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The temporal association between social isolation, distress, and psychotic experiences in individuals at clinical high-risk for psychosis

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Abstract

Background. Psychotic experiences (PEs) and social isolation (SI) seem related during early stages of psychosis, but the temporal dynamics between the two are not clear. Literature so far suggests a self-perpetuating cycle wherein momentary increases in PEs lead to social withdrawal, which, subsequently, triggers PEs at a next point in time, especially when SI is associated with increased distress. The current study investigated the daily-life temporal associations between SI and PEs, as well as the role of SI-related and general affective distress in individuals at clinical high risk (CHR) for psychosis.

Methods. We used experience sampling methodology in a sample of 137 CHR participants. We analyzed the association between SI, PEs, and distress using time-lagged linear mixed-effects models.

Results. SI did not predict next-moment fluctuations in PEs, or *vice versa*. Furthermore, although SI-related distress was not predictive of subsequent PEs, general affective distress during SI was a robust predictor of next-moment PEs.

Conclusions. Our results suggest that SI and PEs are not directly related on a moment-to-moment level, but a negative emotional state when alone does contribute to the risk of PEs. These findings highlight the role of affective wellbeing during early-stage psychosis development.

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Introduction

It is estimated that less than 1% of the global population will be diagnosed with a psychotic disorder during their lifetime (Moreno-Küstner, Martín, & Pastor, 2018). This is in contrast to psychotic experiences (PEs), commonly conceptualized as subthreshold manifestations of hallucinations and delusions (Yung & Lin, 2016). While psychosis also includes negative symptoms (Correll & Schooler, 2020), the current study mostly focuses on subclinical manifestations of positive and disorganized symptoms. PEs are much more prevalent than psychotic disorders, occurring in about 5.8–7.2% of individuals worldwide (Linscott & van Os, 2013; McGrath et al., 2015). Intermittent and subclinical expressions of psychosis often occur outside of a clinical diagnosis (Fusar-Poli et al., 2013; Guloksuz et al., 2020), but they are associated with increased risk for developing a psychotic disorder later on (Linscott & van Os, 2013). The prevalence of subclinical PEs whereby individuals do experience significant distress and functional inhibition is estimated to be around 4% (Van Os, Linscott, Myin-Germeys, Delespaul, & Krabbendam, 2009). Individuals that seek help for these experiences are often considered to be at clinical high risk (CHR) for psychosis (Fusar-Poli, 2017). As the term CHR implies, these individuals face a higher risk of developing a psychotic disorder later in life, but their experiences do not yet meet the threshold for a psychotic disorder (Fusar-Poli, 2017). Investigating the occurrence of PEs in early stages of psychosis, particularly in CHR individuals, could provide valuable insight into the course of psychosis development. Research suggests that social isolation (SI) may be one of the early markers of psychosis development (Gayer-Anderson & Morgan, 2013; Velthorst et al., 2009).

SI is common in people with psychotic disorders. In comparison to individuals without psychosis, their social networks tend to be smaller (Stain et al., 2012), they have fewer close friends (Erickson, Beiser, Iacono, Fleming, & Lin, 1989; Giacco et al., 2012), and experience difficulty maintaining relationships with friends and family (Macdonald, Sauer, Howie, & Albiston, 2009). Even though they report similar enjoyment during social situations, individuals with psychosis appear more likely to feel stress and prefer to be alone when in company (Mote & Fulford, 2020). Their relative SI also corresponds to affective distress; often feeling unsupported by others (Sündermann, Onwumere, Kane, Morgan, & Kuipers, 2014) while also desiring more social contact (Tee et al., 2022).

Importantly, these objective and affective components of SI can already be identified at the lower end of the psychosis continuum. Specifically, individuals at CHR for psychosis report smaller social networks and fewer close friends compared to typical individuals (Robustelli, Newberry, Whisman, & Mittal, 2017). They also interact less with other people compared to controls, despite their intact ability to enjoy social interactions (Hermans et al., 2021). CHR individuals experience more subjective isolation: they feel less supported by others, less satisfied with their relationships with family and friends, and more lonely than typical individuals (Robustelli et al., 2017).

Some authors have suggested that SI in psychosis stems from the loss of contact with others due to psychiatric residential care (Lipton, Cohen, Fischer, & Katz, 1981). However, the observed SI at the CHR stage suggests that social problems have already arisen prior to an acute phase of illness. This may mean that SI already plays a role in the early development of PEs in CHR individuals. While SI during early-stage psychosis has often been documented (Gayer-Anderson & Morgan, 2013; Robustelli et al., 2017; Velthorst et al., 2009), the temporal dynamics between isolation and PEs at the moment-to-moment level remains unclear. The outstanding question is whether being alone precedes PEs, or whether PEs relate to more isolation at a subsequent moment in time. To understand how these short-term dynamics take place in everyday life, we need ecologically valid methodology that circumvents issues such as retrospective cognitive bias (Hassan, 2005). Experience sampling methodology (ESM) is suitable for this purpose. ESM, now a widely used assessment technique in mental health research, is a self-report diary technique that can capture fluctuations in internal states as they occur in daily life (Myin-Germeys et al., 2009, 2018; Myin-Germeys & Kuppens, 2022).

Previous ESM research in patients with long-term psychosis found that being in a familiar social context was associated with a decrease in delusional experiences at the next moment, while being alone was associated with an increase in subsequent delusional experiences (Myin-Germeys, Nicolson, & Delespaul, 2001a). However, a more recent study in individuals diagnosed with psychotic disorders, first-degree relatives of psychosis patients, and controls found that SI did not predict subsequent paranoia in any of the groups (Fett, Hanssen, Eemers, Peters, & Shergill, 2022). In this study also no association was found between paranoia and subsequent SI (Fett et al., 2022). Other research suggests there may be a self-perpetuating cycle wherein moments of increased PEs lead individuals to seek more solitude, limiting their social interactions, which in turn increases the occurrence and severity of PEs (Gayer-Anderson & Morgan, 2013). These conflicting findings show that it is unclear how SI and general PEs interact on a momentary level, especially in CHR populations.

Understanding the relationship between SI and early-stage PEs may also require studying individuals' affective state while alone (Lim & Gleeson, 2014). This is important, because while being alone may be pleasant, it may also be distressing (Hawkley & Cacioppo, 2010). It might therefore be relevant to investigate the potential difference between moments that individuals feel satisfied with being alone *v.* moments when they would prefer to have company. Distressing experiences of isolation may particularly relate to subsequent PEs, as stress is one of the largest environmental risk factors for psychosis, and stressful everyday situations have been associated with increased PEs in CHR individuals (Fusar-Poli et al., 2017; Myin-Germeys & van Os, 2007; Tessner, Mittal, & Walker, 2011). Furthermore, research suggests that minor daily stress also relates to PEs in an indirect way, namely through altered affective states (Klippel et al., 2018). Individuals vulnerable to psychosis show stronger affective responses to minor daily stress than typical individuals (Myin-Germeys & van Os, 2007), which might include unwanted SI. The idea is that changes in stress lead to increased negative affect, which, in turn, influences PEs, especially during early stages of psychosis (Klippel et al., 2018; van der Steen, 2018). The question arises as to which factors, stress related to being alone (solitary stress), or people's affective state (negative affect), predict subsequent PEs more accurately.

This study aims to investigate how SI and PEs are temporally related in individuals at CHR for psychosis. We also look at individuals' preference regarding being alone, defined here as solitary stress (SS), and negative affect (NA) when alone. Using ESM, we will test the following hypotheses: (I) momentary SI predicts subsequent PEs, (II) momentary intensity of PEs predicts subsequent

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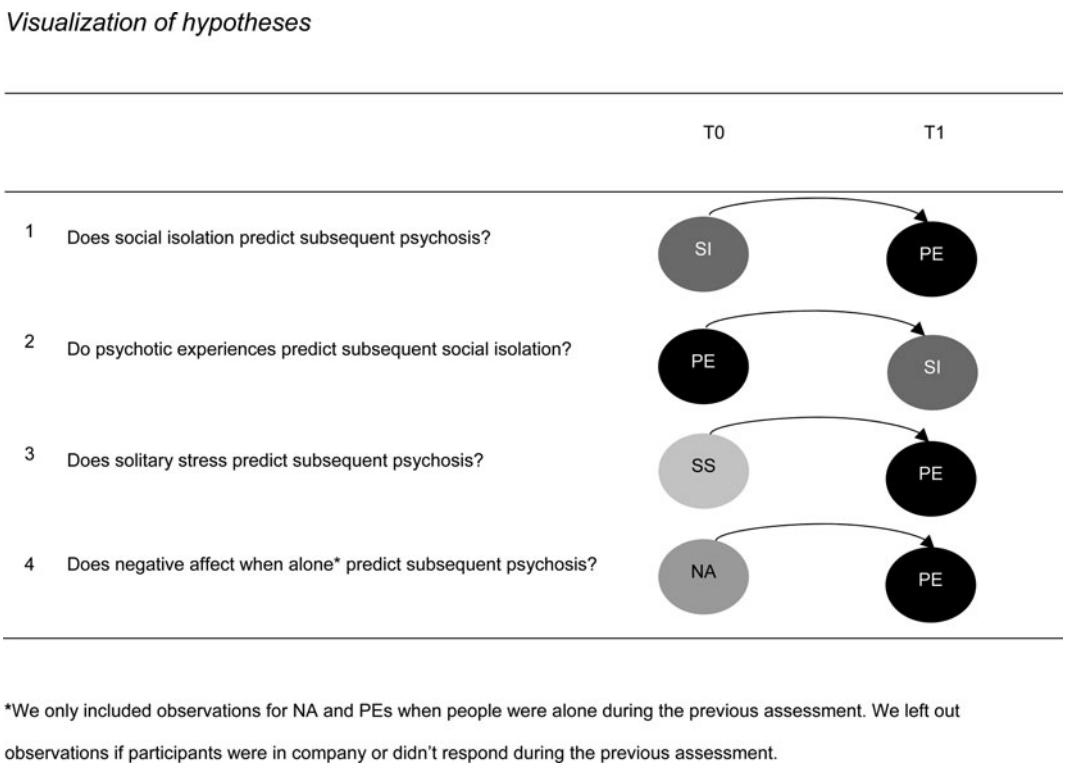

Figure 1. Visualization of hypotheses.

SI, (III) intensity of momentary SS predicts subsequent PEs, (IV) intensity of momentary NA when alone predicts subsequent PEs, and (V) explore whether SS or NA when alone is a more accurate predictor of subsequent PEs. The visualization of our hypotheses can be found in Fig. 1.

Method

This paper has not been pre-registered due to the frequent use of the two datasets previous to our paper, particularly the EU-GEI dataset. The data can be accessed through approval by the EU-GEI and INTERACT steering groups respectively, or by contacting the corresponding author.

Sample

This study combines data from the EU-GEI and INTERACT projects (EU-GEI, 2016; Myin-Germeys et al., 2022). The EU-GEI project is an international longitudinal study on the interaction between genetic, clinical, and environmental factors relating to schizophrenia (EU-GEI, 2016). All EU-GEI participants included in the present study resided in one of the following cities: Amsterdam, The Hague, London, or Melbourne. The sample consisted of 81 CHR participants, their age ranging from 15 to 35 years old. The inclusion criteria for CHR participants were based on the Comprehensive Assessment of At Risk Mental State (CAARMS) (Yung et al., 2005). The EU-GEI study protocol was approved by local Medical Ethics Committees of the three sites. Participants signed informed consent prior to assessments commencing. Participants were excluded if (1) they had a current or past psychotic disorder according to the CAARMS (Yung et al., 2005) and Structured Clinical Interview for DSM Disorders (SCID) (First, Gibbon, & Williams, 2002), (2) their psychotic symptoms could be explained by a medical disorder or substance use, or (3) their IQ scores were below 60, as assessed through a short version of the Wechsler Adult Intelligence Scale (WAIS) (Ryan, Weilage, & Spaulding, 1999; Ward, 1990).

The INTERACT study is a multi-center randomized controlled trial investigating the efficacy of Acceptance and Commitment Therapy (ACT) in Daily Life during early psychosis (Myin-Germeys et al., 2022). Participants were individuals at CHR or first-episode psychosis patients (FEP). We included baseline ESM data from the 96 CHR participants. We left out FEP participants due to possible medication effects. Participants were referred to the INTERACT study by various institutions across the Netherlands and Flanders in Belgium. The inclusion criteria for CHR participants were (1) being between 15 and 46 years old, (2) being at high-risk for psychosis (with no use beforehand of antipsychotic medication) as measured by the CAARMS (Yung et al., 2005), (3) adequate command of the Dutch language, and (4) being able to sign informed consent. Participants were excluded if they had a primary diagnosis of alcohol/substance abuse according to the Mini-International Neuropsychiatric Interview (Sheehan et al., 1998), or a severe brain, endocrine, or cardiovascular disease. The INTERACT study was approved by the MERC at Maastricht University Medical Centre, the Netherlands and the University Clinic Leuven, Belgium (Reininghaus et al., 2019).

ESM

ESM procedure

Over a period of 6 consecutive days, 10 'beep' signals per day were emitted by the PsyMate™ app (https://www.psymate.eu/), indicating an ESM assessment (Verhagen et al., 2017). However, INTERACT participants who did not answer at least 20 beeps (i.e. 33%) by the end of this period were asked to continue the

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assessment until they did, meaning that some participants answered beeps for more than 6 days. Stratified random sampling was used, scheduling ESM questionnaires randomly within time blocks of 90 min, with responses being required within 15 min of the beep. The time interval between beeps ranged from 15 to 180 min. To control for the difference in data collection duration between the two datasets, we only looked at a subsample of 6 days for each INTERACT participant (the same period as with the EU-GEI dataset). For each participant, we selected the 6 days wherein they answered beeps most frequently. This left out 530 observations.

ESM measures

The EU-GEI study's London and Melbourne sites used English items, and the INTERACT study and the EU-GEI study's Amsterdam and The Hague sites used the Dutch version of the same items. For the reliability of our scales, we used Cronbach's α to measure the internal consistency of each variable both within and between subjects. Cronbach's α assesses internal consistency by comparing the covariance of items for each variable with the overall variance of that variable.

Psychotic experiences: we had seven items measuring PEs, including 'I feel unreal', 'I hear things that aren't really there', 'I see things that aren't really there', 'I feel paranoid', 'I can't get these thoughts out of my head', 'It's hard to express my thoughts into words', and 'my thoughts are influenced by others'. Participants could respond on a 7-point Likert scale that ranged from 1 ('not at all') to 7 ('very much'). Next, we calculated the mean across the seven items on a beep level. We used Cronbach's α to calculate the reliability of our items, resulting in a within-subject internal consistency of 0.69, and a between-person consistency of 0.83.

Social isolation: we assessed whether people were alone through the item 'Who are you with?'. Participants answered one of the following: 'nobody', 'partner', 'friends', 'family resident', 'family non-resident', 'colleagues', 'acquaintances', 'strangers/others'. We recoded the responses into a binary item where 0 indicated people were alone, 1 indicated they had company.

Solitary stress: based on previous research into stress in social contexts, we sub-selected items specifically related to being alone unwillingly (Reininghaus et al., 2016). We asked participants that were alone to rate their isolation through following two items: 'I would prefer to have company' and 'I find it pleasant to be alone'. Participants could answer the items through a 7-point Likert scale that ranged from 1 ('not at all') to 7 ('very much'). We used reverse coding for the second item and calculated the mean score of the two items to assess SS in daily life. The within-subject internal consistency was 0.50, the between-person consistency was 0.71.

Negative affect: we assessed NA with five items, including 'I feel insecure', 'I feel down', 'I feel lonely', 'I feel anxious', and 'I feel annoyed'. The items were rated on a 7-point Likert scale ranging from 1 ('not at all') to 7 ('very much'). We calculated the mean score for these items to assess NA in daily life. The within-subject internal consistency was 0.72, and the between-person consistency was 0.83.

Statistical analysis

All reported analyses were conducted in Stata 14.2 except for the last hypothesis, which, due to its complexity, we conducted in R version 4.0.5 using the lme4 package. We used a different platform for the last hypothesis comparing the predictive accuracy of SS and NA, since the resources used for writing the code were only available in R. A visualization of the hypotheses can be found in Fig. 1. ESM data have a multilevel structure, whereby each participant provides multiple observations. We investigated whether lagged values of SI, preference regarding being alone or SS and NA when alone predicted subsequent PEs (hypotheses 1, 3, and 4 respectively) using multilevel linear regression models, which account for within-subject and within-day clustering of repeated observations. We used multilevel mixed-effects logistic regression to look at whether lagged PEs predict the odds of subsequent SI (hypothesis 2). We person-mean centered the continuous predictors PEs, SS, and NA (hypotheses 2, 3, and 4 respectively). We accounted for autocorrelation of the outcome variable PE by looking at the autocorrelation of the residuals.

We added random intercepts and slopes to the model, and assumed all within-person errors to be identically distributed for parsimony. We used a maximum-likelihood estimation to use all available data, assuming data are missing at random and that the model encompasses all possible related variables. In line with previous research, we controlled for the potential confounders age, gender, and race (Hermans et al., 2021; Rauschenberg et al., 2017).

We used blocked cross-validation to compare SS and NA as predictors of subsequent psychosis (Bulteel, Mestdagh, Tuerlinckx, & Ceulemans, 2018; Lafit, Meers, & Ceulemans, 2021)[†1]. Blocked cross-validation takes into account the time series structure of the data, dividing data into sets of consecutive observations (Lafit et al., 2021). It takes those sets or blocks of consecutive data points to train and test a certain model. Each block is used as a test set, whereas the remaining K–1 blocks serve as a training set. We created 10 blocks of observations: nine to train and one to test the model. The process was repeated so each block of data was used once as a test set. Then we compared the results of each run, calculating how accurately the model predicted the outcomes. We first investigated the predictive accuracy of the model whereby SS, age, gender, and race predicted subsequent PEs. We also added random intercepts to account for interpersonal differences in the outcome. We then computed the mean squared prediction error (MSPE) and its standard deviation to look at how much of the outcome was not predicted by our model. After we ran the model for SS, we repeated the same process with NA as a predictor. Finally, we compared the two models to see which one had the lowest MSPE, thereby inferring which one predicted unseen data better.

Results

Sample characteristics

We removed participants that responded to less than a third of beeps or that provided no demographic information. This excluded 38 participants from the INTERACT sample and two from the EU-GEI sample. Our final sample consisted of 137 CHR participants (79 from EU-GEI, 58 from INTERACT). The supplementary materials contain an overview of between-group differences between the final sample and participants that were excluded due to low compliance (online Supplementary Table S1). There was a significant difference in gender distribution ($p = 0.006$), with included participants being mostly female ($n = 80$, 58.4%) while excluded participants were mostly male ($n = 29$, 65.9%).

An overview of the sample characteristics and comparisons between the datasets can be found in online Supplementary

[†]The notes appear after the main text.

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Table S2. We found significant differences between the two studies regarding race, Global Assessment of Functioning (GAF) disability scores (Hall, 1995), and compliance, with individuals in the EU-GEI study being more racially diverse, having higher disability scores and higher compliance. We also assessed whether we should control for differences between our two datasets based on our main variables. We added 'study' as a fixed effect to each model. We also assessed the value of 'study' as a random effect through the intra-class correlation (ICC) (online Supplementary Table S3). We initially wanted to conduct a log-likelihood ratio test, but received error messages where the degrees of freedom remained the same, implying that the added random effect had no effect in the model. The ICC, which measures the variance explained by study, was close to zero for each model, meaning there was no significant improvement when adding it to the analysis. We therefore left out 'study' as a confounder variable.

Momentary SI does not predict subsequent PEs or vice versa

We found neither a significant association between SI and subsequent PEs (Table 1), nor between PEs and subsequent SI (Table 1). A full overview including covariates and random effects can be found in supplementary materials, with online Supplementary Table S4 detailing the SI predictor model and online Supplementary Table S5 the PEs predictor model. We therefore could not conclude that SI and PEs are temporally related in these studies.

Momentary solitary stress does not predict subsequent PEs

There was also no significant association between SS and subsequent PEs (Table 1), meaning dissatisfaction with current lack of company did not appear to precede PEs. A full overview of the analysis, including covariates and random effects, can be found in online Supplementary Table S6.

Momentary negative affect when alone does predict subsequent PEs

NA when alone did appear to be predictive of subsequent PEs (Table 1). A full overview of the analysis, including covariates and random effects, can be found in online Supplementary Table S7. An example of how we selected data for this analysis can be found in online Supplementary Table S8 as well.

Table 1. The momentary association between social isolation (SI), solitary stress (SS), negative affect when alone (NA), and psychotic experiences (PEs)

	PEs (t0)			
	B (s.e.)	95% CI	*p*	Ppn (obs)
SI (t-1)	−0.02 (0.03)	−0.08 to 0.04	0.551	135 (2943)
SS(t-1)	0.02 (0.02)	−0.01 to 0.06	0.200	130 (1231)
NA (t-1)	0.13 (0.03)	0.08 to 0.21	>0.001**	130 (1233)
	SI (t0)			
	B (s.e.)	95% CI	*p*	Ppn (obs)
PEs (t-1)	0.08 (0.07)	−0.05 to 0.21	0.225	135 (2939)

PEs, psychotic experiences; SI, social isolation; SS, solitary stress; NA, negative affect when alone; B, unstandardized point estimate; s.e., standard error; CI, confidence interval; Ppn, participants; obs, observations.
Gender: men as dummy variable; race: white as dummy variable; study: EU-GEI dataset as dummy variable.
**>0.001.

Negative affect predicts subsequent PEs more accurately than solitary stress

We compared NA when alone and SS as predictors of subsequent PEs using K-blocked cross-validation. The NA model has the lowest MSPE and standard deviation, meaning NA had a better predictive accuracy than SS for subsequent PEs (Table 2).

Post-hoc analysis

In the current paper, we found no association between SI and PEs on a moment-to-moment basis. We therefore conducted a post-hoc multilevel mixed-effects linear regression analysis to investigate whether SI predicted PEs in the moment itself, with random slopes and intercepts, and an unstructured variance–covariance matrix.

We found no significant association between SI (being either alone or in company) and concurrent PEs (Table 3).

Discussion

We investigated the momentary dynamics between SI, PEs, and the role of stress in CHR individuals. We found no direct influence of SI on subsequent PEs or *vice versa*. This means, on a momentary level, we found no support for the self-perpetuating hypothesis between PEs and SI (Gayer-Anderson & Morgan, 2013). We also found no association between SS and subsequent PEs, but high NA when alone did strongly predict PEs at a next time point. These findings underscore the importance of NA in psychosis proneness (Betz et al., 2020; van Os et al., 2022).

The temporal interplay between social isolation and psychotic experiences

Despite previous studies showing an overall association between psychosis and SI (Gayer-Anderson & Morgan, 2013), we did not find such association on a momentary level within an at-risk sample. Aligning with previous research (Fett et al., 2022), our findings indicate that, on a momentary level, being alone does not influence the occurrence of PEs in CHR individuals. Surprisingly, we also found no association between SI and PEs within the same moment, which is in contrast with a prior study into a clinical sample that showed that patients report more PEs when alone compared to when they are in company (Fett et al., 2022). These differing findings may be explained by the type of symptoms being investigated and the stage of psychosis development.

Table 2. Comparing the predictive accuracy of negative affect and solitary stress

	MSPE	MSPE.sd
SS	2.78	0.64
NA	0.61	0.16

SS, solitary stress; NA, negative affect; MSPE, mean squared prediction error; MSPE.sd, mean squared prediction error standard deviation.

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Table 3. The concurrent association between SI and PEs

	PEs			
	B (s.e.)	95% CI	*P*	Ppn (obs)
SI	−0.03 (0.03)	−0.08 to 0.02	0.220	137 (4494)
Study	0.10 (0.17)	−0.22 to 0.43	0.535	137 (4494)
Age	−0.04 (0.02)	−0.07 to −0.01	0.022*	137 (4494)
Gender (f)	0.23 (0.16)	−0.09 to 0.54	0.157	137 (4494)
Race (Black)	0.51 (0.26)	−0.01 to 1.01	0.045	137 (4494)
Race (Asian)	−0.08 (0.55)	−1.16 to 1.01	0.892	137 (4494)
Race (other)	0.04 (0.26)	−0.47 to 0.54	0.881	137 (4494)

PEs, psychotic experiences; SI, social isolation; B, unstandardized point estimate; s.e., standard error; CI, confidence interval; Ppn, participants; obs, observations.
Gender: men as dummy variable; race: white as dummy variable; study: EU-GEI dataset as dummy variable.

A possible explanation for the discrepancy between the current study's and previous findings relates to the kind of PEs being investigated. Fett et al. (2022) specifically investigated paranoia, whereas our study focused on various kinds of mostly positive PEs taken together (including hallucinations and non-paranoid delusional experiences). Research indicates that being in company influences vigilance; individuals are less likely to monitor and detect threats when in the presence of others (Gomes & Semin, 2020). Similarly, paranoid individuals may be more likely to isolate to feel safer, thereby missing out on benevolent social interactions that could challenge or distract from the idea of being under threat (Fett et al., 2022; Freeman, 2007). As a result, paranoid experiences may relate more strongly to SI compared to other PEs. Our study found no momentary association between SI and general PEs, but the relationship may differ for specific symptoms such as paranoia.

Aligning with other research, we also found no moment-to-moment association between PEs and subsequent SI (Fett et al., 2022). This finding does not support the hypothesis that CHR individuals tend to withdraw after experiencing PEs. Reduced social contact may thus not be an inherent part of momentary fluctuations in psychosis proneness. Instead, increases in SI could reflect a lack of opportunity for social interaction (Kasanova, Oorschot, & Myin-Germeys, 2018). For example, people with PEs may have less chances to interact with others through employment, since stigma and/or systemic barriers could make workplaces inaccessible (Hampson, 2014). After all, it appears that the ability to enjoy social interactions is intact during early stages of psychosis, including the CHR state (Hermans et al., 2021), yet people with psychosis show reduced anticipation and initiative toward pleasurable activities (Marder & Galderisi, 2017). They also experience a reduction in support and contact with existing relationships during subclinical stages of psychosis (Gayer-Anderson & Morgan, 2013). In that case, PEs may not relate to immediate changes in social behavior, but more to widespread, sustained, and often external difficulties in people's social life.

An alternative explanation for the discrepancy between our findings at other literature refers to the stage of psychosis development being investigated. Previous findings from ESM studies report a difference between clinical and non-clinical populations. Fett et al. (2022) found a positive association between PEs and SI in patients with non-affective psychotic disorders. Similar to other ESM studies (Krijnen, Lemmers-Jansen, Fett, & Krabbendam, 2021; Verdoux, Husky, Tournier, Sorbara, & Swendsen, 2003), they found no association in non-clinical populations (Fett et al., 2022). These contrasting findings suggest that the association between PEs and SI develops with illness progression, possibly as a result of individuals learning to recognize early signals of PEs, triggering them to withdraw. This means our findings regarding the lack of momentary association between SI and PEs may be specific to CHR individuals and cannot be generalized across the psychosis spectrum.

Finally, the lack of momentary association does not rule out an association between SI and the occurrence of PEs. We measured SI's predictive value on a moment-to-moment basis, over a 90 min time-interval. Other time-intervals could lead to different findings. For example, the influence of SI might take place over a few hours or even a day. In that case, we wouldn't have an association on a moment-to-moment level, but on a micro time-scale nonetheless. There is therefore need for more research into SI and PEs over different time intervals.

Distress-related predictors of subsequent psychotic experiences

According to our findings, being alone and dissatisfied, previously conceptualized as part of social stress (Reininghaus et al., 2016) and called SS in our study, does not predict an increase in PEs. This is a surprising finding, considering the vast amount of research linking stress to fluctuations in PEs (Myin-Germeys & van Os, 2007; Palmier-Claus, Dunn, & Lewis, 2012; Vaessen, 2018). The reason our results do not align with previous research into stress and PEs might relate to the low internal consistency of the SS variable (see 'ESM measures' section), which we discuss in detail below (see 'Limitations' section). However, the question arises which other factors might influence abovementioned relationship. A recent ESM study suggested that stress and PEs are associated through the mediating role of NA (Klippel et al., 2022). Our findings support this hypothesis, since NA when alone was a stronger predictor than SS of subsequent PE.

The results indicate that being alone in and of itself does not appear to increase the risk for PEs at a next point in time, but feeling negative while alone does. Importantly, emotional distress appears to increase the risk of consequent PEs regardless of social context (Kramer et al., 2014) or stage of psychosis development (Monsonet, Kwapil, & Barrantes-Vidal, 2022). Other ESM studies also highlight the role of affect by suggesting that it is not social contact in general, but particularly the presence of family or acquaintances that decreases the risk of subsequent PEs in patient samples (Myin-Germeys, van Os, Schwartz, Stone, & Delespaul, 2001b). Taken together, it appears that PEs do not relate directly to whether a person is alone or not, but to the affective quality of being alone/in company. This suggests that fluctuations in early PEs are not primarily related to being alone, but rather affect-driven. It therefore seems that, when aiming to reduce the chances of PEs occurring in the short term, the focus should be on improving affective wellbeing in social context, rather than increasing social interactions *per se*.

Limitations

Our study has a number of limitations. First, our ESM observations could be influenced by self-report biases, such as the tendency of participants to habitually choose extreme response options (Lima-Costa & Hauck-Filho, 2019). Nevertheless, ESM has been shown to be a valid and reliable assessment tool for research into

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early psychosis (Myin-Germeys et al., 2001a, 2001b; Myin-Germeys et al., 2009; Palmier-Claus et al., 2012). Second, ESM data collection can be intense and burdensome for participants. Our data may be skewed in favor of participants that were highly motivated and therefore responded to more prompts. Our comparison between the datasets shows that there is a significant difference in compliance (online Supplementary Table S2), with the INTERACT in particular struggling with initial low compliance. As a solution, participants that did not meet the required number of beeps during data collection were asked to answer prompts for longer than 6 days. In order to merge INTERACT with EU-GEI data, we selected the 6-day period with most responses for each INTERACT participant. This means the chosen periods may reflect times where participants had more time/motivation to answer prompts. Third, the internal consistency of our SS variable was relatively low. This means our assessment of unwanted SI could be improved, e.g. by improving items assessing individuals' subjective appraisal of SI. For now, there does not appear to be a consensus on how to operationalize subjective aspects of SI. We hope future studies will shed light on this issue. Lastly, there were also significant differences in GAF disability scores and racial diversity between the studies (online Supplementary Table S2). It may be possible that individuals with higher rates of disability and/or ethnic minority status experience more unwanted SI due to (internalized) stigma and discrimination (Hampson, Watt, & Hicks, 2020; Wong, Collins, Cerully, Seelam, & Roth, 2017). The role of SI and distress for early-stage PEs may then differ for these more vulnerable individuals.

Conclusion

Our study investigated the moment-to-moment association between SI, distress, and PEs in CHR individuals. We found neither a direct influence of SI on fluctuations in PEs, nor a direct influence of PEs on changes in SI. This means SI has no immediate role in the momentary occurrence of PEs in CHR individuals. However, more research is needed to look into the association between SI and specific PEs such as paranoia. We also looked at subjective experience and found that feeling distressed about SI did not relate to subsequent PEs. However, NA when alone did predict subsequent PEs. This means that CHR individuals who are alone and experience NA have a higher risk of developing PEs at a next time point. These findings highlight the proximal role of affective well-being in early-stage psychosis. It appears that it is not the state of being alone that relates to fluctuations in PEs, but rather how individuals are feeling when alone.

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Note

1 We didn't compare effect sizes of SS and NA due to the lack of a benchmark procedure to compute standardized effect sizes for multilevel models (Rights & Sterba, 2019).

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