

Online supplement

DNA preparation

Genomic deoxyribonucleic acid (DNA) was obtained from consenting participants between the ages of 28 and 30. In most cases (91.4%), DNA was extracted from peripheral blood using a salting-out extraction procedure.²⁸ To control for laboratory processing errors, three 5 ml EDTA blood tubes were drawn from the majority of participants and two tubes were independently processed for DNA extraction on separate days, with the third unopened tube retained frozen as a back-up. The resulting duplicate DNA preparations were stored in two parallel collections. Sample labelling and handling was rigorously controlled and audited throughout all laboratory procedures. Once the entire cohort was recruited, gender-typing polymerase chain reaction (PCR) analysis was carried out on both collections, using an in-house XY multiplex PCR (protocol available from the author on request) and the results compared. Of the 793 duplicate samples extracted from blood, there was one gender disagreement (0.13% error rate). This mismatch was resolved by disposal of both samples, and extraction of the third stored blood sample from that participant. For those participants not wishing or not able to undergo phlebotomy (8.6% of participants), saliva was collected using OrageneTM collection kits (DNA Genotek, Ottawa, Canada) and DNA was extracted according to the supplier's instructions. Duplicate samples were not obtained for these individuals, although gender-typing PCR was carried out as described above. Finally, an additional quality control comes from some 40 internal duplicates, that is, DNA samples that resulted from independent collection on different occasions (such as blood samples and OrageneTM saliva samples provided at different times). Genotypes from these samples were cross-checked to ensure they yielded identical results (100% concurrence).

Description of measures

Childhood adversity/maltreatment (0–16 years)

The following measures were used to assess the extent of exposure to stress/adversity during childhood.

Childhood sexual abuse

Exposure to childhood sexual abuse was assessed on the basis of retrospective reports obtained at ages 18 and 21 years. Participants were questioned about their experience of a range of 15 abusive experiences prior to age 16, and for each incident reported further detail was gathered on the nature and context of the abuse.^{17,18} On the basis of this questioning participants were classified into four groups reflecting the most severe form of abuse reported at either age: no childhood sexual abuse; non-contact childhood sexual abuse (for example indecent exposure, lewd or threatening sexual comments); contact childhood sexual abuse involving inappropriate touching of genital areas; attempted/completed sexual penetration.

Childhood physical abuse

Exposure to childhood physical abuse was assessed on the basis of retrospective reports obtained at ages 18 and 21 of the extent to which the participant's parent(s) were reported to have used methods of physical punishment during childhood (<16 years).^{17,19} Separate reports were obtained for use of physical punishment by each parent. For the purposes of the present analysis participants were classified into three groups reflecting the most severe form of physical punishment by either parent reported at either age. These groups were: parents never or rarely

used physical punishment; at least one parent regularly used physical punishment; at least one parent used frequent, severe or harsh physical punishment.

Inter-parental violence

This was assessed at age 18 using selected items from the Conflict Tactics Scale²⁹ to assess the extent to which the participant had witnessed incidents of inter-parental conflict and physical violence during childhood. Separate reports were obtained for father-initiated and mother-initiated violence. These items were combined to form a scale measure reflecting the extent of inter-parental violence.²⁰ For analysis purposes participants were classified into three groups ranging from those reporting no inter-parental violence (50% of the sample) to those whose scores placed them in the top 10% of the distribution of inter-parental violence.

Changes of parents

As part of the annual assessments from age 1 to 16 years information was obtained on changes of parents since the previous assessment. An overall measure of family stability during childhood was developed based on a count of the number of changes of parents experienced by the child from birth to age 16 years. This count included all changes due to parental separation/divorce, reconciliation, remarriage/cohabitation, parental death, fostering and other changes of custodial parents. For analysis purposes the sample was classified into four groups (0, 1–2, 3–4, 5+ changes) based on the distribution of number of changes of parents by age 16.

Parental punitive behaviour

As part of the assessments when the study children were aged 3, 4 and 5 years, interviewer observations of the quality of mother–child interaction were obtained using the Avoidance of Restriction and Punishment subscale of the HOME Inventory.²¹ This scale comprised a total of eight items reflecting such behaviours as: shouting at the child, expressing annoyance and hostility to the child, spanking or slapping the child, scolding or putting down (demeaning) the child. Scale scores were calculated for each year using an unweighted sum of the items. Scores were then averaged over the three assessments to provide an overall measure of the extent of punitive parenting behaviours in early childhood.

Childhood adversity score

The above measures were used to construct an overall index of the extent of stress/adversity experienced by the child to age 16 years based on a sum of five dichotomous indicators of adverse childhood experiences. These indicators were whether the individual:

- reported childhood sexual abuse involving genital contact or attempted/completed intercourse;
- reported experiencing frequent, severe or harsh physical punishment from a parent;
- fell into the top decile on the measure of childhood inter-parental conflict;
- had experienced more than three changes of parents during childhood;
- was observed to be exposed to three or more punitive parenting behaviours in early childhood.

Overall, 69% of the sample was classified as experiencing no adversity; 20% as having one adverse experience; and 11% as experiencing two or more adversities.

Adolescent/adult stressful life events

As part of the participant interview at each assessment from age 15 onwards participants were questioned using a life-event checklist that examined the range and severity of adverse life events experienced for each 12-month period since the previous assessment. At ages 15 and 16 this checklist was based on the Feeling Bad Scale.³⁰ From age 18 onwards this scale was updated to include elements from adult life-events checklists, including the Social Readjustment Rating Scale³¹ and the life-events scale reported by Henderson *et al.*³² The full scale comprised a list of 30 adverse life events spanning such domains as: employment problems; serious financial difficulties; partner relationship problems; serious relationship problems with friends or other family members; serious illness or accident of the participant, other close friends or family members; sexual or physical assault victimisation; pregnancy, pregnancy loss and parenthood. For each event the participant was asked to report whether they had experienced the event in each 12-month period since the previous assessment; and if they had experienced the event, to rate the extent to which the event caused them to become upset/distressed on a four-point scale ranging from not upset/distressed to very upset/distressed.

Using these data, two measures were constructed to reflect the overall extent or severity of exposure to stressful life events in the preceding 3 years at ages 18, 21, 25 and 30 years. The first measure was the total life-event score and this measure was based on an unweighted sum of the total number of life events that the individual reported over the 3-year period. For analysis purposes the life-event score at each age was classified into a series of class intervals as follows: 0, 0–1 event; 1, 2–4 events; 3, 5–7 events; 4, 8–10 events; 5, 11+ events. The second measure was the weighted life-event score. A disadvantage of the previous measure was that it did not take into account the extent of distress that each event caused for the individual. To address this issue a weighted life-event score was constructed by summing the total life events reported, with each event weighted by the level of distress that it caused, to provide a measure of the overall severity of life stress. For analysis purposes the weighted life-event score at each age was classified into four class intervals ranging from scores that placed individuals in the lowest 35–40% of the distribution of life stress to scores that placed them in the highest 10% of the sample.

Other measures of adult adversity (16–30 years)

The above life-event report data were supplemented by the following additional measures of life-course stress/adversity over the period from age 16 to 30 years. In each case the measure was obtained as part of in-depth questioning of the participant on aspects of their life experience.

Prolonged unemployment

At each assessment from age 18 to 30 years participants were questioned in detail about their employment history since the previous assessment. As part of this questioning, information was obtained on the extent and duration of any periods of unemployment. For the purposes of this analysis participants were classified as having experienced prolonged unemployment if they reported having been unemployed and seeking work for a period of 12 months or longer since the previous assessment.

Welfare dependence

At each assessment participants were also questioned about sources of income since the previous assessment. As part of this questioning, information was obtained on receipt of government welfare support, including unemployment, sickness, invalid's, domestic purposes and related benefits. Participants were classified as welfare dependent if they reported receiving welfare payments at any time since the previous assessment.

Poverty/depressed living standards (age 30 only)

At age 30, participants were questioned using the short form Economic Living Standards Index (ELSI)²² to assess the extent of current material/economic deprivation. The ELSI scale combines a mix of items reflecting social and material deprivation, economic hardship with self-report ratings of living standards and income adequacy to derive an overall scale score reflecting the overall quality of material living standards experienced by the individual. For the purposes of the present analysis participants were classified into four groups on the basis of their ELSI scores, ranging from those whose scores placed them in the 50% of the sample with the highest living standards (group 1) to those whose scores placed them in the 10% of the sample with the lowest living standards (group 4).

Inter-partner violence victimisation

At ages 21, 25 and 30, participants were questioned concerning their partner relationship experiences over the past 12 months, and in particular the extent and nature of any incidents of inter-partner conflict and violence. Questioning was based on the Conflict Tactics Scale.²³ For the purposes of the present analysis participants were classified as being a victim of inter-partner violence if they reported any incident of physical assault or serious threats of physical assault by a partner in the past 12 months.

Abortion/unwanted pregnancy (females only)

At each assessment from age 16 to 30 years female participants were questioned in detail concerning any pregnancies occurring since the previous assessment and the outcome of each pregnancy. At age 30, women were further questioned about their lifetime pregnancy history, with additional information being obtained on planning of pregnancy, the women's reaction to each pregnancy and whether the pregnancy was wanted. Using these data it was possible to construct a detailed history for each woman on the timing, planning, wantedness and outcome of each pregnancy. For the purposes of the present analysis a dichotomous measure was constructed at each age based on the woman's history of unwanted pregnancy resulting in abortion, or unwanted pregnancy coming to term where the woman reported severe distress or other adverse reaction to the pregnancy.

Mental health outcomes

At ages 18, 21, 25 and 30, participants were administered a comprehensive mental health interview that assessed aspects of the individual's mental health and psychosocial adjustment over the period since the previous assessment. As part of this interview, participants were assessed on DSM-IV²⁴ symptom criteria for major depression and a range of anxiety disorders (generalised anxiety disorder, panic disorders, agoraphobia, social phobia, specific phobia). Questioning was based on the relevant sections of the Composite International Diagnostic Interview (CIDI).²⁵ Participants were also asked about the extent and timing of any

suicidal thoughts since the previous assessment. These data were used to construct four outcome measures at each age. These measures were:

- (a) symptoms of major depression: the number of DSM–IV major depression symptom criteria reported for the previous 12 months;
- (b) major depression: a dichotomous measure reflecting whether the participant met diagnostic criteria for a major depressive episode in the previous 12 months;
- (c) anxiety disorder: a dichotomous measure reflecting whether the participant met diagnostic criteria for any anxiety disorder in the past 12 months;
- (d) suicidal ideation: a dichotomous measure reflecting whether the participant reported suicidal thoughts in the past 12 months.

In addition, at ages 18, 21 and 25, interviews were conducted with a significant other nominated by the participant. As part of

this interview the significant other was questioned about the participant's mental health, including symptoms of major depression occurring in the past 12 months. These data were used to construct a separate informant report of number of depressive symptoms at each age.

Additional references

- 28 Lahiri DK, Nurnberger JI Jr. A rapid non-enzymatic method for the preparation of HMW DNA from blood for RFLP studies. *Nucleic Acids Res* 1991; **19**: 5444.
- 29 Straus MA. Measuring intrafamily conflict and violence: the Conflict Tactics (CT) Scales. *J Marriage Fam* 1979; **41**: 75–88.
- 30 Lewis CE, Seigel JM, Lewis MA. Feeling bad: exploring sources of distress among pre-adolescent children. *Am J Public Health* 1984; **74**: 117–22.
- 31 Holmes SJ, Rahe R. The Social Readjustment Rating Scale. *J Psychosom Res* 1967; **11**: 213–8.
- 32 Henderson S, Byrne DG, Duncan-Jones P. *Neurosis and the Social Environment*. Academic Press, 1981.