified as CHR-P.

Reduced Expression of Emotion as a Detectable Symptom of Conversion Risk

Reduced expression of emotion, particularly facial affect recognition, offers a distinct opportunity for the detection of conversion risk (Pelletier-Baldelli & Holt, 2019). Behavioral change—e.g., from a state of normal affect to affective flattening—is detectable even without verbal interaction and, in many cases, from

a physical distance. Furthermore, the symptom is overtly observable by non-clinicians, including peers, family and teachers, which suggests this symptom can be a target of early CHR-P detection strategies. Assessments can even be made using Internet-based technologies, as has proven necessary during the recent pandemic. Mental health workers with no special training would be able to recognize it and refer the individual to CHR-P or early psychosis services for further evaluation. These features could help improve detection strategies.

LIMITATIONS

The primary limitations of this study are attrition rate and small sample size. These represent a loss of valuable information and may weaken the study's generalizability. However, we found no differences in baseline characteristics between completers and drop-outs. Attrition thus appears to be random, and the sample can be assumed to be representative regarding baseline characteristics (Bjornestad et al., 2021). The limited model fit ("fair") and wide confidence intervals may be attributable to the small sample size. The study findings need replication in larger representative samples. Finally, on a more general note, the main inclusion criterion for most CHR studies, including this one, is elevated positive symptom scores. This limits variability and may reduce statistical power; however, it also underscores the main message of this study, being that the inclusion of negative symptoms as part of CHR should be considered.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available because according to Norwegian law, data sharing requires approvals from the Regional Committees for Medical and Health Research Ethics, and from the Data Protection Officer at Stavanger University Hospital, on the basis of specific research proposals. Requests to access the datasets should be directed to jone.r.bjornestad@uis.no

DISCLOSURE STATEMENT

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SUPPLEMENTARY MATERIAL

Supplemental data for this article can be accessed on the publisher's website.

ORCID

Tore Tjora http://orcid.org/0000-0002-4024-2288

Wenche Ten Velden Hegelstad http://orcid.org/0000-0003-1148-8825

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