(four lessons); c) caring for me (three lessons); d) providing everyday care (five lessons); and e) dealing with changing behaviour (ten lessons). Each lesson presents information about a specific topic and provides engaging, interactive exercises related to this topic. The user is given instant feedback.

Since attrition is common in online programmes, tailoring components and duration of the lessons to the individual is important, the more so because caregivers often experience time constraints due to their caregiving role[6]. iSupport enables caregivers to choose lessons that are appealing and most relevant to them.

iSupport has been developed as an online or web-based self-help programme, but it can also be linked to a caregiver platform (for example a Facebook group), a coach or a face-to-face support group. Contacts with other caregivers or a coach might have added value; however, the human resources that are needed to moderate or guide are not always available, in particular in less developed countries.

When countries want to implement iSupport, translation and adaptation of the programme is needed. We assume that iSupport can be useful in different cultural contexts for different groups of caregivers, if appropriate adaptations to context and culture are made for ecological validity[9]. For example, for caregivers of people with dementia, generational differences within cultures should be examined.

The WHO provides a standardized guide for translation and adaptation (available upon request from whodementia@who.int) to ensure that the local version of iSupport is accurate and in line with the generic version, but at the same time appropriate for the local target group of family caregivers. The guide describes the process to translate and adapt the generic English version and the actual changes that might be (in)appropriate in the programme, such as specific words, names, and links to local Alzheimer's organizations and care and support services.

In several countries, iSupport is currently being adapted and implemented, for example in India, China, Japan, Portugal, Brazil, Australia and the Netherlands. In a next step, the usability and effectiveness of iSupport will be studied and will guide the further improvement of this global course. Upon request by some countries, a generic hardcopy manual of iSupport for adaptation and implementation to local contexts will become available shortly.

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Evocative gene-environment correlation between genetic risk for schizophrenia and bullying victimization

Bullying victimization (BV) is a risk factor for the development of psychotic experiences and psychotic disorders[1,2]. We used data from TRAILS (TRacking Adolescents' Individual Lives Survey), a longitudinal cohort study of Dutch pre-adolescents[3], to study the relationship between polygenic risk score for schizophrenia (SCZ-PRS) and BV, and the possible role of BV in mediating the effect of genetic risk for schizophrenia on the development of psychotic symptoms later in life.

Three assessment waves of TRAILS – T1 (10-12.5 years old), T2 (12.4-14.6 years old) and T3 (14.8-18.3 years old) – were considered. We assessed IQ using the Wechsler Intelligence Scale for Children (WISC), administered at T1; BV through peer nomination scores at T1 and T2; social competence at T1 using the Revised Class Play (RCP); teacher-reported relational aggression by Likert scales at T2; and lifetime psychotic experiences using the Community Assessment of Psychic Experiences Scale at T3.

We imputed TRAILS genotypic data using Sanger Imputation Service (1000 Genomes Project Phase 3 reference GRCh37/hg19). We excluded siblings and pupils on special education, checked genotype quality, derived genomic components to control for ancestry, and computed individual polygenic risk scores (PRS) for schizophrenia, attention-deficit/hyperactivity disorder, autism, bipolar disorder, major depression, and obsessive-compulsive disorder, using standard procedures[4]. We focused on PRS-6 (including variants with association p-value <0.05), a measure of genetic risk yielding the highest prediction

accuracy for schizophrenia[5]. We divided the sample into PRS tertiles, reflecting low, medium and high risk.

We explored whether BV was uniformly distributed across genetic groups, and whether BV mediated the path from genetic risk to psychotic experiences. For the former assessment, we computed an ANOVA using BV at T1 and T2 (separately) as dependent variables; PRS tertiles as factor; gender, WISC and five genomic ancestry components as nuisance covariates (bias corrected-accelerated bootstrap, 1000 runs). For the latter assessment, we computed mediation analyses using psychotic experiences at T3 as dependent variable, BV at T1 and T2 (separately) as mediators, and the PRS as multi-categorical predictor (sequential contrast; same covariates as above plus victimization-psychosis time interval; mean-centering; bootstrap with 5000 runs; Cribari-Neto correction).

To account for different BV reporters, we additionally computed a mediation model using the rank product of peer nomination and relational aggression scores at T2. We tested other peer nomination scores and genetic risk for other disorders to assess specificity of the effects. We additionally explored whether the effect of the SCZ-PRS on BV was mediated by social competence assessed at T1.

Analyses at T1 returned no significant PRS effects (N=650, all p>0.05). ANOVA at T2 returned a significant PRS effect on BV (N=625, $F_{2,611}$=3.4, p=0.033, partial η^2=0.011; observed power = 64%). High PRS individuals had greater peer nomination scores compared to medium PRS subjects (N=417, p=0.017) as well as to a merged sample of low/medium risk individuals (N=625, $F_{1,613}$=6.3, p=0.012, partial η^2=0.01, observed power = 71%). SCZ-PRS was directly associated with BV at T2, without significant mediation by social competence at T1 (N=558, partially standardized effect = 0.011). T2 mediation analysis revealed a significant indirect effect of genetic risk on psychotic experiences at T3 (N=610, partially standardized effect = 0.031). Victims suffered more frequent psychotic experiences at T3 (N=610, p=0.018). These results suggest that BV partially mediated the effect of SCZ-PRS on the frequency of psychotic symptoms developed at T3.

When BV was assessed based on both peer and teacher report at T2, the effect was even larger, despite the reduced sample size (N=390, p=0.002). Only genetic risk for schizophrenia, and not for other disorders, was associated with BV. Only BV peer nomination, not other peer nomination measures, was associated with later psychotic symptoms.

In summary, we found that 13-14-year-old adolescents with greater SCZ-PRS experienced more severe bullying than their peers with lower SCZ-PRS, and that BV partially mediated the effect of genetic risk on the development of later psychotic symptoms. A possible mechanism through which this mediation may occur is evocative gene-environment correlation, i.e., the genetic risk carrier evoking particular reactions of other individuals, such as bullying. The effect is small (1% of the variance), but it is in line with other reported effects, e.g., SCZ-PRS explains at most 1.2% of the variance in symptoms across patients with schizophrenia.

Our sample sizes are small for a behavioral genetics study, a limitation we attempted to address by cumulating risk variants into PRS tertiles. Peer nomination is just one way to assess BV and results may differ based on other reporters[6,7]. However, findings persisted when assessing BV based on peer/teacher reports. Importantly, we did not use self-reports, which may be influenced by paranoia. The prospective data collection reduced the risk of retrospective memory bias.

We studied risk for schizophrenia, but used psychotic episodes as a clinical proxy. Schizophrenia risk may overlap only partially with risk for psychosis, but risk variants for psychosis are not known. To the extent that genetic risk translation into clinical symptoms is mediated by environmental risk[8], our findings call for efforts to antagonize BV of vulnerable individuals to support mental health prevention[6,9].

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