

Course of Disinhibited Social Engagement Disorder From Early Childhood to Early Adolescence

Katherine L. Guyon-Harris, PhD, Kathryn L. Humphreys, PhD, EdM, Nathan A. Fox, PhD, Charles A. Nelson, PhD, Charles H. Zeanah, MD

Objective: Disinhibited social engagement disorder (DSED) is poorly understood beyond early childhood. The course of DSED signs in a sample of children who experienced severe, early deprivation from early childhood to early adolescence was examined using variable-centered (linear mixed modeling) and person-centered (growth mixture modeling) approaches.

Method: The study included 124 children with a history of institutional care from a randomized controlled trial of foster care as an alternative to institutional care and 69 community comparison children matched by age and sex. DSED signs were assessed at baseline (mean age 22 months), 30, 42, and 54 months of age, and 8 and 12 years of age using a validated caregiver report of disturbed attachment behavior.

Results: Variable-centered analyses based on intent-to-treat groups indicated that signs of DSED decreased sharply for children randomized to foster care and decreased slightly but remained high for children randomized to care as usual. Person-centered analyses showed 4 profiles (i.e., elevated, persistent modest, early decreasing, and minimal). Elevated and persistent modest courses were associated with greater placement disruptions ($F_{3,99} = 4.29$, p = .007, partial eta-squared [η^2] = 0.12), older age at placement into foster care ($F_{3,56} = 3.41$, p < .05, partial $\eta^2 = 0.16$), and more time in institutional care ($F_{3,115} = 11.91$, p < .001, partial $\eta^2 = 0.24$) compared with decreasing and minimal courses.

Conclusion: Early and sustained placement into families after deprivation is associated with minimal or decreasing signs of DSED across development. Shortening the amount of time children spend in institutions and preserving placements could help decrease signs of DSED into early adolescence in previously institutionalized children.

Key words: disinhibited social engagement disorder, institutional care, deprivation, disinhibited attachment disorder, indiscriminate behavior

J Am Acad Child Adolesc Psychiatry 2018;57(5):329-335.







isinhibited social engagement disorder (DSED) is one of the most pervasive clinical sequelae of severe neglect. In young children, it is characterized by overly familiar verbal or physical behavior, willingness to depart with an unfamiliar adult without hesitation, and a tendency to fail to track or check back with a caregiver in unfamiliar settings. DSED also is referred to as "indiscriminant friend-liness," "indiscriminant sociability," or "disinhibited social behavior" because affected children exhibit overly familiar behavior or seek comfort and support from relatively unfamiliar adults even in the presence of a familiar caregiver. 3-5

Indiscriminant behavior in early childhood has been studied extensively. Signs of DSED in early childhood have been consistently identified in samples of children living in foster care and in samples of children living in or previously removed from institutions. ⁶⁻¹² However, despite a strong association with early psychosocial deprivation, past research indicates that removal of children from institutional care does not decrease signs of DSED for all children. ^{6,9,13,14} Children with signs of DSED in early life are at increased risk for psychopathology and difficulties with peers. ¹⁵⁻¹⁸

In middle childhood and adolescence, signs of DSED also are associated with a history of psychosocial deprivation ¹⁹⁻²²; however, more work is needed to explore how manifestations of DSED in middle childhood and adolescence relate to the well-studied early childhood phenotype. A longitudinal perspective can be especially valuable to

examine the course of signs of DSED from early childhood to adolescence in children who experienced deprivation.

Only a few studies have examined the course of DSED across development. Previously, we reported that signs of DSED decreased significantly from baseline (average age 22 months) to 8 years in children in Romania exposed to institutional care. Lawler *et al.* reported on physical (e.g., overly familiar physical behavior) and nonphysical (e.g., overly familiar verbal behavior) disinhibited social behavior from 26 to 48 months of age in a sample of internationally adopted children residing in the United States. In general, signs of DSED remained high over time; however, the study followed children through 4 years of age.

The most extensive examination of the course of DSED beyond early childhood was in the English and Romanian Adoptees Study (ERAS). 9,21,22 Investigators examined DSED signs from 4 years to early adulthood in sample of children raised in Romanian institutions and later adopted by families in the United Kingdom. Signs of DSED for these previously institutionalized children were stable after adoption at 4 to 6 years of age (62% had no change in DSED signs) and persisted but slightly decreased in frequency at 6 to 11 years (54% had persistent mild to marked DSED signs). Signs of DSED in a subset of children in the ERAS who spent more than 6 months in an institution were examined in a follow-up study that extended into early adulthood (22–25 years). The proportion of children demonstrating at least mild signs of DSED appeared to plateau at approximately 15% after 11 years of age and

remain at approximately 15% into early adulthood. Taken together, past work has demonstrated that signs of DSED can persist after early childhood; however, all such approaches have focused on group-level changes, rather than allowing for potential variability in the developmental course of DSED.

Change over time can be characterized using variable-centered (e.g., linear mixed modeling) or person-centered (e.g., growth mixture modeling) approaches. Each approach provides different yet complementary information about growth trajectories over time.²⁴ Variablecentered approaches identify across-sample, fixed-group trends examining mean change and relations between variables for an entire sample or pre-identified groups within a sample.²⁵ With variablecentered approaches, all research participants in a given sample or group are assumed to be drawn from a single population and thus are expected to change in similar and predictable ways over time. In contrast, person-centered analyses allow for a nuanced examination of individual differences outside predetermined groups of interest by examining the presence of meaningful data-derived subgroups defined by unique profiles or trajectories within a sample.²⁶ A combination of variable-centered and person-centered techniques offers the most comprehensive analysis of the longitudinal course of signs of DSED over time. The variablecentered analyses provide a context within which to review and critique findings from person-centered analyses because person-centered analyses are inherently exploratory and therefore susceptible to misinterpretation and overextension.²⁷

We examined data from the Bucharest Early Intervention Project (BEIP), the only randomized controlled trial (RCT) of foster care as an alternative to care as usual. This allowed us to examine signs of DSED from early childhood to early adolescence in children exposed to severe, early deprivation compared with age- and sex-matched children who were never institutionalized.²⁸ Previously, we reported that signs of DSED are more often identified in young children raised in institutions than in those never institutionalized. 8,23 Further, we reported that removal from institutions and placement in foster care leads to decreases in signs of DSED in early childhood^{6,23} and early adolescence. ¹⁹ What is not clear from previous analyses are the group- and individual-level patterns of change in DSED or the variables associated with different patterns of DSED signs across development.

Based on previous findings about DSED from the BEIP, 6,19,23 we predicted that, from early childhood to early adolescence, children who did not experience early deprivation would not have meaningfully increased levels of DSED signs, that children randomized to foster care would demonstrate a rapid decrease in DSED signs, and that children randomized to care as usual would demonstrate a slow, but more modest, decrease in signs of DSED. We predicted that person-centered analyses would show patterns similar to variable-centered analyses, recognizing the potential for the emergence of additional profiles that could not be predicted a priori given that person-centered analyses are exploratory in nature. We predicted person-centered analyses would demonstrate that persistent signs of DSED are associated with longer duration in institutional care and an older age at placement into families.

METHOD

Participants

Research participants included 193 children with usable data from the BEIP and community comparison children. The original sample consisted of 136 infants and toddlers recruited from institutions in Bucharest and randomized after a baseline assessment (mean [M] age 22.49 months, standard deviation [SD] 5.63) into a care as usual group (CAUG; n = 68) or a foster care group (FCG; n = 68).²⁸ The neverinstitutionalized group (NIG; n = 72) consisted of an additional group of community comparison children recruited at baseline. Community comparison children were recruited from the hospitals in which the everinstitutionalized children were born and matched in age and sex. Participation varied across data collection; analyses in this report included 61 CAUG children, 63 FCG children, and 69 NIG children (Figure S1, available online). In addition to a baseline assessment, research participants were assessed at 30, 42, and 54 months of age, at which time the RCT intervention ended, and oversight of the foster care network was transferred to local governmental control. Follow-up assessments were conducted at 8 and 12 years of age. Details about the original sample are available in Supplement 1 (available online).

The BEIP was conducted in collaboration with the Institute of Maternal and Child Health of the Romanian Ministry of Health. Protocols were reviewed and approved by the local Commissions on Child Protection in Bucharest and institutional review boards of the 3 principal investigators (N.A.F., CA.N., and C.H.Z.). All assessments at the 8- and 12-year follow-ups were reviewed by a standing data safety monitoring board in Bucharest. The 12-year follow-up also was reviewed by an ethics committee at Bucharest University. As required by Romanian law, each child's legal guardian provided consent to participate. Assent was obtained from the children at 8 and 12 years of age for each procedure. Discussions of ethical considerations of the study by us and by others are available elsewhere. 29-33

Procedure

Children were randomly assigned to the CAUG or FCG after baseline assessment. These groups were indistinguishable in demographic and caregiving quality features.³⁴ All placement decisions after randomization were made by Romanian child protection officials. Analyses were based on original RCT placement (i.e., using an intent-to-treat design).

Measures

Disturbances of Attachment Interview. Signs of DSED were assessed using a semistructured interview of caregivers about signs of disordered attachment that has been widely used and validated at younger ages. 8,12,13,23,35 The Disturbances of Attachment Interview was translated into Romanian, back-translated into English, and assessed for meaning at each step by bilingual research staff. The mother reported on children living with biological or foster parents and an institutional caregiver who knew the child well reported on children living in the institution. Caregivers responded to probes about their child's attachment behavior and the behaviors were rated as rarely or never present, somewhat or sometimes present, or clearly present. The disinhibited social behavior scale was composed of 3 items (lack of shyness around strangers; getting too close physically; asking overly personal or intrusive questions). The use of only 3 items to assess DSED was necessary because these items were identical across assessment waves, which allowed for consistency of measurement. Additional items added to identify signs of DSED in older children were included at later waves and were not included in the present study. The range for possible scores on the disinhibited social behavior scale was 0 to 6, with higher scores indicating more signs of DSED.

Intervention

The BEIP team recruited and trained 56 foster parents to care for 68 children. 28,36 The foster parents were supported by social workers in

Journal of the American Academy of Child & Adolescent Psychiatry

Volume 57 / Number 5 / May 2018

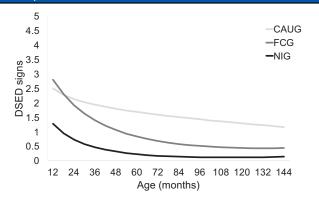
Bucharest who received regular consultation from clinicians in the United States. Parents were explicitly encouraged to care for their foster children as if they were their own children and to make full and lasting commitments to them.

Data Analysis

Signs of DSED were assessed longitudinally using variable- and personcentered approaches. The first approach, linear mixed modeling, used a variable-centered method to examine the effect of group assignment and institutional care history on trajectories of DSED signs. Linear mixed modeling accounts for the non-independence of repeated measures within individuals and handles data from research participants with different numbers of observations and intervals between assessment waves. Restricted maximum likelihood estimation in mixed models in SPSS 23³⁷ was used. Degrees of freedom were calculated using the Satterthwaite method³⁸ to decrease type I error rates, which can result in fractional degrees of freedom. Linear, quadratic, and cubic terms for child age in months (i.e., age, age squared, and age cubed) and age-by-group interactions were tested to examine developmental changes in DSED. Fixed slope and random intercept terms were included. Because greater changes were observed earlier in development, a natural logarithmic transformation was applied to the age values after subtracting a constant from each value so that the youngest age was represented by a value of 0. The actual ages represented by the transformed age variables are presented in Figure 1. Main effects and interaction terms with group were tested for the linear, quadric, and cubic metrics for age. Additional predictors were retained in the model if the terms were at least trend level (p < .10) in the prediction of DSED signs.

Growth mixture modeling is a person-centered, data-driven approach that identifies latent subgroups within the larger sample with similar growth trajectories across assessment waves. Probabilities of membership to each identified profile (trajectory) are used to classify research participants into profiles. Data were analyzed using Mplus 7³⁹; missing data were addressed using the maximum likelihood ratio, a type of full-information maximum likelihood estimation. Models for a 2-, 3-, 4-, and 5-profile solution were tested to determine the optimal number of profiles for the data. Each model was evaluated based on fit statistics and considerations of theory. Fit indices examined included the Bayesian

FIGURE 1 Estimated Signs of Disinhibited Social Engagement Disorder (DSED) as a Function of Group Across Development



Note: CAUG = care as usual group; FCG = foster care group; NIG = never institutionalized group.

information criteria statistic value, Lo-Mendel-Rubin likelihood ratio test, ⁴⁰ and bootstrap likelihood ratio test. The model with the lowest Bayesian information criteria statistic value is considered the best-fitting model. ⁴¹ The Lo-Mendel-Rubin likelihood ratio test ⁴⁰ and bootstrap likelihood ratio test determine whether the addition of each class improves on the previous model. For example, the indices test whether a 3-profile model fits the data better than a 2-profile model.

RESULTS

Linear Mixed Modeling Analysis of DSED Signs

DSED scores were examined as a function of age using linear mixed modeling. Group status (i.e., CAUG, FCG, and NIG) was examined in relation to the intercept and slope across development. Three age models were examined (linear, quadratic, and cubic age), and given that the cubic age term interacted with group status (p = .051), this model was retained (Table S1, available online). As observed in Figure 1, the FCG and CAUG, on average, had more DSED signs in early life (e.g., until approximately 20 months of age) compared with the NIG and did not differ from one another. Further, as predicted, the intent-to-treat effects became more apparent as time in foster placement continued to the end of the formal intervention (54 months of age), at which age the FCG had significantly fewer DSED signs than the CAUG. The FCG, on average, had low levels of signs of DSED from 54 months until early adolescence, whereas the CAUG, whose DSED signs decreased from early childhood, on average had relatively increased signs throughout childhood and into early adolescence.

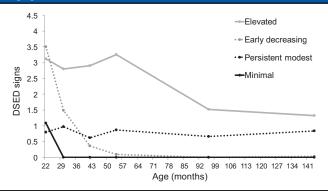
Growth Mixture Modeling of DSED Signs

Latent profiles of DSED signs from baseline to 12 years of age were examined using growth mixture modeling. Given model fit parameters, models were specified using a Poisson error distribution. Models for 2-through 5-profile solutions were tested to arrive at the optimal number of profiles. Fit indices are presented in Table S2 (available online). The Bayesian information criteria and Lo-Mendel-Rubin likelihood ratio test values suggested that the 3-profile model provided the best fit; however, the Bayesian information criterion value for the 4-profile model was similar, and the bootstrap likelihood ratio test indicated that a 4-profile model improved on a 3-profile model. Furthermore, the bootstrap likelihood ratio test has been shown to have better performance compared with the Lo-Mendel-Rubin likelihood ratio test in identifying the most appropriate number of profiles. Therefore, the 4-profile model was chosen as the final model based on fit indices and empirical considerations.

Trajectories for the 4-profile solution are presented in Figure 2. One profile, labeled "elevated," is composed of children who had high levels of DSED signs early in life that continued to be elevated across assessment waves with a gradual decrease into adolescence. Another, labeled "early decreasing," is composed of children who initially had high scores in early life followed by a pronounced decrease in DSED signs across waves. The remaining 2 profiles depict relatively stable courses of signs over time. One profile, labeled "persistent modest," is composed of children who consistently were rated in the low to moderate range across assessment waves. The other profile, labeled "minimal," is composed of children who consistently demonstrated few to no signs of DSED across waves.

Associations With Group and Sex. A significant relation between group and profile was found, indicating that the profiles contain different distributions of children across groups ($\chi^2_6 = 72.60$, p < .001; Table 1 presents the distribution of the number of children in each DSED

FIGURE 2 Observed Signs of Disinhibited Social Engagement Disorder (DSED) Over Time for Each Profile



symptom profile by group membership). The elevated and persistent modest profiles were composed mostly of children from the CAUG and FCG. The early decreasing profile was composed mostly of children from the FCG and NIG and only a small number of children from the CAUG (n = 5). The minimal profile was composed of the largest proportion of NIG children. There was no relation between sex and DSED profile ($\chi^2_3 = 4.29$, p = .232).

Associations With Age of Placement and Institutional Care History. DSED profiles were compared for age at placement into foster care (in the FCG only [n=63]) and age at first placement into a family (for FCG and CAUG children ever placed in family care [n=124]).

Among all ever-institutionalized children, placement disruptions and percentage of time spent in the institution through 54 months of age and from 54 months to 12 years of age were compared between profiles. We found a significant association between age at placement into foster care and DSED profile ($F_{3,56} = 3.41$, p < .05, partial eta-squared [η^2] = 0.16; Table S3, available online). FCG children in the elevated (M 25.99, SD 6.00) and early decreasing (M 23.98, SD 7.16) profiles were, on average, placed into foster care at significantly older ages than children in the minimal profile (M 18.61, SD 7.27).

Age placed into a family for children in the FCG and CAUG also was associated with DSED profile ($F_{3,114} = 7.24$, p < .001, partial $\eta^2 = 0.16$). Children in the elevated (M 35.59, SD 15.76) and persistent modest (M 35.83, SD 17.93) profiles were, on average, first placed into families at significantly older ages than children in the early decreasing (M 25.35, SD 13.11) and minimal (M 18.18, SD 6.97) profiles. Therefore, placement into families at an older age was associated with elevated and modest levels of DSED signs across development.

Placement disruptions through 54 months of age did not differ significantly by DSED profile ($F_{3,111}=1.05$, p=.374 partial $\eta^2=0.03$), however, placement disruptions through 12 years of age, controlling for disruptions through 54 months, did differ significantly by profile ($F_{3,99}=4.29$, p=.007 partial $\eta^2=0.12$). Children in the elevated profile, on average, experienced more disruptions during childhood and early adolescence (M 3.49, SD 1.65) than children with the minimal profile (M 2.42, SD 0.90). Children in the persistent modest profile, on average, experienced more disruptions in placement during childhood and early adolescence (M 4.45, SD 1.77) compared with all other profiles.

Percentage of time in institutional care through 54 months of age differed significantly between DSED profiles ($F_{3,115} = 11.91$, p < .001, partial $\eta^2 = 0.24$). Children in the elevated (M 62.63, SD 23.05) and

persistent modest (M 61.48, SD 27.62) profiles, on average, spent a larger percentage of time in institutional care through 54 months of age compared with children in the early decreasing (M 39.18, SD 19.22) and minimal (M 29.60, SD 12.65) profiles. Therefore, a larger percentage of time spent in institutional care was associated with elevated and modest persistent signs of DSED across development. Percentage of time in institutional care through 12 years of age, controlling for through 54 months, did not differ significantly by profile ($F_{3,99} = 0.41$, p = .749, partial $\eta^2 = 0.01$).

DISCUSSION

The present study examined the course of DSED from early childhood to early adolescence in 124 children with a history of institutional rearing and 69 community comparison children. Patterns of DSED signs across development were identified using variable- and person-centered statistical approaches. Signs of DSED persisted from early childhood to early adolescence for children with a history of institutional rearing, especially if they were placed in families at older ages, had more placement disruptions, and spent more time in institutional care. Trajectories of minimal and early decreasing signs of DSED were common among children with and without institutional care histories. For those with a history of institutional care, minimal or decreasing signs of DSED were associated with earlier and sustained placement in families and less time in institutional care.

The use of variable- and person-centered analyses provided different perspectives on the longitudinal course of DSED from early childhood to early adolescence. Variable-centered analyses examined patterns of change within each intervention group (assigned at baseline) and demonstrated that signs of DSED for children with a history of institutional placement decreased from baseline to 54 months of age, with the sharpest decrease observed in the FCG, reflecting a robust effect of the RCT intervention and consistency with prior work from this sample. These findings extend prior work from this sample by showing that DSED signs remain stable or slightly decrease into adolescence, as suggested by the decrease in DSED signs from 54 months to 8 years of age in a previous report on this sample. Particularly given the long-term persistence of signs of DSED in some children after early deprivation, decreasing exposure to institutional care through family placements should be a priority for abandoned infants and young children.

Our findings differ from those of Lawler et al. 14 who reported high, sustained levels of DSED signs through 48 months in internationally adopted children placed in families in the United States. The fact that not all children in the BEIP exhibited high, sustained levels if indiscriminate behavior could be due to the fact that a larger proportion of children in the BEIP were placed earlier in life compared with children in the study by Lawler et al. After 54 months, the age at which support for the foster care intervention was transferred to local Romanian authorities, DSED signs appeared to plateau for the CAUG and FCG, indicating that at least on the group level, there was stability of DSED levels into adolescence. These findings are consistent with those of Sonuga-Barke et al. 22 who reported a sustained plateau of symptoms across middle childhood and adolescence in their sample of post-institutionalized Romanian children adopted into the United Kingdom. Therefore, we provide evidence that signs of DSED can emerge early in life and that increased levels in early life can persist into early adolescence and adulthood.

Person-centered analyses identified common patterns of change in the data. The elevated, minimal, and early decreasing profiles were similar to those observed in the variable-centered analyses and contained expected proportions of children from the NIG, FCG, and CAUG. There

TABLE 1 Group Membership and Sex by Disinhibited Social Engagement Disorder (DSED) Symptom Profile

	Elevated (n = 63) n (%)	Early Decreasing (n = 36) n (%)	Persistent Modest (n = 39) n (%)	Minimal (n = 55) n (%)
CAUG (n = 61)	35 (55.5)	5 (14)	20 (51)	1 (2)
FCG (n = 63)	20 (32)	18 (50)	11 (28)	14 (25)
NIG (n = 69)	8 (12.5)	13 (36)	8 (21)	40 (73)
Girls (n = 101)	27 (43)	19 (53)	21 (54)	34 (62)
Boys (n = 92)	36 (57)	17 (47)	18 (46)	21 (38)

Note: CAUG = care as usual group; FCG = foster care group; NIG = never-institutionalized group.

were some, albeit few, children in the minimal profile from the FCG and CAUG, highlighting that a small subset of severely deprived children develop no signs of DSED. A study by Minnis *et al.*⁴³ showed a strong genetic component for signs of attachment disorders such as DSED, offering 1 possible explanation of why some children in the FCG and CAUG, despite experiencing deprivation, did not show signs of DSED, but this remains to be explored further. The persistent modest profile, composed of children who exhibit persistently mild elevations of DSED signs over time, is a previously unidentified pattern of DSED signs not hypothesized a priori, highlighting the wide variability in signs of DSED and the advantage of using multiple statistical approaches. Persistence of signs of DSED might or might not be worrisome depending on functional impairment. Future work is needed to further explore potential outcomes associated with persistently modest levels of DSED.

Examining profiles identified from growth mixture modeling contributed insight about the specific factors associated with individual variability in DSED signs over time. Consistent with previous work examining patterns of DSED after institutional care, no sex differences were found. The most important predictors of variability in signs of DSED over time included age at placement into foster care (FCG children), age first placed into a family (ever-institutionalized children), disruptions in placement, and percentage of time spent in the institution.

Age at placement into foster care emerged as a potential predictor of outcomes, which has been a common finding in the BEIP.³¹ Such findings highlight the importance of early intervention, because earlier placement into families has been linked to not only fewer signs of DSED but also a better course of DSED across development. We previously reported that children placed before the 24 months of age show fewer DSED signs than children placed after 24 months. ²³ In 2 separate reports from the same research group, Rutter et al. 21 and Sonuga-Barke et al. 22 reported that placement before 6 months was associated with fewer DSED signs throughout childhood and adolescence. In the present study, children with persistently elevated or modest signs of DSED who were from the FCG were placed into foster care at significantly older ages than children with few or no signs of DSED. Over the course of the study, most children in the CAUG were placed eventually into families (e.g., government foster care, adopted within Romania, or returned to biological parents/extended families). Children in the elevated and persistent modest profiles were found to be placed into families at significant older ages than children in the early decreasing and minimal profiles. Therefore, age at placement might not only lessen the occurrence of signs of DSED signs but also protect against the persistence of signs into early adolescence. These findings underscore the importance of placing children into families at a young age and suggest that early

placement can lead to decreases in DSED signs and prevent persistence into early adolescence. Furthermore, they point to a potential sensitive period in early childhood for the impact of adequate caregiving on the development and sustained course of signs of DSED into early adolescence.

Beyond early placement into families, consistency of placement has implications for the course of DSED across development. Previous work by Pears et al. 11 demonstrated associations between placement disruptions and signs of DSED in preschool-age children maltreated in foster care. In the present study, more placement disruptions, particularly during childhood and early adolescence, were associated with more signs of DSED. The difference in findings could be due to different samples or age at assessments. Interestingly, children in the persistent modest profile had the largest number of placement disruptions, indicating that frequent disruptions, particularly after 54 months of age, can contribute to steady, albeit modest, levels of DSED signs into early adolescence. Despite a clear association with age placed into a family and placement disruption for the persistent modest profile, it is unclear how meaningful modest levels of DSED signs are. One study examined the persistence of signs of DSED into adulthood and found little impairment related to DSED in the absence of comorbidity.²² However, additional work is needed to replicate these findings and further examine potential outcomes of this pattern coupled with comorbidity and functional impairment.

Differences among profiles also were found for percentage of time in institutional care through 54 months of age. Spending a larger percentage of time in institutional care early in life was associated with elevated and persistently modest courses of DSED signs across development, whereas spending less time in care was associated with minimal or decreasing DSED signs over time. After controlling for percentage of time in institutional care through 54 months of age, percentage of time in institutional care through 12 years of age did not independently contribute to a different course of DSED signs. Taken together, results indicate that early deprivation has a more robust association with the course of DSED signs across development than later deprivation in institutional care. The less time young children spend in institutional care, the greater the decrease in the persistence of DSED. Furthermore, preventing disruptions and sustaining placements in families into middle childhood and adolescence could have a positive impact on signs of DSED across development.

Importantly, the course of DSED after severe deprivation is influenced by earlier placement of children into families and maintaining stable placements. Previous research on family placement decreasing signs of DSED has been mixed, with many studies reporting that signs of DSED were not significantly decreased after placement into non-neglecting families—at least in some children. 6,9,14,23 Nevertheless, in the present study, we found that placing children into families at a young age could be crucial for improving the course of DSED across development. Another important consideration is the stability of foster care placement. Interventions aimed at decreasing signs of DSED after deprivation should focus on finding family placements for children early in life. Once placed in a family, disruptions throughout childhood and adolescence should be minimized. Preserving placements can involve ongoing support to the family and the provision of services such as psychoeducation about the effects of early deprivation. In persistent cases, treatment might be necessary⁴⁴; however, the evidence base for the treatment of DSED signs is limited and requires further study.

There were some limitations of this work that are important to note. The signs used to assess DSED were consistent across all waves of assessment, which allows consistency in the scale of measurement and items used to assess DSED longitudinally, but this necessarily weakens

333

developmental sensitivity to the clinical phenotype at different ages. As with most studies of DSED, caregiver report was used, and this introduces possible reporter bias. Because of placement changes, caregivers who reported on children with a history of institutional rearing changed over time, introducing variability. Owing to missing data, models were fitted to provide approximations of the pattern of DSED signs across available assessment ages, and thus data were not available for each year in age. A larger sample assessed with greater frequency would increase confidence in the findings reported.

Although previous work has identified patterns of DSED across early childhood 14 and from childhood into young adulthood, 22 this is the first report on the longitudinal course of the same signs of DSED from early childhood into early adolescence. Our longitudinal analyses suggest that signs of DSED vary significantly over time, and that decreasing and stable patterns were apparent from early childhood to early adolescence. Variation was associated with response to a high-quality foster care intervention, duration children spent in institutional care, and stability of placement once children were placed with families. Further research on DSED beyond early adolescence is needed to better understand the presentation and impact of DSED across development and will be beneficial in identifying ways to improve and sustain the well-being of children into adolescence and adulthood who have been exposed to insufficient care.

Accepted March 9, 2018.

Drs. Guyon-Harris, Humphreys, and Zeanah are with the Tulane University School of Medicine, New Orleans, LA. Dr. Humphreys also is with Stanford University, Stanford, CA. Dr. Fox is with the University of Maryland, College Park, and Dr. Nelson is with Boston Children's Hospital and Harvard Medical School, Boston, and the Harvard Graduate School of Education, Cambridge, MA.

This research was supported by the John D. and Catherine T. MacArthur Foundation Research Network on "Early Experience and Brain Development" (Charles A. Nelson, PhD, Chair), the National Institute of Mental Health (NIMH; 1R01MH091363 to Dr. Nelson and F32MH107129 to Dr. Humphreys), the Brain and Behavior Research Foundation (formerly NARSAD) Young Investigator Award 23819 (to Dr. Humphreys), and the Klingenstein Third Generation Foundation Fellowship (to Dr. Humphreys).

The authors thank the Bucharest Early Intervention Project staff in Romania and the children and caregivers who participated in this study.

Disclosure: Dr. Humphreys has received grant support from the NIMH and the Brain and Behavior Research Foundation. She has received honoraria for lectures to professional audiences. She has served as a paid consultant to Zero to Three. Dr. Fox has received grant support from the NIMH and the National Institute of Child Health and Human Development. He has served on the National Scientific Council on the Developing Child. He has received royalties from Taylor and Francis Press and Harvard University Press. He has received honoraria for lectures to professional audiences. Dr. Nelson has received grant support from the NIMH, the John D. and Catherine T. MacArthur Foundation, the Sinneave Foundation, and the Binder Family Foundation. He has served on the scientific advisory board of the Merck Foundation and the National Scientific Council on the Developing Child and has served as a paid consultant to the US Department of Justice. He has received royalties from Harvard University Press, Massachusetts Institute of Technology Press, and Wiley and Sons. He has received honoraria for lectures to professional audiences. Dr. Zeanah has received grant support from the NIMH, the Palix Foundation, the Irving Harris Foundation, the Substance Abuse and Mental Health Services Administration, the Lumos Foundation, and the Institute for Mental Hygiene. He has received royalties from Guilford Press and Harvard University Press. He has received honoraria for lectures to professional audiences. Dr. Guyon-Harris reports no biomedical financial interests or potential conflicts of interest.

Correspondence to Charles H. Zeanah, MD, Department of Psychiatry and Behavioral Sciences, 1430 Tulane Avenue, #8055, New Orleans, LA 70112; e-mail: czeanah@tulane.edu

0890-8567/\$36.00/@2018 American Academy of Child and Adolescent Psychiatry

https://doi.org/10.1016/j.jaac.2018.02.009

REFERENCES

- American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders.
 5th ed. Arlington, VA: American Psychiatric Publishing; 2013.
- Zero to Three. DC: 0-5TM: Diagnostic Classification of Mental Health and Developmental Disorders of Infancy and Early Childhood. Washington, DC: Author; 2016.
- Chisholm K, Carter MC, Ames EW, Morison SJ. Attachment security and indiscriminately friendly behavior in children adopted from Romanian orphanages. Dev Psychopathol. 1995;7:283-294.
- Albus KE, Dozier M. Indiscriminate friendliness and terror of strangers in infancy: contributions from the study of infants in foster care. Infant Ment Health J. 1999; 20:30-41.
- 5. Zeanah CH. Disturbances of attachment in young children adopted from institutions. J Dev Behav Pediatr. 2000;21:230-236. Available at: https://www.researchgate.net/profile/Charles_Zeanah/publication/12434999_Disturbances_of_attachment_in_young_children_adopted_from_institutions/links/54c11e290cf25b4b8071b6b4.pdf. Accessed August 21, 2017.
- Gleason MM, Fox NA, Drury SS, Smyke AT, Nelson CA, Zeanah CH. Indiscriminate behaviors in previously institutionalized young children. Pediatrics. 2014;133: e657-e665.
- Zeanah CH, Scheeringa M, Boris NW, Heller SS, Smyke AT, Trapani J. Reactive attachment disorder in maltreated toddlers. Child Abus Negl. 2004;28:877-888.
- Zeanah CH, Smyke AT, Koga SF, Carlson E. Attachment in institutionalized and community children in Romania. Child Dev. 2005;76:1015-1028.
- O'Connor TG, Rutter M. Attachment disorder behavior following early severe deprivation: extension and longitudinal follow-up. J Am Acad Child Adolesc Psychiatry. 2000; 30:703-712.
- Bruce J, Tarullo AR, Gunnar MR. Disinhibited social behavior among internationally adopted children. Dev Psychopathol. 2009;21:157-171.
- Pears KC, Bruce J, Fisher PA, Kim HK. Indiscriminate friendliness in maltreated foster children. Child Maltreat. 2010;15:64-75.
- Zeanah CH, Smyke AT, Dumitrescu A. Attachment disturbances in young children. II: Indiscriminate behavior and institutional care. J Am Acad Child Adolesc Psychiatry. 2002;41:983-989.

- Gleason MM, Fox NA, Drury S, et al. Validity of evidence-derived criteria for reactive attachment disorder: Iindiscriminately social/disinhibited and emotionally withdrawn/ inhibited types. J Am Acad Child Adolesc Psychiatry. 2011;50:216-231.
- Lawler JM, Koss KJ, Doyle CM, Gunnar MR. The course of early disinhibited social engagement among post-institutionalized adopted children. J Child Psychol Psychiatry Allied Discip. 2016;57:1126-1134.
- Lehmann S, Breivik K, Heiervang ER, Havik T, Havik OE. Reactive attachment disorder and disinhibited social engagement disorder in school-aged foster children—a confirmatory approach to dimensional measures. J Abnorm Child Psychol. 2016;44:445-457.
- Jonkman CS, Oosterman M, Schuengel C, Bolle EA, Boer F, Lindauer RJ. Disturbances in attachment: inhibited and disinhibited symptoms in foster children. Child Adolesc Psychiatry Ment Health. 2014;8:21.
- Tizard B, Hodges J. The effect of early institutional rearing on the development of eight year old children. J Child Psychol Psychiatry. 1978;19:99-118.
- Sonuga-Barke EJ, Schlotz W, Kreppner J. Differentiating developmental trajectories for conduct, emotion, and peer problems following early deprivation. Monogr Soc Res Child Dev. 2010;75:102-124.
- 19. Humphreys KL, Nelson CA, Fox NA, Zeanah CH. Signs of reactive attachment disorder and disinhibited social engagement disorder at age 12 years: effects of institutional care history and high-quality foster care. Dev Psychopathol. 2017;29:675-684.
- Kay C, Green J, Sharma K. Disinhibited attachment disorder in UK adopted children during middle childhood: prevalence, validity and possible developmental origin. J Abnorm Child Psychol. 2016;44:1375-1386.
- Rutter M, Colvert E, Kreppner J, et al. Early adolescent outcomes for institutionallydeprived and non-deprived adoptees. I: Disinhibited attachment. J Child Psychol Psychiatry Allied Discip. 2007;48:17-30.
- 22. Sonuga-Barke EJS, Kennedy M, Kumsta R, et al. 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. Lancet. 2017;389:1539-1548.
- Smyke AT, Zeanah CH, Gleason MM, et al. A randomized controlled trial comparing foster care and institutional care for children with signs of reactive attachment disorder. Am J Psychiatry. 2012;169:508-514.

- 24. Guyon-Harris KL, Humphreys KL, Degnan KA, Fox NA, Nelson CA, Zeanah CH. A prospective study of reactive attachment disorder following early institutional care: considering variable- and person-centered approaches. Attach Hum Dev. In Press.
- Bergman LR, Magnusson D. A person-oriented approach in research on developmental psychopathology. Dev Psychopathol. 1997;9:291-319.
- Muthén B, Muthén LK. Integrating person-centered and variable-centered analyses: growth mixture modeling with latent trajectory classes. Alcohol Clin Exp Res. 2000;24: 882-891.
- 27. Grimm KJ, Ram N, Estabrook R. Growth Modeling: Structural Equation and Multilevel Modeling Approaches. New York: Guilford Press; 2016. Available at: https://www.guilford.com/books/Growth-Modeling/Grimm-Ram-Estabrook/9781462526062/ summary. Accessed July 20, 2017.
- Zeanah CH, Nelson CA, Fox NA, et al. Designing research to study the effects of institutionalization on brain and behavioral development: the Bucharest Early Intervention Project. Dev Psychopathol. 2003;15:885-907.
- Miller FG. The randomized controlled trial as a demonstration project: an ethical perspective. Am J Psychiatry. 2009;166:743-745.
- Millum J, Emanuel EJ. The ethics of international research with abandoned children. Science. 2007;318:1874-1875.
- Nelson CA, Fox NA, Zeanah CH. Romania's Abandoned Children: Deprivation, Brain Development, and the Struggle for Recovery. Cambridge, MA: Harvard University Press; 2014.
- 32. Rid A. When is research socially valuable? Lessons from the Bucharest Early Intervention Project: commentary on a case study in the ethics of mental health research. J Nerv Ment Dis. 2012;200:248-249.
- Zeanah CH, Fox NA, Nelson CA. The Bucharest Early Intervention Project: case study in the ethics of mental health research. J Nerv Ment Dis. 2012;200:243-247.

- Smyke AT, Koga SF, Johnson DE, et al. The caregiving context in institution-reared and family-reared infants and toddlers in Romania. J Child Psychol Psychiatry Allied Discip. 2007;48:210-218.
- Smyke AT, Dumitrescu A, Zeanah CH. Attachment disturbances in young children. I: The continuum of caretaking casualty. J Am Acad Child Adolesc Psychiatry. 2002;41: 972-982.
- 36. Smyke AT, Zeanah CH, Fox NA, Nelson CA. A new model of foster care for young children: the Bucharest early intervention project. Child Adolesc Psychiatr Clin North Am. 2009;18:721-734.
- 37. IBM Corp. SPSS Statistics for Macintosh. Armonk, NY: IBM Corp; 2015.
- 38. Satterthwaite F. International Biometric Society. Biometrics Bull. 1946;2:110-114.
- Muthén LK, Muthén BO. Mplus User's Guide. 6th ed. Los Angeles, CA: Muthen & Muthen; 1998-2010.
- Lo Y, Mendell NR, Rubin DB. Testing the number of components in a normal mixture. Biometrika. 2001;88:767-778.
- D'Unger A, Land K, McCall P, Nagin D. How many latent classes of delinquent/ criminal careers? Results from mixed poisson regression analyses. Am J Sociol. 1998;103: 1593-1630.
- Nylund KL, Asparouhov T, Muthén BO. Deciding on the number of classes in latent class analysis and growth mixture modeling: a Monte Carlo simulation study. Struct Equ Model. 2007;14:535-569.
- Minnis H, Reekie J, Young D, et al. Genetic, environmental and gender influences on attachment disorder behaviours. Br J Psychiatry. 2007;190:490-495.
- 44. Zeanah CH, Chesher T, Boris NW, et al. Practice parameter for the assessment and treatment of children and adolescents with reactive attachment disorder and disinhibited social engagement disorder. J Am Acad Child Adolesc Psychiatry. 2016;55: 990-1003.

SUPPLEMENT 1

Additional information on research participants

Research participants in the present study were drawn from the Bucharest Early Intervention Project, 1 a randomized controlled trial investigating foster care as an alternative intervention for children in institutional care in Romania. Originally, 187 children from 6 institutions in Bucharest, Romania were screened for inclusion in the study. Fifty-one children were excluded for medical reasons, including genetic syndromes and microcephaly. The remaining 136 children were assessed and randomized to the care as usual in the institution group (CAUG; n=68) or the foster care group (FCG; n=68). The

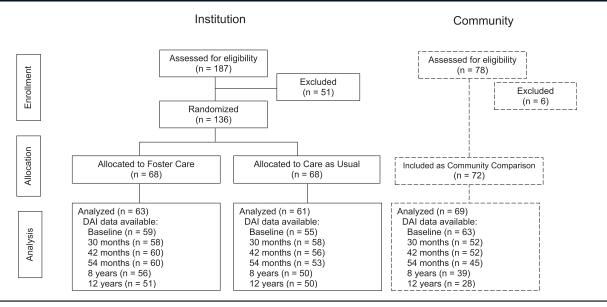
CAUG was composed of 33 boys and 35 girls and the FCG was composed of 34 boys and 34 girls. The groups did not differ based on age, sex, ethnicity, birth weight, developmental quotient, observed caregiving environment, or caregiver-rated behavioral problems.² At baseline, the children were on average 22 months of age (range 6–31 months of age) and had lived in an institution for at least half of their life.

Seventy-two community comparison children matched by age and sex were recruited from the same hospitals in which the FCG and CAUG children were born and composed the never-institutionalized group. This group was composed of 31 boys and 41 girls and did not differ from the ever-institutionalized children in mean age or sex.

REFERENCES

- Zeanah CH, Nelson CA, Fox NA, et al. Designing research to study the effects of institutionalization on brain and behavioral development: the Bucharest Early Intervention Project. Dev Psychopathol. 2003;15:885-907.
- Smyke AT, Koga SF, Johnson DE, et al. The caregiving context in institution-reared and family-reared infants and toddlers in Romania. J Child Psychol Psychiatry Allied Discip. 2007;48:210-218.

FIGURE S1 Consolidated Standards of Reporting Trials (CONSORT) Figure



Note: DAI = Disturbances of Attachment Interview.

TABLE S1 Mixed Modeling Fixed Effect Estimates of Group by Age on Course of Disinhibited Social Engagement <u>Disorder (DSED) Signs</u>

Variable	F	df	p Value
Group	14.98	3, 860.86	<.001
Age (mo)	0.01	1, 832.37	.92
Quadratic age	1.78	1, 821.28	.18
Cubic age	2.43	1, 813.05	.12
Group by age	2.76	2, 834.37	.06
Group by quadratic age	3.13	2, 822.06	.04
Group by cubic age	2.98	2, 813.28	.05

TABLE S2 Fit Indices for Growth Mixture Models

		LMR-LRT		BLRT			
	BIC	Log Likelihood Value	p Value	Log Likelihood Value	p Value		
2-profile	2,662.095	-1,332.561	.024	-1,332.561	<.001		
3-profile	2,664.462	-1,312.629	.003	-1,312.629	.013		
4-profile	2,669.571	-1,305.918	.175	- 1,305.918	.040		
5-profile	_	_	_	_	_		

Note: The 5-profile model did not converge and is not a viable model. BIC = Bayesian information criteria; LMR-LRT = Lo-Mendel-Rubin likelihood ratio test.

TABLE S3 Mean Differences in Age Entered Foster Care (FCG Only) and Age First Placed Into a Family (FCG and CAUG Only)

	E		PL		M		ED				Pairwise
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	F (df)	Partial η^2	Comparisons
Age entered foster care	25.99	6.00	22.06	6.13	18.61	7.27	23.98	7.16	3.41 (3, 56) [*]	0.155	E > M, $ED > M$
Age first placed in a family	35.59	15.76	35.83	17.93	18.18	6.97	25.35	13.11	7.24 (3, 114)***	0.160	E > ED, M , $PL > ED$, M
Placement disruptions through 54 mo	2.75	1.27	3.07	0.98	2.50	0.94	2.67	0.86	1.05 (2, 111)	0.028	_
Placement disruptions through 12 y ^a	3.49	1.65	4.45	1.77	2.42	0.90	3.16	1.21	4.29 (3, 99)**	0.115	E > M, $PL > E$, ED , M
Percentage of time in institution through 54 mo	62.63	23.05	61.48	27.62	29.60	12.65	39.18	19.22	11.91 (3, 115)***	0.243	E > ED, M, $PL > ED$, M
Percentage of time in institution through 12 y ^a	37.69	27.82	34.02	26.88	10.53	4.47	15.82	10.60	0.41 (3, 99)	0.012	_

Note: CAUG = care as usual group; E = elevated; ED = early decreasing; FCG = foster care group; M = minimal; PL = persistent low. ^aControlling for percentage of time through 54 months.

*p < .05; **p < .01; ***p < .01.