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Impact of childhood adversity on the onset and course of subclinical psychosis symptoms — Results from a 30-year prospective community study

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ABSTRACT

The study objective was to examine childhood adversity in association with intra-individual changes and inter-individual differences in subclinical psychosis in a representative community cohort over a 30-year period of observation.

We analyzed two psychosis syndromes derived from the SCL-90-R – schizotypal signs and schizophrenia nuclear symptoms – in 335 participants. Participants were repeatedly assessed between 1978 (around age 20) and 2008 (around age 50). We focused specifically on inter-individual differences and intra-individual changes over time by applying structural equation modeling, generalized linear models, and generalized estimating equations.

Several weak inter-individual differences revealed that increased schizotypal signs are related to various childhood adversities, such as being repeatedly involved in fights and parents having severe conflicts among themselves. We also found a significant positive association between schizotypal signs and the total number of adversities a subject experienced. This pointed toward a modest dose–response relationship. The intra-individual change in schizotypal signs over time was rather weak, although some adjustment did occur. In contrast, inter-individual schizophrenia nuclear symptoms were mainly unrelated to childhood adversity. However, some striking intra-individual changes in distress were noted over time, especially those linked with severe punishment and the total adversity score.

In conclusion, we have confirmed previous positive findings about the association between childhood adversity and subsequent subclinical psychosis symptoms: An increase in adversity is weakly related to an increase of the psychosis symptom load. However, depending on the kind of adversity experienced the psychosis symptom load decreases gradually in adult life.

1. Introduction

How one's environment impacts the onset and course of schizophrenia has garnered longstanding interest within the field of psychiatry. Although at times the question of heritability has prevailed, much evidence has been found in the last two decades for factors that increase the risk of schizophrenia, in particular the effects of growing up in an urban setting, belonging to a minority group, or using cannabis (van Os et al., 2010).

Childhood adversity is another putative risk factor for schizophrenia (Read et al., 2005), but evidence for this has been inconsistent until recently (Morgan and Fisher, 2007). In light of several meta-analyses, i.e., case–control, prospective, and cross-sectional studies, childhood adversity was recently endorsed on a much broader empirical basis (Varese et al., 2012; Matheson et al., 2013). Such adversity also seems to be a risk factor for other psychiatric disorders (Angst et al., 2011; Hengartner et al., 2013a) including subclinical states in general and subclinical psychosis symptoms in particular (Kessler et al., 2010).

Keen interest is growing about subclinical psychosis, with research focusing on attenuated symptoms as part of programs for early recognition, psychosis prevention, and intervention. Subclinical symptoms are quite frequent in the general population (Scott et al., 2006; Rössler et al., 2007) as well as in socio-culturally different countries (Loch et al., 2011). A recent systematic review of 61 reported incidence and prevalence studies of population rates for those symptoms revealed a median prevalence rate of 7.2% and a median annual incidence rate of 2.5%, albeit with significant variation in those rates (Linscott and van Os, 2013).

We have previously assessed subclinical psychosis with higher-order syndromes, as derived from the SCL-90-R, in several independent

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community samples and populations (Rössler et al., 2007, 2011a, 2013a), and have especially relied upon data from the "Zurich Study" (Angst et al., 2005). Within that unique, small community sample, followed longitudinally over 30 years, we have identified subclinical psychosis syndromes with relevant distress and functional disability (Rössler et al., 2007). None of the participating individuals in that study developed a full-blown psychotic disorder (Rössler et al., 2013b). However, many participants with persistent subclinical psychosis syndromes were considered at risk of developing other mental disorders (Rössler et al., 2011b).

As mentioned above several investigations have already focused on the relationship between childhood adversity and psychosis, but no investigation could rely on such a long observational period after participants' exposure to childhood adversities. Thus, the aims of this study were 1) to detect associations of childhood adversity with intra-individual changes (i.e., within-subject effects) and inter-individual differences (between-subject effects) in subclinical psychosis syndromes and 2) to analyze any possible dose–response relationships, i.e., whether several adversities lead to a larger symptom load in a longitudinal community cohort over a 30-year period.

2. Methods

2.1. Sampling

The screening procedure in the Zurich Study took place in 1978 with a sample of 4547 subjects (2201 males; 2346 females) born in 1958 and 1959 and representative of the canton of Zurich in Switzerland. At that time, the male participants were 19 years old (at mandatory conscription) and the females 20 years old (complete electoral register). In Switzerland each male citizen has to present himself for military conscription. With permission from the authorities and independently of the military procedure, we could screen randomly half of the conscripts. The refusal rate was 0.3%. The females were identified at the age of 20 by the complete electoral register; half of the women chosen randomly received mailed questionnaires and 75% of them responded. A lower educational level was over-represented among non-responding women; in order to correct for that the female interview sample was matched by educational level to the male sample. All subjects received the Symptom Checklist 90-R (SCL-90-R) (Derogatis, 1977), a comprehensive self-report questionnaire consisting of 90 questions, which covers a broad range of psychiatric symptoms, and a demographic questionnaire.

With regard to the second phase, a stratification procedure was applied in order to enrich the interview sample with cases at risk for the development of psychiatric syndromes. Stratification was based on a cut-off value of the SCL-90-R global severity index (GSI) score. Two-thirds of the interview sample comprised high scorers (defined by the 85th percentile or above on the SCL-90-R GSI scores) and one-third of the interview sample were randomly selected from the rest of the initial sample (GSI scores below the 85th percentile). 591 subjects (292 males, 299 females) were selected for interview. Such a two-phase procedure is fairly common in epidemiological research (Dunn et al., 1999), and is applied to enrich the interview sample with persons at risk for psychopathological syndromes.

Face-to-face interviews were conducted in 1979 (N = 591), 1981 (N = 456), 1986 (N = 457), 1988 (N = 424), 1993 (N = 407), 1999 (N = 367), and 2008 (N = 335). Over that span of seven assessment waves, 57% of the original cohort continued to participate. The initial allocation into the two groups according to the 85th percentile cut-off value did not change over the study interview period, although dropouts were rather extremely high or low scorers on the GSI (Eich et al., 2003). When we repeated those dropout analyses for the last interview in 2008, we also found that those participants who dropped out did not differ significantly in their socio-economic status and education at the onset of the study from subjects who remained for the entire study. Neither did their initial psychopathologic impairments differ according to the nine SCL-90-R subscales. However, a moderate bias existed with respect to sex: dropouts were more frequently male (OR = 1.82; 95%-CI = 1.31–2.53; $p < 0.001$). A detailed description of the sampling procedure has been provided elsewhere (Angst et al., 1984; Rössler et al., 2012). For the investigation described here, we considered only subjects who also participated until the last assessment in 2008 (191 females; 144 males).

2.2. Instrument and measures

The SCL-90-R is a comprehensive self-report questionnaire of 90 items that address a wide variety of psychiatric symptoms. Subjects respond according to a five-point Likert scale of distress that ranges from 1, "not at all" to 5, "extremely". The SCL-90-R is intended to cover the most recent four-week period of psychopathology on each measurement occasion. Its 90 items are grouped along nine subscales that reflect a broad spectrum of symptoms. We applied two subscales relevant to subclinical psychosis — "paranoid ideation" and "psychoticism". The SCL-90-R has historically shown good internal consistency and test–retest reliability (Derogatis, 2000; Schmitz et al., 2000). However, the factor structure has led to contradictory results. Commonly, fewer than nine factors are identified (Schmitz et al., 2000), and the "psychoticism" subscale yields the least consistent results (Olsen et al., 2004). To overcome those shortcomings, we used factor-analytic methods to rearrange those psychosis subscales slightly. The modification of those two psychosis dimensions has been detailed previously (Rössler et al., 2007).

Our first new subscale was used to evaluate social and interpersonal deficiencies, as evidenced by a reduced capacity for close relationships as well as ideas of reference, odd beliefs, and suspicion/paranoid ideation. As such, this factor was reminiscent of criteria required for diagnosing a schizotypal personality disorder. Thus, we named this new subscale "schizotypal signs" (STS). Our second new subscale included the items of thought insertion, thought broadcasting, thought control, and hearing voices. These symptoms represent attenuated forms of the nuclear symptoms of schizophrenia and we named this subscale "schizophrenia nuclear symptoms" (SNS). Since their introduction, those subscales of subclinical psychosis have been replicated and applied in other samples (Breetvelt et al., 2010; Rössler et al., 2011a, 2013a). Here, the internal consistency (Cronbach's α) of STS over all interviews ranged from $\alpha = 0.800$ to $\alpha = 0.869$, with a mean $\alpha = 0.821$. Cronbach's α of SNS ranged from $\alpha = 0.497$ to $\alpha = 0.694$, with a mean $\alpha = 0.595$. To assess discriminant and convergent validity we correlated our psychosis subscales with the three subscales of the Schizotypal Personality Questionnaire brief-form (SPQ-B) (Raine and Benishay, 1995). Pearson *r* values for the associations of STS with the SPQ-B subscales "cognitive-perceptual", "interpersonal", and "disorganized" were 0.370, 0.485, and 0.357, respectively. Correlation coefficients for SNS with the same SPQ-B subscales were 0.319, 0.249, and 0.228. Those associations were obtained using the same data from the Zurich Study.

We additionally employed a longitudinal measure of subclinical psychosis by computing the area under the curve with respect to the ground (AUC_G). The following formula, proposed by Pruessner et al. (2003), was applied:

$$AUC_G = \sum_{i=1}^{n-1} \frac{\left(m_{(i+1)} + m_i\right) t_i}{2}$$

where t_i is the time interval between two measurements; m_i, an individual measurement value; and n, the total number of repeated measures. The AUC_G value increases when a subject reports several high scores on the psychosis subscales. By contrast, an individual with consistently low

or only a few elevated psychosis scores over time obtains a rather low AUC_G value.

Childhood adversity was assessed with the "Structured Psychopathological Interview and Rating of the Social Consequences of Psychological Disturbances for Epidemiology" (SPIKE) (Angst et al., 1984). This semi-structured interview, developed for epidemiological surveys in psychiatric research, evaluates data about socio-demography, somatic syndromes, psychopathology, substance use, medication, health services, impairment, and social activity. Its reliability and validity have been reported elsewhere (Angst et al., 2005). The experience of childhood adversity was used as a retrospective question during the 1986 and 1988 assessment waves (see Angst et al., 2011 for more information). Items included in the analysis are listed in Table 3. The rather few items referring to childhood adversity were assessed as part of the semi-structured clinical interview and were well endorsed and elaborated throughout the interview. Each item was then coded as a dichotomous variable with 0 if absent and 1 if endorsed by the participant. A total adversity score was calculated by summing all 8 item-scores, thus resulting in a continuous variable ranging from 0 to 8.

2.3. Statistical analysis

Values on both psychosis subscales were missing completely at random (MCAR) according to Little's MCAR test ($\chi^2 = 1595.014$, df = 1546, $p = 0.188$). Therefore, to obtain complete data from all 335 participants on both subscales, we conducted a missing value analysis (MVA). Altogether, 152 participants (45.4%) had at least one missing value, such that 972 values (10.4%) were imputed. No variable was missing in more than 56 cases (16.7%). The MVA was performed with the full information maximum likelihood estimation using all available data, which is the standard procedure integrated in Mplus (Muthén and Muthén, 1998–2012) and which is highly recommended by Schafer and Graham (2002).

Latent true change (LTC) models (Steyer et al., 1997; McArdle, 2009) are run within the framework of structural equation modeling (SEM). The advantage of SEM over "classical" techniques, such as analysis of variance or linear regression, is that it allows one to take measurement error into account. That is even more important in studies with repeated measures, where the effect of such an error may multiply over several measurement occasions. By contrast, analyses that are based solely on manifest, observed variables may yield biased interrelations among the underlying constructs. Kline (2005) has provided a comprehensive introduction to SEM.

With LTC models one may examine and identify inter-individual differences in intra-individual changes over time. As opposed to autoregressive models, LTCs are fitted with difference-scores between measurement occasions. That is, they assess intra-individual changes with latent variables that are adjusted for measurement error. We fitted an LTC model for each STS and SNS separately. A graphical illustration, as exemplified for STS, is given in Fig. 1. We followed closely the LTC modeling for Mplus, as detailed by Geiser (2011). Every state subsequent to the initial measurement in 1979 could be perfectly explained by that first state and the latent change variables. Thus, the residual variance of all states from 1981 to 2008 was consequently fixed as 0. Path coefficients from state 1979 to all other states and the loadings of the difference scores on the respective states were set to 1. State 1979 and the latent change variables were allowed to covariate freely.

Factorial measurement invariance should be established in LTC models to ensure that one does not compare "apples with oranges" when examining any change in latent constructs over time (McArdle, 2009). Therefore, we fixed the factor loadings of the second indicator so that those parameters took on the same value at each measurement occasion. Another important part of fitting an LTC model is the adequate modeling of indicator-specific method effects because residuals of indicators are often interrelated over time when repeatedly measured (Sörbom, 1975). Several approaches allow one to account for indicator-specific method effects. Here, we implemented a procedure with an indicator-specific latent factor, as discussed by Eid et al. (1999) and Geiser and Lockhart (2012). Using this method, we fitted an indicator-specific latent factor that loaded exclusively on the second indicator at every measurement occasion. The first state indicator served as the reference, and the indicator-specific factor was defined as the residual factor of the state factors. Consequently, the indicator-specific factor stringently had a mean equal to 0, and was not correlated with any state factors or latent change scores. Predictors were defined according to a split-half approach based on items for the respective subscale. As recommended, we applied a robust maximum likelihood

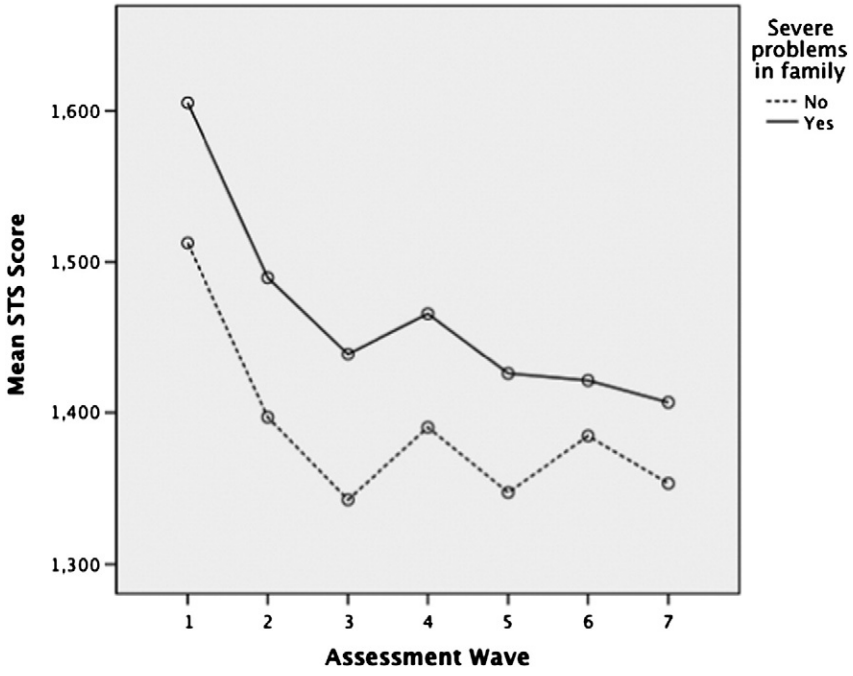

Fig. 1. Latent schizotypal signs (STS) state scores over time in association with severe family problems during childhood.

estimator because of its robustness to multivariate non-normality of continuous data (Brown, 2006).

To evaluate the goodness of model fit we applied the χ^2-test of model fit and the following approximate fit indices: comparative fit index (CFI), Tucker–Lewis index (TLI), root mean square error of approximation (RMSEA), and standardized root mean square residual (SRMR). According to χ^2-tests, a good-fitting model should provide insignificant results (i.e., above the 0.05 threshold). However, as the sample size increases, a χ^2 value easily becomes significant and the test then tends to reject well-fitting models as well (Steiger, 2007). Recommended cut-off values for approximate fit indices are a CFI and TLI > 0.95, an RMSEA < 0.06, and an SRMR < 0.08 (Schreiber et al., 2006). Our LTC model was carried out with the Mplus version 7 for Macintosh (Muthén and Muthén, 1998–2012).

All subsequent analyses were conducted with individual factor scores on the latent variables, as obtained from the LTC model detailed above. Longitudinal analyses of associations between childhood adversity and the repeated measures of latent psychosis states were performed with a series of generalized estimating equations (GEE). These analyses were introduced to fit regression models that account for within-subject correlation, which is an inherent part of longitudinal studies that rely on repeated measures (Zeger et al., 1988). Distribution and link-function for both psychosis subscales were chosen according to their graph and the quasi-likelihood under independence model criterion. Finally, the best fit to the data for both subscales was obtained with an inverse Gauss distribution with log link-function. Intercept and slope were included in all GEE models. The within-subject covariance structure was specified with the "unstructured" correlation type to avoid placing any constraints on the covariance structure. Associations of AUC_G as well as latent psychosis state and change variables with childhood adversity were then examined with generalized linear models (GLM). According to their graphs, as well as Akaike and Bayesian information criteria, we fitted models of normal distribution with an identity-link function for latent change variables and a gamma distribution with a log-link function for the latent state variables and AUC_G. For both GEE and GLM, we used a robust estimator to reduce the effects of outliers and influential observations. Because adolescent cannabis use was an important risk factor for subclinical psychosis in this cohort (see Rössler et al., 2012) we adjusted all analyses for that important covariate. Computations for GEE and GLM were performed with SPSS 20 for Macintosh.

3. Results

Inspection of the LTC model for STS revealed a good fit to the data. The χ^2 was 76.001 (df = 61), p = 0.094; RMSEA = 0.027; CFI = 0.993; TLI = 0.990; and SRMR = 0.025. For the SNS subscale, the indices also revealed a close fit. The χ^2 was 59.449 (df = 61), p = 0.532; RMSEA = 0.001; CFI and TLI = 0.999; and SRMR = 0.040. A graphic illustration of the LST model, as exemplified by the STS subscale, is given on request. The correlation–covariance matrices of both psychosis subscales are also provided on request.

The frequencies of the participants that indicated a given childhood adversity were as follows: broken home: 16.5%; family problems: 45.1%; conflicts between parents: 27.7%; conflicts with parents: 31.7%; sexual abuse: 5.0%; severe punishment: 17.0%; disliked, rejected: 15.3%; and repeated fights: 7.4%. The total adversity score ranged from 0 to 8 with a mean and standard deviation of 1.67 and 1.68. Altogether 22.8% of all participants reported cannabis use during adolescence, whereof 16.8% indicated moderate use and 6.0% heavy use.

Associations between repeated latent states of subclinical psychosis and childhood adversity are presented in Table 1. The GEE results, adjusted for cannabis use, showed that repeated STS measures were significantly and positively related to the following childhood adversity variables over adulthood: family problems (b = 0.044), conflicts between parents (b = 0.062), being disliked/rejected (b = 0.057), repeatedly involved in fights (b = 0.080), and total adversity score (b = 0.019). SNS was uniquely and negatively associated with family problems (b = −0.030), indicating that subjects who experienced them reported lower SNS scores on average. All those associations corresponded to weak effect sizes.

Table 1
Results of a series of bivariate generalized estimating equations (GEE): Childhood adversity associated with schizotypal signs (STS) and schizophrenia nuclear symptoms (SNS) from age 20 years to 50 years, adjusted for cannabis use. Significant associations are emphasized in bold type.

Predictor	STS		SNS	
	b (SE)	Sig.	b (SE)	Sig.
Broken home	0.016 (0.026)	0.534	−0.022 (0.016)	0.168
Family problems	**0.044 (0.019)**	0.020	**−0.030 (0.013)**	0.021
Conflicts between parents	**0.062 (0.020)**	0.002	−0.005 (0.016)	0.768
Conflicts with parents	0.023 (0.022)	0.288	0.004 (0.014)	0.756
Sexual abuse	0.060 (0.047)	0.200	0.007 (0.027)	0.803
Severe punishment	0.028 (0.025)	0.255	0.017 (0.020)	0.395
Disliked, rejected	**0.057 (0.025)**	0.023	−0.017 (0.020)	0.378
Repeated fights	**0.080 (0.036)**	0.028	0.028 (0.021)	0.192
Total adversity score	**0.019 (0.006)**	0.001	−0.004 (0.004)	0.413

Interpretation of the GEE is not straightforward because inter-individual differences in states can be confounded with intra-individual changes in those states. That is, the significant negative association between family problems and repeated SNS states may indicate that subjects reporting such problems have lower SNS values averaged over time (inter-individual difference in states, i.e., between-subject effects). Alternatively, those persons may show a significant decrease in SNS over time relative to subjects without family problems (intra-individual change, i.e., within-subject effects). Therefore, we first addressed this issue by inspecting the graphs of the repeated measures. The plots revealed that all significant regression coefficients in the GEE analyses of STS were mainly attributable to inter-individual state differences. This relationship is exemplified in Fig. 1, which illustrates the association between severe family problems and repeated latent states of STS.

Second, we took the latent change variables and related them to childhood adversity variables via GLM. In doing so, we specifically focused on group differences in subtle intra-individual changes. The results for STS are reported in Table 2. Intra-individual changes from 1979 to 1981 differed significantly in association with sexual abuse (b = 0.097) and severe punishment (b = −0.061). With regard to the former factor, inspection of the mean scores revealed that subjects who were abused showed a smaller decrease in STS from 1979 to 1981 than subjects who were not abused (corresponding to a medium effect size). By contrast, the negative association with punishment indicated that severely punished subjects showed a larger decrease over that time span than unpunished subjects, although the corresponding effect size was again small. The results in Table 2 confirmed that intra-individual changes play only a minor role in STS. Thus, most of the significant associations gained from the GEE analyses (cf., Table 3) relied mainly on inter-individual differences rather than on an intra-individual change.

For SNS (Table 3), the models yielded a small but significant intra-individual change related to broken home from 1986 to 1988 (b = 0.030). This indicated that persons reporting broken home showed a smaller decrease in SNS than did unpunished subjects. Subjects who were sexually abused (b = 0.038) or disliked/rejected during childhood (b = 0.030) reported a smaller decrease in SNS from 1981 to 1986 than those who were not sexually abused or disliked/rejected. In return, the decrease in SNS from 1988 to 1993 was slightly larger in subjects who indicated severe punishment (b = −0.044). Finally, the total adversity score revealed that, as the number of reported adversities rose, the distress in SNS significantly varied from 1981 to 1986 (b = 0.008) as

Table 2
Results of a series of bivariate generalized linear models (GLM): Childhood adversity in association with intra-individual change in schizotypal signs (STS) over time, adjusted for cannabis use. Significant associations are emphasized in bold type.

Predictor	Change 81 − 79	Change 86 − 81	Change 88 − 86	Change 93 − 88	Change 99 − 93	Change 08 − 99
	b (SE)	b (SE)	b (SE)	b (SE)	b (SE)	b (SE)
Broken home	0.004 (0.03)	−0.014 (0.02)	0.032 (0.02)	−0.004 (0.03)	−0.003 (0.03)	−0.006 (0.03)
Family problems	0.000 (0.02)	0.007 (0.02)	−0.016 (0.02)	0.002 (0.02)	−0.041 (0.02)	0.017 (0.02)
Conflicts between parents	0.007 (0.02)	−0.018 (0.02)	0.022 (0.02)	−0.049 (0.03)	0.037 (0.02)	−0.008 (0.02)
Conflicts with parents	0.005 (0.02)	−0.006 (0.02)	0.004 (0.02)	−0.008 (0.02)	0.000 (0.02)	0.009 (0.03)
Sexual abuse	**0.097 (0.04)****	−0.016 (0.04)	−0.033 (0.04)	−0.024 (0.06)	−0.043 (0.05)	−0.025 (0.06)
Severe punishment	**−0.061 (0.03)***	0.020 (0.03)	0.024 (0.02)	−0.040 (0.03)	0.017 (0.03)	−0.009 (0.03)
Disliked, rejected	−0.016 (0.03)	−0.032 (0.03)	0.033 (0.02)	−0.001 (0.03)	−0.015 (0.03)	−0.002 (0.03)
Repeated fights	−0.033 (0.05)	−0.036 (0.05)	0.021 (0.04)	0.004 (0.04)	0.018 (0.04)	−0.056 (0.05)
Total adversity score	−0.002 (0.006)	−0.003 (0.006)	0.005 (0.005)	−0.008 (0.007)	−0.001 (0.007)	−0.001 (0.008)

* $p < 0.05$.
** $p < 0.01$.

well as from 1988 to 1993 (b = −0.009), although corresponding effect sizes were again modest. Nevertheless, intra-individual change in SNS was fairly more common than in STS.

The results reported in Table 4 serve as confirmation and a recapitulation of our previous findings. An increased STS state in 1979 was significantly albeit modestly associated with family problems (b = 0.048), conflicts between parents (b = 0.061), being disliked/rejected (b = 0.058), repeated fights (b = 0.086), and the total adversity score (b = 0.020). For the last state in 2008, we found only a significant difference in association with conflicts between parents (b = 0.069) and the total adversity score (b = 0.016), indicating that subjects who experienced those conflicts and several adversities reported higher mean values. As a supplemental measure of inter-individual differences over the entire observational period, the AUC_G showed significant associations with family problems (b = 0.043), conflict between parents (b = 0.066), and the total adversity score (b = 0.018). No single adversity variable was significantly related to the overall intra-individual change in STS from 1979 to 2008.

For SNS, mean differences linked with childhood adversity were significant for broken home in 1979 (b = −0.054) and family problems in 2008 (b = −0.026), indicating that those adversities were associated with lower distress when adjusted for adolescent cannabis use. A statistically significantly higher AUC_G was uniquely found in association with conflicts between parents (b = 0.033), although this effect was again relatively small. Finally, the GLM yielded no significant overall intra-individual change from 1979 to 2008. Finally, and probably most importantly, no association reported for STS or SNS above did exceed a medium effect size (all Cohen's d < 0.5), but the effects of childhood adversity were adjusted for cannabis use during adolescence and thus independent of that important covariate.

4. Discussion

Childhood adversity is a common experience, with some estimates suggesting that about 1/3 of the population worldwide is affected (Kessler et al., 2010). Although its association with psychosis has been consistently confirmed in several meta-analyses covering different study designs (Varese et al., 2012; Matheson et al., 2013), the etiological link is not clear. Adversity is neither a necessary nor sufficient factor for the onset of a psychotic disorder (Sideli et al., 2012). In addition, childhood adversity is related to various other psychiatric conditions (Kessler et al., 2010; Angst et al., 2011; Hengartner et al., 2013a). We could also demonstrate that subclinical psychosis generally represents a risk factor for the development of common mental disorders and a liability for co-occurring disorders. This refers in particular to dysthymia, bipolar disorder, social phobia, and obsessive–compulsive disorder (Rössler et al., 2011b). As such the association of childhood adversity as a risk factor for various psychiatric conditions including subclinical psychotic states does not come as a surprise.

It is quite likely that biological vulnerabilities and environmental factors, such as childhood adversity, jointly influence the onset and outcome of mental disorders (van Os et al., 2010). Because psychotic disorders, in particular schizophrenia, have a high diagnostic threshold, they are quite rare diseases. The average annual incidence is about 0.2 per 1000 persons, with a lifetime prevalence of 0.4 to 0.7% (Rössler et al., 2005). By comparison, subclinical psychosis symptoms are much more frequent in the general population and, thus, are much more sensitive to detected associations with instances of childhood adversity.

We examined how subclinical psychosis symptoms might be related to childhood adversity, using a representative community cohort that spanned 30 years and involved participants from the age of 19/20

Table 3
Results of a series of bivariate generalized linear models (GLM): Childhood adversity in association with intra-individual change in schizophrenia nuclear symptoms (SNS) over time, adjusted for cannabis use. Significant associations are emphasized in bold type.

Predictor	Change 81 − 79	Change 86 − 81	Change 88 − 86	Change 93 − 88	Change 99 − 93	Change 08 − 99
	b (SE)	b (SE)	b (SE)	b (SE)	b (SE)	b (SE)
Broken home	0.013 (0.02)	0.024 (0.01)	**0.030 (0.01)***	−0.020 (0.01)	−0.004 (0.01)	−0.001 (0.01)
Family problems	−0.013 (0.02)	0.009 (0.01)	0.009 (0.01)	−0.019 (0.01)	−0.008 (0.01)	0.010 (0.01)
Conflicts between parents	0.014 (0.02)	0.015 (0.01)	0.009 (0.01)	−0.020 (0.01)	−0.016 (0.01)	−0.005 (0.01)
Conflicts with parents	−0.017 (0.02)	0.013 (0.01)	0.006 (0.01)	−0.005 (0.01)	−0.004 (0.01)	0.007 (0.01)
Sexual abuse	−0.015 (0.03)	**0.038 (0.02)***	0.027 (0.02)	−0.031 (0.03)	−0.006 (0.01)	0.011 (0.01)
Severe punishment	−0.042 (0.02)	0.022 (0.01)	0.026 (0.02)	**−0.044 (0.02)****	−0.011 (0.01)	0.015 (0.01)
Disliked, rejected	−0.002 (0.02)	**0.030 (0.01)***	0.015 (0.02)	−0.020 (0.01)	−0.015 (0.01)	0.008 (0.01)
Repeated fights	0.018 (0.04)	−0.025 (0.03)	0.019 (0.02)	0.000 (0.03)	−0.015 (0.01)	0.003 (0.02)
Total adversity score	−0.003 (0.005)	**0.008 (0.003)***	0.007 (0.004)	**−0.009 (0.004)***	−0.004 (0.002)	0.002 (0.003)

* $p < 0.05$.
** $p < 0.01$.

Table 4
Results of a series of bivariate GLM: Childhood adversity associated with inter-individual differences in states and AUC_G, and overall intra-individual change in STS and SNS from age 20 years to 50 years, adjusted for cannabis use. Significant associations are emphasized in bold type.

Predictor	STS				SNS			
	State 79	State 08	AUC_G	Change 08 − 79	State 79	State 08	AUC_G	Change 08 − 79
	b (SE)	b (SE)	b (SE)	b (SE)	b (SE)	b (SE)	b (SE)	b (SE)
Broken home	0.018 (0.03)	−0.003 (0.03)	0.010 (0.03)	−0.018 (0.04)	**−0.054 (0.02)***	−0.029 (0.02)	−0.028 (0.02)	0.036 (0.02)
Family problems	**0.048 (0.02)***	0.038 (0.03)	**0.043 (0.02)***	−0.027 (0.03)	−0.012 (0.02)	**−0.026 (0.01)***	−0.025 (0.01)	−0.006 (0.02)
Conflicts between parents	**0.061 (0.02)****	**0.069 (0.03)***	**0.066 (0.02)****	−0.001 (0.04)	0.017 (0.02)	0.020 (0.01)	**0.033 (0.02)***	−0.003 (0.02)
Conflicts with parents	0.021 (0.02)	0.033 (0.03)	0.026 (0.02)	0.006 (0.04)	−0.007 (0.02)	−0.005 (0.01)	−0.010 (0.01)	−0.014 (0.02)
Sexual abuse	0.048 (0.04)	0.022 (0.07)	0.065 (0.05)	−0.001 (0.10)	−0.006 (0.05)	0.016 (0.04)	0.009 (0.04)	0.018 (0.05)
Severe punishment	0.043 (0.03)	0.018 (0.03)	0.020 (0.03)	−0.056 (0.04)	0.028 (0.03)	0.005 (0.02)	0.006 (0.02)	−0.044 (0.03)
Disliked, rejected	**0.058 (0.03)***	0.048 (0.03)	0.050 (0.03)	−0.029 (0.04)	−0.009 (0.03)	0.002 (0.02)	0.003 (0.02)	0.014 (0.02)
Repeated fights	**0.086 (0.04)***	0.046 (0.05)	0.068 (0.04)	−0.076 (0.07)	−0.007 (0.03)	−0.007 (0.02)	−0.003 (0.02)	−0.013 (0.04)
Total adversity score	**0.020 (0.006)****	**0.016 (0.008)***	**0.018 (0.006)****	−0.009 (0.011)	0.004 (0.006)	−0.002 (0.004)	−0.002 (0.004)	−0.002 (0.006)

* $p < 0.05$.
** $p < 0.01$.

until they were 49/50 years old. Although several other studies have focused on the relationship between these two components, none had yet comprised such a long observation period or separately examined, in detail, within- and between-subject effects. Here, we implemented sophisticated and in-depth statistical methods, including GEE and SEM. In doing so, we applied two syndromes of subclinical psychosis, schizotypal signs and schizophrenia nuclear symptoms. In addition, all analyses were adjusted for adolescent cannabis use, which is quite prevalent in the general population and which constitutes an important risk factor for psychosis (Rössler et al., 2012). Several of our major findings are highlighted below:

First, the relationship between childhood adversity and schizotypal signs reflected mainly inter-individual mean differences and, to a lesser extent, intra-individual changes over time. This indicated that subjects who were affected by such adversity reported, on average, higher total distress (measured by the SCL-90-R) over the entire 30-year period of observation than did unaffected subjects. However, most significant effects were weak and only one association (for sexual abuse) reached a medium effect size. Thus, in our sample the impact of childhood adversity on subclinical psychosis needs to be considered as modest.

We also noted a different longitudinal trajectory that was principally characterized by slight symptom remission in relation to childhood adversity. Except for conflicts between parents and the total adversity score, none of the forms of childhood adversity that were significantly related to increased schizotypal signs at age 20/21 showed enduring effects up to the age of 49/50. That is, our data revealed that, subsequent to significant effects of childhood adversity on schizotypal signs in early adulthood, some kind of psychological adjustment occurred that was manifested as a reduction in symptoms later in adult life. Both groups (affected vs. unaffected) gradually approximated in their distress in schizotypal signs before the final assessment at age 49/50, although most direct measures of that intra-individual change over time did not reach statistical significance. In this respect it has been suggested that adaptive coping may substantially attenuate the detrimental effects of childhood adversity (Walsh et al., 2010; Hengartner et al., 2013b). However, the total distress score also demonstrated that, even after 30 years, persons who were affected by various childhood adversities still displayed slightly elevated distress when compared with subjects who had either no or single adversities. Thus, our data also pointed toward a small inter-individual, dose–response relationship.

Second, schizophrenia nuclear symptoms were, for the most part, inter-individually not related to childhood adversity. Although a few statistically significant associations occurred, they were of rather small effect sizes. However, some striking intra-individual changes in distress over time were identified that were related, in particular, to severe punishment and the total adversity score. This suggested that subjects with a history of severe punishment and several other adversities adapted significantly in later life. Those intra-individual changes indicated that the initial distress attributable to childhood adversity varied significantly over time. Thus, although schizophrenia nuclear symptoms were not related to childhood adversity with respect to inter-individual differences in total distress, we found modest intra-individual changes over time in schizophrenia nuclear symptoms when related to severe punishment and the total score. That latter association pointed again toward a dose–response relationship, although once positively and once negatively associated.

Our study did contain both strengths and weaknesses. The data were restricted to a relatively small age cohort, within which persons were interviewed seven times from the ages of 20/21 to 49/50. The relatively small numbers led to moderate statistical power, which may have created some Type-II errors. However, because with the exception of one association no effect reached a medium effect size, we are convinced that we did not miss a strong association. Overall, the majority of variables that we used to define childhood adversity were significant inter-individual risk factors, at least for the schizotypal signs syndrome. Conversely, schizophrenia nuclear symptoms were more closely related to intra-individual changes over time. Whereas schizotypal signs constitute a very pervasive psychopathology that is characterized by severely disordered social communication, schizophrenia nuclear symptoms might rather represent single events in the lives of affected persons. Our study – even if prospective – might have been further limited by the fact that the childhood adversity variables were assessed retrospectively in young adulthood, but nonetheless 15 to 20 years after the event. Retrospectively assessed responses must eventually be regarded cautiously (Hardt and Rutter, 2004). Nevertheless, other researchers have noted that the reliability of retrospective reports of childhood abuse in patients with psychosis has proven to be stable over a long period of time (Dvir et al., 2013). Finally, distress in both measures of subclinical psychosis considerably decreased over time. We do not know, which impact treatment had on the longitudinal course of our subclinical psychosis measures. Nevertheless, this decrease might also be attributed to a methodological artifact called “regression to the mean”, which occurs when a stratified sample with high-scores is followed over time (Barnett et al., 2005). As such, a proportion of the decrease observed in those measures may not represent real change, but rather a methodological bias.

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The foundation had no further role in experimental design; the collection, analysis, and interpretation of data; the writing of this report; or the decision to submit this paper for publication.

Contributors

Wulf Rössler took responsibility for all assessment waves of the Zurich Cohort Study since 1999, and also drafted and revised the manuscript. Michael P. Hengartner conceived and conducted all statistical analyses and substantially contributed to drafting and critical revision of the manuscript. Vladeta Ajdacic-Gross and Helene Haker substantially contributed to drafting and critical revision of the manuscript. Jules Angst designed the Zurich Cohort Study, was responsible for assessment waves until 1993, and substantially contributed to drafting and critical revision of the manuscript.

Conflict of interest

All authors declare that there are no conflicts of interest.

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