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Adolescents hospitalised for suicidality: biomarkers, social and affective predictors: a cohort study

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ABSTRACT

Objectives The present research examines genomics and in vivo dynamics of family context and experienced affect following discharge from psychiatric hospitalisation for suicidal thoughts and behaviours (STBs). The purpose of this paper is to provide an overview of a new model, description of model-guided integration of multiple methods, documentation of feasibility of recruitment and retention and a description of baseline sample characteristics.

Design The research involved a longitudinal, multimethod observational investigation.

Setting Participants were recruited from an inpatient child and adolescent psychiatric hospital. 194 participants ages 13–18 were recruited following hospitalisation for STB.

Primary and secondary outcome measures Participants underwent a battery of clinical interviews, self-report assessments and venipuncture. On discharge, participants were provided with a phone with (1) the electronically activated recorder (EAR), permitting acoustic capture later coded for social context, and (2) ecological momentary assessment, permitting assessment of in vivo experienced affect and STB. Participants agreed to follow-ups at 3 weeks and 6 months.

Results A total of 71.1% of approached patients consented to participation. Participants reported diversity in gender identity (11.6% reported transgender or other gender identity) and sexual orientation (47.6% reported heterosexual or straight sexual orientation). Clinical interviews supported a range of diagnoses with the largest proportion of participants meeting criteria for major depressive disorder (76.9%). History of trauma/maltreatment was prevalent. Enrolment rates and participant characteristics were similar to other observational studies.

Conclusions The research protocol characterises in vivo, real-world experienced affect and observed family context as associated with STB in adolescents during the high-risk weeks post discharge, merging multiple fields of study.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Integration of interviewing, self-report, ecological and biological approaches to examine a high-risk transition.
⇒ The use of the electronically activated recorder to observe and characterise social interactions during the transition from inpatient psychiatric hospitalisation to daily lives.
⇒ Assessment of participants' internal experiences through ecological momentary assessment.
⇒ The incorporation of epigenetic methods to characterise the potential effects of early adversity on epigenetic profiles.
⇒ Limitations include sample size and absence of a control group of youth with no history of suicidal thoughts and behaviours.

Suicide rates have increased alarmingly—a 30% increase between 2000 and 2017—with increases in youth suicide in recent years.[1 2] About 1 in 20 community youth report lifetime suicidal ideation.[3] In 2017, a national sample of adolescents reported suicidal behaviours in the past year, with 7.4% reporting a suicide attempt, 13% reporting a suicide plan and 17% having seriously considered suicide.[4 5] The developmental shift from childhood to adolescence marks a sharp increase in suicidal thoughts and behaviours (STBs) as well as death by suicide, making it especially important for investigations of STB to be conducted with adolescent populations. Individual-level risk factors for adolescent suicide cut across gender and race/ethnicity and include prior attempts, preoccupation with death, violence exposure, disruptive behaviour or mood disorder, and family history of suicide.[6–9] Environmental risk factors include poverty, school problems and, in particular, family conflict and childhood maltreatment.[9 10] In spite of improvements in the efficacy and availability of treatments for many psychiatric disorders, the suicide rate in the USA has increased.[11] Moreover, despite inpatient and follow-up interventions, individuals discharged from psychiatric hospitalisation are at significantly increased risk of suicidal behaviour.[12–16] One-third to one-half of psychiatrically hospitalised youth are readmitted, with the highest readmission risk within a month post discharge and more than

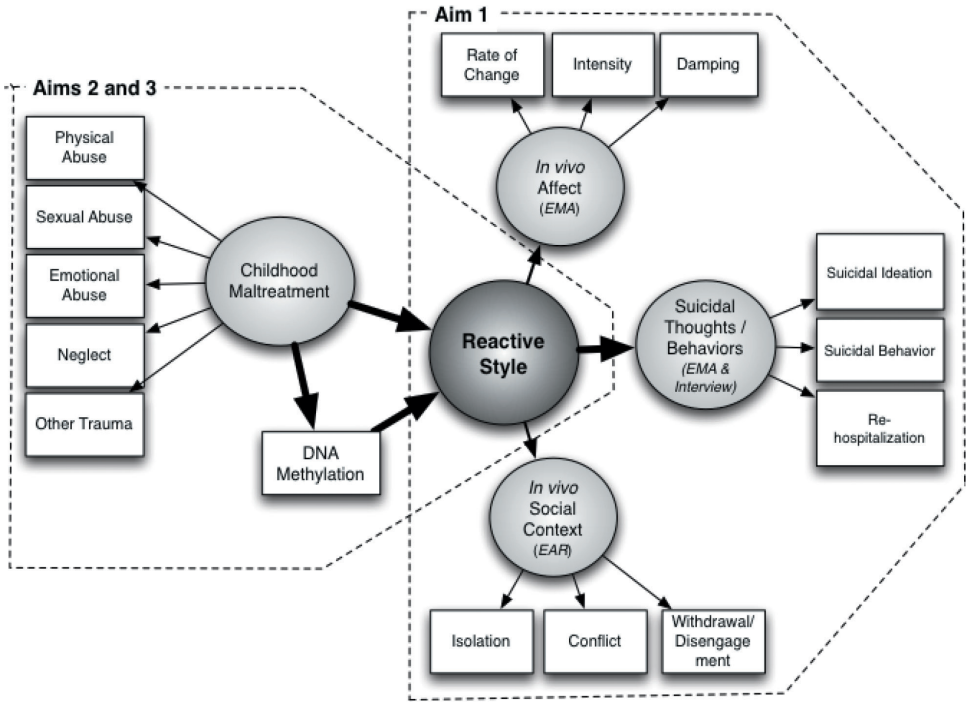

Figure 1 Conceptual model.

80% of readmissions occurring within 3 months.[16–24] We describe here the methods and baseline characteristics of an innovative, multimethod investigation aimed at modelling and integrating known predictors and correlates of STB in a sample of adolescents hospitalised for STBs.

The present investigation examines the high-risk postdischarge transition of adolescents hospitalised for STB to their home environments. Shown in figure 1, we have conducted a rich characterisation of the interplay of experienced affect and social context, as operationalised by the coupling of social context and negative affect in terms of both reactivity of affect and recovery from dysregulation. We apply in vivo ecological sampling permitted by the electronically activated recorder for audio capture of objectively observed social interactions and ecological momentary assessment (EMA) for assessment of experienced affect. We assert that social context and affect are closely tied and that a reactive style involving close coupling of stressful social context with affect reactivity (rapidly changing, intense affect, with slow return to baseline) increases risk of STBs. We further inform frameworks for understanding influences on STB (and potential points for intervention) through epigenetic methodology assessing DNA methylation (DNAm) in peripheral blood samples, an epigenetic modification to DNA that can result in altered gene transcription.

STBS AS TRANSDIAGNOSTIC

Suicide cuts across diagnostic categories and is commonly observed in mood (32%–44%), substance use (18%–23%), post-traumatic stress (23%) and personality (13%–15%) disorders[24 25]; notably, common across these diagnoses is a component of stress sensitivity/affect reactivity, as well as enhanced risk conferred by early life trauma. Indeed, heritability studies suggest that STB functions independent of specific psychiatric disorder[26] and that cluster B traits, partly characterised by affective reactivity, mediate the link between familial predisposition and suicide attempts/severity.[27] Given the prevalence of STB in mood disorders and borderline personality disorder (BPD),[28] with STB similarly serious irrespective of diagnosis,[29] suicidal behaviour may best be studied through intermediary phenotypes.[26] A wealth of evidence across diagnostic groups and methodologies supports the importance of impulsivity, aggressive–impulsive traits, anger-related traits, affect lability/dysregulation and negative affect in STB,[26 30–35] all of which may be facets of a latent reactivity construct. Importantly, even when individuals believe themselves to behave impulsively or 'without thought', affect appears to influence behaviour.[36 37] Converging research supports a central role for affect 'reactivity' in aetiology and course of STB, with adolescent research highlighting the developmental impact of childhood maltreatment on transdiagnostic difficulties in emotion regulation.[38] Supporting the importance of considering these more nuanced aspects of negative affect, an EMA study of female twins reported 18% heritability for negative affect and 35% heritability for *variability* in negative affect.[39]

The importance of affect reactivity is further supported by prospective EMA research linking increasing negative affect to the prediction of self-harm behaviour and suicidal ideation.[40 41] Interestingly, when prompted by EMA to indicate what they were doing when they first

thought of suicide, the largest proportion (35%) of youth reported they were 'socialising'.[41] However, when prompted to indicate whom they were with when they first thought of suicide, 42% of youth reported they were alone. These paradoxical findings suggest that social context is important to suicide risk and that objective characterisation of this context in which suicide risk becomes elevated is needed to reduce self-report bias. Extrapolating from related research, we expect that individuals who experience increases in suicidal ideation/behaviour during the investigation will show rapid and intense increases in negative affect in response to experiences (ie, reactivity in experienced affect). Importantly, we expect that social interactions will be an especially salient influence on affective reactivity in adolescents transitioning from psychiatric hospitalisation.

Importance of social context

Research supports the influence of family, particularly parents, in adolescent STB,[42–52] with increasing recognition of the role of parents in socialisation of emotion regulation.[53] Although research has shown that hospitalised adolescents report more peer relationship difficulties than non-hospitalised comparison youth, perceived family maladjustment differed between suicidal hospitalised youth and hospitalised adolescents who were not suicidal,[54] highlighting the unique importance of the parent–child relationship. A focus on parent–child relationships is also practical for translation to intervention, as parents may be recruited to play a critical role in treatment.[55 56] Although a wealth of studies have reinforced the key role of family in STB, hospitalisation and rehospitalisation, we are unaware of any study that prospectively examines the parent–adolescent relationship processes that unfold in the weeks post discharge; furthermore, the majority of studies focus on adolescent *perceptions* of their family interactions, whereas the present investigation involves objective audio capture of actual interactions.

Studies examining EAR data can objectively code interactions, including conflictual parent–child interactions, reliably and with high fidelity.[57] Prior work has shown that youth *perceive* that their thoughts of suicide increase while they are alone.[41] However, it is possible that actual disruptions to affect could begin during conflict, with adolescents becoming aware of mounting distress and STB only later when alone. Our work has shown that although youth perceive self-harm to be impulsive, these behaviours can be predicted by elevations in negative affect experienced up to 24 hours in advance.[40] Alternatively, certain interactions could be protective; for example, perceived family support predicts less extreme fluctuations in negative affect as well as the coupling of negative affect with daily stress such that family support facilitated stress resistance.[58] Understanding the in vivo interplay of social context and experienced emotion in the weeks following discharge is critical for novel treatment development.

Long-term effects of trauma and maltreatment

Trauma history represents another consistent and significant risk factor for both hospitalisation and rehospitalisation.[24 59 60] Consistent with the importance of trauma as well as affect in the proposed model, we recently found that rehospitalisation was predicted by post-traumatic stress disorder (PTSD) (but not other axis I disorders), childhood sexual abuse, BPD and affect intensity.[24] Even after accounting for demographics and family environment, onset and persistence of STB among adolescents are predicted by trauma,[59–66] and recent research points to differences in the impact of these effects during early adolescence relative to middle adolescence.[67] As we have described, the influence of trauma history on suicide risk may take a number of pathways including trauma-related psychopathology (ie, PTSD, depression, substance abuse and personality disorders) and impairments in social and emotional functionings.[68] Trauma may impact an individual's ability to recruit, or benefit from, social support.[68] Over time, post-traumatic symptoms have been associated with impaired psychosocial functioning with family and friends[69] and may erode social support.[70 71] Trauma and post-traumatic symptoms are associated with negative perceptions of social support and interpersonal resources[72 73] and with feelings of loneliness and social isolation.[74–76] We propose that a history of maltreatment establishes problematic social and emotional dynamics that enhance risk of STB for youth through an enhanced coupling of social context and experienced affect, and that these youth will have more difficulty with damping or recovery from disruptions in affect.

One key pathway whereby early maltreatment and trauma may impact long-term functioning is through biological—particularly epigenetic—alterations. Epigenetics are relevant to suicide research and intervention and the present research question in particular. Affective lability evidences substantial (but incomplete) heritability (45%), suggesting that genetically influenced biological factors as well as environmental influences make an important contribution to affect reactivity.[77] Converging evidence suggests that the pathway critical to *social* and *affect reactivity* (and sensitive to environmental influences) is the hypothalamic–pituitary–adrenal (HPA) axis. Research also points to evidence of the relevance of *social relationships* in HPA neurobiology and psychobehavioural outcomes of trauma.[78–83] Unfortunately, the practical implications of DNA genotypes is limited by their often modest effect sizes and immutability.[84] Epigenetics (specifically, DNAm) is a powerful mechanism whereby environmental effects, particularly early life stress and maltreatment, translate to enduring psychobehavioural outcomes.[84–88] DNAm, which occurs predominantly in CpG sites (DNA regions where a cytosine nucleotide is next to a guanine), involves structural modification of DNA, permitting molecular adaptability and complexity by allowing gene expression to respond to the environment. Numerous animal and human studies have shown DNAm alterations associated with early life adversity and

maltreatment.[86 88–91] Research has demonstrated differential DNAm related to STB and even STB treatment outcomes.[92–98]

New model for understanding STB

The present study further refines affect characterisation and, by coupling affect to social processes during the high-risk transition home, has implications for intervention. Boker and colleagues[99] note that the process of emotion regulation can be represented using a damped oscillator model, a dynamical systems (DS) approach planned here. Affect reactivity is composed of several related constructs, including magnitude of emotion, rate of emotion change (ie, frequency of oscillations) and damping/amplifying (ie, latency to return to homeostatic baseline). These models permit the examination of context and affect as a coupled DS. Influences on these parameters, such as historic (ie, childhood maltreatment) or biological predictors (ie, DNA/DNAm) can be explicitly modelled. Indeed Boker *et al* previously demonstrated that high levels of dispositional resilience were linked to greater damping of negative affect (ie, rapid stress recovery), as well as decreased coupling of negative affect (ie, less linked to stress events).[58] We propose that a more *reactive style* will be characterised by close coupling of stressful social context (eg, isolation and conflictual interactions) with affect reactivity (eg, rapidly changing, intense affect, with poor damping). We expect that this reactive style will be predicted by childhood maltreatment as well as DNA/DNAm and, in turn, predict increased risk of STB. No prior studies have applied a DS approach to measurement of affect reactivity in suicidal individuals nor have studies explored how affect reactivity may be coupled to interpersonal interactions.

The purpose of this paper is, first, to outline a conceptual model and research protocol that leverages multiple approaches to integrate clinical, biomarker, self-report and ecological approaches to better understand influences on adolescent suicidal ideation and/or behaviour during the high-risk transition home from psychiatric hospitalisation. Second, this paper provides an overview of procedures of confidentiality, privacy and procedures for addressing suicide risk during an ecologically involved protocol, increasing the likelihood that other researchers can replicate and extend this multimethod approach. Third, we provide an overview of baseline characteristics of the enrolled sample as well as the overall retention for follow-up visits, demonstrating feasibility of recruitment to research involving integration of biological and ecological methods. Future publications with this sample will refer back to this overview, providing helpful context for the findings observed in forthcoming work.

METHODS

The current investigation was conducted at an academic child and adolescent psychiatric hospital in the Northeastern USA. Study procedures involved an in-hospital baseline, including clinical interviews with adolescents and self-report assessments with both parents and adolescents. Youth also provided blood samples while hospitalised at baseline. Families were trained on EMA and EAR protocols during their hospitalisation, and adolescents began ecological procedures immediately on discharge. Participants completed comprehensive follow-up interviews and questionnaire assessments at 3 weeks and 6 months post discharge.

Participants

Participants included youth recruited from an inpatient child and adolescent psychiatric hospital. Inclusion criteria for youth recruitment were (1) hospitalisation for suicidal thoughts or behaviours; (2) past-month STB verified by interview (Self-Injurious Thoughts and Behaviours Interview (SITB-II)); (3) aged 13–18; (4) ability to speak, read and understand English sufficiently well to complete study procedures; (5) consent of a parent or legal guardian; (6) adolescent assent and (7) comfort with the use of smartphone technology for EMA assessments. Exclusion criteria included (1) psychotic symptoms that are primary and (2) developmental delay or pervasive developmental disorder. Recruitment procedures involved research assistants conducting daily chart reviews of newly admitted patients for suicide risk and obtaining consent from the treating physician to approach. Patients meeting this initial criterion were approached by research staff, provided a description of the study and study aims, and for interested youth, a separate meeting was scheduled with the guardian present to obtain consent. Consenting families then completed a baseline assessment in the hospital, for which adolescents were reimbursed $50.

Baseline assessment

Shown in table 1, baseline procedures took place during hospitalisation and included EMA/EAR training, venipuncture for blood sampling to collect DNA/DNAm, clinical interviews, computer tasks and self-reports.

EMA procedures

The EMA device signalled five times daily during study hours (~10:00 to 23:00 on weekends and ~15:00 to 21:00 on weekdays), at random intervals throughout the day, instructing participants to complete a brief questionnaire assessing affect, behaviours and perceived social context. This procedure resulted in a maximum of 105 possible repeated measures assessments over the 3-week duration of the EMA. Participants were trained to complete an event-queued assessment whenever they experienced feeling strong suicidal ideation or had the urge to engage in some type of self-harm or suicidal behaviour. In the event that individuals endorsed a strong desire to engage in self-harm or suicidal behaviour at any time during EMA, the EMA device was set up to activate an emergency protocol including encouraging participants to talk to their parent(s), contact emergency services or to call 911.

Table 1 Self-report and interview measures

Measure	Timepoint		
	Baseline	3 weeks	6 months
Self-report			
ADD Health	x	x	x
Adolescent Alcohol and Drug Involvement Scale	x		
Adolescent Drinking Questionnaire	x	x	x
Affect Intensity Measure	x	x	x
Affective Reactivity Index-Self	x	x	x
Center for Epidemiological Studies Depression scale for Children	x	x	x
Childhood Trauma Questionnaire	x		x
Children's Ruminative Response Scale	x	x	x
Conflict Behaviour Questionnaire	x	x	x
The Connor-Davidson Resilience Scale	x		
Difficulties in Emotion Regulation Scale	x		
Digital Monitoring Survey	x		x
Emotion Reactivity Scale	x		
Emotion Socialisation Measure	x	x	x
Excessive Reassurance Seeking Scale	x		x
Family Assessment Device	x	x	x
Hopelessness Scale for Children	x	x	x
Implicit Theories of Emotion Scale	x	x	x
Interpersonal Needs Questionnaire	x	x	x
Modified Version of Fagerstrom Tolerance Questionnaire	x		
Perceived Social Support Conflict	x	x	x
Sensitivity to Punishment and Sensitivity to Reward Questionnaire—Short Form	x		
Youth Self-Report	x		x
Computer-administered behavioural tasks			
Now or Later (Delay Discounting Task)	x	x	x
Suicide/Death Implicit Association Test	x	x	x
Self-Referent Encoding Task	x		
Stoplight	x		
Interview			
Clinician-Administered PTSD Scale	x		x
Columbia Suicide Severity Rating Scale	x	x	x
Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime Version	x		x
Life Events Checklist	x		x
Self-Injurious Thoughts and Behaviours Interview	x	x	x
Timeline Followback	x	x	x
Life Stress Interview		x	
Wechsler Abbreviated Scale of Intelligence	x		

EMA measures

EMA measures were largely derived from previously validated measures. We assessed whether the participant was alone or with others, and if they recently used drugs or alcohol. Next, a series of questions assessed attitudes and cognitions related to the experience of affect and distress tolerance. Next, a series of items derived from the PANAS-X assessed for the presence of various forms of affect associated with STB (eg, anger, sadness and hopelessness). The presence of an experienced life stressor

and the presence of suicidal ideation, suicidal behaviour or non-suicidal self-injurious thoughts and behaviours were also assessed at the end of each EMA assessment. Random and event-cued assessments were identical. A third end-of-day assessment schedule briefly assessed treatment and medication adherence.

EAR procedures

Each participant received detailed instructions on how to wear the EAR, and information on the study's privacy and confidentiality policies. The voluntary nature of their participation and the importance of protecting their privacy were emphasised. Participants were encouraged to bring the device with them as much possible and to only take it off overnight and when its proper functioning would be jeopardised (similar to how they might approach their own cellphones). Participants were provided with a case that had a clip so that the device could be worn on a belt. Scheduling of EAR recordings was customised for individual participants to assure that recordings did not take place during either school or during participation in partial hospitalisation programming. This meant that, during the school year, weekday monitoring occurred 15:00–23:00 and weekend monitoring windows were 09:00–23:00. The EAR sampling period corresponded with the 3-week EMA assessment period and was set to record 30 s every 12 min or 5% of the total assessment window. Based on prior studies, this sampling had the potential to result in about 50–70 valid waking recordings and about 15–25 recorded conversations per participant per full day of monitoring. The study implemented several safeguards to protect participants' privacy and to ensure data confidentiality. The study used a National Institutes of Health Certificate of Confidentiality, and participants were encouraged to notify the researchers if there were any windows of time during which they wanted recordings to be destroyed. At the time of consent, participants also completed a brief training and quiz to assure that they understood the EAR functioning, including understanding that the EAR was not a tool for communicating with researchers and that if they wished to report any STB to researchers they would need to contact/interact with staff directly. Recorded sound files were coded by trained research assistants using a coding scheme that was adapted from past work; specifically, the Social Environment Coding of Sound Inventory (SECSI) was modified to assess adolescent social environment and behaviour.[100] Consistent with the focus on concrete, acoustically detectible interaction features, prior EAR studies have found good intercoder reliabilities for standard SECSI variables (including conflictual conversations).[101]

Follow-up assessment schedule

Follow-up assessments took place on completion of the EMA assessments (3 weeks post discharge) and again 6 months post discharge. As diagnosis is unlikely to change within 3 weeks, diagnostic interviews were not repeated until the 6-month follow-up. As shown in table 1, both follow-ups were otherwise identical in most interview and questionnaire assessments. Adolescents also completed an EAR evaluation questionnaire at the 3-week follow-up to assess comfort with wearing the EAR. Adolescents also completed computerised tasks at both follow-ups. To ensure participant safety, our REDCap database was constructed to flag critical items (ie, risk of suicide) for review by the research team, and for participants endorsing those items in self-report or interview, staff implemented a series of assessments, and a licensed clinician, experienced with STB, oversaw procedures related to assuring participant safety.

Interview measures

The SITB-I and Columbia-Suicide Severity Rating Scale were used to assess the presence, frequency and characteristics of a wide range of self-injurious thoughts and behaviours, including suicidal ideation, suicide plans, suicide gestures, suicide attempts and non-suicidal self-injury.[102] We assessed current diagnosis at baseline and 6-month follow-ups using the Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime Version,[103] a widely used and well-validated assessment tool that we have already updated for the Diagnostic and Statistical Manual of Mental Disorders-5 in our current studies. Given the posited relevance of trauma, the Clinician-Administered PTSD Scale for Children and Adolescents (CAPS-CA), paired with the Life Events Checklist, was used to assess trauma exposure and PTSD diagnosis and symptom severity.[104] The Timeline Followback assessed for particular thoughts and behaviours related to self-injury, substance use and sexual behaviours over the prior 3–4 weeks. Vocabulary and matrix reasoning subscales from the Wechsler Abbreviated Scale of Intelligence were conducted at baseline. Clinical interviews were audiotaped for inter-rater reliability.

Adolescent questionnaire measures

Given our focus on affect dynamics, we used a number of cross-sectional questionnaires to assess a number of relevant/overlapping constructs at baseline, on completion of the EMA/EAR protocol, and at 6-month follow-up. The Emotion Reactivity Scale, a 21-item measure of emotion sensitivity, intensity and persistence, has shown strong psychometrics including excellent internal consistency (α=0.94) and convergent and divergent validity.[105] The Conflict Behaviour Questionnaire assesses perceived conflict and communication between adolescents and parents, with parallel versions for adolescents and parents.[106] Additional questionnaire measures that are relevant to the proposed research question include Difficulties in Emotion Regulation Scale, Family Assessment Device, Adolescent Drinking Questionnaire, ADD Health, Emotion Socialisation Measure, Sensitivity to Punishment and Sensitivity to Reward Questionnaire, Interpersonal Needs Questionnaire, Hopelessness Scale for Children, Affect Intensity Measure, Affective Reactivity Index-Self,

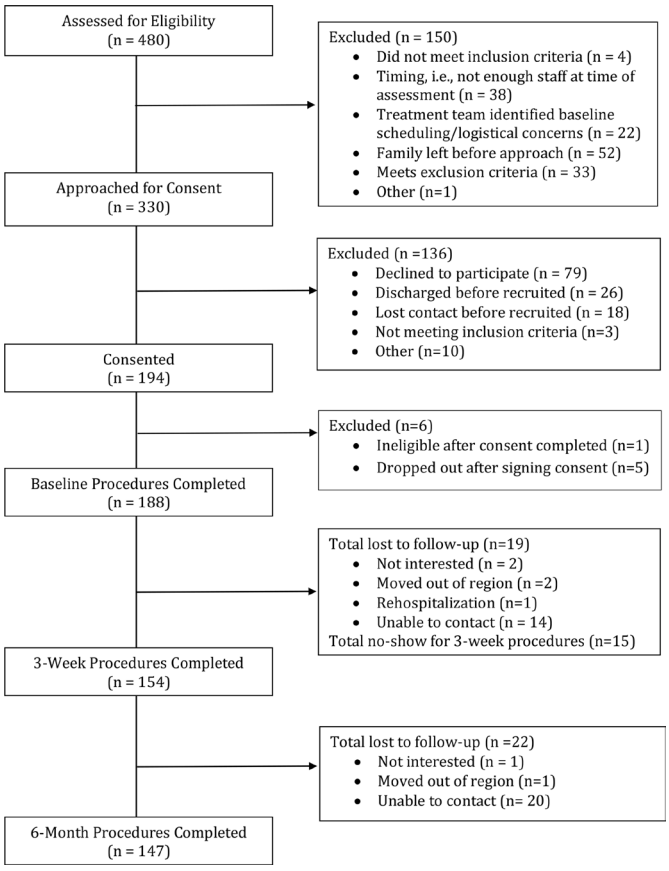

Figure 2 Consolidated Standards of Reporting Trials: enrolment and retention.

Sexual Orientation Questionnaire, Childhood Trauma Questionnaire, Children's Ruminative Response Scale, Implicit Theories of Emotion Scale, Youth Self-Report, Center for Epidemiological Studies Depression Scale for Children, Perceived Social Support/Conflict, The Connor-Davidson Resilience Scale and Family Risk and Protective Factors. Participants also completed the child and adolescent version of the Excessive Reassurance Seeking Scale, a four-item self-report questionnaire, rated on a Likert scale ranging from 1 (not at all) to 7 (very much).

Retention

Our study employed multiple strategies to ensure participant retention and adherence. First, we collected multiple forms of contact information for each participant (eg, home phone, cell phone and e-mail). Second, participants were compensated for each of the three possible assessments (baseline at $50, post-EMA/EAR 3 weeks at $50, and 6-month follow-up at $60) that they completed. Third, participants were compensated for each of the random EMA assessments they completed (with a bonus if they completed >75% of assessments). Fourth, we collected the EMA device and conducted the 6-month follow-up at participants' homes if they were unable or unwilling to come to our offices. If needed, transportation was also provided for participants to complete the follow-up assessments.

Patient and public involvement

Patients and the public were not involved in the design, implementation, analysis or dissemination of this research.

RESULTS

Enrolled participants included a total of 194 participants, ages 13–18 (mean=15.14, SD=1.44) hospitalised for STBs. As shown in figure 2, of 273 participants approached, a total of 71.1% consented to participation, an enrolment rate comparable with other research recruiting out of this population. After enrolment, 179 participants provided blood samples. Participants were considered retained if they attended a follow-up visit; demographic variables (sex, gender, sexual orientation, race and ethnicity) were unrelated to retention (all p values >0.05).

As shown in table 2, consistent with the demographics of the inpatient unit from which we recruited, participants were most likely to report their gender as girl/woman. Also consistent with youth self-reported gender on the adolescent psychiatric inpatient units during this study period, a number of youth (11.6% of participants) reported either transgender (13 participants) or other (eight participants) gender identity, and less than half identified as heterosexual or straight (47.6%). In part due to the requirement that the primary spoken language in the home needed to be English (for EAR coding purposes), the majority of participants (14.9%) reported that they were not Hispanic. Consistent with the unit demographics, participants reported white race (71.2%), followed by more than one race (16.5%) and by Black or African–American race (9.4%).

As shown in table 3, just over half (55.5%) of the participants were admitted to the adolescent inpatient unit due to an admitting professional's (ie, psychiatrist, psychologist, social worker, etc) assessment supporting adolescent suicidal ideation with a plan. The next most common reason for admission was suicidal ideation without a plan, with a quarter (25.4%) of participants reporting suicidal ideation without a plan. Another 18.5% of participants were admitted following a suicide attempt.

As shown in table 4, baseline clinical interview procedures (using the Schedule for Affective Disorders and Schizophrenia for School-Age Children and CAPS-CA interviews) were conducted, with mood disorders representing the most commonly observed diagnoses. Indeed, three-quarters (76.9%) of the participants met the criteria for a major depressive disorder. Over a third of the participants (38.2%) met the criteria for a persistent depressive disorder. A number of participants met the criteria for anxiety disorders, including generalised anxiety disorder (34.9%), panic disorder (29.6%) and social anxiety disorder (29.6%). A lower proportion of participants met criteria for behavioural disorders, including 15.1% attention deficit hyperactivity disorder and 9.1% oppositional defiant disorder. Relatively fewer participants met the criteria for substance and alcohol use disorders.

Table 2 Demographic characteristics of participants at baseline

	n	%
Sex at birth		
Male	55	30.4
Female	129	69.6
Self-reported gender		
Boy/man	50	27.9
Girl/woman	108	60.3
Transgender	13	7.2
Other	8	4.4
Sexual orientation		
Heterosexual or straight	79	47.6
Gay or lesbian	11	6.6
Bisexual	43	25.9
Not sure	13	7.8
None of the above	20	12.0
Ethnicity		
Hispanic	26	14.9
Not Hispanic	148	85.1
Race		
American Indian/Alaskan Native	3	1.8
Asian	2	1.2
Black or African–American	16	9.4
White	121	71.2
More than one race	28	16.5

Table 4 Diagnostic characteristics of participants at baseline

	n	%
Mood misorders		
Major depressive disorder	143	76.9
Persistent depressive disorder	71	38.2
Bipolar disorder	2	0.1
Disrupted mood dysregulation disorder	3	1.6
Anxiety disorders		
Panic disorder	55	29.6
Agoraphobia disorder	7	3.8
Social anxiety disorder	55	29.6
Specific phobia disorder	4	2.2
General anxiety disorder	65	34.9
Obsessive compulsive disorder	9	4.8
Behavioural disorders		
Attention deficit hyperactivity disorder	28	15.1
Oppositional defiant disorder	17	9.1
Conduct disorder	3	1.6
Eating disorders		
Anorexia nervosa	3	1.6
Binge eating disorder	6	3.2
Bulimia nervosa	1	0.5
Substance use		
Alcohol use disorder	2	1.1
Substance use disorder	15	8.1

On completion of the ecological procedures, participants were provided with the opportunity to request deletion of any audio files. Only one participant requested the deletion of any audio files (specifically, the participant asked that the researchers delete EAR files on one particular evening).

DISCUSSION

We provide here the description of an innovative, multimethod research investigation involving youth recruited during inpatient hospitalisation for STBs. As described here, youth and guardians were willing to participate in this novel research at similar rates as observed in other studies recruiting adolescents hospitalised for STBs. Enrolled participants showed baseline characteristics that were also comparable to the demographics and diagnoses observed on the units from which participants were recruited and were comparable to past research recruiting adolescents hospitalised with STBs. Future publications examining the multimethod outcomes of this sample assessed during the critical postdischarge period will provide important and clinically relevant context for adolescents hospitalised for STBs. The clinical significance of this research is enhanced by our focus on mechanisms that may later become targets for treatment.

Table 3 Reason for inpatient admission of participants at baseline

	n	%
Suicide attempt	35	18.5
Suicidal ideation with plan	105	55.6
Suicidal ideation without plan	48	25.4
Aggressive behaviour	1	0.5

The scientific significance of this work involves its critical contribution to frameworks for understanding the impact of early life abuse on neurobiology and, in turn, on the social–affective processes that unfold for suicidal adolescents during the high-risk transition from inpatient psychiatric hospitalisation. The American Foundation for Suicide Prevention, Columbia, and the National Institutes of Mental Health convened a workshop to characterise the diathesis for STB.[32] Many of the intermediary phenotypes identified as promising may share a common underlying component of stress sensitive affect reactivity and have been found to distinguish clinically relevant aspects of STB. The concept of a shared neurocircuitry underlying seemingly disparate functions of cognition, affect and social behaviour is consistent with the

Research Domain Criteria, 'effort to define basic dimensions of functioning… to be studied across multiple units of analysis, from genes … to behaviors, cutting across disorders as traditionally defined', and familiar to affective neuroscience,[36 37] which applies designs such as the present investigation to integrate social, affective and DNA/DNAm processes.

The close link between central and peripheral processes in stress-related disorders may be related to the high level of communication between central and peripheral processes in the initiation, maintenance and termination of the HPA axis. This framework has extended to epigenetic research, in which researchers concluded that 'glucocorticoid-induced epigenetic alterations have a broader validity in non-neuronal cells and that they may involve the DNA methylation machinery'.[107] Epigenetic methods provide an important biomarker for reactive style, *proposed here to be important during high stress periods such as during the transition from hospitalisation*. The 'signature model' of DNAm assumes an association between DNAm and a phenotype but makes no assertions related to brain DNAm; DNAm in hospital could serve as a biomarker for a stress reactive phenotype that could place youth at increased risk of STB during stressful times such as transition out of hospitalisation.

An important benefit of studies, such as the present research, focused on *translational* intermediary phenotypes such as emotional reactivity, is characterisation of mechanisms that may later become targets for treatment.[108–112] Information garnered from the present study will inform points of intervention, including when and how to intervene with patients during the sensitive post-discharge period. EMA methods may be employed to identify and describe the impact of context on thoughts, emotions and behaviours.[113] EMA has been used to explore a variety of processes and can be integrated easily with other scientific approaches.[114–118] EMA is particularly useful in the study of emotion, as traditional cross-sectional or daily assessments may be insufficiently frequent to capture variability in mood and insufficiently random to provide the background fluctuations against which reactions to stressful events can be contrasted. Internet-based methods, particularly when participants self-select assessment timing, limit assessments to situations in which participants have computer access or times when they 'feel like' responding, confounding participant responses. Since the present research was funded, although a few studies have applied EMA to understanding post-hospitalisation STB,[119] no studies have involved the sample size or comprehensive and integrated approach used here. As we have described before, the use of mobile technology/devices in research design is ideally suited to rapid translation into digital health approaches spanning from symptom monitoring to text messaging and just-in-time adaptive interventions.[120] Research incorporating technology into psychological and behavioural treatment has shown exponential growth in recent years, particularly since the COVID-19 pandemic has impacted traditional service delivery models.

The EAR complements traditional EMA-based experiential assessments by adding an objective (in the sense of traceable) observed behavioural perspective to the subjective experiential perspective. Implementing in vivo observational methods is particularly important when measuring evaluative constructs (eg, conflict and disengagement) that, in self-report, are prone to socially desirable responding (eg, impression management and self-deceptive enhancement). The present study is the first to implement the joint assessment of both perspectives on daily life in youth, that is, the experiential (via EMA) and social (via EAR) sides of daily life. Researchers have begun to explore the ways that audio sampling such as via the EAR might also be incorporated into intervention efforts, with early insights about clinician perceptions of both potential barriers and opportunities availed through audio sampling pointing to the importance of continued basic research to inform impactful intervention development in this area.[121]

It is hoped that future research will build on the limitations of this work. First, the sample size is small by some genomics standards, limiting some of the possible genomics analyses. Second, the sample is composed entirely of adolescents hospitalised for STBs; the study might have been strengthened by a comparison group such as adolescents who were transitioning home from a medical hospitalisation or from another period of time away from home (ie, time away at camp or visiting someone else). Third, although the EAR data are rich in content, the laborious nature of coding the EAR samples limits the immediate utility of the EAR to rapid translation to intervention. Fourth, although the sample is diverse in gender identity and sexual orientation, the majority of participants reported that they are white. Fifth, although rates of enrolled participants were comparable to past research with this recruitment site, it is possible that the participants who declined study participation were different in some way from enrolled participants. Finally, the study would have been strengthened by blood collection at each follow-up assessment to permit examination of how patterns of methylation may have changed over time.

It is also important to note that this study was designed to focus on the family environment due to past research demonstrating the importance of family factors and the potential relevance for translation for intervention. However, peer relationships are a critical part of adolescent development, and peer social support as well as peer bullying experiences have been shown to be important predictors of adolescent STB.[122 123] This limitation is slightly reduced by the use of the EAR, which permits identification (and coding) of interactions during non-school hours that occurred with peers. Future research that more systematically integrates peer relationships into the design will be important to more comprehensively evaluate ways that peer relationships could be targeted for intervention efforts.

Findings coming from this important research sample will inform our understanding of the high-risk transition from inpatient hospitalisation and will permit new

innovations in the applications of technology, as impacted by adolescent history, biology and social context. However, the present research also serves as a model for integration of multiple methodological components to permit a more comprehensive understanding of the real-world experience of adolescents hospitalised for STBs. Moving forward, we found that the field will benefit from efforts to characterise and intervene that, similar to the present research, propose integrated and multilevel assessments of clinically meaningful and modifiable processes.

Contributors Principal investigator NRN was responsible for the design of the research as related to the integration of multiple methods and analytical approaches in adolescents discharged from inpatient hospitalisation as well as all aspects of study implementation; as principal investigator and guarantor, NRN is responsible for the overall content. Coinvestigator MA was responsible for advising design and implementation of ecological momentary assessment procedures and contributed significantly to the overall study design. Coinvestigator SB contributed expertise related to dynamical systems modeling. LB was instrumental in study implementation and contributed to the paper. VK contributed expertise related to analysis of genetic and epigenetic samples to the original study submission. JEM contributed to original study design as related to phenotyping as well as oversight of all aspects of blood sample collection, storage and initial processing. AS contributed to the initial design, particularly related to interview and self-report assessment of adolescents hospitalised for suicidal thoughts and behaviours, as well as to study recruitment and the paper. MRM contributed expertise related to the audio sampling and coding and oversaw all coding of the audio samples.

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