Child-to-adult neurodevelopmental and mental health trajectories after early life deprivation: the young adult follow-up of the longitudinal English and Romanian Adoptees study

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Summary

Background Time-limited, early-life exposures to institutional deprivation are associated with disorders in childhood, but it is unknown whether effects persist into adulthood. We used data from the English and Romanian Adoptees study to assess whether deprivation-associated adverse neurodevelopmental and mental health outcomes persist into young adulthood.

Methods The English and Romanian Adoptees study is a longitudinal, natural experiment investigation into the long-term outcomes of individuals who spent from soon after birth to up to 43 months in severe deprivation in Romanian institutions before being adopted into the UK. We used developmentally appropriate standard questionnaires, interviews completed by parents and adoptees, and direct measures of IQ to measure symptoms of autism spectrum disorder, inattention and overactivity, disinhibited social engagement, conduct or emotional problems, and cognitive impairment (IQ score <80) during childhood (ages 6, 11, and 15 years) and in young adulthood (22–25 years). For analysis, Romanian adoptees were split into those who spent less than 6 months in an institution and those who spent more than 6 months in an institution. We used a comparison group of UK adoptees who did not experience deprivation. We used mixed-effects regression models for ordered-categorical outcome variables to compare symptom levels and trends between groups.

Findings Romanian adoptees who experienced less than 6 months in an institution (n=67 at ages 6 years; n=50 at young adulthood) and UK controls (n=52 at age 6 years; n=39 at young adulthood) had similarly low levels of symptoms across most ages and outcomes. By contrast, Romanian adoptees exposed to more than 6 months in an institution (n=98 at ages 6 years; n=72 at young adulthood) had persistently higher rates than UK controls of symptoms of autism spectrum disorder, disinhibited social engagement, and inattention and overactivity through to young adulthood (pooled p<0·0001 for all). Cognitive impairment in the group who spent more than 6 months in an institution remitted from markedly higher rates at ages 6 years (p=0·0001) and 11 years (p=0·0016) compared with UK controls, to normal rates at young adulthood (p=0·76). By contrast, self-rated emotional symptoms showed a late-onset pattern with minimal differences versus UK controls at ages 11 years (p=0·0449) and 15 years (p=0·17), and then marked increases by young adulthood (p=0·0005), with similar effects seen for parent ratings. The high deprivation group also had a higher proportion of people with low educational achievement (p=0·0195), unemployment (p=0·0124), and mental health service use (p=0·0120, p=0·0032, and p=0·0003 for use when aged <11 years, 11–14 years, and 15–23 years, respectively) than the UK control group. A fifth (n=15) of individuals who spent more than 6 months in an institution were problem-free at all assessments.

Interpretation Notwithstanding the resilience shown by some adoptees and the adult remission of cognitive impairment, extended early deprivation was associated with long-term deleterious effects on wellbeing that seem insusceptible to years of nurturance and support in adoptive families.

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Introduction

The role of social and emotional deprivation in the pathogenesis of mental health problems is a long-standing focus of psychiatry.[1] One hypothesis, held by many to be self-evident, is that such adverse exposures have an especially pernicious and persistent effect when experienced early in life during sensitive periods of development.[2] Although animal studies strongly support this view,[3] equivalently robust evidence in human beings has been difficult to find. Experimental exposure of children to deprivation is ethically unacceptable,[4] but drawing inferences from associations between early

Research in context

Research before this study

We searched ISI Web of Science and MEDLINE on July 1, 2016, for longitudinal studies on the effects of early institutional deprivation on development with adult outcome data published in English since 1990. Search terms included "deprivation", "institutional", "early adversity", "children", "autism," "disinhibited attachment/social engagement", "hyperactivity", "inattention", "IQ", "cognition", "behaviour problems", "conduct problems", "depression", "anxiety", and "emotional problems". Although there are a number of longitudinal cohort studies of the effects of early institutional deprivation, they did not follow up individuals into adult life.

Added value of this study

To our knowledge, this is the first large-scale study to follow a cohort of children who suffered profound but circumscribed periods of institutional deprivation through to adult life, allowing direct comparison of their post-institutional developmental trajectories across multiple neurodevelopmental and mental health domains. It extends our previous work and that of studies such as the Bucharest Early Intervention Project by providing evidence of a striking persistence into young adulthood of core neurodevelopmental problems in three symptom domains: inattention and overactivity, disinhibited social engagement, and autism spectrum disorder, despite the positive influence of well resourced, caring, and supportive adoptive families. By contrast, early problems in cognitive impairment were rarely carried into young adulthood. There was an emergence of emotional problems among the young adults who experienced extended deprivation. Despite the extent of problems in this group overall, there was a substantial minority who appeared resilient, showing no core problem at any age.

Implications of all the available evidence

Time-limited but intense periods of early institutional deprivation can have profound effects on development and mental health that can persist beyond adolescence and into young adulthood in ways that both compromise functioning and lead to clinically significant problems. These effects are consistent with models that propose that early environmental adversity can have deep-seated neurobiological effects. Practitioners and policy makers need to take histories of deprivation and other forms of adversity into account when assessing and treating individuals with mental health and neurodevelopmental problems. Most importantly, adolescent-to-adult transitional services need to carefully consider the needs of such patients and ensure continuation of appropriate care as young people enter adult life.

adversity and later mental disorder in observational studies is compromised by heterogeneity in exposure type, timing, and severity; confounding between initial and continuing adversity; and familial correlations between genetic and environmental risks.[5]

The English and Romanian Adoptees study addresses these limitations by using data from a natural experiment, the adoption by UK families of young children who had spent nearly all their early lives in Romania's grossly depriving institutions during the regime of Nicolae Ceaușescu.[6] In the institutions, most children experienced extremely poor hygiene, insufficient food, little personalised care, and social and cognitive understimulation. By contrast, following their arrival in the UK (between 2 weeks and 43 months of age), the children joined socioeconomically advantaged, stable, caring, and supportive families. We previously assessed these children's development at ages 6, 11, and 15 years (and a subsample at 4 years). Profound developmental delay for most children at UK entry[7] was followed by a period of rapid recovery for many adoptees.[8] By age 6 years, children with limited exposure to deprivation (<6 months) were largely indistinguishable from a group of non-deprived UK adoptees. However, for many, but not all, children exposed to more extended deprivation (>6 months) significant impairment of social and cognitive functioning persisted through to adolescence.[9] Core to this pattern were symptoms of disinhibited social engagement, autism spectrum disorder (termed quasi-autism; includes especially notable communication and obsessional problems), inattention and overactivity, and cognitive impairment. Although initially absent, signs of emotional problems began to emerge in adolescence.[10,11] Similar effects have been found in other institutionalised, although less severely deprived, populations.[12–14]

Although other studies have examined the adult outcomes of groups of international adoptees,[15] the recent completion of the English and Romanian Adoptees young adult follow-up (age 22–25 years) allows us, for the first time, to chart childhood-to-adult developmental trajectories in a large group of individuals affected by early profound global institutional deprivation. We had several hypotheses. First, that Romanian adoptees who spent less than 6 months in an institution and UK adoptee controls would display similarly low levels of symptoms at all ages. Second, that increased rates of inattention and overactivity, disinhibited social engagement, autism spectrum disorder, and cognitive impairment symptoms would persist despite continued good-quality adoptive care in the adoptees who spent more than 6 months in an institution. This hypothesis is based on animal research highlighting the deep-seated nature of such effects and previous evidence of childhood persistence from the English and Romanian Adoptees study.[6] Third, that emotional problems would escalate between adolescence and adulthood in the group who experienced more than 6 months of deprivation,

reflecting the especially challenging nature of the adolescent-to-adult transition for this group. We aimed to test these hypotheses using available data from the English and Romanian Adoptees study.

Methods

The English and Romanian Adoptees study

The English and Romanian Adoptees project is a longitudinal investigation into the development of children adopted into UK families from Romania in the early 1990s. The vast majority of the adoptees experienced extreme early global deprivation up to 43 months of age. 165 Romanian and 52 UK adoptees and their adoptive families were recruited in the years following their entry into the UK between February, 1990, and September, 1992. Ethical approval for the young adult follow-up was received from the University of Southampton Research Ethics Committee. At each assessment wave, all adoptees and family members gave written informed consent or verbal assent (where developmentally appropriate).

Procedures and assessments

Assessments took place in the individuals' homes. Questionnaires were completed online or returned by post. For practical and scientific reasons, different assessment instruments were used at different ages. We collected parent reports, available at all age assessments, of six neurodevelopmental and mental health outcomes (autism spectrum disorder, inattention and overactivity, disinhibited social engagement, conduct problems, emotional problems, and cognitive impairment). Self-ratings of emotional and conduct problems, which are considered valuable complements to parent ratings in the adolescent and adult years,[16,17] were also collected for children aged 11 years, 15 years, and in young adulthood (age 22–25 years). Each outcome was characterised by three core symptom domains, measured, as far as possible, by equivalent ratings at each age. Indicators were extracted from available questionnaires and interviews using standard thresholds for symptom domain endorsement wherever possible (see appendix for specific wording of items at each age).

See Online for appendix

Inattention and overactivity covered the symptom domains hyperactivity, sustained attention, and distractibility, measured using items from the Revised Rutter scale[18] at ages 6 years and 11 years; the Strengths and Difficulties Questionnaire[19] at age 15 years; and the Conners Comprehensive Behavior Rating Scale[20] in young adulthood. The same questionnaires were used to derive measures of conduct problems (covering the domains dishonesty, fighting, and defiance) and emotional problems (depressed mood, worry, and social anxiety). For each Revised Rutter scale and Strengths and Difficulties Questionnaire domain, a symptom was judged endorsed when a rating of 2 (certainly applies) was made (0–2 scale). For the Comprehensive Behavior Rating Scale, the equivalent rating was often/very often (rating of 2 or 3; 0–3 scale).

Assessment of disinhibited social engagement was based on researcher ratings of parents' responses to age-appropriate variations of three interview questions relating

	Prevalence of characteristics (%)			Difference between groups, χ^2 (p value)		
	UK group (n=52)	R<6 group (n=67)	R>6 group (n=98)	UK *vs* R<6	UK *vs* R>6	R<6 *vs* R>6
Female sex	34·6%	49·3%	59·2%	2·56 (p=0·11)	8·20 (p=0·0042)	1·59 (p=0·21)
Low birthweight <2500 g	11·5%	22·0%	32·9%	2·15 (p=0·14)	7·92 (p=0·0049)	2·03 (p=0·15)
High SES	87·2%	86·9%	82·4%	0·00 (p=0·96)	0·54 (p=0·46)	0·55 (p=0·46)
Parents' marriage intact	83·7%	73·5%	70·5%	1·42 (p=0·23)	2·42 (p=0·12)	0·12 (p=0·73)
Good parent–child relationship*	50·0%	60·5%	68·1%	0·81 (p=0·37)	2·70 (p=0·10)	0·53 (p=0·47)
Parental support						
Parent report†	100%	100%	98·3%	NA	0·70 (p=0·40)	0·80 (p=0·37)
Child report‡	79·4%	75·7%	75·5%	0·14 (p=0·71)	0·17 (p=0·68)	0·00 (p=0·99)
Young adult unemployment	14·3%	10·0%	36·1%	0·40 (p=0·53)	6·26 (p=0·0124)	10·62 (p=0·0011)
Low education§	19·0%	32·7%	40·3%	2·16 (p=0·14)	5·45 (p=0·0195)	0·73 (p=0·39)
Mental health service use¶						
Up to 11 years of age	5·8%	13·8%	21·6%	2·05 (p=0·15)	6·32 (p=0·0120)	1·57 (p=0·21)
11–14 years of age	8·5%	14·8%	31·0%	0·98 (p=0·32)	8·71 (p=0·0032)	5·16 (p=0·0231)
15–23 years of age	9·5%	22·9%	43·1%	2·90 (p=0·0890)	13·34 (p=0·0003)	4·77 (p=0·0289)

UK=UK adoptees. R<6=Romanian adoptees who spent less than 6 months in an institution. R>6=Romanian adoptees who spent more than 6 months in an institution. SES=skilled, managerial, technical, and professional occupations. NA=not available. *Defined as an average score of 4 or more (out of 5) on the 25-item Inventory of Parent and Peer Attachment.[27] †Defined as at least one parent reported providing support on parenting interview. ‡Supportive parent (adoptee report) defined as an average score of 3 or more (out of 5) on the 13-item support subscale of the Parental Attachment Questionnaire.[28] §GCSE qualifications or lower. ¶Only significant mental health service use was included: at least two sessions with a general practitioner or mental health practitioner if either a formal diagnosis was made or prescription of medication given, or at least six sessions when no diagnosis or medication was received.

Table 1: **Comparison of demographic, family, and young adult circumstances and lifetime mental health service use between groups**

to interactions with strangers, tapping the constructs of being "too friendly", showing "inappropriate intrusiveness", and being "unaware of social boundaries". A rating of "definite evidence of disinhibition" (rating of 2 on a 0–2 scale) represented a positive endorsement (appendix).[8]

Domains of autism spectrum disorder symptoms were assessed using 15 items from the Social Communication Questionnaire[21] deemed to be developmentally relevant at all ages (appendix). Each symptom domain (social reciprocal interaction, communication, and repetitive and stereotyped behaviours) consisted of five items (appendix). A symptom domain was deemed endorsed if at least three items were rated 1 (0–1 scale).

Cognitive impairment was based on age-appropriate standardised IQ assessments: the McCarthy Scales of Children's Abilities General Cognitive Index (age 6 years),[22] the short form of the Wechsler Intelligence Scale for Children (block design, object assembly, vocabulary, and similarities) at ages 11 years and 15 years,[23] and block design and vocabulary subscales from the short-form Wechsler Abbreviated Scale of Intelligence in adulthood.[24] General Cognitive Index values were adjusted to account for apparent inflation of scores since the norms were established in 1970.[25] As in previous studies of the English and Romanian Adoptees study population, cognitive impairment was judged present when individuals had an IQ of less than 80.

Family context, mental health service use, and young adult functioning data were derived from interviews on adoption breakdown (defined here as the child leaving the care of the family before age 18 years); adoptees' mental health service use (parent-report); educational attainment and employment status; and parental socioeconomic status (based on parents' occupation) and marital status. To assess parental supportiveness, young adult adoptees completed the 13-item support subscale of the Parental Attachment Questionnaire,[26] while mothers' and fathers' responses to specific interview questions were coded. Young adult adoptees rated their relationship with their parents using the 25-item Inventory of Parent and Peer Attachment (appendix).[27]

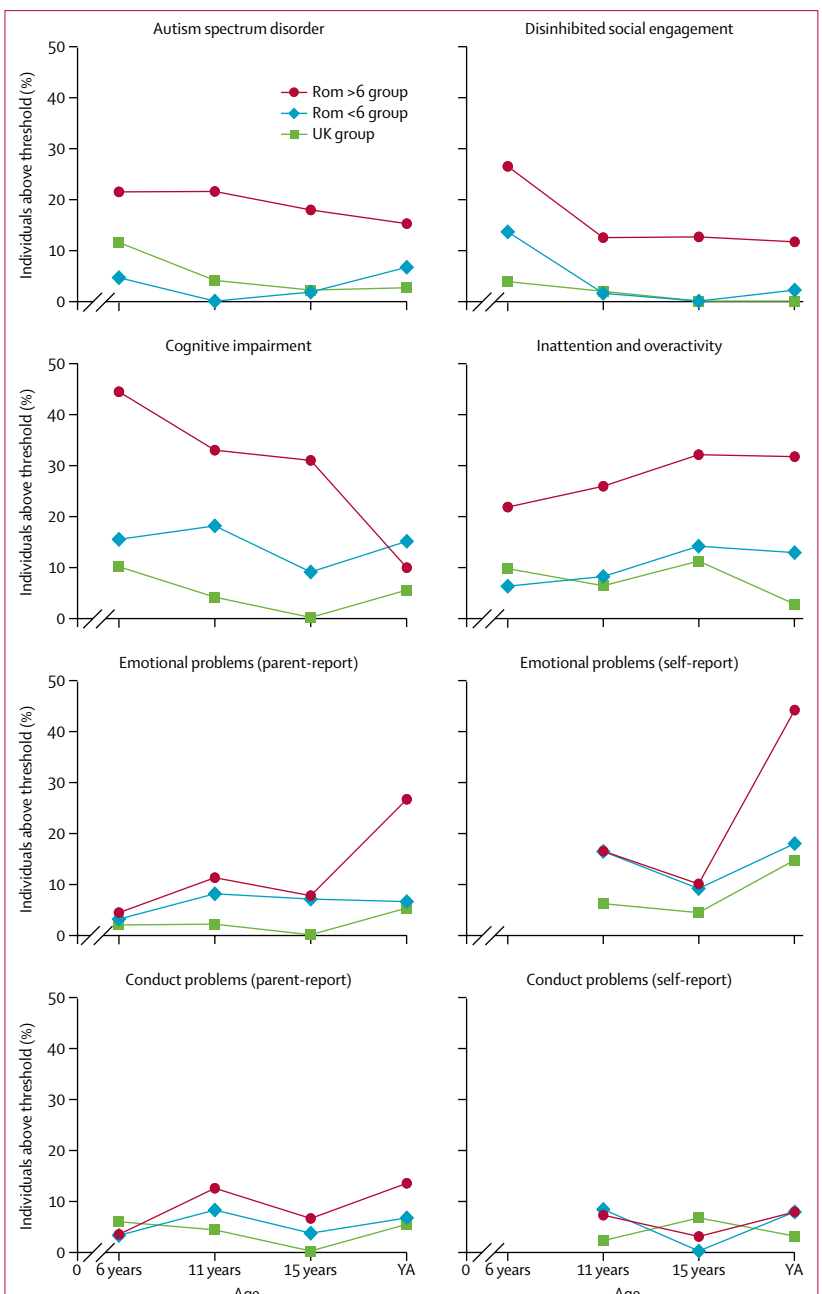

Figure 1: **Developmental trajectories for neurodevelopmental and mental health symptoms**
Threshold defined as either two of three three-symptom domains endorsed or an IQ score of 80 or less. Rom>6=Romanian adoptees who spent more than 6 months in an institution. Rom<6=Romanian adoptees who spent less than 6 months in an institution. UK=UK adoptees. YA=young adult follow-up (22–25 years of age).

Statistical analysis

As previously, we divided the Romanian adoptees into two groups: Romanian adoptees who spent less than 6 months in an institution (n=67 at entry; including 21 adoptees placed directly from their homes) and Romanian adoptees who spent more than 6 months in an institution (n=98 at entry). Previous analyses validated this distinction by showing a step-change in risk within the group with between 6 and 12 months of deprivation[28] and a similar low rate of problems in the UK and Romanian adoptees with less than 6 months of deprivation.[6]

We used mixed-effects logistic regression models for ordered categorical outcome variables to test for differences across development between the three groups, while supplementary analyses compared the UK and the other two groups separately (appendix). We ran models to compare the number of symptom domains endorsed for each outcome (0, 1, 2, or 3 for all outcomes except cognitive inhibition, which was coded 0 or 1) and to test for symptom trends over age; differences in age-trends between groups; and contrasts of simple effects within assessment waves comparing

groups. We used χ^2 and McNemar tests to assess group differences in binary outcomes or covariates, as well as co-occurrence of symptoms among outcome domains (binary indicator, coded 1 if two or more of three symptom domains were endorsed for each outcome). To help to illustrate outcome co-occurrence, we combined the UK control and less than 6 months deprivation groups into a low deprivation group and compared with the more than 6 months deprivation group (for further details see appendix). We did McNemar tests and frequency tests using SPSS version 23. All other analyses were done using Stata version 13.1.

We used largely illustrative cutoffs to provide consistency across outcome domains and over time. Although necessarily arbitrary to some degree and not representative of precise clinical cutoffs we attempted, as far as possible, to map these cutoffs onto acknowledged thresholds of clinically significant expressions across disorders.

We investigated missing data for all outcome variables using multivariate tests that modelled random dropout from the study and selective attrition (appendix). Additionally, to exclude the possibility of systematic differences in genotype that might explain differences in duration of deprivation, we used DNA taken at 15 years' follow-up to compare minor allele frequencies of a small set of candidate genes between the groups of Romanian adoptees that spent more or less than 6 months in institutions using χ^2 tests. We also adjusted additional tests of group levels, assessment wave trends, and interactions of group by wave for standard scores of birthweight and for sex (appendix).

Role of the funding source

The funders had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

In the UK adoptees control group, data for the outcomes reported here were available for 52 (100%) children at ages 6 years and 11 years, 47 (90%) at age 15 years, and 39 (75%) in young adulthood. The average age at young adult assessment was 23·6 years. The equivalent figures

	Age 6 years			Age 11 years			Age 15 years			Young adulthood		
	R<6 *vs* UK	R>6 *vs* UK	R>6 *vs* R<6	R<6 *vs* UK	R>6 *vs* UK	R>6 *vs* R<6	R<6 *vs* UK	R>6 *vs* UK	R>6 *vs* R<6	R<6 *vs* UK	R>6 *vs* UK	R>6 *vs* R<6
Autism spectrum disorder symptoms	0·0 (0·5); p=0·96	1·4 (0·5); p=0·0062	1·4 (0·4); p=0·0014	0·8 (0·8); p=0·32	3·2 (0·7); p<0·0001	2·5 (0·5); P<0·0001	2·0 (1·0); p=0·0462	3·7 (1·0); p=0·0001	1·7 (0·6); p=0·0031	1·4 (1·0); p=0·13	3·1 (0·9); p=0·0008	1·7 (0·6); p=0·0080
Disinhibited social engagement symptoms	1·3 (0·7); p=0·0669	2·7 (0·6); p<0·0001	1·4 (0·5); p=0·0025	0·5 (1·0); p=0·65	3·2 (0·8); p=0·0001	2·7 (0·7); p=0·0001	0·1 (1·1); p=0·96	2·3 (0·8); p=0·0053	2·2 (0·9); p=0·0156	–0·7 (1·4); p=0·63	2·5 (0·8); p=0·0025	3·1 (1·2); p=0·0097
Cognitive impairment (IQ score <80)	0·6 (0·9); p=0·47	4·4 (0·9); p<0·0001	3·8 (0·8); p<0·0001	3·3 (1·9); p=0·0752	5·4 (1·9); p=0·0048	2·1 (0·8); p=0·0105	NE	NE	4·0 (1·1); p=0·0003	1·7 (1·9) p=0·37	0·6 (2·0); p=0·77	–1·1 (1·3); p=0·41
Inattention and overactivity symptoms	0·2 (0·6); p=0·76	1·7 (0·6); p=0·0030	1·5 (0·5); p=0·0024	1·4 (0·7); p=0·0386	2·4 (0·7); p=0·0003	1·0 (0·5); p=0·0448	0·9 (0·7); p=0·24	2·5 (0·7); p=0·0003	1·6 (0·5); p=0·0020	1·6 (0·9); p=0·0688	3·6 (0·8); p<0·0001	1·9 (0·6); p=0·0026
Parent-rated emotional symptoms	–0·2 (0·7); p=0·78	–0·2 (0·6); p=0·81	0·0 (0·6); p=0·96	1·4 (0·8); p=0·0691	1·7 (0·7); p=0·0205	0·3 (0·5); p=0·62	1·3 (1·0); p=0·18	2·3 (0·9); p=0·0070	1·0 (0·7); p=0·11	0·0 (0·7); p=0·96	1·9 (0·6); p=0·0017	1·9 (0·6); p=0·0010
Self (adoptee)-rated emotional symptoms	NA	NA	NA	0·8 (0·5); p=0·12	0·9 (0·5); p=0·0449	0·1 (0·4); p=0·74	0·2 (0·5); p=0·68	0·6 (0·5); p=0·17	0·4 (0·4); p=0·35	0·5 (0·6); p=0·34	1·9 (0·5); p=0·0005	1·3 (0·5); p=0·0045
Parent-rated conduct problem symptoms	–0·4 (0·8); p=0·63	0·2 (0·7); p=0·80	0·5 (0·6); p=0·38	0·4 (0·8); p=0·64	1·7 (0·7); p=0·80	1·3 (0·6); p=0·0403	1·0 (0·8); p=0·21	1·5 (0·8); p=0·0491	0·5 (0·6); p=0·45	–0·1 (0·9); p=0·93	2·1 (0·7); p=0·0052	2·1 (0·7); p=0·0017
Self (adoptee)-rated conduct problem symptoms	NA	NA	NA	–0·4 (0·5); p=0·41	0·4 (0·4); p=0·33	0·8 (0·5); p=0·0759	0·5 (0·7); p=0·49	0·6 (0·7); p=0·39	0·1 (0·5); p=0·84	0·4 (0·5); p=0·35	0·1 (0·5); p=0·89	–0·4 (0·5); p=0·40

Data are log odds (SE); p value. UK=UK adoptees. R<6=Romanian adoptees who spent less than 6 months in an institution. R>6=Romanian adoptees who spent more than 6 months in an institution. NE=not estimable. NA=not available.

***Table 2*: Differences between deprivation groups at each assessment wave**

in the Romanian group were 66 (99%), 65 (97%), 62 (93%), and 50 (75%) for those with less than 6 months of deprivation and 98 (100%), 96 (98%), 89 (91%), and 72 (73%) for those with more than 6 months' deprivation. The average age at young adult assessment for the less than 6 month group was 23·5 years and for the more than 6 month group was 24·5 years. Missing data and participant dropout were largely consistent with an assumption of data missing completely at random (appendix). The exception to this was parent ratings of emotional problems, where dropout was predicted by previous low or average scores.

One family had an adoption breakdown. With this exception, adoptive families generally continued to provide a positive environment in adulthood with no difference between groups in terms of family socioeconomic status, intactness of parents' marriage, child's perception of parent relationship quality, and parent or adoptee perceptions of family support (table 1).[28]

Figure 1 shows developmental trends in binary indicators of all outcomes (statistical values reported in tables 2, 3, and the appendix). Outcomes mostly did not differ between the control group of UK adoptees and the group of Romanian adoptees who spent less than 6 months in an institution, with both groups showing consistently low levels of symptoms (figure 1, table 2). By contrast, the group of Romanian adoptees who spent more than 6 months in an institution had early onset and persistently higher rates of symptoms for autism spectrum disorder, disinhibited social engagement, and inattention and overactivity compared with both the UK adoptees control group and the less deprived Romanian adoptees group (figure 1, table 2). Group differences in these domains established at age 6 years persisted to adulthood (table 2). Substantially elevated rates of cognitive impairment at age 6 years gradually resolved during development so that the group with more than 6 months' deprivation was indistinguishable from the other groups by adulthood (figure 1, table 2). Emotional problems followed a different, late-onset pattern: there were no differences between groups at age 6 years, and the pattern was largely unchanged at ages 11 and 15 years, but there was a significant increase in the number of both parent-rated and self-rated emotional symptoms seen in the group with more than 6 months deprivation during the transition to adulthood (figure 1, table 3). Conduct problems followed a similar, but less marked, pattern (parent rating only; tables 2, 3). Adjusting models for sex and birthweight did not change the results (appendix).

Many individuals in the group who experienced more than 6 months of deprivation had symptoms of multiple problems (figure 2). More than a fifth of the group had two or more problems during childhood and adolescence (figure 2); however, this proportion dropped significantly to 8·5% (n=6; p for change=0·012) in young adulthood. 15 (21%) individuals in the most deprived group did not meet criteria for any adverse outcomes at any age. By contrast, 33 (34%) persisted in meeting criteria for at least one problem at ages 6, 11, and 15 years; this figure dropped to 25% (n=18) if young adult outcomes were included. Different individuals displayed different patterns of overlapping problems, with every pair of co-occuring problems being displayed at some age by at least some individuals who experienced more than 6 months of deprivation (figure 2).

Extended early deprivation was associated with low

	Change from age 6 years to age 11 years			Change from age 11 years to age 15 years			Change from 15 years to young adulthood		
	UK	R<6	R>6	UK	R<6	R>6	UK	R<6	R>6
Autism spectrum disorder symptoms	–2·0 (0·6); p=0·0011	–1·3 (0·5); p=0·0076	–0·2 (0·3); p=0·44	–1·3 (0·9); p=0·17	–0·4 (0·5); p=0·94	–0·8 (0·3); p=0·0083	1·1 (1·0); p=0·28	0·5 (0·5); p=0·32	0·4 (0·4); p=0·30
Disinhibited social engagement symptoms	–1·4 (0·9); p=0·11	–2·2 (0·6); p=0·0005	–0·9 (0·3); p=0·0019	–0·0 (0·1); p=0·71	–0·4 (1·0); p=0·67	–1·0 (0·4); p=0·0290	0·3 (0·8); p=0·68	–0·4 (1·4); p=0·78	0·5 (0·4); p=0·20
Cognitive impairment (IQ score <80)	–2·3 (1·9); p=0·23	0·4 (0·9; p=0·66	–1·3 (0·7); p=0·0478	NE	–2·1 (1·1); p=0·0512	–0·2 (0·7); p=0·76	NE	0·9 (1·1); p=0·42	–4·2 (1·2); p=0·0006
Inattention and overactivity symptoms	–0·7 (0·6); p=0·19	0·5 (0·4); p=0·24	–0·1 (0·3); p=0·80	0·6 (0·7); p=0·37	0·1 (0·4); p=0·77	0·8 (0·3); p=0·0022	–1·2 (0·9); p=0·17	–0·4 (0·6); p=0·51	–0·1 (0·4); p=0·79
Parent-rated emotional symptoms	–0·6 (0·8); p=0·50	1·0 (0·4); p=0·0209	1·3 (0·4); p=0·0038	–0·9 (0·8); p=0·31	–1·0 (0·6); p=0·0891	–0·2 (0·4); p=0·68	2·1 (0·8); p=0·0070	0·8 (0·6); p=0·19	1·7 (0·5); p=0·0011
Self (adoptee)-rated emotional symptoms	NA	NA	NA	0·1 (0·5); p=0·89	–0·5 (0·5); p=0·30	–0·2 (0·3); p=0·51	0·7 (0·5); p=0·19	1·0 (0·5); p=0·0333	2·0 (0·4); p<0·0001
Parent-rated conduct problem symptoms	–0·7 (0·6); p=0·25	0·1 (0·5); p=0·84	0·9 (0·4); p=0·0294	–0·3 (0·8); p=0·69	0·3 (0·5); p=0·57	–0·5 (0·4); p=0·22	0·9 (0·6); p=0·17	–0·2 (0·6); p=0·70	1·4 (0·5); p=0·0068
Self (adoptee)-rated conduct problem symptoms	NA	NA	NA	–1·4 (0·6); p=0·0263	–0·5 (0·6); p=0·39	–1·2 (0·4); p=0·0045	1·7 (0·6); p=0·0069	1·7 (0·5); p=0·0007	1·2 (0·5); p=0·0081

Data are log odds (SE); p value. UK=UK adoptees. R<6=Romanian adoptees who spent less than 6 months in an institution. R>6=Romanian adoptees who spent more than 6 months in an institution. NE=not estimable. NA=not available.

Table 3: **Adjacent contrasts testing differences between assessment waves within deprivation groups**

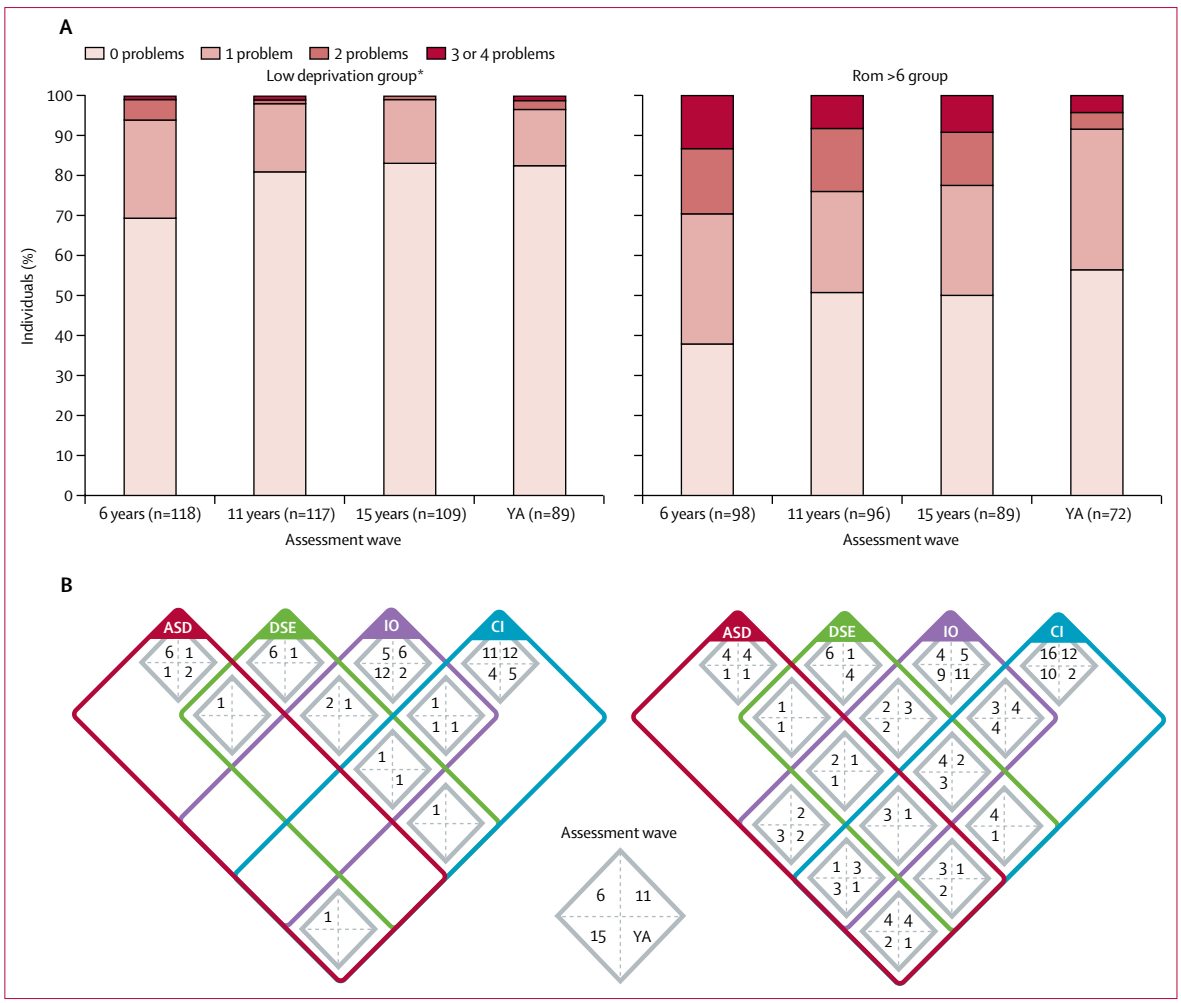

Figure 2: **Proportion of individuals with more than one outcome (A) and number with outcomes that overlapped (B) throughout development**
Assessment waves were at 6 years of age, 11 years of age, 15 years of age, and YA (22–25 years of age). YA=young adult. ASD=autism spectrum disorder symptoms. DSE=disinhibited social engagement symptoms. IO=inattention and overactivity symptoms. CI=cognitive impairment. *Combines Romanian adoptees with less than 6 months deprivation and non-deprived UK adoptees.

educational attainment and unemployment in early adulthood (table 1). Mental health service use at all ages was significantly higher in the group who experienced more than 6 months of deprivation than in the group of UK adoptees (table 1). Lifetime contact with services was very high in the 33 individuals in the most deprived group with persistent problems (67% [n=22] compared with the 28% [n=18] who reported no persistent problems; p=0·0003). At young adult follow-up, in the group who experienced more than 6 months in a Romanian institution, three individuals had referrals for borderline personality disorder, two had referrals for bipolar disorder, and two had referrals for psychosis.

Discussion

We provide compelling evidence that time-limited exposure to severe adversity, occurring because of institutional deprivation in early childhood, can have a profound and lasting psychological impact despite subsequent environmental enrichment in well resourced and supportive families. Our findings are in line with animal models describing long-lasting and deep-seated neurobiological and behavioural alterations after environmental adversity during circumscribed early developmental periods.[29] The presence of multiple neurodevelopmental and mental health problems, with characteristic developmental trajectories, creates a distinctive, complex, and heterogeneous clinical picture; any two affected children rarely presented with the same clinical profile over time. Nevertheless, taking the group as a whole, three outcome domains (autism spectrum disorder, disinhibited social engagement, and inattention and overactivity) followed similar, somewhat overlapping, developmental trajectories, and appear to form an early onset, highly persistent, impairing, and clinically significant deprivation-specific core of characteristics.

The pattern of inappropriate social engagement with strangers (disinhibited social engagement) has, until now, been considered a childhood-limited feature.[30] However, given the previous evidence of persistence into adolescence in the presented sample, it is perhaps not surprising that it continued as a core of deprivation-related characteristics in adulthood. Childhood autism spectrum disorder and inattention and overactivity can both persist into adulthood.[31] The deprivation-related autism spectrum disorder phenotype was originally termed quasi-autism because initial results for children at age 6 years suggested a severe but remitting variant with a distinctive profile that was marked especially by aberrant patterns of social communication and obsessive behaviours.[7] The young adult presentation of this disorder continues to reflect this original formulation, especially in the communication domain, although the extent of long-term persistence appears higher than originally expected.

Deprivation-related cognitive impairment followed a markedly different trajectory in its pattern of remission and normalisation. This course suggests either that institutional deprivation operates in different ways for cognitive impairment, making it more remediable, or that adoptive family life provided a more powerful remediating context for cognitive impairment. Either way, our results provide compelling evidence for long-term neuroplasticity in human beings.

Unlike other outcomes, emotional problems showed a later-emerging pattern in the extended deprivation group, from age 6 years, when levels were practically identical across the groups, to young adulthood, where emotional problems were three-to-four-times higher than in other groups (figure 1). Although other forms of early adversity have been associated with adult depression and anxiety,[32] given their relative absence in this sample at earlier sampling waves, it is striking to see how emotional problems had become such a central feature of deprivation-related clinical burden. These outcomes might be a developmental consequence of the adoptees' experience of early-onset problems. Alternatively, they could be the result of a long-standing, but latent, vulnerability linked to early stress system sensitisation that is only expressed later in life. Finally, it is important to note that a substantial minority of the group who were deprived for more than 6 months were problem-free from age 6 years onwards and had positive young adult outcomes. Understanding the origins of this resilience is a major focus of ongoing work, with preliminary studies pointing towards genetics[33] and epigenetics[4] as important contributors.

Despite the many strengths of the design of the longitudinal English and Romanian Adoptees study, there are a number of possible limitations to consider. We had limited information on possible preinstitutional risks. Maternal smoking, substance use, or stress exposures during pregnancy have been associated with increased risk of neurodevelopmental problems.[34] However, it seems unlikely that these factors could account for the association shown here between deprivation duration and poor outcome. The effects of deprivation reported here are much larger than previous estimates for prenatal exposure risk. Also, it seems unlikely that children who spent more than 6 months in institutions would have been exposed to sufficiently greater prenatal risk than those who had spent less than 6 months in institutions, partly because the timing of adoption was largely determined by the fall of Ceaușescu's regime. Consistent with this view, we found no statistically significant differences in birthweight, a perinatal marker of prenatal risk, between the two institutional groups (table 1), and adjustment for birthweight did not change results of longitudinal models (appendix). Likewise, there was no evidence that these two groups differed in terms of a number of known genetic markers of neurodevelopmental risk (appendix). In fact, the high rates of mortality[35] from infection in the institutions (some have estimated a 40% death rate each winter) might have, over time, enriched the long-term institutionalised group with more, rather than less, resilient children.

A second potential limitation was that outcomes were measured using different questionnaires, with different formats for response scaling used at different ages. As a result, we needed to identify equivalent thresholds for the endorsement of symptom domains. Our thresholding decisions were further validated by the overall low and stable pattern of symptoms in the UK group and the group who spent less than 6 months in institutions and the high levels of contact with mental health services and poor adult functioning in the group who spent more than 6 months in institutions. However, this approach inevitably restricted the scope of the assessments to the constructs measured at age 6 years. A third limitation was that, by contrast to the previous assessment phases, there was more attrition between adolescence and young adulthood, although this appeared to be non-selective (appendix). Finally, because duration and timing of deprivation overlapped, we were unable to address the key issue of sensitive developmental windows in any detail.

Our finding that early institutional deprivation is associated with a pervasive pattern of long-term impairment and burden is relevant to the health and wellbeing of the very large numbers of children worldwide still exposed to depriving and neglectful conditions.[36,37] Even when the deprivation experienced is less severe than in the Romanian institutions, studies suggest that the cluster of neurodevelopmental problems seen in the English and Romanian Adoptees study sample are common in other samples of institutionalised but well cared for children and adolescents.[12–14,38] Questions about the extent to which such problems will persist to adulthood in these groups, and whether our findings can be generalised to children who experience other forms of

abuse or trauma, remain to be investigated fully. Our findings highlight the importance of documenting early-life adversity during clinical assessments. Records of adversary can aid in the planning of services to address the especially persistent and complex nature of the problems such individuals have. Our results suggest that taking account of such histories is likely to be important in planning adult transitional services so that affected individuals have continued access to the specialist services they need.

Contributors

MR initiated the English and Romanian Adoptees study. EJS-B (principal investigator), BM, JK, RK, and WS (co-principal investigators) devised the young adult follow-up and MK and NK collected the data. The Article was conceived by EJS-B, who wrote the first draft with further input from JK, BM, RK, WS, DG and MK. WS conducted the statistical analysis in conjunction with EJS-B and support from MK. All authors interpreted data, reviewed drafts, and approved the final version of the article.

Declaration of interests

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