Towards Health & Resilience in Volatile Environments (THRIVE) - a multi-level neurobiological study with vulnerable young adults

Published: 05-07-2022
Last updated: 11-07-2024

The aim of the THRIVE study is to examine three key objectives: 1. Does friendship support relate to reduced neural stress responses in young adults with CA?2. Does friendship support relate to enhanced self-esteem stability in young adults with CA?...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON53797

Source
ToetsingOnline

Brief title
THRIVE Study

Condition

- Other condition

Synonym
Feedback learning, Stress response

Health condition

neurowetenschappenlijk onderzoek

Research involving

Human

Sponsors and support

Primary sponsor: Universiteit Leiden
Source(s) of monetary or material Support: Ministerie van OC&W,Sara van Dam z.L. Foundation;Royal Netherlands Academy of Arts & Science grant (knaw WF/2407/SD2019-2); Elise Mathilde Foundation (W20303-5-EML)

Intervention

Keyword: Adolescent, Childhood adversity, Neurobiology, Resilience factors

Outcome measures

Primary outcome

The goal of the THRIVE study is to examine the neurobiological mechanisms of friendship support in young adults (aged 18-24 years) with a history of CA. For that we will investigate three potential mechanisms: neural stress responses, self-esteem stability, positive autobiographical memory specificity.

Hence, we will use the following main study parameters:

Main predictors

Childhood adversity

To estimate childhood adversity (CA), we will use a principal component analysis to estimate a latent factor predicting variance across all items that have assessed CA experiences (using the Childhood Trauma Questionnaire, Multidimensional Peer Victimization Scale, and the Youth and Childhood Adversity Scale). The latent factor score for CA will then be extracted and utilized in all subsequent analyses.

Friendship support

To assess friendship support, we will use a principal component analysis to estimate a latent factor predicting variance across items that have assessed perceived friendship support (using the Cambridge Friendship Questionnaire, McGill Friendship Questionnaire-Friendship Functions, and the Multidimensional Scale of Perceived Social Support). The latent factor score for friendship support will then be extracted and utilized in all subsequent analyses.

Main outcomes

Neural stress responses

Neural stress responses will be examined with the Montreal Imaging Stress Task (MIST; Dedovic et al., 2005), a psychosocial stressor, comprising a series of computerized mental arithmetic tasks with an induced failure component (detailed in section 5.2.4.2).

Outcome measures include:

1. Neural activity in the limbic system (Regions of Interest (ROIs): insula, hippocampus, amygdala, anterior cingulate cortex (ACC), and ventral striatum) during the MIST (i.e., stress vs. control) (Noack et al., 2019).
2. Self-reported mood (on a visual analogue scale) as well as hormonal (salivary cortisol) stress responses will be assessed before and after the MIST to ensure the test is indeed perceived as stressful and elicits a hormonal stress response.

Self-esteem stability

We will assess self-esteem stability using a task in which participants report on their self-esteem after receiving computer-generated approval and disapproval feedback (ostensibly from peers) on an online personality profile (Will et al., 2017; see 5.2.4.2 for more details regarding this task).
Self-esteem stability is operationalized as the extent to which self-esteem goes up or down as a function of approval or disapproval feedback, and it will be assessed both in a baseline self-esteem state as well as in an induced high or low self-esteem state.

Outcome measures include:

1. Self-esteem stability in response to social feedback (i.e., fluctuations in self-esteem in response to approval and disapproval feedback). This is measured through subjective ratings in response to the question *How good do you feel about yourself right now?* (on a visual analog scale submitted through button presses).
2. Neural activity co-varying with feedback-induced changes in self-esteem, with a specific focus insula-vmPFC connectivity during feedback-induced changes in self-esteem (Will et al., 2017).

Positive autobiographical memory specificity

Positive autobiographical memory specificity will be examined through the ratio of total specific to total categorical (overgeneral) responses to positive cues in the Autobiographical Memory Task (AMT; Askelund et al., 2019).

Outcome measures include:

1. Memory specificity for both positive and negative autobiographical memories as assessed through written responses in the Autobiographical Memory Task (AMT). We will assess responses to both positive and negative cues in order to examine whether potentially significant effects are due to memory specificity in general or specific to positive memory specificity.

Resilient functioning

Resilient functioning will be quantified as the degree to which an individual functions better or worse than expected given their self-reported history of CA (for details using this quantification see (Anne-Laura van Harmelen et al., 2017)). For that, we will use principal component analyses to estimate a single latent factor score that reflects current psychosocial functioning across various domains (i.e., mental health, drug and alcohol use, perceived stress, and aggressive behaviors towards self and others as assessed with the Drugs, Alcohol, and Self-Injury Inventory, International Self-Report Delinquency Questionnaire, Mood and Feelings Questionnaire, State-Trait Anxiety Inventory, Patient Health Questionnaire, and Perceived Stress Scale) as well as a single latent factor score that reflects CA experiences (assessed with the Childhood Trauma Questionnaire, Multidimensional Peer Victimization Scale, and Youth and Childhood Adversity Scale). Individual degree of resilient functioning will then be estimated as the residual variation from the best fitting relationship (comparing linear, quadratic, and cubic models) between our latent factor for psychosocial functioning and our latent factor for CA (see Figure 1).

As such, in our approach resilient functioning reflects the degree to which psychosocial functioning across domains is better (or worse) than expected given an individual*s CA experiences. Using this method, individual residual variation scores will be extracted to indicate individual degree of resilient functioning as compared to the overall sample. Please refer to Ioannidis et al., 2020 for an extensive discussion of the benefits and pitfalls of using this approach to quantify resilient functioning after CA.

Secondary outcome

The secondary study parameters include age, gender identity, sex assigned at birth, ethnic orientation, sexual orientation, highest level of education, occupation, caregiver household income, caregiver education status and covid related experiences. These factors will be analyzed in exploratory post-hoc analyses and added as covariates in our models.

Study description

Background summary

Up to 50% of all children and adolescents growing up worldwide are exposed to at least one form of childhood adversity (CA; e.g., abuse, neglect, bullying, or poverty) (Bellis, Hughes, Leckenby, Perkins, & Lowey, 2014; McLaughlin, 2016). CA can be defined as *exposure during childhood or adolescence to [highly stressful and potentially traumatic] environmental circumstances that are likely to require significant psychological, social, or neurobiological adaptation [*]* (McLaughlin, 2016; p. 363). As such, CA refers to a wide range of negative life experiences including child maltreatment (emotional, sexual, and physical abuse, and emotional and physical neglect) as well as intra-family adversity (e.g., martial distress/conflict, parental alcohol dependence, aggressive parenting behavior, parental violence, parental mental health problems, or stressful family-level life events) (Fritz, de Graaff, Caisley, van Harmelen, & Wilkinson, 2018). In addition, CA is a strong predictor of problems in adolescence, such as depression or anxiety, behavioral problems,

and aggression towards the self and others (Gilbert et al., 2009; Green et al., 2010). However, not all individuals with a history of CA move on to develop such internalizing or externalizing problems. Those individuals adapt well despite their early-life stressful experiences and can therefore be described as resilient. Social relationships are an important resource for resilient functioning (Ungar, Ghazinour, & Richter, 2013). Friendships, defined as voluntary, reciprocal, and nurturing relationships, may be a particularly important source of social support for young adults (Orben, Tomova, & Blakemore, 2020). We have shown that friendship support improves mental well-being in adolescents and young adults with a history of CA (A-L van Harmelen, Blakemore, Goodyer, & Kievit, 2021; Anne-Laura van Harmelen et al., 2016, 2017). However, the exact mechanisms through which friendships aid resilient functioning are currently unknown (Gunnar, 2017; Scheuplein & van Harmelen, 2022). To inform intervention and prevention efforts aimed towards increasing resilience in individuals with CA, the THRIVE study will examine three potential mechanisms (i.e., neural stress responses, self-esteem stability, positive autobiographical memory specificity) through which friendships may aid resilient functioning in young adults with CA.

Study objective

The aim of the THRIVE study is to examine three key objectives:
1. Does friendship support relate to reduced neural stress responses in young adults with CA?
2. Does friendship support relate to enhanced self-esteem stability in young adults with CA?
3. Does friendship support relate to greater positive autobiographical memory specificity in young adults with CA?

In addition, we will examine whether friendship support relates to improved resilient functioning through its effects on the three mechanisms (i.e., neural stress responses, self-esteem stability, positive autobiographical memory specificity).

Study design

This cross-sectional study will be conducted in Dutch and consists of a screening and two main sessions. The screening will be conducted via telephone during which interested participants will be screened for our inclusion and exclusion requirements (see appendix E4 for the telephone screening). Eligible participants will then be invited to the first online session (Session 1) during which they will be asked to complete self-reports assessing CA experiences, personality characteristics, and perceived social support. After completing Session 1, participants will be invited for an in-unit assessment (Session 2) at the Leiden University Medical Center (LUMC). Session 2 will consist of MRI scanning, saliva sampling, self-reports, and cognitive tasks

(Autobiographical Memory Task (AMT), Self-Esteem Task, Montreal Imaging Stress Task (MIST); see section 3 for a detailed explanation of the full study procedure).

Study burden and risks

Group relatedness Our participants will comprise of healthy young adults (18-24-year-olds without a current (past month) mental health diagnosis) with a self-reported history of CA. One out of two young people growing up worldwide are exposed to at least one form of CA, making it very prevalent in the general population (Bellis et al., 2014). In the light of potential burdens associated with participation in the THRIVE study, we have selected our exclusion criteria to ensure that our sample will not consist of very vulnerable individuals. Meaning, we will screen and exclude individuals based on a self-reported current (past month) mental health diagnosis, high depressive symptomatology (i.e., >14 on the PHQ; (Urtasun et al., 2019) indicating *severe depressive* symptoms) and/or current suicidal ideation (i.e., score >0 on question 9 of the PHQ). See section 4.2 & 4.3 for more details and appendix E4 for our telephone screening. Benefits of the study Although we know that friendships improve mental health and well-being in young people with CA, the underlying mechanisms of this effect are unknown (Scheuplein & van Harmelen, 2022). Our study will establish whether and how friendships improve mental health and well-being through their effects on three potential mechanisms of vulnerability (neural stress responsivity, self-esteem stability, and positive autobiographical memory specificity) in young adults with CA. An improved understanding about the protective role of friendships and their impact on these mechanisms of vulnerability has the potential to inform novel intervention and prevention efforts. These efforts could for example aim to mimic the beneficial effects of friendship support through specifically targeting the mechanisms of vulnerability. Burdens and risks associated with participation There are two types of burdens/risks associated with participation in the THRIVE study. First, the burden associated with Magnetic Resonance Imaging (MRI). MRI may in some cases be perceived as slightly uncomfortable, however, the burden is minimal, and we have proper procedures in place to make MRI scanning a relatively safe situation. Some participants can become claustrophobic while inside the scanner, in which case the session can be terminated immediately if the participant*s requests so. To reduce the risk of distress due to MRI, interested participants will be screened via telephone for standard MRI contraindications (e.g., claustrophobia, braces, or pregnancy) as well as prior to the start of the in-unit session. Second, our study population will consist of young adults with CA, who despite their experiences do not have mental health problems (i.e., we exclude those with a self-reported mental health diagnosis, as well as those scoring above the severe range for depression on the PHQ). In this resilient sample, recalling CA experiences, negative autobiographical memories, as well as completing the cognitive tasks (Self-Esteem Task and MIST) may still be perceived as stressful by some. The Autobiographical Memory Task (AMT), Self-Esteem Task, and MIST have been used

by the principal investigator and co-investigators in previous studies that included adolescents and young adults (i.e., 14 years and older). For instance, in a large sample of 14-year-old adolescents with a self-reported history of CA, we assessed positive and negative autobiographical memories (Askelund, Schweizer, Goodyer, & van Harmelen, 2019). In the Resilience after Individual Stress Exposure (RAISE) study, we assessed neural stress responses using the MIST in adolescents and young adults with self-reported CA experiences (Moreno-Lo*pez et al., 2021). Moreover, we have extensive experience assessing reactions to social stressors such as social exclusion in samples of adolescents (12-15 years; (Will, van Lier, Crone, & Gu*rog*lu, 2016)) and young adults (mean age = 18 years; (Anne-Laura van Harmelen et al., 2014)) with mental health disorders and histories of CA experiences (e.g., emotional maltreatment). Across these studies, participants did not report lasting emotional distress as a function of our experimental tasks. This may be due to our sensitive approach in our assessments as well as our interactions with the participants. Our sensitive approach means that we prioritize participants well-being during all aspects of the assessment day; making sure they understand that some tasks will be stressful, and that they know they can stop participation at any given time. During the debriefing, we make sure that participants have ample time to discuss their experiences and feelings and leave in a good mood. Furthermore, our recruitment strategy further ensures that those most sensitive to stress may not volunteer for our study. During recruitment the RAISE study, it was clearly stated that participants would undergo stressful tasks, which likely resulted in a self-selection bias of less easily distressed participants for these studies. In the current THRIVE study, we will adhere to a similar recruitment and assessment approach. In addition, we will screen and exclude interested participants that are particularly vulnerable to stress (i.e., excluding those with a self-reported current (past month) mental health diagnosis, high depressive symptomatology, and current suicidal ideation (both assessed with the PHQ during our telephone screening); see section 4.2 & 4.3 for more details and appendix E4 for our telephone screening). These measures have been chosen to minimize the possibility of participants becoming distressed during the study. However, in case a participant does experience distress during the study, we have a substantial risk protocol in place to alleviate distress in the most secure, empathic, and effective way possible.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Right-handed young adults aged between 18-24 years (inclusive).
Able and willing to provide digital informed consent.
Able to speak, write, and understand Dutch fluently.
Any experience of CA as retrospectively assessed with the YCAS (i.e., death of a very close friend or family member, major upheaval between parents, traumatic sexual experience, victim of violence, extreme illness or injury, and any other major traumatic event) up until the age of 18.

Exclusion criteria

Current (past month) diagnosis of mental health problems.
High depressive symptoms and/or current self-injury or active suicidal thoughts.
History of significant head trauma, premature birth, or learning disabilities.
Current neurodevelopmental disorders like autism spectrum disorder (ASD) or attention deficit hyperactivity disorder (ADHD).
MRI contraindications (e.g., metal implants, surgical clips, pacemakers, claustrophobia, or pregnancy).

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	13-10-2022
Enrollment:	124
Type:	Actual

Ethics review

Approved WMO

Date:	05-07-2022
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	02-08-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	06-11-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL80017.058.21