PI: **Schleider, Jessica Lee**	Title: Harnessing Network Science to Personalize Scalable Interventions for Adolescent Depression	
Received: 08/27/2018	FOA: RM18-010 Clinical Trial:Optional	Council: 05/2019
Competition ID: FORMS-E	FOA Title: NIH Director's Early Independence Award (DP5 - Clinical Trial Optional)	
1 DP5 OD028123-01	Dual: DE,RM	Accession Number: 4207606
IPF: 5992612	Organization: STATE UNIVERSITY NEW YORK STONY BROOK	
Former Number: 1DP5DE028760-01	Department: Psychology	
IRG/SRG: ZRG1 PSE-H (70)	AIDS: N	Expedited: N
Subtotal Direct Costs (excludes consortium F&A) Year 1: 250,000 Year 2: 250,000 Year 3: 250,000 Year 4: 250,000 Year 5: 250,000	Animals: N Humans: Y Clinical Trial: Y Current HS Code: 30 HESC: N HFT: N	New Investigator: Y Early Stage Investigator: Y
Senior/Key Personnel:	*Organization:*	*Role Category:*
Jessica Schleider	HARVARD UNIVERSITY	PD/PI

Reference Letters

[redacted]

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

3. DATE RECEIVED BY STATE	**State Application Identifier**

1. TYPE OF SUBMISSION*

❍ Pre-application ● Application ❍ Changed/Corrected Application

4.a. Federal Identifier

b. Agency Routing Number

c. Previous Grants.gov Tracking Number

2. DATE SUBMITTED 2018-08-31

Application Identifier

5. APPLICANT INFORMATION

Organizational DUNS*: [redacted]

Legal Name*: The Research Foundation of the State University New York
Department: Office of Sponsored Program
Division: SBRO
Street1*: [redacted]
Street2:
City*: [redacted]
County: [redacted]
State*: [redacted]
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: [redacted]

Person to be contacted on matters involving this application
Prefix: [redacted] First Name*: [redacted] Middle Name: [redacted] Last Name*: [redacted] Suffix:
Position/Title: Grants Administrator
Street1*: [redacted]
Street2:
City*: [redacted]
County: [redacted]
State*: [redacted]
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: [redacted]
Phone Number*: [redacted] Fax Number: [redacted] Email: [redacted]

6. EMPLOYER IDENTIFICATION NUMBER *(EIN) or (TIN)** [redacted]

7. TYPE OF APPLICANT* M: Nonprofit with 501C3 IRS Status (Other than Institution of Higher Education)

Other (Specify):
Small Business Organization Type ❍ Women Owned ❍ Socially and Economically Disadvantaged

8. TYPE OF APPLICATION*

● New ❍ Resubmission
❍ Renewal ❍ Continuation ❍ Revision

If Revision, mark appropriate box(es).
❍ A. Increase Award ❍ B. Decrease Award ❍ C. Increase Duration
❍ D. Decrease Duration ❍ E. Other *(specify)* :

Is this application being submitted to other agencies?* ❍Yes ●No What other Agencies?

9. NAME OF FEDERAL AGENCY*
National Institutes of Health

10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER
TITLE:

11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT*
Harnessing Network Science to Personalize Scalable Interventions for Adolescent Depression

12. PROPOSED PROJECT
Start Date* 09/01/2019
Ending Date* 08/31/2024

13. CONGRESSIONAL DISTRICTS OF APPLICANT
NY-001

SF 424 (R&R) APPLICATION FOR FEDERAL ASSISTANCE

14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION

Prefix: Ms. First Name*: Jessica Middle Name: Lee Last Name*: Schleider Suffix:
Position/Title:
Organization Name*: HARVARD UNIVERSITY
Department: Psychology
Division:
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*: [redacted]
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: [redacted]
Phone Number*: [redacted] Fax Number: Email*: [redacted]

15. ESTIMATED PROJECT FUNDING

a. Total Federal Funds Requested* [redacted]
b. Total Non-Federal Funds* [redacted]
c. Total Federal & Non-Federal Funds* [redacted]
d. Estimated Program Income* [redacted]

16.IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?*

a. YES ○ THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:
DATE:

b. NO ● PROGRAM IS NOT COVERED BY E.O. 12372; OR
○ PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

17. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)

● I agree*

** The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.*

18. SFLLL or OTHER EXPLANATORY DOCUMENTATION File Name:

19. AUTHORIZED REPRESENTATIVE

Prefix: Ms. First Name*: [redacted] Middle Name: [redacted] Last Name*: [redacted] Suffix:
Position/Title*: Grants Administrator
Organization Name*: The Research Foundation for the State University New York
Department: Office of Sponsored Programs
Division: SBRO
Street1*: [redacted]
Street2:
City*: [redacted]
County: [redacted]
State*: [redacted]
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: [redacted]
Phone Number*: [redacted] Fax Number: [redacted] Email*: [redacted]

Signature of Authorized Representative* [redacted]

Date Signed* [redacted]

20. PRE-APPLICATION File Name:

21. COVER LETTER ATTACHMENT File Name:Cover_Letter_DP5.pdf

424 R&R and PHS-398 Specific
Table Of Contents

SF 424 R&R Cover Page....1
Table of Contents....3
Performance Sites....4
Research & Related Other Project Information....5
Project Summary/Abstract(Description)....6
Project Narrative....7
Facilities & Other Resources....8
Equipment....13
Research & Related Senior/Key Person....14
PHS398 Cover Page Supplement....21
PHS 398 Modular Budget....23
Personnel Justification....29
Additional Narrative Justification....30
PHS 398 Research Plan....32
Specific Aims....33
Research Strategy....34
PHS Human Subjects and Clinical Trials Information....46
Study 1: Phase 1: Establishing Guidelines for Computing Personalized Symptom Net for Adolescent Depressive Symptoms....48
Inclusion Enrollment Reports....53
Study 2: Phase 2: Personalized Symptom Network Parameters as Predictors of Resp to Single-Session Interventions for Depression in Adolescents....63
Inclusion Enrollment Reports....68
Bibliography & References Cited....85
Letters of Support....90
Resource Sharing Plan(s)....104

Project/Performance Site Location(s)

Project/Performance Site Primary Location

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: The Research Foundation of the State University New York

Duns Number: [redacted]

Street1*: [redacted]

Street2:

City*: [redacted]

County: [redacted]

State*: [redacted]

Province:

Country*: [redacted]

Zip / Postal Code*: [redacted]

Project/Performance Site Congressional District*: NY-001

Project/Performance Site Location 1

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: STATE UNIVERSITY NEW YORK STONY BROOK

DUNS Number: [redacted]

Street1*: [redacted]

Street2: [redacted]

City*: [redacted]

County:

State*: [redacted]

Province:

Country*: [redacted]

Zip / Postal Code*: [redacted]

Project/Performance Site Congressional District*:

Additional Location(s) File Name:

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* ● **Yes** ❍ **No**

1.a. If YES to Human Subjects

Is the Project Exempt from Federal regulations? ❍ Yes ● No

If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 _ 7 _ 8

If NO, is the IRB review Pending? ● **Yes** ❍ **No**

IRB Approval Date:

Human Subject Assurance Number [redacted]

2. Are Vertebrate Animals Used?* ❍ **Yes** ● **No**

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ❍ Yes ❍ No

IACUC Approval Date:

Animal Welfare Assurance Number

3. Is proprietary/privileged information included in the application?* ❍ **Yes** ● **No**

4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* ❍ **Yes** ● **No**

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ❍ Yes ❍ No

4.d. If yes, please explain:

5. Is the research performance site designated, or eligible to be designated, as a historic place?* ❍ **Yes** ● **No**

5.a. If yes, please explain:

6. Does this project involve activities outside the United States or partnership with international collaborators?* ● **Yes** ❍ **No**

6.a. If yes, identify countries: Netherlands

6.b. Optional Explanation:

	Filename
7. Project Summary/Abstract*	Project_Summary_Abstract.pdf
8. Project Narrative*	Project_Narrative_08.04.18.pdf
9. Bibliography & References Cited	references_cited_7_20_18.pdf
10.Facilities & Other Resources	Facilities_Resources_8_10_18.pdf
11.Equipment	Equipment.pdf

Funding Opportunity Number: RFA-RM-18-010. Received Date: 2018-08-27T12:22:32.000-04:00

Project Summary/Abstract

Major depression (MD) is the leading cause of disability in youth, with a global economic burden of >$210 billion annually. However, up to 70% of youth with MD do not receive services. Even among those who do access treatment, 30-65% fail to respond, demonstrating a need for more potent, accessible interventions. A challenge underlying limited treatment potency is MD's heterogeneity: An MD diagnosis reflects >1400 symptom combinations, creating a need for treatments matched to personal clinical need. Separately, low treatment accessibility stems from the structure of existing interventions. Most span many weeks and are designed for delivery by highly trained clinicians, making them difficult to scale. This proposal aims to address the need for accessible, potent youth MD interventions by integrating methods and findings from previously separate areas: single-session intervention (SSI) research and network science. In a meta-analysis of 50 randomized trials, the investigator has found that SSIs can reduce diverse youth psychiatric problems, including MD. The investigator also found that a web-based SSI teaching growth mindset (the belief that personal traits are malleable) reduced depression and anxiety in high-symptom youth across 9 months. Thus, well-targeted SSIs can yield lasting benefits—but given MD's heterogeneity, there is a need for tools that can match youth to SSIs optimized for personal symptom structures. The proposed project harnesses computational advances from the *network approach to psychopathology*, which views psychiatric disorders as causal interactions between symptoms, to evaluate such a tool. The first goal is to establish a new method of characterizing MD symptom structures; the second is to test parameters from these structures as predictors of response to two SSIs targeting distinct MD features (behavioral vs. cognitive symptoms). Specifically, Aim 1 is to establish guidelines for computing personalized symptom networks using experience sampling method (ESM) data from youth with MD collected 7x/day for 3 weeks (N=50, ages 11-16; 147 time-points each). This will include a comparison of two leading approaches for computing network parameters, such as outward centrality (the degree to which a symptom prospectively predicts other symptoms). Aim 2 is to test network parameters as SSI outcome predictors among youth with MD (N=180). Youth will be randomized to a behavioral activation (BA) SSI (adapted from evidence-based BA SSIs); the mindset SSI noted above; or a control SSI. Network parameters will be tested as predictors of SSI response. For instance, youth with stronger centrality on a behavioral symptom (e.g. withdrawal from pleasurable activities) may respond more favorably to the BA SSI, and youth with stronger centrality on a cognitive symptom (e.g. hopelessness) to the mindset SSI. Results may identify a novel means of matching youth to targeted MD SSIs by personal need. The project will also include the first RCT comparing two youth MD SSIs, with the longest follow-up of any SSI trial to date (2 years), gauging their relative promise to reduce youth MD.

Project Narrative

The goal of this project is to integrate advances in network analysis and intervention science—specifically, research on single-session interventions (SSIs)—to identify potent, accessible strategies for reducing depression in adolescents. The first goal is to establish guidelines for characterizing adolescents' depression symptom structures, using experience sampling method data to compare two approaches for computing personalized symptom networks; the second goal is to test whether parameters from these personalized symptom networks predict adolescents' clinical response to evidence-based SSIs targeting distinct features of depression. Results may identify a novel, powerful approach to matching adolescents to targeted SSIs based on personalized clinical need.

Facilities & Other Resources

Positions details:

• During the award period, the Early Independence investigator must be scientifically independent and administratively independent. The appointment need not be permanent or tenure-track and may be contingent upon receipt of the Early Independence Award. Describe in detail the position to which the Early Independence investigator will be appointed and how the PD/PI's independence will be ensured during the course of the award:

Dr. Schleider is an extremely promising young clinical scientist in the area of child and adolescent psychopathology and intervention. She was hired as a tenure-track Assistant Professor in the Psychology Department, where she will begin in the fall 2018 semester, shortly after completing the requirements for her Ph.D. While Psychology is generally not inclined to hire junior faculty without postdoctoral training, Dr. Schleider's productivity, focus, and the innovative research led our faculty to unanimously select her as our first-choice candidate. Dr. Schleider will strengthen and expand the department's already strong and well-funded program in developmental psychopathology and evidence-based intervention.

• Describe plans for maintaining protected time for the Early Independence investigator so that s/he will be able to devote at least 9.6 person-months every year (i.e., 80% effort of a 12-month appointment) to conducting independent research during the project period, with at least the first two years being devoted entirely to the Early Independence Award project. Clinicians should be permitted to perform clinical duties to the extent necessary to maintain credentials:

The standard teaching load in Psychology is three courses per year (2 in one semester, 1 in the other semester). To facilitate the development of Dr. Schleider's research program at Stony Brook, Dr. Schleider will be permitted to reduce her teaching load in order to devote the required amount of effort to the proposed project. Additionally, Clinical Psychology faculty can receive teaching credit for one course per academic year for the clinical supervision and training of our Doctoral students. As part of her integration into the Department, Dr. Schleider will take on the role of overseeing some of the supervision and training of Doctoral students in treatment of child and adolescent cases. Importantly, Dr. Schleider's clinical supervisory activities will also serve to maintain her clinical skills and credentials; further, they will be directly linked to the populations and topics core to her research.

• Describe the process and criteria used to select the PD/PI.

Dr. Schleider was selected as Stony Brook University's nominee for this award following a thorough internal review. This process entailed a faculty review of the applications which were then scored and rated on fit and merit.

• Describe the institutional organizational structure within which the Early Independence PD/PI's position will be administered (school, department, etc.), and explain how this administrative structure will best meet the goal of supporting the success of the Early Independence PD/PI. Include details of responsibilities for integrating the Early Independence investigator and his/her scientific project into the institutional culture and the faculty community. Describe the management of problematic situations as well as institutional expectations related to the retention or transfer of the PD/PI at the end of the funding period.

The research environment at Stony Brook University (SBU) is strong and well-resourced. SBU is one of only 62 institutions in the country awarded membership in the prestigious Association of American Universities (AAU), representing the leading public and private research universities in the United States and Canada. The Psychology Department at Stony Brook is an ideal venue for development of early career faculty in Dr. Schleider's field. We are a member of the elite Association of American Universities (AAU), and Psychology is one of the largest and most respected departments in the College of Arts & Sciences. The National Research Council ranks the department in the top quartile, and our Clinical Psychology Doctoral Program (which Dr. Schleider will join as a faculty member) is ranked #4 in the country by U.S. News and World Report. The program is a longstanding leader in the development of evidence-based interventions, a charter member of the

Academy of Psychological Clinical Science, and accredited by both the American Psychological Association and the Psychological Clinical Science Accreditation System. As such, the Clinical Psychology Doctoral Program attracts highly competitive applicants [redacted] who strengthen and grow the research programs of our faculty In her faculty position, Dr. Schleider will be provided all the rights, privileges, and opportunities associated with a tenure-track faculty role at a major R1 institution, including attendance and voting rights at faculty meetings, running her own lab and lab meetings, and some teaching and clinical supervisory responsibilities.

• If the candidate is not a U.S. Citizen or permanent resident, the sponsoring institution must include information about the candidate's visa status and assurance that the candidate's visa provides sufficient time to complete the award at a U.S. institution.

Not Applicable

Institutional resources commitment:

• Describe details of the laboratory space to be provided to the Early Independence investigator, including physical structure and space layout along with the availability of support staff.

The proposed research will be conducted within PI Schleider's future laboratory, the Laboratory for Scalable Mental Health (LSMH). The LSMH will be located on the third and fourth floors of the Psychology Department building on the SBU Main Campus, will consist of approximately 1000 square feet total (4 rooms and a faculty office), and will be designated specifically for the PI's research program. PI Schleider will serve as the primary research advisor for one master's-level student during the 2018-19 academic year; additional doctoral students will be admitted by the beginning of the award period. Additionally, PI Schleider has recruited a team of six research assistants, whom she will supervise beginning September 2018. The LSMH will contain multiple spaces to be used for this study. First, there will be 2 sound-attenuated rooms of 104 sq. ft. each. One will be dedicated to diagnostic, behavioral, and self-report intake assessments with adolescents, as well as computer-based intervention administration. The second room will serve as a private space for caregivers to complete their assessment batteries. Additionally, the LSMH will include a 234 sq. ft. rectangular room, to be equipped with a conference table and chairs, where psychophysiological data collection may occur. PI Schleider owns a full set of Biopac equipment (including a Biopac MP150 Starter System, an EDA electrical activity amplifier, an ECG electrocardiogram amplifier, a skin conduction transducer, disposable electrodes, gel, and tape), as well as a linked computer equipped with AcqKnowledge software, for psychophysiological data acquisition, cleaning, and analysis. The space's conference room-like setup will enable administration of in-vivo stress inductions such as the Trier Social Stress Test. The LSMH will be HIPAA-compliant in terms of storage and maintenance of confidential data, including minimum two-lock protection public spaces and storage cabinets for paper data, and a secure 32 TB RAID 60 server. Beyond this, the LSMH contains an additional shared, private office space (234 sq. feet) with carrels for research assistants, students, and project coordinators; and access to a shared large conference room (529 sq. ft.) for full-lab meetings. All of the spaces have been prewired with multiple CAT-5 ports, currently configured as one phone and two 1GB Ethernet drops. The Ethernet drops connect to the RAID 60 server. Dell Optiplex 9020 Workstations (Quad Core, 3.40GHz, 8MB, w/HD4600 Graphics processors; 8GB DDR3 SDRAM at 1600MHz; 320 GB Hard Drives) accompany each carrel and the acti32Champ system. These Workstations will contain the software (Microsoft Office, MPlus, Stata, R, Qualtrics, and SPSS) needed to conduct and manage this research. A machine shop and electronic shop are also housed in the same building as the SCTL. The PI's office (234 sq. ft) will be located one floor beneath the lab; office of future graduate students will be on various floors in the same building. The University Library is next-door to the PI's office and laboratory and provides access to state-of-the-art electronic resources including scholarly journals and scientific databases.

• Describe other administrative and support functions that will be available to the Early Independence investigator (for example, human resources, supply and equipment ordering systems, administrative assistance, etc.).

In terms of research support staff for her research program, Dr. Schleider will have multiple Departmental opportunities. First, the College provides funding for Doctoral students within the program, and junior faculty

are given first priority in admitting new students. Thus, Dr. Schleider will be provided with several Department-funded full-time doctoral students. Additionally, grant-supported faculty may enlarge their labs by funding additional graduate students; thus, should Dr. Schleider receive this Award, she will be able to expand her lab more quickly, ensuring that she enough students to support this and multiple other projects. Second, Dr. Schleider has access to a large pool of undergraduates (1500 Psychology majors), who may sign up for up to 9 hours/week of Research Assistant experience for course credit. Indeed, Dr. Schleider has already remotely recruited 6 Stony Brook undergraduates to join her new lab as research assistants, starting in the fall. The quality and diversity of the undergraduates is excellent; Stony Brook is among the 10 most selective public AAU universities in the country. Likewise, there is a standalone 1 year Psychology Master's degree program, wherein students may elect to participate as members of faculty labs; Dr. Schleider has already arranged to serve as the primary research mentor for one Master's student during the 2018-19 academic year. In sum, Dr. Schleider has access to an effectively limitless supply of Research Assistant support to conduct this project. Third, Dr. Schleider will have access to resources through her startup funds to hire a part-time, paid undergraduate lab coordinator to help establish her lab during the early years of her appointment. However, should she receive this Award and she will have sufficient resources to hire a full-time post-baccalaureate lab coordinator for the duration of this project, which will be essential to building the large-scale clinical research program she envisions. The Department also provides all faculty access to the highly experienced administrative and technical support staff. For instance, the Assistant to the Chair aid faculty with all hiring and purchases and aids in submission and administration of grants. The Psychology department also has a Building Manager and two full-time Electronics Shop experts who aid and support infrastructural and technical needs of its faculty. Finally, in terms of the logical (e.g., recruitment), statistical, and methodological aspects of her proposal, Dr. Schleider has access to substantial support from other faculty within and outside of the Department, as noted in multiple accompanying letters of support.

• Describe the institutional financial commitment to the Early Independence investigator. Matching funds are not required; however, an appropriate level of institutional support is expected. Institutional commitment to the development of the PD/PI as a successful and independent research scientist will be given considerable attention during the review and selection process.

SBU provides access to numerous research related resources, including multiple libraries, computing, and technology facilities. The psychology department provides a fully equipped computer, electronic, and wood shop, administrative assistants who assist in management of payroll and personnel issues, and an administrative grants assistant at no cost to faculty. The Psychology department has its own photocopiers, scanners, and supply room. The university has numerous additional resources including mail and document services, art and photographic services, and computing and information technology services. Of particular relevance to this proposal, the University's Clinical and Translational Science Center provides statistical consultation, counsel and assistance with clinical trial recruitment, and project and data management support for SBU investigators. Additionally, SBU provides faculty with free access to high-performance computing clusters—using top-of-the-line components from Penguin, DDN, Intel, Nvidia, Mellanox, and numerous other technology partners—enabling execution of complex computational techniques, such as network analysis.

• If the Early Independence investigator already has a commitment of funding for independent research (such as through another independent research program or institutional start-up funds), describe how the Early Independence Award will affect the other funding.

In her faculty position, Dr. Schleider will be provided all the rights, privileges, and opportunities associated with a tenure-track faculty role at a major R1 institution, including attendance and voting rights at faculty meetings, running her own lab and lab meetings, and some teaching and clinical supervisory responsibilities. Notably, the primary expectation of Dr. Schleider's position is research productivity, as at least 80% of her time is expected to be dedicated to conducting her own, independent research. To support this, Dr. Schleider has been provided a highly competitive start-up package [redacted] for professional support, technical equipment, subject recruitment and payment, testing materials, and lab development; this funding would not be affected by the receipt of the NIH Director's Early Independence Award. As her appointment is within the College Arts & Sciences, her position is a 9-month appointment. However, she is able to pay herself a summer salary for 2 months out of her start-up budget, and should she obtain external grant funding, she may pay herself up to 3 months of summer funding. If she receives this Award, she will be able to cover 100% of her summer funding

for the duration of the grant, maximizing her ability to further build her independent research program throughout the calendar year

Institutional career development commitment:

• Describe plans for assuring scientific independence. Particularly if the Early Independence investigator is staying at the same institution at which s/he trained, indicate how independence from degree/fellowship mentors will be established and maintained.

In September 2018, Dr. Schleider will begin a tenure-track position at SBU, serve as PI for her own laboratory in the Department of Psychology, and will build her research program (including the proposed project) fully independently from her former mentors, none of whom are affiliated with SBU. Dr. Schleider has established a solid foundation for undertaking the proposed project independently. Indeed, she led multiple research projects during her graduate training with conceptual guidance but significant methodological independence from her former mentors, requiring only consultation from them in her recent work.

• Describe plans for integrating the Early Independence investigator into institutional scientific and administrative activities at the institution. Describe the scientific collaborative activities (attendance at faculty meetings, laboratory meetings, participation in institutional scientific retreats, etc.) and career development resources (courses in laboratory management and grant writing, etc.) that will be available to ensure the Early Independence investigator is successful.

Dr. Schleider will be provided with many avenues for integration into the scientific community at Stony Brook, several of which she has begun to capitalize on. Within Psychology, there are regular departmental faculty meetings and colloquia, and there are also weekly faculty meetings for the clinical doctoral program. Additionally, although she has not yet arrived, Dr. Schleider has initiated collaborations with faculty in Psychology and begun discussions of future collaborations with faculty in other departments (Psychiatry, Pediatrics). Accordingly, she has been invited to present on her research to the Child and Adolescent Psychiatry faculty upon her arrival. Dr. Schleider also has department formal support to pursue Joint Appointments in both Psychiatry and Pediatrics following the start of her faculty appointment, which Dr. Levy (Chair of the department) will be very pleased to help to facilitate. The Psychology Department will actively support Dr. Schleider's efforts to obtain further support for this project from individuals throughout the Stony Brook community.

• Describe the mentoring structure, including membership, meeting frequency, and meeting format. Though the Early Independence investigator must be scientifically independent, it is important that senior colleagues are available as resources and periodically meet with the awardee.

The College of Arts and Sciences has a well-specified tenure review process, including two pre-tenure reviews that establish clear benchmarks for junior faculty. There is also ample support from senior faculty throughout the junior period. For instance, The College of Arts and Science has a formal junior faculty mentorship program, in which Dr. Schleider will meet semiweekly with a senior faculty mentor within Clinical Psychology (Dr. Joanne Davila); several times per semester with a faculty member outside of her area, but within Psychology; once a semester with the Chair of the department, and regularly with a third senior faculty member outside of our Department. Dr. Schleider has also already established informal mentorship relationships with faculty members within Psychology (e.g., Drs. Daniel Klein, Matthew Lerner, and Nicholas Eaton, as detailed in additional Letters of Support) and outside of Psychology (e.g., Drs. Paul Mitrani and Margaret McGovern). In mentor meetings, Dr. Schleider will receive feedback and guidance regarding research progress and tenure benchmarks. Additionally, junior faculty are openly encouraged to come to the Chair or Associate Chairs of the department or the Associate Dean for Faculty Affairs for ongoing guidance. Because of these features, junior faculty in the Psychology Department have an especially high historical success rate in obtaining tenure. Dr. Schleider will be similarly supported to achieve tenure during the early phase of her career.

• The primary goal for an Early Independence investigator is to establish an independent scientific research program. However, if an Early Independence investigator has an interest in (limited) teaching, describe what opportunities will be available.

The Psychology Department has designed Dr. Schleider's teaching load to directly complement her research program. Specifically, Dr. Schleider's teaching will focus on undergraduate and graduate courses on Developmental Psychopathology, allowing her to remain abreast of topics that are central to her research. Finally, Dr. Schleider is permitted to buy out of two courses per year. Thus, should she receive this Award, her effective course load will be reduced to just one formal course per year for the duration of the award. She will not have direct patient care responsibilities beyond supervision.

• Describe expectations and opportunities for the Early Independence investigator to establish a record of independent funding by submitting and accepting grants from sources other than the Early Independence Award.

The Psychology Department is strongly committed to supporting its junior faculty members. As such, Dr. Schleider will be encouraged (though not required) to apply for additional funding to support her work as necessary, and grant writing guidance will be provided individually in her mentor meetings; however, it is unlikely that much encouragement will be needed in Dr. Schleider's case, as she is actively developing multiple research grants applications for the coming years. Dr. Levy, the Department Chair is personally committed to supporting Dr. Schleider's career development, and this award in particular. Dr. Levy has offered Dr. Schleider the opportunity to meet regularly with her throughout the award period to review and discuss logistics of the project, including as navigating and capitalizing Departmental and Institutional supports and resources. These structures are designed to guide and facilitate Dr. Schleider's professional growth as well as to ensure all necessary resources are proactively accessible.

Equipment

All of the equipment required to do the intervention-related, behavioral, and psychophysiological components of this research will be located in the PI's laboratory at Stony Brook University. This includes including several desktop and laptop computers and a full set of Biopac equipment, including a Biopac MP150 Starter System, an EDA electrical activity amplifier, an ECG electrocardiogram amplifier, a skin conduction transducer, electrodes, gel, and tape, and a linked computer equipped with AcqKnowledge data acquisition software. The PI's lab will also be equipped with a lab telephone line for correspondence with study participants; and a laser printer, scanner, and fax machine for administrative purposes. For the experience sampling method (ESM) data collection components of the project, fifteen smartphones will be purchased as part of this grant to accommodate adolescent participants who do not own smartphones themselves. One smartphone will be lent to each such participant for the duration of the 3-week ESM data collection period.

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Prefix: Ms. First Name*: Jessica Middle Name Lee Last Name*: Schleider Suffix:

Position/Title*:
Organization Name*: HARVARD UNIVERSITY
Department: Psychology
Division:
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*: [redacted]
Province:
Country*: [redacted]
Zip / Postal Code*:

Phone Number*: [redacted] Fax Number:

E-Mail*: [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: PD/PI Other Project Role Category:

Degree Type: MA; PhD Degree Year: 2014; 2018 (expected)

Attach Biographical Sketch*: File Name: Schleider_Biosketch_8.20.2018.pdf

Attach Current & Pending Support: File Name: Current_and_Pending_Support_8_20_2018.pdf

Tracking Number: GRANT12700349 Funding Opportunity Number: RFA-RM-18-010 . Received Date: 2018-08-27T12:22:32.000-04:00

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Jessica Lee Schleider

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: Doctoral Candidate, Clinical Psychology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Swarthmore College	B.A.	05/2012	Psychology
Harvard University	M.A.	11/2014	Clinical Psychology
Yale University School of Medicine	Internship	06/2018	Clinical Psychology
Harvard University	Ph.D. (expected)	11/2018	Clinical Psychology

Personal Statement

I am well positioned to successfully carry out the proposed research project. Beginning with my undergraduate training at Swarthmore College, where I studied predictors and outcome mediators in school-based depression prevention programs, I have remained dedicated to a single professional goal: rapid advancement of scalable, precise interventions that will dramatically reduce youth internalizing disorders. Toward this objective, I have pursued extensive training in intervention and dissemination science, developmental psychopathology, social psychology, human physiology, technology-based data collection and treatment design, and advanced statistical techniques, including mixed-effects linear modeling and network analysis. Alongside these experiences, much of my clinical work has involved delivering interventions to youth with internalizing disorders. As a clinician, I have witnessed the pressing need for more accessible youth depression interventions, as well as the clinical impact that brief (and even single-session) interventions can yield when targeted to individual needs. Together, my research and clinical experiences have enabled me to grow a program of research on developing and evaluating precise, scalable interventions for youth depression and anxiety. To date, I have published the first meta-analysis supporting the promise of single-session interventions (SSIs) for youth mental health. Separately, integrating methods and findings from social-developmental psychology, human physiology, and clinical science, I designed and evaluated a targeted SSI that improved physiological stress recovery and reduced adolescent depression and anxiety across nine months. In conducting these and other studies, I have gained substantial experience in project management; training and supervising students and research assistants; and building partnerships with cross-disciplinary researchers and community agencies. The proposed project represents a direct extension of my previous work, markedly extending its scope and impact. It will be the first study to integrate advances in network analysis and SSI research, which may help entify potent, personalized, accessible strategies for reducing adolescent depression. My background, expertise, and record of success as a clinical scientist—combined with the Host Institution's highly supportive research environment and the added expertise of my Consultant and Collaborator (Drs. Laura Bringmann and Nicholas Eaton)—ideally position me to lead this project to completion.

B. Positions and Honors

Positions and Employment

2006-2008 Teaching Fellow, Middle School Math and English, Breakthrough New York (New York, NY)
2012-2018 Graduate Student, Clinical Psychology, Harvard University (Cambridge, MA)

2017-2018	Doctoral Intern in Clinical and Community Psychology, Department of Psychiatry, Yale University School of Medicine (New Haven, CT)
Starting 9/1/2018	Assistant Professor, Department of Psychology, Stony Brook University (Stony Brook, NY)

Other Experience and Professional Memberships

2013-2016	Mentor, Dissemination/Implementation Science Special Interest Group Mentorship Program
2017-2018	Mentor, Association for Psychological Science Undergraduate Mentorship Program
2017-2018	Mentor, Society for Clinical Child and Adolescent Psychology Mentorship Program
2012-Present	Member, Association for Psychological Science
2012-Present	Member Association for Behavioral and Cognitive Therapies (ABCT)
2012-Present	Member, Society for a Science of Clinical Psychology
2014-Present	Member, American Psychological Association (Division 53)
2014-Present	Member, Anxiety and Depression Association of America

Honors

2008	National Gold Medal, Scholastic Art & Writing Awards
2010	Starfield Summer Research Award, Swarthmore College
2012	Solomon Asch Award (for most outstanding thesis in psychology), Swarthmore College
2012	Phi Beta Kappa, Swarthmore College
2013	Karen Stone Award (based on high potential for independent research career), Harvard University
2013-2017	Restricted Funds Conference Award (x5), Harvard University
2015	Travel Award, International Society for Research in Child and Adolescent Psychopathology
2015	Elizabeth Munsterberg Koppitz Fellowship, American Psychological Foundation
2015	Ruth L. Kirschstein Individual Predoctoral National Research Service Award, National Institute of Mental Health
2015	Julius B. Richmond Fellowship, Harvard Center on the Developing Child
2016	Student Achievement Award, Society for Clinical Child and Adolescent Psychology, Division 53, American Psychological Association
2016	Derek C. Bok Certificate of Distinction in Teaching, Harvard University
2016	Delaware Project Student Research Award, Honorable Mention, The Delaware Project
2017	Dissertation Completion Fellowship, Harvard University
2017	Alies Muskin Career Development Leadership Award, Anxiety & Depression Association of America
2017	Anne Anastasi General Psychology Graduate Student Research Award, Society for General Psychology, Division 1, American Psychological Association
2017	Outstanding Student Researcher Award, Society for a Science of Clinical Psychology, American Psychological Association

C. Contributions to Science

1. Single session interventions for youth mental health problems. An overarching goal of my work is to further the development of novel, precisely targeted, brief interventions for youth mental health problems, designed with potential for scalability. Although over 200 psychosocial interventions are identified as "effective" or "promising" in treating youth psychological problems (https://www.samhsa.gov/ebp-resource-center), access to services is strikingly low. There are many possible reasons for this discrepancy: Youth therapies can be costly and time-intensive, and they are not always accessible to those in need. Thus, there is a need for brief, scalable interventions for youth mental health problems—particularly those deliverable beyond brick-and-mortar clinics and via nontraditional means (e.g. web-based programs) to maximize accessibility. My work has shown that single-session interventions (SSIs) may hold potential to address this need. SSIs include core, theoretically driven elements of comprehensive, evidence-based therapies. However, their brevity and flexible format could make them disseminable to those who might not otherwise access care—and for whom a targeted, light touch treatment might be just enough. SSIs' promise is supported by a recent meta-analysis (role: PI) in which I evaluated the effects of SSIs for youth mental health problems. Across 50 RCTs (N=10,508 youths), SSIs showed a significant beneficial effect (mean *g*=0.32). This effect emerged even for self-administered interventions (i.e., those that did not involve a therapist). Thus, for some, SSIs may present a

cost-effective alternative or adjunct to traditional psychiatric services, which are often inaccessible to youths in need. I intend to dedicate my career to developing and testing effective, scalable youth interventions, using single-session designs and other brief, cost-effective frameworks, to help reduce depression and anxiety in youth.

- Schleider, J. L., & Weisz, J. R. (2017). Little treatments, promising effects? Meta-analysis of single session interventions for youth psychiatric problems. *Journal of the American Academy of Child & Adolescent Psychiatry*, *56*, 107-115.
- Schleider, J. L., & Weisz, J. R. (2017). Can less be more? The promise (and perils) of single-session youth mental health interventions. *The Behavior Therapist*, *40*, 256-261.

2. Growth mindsets and youth mental health. As noted above, the overall objective of my research program is to develop and disseminate accessible, potent interventions for youth depression and anxiety. Toward this goal, I have examined a particular type of youth cognition—called 'mindsets'—as a potentially potent intervention target. Mindsets are beliefs about whether personal traits are immutable (called a "fixed mindset") or malleable through effort (called a "growth mindset"). Historically, the mindset construct has been applied primarily in the educational domain. Research has shown, for example, that viewing intelligence as malleable increases children's effort on challenging academic tasks quickens recovery from academic setbacks. Drawing on this work, I have explored ways in which the mindset model might inform the promotion of *emotional* resilience in youth, including the prevention and treatment of psychological disorders. Through a meta-analysis on this topic, I observed that youths holding fixed mindsets of personal traits have shown more pronounced mental health problems overall. This association was evident across mindset domains (i.e. mindsets of intelligence, personality, and social abilities), and youth problem types (internalizing versus externalizing). In a school-based longitudinal study following early adolescents across an academic year, I found that fixed mindsets were prospectively linked with increased youth psychopathology, particularly internalizing problems. Mindsets may therefore represent a *cognitive vulnerability* to psychological distress in youth—particularly in the face of adversity—by providing a framework for understanding and coping with setbacks. For example, youths who hold fixed views of personal traits (i.e., beliefs that they cannot become smarter, less shy, or more socially skilled, regardless of personal effort) may feel unable to control unwanted life events, and thus be more vulnerable to anxiety, depression, or aggression. Thus, fixed mindsets may set the stage for maladaptive stress coping and mental health problems over time. Given this possibility, I tested whether mindsets might be a promising intervention target. With support from an NIMH NRSA (F31) and foundation grants, I developed and evaluated a single-session, computer-based intervention teaching growth mindsets of personality—including shyness, sadness, and likeability. For my dissertation, I tested whether this intervention improved social stress recovery and reduced internalizing problems in high-symptom early adolescents. Compared to a control program, the 30-minute mindset intervention strengthened youths' post-intervention physiological recovery from a lab-based social stressor, as well as perceived emotional and behavioral control. Further, compared to control group youths, youths who received the mindset intervention experienced significantly greater improvements in parent-reported depression and anxiety, youth-reported depression, and perceived primary control from baseline to 9-month follow-up. Results suggest a mechanism-targeted, low-cost strategy for reducing youth internalizing distress, with high potential for scalability.

- Schleider, J. L., & Weisz, J. R. (2018). A single-session growth mindset intervention for adolescent anxiety and depression: Nine-month outcomes of a randomized trial. *Journal of Child Psychology and Psychiatry, 59,* 160-170.
- Schleider, J. L., & Weisz, J. R. (2016). Reducing risk for anxiety and depression in adolescents: Effects of a single-session intervention teaching that personality can change. *Behaviour Research and Therapy*, *87*, 170-181.
- Schleider, J. L., & Weisz, J. R. (2016). Implicit theories relate to youth psychopathology, but how? A longitudinal test of two predictive models. *Child Psychiatry & Human Development, 47*, 603-617.
- Schleider, J. L., Abel, M., & Weisz, J. R. (2015). Implicit theories and mental health problems in youths: A random-effects meta-analysis. *Clinical Psychology Review*, *35*, 1-9.

3. Family processes and intervention design. In addition to examining youth mindsets as a possible intervention target, I have also examined family processes as possible targets that might inform the design of scalable, precise interventions for youth depression and anxiety. I have conducted several studies examining relations among familial risk, youth psychopathology, and youth treatment response. For instance, I found that parental psychopathology predicted diverse mental health problems in offspring, but only in single-parent

homes, suggesting that a parenting partner might mitigate the adverse impacts of parental psychopathology. I also found that in families of youths treated for anxiety disorders, higher pre-treatment parent psychopathology predicted greater reductions in caregiver strain and family dysfunction during treatment, which jointly predicted more favorable youth treatment outcomes. Together, this work has helped me develop a new theoretical model, the "triadic model of family process," to help guide the systematic development and evaluation of family-focused intervention strategies. This model outlines networks of parent-level (e.g. parental psychopathology), dyad-level (e.g. sibling conflict), and family-level risk factors (e.g. family stability) that may jointly shape youth processes underlying internalizing dysfunction (e.g., low perceived control). I have recently begun to apply the triadic model to intervention design: I found that a novel, 10-minute, web-based intervention targeting parent-level factors (specifically, maladaptive cognitions) increased parents' optimism about the effectiveness of psychotherapy, both for themselves (*d* = .47) and their children (*d* = .43), compared to an active control. In the future, I will continue using the triadic model to guide the development of targeted, family-focused strategies for reducing youth internalizing problems and improving access to youth mental health services.

- Schleider, J. L., & Weisz, J. R. (2017). Family process and youth internalizing problems: A Triadic Model of etiology and intervention. *Development and Psychopathology, 29*, 273-301.
- Schleider, J. L., Ginsburg, G. S., Keeton, C. P., Weisz, J. R., Birmaher, B., Kendall, P. C., Piacentini, J., Sherrill, J., & Walkup, J. T. (2015). Parent symptoms and treatment outcomes for anxious youth: Roles of family functioning and caregiver strain. *Journal of Consulting and Clinical Psychology*, *83*, 213-224.
- Schleider, J. L., Chorpita, B. F., & Weisz, J. R. (2014). Relation between parent psychiatric symptoms and youth problems: Moderation through family structure and youth gender. *Journal of Abnormal Child Psychology*, *42*, 195-204.
- Schleider, J. L., & Weisz, J. R. (2018, in press). Parent expectancies and preferences for mental health treatment: The roles of emotion mindsets and views of failure. *Journal of Clinical Child and Adolescent Psychology*.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/1teWtijC69eIsy/bibliography/55672483/public/?sort=date&direction=ascending

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing and Anticipated Research Support

Clinical Trial Sponsorship, Limbix Health Inc. Schleider (PI) 09/2018-09/2020
Optimizing growth mindset interventions for adolescent depression: Acceptability and effectiveness of a virtual reality approach.
This study will examine the acceptability and effectiveness of a novel, virtual reality-based intervention teaching growth mindset (the belief that personality can change) to adolescents with depression.
Role: PI. I will be responsible for overseeing all aspects of the study.

Completed Research Support

William H. Talley Fellowship, Harvard University Schleider (PI) 01/2017-01/2018
Parental preferences and expectations for child mental health treatment: Effects of viewing emotion and anxiety as malleable.
This study examined whether brief (10-15 minute), online interventions teaching growth emotion mindsets (viewing emotions as malleable), adaptive failure beliefs (viewing failure as enhancing rather than debilitating), or both could improve parents' expectancies and preferences for receiving mental health treatment.
Role: PI. I was responsible for overseeing all aspects of this study.

MetricWire Research Project Sponsorship, MetricWire Inc Schleider (PI) 02/2017-06/2018
Harnessing mobile technology to reduce anxiety and depression in early adolescents: A pilot feasibility trial of two app-based interventions.
This study examined the feasibility and acceptability of brief, moble app-based interventions teaching mindful meditation skills and growth mindset (the belief that personality can change), respectively, to youth with elevated internalizing symptoms.
Role: PI. I was responsible for overseeing all aspects of this study.

F31 MH108280, National Institute of Mental Health Schleider (PI) 08/2015-07/2018
Effects of a single-session implicit theories of personality intervention on social stress recovery and long-term psychological functioning in early adolescents
This study examined whether a single-session, web-based intervention teaching growth mindset of personality (the belief that personality is malleable) could reduce depression and anxiety, improve perceived control, and strengthen physiological stress recovery in high-symptom adolescents across 9 months.
Role: PI. I was responsible for overseeing all aspects of this study.

Elizabeth Munsterberg Koppitz Fellowship, Schleider (PI) 09/2015-08/2016
American Psychological Foundation
Effects of a single-session implicit theories of personality intervention on early adolescent psychopathology.
This fellowship provided additional funding for direct study costs associated with the fellowship noted above (F31 MH108280), including participant payment and psychophysiological equipment.
Role: PI. I was responsible for overseeing all aspects of the study.

Julius B. Richmond Fellowship Schleider (PI) 09/2015-05/2016
Harvard Center on the Developing Child
Awarded for research supporting resilience in at-risk children. This fellowship provided additional funding for direct study costs associated with the fellowship noted above (F31 MH108280), including study recruitment costs.
Role: PI. I was responsible for overseeing all aspects of the study.

William H. Talley Fellowship, Harvard University Schleider (PI) 09/2013-08/2014
Implicit theories of thoughts, feelings, and behavior in youths: Longitudinal links to parental evaluation and psychopathology
This school-based study examined longitudinal associations between implicit theories (mindsets) regarding the malleability of thoughts, feelings, and behavior; parental criticism; and psychopathology in early adolescents.
Role: PI. I was responsible for overseeing all aspects of this study.

Stimson Fund Research Grant, Harvard University Schleider (PI) 09/2012-08/2013
Relation between parent psychiatric symptoms and youth problems: Moderation through family structure and youth gender
This study examined whether family structure and youth sex moderated the association between psychopathology in parents and internalizing and externalizing problems in their children.
Role: PI. I was responsible for overseeing all aspects of this study.

Hans Wallach Fellowship, Swarthmore College Schleider (PI) 05/2011-08/2011
Sequential comorbidity of anxiety and depression in youth
The goal of this project was to produce a systematic narrative review of the association between childhood anxiety and subsequent depression in adolescence.
Role: PI. I was responsible for overseeing all aspects of this study.

Current and Pending Support

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

Expiration Date: 03/31/2020

1. Vertebrate Animals Section

Are vertebrate animals euthanized? ❍ Yes ● No

If "Yes" to euthanasia

Is the method consistent with American Veterinary Medical Association (AVMA) guidelines?

❍ Yes ❍ No

If "No" to AVMA guidelines, describe method and provide scientific justification

2. *Program Income Section

*Is program income anticipated during the periods for which the grant support is requested?

❍ Yes ● No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

*Budget Period *Anticipated Amount ($) *Source(s)

Tracking Number: GRANT12700349 Funding Opportunity Number: RFA-RM-18-010 . Received Date: 2018-08-27T12:22:32.000-04:00

PHS 398 Cover Page Supplement

3. Human Embryonic Stem Cells Section

*Does the proposed project involve human embryonic stem cells? ○ Yes ● No

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, check the box indicating that one from the registry will be used:

❑ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

Cell Line(s) (Example: 0004):

4. Inventions and Patents Section (Renewal applications)

*Inventions and Patents: ○ Yes ● No

If the answer is "Yes" then please answer the following:

*Previously Reported: ○ Yes ○ No

5. Change of Investigator/Change of Institution Section

❑ Change of Project Director/Principal Investigator

Name of former Project Director/Principal Investigator

Prefix:

*First Name:

Middle Name:

*Last Name:

Suffix:

❑ Change of Grantee Institution

*Name of former institution:

Tracking Number: GRANT12700349 Funding Opportunity Number: RFA-RM-18-010 . Received Date: 2018-08-27T12:22:32.000-04:00

NIH MODULAR JUSTIFICATION

Personnel

Jessica L. Schleider, Ph.D Candidate, Harvard University
(Effort = 3.0 summer months and 6.6 academic for a total of 9.6 person months in years 1-5)
Dr. Schleider is currently a PhD candidate at Harvard University and her faculty position will begin on September 1, 2018 at Stony Brook University. She will act as the Primary Investigator on this project and as such will be responsible for managing and maintaining the quality of all aspects of the project. She will lead weekly staff meetings to monitor and coordinate all project-related activities; hire, train, and supervise staff; monitor the budget; and take primary responsibility for data analyses and writing scientific papers from the project.

[redacted]

Graduate Research Assistant (effort=9 months in years 1-5)
To Be Hired. There is one funded graduate assistant line associated with this project, which will be filled by a doctoral student in clinical psychology from the PI's laboratory. The Graduate RA will assist with clinical assessments throughout the course of the project, as well as data processing, data analyses, intervention implementation and oversight, and data processing and analyses, and writing scientific manuscripts.

As required by Stony Brook University, in-state tuition is budgeted for the Graduate RA (see below).

Bachelor's-Level Project Coordinator (effort=12 months in years 1-5)
To Be Hired. The Project Coordinator will organize all aspects of the study, including scheduling and tracking participants; monitoring the completion of all lab-based and online assessments; recruiting and overseeing undergraduate RAs; submitting and monitoring participant payments; maintaining family & professional contact lists; ordering and upkeep of equipment and supplies; preparing and sending project newsletters to study participants; storage and oversight of confidential data; and assisting in the preparation of reports for the IRB and NIH. This position is budgeted at 100% effort (12.0 person months) for years 1-5.

[redacted]

Other

Graduate Student Tuition: Funds are requested to cover tuition [redacted] for one graduate student research assistant in years 1-5.

Subscription to LifeData for years 1-4. LifeData is a secure, HIPAA-compliant platform for experience sampling method (ESM) data collection, which is needed for Phases 1 and 2 of the project. A subscription to LifeData costs $3,480/year and is needed for years 1-4 of the project.

Recruitment: Funds are requested to cover costs of recruiting participants (e.g., travel costs for study personnel to recruitment sites; printing informational pamphlets and fliers; access to commercial mailing lists; estimated cost of $8,000 in total across years 1-4 of the grant period).

Subject Payment: Funds are requested for subject payments. For Phase 1 (Study 1), each family will receive $30 for a 90-minute baseline lab visit and another 90-minute follow-up visit. Additionally, adolescents will have the opportunity to earn an additional $5-10 during an Experience Sampling Method (ESM) data collection period, which will occur between the two lab visits. Adolescents will be prompted to complete the same 2-minute, 8-item survey 7 times per day for 21 days via a smartphone-based app. They will receive $5 for completing ≥75% of surveys or $10 for completing ≥90% of surveys. Thus, in total, the 50 participating families in Phase 1 may earn up to $70. The total amount in subject payment requested for Phase 1 is $3,500. Phase 1 payments will be disbursed in years 1-2 of the grant period.

For Phase 2 (Study 2), each participating family (one youth, one parent) will complete a 90-minute baseline lab visit and, approximately one month later, a second 2-hour lab visit. In between these lab visits, the adolescent will complete a 3-week ESM data collection period. Subsequently, each family will complete two additional 90-minute follow-up visits to the lab (at 3 and 12 months) and four 30-minute web-based follow-up surveys (at 6, 9, 18, and 24 months). Each family will receive $30 per in-person lab visit and $5-10 for completing the ESM data collection period ($5 for completing ≥75% of surveys or $10 for completing ≥90% of surveys). Additionally, for each online follow-up survey a participating youth/parent pair completes, their family's name will be entered once into a lottery for one of fifteen $50 gift cards, to be conducted after data collection is complete. Thus, each family participating in Phase 2 may earn up to $130 for completing all in-person visits and the ESM data collection period; families may also win an additional $50 gift card through a lottery (each family is eligible to win one lottery prize). The total amount in subject payment requested for Phase 2 is $22,350. Phase 2 payments will be disbursed in years 2-5 of the grant period.

Material and Supplies: Funds are requested for 15 individual smartphones (approximately $80 each to purchase via TracFone and $125/year per device, during years 1-4 of the grant, for limited service plan to enable Wifi access and LifeData usage). These smartphones are needed for adolescent participants in Phases 1 or 2 who do not own smartphones themselves; they will be lent to such participants for the duration of the 3-week ESM data collection period. Funds are also requested for disposable electrodes needed for psychophysiological data collection. Total funds requested for equipment: $9,500.

Travel: Funding is requested for travel expenses to attend professional meetings to present the proposed research, such as the Association for Behavioral and Cognitive Therapies (ABCT) annual meeting, the Anxiety and Depression Association of America (ADAA) annual meeting,

the Association for Psychological Science (APS) annual meeting, and others. Estimated costs are $3,000 for airfare and lodging per year (using the University's established rates).

I. Indirect Costs

Indirect costs are charged in accordance with the institution's most current Indirect Cost Rate Agreement dated 5/8/18 negotiated through DHHS, our federal cognizant agency.

PHS 398 Research Plan

OMB Number: 0925-0001
Expiration Date: 03/31/2020

Introduction	
1. Introduction to Application (for Resubmission and Revision applications)	
Research Plan Section	
2. Specific Aims	Specific_Aims_8_10_18.pdf
3. Research Strategy*	Research_Strategy_8.22.18.pdf
4. Progress Report Publication List	
Other Research Plan Section	
5. Vertebrate Animals	
6. Select Agent Research	
7. Multiple PD/PI Leadership Plan	
8. Consortium/Contractual Arrangements	
9. Letters of Support	EIA_LETTERS_OF_SUPPORT_-_ALL_8.13.18.pdf
10. Resource Sharing Plan(s)	Resource_Sharing_Plan_7_20_18.pdf
11. Authentication of Key Biological and/or Chemical Resources	
Appendix	
12. Appendix	

Tracking Number: GRANT12700349
Funding Opportunity Number: RFA-RM-18-010. Received Date: 2018-08-27T12:22:32.000-04:00

Specific Aims. Research Objectives. Efforts to reduce major depression (MD) in youth have advanced greatly, yet 30-65% of youth who receive treatment fail to respond.[1-2] The multifarious nature of MD contributes to this problem. An MD diagnosis reflects >1400 possible symptom combinations,[3] highlighting the need for treatments matched to personal clinical need. Compounding the problem of potency, existing treatments are not uniformly accessible: up to 70% of youth with MD do not access services.[4-5] Given the global economic burden of MD (>$210 billion annually[6]), there is a need for *potent*, *accessible* interventions. The goal of my research program is to help address this need by developing brief, mechanism-targeted interventions for MD and related disorders in youth, and streamlining their dissemination to those most likely to benefit. For example, I have identified growth mindsets (beliefs about the malleability of personal traits) as promising targets.[7-12] In an RCT (N=96), I found that a web-based single-session intervention (SSI) teaching growth mindsets improved youths' stress recovery and reduced depression and anxiety over 9 months (ds=.28-.60).[11-12] Indeed, across 50 RCTs, I found that SSIs reduced diverse youth psychiatric problems (mean g=0.32; N=10,508), with SSIs for MD producing modest effects (mean g=0.21).[13] Thus, well-targeted SSIs may yield lasting benefits. In addition to continuing to develop precise and even more potent MD SSIs, testing tools to pair youth with SSIs based on individual need is a key next step for my work. Given MD's heterogeneity, novel methods of characterizing symptoms may guide efforts to match youth to SSIs that best fit their clinical needs.

This proposal aims to accelerate innovation in youth MD treatment by establishing a new method of characterizing MD symptom structures, and testing parameters from these structures as predictors of response to two SSIs targeting distinct MD features (behavioral vs. cognitive symptoms). To achieve this, I will harness computational advances from the *network approach to psychopathology,* which views psychiatric disorders as causal interactions between symptoms.[14-17] **Aim 1** is to establish guidelines for computing idiographic symptom networks using experience sampling method (ESM) data from youth ages 11-16 with depression, collected 7x/day for 3 weeks (N=50; 147 time-points each). This will include a comparison of two leading approaches (multilevel factorial vs. vector autoregressive modeling[17-20]) for computing network parameters, such as outward centrality (the degree to which a symptom prospectively predicts other symptoms). Next, integrating network science and youth intervention research for the first time, **Aim 2** is to test network parameters as outcome predictors for two SSIs targeting behavioral and cognitive MD symptoms, respectively, in youth with depression (N=180). Following an ESM period, youth will be randomized to a behavioral activation (BA) SSI (adapted from empirically supported single-session and very brief BA interventions[21-23]); the mindset SSI noted above[11-12]; or a control SSI[11-12]. I expect network parameters to predict differential SSI response. For instance, youth with stronger centrality on a behavioral symptom (e.g. anhedonia; withdrawal from pleasurable activities) will respond more favorably to the BA SSI, and youths with stronger centrality on a cognitive symptom (e.g. hopelessness), to the GM SSI. I also expect youth with stronger bidirectional links between cognitive and behavioral symptoms to respond favorably to either SSI, versus the control. Results may yield a novel means of matching youths to targeted MD SSIs. The study will also include the first RCT of two youth MD SSIs, with the longest follow-up of any SSI trial to date (2 years),[13] to gauge their relative promise in reducing youth MD.

Institutional Support. Stony Brook University (SBU) has hired me as a tenure-track Assistant Professor of Psychology starting September 2018 and will provide excellent infrastructure and support for my research objectives. The position includes generous lab space and start-up funds; continuous departmental PhD student funding; limited teaching and clinical responsibilities, designed to augment my research program; and free access to administrative and technical staff. SBU will also provide a formal mentorship team of senior colleagues to support the launch of my independent career. At minimum, I will meet biweekly with a Senior Faculty Mentor in Clinical Psychology (Dr. Joanne Davila); monthly with two Senior Faculty Mentors outside of Clinical Psychology; bimonthly with my Department Chair (Dr. Sheri Levy); and annually with the Dean regarding tenure progress, creating a strong support system from which to achieve my research objectives.

Early Independence Rationale. I am fully prepared to accomplish the project proposed. At Swarthmore College, Harvard University, and Yale School of Medicine, I gained a decade of training in intervention science, complex statistical techniques, and developmental psychopathology. I led several studies on predictors and mechanisms of youth treatment response[11-12; 24-27]; two meta-analyses[7;13]; a school-based longitudinal study[8-9]; and 3 trials of SSIs I designed for youth, parents, and teachers.[11-12; 27-28] Through my F31/ NRSA, I gained training in physiological methods and applying social psychological theory to SSI design. Via courses and informal mentorship, I learned advanced statistical methods (e.g. multilevel modeling), network science, and online and mobile data collection. I have secured >$150,000 in research funding and published 25 papers (19 as first author). I mentored 22 RAs, advising 10 in co-authoring posters or papers; two in winning research grants; 10 in securing full-time RA jobs; and 8 in graduate program acceptances. Thus, I am well prepared to leverage my scientific training, leadership, and achievements to accomplish the objectives proposed.

Rationale for Omitting Post-Doc

Over the past decade, I have remained dedicated to a singular scientific vision: to develop and disseminate brief, mechanism-targeted interventions that will dramatically reduce youth depression and anxiety. Efforts to develop effective interventions have advanced greatly, yet they have not markedly reduced these disorders' individual or societal burdens. There is an especially urgent need for novel approaches to reducing youth depression—the leading cause of youth disability—as first-line treatments yield modest symptom reductions overall.[29] To accelerate progress in this domain, I have pursued intensive training in intervention and prevention science; developmental psychopathology; social psychology; human physiology; technology-based data collection and treatment design; and advanced statistical techniques. My activities and accomplishments to date demonstrate my readiness to launch an independent research program on developing precise, effective, accessible interventions, with the goal of reducing youth depression and anxiety on a large scale.

First, as an undergraduate at Swarthmore College working with Dr. Jane Gillham, I carried out several independent studies on change mechanisms in cognitive-behavioral interventions for depression in adolescent girls, as well as risk factors for adolescent anxiety in at-risk youth. I then trained in the Clinical Psychology Doctoral Program at Harvard University with Dr. John Weisz, an internationally recognized leader in youth mental health and intervention science. I obtained extensive training in developmental psychopathology, treatment evaluation, and dissemination science. I designed and led two meta-analyses; multiple projects using data from youth treatment trials, at Harvard and via external collaborations (e.g. with Dr. Golda Ginsburg at University of Connecticut; the Child/Adolescent Anxiety Multimodal Study Team; and Dr. Wendy Silverman at Yale School of Medicine); a school-based longitudinal study, which I launched in collaboration with Cambridge Public Schools; and two RCTs of novel single-session interventions (SSIs), including a trial testing a web-based growth mindset SSI I developed for adolescent anxiety and depression. Through an F31 NRSA from the National Institute of Mental Health, I obtained training in physiological data collection and analysis (using ECG, respiratory and EDA parameters, from Dr. Michelle Bosquet-Enlow at Boston Children's Hospital), and in using these parameters to index treatment response. I also learned to translate basic social psychological theory into the design of brief, web-based interventions for health outcomes from social and developmental psychologists Drs. Carol Dweck (Stanford University) and David Yeager (University of Texas). Most recently, as a Clinical Psychology Doctoral Intern at Yale School of Medicine working with Drs. Derrick Gordon and Carolyn Sartor, I enhanced my training in community-based intervention research, piloting a novel SSI for teachers in high-need public schools. I also furthered my statistical training, using cross-lagged panel analysis to model longitudinal reciprocal links among depression, anxiety, and alcohol use in adolescents. Via Harvard coursework and informal mentorship from aforementioned faculty, I built expertise in advanced quantitative techniques (e.g., multilevel modeling), network science, and online and ESM data collection.

In pursuing these experiences, I have gained many of the technical and leadership skills necessary to my planned program of research, including securing research funding through federal, foundation, and University-based grants totaling >$150,000; building a mini-lab of undergraduate and graduate trainees; and disseminating my research through publication of 25 peer-reviewed articles and chapters, including 19 first-authored papers. Although several postdoctoral opportunities were available that might have broadened my expertise in relevant areas, I felt prepared this year to apply for academic faculty positions to pursue my scientific vision as an independent investigator. I ultimately received an offer for a tenure-track Assistant Professor position at Stony Brook University (SBU): a top-tier institution offering excellent institutional support, including continuous graduate student funding and administrative resources, and cross-disciplinary support for my program of research (see Host Institution Interaction for details). Given this high level of Host Institution support, my preparedness as an independent clinical scientist, and the urgent need for improved approaches to reducing youth depression and anxiety, it made sense for me to omit the postdoctoral phase and accept the position at SBU, which I will begin in September 2018. This path will maximize my ability to contribute to my field at a very early career stage; spur needed progress in the reduction of youth depression; and build an excellent foundation for my research program, laboratory, and professional goals.

Evidence of Transition to an Independent Position

At the time of this application (August 2018), I am a PhD candidate in Clinical Psychology at Harvard University under the mentorship of Dr. John Weisz. I successfully defended my dissertation in January 2017 and completed my doctoral internship at Yale University School of Medicine on June 30, 2018. My expected degree conferral date is November 2018, the next available conferral date following my internship completion. Thus, I do not yet have research independence. My start-date as a tenure-track Assistant Professor at SBU (the Host Institution) will be September 1, 2018, prior to the start of the Early Independence Award.

Personal/career development plan.

I have several strengths that prepare me to launch a productive, independent research career. First, I have a track record of independence and success as a clinical scientist: In graduate school, I established a research program on developing and evaluating mechanism-targeted, scalable interventions for youth depression and anxiety. I secured federal, foundation, and competitive University-sponsored grants for this work, which yielded multiple publications. Second, I am highly collaborative in my scientific approach. My work is interdisciplinary and translational, applying theory from basic social-developmental psychology to build novel clinical interventions. As such, I work with researchers across these areas, within and outside my graduate institution. Third, I have successfully partnered with community organizations on research: a key skillset for conducting youth intervention studies. For instance, I led a 3-wave longitudinal study in Cambridge Public Schools and an intervention trial in New Haven Public Schools; I also built ties with community agencies to create recruitment channels for another clinical trial. Finally, I am trained in many relevant methodologies, including advanced quantitative methods (e.g. mixed-effects and growth curve modeling); psychophysiology (electrodermal activity/EDA; respiratory sinus arrhythmia/RSA); web- and mobile data collection and intervention design; and multi-method assessment. This award would allow me to capitalize on these strengths to build a comprehensive research program very early in my independent career. It would also spur cross-disciplinary collaborations, and augment my methodological expertise in key respects, to optimize and accelerate the impact of my work on novel youth depression treatments.

I also have weaknesses that this award would address directly. First, while I have used network analysis to estimate cross-sectional networks of youth depressive symptoms,[30] I have not had the opportunity to estimate within-person symptom networks. Indeed, constructing personalized networks and testing whether they predict treatment response is a new frontier in intervention science: one that may optimize our ability to match youths to brief interventions that target personal symptom structures. This award would allow me to gauge the potential of this innovative approach. Second, while I have directed large research projects and budgets, I have not managed a research program at the R01 scale. Third, I have not yet established myself as an independent scientist at the faculty level. This award would allow me to directly address each of these weaknesses.

The DP5 would greatly accelerate my establishing an independent research career, beyond the benefits provided by my future tenure-track position. First, it would allow me to buy out of teaching one semester-long course annually (resulting in a 1-1 load) and provide summer salary, maximizing my capacity to prioritize research endeavors. Second, the DP5 would provide funds for hiring a research team of the size, and with the skill set, needed for my planned research, including full-time research staff, as early as possible. Hiring an appropriate full-time team will be critical to achieving my scientific vision, given the complex, time-intensive nature of longitudinal and intervention research with youth. Third, given the scope and novelty of the proposed project, there is *no other funding mechanism* that would allow me to pursue it in full, including traditional R-series awards a much longer timeline and might sacrifice key project elements (e.g., linking network parameters to intervention outcomes within one study; limiting costlier elements of outcome batteries requiring multiple lab visits; interrupting study sequences to seek funding). This award would help me rapidly establish a cohesive, integrated research program on innovative approaches to reducing depression in youth.

My long-term career goals are to develop brief, mechanism-targeted interventions for youth internalizing disorders; establish tools to match youths to targeted interventions; and streamline dissemination of these tools and interventions to real-world settings. Toward this vision, my near-term goal is to build a consistently funded research program on brief, targeted depression and anxiety interventions for youth, as well as tools that may predict response to specific interventions. Simultaneously, I aim to establish a *Lab for Scalable Mental Health Lab* (LSMH) at SBU. The LSMH may serve as a site for effectiveness trials of novel interventions, and for tools designed to match youth to indicated interventions. Over time, I intend to partner with community agencies, schools, and pediatric clinics to gauge the viability of disseminating brief interventions in nontraditional settings. Such partnerships may identify strategies for increasing youths' access to targeted treatments. They may also suggest ways to further improve brief interventions and matching-tools, which could be tested in studies through the SMHL. This award would dramatically accelerate my pursuit of these objectives.

Evidence of training ability and leadership

Many previous activities have prepared me to lead a laboratory, train staff, and mentor students. I have led and managed numerous research projects, including lab-based and online intervention trials, school-based longitudinal studies, and meta-analyses. This involved securing and managing a budget of >$150,000 in grant funding, and recruiting and supervising large research assistant (RA) teams to ensure the projects' successful execution. Specifically, in a 'mini-lab' I built at Harvard, I trained 22 undergraduate and graduate-level RAs in community-based study recruitment, clinical trial design and management, clinical screening and assessment with youth and families, multilevel (physiological, subjective, behavioral) data collection, and meta-analytic

coding. From this training, I led our team in recruiting over 160 youths and families across a lab-based RCT and a school-based longitudinal study; over 800 parents for online longitudinal studies and intervention trials; and in conducting two meta-analyses. I advised 9 RAs in completing independent studies based on these projects, which resulted in co-authored presentations or publications. I also advised one RA on his psychology thesis, which received departmental honors. I mentored each student in scientific writing and statistical methods needed for their projects. I also supported 2 in securing competitive national and University-based research grants; 3 in winning postgraduate fellowships; 10 in obtaining full-time post-baccalaureate research positions; and eight in gaining acceptance to Ph.D., M.D., or M.A. programs. I wrote recommendation letters for each of these students in support of their successes. Separately, I serve as a Mentor in formal mentorship programs through 3 professional organizations (the Association for Psychological Science, Society for Clinical Child and Adolescent Psychology, and Association for Behavioral and Cognitive Therapies). I have mentored undergraduates in navigating the Ph.D. program application process, and early graduate students in planning their career trajectories. I have also taken on service and leadership roles in my field. I serve as peer reviewer for 22 journals in psychology and psychiatry, and in January 2018, I was invited to serve as Consulting Editor for the *Journal of Clinical Child and Adolescent Psychology* (the official journal for Division 53 of the American Psychological Association) where I am the only pre-doctoral Editorial Board member. Thus, many experiences have prepared me for the leadership, training, and mentorship roles I will take on an independent investigator.

Host institution interactions.

The host institution (Stony Brook University; SBU) has offered ample arrangements to provide support and feedback during my early career, with a view towards sustained integration into the scientific community (details enumerated in letters from Dean, Department Chair, and relevant senior colleagues, included in Facilities & Other Resources). SBU has hired me as a tenure-track Assistant Professor of Psychology. The position will include highly generous lab space and start-up funds; limited teaching and clinical responsibilities designed to directly augment my research program; arrangements for course reductions and summer salary to facilitate my early career transition; Departmental funding for 2-4 graduate students at any given time; opportunities to fund additional students, Post-Docs, and lab staff out of grants; and free access to Departmental administrative and technical staff (further details are included in letters of support from Dean X and Department Chair Levy). SBU has also provided me multiple avenues of mentorship from senior colleagues meant to provide me support and feedback to launch my independent career. These include biweekly meetings with a within-area Senior Faculty Mentor; and periodic meetings with an out-of-area Senior Faculty Mentor; regular informal meetings with other senior colleagues, including my Department Chair and other senior colleagues who have provided letters in this proposal; and annual meetings regarding tenure progress with the Dean and Associate Dean. Additionally, my Department Chair has endorsed my seeking additional faculty appointments in Psychiatry and Pediatrics upon the start of my position, and I have already begun to build connections with Chairs of both departments to integrate myself as an active member of SBU's cross-disciplinary research community (see support letters included in this proposal). I have also begun collaborations on research projects with colleagues in my future Department for which grant applications and IRB proposals are in progress. My connections within and outside of the Psychology Department will substantially aid in my establishing a robust, institutionally interconnected research program at SBU.

Research Challenge

Psychiatric disorders are the leading cause of disability worldwide, and 40.5% of this burden is attributable to major depression (MD).[31] Rates of MD increase markedly in adolescence, with nearly 20% of youth experiencing MD between ages 12 and 18.[32] Adolescent-onset MD accounts for 66% of lifetime MD cases and predicts interpersonal problems, substance abuse, and a 20-fold increased risk for attempting suicide.[33-34] Despite this early onset and protracted course, up to 70% of US adolescents with MD do not receive services.[4-5] Even among those who do access treatment, 30-65% fail to respond.[1-2] These findings highlight the urgent need for more potent and accessible MD interventions for adolescents.

A key challenge underlying the limited potency of MD treatments involves the heterogeneity of depression.[35] MD diagnostic criteria place youths with 5 of 9 diverse symptoms (such as excessive guilt, fatigue, and hopelessness) into a single category including >1400 possible symptom combinations.[3] This heterogeneity has led to the creation of MD interventions that address a wide range of symptoms, some of which may be unrelated to the clinical needs of an individual. Recently, intervention scientists have called for more focused, personalized treatments, and a departure from treatments characterized by "extreme comprehensiveness" (e.g., cognitive behavioral therapy) and those for which specific mechanisms of action remain unclear (e.g., SSRIs).[36-37] Developing tools that can identify symptoms most central to an individual's MD-related distress may enable matching of adolescents to targeted treatments by personal clinical need.

Separately, the challenge of low accessibility of MD interventions results partly from the way in which treatments are designed. Existing youth MD interventions tend to span many weeks, and are intended for delivery in brick-and-mortar clinics by highly trained clinicians.[29] These features make them difficult to disseminate on a broad scale. Further, between 28-59% of youths who do access mental health treatment drop out prematurely, exacerbating the problem of scarcity of services.[38-39] In sum, given unmet needs for adolescent MD treatment, creating brief treatments deliverable by nontraditional means is a needed direction for future work—particularly treatments targeting key mechanisms underlying individual difficulties.[40]

Emerging research on network analysis may guide efforts to strengthen the *potency* of MD interventions. The "network approach to psychopathology" states that individual symptoms interact with and cause one another to create and maintain psychiatric disorders.[14-17] Network analysis is a leading approach to quantifying these symptom-symptom interactions. This approach can identify outwardly central symptoms, defined as symptoms that most strongly predict increases in other symptoms in a network; and network density, or the mean strength of the interconnections among all symptoms in a network.[16-19] As in a domino effect, an outwardly central symptom is likely to have greater influence across an entire network due to its strong causal links to other symptoms.[14] Studies of MD symptom structures support this theory. For instance, MD symptom network density predicted greater odds of persistent (versus remitted) MD across 2 years in a large, clinic-referred sample.[41] In another study, baseline severity of MD symptoms identified as most central (e.g., anhedonia) predicted MD onset 6 years later.[42] However, these studies relied on cross-sectional, group-level symptom networks, which may not predict MD outcomes for specific individuals: indeed, group-level data often yield inaccurate estimates of individual experiences, suggesting that intensive, repeated-measures data (data collected from individuals at many time-points) may bolster predictive accuracy.[43] Separately, personalized network structures have not been tested as predictors of MD intervention outcome. For instance, individuals given a treatment targeting their most outwardly central symptom—versus a standard, broad-based treatment—might respond more favorably. By applying newly developed techniques for computing individual networks from within-person data[14-17], future research may test this possibility directly.

Whereas network analysis may help address the problem of *potency*, emerging work suggests that single-session interventions (SSIs) may increase *accessibility* of youth MD interventions.[13] SSIs include core elements of comprehensive, evidence based treatments, but their brevity makes them easier to disseminate to diverse settings.[13, 40] Indeed, SSIs can successfully treat youth psychiatric problems: In a meta-analysis of 50 RCTs, I found that SSIs reduced youth mental health difficulties of multiple types (mean g=0.32), including self-administered SSIs (e.g., web-based SSIs; mean g=0.32).[13] Two SSIs have been shown to reduce adolescent MD symptoms. The first is a *growth mindset (GM) SSI*: a web-based program teaching the belief that personal traits are malleable, which has prevented and reduced adolescent MD in recent RCTs.[11-12,44] For example, I found that a GM SSI led to significant 9-month MD symptom reductions in high-symptom adolescents, versus a supportive therapy control (ds=0.60, 0.32 per parent and youth reports).[12] The second is a *behavioral activation (BA) SSI,* which promotes value-based activity engagement to elicit feelings of pleasure and accomplishment.[21] In RCTs, BA SSIs have reduced MD symptoms in moderately depressed adolescents across 2 weeks (d=1.61) and 1 month (d=0.57).[21-22] Notably, GM and BA SSIs target different MD symptoms: whereas GM SSIs target and have effected change by reducing maladaptive cognitions, BA SSIs target anhedonia (through activity engagement). Thus, adolescents with different MD symptom structures may differentially benefit from GM or BA SSIs, although this possibility has not been tested.

The proposed project will integrate advances in network analysis and SSI research to identify potent, accessible strategies for reducing adolescent MD. In **Aim 1**, I will ascertain guidelines for characterizing MD symptom structures in adolescents, using ESM data to compare two approaches for computing personalized symptom networks. In **Aim 2**, through a three-arm RCT, I will test whether parameters from adolescents' MD symptom structures predict clinical response to SSIs. Adolescents with high MD symptoms will be randomized to receive one of two evidence-based SSIs (GM or BA) targeting distinct MD features, or a control SSI. I expect network parameters to predict SSI response. For instance, adolescents with higher outward centrality on a cognitive symptom (e.g. hopelessness) will respond more favorably to the GM SSI, and those with higher outward centrality on a behavioral symptom (e.g. anhedonia; pleasurable activity withdrawal), to the BA SSI. I also expect adolescents with stronger bidirectional links between multiple types of MD symptoms to respond more favorably to either SSI. Results may identify a novel approach to *matching* adolescents to targeted MD SSIs by personalized need. The study will also include the first RCT comparing two youth MD SSIs, with the longest follow-up of any SSI trial to date, gauging their relative promise to help reduce adolescent MD.

I chose this challenge due to my experiences working with youth with MD, whose families often struggle to find effective youth MD services. I have also witnessed the clinical impact that well-targeted interventions can

yield, reinforcing my goal of building potent, personalized, accessible strategies to reduce youth MD. My work shows the potential of well-targeted MD SSIs; it also supports the notion that they may operate by shifting key targets, reflecting specific MD features. Thus, my commitment to this challenge stems from the urgent need for progress and the potential of SSIs, network analysis, and their integration to help achieve it.

Approach

Overview. This study will progress in two phases. In phase 1 (addressing **Aim 1**), I will establish guidelines for computing idiographic symptom networks using experience sampling method (ESM) data from adolescents with elevated depression (N=50, ages 11-16; 147 time-points each). As a secondary aim, I will assess the predictive validity of parameters from these networks, or the degree to which network parameters predict changes in core depression-related deficits (anhedonia,[45-46] low agency,[47-48] blunted stress recovery[49-50]). After completing a study eligibility screener, adolescents and parents will complete a baseline battery assessing depression and related symptomatology; anhedonia (per self-report and a behavioral task), low agency (per self-reported hopelessness, fixed mindsets, and low perceived control), and impaired stress recovery (per RSA and EDA recovery from a lab-based stressor); and contextual depression risk factors at the peer (loneliness; peer victimization) and family levels (parental psychopathology). Adolescents will then participate in an ESM period. They will be prompted via smartphones to complete the same 2-minute survey of depression-related difficulties 7x/day for 3 weeks. Similar ESM protocols have been implemented with low missing data rates [17-20,51-54] (mean compliance rate in clinic-referred adolescents=89.3% across mobile-based ESM studies with ≥6 daily surveys[55]). Two months later (3 months post-baseline), adolescents and parents will complete a second lab-based battery, including the same measures as at baseline. In stage one of analyses, in collaboration with Consultant Bringmann (a quantitative psychologist and expert in intra-individual network analysis) and on-site support from Collaborator Eaton (a clinical psychologist with expertise in quantitative modeling of the structures underlying psychopathology, including network analysis[56-61]), I will assess which of two leading approaches to computing within-person symptom networks (multilevel factorial vs. vector autoregressive modeling for ESM data[14-17]) yields more stable idiographic network parameters for *overall network density* and *outward centrality* of each symptom assessed. Next, to test predictive validity of these parameters, I will use mixed-effects linear models to test the prediction that idiographic network structures prospectively predict changes in depression-related deficits (anhedonia, low agency, and blunted stress recovery). Results will identify the statistical approach that best estimates personalized symptom parameters for this population, building guidelines for future research. They will also gauge the predictive validity of idiographic network parameters by testing their prospective links to clinically relevant outcomes.

Methodological guidelines established in Phase 1 will directly inform Phase 2 (addressing **Aim 2**). Here, I will test whether personalized parameters from adolescents' MD symptom structures (outward symptom centrality and overall network density) predict response to targeted single-session interventions (SSIs). After completing an eligibility screener, adolescents with elevated depression (N=180; ages 11-16) and parents will complete a baseline battery and ESM period, as in Phase 1. Adolescents will then return to the lab, where they will be randomly assigned to receive one of three online SSIs: a GM, BA, or supportive therapy (ST) SSI. Adolescents will be assigned to one of the three SSIs via a computer-based randomizer; neither adolescents nor the research team will be aware of condition assignment until the end of the study period. Immediately pre- and post-SSI, adolescents will complete a limited number of self-report measures as manipulation checks, and to assess shifts in proximal outcomes relevant to each SSI (growth mindset; anhedonia; hopelessness; perceived control). Three months post-intervention, adolescents and parents will return for a follow-up battery, assessing the same factors as at baseline. A final lab visit (comprising the same battery) will be held 12 months post-intervention. Additionally, to enable analysis of outcome trajectories across a two-year period, adolescents and parents will complete online follow-up surveys (including all adolescent- and parent-report surveys included in the lab-based batteries) at 6-, 9-, 18-, and 24-months post-intervention. First, personalized network parameters will be computed from ESM data, using methods ascertained in Phase 1. I will then test personalized symptom parameters as predictors of SSI response. I expect that adolescents with a more outwardly central *cognitive* symptom (e.g. hopelessness or low perceived control) will respond more favorably to the GM SSI, and those with a more outwardly central *behavioral* symptom (e.g. anhedonia; withdrawal from pleasurable activities), to the BA SSI. (Note that each symptom's outward centrality will be indexed through continuous predictor variables; thus, there is no requirement or expectation that distinct groups of adolescents will emerge with outwardly central cognitive *or* behavioral symptoms.) I also predict that adolescents with higher overall network density, indexing stronger causal links among behavioral and cognitive symptoms, will respond more favorably to either active SSI. SSI response will be operationalized as declines in overall depressive symptoms (primary outcome) and improvements in core deficits linked with depression (secondary

outcomes: anhedonia, low agency, blunted stress recovery), from baseline to proximal (3-month) and longer-term (12- and 24-month) follow-ups.

Preliminary Studies. As noted in the RFA, preliminary data are not required for this award. However, I have conducted several preliminary studies that inform this project. For instance, in longitudinal studies and clinical trials, I have examined subjective and physiological predictors of youth symptom trajectories, SSI outcomes, or both.[8-9,11-12,24-26,28] Of particular relevance for Phase 2, I conducted a meta-analysis of 17 studies (N=6,543 youth, ages 4-17) that showed a significant overall relation between stronger fixed mindsets and more severe depression and anxiety (meta-analytic r=.30, p<.001).[7] In a subsequent school-based longitudinal study (N=59, ages 11-14), I found that youths' increases in depression and anxiety symptoms were linked with 6-month increases in fixed mindsets regarding thoughts (β=-.29, p=.02), emotions (β=-.27, p=.04), and behavior (β=-.29, p=.02).[8] Based on these findings, I developed and examined the effects of a web-based GM SSI on stress recovery and anxiety and depression in high-symptom adolescents (N=96, ages 12-15).[11] The GM SSI led to post-intervention increases in adolescents' perceived primary control (d=.34, p<.001) and secondary control (d=.19, p=.03) relative to a comparison (supportive therapy) SSI. Further, per EDA and HRV recovery slopes, adolescents receiving the GM SSI recovered from a lab-based stress task over 3 times as fast as comparison group adolescents (ds>.50, ps<.05). The GM SSI also predicted steeper 9-month declines in youth depression symptoms per parent (B=-.99, p=.047) and adolescent reports (B=-1.37, p=.03), based on mixed-effects linear models (the approach proposed in Phases 1 and 2).[12] Further, the GM SSI predicted steeper improvements in primary control across the follow-up (B=1.24, p=.047), and larger 9-month reductions in adolescent depressive symptoms per parent (d=.60) and youth-report (d=.32), and anxiety symptoms per parent-report (d=28).

Together, these results suggest the relevance of mindsets and low perceived control (i.e., difficulties linked to *cognitive* symptoms of depression) to youth depression and anxiety. They also suggest that web-based GM SSI can reduce depression in high-symptom adolescents, versus an active control SSI. They also establish the GM and control SSIs as acceptable and equivalent along key metrics: adolescents in the above RCT reported no differences in their program comprehension (p=0.72), interest in the material, (p=0.14), or effort on activities (p=0.37) by SSI assignment.[11] The research described above also confirms my familiarity with many of the methods and protocols in the proposed project and my success in retaining youths and families through follow-up (retention in my 6-month school-based study was 100%; and the 9-month retention rate of 77% in the GM SSI RCT is similar to retention rates achieved in large-scale, multisite clinical trials targeting youth depression).

My work also lends broader support to SSIs targeting youth psychopathology. In a meta-analysis of 50 RCTs (N=10,508 youths, ages 3-19), I found that SSIs demonstrated a significant positive effect (g=.32) across varying levels of youth problem severity and diagnostic status.[13] Importantly, significant SSI effects emerged even for self-administered (e.g. web-based) interventions (g=.32), supporting the Phase 2 focus on web-based SSIs. This meta-analysis also led me to identify the most effective SSIs for adolescent depression identified to date: the GM SSI described above, and a behavioral activation (BA) SSI, which significantly reduced depression severity in elevated-symptom adolescents in two RCTs (ds=0.57, 1.61).[21-22] These results support my selection of the GM and BA SSIs for Phase 2 of this study.

Although I have completed a study assessing cross-sectional networks of depressive symptoms in clinic-referred children and adolescents,[30] I do not have pilot data on intra-individual depression symptom networks. Indeed, this represents a new frontier for youth depression research and treatment. It is also an area of expertise for Consultant Bringmann, who has pioneered the use of vector autoregressive modeling for depression symptom networks using ESM data,[17-19] and for Collaborator Eaton, a clinical psychologist with expertise in structural models of in psychopathology, including network approaches.[56-61] Consultant Bringmann will provide statistical consultation on all ESM-related analyses in this study (e.g., model estimation and comparison; network parameter extraction). Collaborator Eaton will provide on-site consultation on technical aspects of analyses (e.g., writing, revising code) and results interpretation within a clinical context.

Sample and Procedures. I will recruit youth ages 11-16, as depression increases markedly in adolescence, and youth in this age-range have responded well to GM and BA interventions. I expect to recruit more girls than boys (2:1 ratio), as girls are twice as likely as boys to meet criteria for depression after age 12, and sex differences in depression symptom levels peak in adolescence.[62] Racial/ethnic distribution targets will track those of the local census; selective sampling methods (drawn from those successfully used by Departmental colleagues, with their consultation; see letter of support) will be used to attain adequate minority representation. Figure 1 (below) shows procedures for Phases 1 and 2 for eligible youths. In Phase 1, I plan to recruit 50 adolescents from clinical and nonclinical settings. I intend to utilize connections in Psychiatry and Pediatrics to develop recruitment channels (see letters of support from Dr. Mitrani, Dr. McGovern, and Chair Levy) along with connections I plan to establish with local schools with facilitation from Departmental

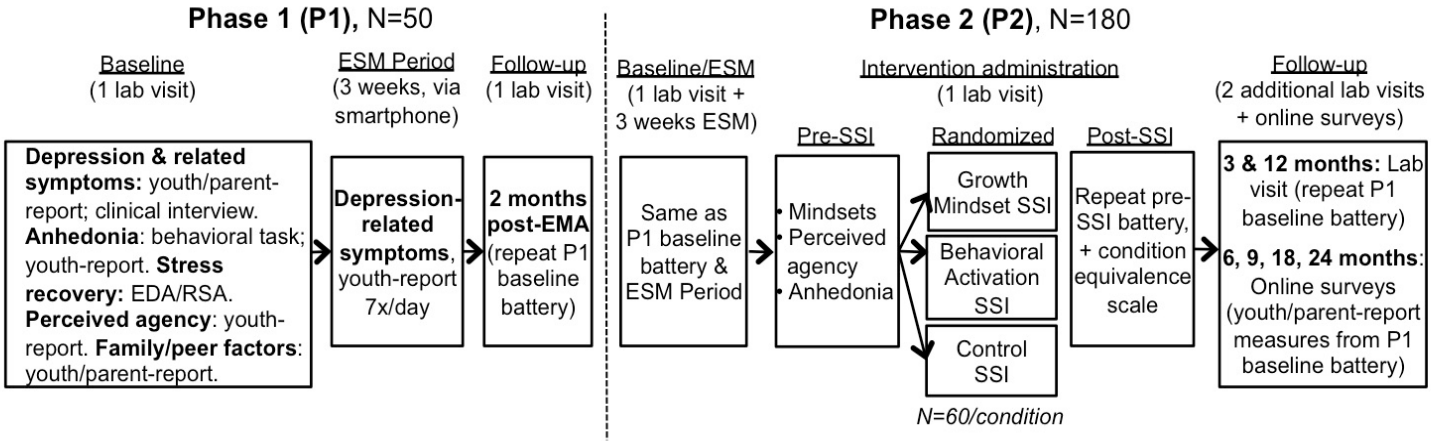

Figure 1. Study flow in P1 and P2 for youth meeting eligibility criteria. P1 and P2 samples will not overlap.

colleagues (see letter of support from Dr. Lerner), community-based strategies used by Psychology colleagues (e.g., commercial mailing lists), and approaches I have applied in my own work. Interested families will then contact our lab; to determine eligibility, the Project Coordinator will conduct a phone screen with parents and adolescents. Inclusion criteria will include (1) the adolescent is age 11-16 (inclusive), with one parent willing to participate; (2) the adolescent reports elevated depressive symptoms (≥84%ile for age and sex, reflecting subclinical or higher symptom elevations) based on the Children's Depression Inventory-2.[63] Exclusion criteria will include inability to complete assessments, psychotic symptoms, and active suicidality requiring immediate treatment. Concurrent treatment will be monitored but will not preclude eligibility. Eligible adolescents and one parent will complete a baseline lab-based battery, detailed below. This battery will be followed by a 3-week ESM period. Adolescents will be prompted to complete the same 2-minute, 8-item survey 7 times per day for 21 days, via a smartphone-based app (LifeData). Notifications to complete surveys will occur every 2-3 hours, from 7:30am to 9:30pm on weekdays and 8:00am to 10:00pm on weekends. Responses will be deemed valid if completed within 1 hour of notification, ensuring at least 1-hour lags between surveys. Adolescents will receive an ESM tutorial at the initial lab visit, and a research team member will review each survey question with the adolescent to ensure comprehension. Adolescents with a personal smartphone will be assisted in downloading the ESM app; those without a smartphone will be provided with one for the ESM period. To support survey completion, adolescents will win a bonus for completing >75% of surveys ($5.00) or a larger bonus for completing >90% of surveys ($10). Two months post-ESM (3 months post-baseline), adolescents and parents will complete a follow-up battery at lab, including the same measures as at baseline.

In Phase 2, we will recruit 180 subjects meeting the above eligibility criteria. Phase 1 participants will be ineligible for Phase 2. After completing a baseline battery and ESM period, adolescents will be randomly assigned to receive 1 of 3 web-based SSIs at a second lab visit: the GM, BA, or supportive therapy (ST) SSI. Immediately pre- and post-SSI, adolescents will complete a limited number of self-report questionnaires to index shifts in proximal outcomes. Adolescents and parents will return to lab follow-up assessments at 3- and 12-months post-intervention (same battery as at baseline). To enable longitudinal analysis of outcome trajectories, adolescents and parents will complete online follow-up questionnaires (including subjective reports of clinical and functional outcomes) 6, 9, 18, and 24 months post-intervention. Families will be debriefed by phone, and initial SSI condition assignment will be revealed, after 24-month follow-up is complete. At this time, adolescents will be offered the opportunity to remotely complete the SSIs they did not originally receive.

Measures. **Lab-Based Battery.** Measures listed below will be included in the lab-based batteries in phases 1 and 2 at baseline and follow-ups. Online follow-up batteries in Phase 2 will include all youth- and parent-report questionnaires from the lab-based battery. Although conducting full, lab-based batteries at all follow-ups would be ideal, we opted to conduct interim assessments online to reduce participant burden and project costs.

Demographics and pubertal development**.** Parents will report demographic, family, and other background information (e.g. age, sex, race, mental health treatment history). Parents will also complete the Pubertal Development Scale[64] with regard to their adolescent, given effects of puberty on depression onset.[65]

Depression and related symptomatology*. Children's Depression Inventory-2.*[63] Adolescent depressive symptom severity will be assessed using the CDI-2 Child and Parent forms. The CDI-2 is a reliable, valid measure of youth depression severity, normed for youth age and sex and yielding raw and *T* scores. Changes in CDI-2 scores will serve as the primary index of SSI effects in the Phase 2 RCT. Changes in scores on other assessments detailed in the sections below, will serve as secondary RCT outcomes in Phase 2.

Kiddie-SADS diagnostic interview.[66] Depressive disorders and commonly comorbid psychiatric disorders

will be assessed using selected KSADS modules, a semi-structured diagnostic interview with established reliability and validity. We will administer modules assessing depressive disorders, generalized and social anxiety disorders, mania, oppositional defiant disorder, ADHD, and conduct disorder. The KSADS will be administered by research-reliable examiners only (e.g. the PI, Project Coordinator, or graduate students).

Multidimensional Anxiety Scale for Children.[67] Given high comorbidity between depression and anxiety,[68] adolescent anxiety symptom severity will be assessed via adolescent and parent reports using the MASC: a reliable, valid, widely used youth anxiety assessment with analog parent and youth-report forms. The MASC is normed for age and gender and yields raw and *T* scores.

Stress Recovery. *Modified Trier Social Stress Task.*[69] Physiological stress recovery will be indexed through a modified TSST, which I used in a prior RCT testing a GM SSI for high-symptom adolescents.[11-12] First, participants complete a 5-min baseline period to assess resting EDA and RSA while watching a neutral film clip about ocean life. Next, the experimenter instructs participants to prepare and then deliver a 3-min speech. The goal of the speech, as explained to the participants, is to "talk about what it means to be a good friend, and what parts of being a good friend you do and do not have." Participants are informed that the speech will be evaluated by two observers. Immediately prior to delivering the speech, two RAs ("observers") enter the room, carrying clipboards and pencils, ostensibly to evaluate the participant's performance. One observer carries a stopwatch and instructs the participant to begin and end his/her speech. At regular intervals, observers make small marks on clipboards to give the appearance of evaluation; they leave the room when the speech ends. Following the speech, participants undergo a 5-min recovery period, again watching a film clip about ocean life.

I will assess participants' autonomic nervous system reactivity continuously during the baseline, speech, and recovery periods using Biopac MP150 hardware, which has capability of measuring the electrocardiogram (ECG, 1.0 kHz); timing, flow and volume respiratory parameters, and EDA. To address posture and motor variability, participants will be asked to sit in the same chair throughout the TSST. They will be asked to minimize physical movement to help control for metabolic effects of movement on parameters of interest. I will edit and analyze data within AcqKnowledge 5.2 software, enabling analysis of complex waveforms, artifact detection, and calibration of respiratory parameters. Parameters I will analyze are RSA (HRV-derived), and EDA. RSA indexes parasympathetic nervous system reactivity; EDA indexes sympathetic nervous system reactivity. I will assess RSA in the time domain (peak-valley index), correcting for influence of respiration.[70] To address possible sympathetic influences on RSA, I will compute an RSA index normalized for mean interbeat-interval.[71] The primary outcome of interest will be slopes of EDA and RSA change during the recovery period (indexing stress recovery rate), controlling for mean baseline EDA and RSA. I will also use mixed modeling to measure magnitude of change from baseline to stressor (indexing total stress reactivity) and between stressor and recovery and baseline and recovery (indexing total stress recovery) per RSA and EDA parameters.

Anhedonia. Anhedonia is a multidimensional construct defined as "impairments in the ability to pursue, experience, and/or learn about pleasure, which is often but not always accessible to conscious awareness."[72] I will therefore include explicit (subjective) and implicit (behavioral) measures of diverse anhedonia dimensions: hedonic capacity, pleasurable activity engagement, approach-oriented coping, and reward motivation.

Snaith-Hamilton Pleasure Scale.[73] Youth-reported hedonic capacity (the ability to experience pleasure) will be assessed via the SHAPS, a 14-item questionnaire wherein participants rate how much they would enjoy hypothetical, pleasant experiences. Items span sensory stimuli, social activities, and hobbies. The SHAPS has shown strong reliability and validity in adolescent samples and is sensitive to acute changes in anhedonia.

Behavioral Activation for Depression Scale.[74] Youths' approach versus disengagement from rewarding activities will be assessed via the BADS, a 25-item youth-report questionnaire with strong reliability, predictive validity, and sensitivity to change following BA for adolescent MD. I will examine 2 of the 4 BADS subscales in this study: Activation (goal-directed engagement in rewarding activities) and Avoidance/Rumination (engagement in rumination and avoidance rather than active coping).

Effort expenditure for Rewards Task.[75] The EEfRT is a behavioral measure of reward motivation, in which reduced motivation toward reward is indexed as a decreased willingness to choose greater-effort/greater-reward over less-effort/less-reward options. In the EEfRT, youth are presented with a series of trials in which they choose between performing button-pressing tasks of varying difficulty to earn rewards. Upon successfully completing a trial, they receive a pre-specified reward, varying from $0-2 (total possible reward: $10). The task contains blocks of effort choice, where participants choose between an easy task (press a button a few times slowly) or a hard task (press a button many times quickly), or a choice between no action and action (i.e. 'effort'). Each trial first displays these options and potential reward. Next, a 'ready' screen appears, and youths begin the trial. Immediately after, youths receive feedback on whether they succeeded (won the reward). Many

studies using the EEfRT have found that adolescents with subclinical, first-episode, and remitted depression show reduced willingness to expend effort for rewards, compared to controls.[76-78]

Perceived agency. *Primary Control Scale for Children*.[79] The PCSC is a 24-item scale measuring youths' perceived ability to influence or alter objective events or conditions through personal effort. Youth rate agreement with statements about their ability to exert primary control (e.g., "I can do well on tests if I study hard"; "I can get other kids to like me if I try"). This PCSC has shown acceptable internal consistency, 6-month test-retest reliability, and strong inverse relations to adolescent depressive symptoms.[79-80]

Secondary Control Scale for Children.[81] The SCSC is a 20-item scale measuring youths' perceived ability to shape the personal impact of objective conditions on oneself, by adjusting oneself to fit those conditions. Youth rate agreement with items reflecting various kinds of secondary control, such as adjusting cognition ("When something bad happens, I can find a way to think about it that makes me feel better"). The SCSC has shown acceptable reliability and validity in a large youth sample.[81]

Implicit Personality Theory Questionnaire.[82-83] The IPTQ asks youth to rate the extent of their agreement with three statements linked to the malleability of personality, using a 1-to-7 Likert scale (e.g. "Your personality is something about you that you can't change very much." Higher summed scores on these three items indicate a stronger fixed personality mindset, a lower scores, a stronger growth personality mindset.

Hopelessness Scale for Children.[84] The HSC assesses youths' sense of hopelessness, including perceptions of whether their personal actions can improve future outcomes. Adolescents rate 17 items as true or false (e.g., "I might as well give up, because I can't make things better for myself"). The HSC has shown adequate reliability and validity in large samples of adolescents experiencing depression.

Family and peer factors. *Multidimensional Peer Victimization Scale*.[85] The MVPS is a self-report scale assessing adolescents' experiences of peer victimization. This study will include the *social manipulation, verbal victimization,* and *physical victimization* scales, totaling 12 items. Adolescents rate how often peers have victimized them in various ways in the past year (e.g. "called me names"; "tried to turn my friends against me").

UCLA Loneliness Scale.[86] The ULS is a widely used self-report scale of loneliness in adolescents. The brief 8-item version will be used here. Adolescents rate agreement with 8 items reflecting loneliness (e.g. "I feel left out"; "I feel isolated from others"). The ULS has shown adequate reliability and validity in adolescent samples.

Brief Symptom Inventory 18.[87] The BSI-18 is a valid, reliable screening tool for adult (here, parental) psychological distress. Adult respondents rate endorsement of 18 physical and emotional complaints on a 0-4 Likert scale. The BSI-18 includes 3 subscales for somatic, anxiety, and depressive symptoms, respectively. The total sum score yields an additional total distress score.

ESM Survey. The ESM survey will include selected items from the Patient Health Questionnaire-9,[88] a widely-used measure of adolescent and adult depressive symptoms. Items will assess symptoms that could plausibly shift in any 2-3 hour period; thus, items assessing sleep and appetite/weight will be excluded. One item assessing suicidal thoughts will also be excluded to maximize survey acceptability to youth and parents, and because assessing suicidality is not critical to study goals. (Risk assessments will be conducted at lab-based assessments; procedures are detailed in the Human Subjects section.) Thus, youths will rate 6 PHQ-9 items (wording adapted for brevity) given a time-frame of "since my last survey": "I felt sad, down, or hopeless"; "I felt bad about myself, like a failure"; "I felt little interest or pleasure"; "I felt tired, low energy"; "It was hard to focus"; and "I moved too slowly OR felt too fidgety." The ESM survey will also include two items, developed for this study, assessing targets of the GM and BA SSIs: perceived agency ("I felt like things were out of my control") and positive activity engagement ("I did things that were fun or important to me").

Interventions. The GM SSI[11-12] is a 30-minute, computer-based intervention self-administered by youth, which I developed and tested previously. The intervention's content is designed to maximize relevance for youth experiencing depression and related difficulties, such as excessive worry. The SSI includes five components: (1) An introduction to the concept of neuroplasticity (describing how and why personal traits and abilities are controlled by thoughts and feelings in their brains, which have constant potential for change); (2) Testimonials from older youth describing their beliefs that people can change, given the brain's inherent malleability; (3) Additional vignettes by older youths, describing times when they used 'growth mindsets' to persevere/cope following peer rejection and negative self-talk; (4) A worksheet describing strategies for applying these ideas to participants' lives; (5) An exercise wherein participants write notes to younger children, using newly gleaned information about the malleability of personality, to help them to cope with setbacks.

The BA SSI will be adapted from existing BA SSIs.[21-22] To date, BA SSIs are designed for delivery by therapists; I will create a web-delivered adaptation, given research supporting the effectiveness of multi-session online BA interventions for youth depression. The piloting process for this adaptation is described below. The web-based BA SSI will include 5 elements: (1) An introduction to the program's rationale: that

engaging in value-based activities that build pleasure and accomplishment can combat sad mood and low self-esteem; (2) Psychoeducation about depression, including how behavior shapes feelings and thoughts; (3) A life values assessment, where youth identify key areas (family relationships, friendships, school, or hobbies) from which they draw (or once drew) enjoyment and meaning; (4) Creation of an activity hierarchy, where youth identify (from pre-generated lists) and personalize (in guided exercises) 3 activities to target for change; and (5) An exercise in which youths write about benefits that might result from engaging in each activity; an obstacle that might keep them from doing the activities; and a strategy for overcoming identified obstacles.

The ST SSI, which I developed and tested previously, is a computer-based, self-administered, 30-minute SSI that encourages youth to identify and express feelings.[11-12] It is designed to control for nonspecific aspects of intervention, including engagement in an interactive computer program, and does not teach or emphasize specific cognitive or behavioral skills, beliefs, or activities. ST activities mirror the structure of the GM SSI. The two programs include the same number of reading and writing exercises. ST also includes vignettes written by older youths, who describe times when they benefited from sharing emotions with friends and family members.

Analytic Plan. **Power analysis.** There are no established methods for estimating power for intra-individual symptom networks. However, such networks have been successfully estimated from fewer within-person data-points than will be collected here (e.g., 60 per individual[17]), using ESM surveys with many more than 8 items (e.g., up to 21 items, yielding hundreds more slope estimations[18]), and in smaller and similarly sized samples as in Phases 1 and 2 (*N*s=1-129).[89-90] Thus, even with some portion of missed ESM surveys (estimated at 10-15%, based on a review of past ESM studies with adolescents[55]), we should have sufficient data to estimate network structures. Regarding the Phase 2 RCT, we used G*Power 3.1 to calculate the sample size needed to achieve sufficient power (1- β) to detect mean group differences of small (.2), medium (.5), and large effects (.8) with α set at .05 and power at 0.95. Sample sizes calculated were 1095, 180, and 72, respectively. Power to detect a small effect size is ideal, but logistical constraints necessitate a more conservative sample size. The sample size of 180 (60 per SSI condition) will reflect power to detect a medium effect size.

Analytic Plan: Aim 1. With Consultant Bringmann and Collaborator Eaton, I will estimate symptom networks from ESM data for each adolescent using multilevel factorial (MF) and vector autoregressive (VAR) models.[17-20] VAR models estimate the extent to which a given symptom (time *t*) can be predicted from all other symptoms at a previous moment (time *t*-1).[19] Each symptom is regressed onto its lagged values and the lagged values of all other symptoms. Here, time *t*-1 and time *t* reference two consecutive ESM surveys; network parameter estimation is based on within-person data only. MF models, in contrast, allow for random, person-specific auto- and cross-regressive effects, using population (fixed) *and* person-level (random) effects to estimate parameters.[20] Simulation studies suggest that MF models may be relatively robust to unequal lags and missing ESM data,[20] but MF and VAR models have not been directly compared. Using both methods, we will compute two types of network parameters for all 50 adolescents: network density (overall strength of links between symptoms, defined as the average of absolute values of symptom-to-symptom slopes in one's network) and outward centrality for each symptom (mean strength of all effects from a given symptom at time *t* to all other symptoms at time *t*+1). As in prior studies comparing dynamical process models' performance, we will use cross-validation scores[90] from MF and VAR models to assess their relative utility.

Toward the secondary Phase 1 aim, I will use mixed-effects linear models to test network parameters as predictors of three-month changes in depression-related deficits. Parameters for network density and outward centrality for each symptom will be continuous predictors in these models, calculated using MF or VAR. Covariates will include pubertal development, family income, age, sex, and time (baseline or 3-month follow-up). Models will include a random intercept and slope, allowing for variation in baseline levels of the outcome variables and rates of change, and an autoregressive error structure. A significant (p<.05) interaction between a network parameter and time would indicate that the parameter significantly predicted 3-month change in the outcome. I hypothesize that (1) greater network density will predict larger 3-month increases in all depression-related deficits (anhedonia, low agency, blunted stress recovery); (2) higher outward centrality of cognitive symptoms will predict larger 3-month declines in agency; and (3) higher outward centrality of behavioral symptoms will predict larger 3-month increases in anhedonia.

Analytic Plan: Aim 2. Networks will be estimated using the approach identified in Phase 1 as producing more stable parameters. To assess network parameters as predictors of SSI outcome, I will use mixed-effects linear models, structured as in Phase 1 analyses with two added variables indexing SSI condition assignment (GM or BA). Change in CDI-2 scores from baseline to proximal (3-month) and across long-term (12-, 24-month) follow-ups will be the primary study outcome. A significant interaction between time and network density would indicate that symptom network density predicted SSI response, regardless of SSI condition. A significant interaction between time, cognitive symptom outward centrality (assessed continuously), and GM

condition would indicate that adolescents with greater outward centrality on a given cognitive symptom responded more favorably to the GM SSI, versus other SSIs. A significant interaction between time, outward centrality of a behavioral symptom, and BA condition would indicate that adolescents with greater outward centrality on a given behavioral symptom responded more favorably to the BA SSI, versus other SSIs. I will also examine main and relative effects of the BA and GM SSIs on youth depression trajectories. Significant interactions between time and an SSI condition variable would indicate that a given SSI significantly improved youth depression symptom trajectories, relative to ST. Finally, additional mixed-effects models (structured as described previously) will assess network parameters as predictors of depression-related deficits (anhedonia, low agency, blunted stress recovery) and associated symptoms (e.g. anxiety severity).

Limitations, Potential Problems, and Alternative Strategies. One challenge of this research will be recruiting 230 adolescents. To address this, I have initiated collaborations with Psychiatry and Pediatrics and will apply community- and school-based recruitment strategies successfully applied by colleagues in Psychology (see letters of support from Psychiatry, Pediatrics, and Psychology faculty). I will also employ community outreach strategies that have led to rapid recruitment in my past work (e.g., recruiting 96 high-symptom adolescents in 3 months). Further, >1,000,000 individuals live in a 20-mile radius of SBU, the only academic medical center in central and Eastern Long Island, creating a large recruitment pool. A second challenge, possible in all ESM and longitudinal studies, is possible missing data. However, clinic-referred adolescents have shown high ESM compliance rates (89.3% on average for studies with >6 surveys per day), and graded monetary incentives will be used to bolster survey completion. Even if completion rates are lower than expected (e.g., 80%), networks will remain estimable; idiographic networks have been estimated from many fewer ESM assessments with MF and VAR models.[17-18] Regarding follow-up, retention in my past longitudinal studies has been 77-100%. I will use multiple strategies to reduce attrition at follow-up (e.g., reminder calls; lotteried rewards). For missing data that does emerge, maximum likelihood estimation will be used in all models. Finally, it is notable that the BA SSI will be a new, online adaptation of therapist-delivered versions, for which materials are freely available. To test acceptability of the new SSI, Phase 1 participants will be invited to complete a pilot study of the web-based BA SSI. I plan to pilot the BA SSI with 15 youth. Revisions to the online BA SSI will be applied prior to Phase 2.

Innovation

This research is highly innovative in several respects. First, personalized network science represents a new frontier in youth depression research: one that may greatly improve our ability to match youth to targeted interventions. However, no previous studies have established guidelines for building personalized depression symptom structures in adolescents. Phase 1 of this project will fill this gap: a critical step toward harnessing network science to optimize youth depression treatment. Results will not only produce guidelines for characterizing personalized youth symptom structures, but they will also ascertain the degree to which these parameters prospectively predict changes in depression-related deficits in high-symptom adolescents, assessed at multiple units of analysis (subjective, behavioral, physiological). This will lay the groundwork for future work applying idiographic symptom structures to youth depression assessment and outcome prediction.

Second, this study will be the first to integrate advances in two rapidly developing but separate fields: network analysis and clinical intervention research—specifically, single-session intervention (SSI) research. This integration may help address the complex challenge of identifying potent, personalized, accessible strategies for reducing adolescent depression. In particular, no prior studies have tested personalized network structures as predictors of youth treatment response. Some studies focused on adults have tested cross-sectional, group-level networks as treatment outcome predictors. However, these group-level networks may not reflect causal, symptom-to-symptom links for specific individuals. In contrast, personalized networks, built from symptom data gathered from many individuals at multiple time-points, hold potential to forward the NIH-wide goal of *precision medicine*: Parameters from personalized networks may predict individual likelihood of response to well-targeted interventions, optimizing efforts to match individuals to supports that fit their unique symptom structures and clinical needs. Phase 2 of this study will be the first to assess whether personalized symptom structures predict clinical response to extremely brief, precisely targeted, evidence-based SSIs for adolescent depression. Given the low potency and limited accessibility of existing depression treatments, the promise of SSIs, and the need for tools to match youths to tailored, brief treatments, Phase 2 results may spur critical progress toward reducing the individual and societal burden of adolescent depression.

Third, this project includes the first randomized controlled trial comparing two evidence-based SSIs for adolescent depression, with the longest follow-up period of any SSI trial to date, an active control intervention, and a multi-level outcome assessment model. SSIs may hold potential to dramatically increase intervention accessibility, yet further investigation remains needed to determine SSIs' promise in reducing youth depression on a large scale. Seven RCTs to date have evaluated SSIs for youth depression, but follow-up

periods ranged from 2 weeks to 9 months; control conditions have varied in rigor (e.g., no-treatment or waitlist controls); and long-term outcome assessments have relied largely on subjective youth reports. This project will be the first trial to evaluate SSI effects on multi-level outcomes (subjective, behavioral, and physiological) and will include a 24-month follow-up. It will also compare two depression-specific SSIs (GM and BA) and an active control, comprised of a supportive therapy SSI I developed previously. Given these design features, this study will dramatically strengthen evidence regarding the capacity of targeted SSIs to reduce depression in adolescents. By including two evidence-based SSIs within the same RCT, this study will also help ascertain which SSI (if either) yields greater overall reductions in youth depression, relative to an active control. This study will also involve the development, piloting, and subsequent evaluation of a novel web-based BA SSI (adapted directly from existing therapist-delivered BA SSIs), yielding a more scalable, accessible iteration of an existing evidence-based treatment.

Relationship to previous work

The proposed project represents a direct extension of my prior work, markedly extending its scope and impact. To date, I have established a research program on developing and evaluating mechanism-targeted, scalable interventions for youth depression and anxiety. For instance, as noted above, I have identified growth mindsets as promising targets. In a longitudinal school-based study and a meta-analysis, I observed that mindsets are cross-sectionally and prospectively linked to youth depression and anxiety. In an RCT, I found that a web-based GM SSI improved youths' physiological stress recovery and perceived control, as well as depression and anxiety symptoms 9 months later. Further, in a meta-analysis of 50 SSI RCTs, I found that these very brief interventions can reduce youth psychopathology of multiple types. Thus, SSIs may yield lasting benefits, and I have identified a specific, targeted SSI that may be effective for youth depression. In conducting the above studies and several others, I have built protocols for recruiting high-symptom youth; designing and evaluating novel SSIs; assessing youth symptoms and functioning via subjective and objective metrics; and analyzing SSI response with advanced modeling techniques. That is, I have established a solid foundation for undertaking the proposed project. I have conducted my research with conceptual guidance but significant methodological independence from my mentors, requiring only consultation from them in recent work. The proposed study differs from my past work in at least two key respects. First, it allows me to test network analysis as a novel tool to help match youth to targeted SSIs, based on personal clinical need. The integration of network analysis and SSI research is a key innovation in this study—and a critical direction for my future work— and may generate a novel approach to matching youths with targeted SSIs. Second, it will include the first RCT comparing two evidence-based SSIs for adolescent depression, including the longest follow-up of any SSI trial to date and the first SSI trial assessing multilevel outcomes (subjective, behavioral, physiological) across long-term follow-up. The proposed project is well positioned to produce rich data and meaningful findings with direct implications for reducing depression in youth. The research is multifaceted, potentially highly impactful, and uniquely feasible with support from the DP5. This award will allow me to further my research career and contribute to my field at a rate and coherence that would otherwise be impossible.

Timeline

Phase 0 (lab establishment; before grant period). Initial study construction, equipment purchasing, and IRB submission will begin in Fall 2018. The lab will be prepared for subject recruitment by Spring 2019. One to two graduate students will join the lab in Fall 2019; a part-time lab coordinator will be hired in Summer 2019. Initial development of the online BA SSI will occur in 2018-2019. Phase 1 (year 1 of grant period; Study 1). Should the DP5 be awarded, equipment for ESM data collection will be purchased (LifeData subscription; smartphones for subjects) and a full-time Project Coordinator will be hired. Graduate and undergraduate evaluators will be trained in study protocols. In 2019-20, the Phase 1 sample (N=50) will be recruited. Phase 1 ESM data collection will be complete by the start of Fall 2020. At that time, network analysis using ESM data will be conducted, guided by Consultant Bringmann and Collaborator Eaton. Three-month follow-ups for Phase 1 will be complete by the end of Fall 2020. Piloting of the BA SSI will occur concurrently with Phase 1; based on pilot feedback, SSI revisions will be implemented by Summer 2020, before Phase 2 initiation. Phase 2 (years 2-5 of grant; Study 2, clinical trial component). In Summer 2020, graduate students, undergraduates, and the Project Coordinator will be trained in SSI administration. An additional graduate student will be recruited for Fall 2020 and will take part in these trainings. In 2020-21 and 2021-22, the Phase 2 sample (N=180) will be recruited. Baseline assessments, ESM periods, and SSI sessions will be complete by Summer 2022. Network construction for Phase 2 participants will occur in Fall 2022 and Spring 2023, supported by Consultant Bringmann and Collaborator Eaton. Papers from Phase 1 will be submitted at this time. Follow-up lab visits (at 3, 12 months) and online data collection (at 6, 9, 18, 24 months) will occur across the remainder of the DP5 period (2022-24). Through Summer 2024, final analyses will be conducted and papers submitted.

PHS Human Subjects and Clinical Trials Information

OMB Number: 0925-0001 and 0925-0002

Expiration Date: 03/31/2020

Are Human Subjects Involved	● Yes ○ No
Is the Project Exempt from Federal regulations?	○ Yes ● No
Exemption Number	❑ 1 ❑ 2 ❑ 3 ❑ 4 ❑ 5 ❑ 6 ❑ 7 ❑ 8
Other Requested Information	

Human Subject Studies

Study#	Study Title	Clinical Trial?
1	Phase 1: Establishing Guidelines for Computing Personalized Symptom Networks for Adolescent Depressive Symptoms	No
2	Phase 2: Personalized Symptom Network Parameters as Predictors of Response to Single-Session Interventions for Depression in Adolescents	Yes

Section 1 - Basic Information (Study 1)

OMB Number: 0925-0001 and 0925-0002

Expiration Date: 03/31/2020

1.1. Study Title *

Phase 1: Establishing Guidelines for Computing Personalized Symptom Networks for Adolescent Depressive Symptoms

1.2. Is this study exempt from Federal Regulations * ○ Yes ● No

1.3. Exemption Number ❑ 1 ❑ 2 ❑ 3 ❑ 4 ❑ 5 ❑ 6 ❑ 7 ❑ 8

1.4. Clinical Trial Questionnaire *

1.4.a. Does the study involve human participants?	● Yes	○ No
1.4.b. Are the participants prospectively assigned to an intervention?	○ Yes	● No
1.4.c. Is the study designed to evaluate the effect of the intervention on the participants?	○ Yes	● No
1.4.d. Is the effect that will be evaluated a health-related biomedical or behavioral outcome?	● Yes	○ No

1.5. Provide the ClinicalTrials.gov Identifier (e.g. NCT87654321) for this trial, if applicable

Section 2 - Study Population Characteristics (Study 1)

2.1. Conditions or Focus of Study

- Aims are (1) to establish guidelines for computing idiographic depressive symptom networks for high-symptom adolescents, and (2) to assess the degree to which parameters from these networks predict changes in core depression-related deficits.

2.2. Eligibility Criteria

Youth must be living with at least one parent or legal guardian, and both the youth and the parent must speak English well enough to complete study assessments and provide consent and assent. Additional inclusion criteria will include: 1. The youth is age 11-16 (inclusive) with one parent willing to participate; 2. The youth reports elevated depressive symptoms (>84th percentile for age and sex, reflecting subclinical or higher symptom elevations) based on the Children's Depression Inventory-2. Exclusion criteria will include inability to complete assessments, psychotic symptoms, and active suicidality requiring immediate treatment, all of which will be assessed via an initial phone screen with the parent and youth. Concurrent treatment will be monitored but will not preclude eligibility.

2.3. Age Limits	Min Age: 11 Years	Max Age: 16 Years
2.4. Inclusion of Women, Minorities, and Children	Inclusion_of_Women_and_Minorities_07.29.18_Study_1.pdf	
2.5. Recruitment and Retention Plan	Recruitment_and_Retention_Plan_Study_1.pdf	
2.6. Recruitment Status	Not yet recruiting	
2.7. Study Timeline	Phase_1_Study_Timeline.pdf	
2.8. Enrollment of First Subject	11/01/2019	Anticipated

Inclusion of Women and Minorities

Because girls are twice as likely to meet criteria for depressive disorders than boys beginning at age 12, and sex differences in depression symptom levels peak in adolescence,[62] I expect to recruit girls and boys in a 2:1 ratio for the proposed research. Thus, approximately 66% of the sample will be female (33 of 50 adolescents in Phase 1; 120 of 180 adolescents in Phase 2).

Participants in the proposed research will be recruited from the local Long Island community. No individuals will be excluded based on gender, ethnicity, and race, as there is no scientific basis for excluding individuals on these factors. Stony Brook is located in Suffolk County, NY; according to the 2017 census, 19.5% of the residents of Suffolk County were Hispanic or Latino (of any race). In addition, 84.5% were White, 8.6% were Black, and 4.2% were Asian. 0.6% were American Indian/Alaska Native, and 0.1% were Native Hawaiian or Pacific Islander, and 1.9% were listed as “two or more races.” Enrollment targets are based upon these distributions. Ongoing work by supporting Departmental colleagues Klein and Lerner has evinced highly successful minority sampling. Thus, in consultation with them, I will use their established strategies in the current proposal in hopes of maintaining minority representation comparable to the general demographic distribution around Stony Brook.

Recruitment and Retention Plan

The PI will follow procedures that she and Departmental colleagues have previously used in recruiting subjects. Youths and families will be recruited from various sources, including schools, afterschool programs, youth mental health clinics and hospitals, private physicians and mental health practitioners, flyer and email advertisements. Additionally, the PI intends to utilize connections in Psychiatry and Pediatrics to develop recruitment channels (see letters of support from Dr. Mitrani, Dr. McGovern, and Chair Levy) along with connections she plans to establish with local schools with facilitation from Departmental colleagues (see letter of support from Dr. Lerner), community-based strategies used successfully by Psychology colleagues (e.g., commercial mailing lists).

Some amount of missing data is anticipated, as is characteristic of virtually all research including experience sampling method (ESM) and longitudinal data collection. However, clinic-referred adolescents have shown high ESM compliance rates (89.3% on average for studies with >6 surveys per day), and graded monetary incentives will be used during the ESM period of this study to bolster survey completion. Even if completion rates are lower than expected (e.g., 80%), networks will remain estimable; idiographic networks have been estimated from many fewer ESM assessments with MF and VAR models.[17-18] Regarding follow-up, retention in the PI's past longitudinal studies has been 77-100%. Multiple strategies will be utilized to reduce attrition at follow-up (e.g., reminder calls by study personnel; lotteried rewards). For missing data that does emerge, maximum likelihood estimation will be used in all statistical models.

Study Timeline

Phase 1: Establishing guidelines for computing idiographic symptom networks for adolescent depressive symptoms

	Year 1: 9/1/19-8/31/20			Year 2: 9/1/20-8/31/21			Years 3-5: 9/1/21-8/31/24 *Dedicated primarily to Phase 2 study.*		
	Fall	Spring	Summer	Fall	Spring	Summer	Fall	Spring	Summer
Formative work (obtain IRB approval, purchase equipment for EMA data collection)	X								
Train project staff (will begin prior to grant period*)	X	X							
Recruitment and consenting; baseline lab session/EMA period	X**	X	X						
3-month follow-up (lab visit)		X	X	X					
Data processing	X	X	X	X	X	X	X	X	X
Data analysis			X	X	X	X	X	X	X
Manuscript Development			X	X	X	X	X	X	X

*Note: Many assessments and protocols in the proposed study will be utilized in other ongoing projects in the lab. Volunteer research assistant and graduate students will be trained in these assessments and protocols prior to the proposed grant period.

**Note: Recruitment estimated to begin during November of fall 2019, following formative work and initial training of project staff in September and October 2019.

Inclusion Enrollment Reports

IER ID#	Enrollment Location Type	Enrollment Location
Study 1, IER 1	Domestic	Department of Psychology, Stony Brook University

Inclusion Enrollment Report 1

Using an Existing Dataset or Resource* : ○ Yes ● No

Enrollment Location Type* : ● Domestic ○ Foreign

Enrollment Country(ies): USA: UNITED STATES

Enrollment Location(s): Department of Psychology, Stony Brook University

Comments:

Planned

Racial Categories	Ethnic Categories				
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/ Alaska Native	1	0	0	0	
Asian	1	1	0	0	
Native Hawaiian or Other Pacific Islander	0	0	0	0	
Black or African American	3	2	2	1	
White	27	14	5	2	
More than One Race	1	0	0	0	

Cumulative (Actual)

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/ Alaska Native	0	0	0	0	0	0	0	0	0	0
Asian	0	0	0	0	0	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	0	0	0	0	0	0	0	0	0	0
White	0	0	0	0	0	0	0	0	0	0
More than One Race	0	0	0	0	0	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	0
Total	0	0	0	0	0	0	0	0	0	0

Section 3 - Protection and Monitoring Plans (Study 1)

3.1. Protection of Human Subjects	Human_Subjects_-_Phase_1_08.20.18.pdf
3.2. Is this a multi-site study that will use the same protocol to conduct non-exempt human subjects research at more than one domestic site?	○ Yes ● No ○ N/A
If yes, describe the single IRB plan	
3.3. Data and Safety Monitoring Plan	DATA_AND_SAFETY_MONITORING_PLAN_8_20_18_study_1.pdf
3.4. Will a Data and Safety Monitoring Board be appointed for this study?	○ Yes ● No
3.5. Overall structure of the study team	Overall_Structure_of_Study_Team_Study_1.pdf

1. RISK TO SUBJECTS

a. Human Subjects Involved and Characteristics. Participants in Phase 1 will be 50 youth with elevated depressive symptoms (ages 11-16; 33 females, 17 males), and one parent per youth. Phase 1 will occur within the first two years of the award, with the majority of data collection occurring in the first year. Participants in Phase 1 will be ineligible to participate Phase 2 (described elsewhere in this application). All participants will be recruited from clinical and nonclinical settings, utilizing connections in Psychiatry and Pediatrics to develop recruitment channels (see letters of support) along with connections to be established with local schools with facilitation from Departmental colleagues (see letter of support from Dr. Lerner), and community-based strategies used successfully by Psychology colleagues (e.g., commercial mailing lists). Selective sampling methods will be used to attain adequate minority representation (i.e., oversampling zip codes lowest on a composite socioeconomic index score to attain minority representation targets). Youth must be living with at least one parent or legal guardian, and both the youth and the parent must speak English well enough to complete study assessments and provide consent and assent. Additional inclusion criteria will include (1) the youth is age 11-16 (inclusive), with one parent willing to participate; (2) the youth reports elevated depressive symptoms (≥84%ile for age and sex, reflecting subclinical or higher symptom elevations) based on the Children's Depression Inventory-2. Exclusion criteria will include inability to complete assessments, psychotic symptoms, and active suicidality requiring immediate treatment, all of which will be assessed via an initial phone screen with the parent and youth. Concurrent treatment will be monitored but will not preclude eligibility. The current research will focus on youth ages 11-16 because as depression increases markedly in adolescence. All research will take place at Stony Brook University in the Department of Psychology.

b. Sources of Materials. Eligible youth in Phase 1 along with one parent per youth will complete a baseline lab-based battery. Research materials collected during this battery will include psychophysiological, diagnostic, behavioral, and self- and parent-report data. Youth will participate in a structured diagnostic interview for diagnosing psychopathology and related symptoms; parents will be interviewed about the youth using an analog structured diagnostic interview. Youth and their parents will fill out questionnaires assessing the youth's symptoms and functioning across multiple domains; parents will self-report information regarding their own well-being and family history. Parents will also fill out measures designed to assess pubertal development. Youths will participate in a lab-based social stress induction, which will include psychophysiological data collection (ECG, EDA recordings) using the Biopac recording system. This battery will be followed by a 3-week experience sampling method (ESM) data collection period, during which adolescents will be prompted to complete the same 2-minute, 8-item survey 7 times per day for 21 days, via a smartphone-based app (LifeData). LifeData is a secure, HIPAA-compliant platform for ESM data collection. Notifications to complete surveys will occur every 2-3 hours, from 7:30am to 9:30pm on weekdays and 8:00am to 10:00pm on weekends. Responses will be deemed valid if completed within 1 hour of notification, ensuring at least 1-hour lags between surveys. Adolescents will receive an ESM tutorial at the initial lab visit, and a research team member will review each survey question with the adolescent to ensure comprehension. Adolescents with a personal smartphone will be assisted in downloading the ESM app; those without a smartphone will be provided with one for the ESM period. Youth and parents will return to the lab for a follow-up assessment at 3-month follow-up, using the same measurement battery as at baseline.

Participants will be assigned a study identification number that will be used to link the aforementioned data. Correspondence between identifying information and study identification number will be kept in a locked file in a locked room in the PI's laboratory. All data will be identified by the study identification number and will not contain the participants' name.

c. Potential Risks. The potential risks of participating in this study are considered minimal. The assessment instruments and social stress induction are commonly used in research with youth populations. Participants may experience some emotional discomfort in discussing various aspects of their lives while completing questionnaires, or during the social stress induction. The interviewers will be trained in all study procedures by the PI. They will aim to minimize potential distress by presenting all assessment material in a supportive manner. If a parent or a youth becomes upset, the interviewer will assist them with processing their distressing emotions. If necessary, the interview or session may be interrupted or terminated. The family (parent and patient) will be clearly informed that they are free to terminate participation at any point in the protocol.

We will follow guidelines developed by Stony Brook University on the management of incidental findings. First, the consent form will clearly state that the procedures in the study are being conducted for research purposes. The consent will be clear that the researchers of this study are not medical doctors and are not trained to assess possible findings of heart rate (ECG) or electrodermal activity (EDA) recordings. There is no

risk involved in obtaining such recordings via non-invasive electrodes (i.e., stickers placed on the skin). There is no risk of behavioral paradigms, tasks, or questionnaires, with the exception of the possibility that subjects may become bored. We will provide breaks and provide snacks between tasks as needed. Finally, as in any clinical research study, there is the risk of violating confidentiality as some of the information is personal and may be sensitive.

2. ADEQUACY OF PROTECTION AGAINST RISKS

a. Recruitment and informed consent. The PI will follow procedures that she and Departmental colleagues have previously used in recruiting subjects. Youths and families will be recruited from various sources, including schools, afterschool programs, youth mental health clinics and hospitals, private physicians and mental health practitioners, flyer and email advertisements, and via clinics in the Stony Brook University Hospital's Departments of Pediatrics and Psychiatry (see letters of support). Verbal consent will be sought for initial phone screening, during which information demographic will be obtained to ascertain potential appropriateness of the youth's participation. If eligibility criteria are met, the youth and one parent will be offered enrollment in the study. For families that appear to be eligible and are interested, our project coordinator will explain the nature of the study to both the youth and their parent, screen for inclusion and exclusion criteria, and schedule a lab-based study session. The project coordinator will review the consent and assent forms briefly over the phone, and encourage the subject and their parent to read it carefully before the scheduled appointment. At the laboratory visit, the project coordinator will obtain informed consent. The parents and the child will understand that they are free to withdraw from the study at any point. Consistent with IRB requirements, the parent will sign a consent form and the child will sign an assent form. Participants will be provided with a copy of the consent document, and the original will be kept on file.

b. Protection against risk. Informed consent and assent will be obtained prior to participation, and risks will be explained carefully to youths and parents. All information with identifying information collected during the project will be kept in a locked storage cabinet to which only PI Schleider and the project coordinator will have access. All data will be stored separately from identifying information and will be password protected. No names will be maintained in data records; rather, information will be coded by ID numbers only. Each individual will receive a unique ID number thereby allowing handling of data on all subjects without using individual names. PI Schleider will be responsible for monitoring the maintenance of confidentiality. In the event of a breach of confidentiality, she will inform the subject and his/her parents that the breach occurred; any breaches of confidentiality will be reported to the Institutional Review Board. Codifying participants by unique identifiers is an extensively-used practice that is highly efficient at protecting anonymous participation. No names or any identifying information would be used in presentation of scientific reports resulting from this study.

Procedures will be repeatedly explained to the youths and parents, giving them a sense of control over what is happening in their environment. Rather than closed yes/no questions, open-ended questions with regard to comfort and well-being will be used throughout the procedures to give participants the opportunity to voice any concerns or discomfort. Participants will also be given the opportunity to ask questions regarding the research procedures at any time during the protocol.

Because this research focuses on adolescents with elevated depressive symptoms, some participants may endorse suicidal ideation or behaviors during the study protocol (e.g., on the Children's Depression Inventory). In this event, risk assessments will be conducted and, when necessary, appropriate consultation with PI Schleider will be held to determine disposition. PI Schleider is a clinical psychologist with extensive training in child and adolescent risk and abuse assessment; her office will be in the same building where research activities will take place. In addition, the Krasner Psychological Center, the community mental health facility operated by the Department of Psychology, is on the same floor as PI Schleider's laboratory space, where this study will take place. In total, there are more than 11 clinical psychologists located within a short walk to PI Schleider's laboratory. In the event that a participant is in imminent danger to themselves or others, their accompanying parent will be informed. The assessor and PI Schleider will meet with the subject and their parent to establish a safety plan. In the event of reported, active suicidal ideation or plan, participants and their parents will be accompanied to the Comprehensive Psychiatric Emergency Program at Stony Brook University Hospital, which is a 10 minute walk from the PI's laboratory. In addition, if a participant endorses suicidal ideation and/or intent in one of the Qualtrics-based follow-up surveys, PI Schleider or study personnel will contact the family within 24 hours to conduct a risk assessment via phone. If needed, a safety plan will be developed, and the PI or study personnel will work with the family to ensure the youth's safety. Additionally, all study participants will be offered referral information for psychotherapy and/or pharmacologic treatment at Stony Brook and the surrounding community. Participants will not be excluded from completing study

procedures if they begin receiving treatment for psychological distress during the study.

Because information relating to child abuse may emerge in the course of interactions with subjects, the staff will follow federal and state child abuse reporting requirements. Participants will be informed of the need to report child abuse prior to eliciting this information. In case of any reported abuse by the child or parent, the parents will be informed about the federal mandated reporting laws, verbally and in writing. In cases where it is necessary to make a child abuse report, the family will always be informed prior to contacting any state agency, and given the option of making a self-referral to protective services.

3. POTENTIAL BENEFITS TO THE SUBJECTS AND OTHERS

PI Schleider has conducted previous studies using many of the same measures used in the current proposal; many children enjoy participating in the assessments (some involve computer-based tasks presented as games, and certain questionnaires involve self-reflection on personal experiences and beliefs) and all youths receive prizes and snacks during the course of the tasks. Families are also presented with monetary reimbursement for participating (up to 60-$70 for Phase 1, depending on ESM survey completion rate). Providing the honorarium to the family, rather than the youth, reduces the possibility that payment could be coercive—it is left up to the family to decide how to allocate the honorarium. Additionally, all participating families will be offered a free report summarizing the results of their initial lab-based assessment. Such a report, if conducted by a community clinician, could cost upwards of several thousand dollars, and receipt of it is therefore a significant benefit to families. Finally, depression in youth often goes undetected. Assessment and continual monitoring of participants' symptoms may help identify clinically-significant problems in this domain.

4. IMPORTANCE OF THE KNOWLEDGE TO BE GAINED

This research may produce important knowledge relevant to reducing depression in adolescents. First, personalized network analysis holds great promise to improve our ability to match youth to targeted interventions. Phase 1 of this study will be the first to establish guidelines for building personalized symptom structures in adolescents. Thus, the present research represents a key step toward applying methods from network science to optimize the treatment of youth depression. Results of Phase 1 will not only produce guidelines for characterizing personalized youth symptom structures, but they will also ascertain the degree to which these parameters prospectively predict changes in depression-related deficits in high-symptom adolescents. These findings will lay necessary groundwork for future work applying idiographic symptom structures to youth depression assessment and outcome prediction, which may forward the development of targeted, precise strategies to reduce the burden of depression in adolescents.

Data Safety and Monitoring Plan

PI Schleider and the Stony Brook University Institutional Review Board (IRB) will have responsibility for continual monitoring of data and safety of participants in the study. Data and safety monitoring will take place continually (i.e., at least weekly) throughout the study. PI Schleider will follow the Stony Brook University IRB policies for expedited reporting of all unexpected adverse events and serious adverse events. She will report to the IRB any non-serious unexpected adverse events and serious adverse events that are related or possibly related to a subject's participation in the research, and that occur while the subject is enrolled in the study or (b) occur within 30 days of the conclusion of the subject's participation in the study. All such events will be reported within 24 hours of PI Schleider's knowledge of the event by phone, fax, or email to the Committee on Research Involving Human Subjects within Stony Brook University's IRB. In addition, PI Schleider will provide the IRB with a full written report detailing the event within 5 working days/7 business days following initial IRB notification. Additionally, if PI Schleider becomes aware of a serious adverse event more than 30 days after the conclusion of a patient's study participation, she will report the event to the IRB at the time that she becomes aware of it. Further, at the time of the annual continuing review, PI Schleider will provide the Stony Brook University IRB with a summary of any adverse events and any other unanticipated problems that occurred since the last review. PI Schleider will collect data on adverse events throughout the course of the study period.

The potential risks of participating in this study are considered minimal. The assessment instruments, intervention components, and social stress induction are all commonly used in research with youth populations. Participants may experience some emotional discomfort in discussing various aspects of their lives while completing questionnaires, or during the social stress induction. Any such distress will hopefully be minimized by presenting all assessment materials in a supportive manner, assuring youths that their participation in the study is fully voluntary, and informing youths that they can leave the study at any time. Therefore, likelihood of any adverse events during the study is considered very low.

PI Schleider will ensure that the study adheres to the IRB-approved protocol and will continually monitor the overall progress of the study. The trained study personnel will ensure the accuracy and completeness of study materials and report any inconsistencies to the PI.

Names will be removed from all of the data and replaced with a participant ID number. All data will remain in a secured and locked location where only the PI and Lab Coordinator will have access. Additionally, every effort will be made to ensure confidentiality. Confidentiality of recorded and all other information obtained in the study will be maintained by labeling the information with a numerical ID number. A computer file and a paper document linking the code to the subject's identity will be located separately and will be accessible only to authorized personnel. No names or identifying information would be used in presentation of scientific reports resulting from this study.

Adolescents' confidentiality will be maintained except as required by law or as required to insure their safety. For example, because this research focuses on adolescents with elevated depressive symptoms, some participants may endorse suicidal ideation or behaviors during the study protocol (e.g., on the Children's Depression Inventory). In this event, risk assessments will be conducted and, when necessary, appropriate consultation with PI Schleider will be held to determine disposition. PI Schleider is trained as a clinical psychologist with several years of experience and training in child and adolescent risk and abuse assessment; her office will be in the same building where research activities will take place. In the event that an adolescent participant is in imminent danger to him/herself, the accompanying parent will be informed. The assessor and PI Schleider will meet with the subject and their parent to establish a safety plan. In the event of reported, active suicidal ideation or plan, participants and their parents will be accompanied to the Comprehensive Psychiatric Emergency Program at Stony Brook University Hospital, which is a 10 minute walk from the PI's laboratory. In addition, if a participant endorses suicidal ideation and/or intent in one of the Qualtrics-based follow-up surveys, PI Schleider or trained study personnel will contact the family within 24 hours to conduct a risk assessment via phone. If needed, a safety plan will be developed, and the PI or study personnel will work with the family to ensure the youth's safety. Additionally, all study participants will be offered referral information for psychotherapy and/or pharmacologic treatment at Stony Brook and the surrounding community. Participants will not be excluded from completing study procedures if they begin receiving treatment for psychological distress during the study.

Additionally, because information relating to child abuse may emerge in the course of interactions with subjects, PI Schleider and project staff will follow federal and state child abuse reporting requirements. Participants will be informed of the need to report child abuse prior to eliciting this information. In case of any reported abuse by the child or parent, the parents will be informed about the federal mandated reporting laws,

verbally and in writing. In cases where it is necessary to make a child abuse report, the family will always be informed prior to contacting any state agency, and given the option of making a self-referral to protective services.

In the event of the adverse events described above or any others, PI Schleider will report the incident and provide all relevant data to the Stony Brook University IRB according to the timeline noted above.

Overall Structure of Study Team

The administrative and data coordinating site for the proposed study is Stony Brook University. Participants will be recruited from clinical and community settings in the Long Island area. Although some data will be collected remotely (e.g., during the experience sampling method component), all data will be stored and analyzed at Stony Brook University's Department of Psychology within PI Schleider's research lab. There is no separate laboratory or testing center for the proposed study.

Section 4 - Protocol Synopsis (Study 1)

4.1. Brief Summary

4.2. Study Design

4.2.a. Narrative Study Description

4.2.b. Primary Purpose

4.2.c. Interventions

Type	Name	Description

4.2.d. Study Phase

Is this an NIH-defined Phase III Clinical Trial? ○ Yes ● No

4.2.e. Intervention Model

4.2.f. Masking ○ Yes ● No

❑ Participant ❑ Care Provider ❑ Investigator ❑ Outcomes Assessor

4.2.g. Allocation

4.3. Outcome Measures

Type	Name	Time Frame	Brief Description

4.4. Statistical Design and Power

4.5. Subject Participation Duration

4.6. Will the study use an FDA-regulated intervention? ○ Yes ● No

4.6.a. If yes, describe the availability of Investigational Product (IP) and Investigational New Drug (IND)/ Investigational Device Exemption (IDE) status

4.7. Dissemination Plan

Section 1 - Basic Information (Study 2)

OMB Number: 0925-0001 and 0925-0002

Expiration Date: 03/31/2020

1.1. Study Title *

Phase 2: Personalized Symptom Network Parameters as Predictors of Response to Single-Session Interventions for Depression in Adolescents

1.2. Is this study exempt from Federal Regulations * ○ Yes ● No

1.3. Exemption Number ❑ 1 ❑ 2 ❑ 3 ❑ 4 ❑ 5 ❑ 6 ❑ 7 ❑ 8

1.4. Clinical Trial Questionnaire *

1.4.a. Does the study involve human participants?	● Yes	○ No
1.4.b. Are the participants prospectively assigned to an intervention?	● Yes	○ No
1.4.c. Is the study designed to evaluate the effect of the intervention on the participants?	● Yes	○ No
1.4.d. Is the effect that will be evaluated a health-related biomedical or behavioral outcome?	● Yes	○ No

1.5. Provide the ClinicalTrials.gov Identifier (e.g. NCT87654321) for this trial, if applicable

Section 2 - Study Population Characteristics (Study 2)

2.1. Conditions or Focus of Study

2.2. Eligibility Criteria

Youth must be living with at least one parent or legal guardian, and both the youth and the parent must speak English well enough to complete study assessments and provide consent and assent. Additional inclusion criteria will include: 1. The youth is age 11-16 (inclusive) with one parent willing to participate; 2. The youth reports elevated depressive symptoms (>84th percentile for age and sex, reflecting subclinical or higher symptom elevations) based on the Children's Depression Inventory-2. Exclusion criteria will include inability to complete assessments, psychotic symptoms, and active suicidality requiring immediate treatment, all of which will be assessed via an initial phone screen with the parent and youth. Concurrent treatment will be monitored but will not preclude eligibility.

2.3. Age Limits	Min Age: 11 Years	Max Age: 16 Years
2.4. Inclusion of Women, Minorities, and Children	Inclusion_of_Women_and_Minorities_07.29.18.pdf	
2.5. Recruitment and Retention Plan	Recruitment_and_Retention_Plan_Study_2.pdf	
2.6. Recruitment Status	Not yet recruiting	
2.7. Study Timeline	Phase_2_Study_Timeline.pdf	
2.8. Enrollment of First Subject	11/02/2020	Anticipated

Inclusion of Women and Minorities

Because girls are twice as likely to meet criteria for depressive disorders than boys beginning at age 12, and sex differences in depression symptom levels peak in adolescence,[62] I expect to recruit girls and boys in a 2:1 ratio for the proposed research. Thus, approximately 66% of the sample will be female (33 of 50 adolescents in Phase 1; 120 of 180 adolescents in Phase 2).

Participants in the proposed research will be recruited from the local Long Island community. No individuals will be excluded based on gender, ethnicity, and race, as there is no scientific basis for excluding individuals on these factors. Stony Brook is located in Suffolk County, NY; according to the 2017 census, 19.5% of the residents of Suffolk County were Hispanic or Latino (of any race). In addition, 84.5% were White, 8.6% were Black, and 4.2% were Asian. 0.6% were American Indian/Alaska Native, and 0.1% were Native Hawaiian or Pacific Islander, and 1.9% were listed as “two or more races.” Enrollment targets are based upon these distributions. Ongoing work by supporting Departmental colleagues Klein and Lerner has evinced highly successful minority sampling. Thus, in consultation with them, I will use their established strategies in the current proposal in hopes of maintaining minority representation comparable to the general demographic distribution around Stony Brook.

Recruitment and Retention Plan

The PI will follow procedures that she and Departmental colleagues have previously used in recruiting subjects. Youths and families will be recruited from various sources, including schools, afterschool programs, youth mental health clinics and hospitals, private physicians and mental health practitioners, flyer and email advertisements. Additionally, the PI intends to utilize connections in Psychiatry and Pediatrics to develop recruitment channels (see letters of support from Dr. Mitrani, Dr. McGovern, and Chair Levy) along with connections she plans to establish with local schools with facilitation from Departmental colleagues (see letter of support from Dr. Lerner), community-based strategies used successfully by Psychology colleagues (e.g., commercial mailing lists).

Some amount of missing data is anticipated, as is characteristic of virtually all research including experience sampling method (ESM) and longitudinal data collection. However, clinic-referred adolescents have shown high ESM compliance rates (89.3% on average for studies with >6 surveys per day), and graded monetary incentives will be used during the ESM period of this study to bolster survey completion. Even if completion rates are lower than expected (e.g., 80%), networks will remain estimable; idiographic networks have been estimated from many fewer ESM assessments with MF and VAR models.[17-18] Regarding follow-up, retention in the PI's past longitudinal studies has been 77-100%. Multiple strategies will be utilized to reduce attrition at follow-up (e.g., reminder calls by study personnel; lotteried rewards). For missing data that does emerge, maximum likelihood estimation will be used in all statistical models.

Study Timeline

Phase 2: Personalized Symptom Network Parameters as Predictors of Response to Single-Session Interventions for Depression in Adolescents

	Year 1: 9/1/19-8/31/20			Year 2: 9/1/20-8/31/21			Year 3: 9/1/21-8/31/22		
	Fall	Spring	Summer	Fall	Spring	Summer	Fall	Spring	Summer
Formative work (obtain IRB approval; register trial on ClinicalTrials.gov)	X	X	X	X	X				
Train project staff (ongoing to accommodate new volunteer RAs)	X	X	X	X	X	X	X	X	X
Pilot, adapt computer-based BA intervention (volunteer participants drawn from Phase 1 study)		X	X						
Recruitment and consenting; baseline lab session/EMA period				X	X	X	X	X	
Lab-based intervention administration (including immediate pre- and post-intervention batteries)				X	X	X	X	X	
3-month follow-up (lab visit)					X	X	X	X	X
6-month follow-up (remote/via Qualtrics)						X	X	X	X
9-month follow-up (remote/via Qualtrics							X	X	X
12-month follow-up (lab-based)								X	X
Data processing				X	X	X	X	X	X

	Year 4: 9/1/22-8/31/23			Year 5: 9/1/23-8/31/24		
	Fall	Spring	Summer	Fall	Spring	Summer
6-month follow-up (remote/via Qualtrics)	X					
9-month follow-up (remote/via Qualtrics)	X	X				
12-month follow-up (lab visit)	X	X	X			
18-month follow-up (remote/via Qualtrics)	X	X	X	X		
24-month follow-up (remote/via Qualtrics)	X	X	X	X	X	
Data Processing	X	X	X	X	X	X
Data Analysis	X	X	X	X	X	X
Manuscript Development						

Inclusion Enrollment Reports

IER ID#	Enrollment Location Type	Enrollment Location
Study 2, IER 1	Domestic	Department of Psychology, Stony Brook University

Inclusion Enrollment Report 1

Using an Existing Dataset or Resource* : ○ Yes ● No

Enrollment Location Type* : ● Domestic ○ Foreign

Enrollment Country(ies): USA: UNITED STATES

Enrollment Location(s): Department of Psychology, Stony Brook University

Comments:

Planned

Racial Categories	Ethnic Categories				
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/ Alaska Native	2	0	0	0	
Asian	6	2	0	0	
Native Hawaiian or Other Pacific Islander	2	0	0	0	
Black or African American	11	5	5	2	
White	97	50	18	8	
More than One Race	4	1	0	0	

Cumulative (Actual)

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/ Alaska Native	0	0	0	0	0	0	0	0	0	0
Asian	0	0	0	0	0	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	0	0	0	0	0	0	0	0	0	0
White	0	0	0	0	0	0	0	0	0	0
More than One Race	0	0	0	0	0	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	0
Total	0	0	0	0	0	0	0	0	0	0

Section 3 - Protection and Monitoring Plans (Study 2)

3.1. Protection of Human Subjects	Human_Subjects_Phase_2_-_08_20_18.pdf
3.2. Is this a multi-site study that will use the same protocol to conduct non-exempt human subjects research at more than one domestic site?	○ Yes ● No ○ N/A
If yes, describe the single IRB plan	
3.3. Data and Safety Monitoring Plan	DATA_AND_SAFETY_MONITORING_PLAN_08_20_18_study_2.pdf
3.4. Will a Data and Safety Monitoring Board be appointed for this study?	○ Yes ● No
3.5. Overall structure of the study team	Overall_Structure_of_Study_Team.pdf

1. RISK TO SUBJECTS

a. Human Subjects Involved and Characteristics. Participants in Phase 2 (Study 2; does qualify as a clinical trial) will be 180 youth with elevated depressive symptoms (ages 11-16; 120 females, 60 males) and one parent per youth. Phase 2 will occur in years 2-5 of the award period. All participants will be recruited from clinical and nonclinical settings, utilizing connections in Psychiatry and Pediatrics to develop recruitment channels (see letters of support) along with connections to be established with local schools with facilitation from Departmental colleagues (see letter of support from Dr. Lerner), and community-based strategies used successfully by Psychology colleagues (e.g., commercial mailing lists). Selective sampling methods will be used to attain adequate minority representation (i.e., oversampling zip codes lowest on a composite socioeconomic index score to attain minority representation targets). Youth must be living with at least one parent or legal guardian, and both the youth and the parent must speak English well enough to complete study assessments and provide consent and assent. Additional inclusion criteria will include (1) the youth is age 11-16 (inclusive), with one parent willing to participate; (2) the youth reports elevated depressive symptoms (≥84%ile for age and sex, reflecting subclinical or higher symptom elevations) based on the Children's Depression Inventory-2. Exclusion criteria will include inability to complete assessments, psychotic symptoms, and active suicidality requiring immediate treatment, all of which will be assessed via an initial phone screen with the parent and youth. Concurrent treatment will be monitored but will not preclude eligibility. The current research will focus on youth ages 11-16 because as depression increases markedly in adolescence, and youth in this age range have responded well to growth mindset (GM) and behavioral activation (BA) interventions. All research will take place at Stony Brook University in the Department of Psychology.

b. Sources of Materials. Eligible youth in Phase 2, along with one parent per youth, will complete a baseline lab-based battery. Research materials collected during this battery will include psychophysiological, diagnostic, behavioral, and self- and parent-report data. Youth will participate in a structured diagnostic interview for diagnosing psychopathology and related symptoms; parents will be interviewed about the youth using an analog structured diagnostic interview. Youth and their parents will fill out questionnaires assessing the youth's symptoms and functioning across multiple domains; parents will self-report information regarding their own well-being and family history. Parents will also fill out measures designed to assess pubertal development. Youths will participate in a lab-based social stress induction, which will include psychophysiological data collection (ECG, EDA recordings) using the Biopac recording system. This battery will be followed by a 3-week experience sampling method (ESM) data collection period, during which adolescents will be prompted to complete the same 2-minute, 8-item survey 7 times per day for 21 days, via a smartphone-based app (LifeData). LifeData is a secure, HIPAA-compliant platform for ESM data collection. Notifications to complete surveys will occur every 2-3 hours, from 7:30am to 9:30pm on weekdays and 8:00am to 10:00pm on weekends. Responses will be deemed valid if completed within 1 hour of notification, ensuring at least 1-hour lags between surveys. Adolescents will receive an ESM tutorial at the initial lab visit, and a research team member will review each survey question with the adolescent to ensure comprehension. Adolescents with a personal smartphone will be assisted in downloading the ESM app; those without a smartphone will be provided with one for the ESM period.

After completing the baseline battery and 3-week ESM period, Phase 2 participants will return to the lab for a second study session, at which point they will be randomly assigned to receive 1 of 3 web-based SSIs: the GM, BA, or supportive therapy (ST) SSI. Immediately pre- and post-SSI, adolescents will complete a limited number of self-report questionnaires to index shifts in proximal psychosocial outcomes. Youth and parents will return to lab follow-up assessments at 3- and 12-months post-intervention (same measurement battery as at baseline). To enable longitudinal analysis of outcome trajectories, youth and parents will complete online follow-up questionnaires (including subjective reports of clinical and functional outcomes) 6, 9, 18, and 24 months post-intervention. Families will be debriefed by phone, and initial SSI condition assignment will be revealed, after 24-month follow-up is complete. At this time, youth will be offered the opportunity to remotely complete the SSIs they did not originally receive. Online follow-up surveys will be collected via Qualtrics, a secure online data collection system.

Participants will be assigned a study identification number that will be used to link the aforementioned data. Correspondence between identifying information and study identification number will be kept in a locked file in a locked room in the PI's laboratory. All data will be identified by the study identification number and will not contain the participants' name.

c. Potential Risks. The potential risks of participating in this study are considered minimal. The assessment instruments, intervention components, and social stress induction are commonly used in research with youth populations. Participants may experience some emotional discomfort in discussing various aspects

of their lives while completing questionnaires, or during the social stress induction. The interviewers will be trained in all study procedures by the PI. They will aim to minimize potential distress by presenting all assessment material in a supportive manner. If a parent or a youth becomes upset, the interviewer will assist them with processing their distressing emotions. If necessary, the interview or session may be interrupted or terminated. The family (parent and patient) will be clearly informed that they are free to terminate participation at any point in the protocol.

We will follow guidelines developed by Stony Brook University on the management of incidental findings. First, the consent form will clearly state that the procedures in the study are being conducted for research purposes. The consent will be clear that the researchers of this study are not medical doctors and are not trained to assess possible findings of heart rate (ECG) or electrodermal activity (EDA) recordings. There is no risk involved in obtaining such recordings via non-invasive electrodes (i.e., stickers placed on the skin). There is no risk of behavioral paradigms, tasks, questionnaires, or interventions, with the exception of the possibility that subjects may become bored. We will provide breaks and provide snacks between tasks and/or interventions as needed. Finally, as in any clinical research study, there is the risk of violating confidentiality as some of the information is personal and may be sensitive.

2. ADEQUACY OF PROTECTION AGAINST RISKS

a. Recruitment and informed consent. The PI will follow procedures that she and Departmental colleagues have previously used in recruiting subjects. Youths and families will be recruited from various sources, including schools, afterschool programs, youth mental health clinics and hospitals, private physicians and mental health practitioners, flyer and email advertisements, and via clinics in the Stony Brook University Hospital's Departments of Pediatrics and Psychiatry (see letters of support). Verbal consent will be sought for initial phone screening, during which information demographic will be obtained to ascertain potential appropriateness of the youth's participation. If eligibility criteria are met, the youth and one parent will be offered enrollment in the study. For families that appear to be eligible and are interested, our project coordinator will explain the nature of the study to both the youth and their parent, screen for inclusion and exclusion criteria, and schedule a lab-based study session. The project coordinator will review the consent and assent forms briefly over the phone, and encourage the subject and their parent to read it carefully before the scheduled appointment. At the laboratory visit, the project coordinator will obtain informed consent. The parents and the child will understand that they are free to withdraw from the study at any point. Consistent with IRB requirements, the parent will sign a consent form and the child will sign an assent form. Participants will be provided with a copy of the consent document, and the original will be kept on file.

b. Protection against risk. Informed consent and assent will be obtained prior to participation, and risks will be explained carefully to youths and parents. All information with identifying information collected during the project will be kept in a locked storage cabinet to which only PI Schleider and the project coordinator will have access. All data will be stored separately from identifying information and will be password protected. No names will be maintained in data records; rather, information will be coded by ID numbers only. Each individual will receive a unique ID number thereby allowing handling of data on all subjects without using individual names. PI Schleider will be responsible for monitoring the maintenance of confidentiality. In the event of a breach of confidentiality, she will inform the subject and his/her parents that the breach occurred; any breaches of confidentiality will be reported to the Institutional Review Board. Codifying participants by unique identifiers is an extensively-used practice that is highly efficient at protecting anonymous participation. No names or any identifying information would be used in presentation of scientific reports resulting from this study.

Procedures will be repeatedly explained to the youths and parents, giving them a sense of control over what is happening in their environment. Rather than closed yes/no questions, open-ended questions with regard to comfort and well-being will be used throughout the procedures to give participants the opportunity to voice any concerns or discomfort. Participants will also be given the opportunity to ask questions regarding the research procedures at any time during the protocol.

Because this research focuses on adolescents with elevated depressive symptoms, some participants may endorse suicidal ideation or behaviors during the study protocol (e.g., on the Children's Depression Inventory). In this event, risk assessments will be conducted and, when necessary, appropriate consultation with PI Schleider will be held to determine disposition. PI Schleider is a clinical psychologist with extensive training in child and adolescent risk and abuse assessment; her office will be in the same building where research activities will take place. In addition, the Krasner Psychological Center, the community mental health facility operated by the Department of Psychology, is on the same floor as PI Schleider's laboratory space, where this study will take place. In total, there are more than 11 clinical psychologists located within a short walk to PI

Schleider's laboratory. In the event that a participant is in imminent danger to themselves or others, their accompanying parent will be informed. The assessor and PI Schleider will meet with the subject and their parent to establish a safety plan. In the event of reported, active suicidal ideation or plan, participants and their parents will be accompanied to the Comprehensive Psychiatric Emergency Program at Stony Brook University Hospital, which is a 10 minute walk from the PI's laboratory. In addition, if a participant endorses suicidal ideation and/or intent in one of the Qualtrics-based follow-up surveys, PI Schleider or study personnel will contact the family within 24 hours to conduct a risk assessment via phone. If needed, a safety plan will be developed, and the PI or study personnel will work with the family to ensure the youth's safety. Additionally, all study participants will be offered referral information for psychotherapy and/or pharmacologic treatment at Stony Brook and the surrounding community. Participants will not be excluded from completing study procedures if they begin receiving treatment for psychological distress during the study.

Because information relating to child abuse may emerge in the course of interactions with subjects, the staff will follow federal and state child abuse reporting requirements. Participants will be informed of the need to report child abuse prior to eliciting this information. In case of any reported abuse by the child or parent, the parents will be informed about the federal mandated reporting laws, verbally and in writing. In cases where it is necessary to make a child abuse report, the family will always be informed prior to contacting any state agency, and given the option of making a self-referral to protective services.

3. POTENTIAL BENEFITS TO THE SUBJECTS AND OTHERS

PI Schleider has conducted previous studies using many of the same measures used in the current proposal; many children enjoy participating in the assessments (some involve computer-based tasks presented as games, and certain questionnaires involve self-reflection on personal experiences and beliefs) and all youths receive prizes and snacks during the course of the tasks. Families are also presented with monetary reimbursement for participating (up to $130 for Study 2, depending on ESM survey completion rates, with potential for additional lotteried $25 gift cards based on completion of online follow-up surveys). Providing the honorarium to the family, rather than the youth, reduces the possibility that payment could be coercive—it is left up to the family to decide how to allocate the honorarium. Additionally, all participating families will be offered a free report summarizing the results of their initial lab-based assessment. Such a report, if conducted by a community clinician, could cost upwards of several thousand dollars, and receipt of it is therefore a significant benefit to families. Further, participants in Phase 2 may directly benefit from participating in the study. Youth receiving the growth mindset or behavioral activation intervention may learn coping skills directly relevant to adaptive coping with setbacks, stress, and low mood. Youth in receiving the control intervention, which provides psychoeducation about emotions and the value of sharing one's emotions with others, may enjoy participating in the program and find the content interesting. At the conclusion of the study, all participating youths will receive the opportunity to complete any of the three online interventions, regardless of initial condition assignment. Finally, depression in youth often goes undetected. Assessment and continual monitoring of participants' symptoms may help identify clinically-significant problems in this domain.

4. IMPORTANCE OF THE KNOWLEDGE TO BE GAINED

This research may produce important knowledge relevant to reducing depression in adolescents. Phase 2 of this research represents the first study to integrate two historically separate fields: network analysis and single-session intervention (SSI) research. This integration may help identify potent, personalized, and scalable (low-cost, accessible) approaches to reducing depression in adolescents. More specifically, no studies to date have examined idiographic (personalized) network structures as predictors of youth treatment outcomes. Some studies, largely focused on adults, have explored cross-sectional, group-level networks as predictors of treatment outcome. However, these group-level networks—based on data from just one time-point—are unlikely to reflect causal, symptom-to-symptom links applicable to individuals. Personalized networks, , may forward the NIH-wide goal of *precision medicine*: In contrast, parameters from *personalized networks*-- which are created from symptom-level data gathered from many individuals across multiple assessment points—may predict individual likelihood of response to well-targeted interventions, optimizing efforts to match individuals to supports that fit their unique symptom structures and clinical needs. Thus, Phase 2 of this study holds potential to forward the NIH-wide goal of precision medicine in mental health care. Results of Phase 2 may catalyze key progress toward reducing depression in adolescents.

Furthermore, Phase 2 includes the first randomized controlled trial comparing two evidence-based SSIs for adolescent depression. SSIs may hold potential to dramatically increase intervention accessibility, yet additional studies are needed to determine SSIs' promise in reducing youth depression on a large scale, across multiple domains of functioning, and over long periods of time. This trial will be the first to examine

SSI effects on subjective, behavioral, and physiological outcomes. It will also compare two computer-based, depression-specific SSIs and an active control. Given these design features, this study will dramatically strengthen evidence regarding the capacity of targeted SSIs to reduce depression in adolescents. By including two evidence-based SSIs within the same RCT, this study will also help determine which SSI (if either) yields greater overall reductions in youth depressive symptoms. Findings may gauge the promise of cost-efficient, powerful strategies for improving youth depressive symptom trajectories during a developmental period marked by social stress, transitions, and psychosocial vulnerability.

Data Safety and Monitoring Plan

PI Schleider and the Stony Brook University Institutional Review Board (IRB) will have responsibility for continual monitoring of data and safety of participants in the study. Data and safety monitoring will take place continually (i.e., at least weekly) throughout the study. PI Schleider will follow the Stony Brook University IRB policies for expedited reporting of all unexpected adverse events and serious adverse events. She will report to the IRB any non-serious unexpected adverse events and serious adverse events that are related or possibly related to a subject's participation in the research, and that occur while the subject is enrolled in the study or (b) occur within 30 days of the conclusion of the subject's participation in the study. All such events will be reported within 24 hours of PI Schleider's knowledge of the event by phone, fax, or email to the Committee on Research Involving Human Subjects within Stony Brook University's IRB. In addition, PI Schleider will provide the IRB with a full written report detailing the event within 5 working days/7 business days following initial IRB notification. Additionally, if PI Schleider becomes aware of a serious adverse event more than 30 days after the conclusion of a patient's study participation, she will report the event to the IRB at the time that she becomes aware of it. Further, at the time of the annual continuing review, PI Schleider will provide the Stony Brook University IRB with a summary of any adverse events and any other unanticipated problems that occurred since the last review. PI Schleider will collect data on adverse events throughout the course of the study period.

The potential risks of participating in this study are considered minimal. The assessment instruments, intervention components, and social stress induction are all commonly used in research with youth populations. Participants may experience some emotional discomfort in discussing various aspects of their lives while completing questionnaires, or during the social stress induction. Any such distress will hopefully be minimized by presenting all assessment materials in a supportive manner, assuring youths that their participation in the study is fully voluntary, and informing youths that they can leave the study at any time. Therefore, likelihood of any adverse events during the study is considered very low.

PI Schleider will ensure that the study adheres to the IRB-approved protocol and will continually monitor the overall progress of the study. The trained study personnel will ensure the accuracy and completeness of study materials and report any inconsistencies to the PI.

Names will be removed from all of the data and replaced with a participant ID number. All data will remain in a secured and locked location where only the PI and Lab Coordinator will have access. Additionally, every effort will be made to ensure confidentiality. Confidentiality of recorded and all other information obtained in the study will be maintained by labeling the information with a numerical ID number. A computer file and a paper document linking the code to the subject's identity will be located separately and will be accessible only to authorized personnel. No names or identifying information would be used in presentation of scientific reports resulting from this study.

Adolescents' confidentiality will be maintained except as required by law or as required to insure their safety. For example, because this research focuses on adolescents with elevated depressive symptoms, some participants may endorse suicidal ideation or behaviors during the study protocol (e.g., on the Children's Depression Inventory). In this event, risk assessments will be conducted and, when necessary, appropriate consultation with PI Schleider will be held to determine disposition. PI Schleider is trained as a clinical psychologist with several years of experience and training in child and adolescent risk and abuse assessment; her office will be in the same building where research activities will take place. In the event that an adolescent participant is in imminent danger to him/herself, the accompanying parent will be informed. The assessor and PI Schleider will meet with the subject and their parent to establish a safety plan. In the event of reported, active suicidal ideation or plan, participants and their parents will be accompanied to the Comprehensive Psychiatric Emergency Program at Stony Brook University Hospital, which is a 10 minute walk from the PI's laboratory. In addition, if a participant endorses suicidal ideation and/or intent in one of the Qualtrics-based follow-up surveys, PI Schleider or trained study personnel will contact the family within 24 hours to conduct a risk assessment via phone. If needed, a safety plan will be developed, and the PI or study personnel will work with the family to ensure the youth's safety. Additionally, all study participants will be offered referral information for psychotherapy and/or pharmacologic treatment at Stony Brook and the surrounding community. Participants will not be excluded from completing study procedures if they begin receiving treatment for psychological distress during the study.

Additionally, because information relating to child abuse may emerge in the course of interactions with subjects, PI Schleider and project staff will follow federal and state child abuse reporting requirements. Participants will be informed of the need to report child abuse prior to eliciting this information. In case of any reported abuse by the child or parent, the parents will be informed about the federal mandated reporting laws,

verbally and in writing. In cases where it is necessary to make a child abuse report, the family will always be informed prior to contacting any state agency, and given the option of making a self-referral to protective services.

In the event of the adverse events described above or any others, PI Schleider will report the incident and provide all relevant data to the Stony Brook University IRB according to the timeline noted above.

Overall Structure of Study Team

The administrative and data coordinating site for the proposed study is Stony Brook University. Participants will be recruited from clinical and community settings in the Long Island area. Although some data will be collected remotely (e.g., during the experience sampling method component), all data will be stored and analyzed at Stony Brook University's Department of Psychology within PI Schleider's research lab. There is no separate laboratory or testing center for the proposed study.

Section 4 - Protocol Synopsis (Study 2)

4.1. Brief Summary

The goal of this study is to integrate advances in network analysis and single-session intervention (SSI) research to identify potent, accessible strategies for reducing depressive symptoms in adolescents. Through a three-arm randomized trial, this study will test whether parameters from adolescents' personalized depressive symptom structures predict clinical response to SSIs. Adolescents with elevated depressive symptoms will be randomized to receive one of two evidence-based SSIs (a growth mindset SSI or a behavioral activation SSI) targeting distinct features of depression (hopelessness/low perceived control, and anhedonia/pleasurable activity withdrawal, respectively), or an active control SSI. Network parameters will be evaluated as predictors of SSI response over short-term (3 month) and longer-term (across 24-months) follow-up periods. For instance, adolescents with higher outward centrality on a cognitive symptom (e.g., hopelessness) may respond more favorably to the growth mindset intervention, and those with a higher outward centrality on a behavioral symptom (e.g., pleasurable activity withdrawal; anhedonia), to the behavioral activation SSI. Additionally, adolescents with stronger bidirectional links between multiple depressive symptoms types may respond more favorably to either SSI relative to the control. Results may identify a novel approach to matching adolescents to targeted depression interventions by personalized need. The study will also serve as the first randomized trial comparing two SSIs for adolescent depressive symptoms, with the longest follow-up of any SSI trial to date, gauging their relative promise to help reduce depression in adolescents.

4.2. Study Design

4.2.a. Narrative Study Description

Major depression (MD) is the leading cause of disability in youth, with a global economic burden of >$210 billion annually. However, up to 70% of youth with MD do not receive services. Even among those who do access treatment, up to 65% fail to respond, demonstrating the need for more potent, accessible interventions. A key challenge underlying limited treatment potency involves MD's heterogeneity: An MD diagnosis reflects over 1400 possible combinations of symptoms, creating a need for treatment matched to personal clinical need. Separately, low treatment accessibility stems from the structure of existing interventions. Most span many weeks and are designed for delivery in brick-and-mortar clinics by highly trained therapists, making them difficult to deliver on a broad scale. This study aims to address the need for accessible, potent youth MD interventions by integrating methods and findings from two previously independent areas: single-session intervention (SSI) research and network science. In a meta-analysis of 50 randomized clinical trials, the PI has found that SSIs can reduce diverse youth psychiatric problems, including MD. The PI also found that a web-based SSI teaching growth mindset (the belief that personal traits are malleable) reduced depression and anxiety symptoms in high-symptom adolescents across 9 months. Thus, well-targeted SSIs may yield lasting benefits -- but given MD's heterogeneity, there is a need for tools that can match youth to SSIs optimized for personal symptom structures.

This study harnesses computational advances from the network approach to psychopathology, which views psychiatric disorders as causal interactions between symptoms, to evaluate such a tool. Specifically, this study will test whether parameters from personalized symptom structures (such as outward symptom centrality, or the degree to which one symptom prospectively predicts others over time; and overall network density, or the strength with which all symptoms in a given network are prospectively associated with one another) predict response to targeted SSIs. After completing an eligibility screener, adolescents with elevated depressive symptoms (N=180, ages 11-16) and parents will complete a baseline battery, and adolescents will complete an experience sampling (ESM) data collection period to assess adolescents' individual depressive symptoms multiple times per day for 3 consecutive weeks. Adolescents will then return to the lab, where they will be assigned to receive one of three online SSIs: a Growth Mindset SSI (teaching that personal traits and abilities are malleable rather than fixed), a Behavioral Activation SSI (guiding participants to engage in personally valued, rewarding activities), or a supportive therapy/control SSI. Immediately pre- and post-SSI, adolescents will complete a limited number of self-report measures as manipulation checks, and to assess shifts in proximal outcomes relevant to each SSI (growth mindset, perceived control, hopelessness). Three months post-intervention, adolecents and parents will return for a follow-up battery, assessing the same factors as at baseline. A final lab visit, comprising the same battery, will be held 12-months post-intervention. Adolescents will also complete online follow-up surveys at 60, 9-, 18-, and 24-months post-intervention to enable analysis of outcome trajectories across a two-year period. Network parameters will be computer from ESM data, and personalized symptom parameters will be tested as predictors of SSI response, both at at post-intervention and across the follow-up period. It is predicted that adolescents with a more outwardly central cognitive symptom at pre-intervention (e.g., hopelessness or low perceived control) will respond more favorably to the GM SSI, and those with a more outwardly central behavioral symptom (e.g. anhedonia; withdrawal from pleasureable activities), to the BA SSI. (Note that each symptom's outward centrality will be indexed through continuous predictor variables; thus, there is no requirement or expectation that distinct group of adolescents will emerge with outwardly central cognitive or behavioral symptoms). It is also predicted that adolescents with higher overall network density, indexing stronger causal links among behavioral and cognitive symptoms, will respond more favorably to either active SSI. SSI response will be operationalized as declines in overall depressive symptoms (primary outcome) and improvements in core deficits linked with depression (secondary

outcomes: anhedonia, low agency, blunted stress recovery), from baseline to proximal (3-month) and longer-term (12- and 24-month) follow-ups.

4.2.b. Primary Purpose: Treatment

4.2.c. Interventions

Type	Name	Description
Other	Growth Mindset Single-Session Intervention (GM SSI)	The GM SSI is a 30-60 minute computer-based intervention, self-administered by youth. Content is designed to maximize relevance for youth experiencing depression and related problems (e.g., excessive worry; social anxiety). It include 5 elements: (1) An introduction to the concept of neuroplasticity, describing how/why personal traits and abilities are controlled by thoughts and feelings in their brains, which have constant potential for change; (2) Testimonials from older youth describing their beliefs that people can change, given the brain's inherent malleability; (3) Further vignettes by older youth describing times when they used 'growth mindset' to cope following peer rejection and negative self-talk; (4) Examples of strategies for applying these ideas to one's own life; (5) An exercise wherein participants write notes to younger youth, using newly gleaned information about the malleability of personality and the brain.
Other	Behavioral Activation Single-Session Intervention (BA SSI)	The BA SSI is a 30-60 minute computer-based intervention, self-administered by youth, adapted from existing BA SSIs (originally designed for delivery by therapists). The BA SSI includes 5 components: (1) An introduction to the program's rationale: that engaging in value-based activites that build pleasure and accomplishment can combat sad mood and low self-esteem; (2) Psychoeducation about depression, including how behavior shapes feelings and thoughts; (3) A life values assessment, where youth identify key aras (family relationships, friendships, school, hobbies) from which that draw (or once drew) enjoyment and meaning; (4) Creation of an activity hierarchy, where youth identify (from pre-generated lists) and personalize (in guided exercises) 3 activities to target for change; and (5) An exercise in which youth write about benefits that might result from engaging in each activity, an obstacle that might keep them from doing the activities, and a strategy for overcoming the obstacle
Other	Supportive Therapy Single-Session Intervention (ST SSI)	The ST SSI is a computer-based, self-administered, 30-60 min, self-administered intervention that encourages youth to identify and express feelings to trusted others. It is designed to control for nonspecific aspects of completing a computer-based, interactive program; it does not teach or emphasize specific cognitive or behavioral skills or activities. ST SSI activities mirror the structure of the GM SSI. The two programs include the same number of reading and writing exercises. ST also includes vignettes written by older youths, who describe times when they benefited from sharing emotions with friends and family members.

4.2.d. Study Phase: Phase 2/3

Is this an NIH-defined Phase III Clinical Trial? ○ Yes ● No

4.2.e. Intervention Model: Single Group

4.2.f. Masking: ● Yes ○ No

☑ Participant ☑ Care Provider ☑ Investigator ☑ Outcomes Assessor

4.2.g. Allocation: Randomized

4.3. Outcome Measures

Type	Name	Time Frame	Brief Description
Primary	Change in Children's Depression Inventory-2 (CDI-2) scores from baseline to 24-month follow-up	Baseline and 3-, 6-, 9-, 12-, 18-, and 24-month (final) follow-up	Youth-reported youth depressive symptoms
Primary	Change in Children's Depression Inventory-2, Parent (CDI-2-P) scores from baseline to 24-month follow-up	Baseline and 3-, 6-, 9-, 12-, 18-, and 24-month (final) follow-up	Parent-reported youth depressive symptoms
Secondary	Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS)	Baseline and 3- and 12-month follow-up	Selected modules from the K-SADS will be used to assess the presence of psychiatric diagnoses (depressive disorders, generalized and social anxiety disorders, mania, oppositional defiant disorder, ADHD, and conduct disorder)
Secondary	Change in Multidimensional Anxiety Scale for Children-Child Form scores from baseline to 24-month follow-up	Baseline and 3-, 6-, 9-, 12-, 18-, and 24-month (final) follow-up	Youth-reported youth anxiety symptoms
Secondary	Change in Multidimensional Anxiety Scale for Children-Parent Form scores from baseline to 24-month follow-up	Baseline and 3-, 6-, 9-, 12-, 18-, and 24-month (final) follow-up	Parent-reported youth anxiety symptoms
Secondary	Electrodermal activity (EDA) recovery slope	Assessed at immediate post-intervention only	Rate of psychophysiological stress recovery, as indicated by declines in EDA, following a lab-based social stressor (a modified version of the Trier Social Stress Task)
Secondary	Respiratory Sinus Arrhythmia (RSA) recovery slope	Time Frame: Assessed at immediate post-intervention only	Rate of psychophysiological stress recovery, as indicated by increases in RSA, following a lab-based social stressor (a modified version of the Trier Social Stress Task)
Secondary	Change in Snaith-Hamilton Pleasure Scale scores from baseline through 24-month follow-up	Baseline, immediately pre- and post-intervention, and 3-, 6-, 9-, 12-, 18-, and 24-month (final) follow-up	Youth-reported hedonic capacity (the ability to experience pleasure)
Secondary	Change in Behavioral Activation for Depression Scale scores from baseline through 24-month follow-up	Baseline, immediately pre- and post-intervention, and 3-, 6-, 9-, 12-, 18-, and 24-month (final) follow-up	Youth-reported approach versus disengagement from rewarding activities
Secondary	Effort Expenditure for Rewards Task (EEfRT)	Baseline and 12 month follow-ups	Behavioral measure of reward motivation, in which reduced motivation toward reward is indexed as a decreased willingness to choose greater-effort/ greater-reward over less-effort/less-reward options
Secondary	Primary Control Scale for Children (PCSC)	Baseline, immediately pre- and post-intervention, and 3-, 6-, 9-, 12-, 18-, and 24-month (final) follow-up	Youth-reported perceived primary (behavioral) control
Secondary	Secondary Control Scale for Children (SCSC)	Baseline, immediately pre- and post-intervention, and 3-, 6-, 9-, 12-, 18-, and 24-month (final) follow-up	Youth-reported perceived secondary (emotional) control

Secondary	Hopelessness Scale for Children (HSC)	Baseline, immediately pre- and post-intervention, and 3-, 6-, 9-, 12-, 18-, and 24-month (final) follow-up	Youth-reported hopelessness
Secondary	Implicit Theory of Personality Questionnaire (ITPQ)	Baseline, immediately pre- and post-intervention, and 3-, 6-, 9-, 12-, 18-, and 24-month (final) follow-up	Youth-reported beliefs about the malleability of personality
Secondary	UCLA Loneliness Scale	Baseline and 3-, 6-, 9-, 12-, 18-, and 24-month (final) follow-up	Youth-reported loneliness
Secondary	Brief Symptom Inventory-18	Baseline and 3-, 6-, 9-, 12-, 18-, and 24-month (final) follow-up	Parent-reported parental psychological distress
Secondary	Multidimensional Peer Victimization Scale	Baseline, 12 months, 24 months	Youth-reported peer victimization

4.4. Statistical Design and Power — Statistical_Design_and_Power.pdf

4.5. Subject Participation Duration — 25 months

4.6. Will the study use an FDA-regulated intervention? — ○ Yes ● No

4.6.a. If yes, describe the availability of Investigational Product (IP) and Investigational New Drug (IND)/ Investigational Device Exemption (IDE) status

4.7. Dissemination Plan — Dissemination_Plan.pdf

Statistical Design and Power

Power analysis. There are no established methods for estimating power for intra-individual symptom networks. However, such networks have been successfully estimated from fewer within-person data-points than will be collected here (e.g., 60 per individual[17]), using ESM surveys with many more than 8 items (e.g., up to 21 items, yielding hundreds more slope estimations[18]), and in smaller samples than in the proposed study (*N*s=1-129).[89-90] Thus, even with some portion of missed ESM surveys (estimated at 10-15%, based on a review of past ESM studies with adolescents[55]), we should have sufficient data to estimate network structures. Regarding proposed RCT, we used G*Power 3.1 to calculate the sample size needed to achieve sufficient power (1- β) to detect mean group differences of small (.2), medium (.5), and large effects (.8) with α set at .05 and power at 0.95. Sample sizes calculated were 1095, 180, and 72, respectively. Power to detect a small effect size is ideal, but logistical constraints necessitate a more conservative sample size. The sample size of 180 (60 per SSI condition) will reflect power to detect a medium effect size.

Analytic Plan. With Consultant Bringmann and Collaborator Eaton, I will estimate symptom networks from ESM data for each adolescent using multilevel factorial (MF) and vector autoregressive (VAR) models, depending on results of Phase 1 of the proposed project (see Study Record 1).[17-20] VAR models estimate the extent to which a given symptom (time *t*) can be predicted from all other symptoms at a previous moment (time *t*-1).[19] Each symptom is regressed onto its lagged values and the lagged values of all other symptoms. Here, time *t*-1 and time *t* reference two consecutive ESM surveys; network parameter estimation is based on within-person data only. MF models, in contrast, allow for random, person-specific auto- and cross-regressive effects, using population (fixed) *and* person-level (random) effects to estimate parameters.[20] Simulation studies suggest that MF models may be relatively robust to unequal lags and missing ESM data,[20] but MF and VAR models have not been directly compared. Using both methods, we will compute two types of network parameters for all 50 adolescents: network density (overall strength of links between symptoms, defined as the average of absolute values of symptom-to-symptom slopes in one's network) and outward centrality for each symptom (mean strength of all effects from a given symptom at time *t* to all other symptoms at time *t*+1). As in prior studies comparing dynamical process models' performance, we will use cross-validation scores[90] from MF and VAR models to assess their relative utility. Networks in Phase 2 will be estimated using the approach identified in Phase 1 (described in Study Record 1) as producing more stable parameters.

To assess network parameters as predictors of SSI outcome, I will use mixed-effects linear models, I will use mixed-effects linear models to test network parameters as predictors of three-month changes in depression-related deficits. Parameters for network density and outward centrality for each symptom will be continuous predictors in these models, calculated using MF or VAR (depending on Phase 1 results). Covariates will include pubertal development, family income, age, sex, SSI condition assignment, and time. Models will include a random intercept and slope, allowing for variation in baseline levels of the outcome variables and rates of change, and an autoregressive error structure. Change in CDI-2 scores from baseline to proximal (3-month) and across long-term (12-, 24-month) follow-ups will be the primary study outcome. A significant interaction between time and network density would indicate that symptom network density predicted SSI response, regardless of SSI condition. A significant interaction between time, cognitive symptom outward centrality (assessed continuously), and GM condition would indicate that adolescents with greater outward centrality on a given cognitive symptom responded more favorably to the GM SSI, versus other SSIs. A significant interaction between time, outward centrality of a behavioral symptom, and BA condition would indicate that adolescents with greater outward centrality on a given behavioral symptom responded more favorably to the BA SSI, versus other SSIs. I will also examine main and relative effects of the BA and GM SSIs on youth depression trajectories. Significant interactions between time and an SSI condition variable would indicate that a given SSI significantly improved youth depression symptom trajectories, relative to ST. Finally, additional mixed-effects models (structured as described previously) will assess network parameters as predictors of depression-related deficits (anhedonia, low agency, blunted stress recovery) and associated symptoms (e.g. anxiety severity).

Dissemination Plan

PI Schleider will facilitate dissemination of study results through ClinicalTrials.gov registration and reporting. PI Schleider will be responsible for handling ClinicalTrials.gov requirements for this project. She will register the trial prior to enrollment of the first subject. Once a record is established, PI Schleider will confirm accuracy of record content; resolve problems; and maintain records including content update and modifications. PI Schleider will also be responsible for results reporting and Adverse Events reporting at the conclusion of the project.

Delayed Onset Studies

Delayed Onset Study#	Study Title	Anticipated Clinical Trial?	Justification
The form does not have any delayed onset studies			

1 March, J. S., Silva, S., Petrycki, S., Curry, J., Wells, K., Fairbank, J., ... & Severe, J. The Treatment for Adolescents With Depression Study (TADS): long-term effectiveness and safety outcomes. *Archives of General Psychiatry* **64**, 1132-1144 (2007).

2 Vitiello, B., Emslie, G., Clarke, G., Wagner, K. D., Asarnow, J. R., Keller, M., ... & DeBar, L. Long-term outcome of adolescent depression initially resistant to SSRI treatment. *Journal of Clinical Psychiatry* **72**, 388-396 (2011).

3 Fried, E. I., & Nesse, R. M. Depression is not a consistent syndrome: an investigation of unique symptom patterns in the STAR*D study. *Journal of Affective Disorders* **172** 96-102 (2015).

4 Forman-Hoffman, V., McClure, E., McKeeman, J., Wood, C.T., Cook Middleton, J., Skinner, A.C., et al. Screening for Major Depressive Disorder in Children and Adolescents: A Systematic Review for the U.S. Preventive Services Task Force. Evidence synthesis no. 116. AHRQ publication no. 13-05192-EF-1. Rockville, MD, *Agency for Healthcare Research and Quality* (2016).

5 Avenevoli, S., Swendsen, J., He, J. P., Burstein, M., & Merikangas, K. R. Major depression in the National Comorbidity Survey–Adolescent Supplement: prevalence, correlates, and treatment. *Journal of the American Academy of Child & Adolescent Psychiatry* **54**, 37-44 (2015).

6 Greenberg, P. E., Fournier, A. A., Sisitsky, T., Pike, C. T., & Kessler, R. C. The economic burden of adults with major depressive disorder in the United States (2005 and 2010). *The Journal of Clinical Psychiatry* **76**, 155-162 (2015).

7 Schleider, J. L., Abel, M., & Weisz, J. R. Implicit theories and mental health problems in youths: A random-effects meta-analysis. *Clinical Psychology Review* **35**, 1-9 (2015).

8 Schleider, J. L., & Weisz, J. R. Mental health problems and implicit theories of thoughts, feelings, and behavior in early adolescents: Are girls at greater risk? *Journal of Social and Clinical Psychology* **35**, 130-151 (2016).

9 Schleider, J. L., & Weisz, J. R. Implicit theories relate to youth psychopathology, but how? A longitudinal test of two predictive models. *Child Psychiatry & Human Development* **47**, 603-617 (2016).

10 Schleider, J. L. & Schroder, H. S. (2018). Implicit theories of personality across development: impacts on coping, resilience, and mental health. In V. Ziegler-Hill & T. K. Shackelford (Eds.), *The SAGE Handbook of Personality and Individual Differences*. Sage Publications.

11 Schleider, J. L., & Weisz, J. R. Reducing risk for anxiety and depression in adolescents: Effects of a single-session intervention teaching that personality can change. *Behaviour Research and Therapy* **87**, 170-181 (2016).

12 Schleider, J. L., & Weisz, J. R. A single-session growth mindset intervention for adolescent anxiety and depression: Nine-month outcomes of a randomized trial. *Journal of Child Psychology and Psychiatry* **59***,* 160-170 (2018).

13 Schleider, J. L., & Weisz, J. R. Little treatments, promising effects? Meta-analysis of single session interventions for youth psychiatric problems. *Journal of the American Academy of Child & Adolescent Psychiatry* **56**, 107-115 (2017).

14 Borsboom, D., & Cramer, A.O.J. Network analysis: An integrative approach to the structure of psychopathology. *Annual Review of Clinical Psychology* **9** 91-121.

15 McNally, R. J. Can network analysis transform psychopathology? *Behaviour Research and Therapy* **86**, 95-104 (2016).

16 Borsboom, D. Psychometric perspectives on diagnostic systems. *Journal of Clinical Psychology* **8**, 1089-1108 (2008).

17 Bringmann, L. F., Vissers, N., Wichers, M., Geschwind, N., Kuppens, P., Peeters, F., et al. A network approach to psychopathology: New insights into clinical longitudinal data. *PLoS One* **4**, e60188 (2013).

18 Bringmann, L. F., Lemmens, L. H. J. M., Huibers, M. J. H., Borsboom, D., & Tuerlinckx, F. Revealing the dynamic network structure of the Beck Depression Inventory II. *Psychological Medicine* **45**, 747-757 (2015).

19 Bringmann, L. F., Pe, M. L., Vissers, N., Ceulemans, E., Borsboom, D., Vanpaemel, W., ... & Kuppens, P. Assessing temporal emotion dynamics using networks. *Assessment* **23**, 425-435 (2016).

20 Liu, S. Person-specific versus multilevel autoregressive models: Accuracy in parameter estimates at the population and individual levels. *British Journal of Mathematical and Statistical Psychology* **70**, 480-498 (2017).

21 Gawrysiak, M., Nicholas, C. R. N., & Hopko, D. R. Behavioral activation for moderately depressed university students: Randomized controlled trial. *Journal of Counseling Psychology* **56**, 468-475 (2009).

22 Armento, M. E. A., McNulty, J. K., & Hopko, D. R. Behavioral activation of religious behaviors (BARB): Randomized trial with depressed college students. *Psychology of Religion and Spirituality* **4**, 206-222 (2012).
23 Van Vorhees, B. W., Ellis, J., Stuart, S. Fogel, J., & Ford, D. E. Pilot study of a primary care internet-based depression prevention intervention for late adolescents. *The Canadian Child and Adolescent Pyschiatry Review* **14**, 40-43 (2005).
24 Schleider, J. L., Ginsburg, G. S., & Drake, K. Perceived peer victimization predicts anxiety outcomes in a prevention program for offspring of anxious parents. *Journal of Clinical Child and Adolescent Psychology* (2018, in press).
25 Schleider, J. L., Ginsburg, G. S., Keeton, C. P., Weisz, J. R., Birmaher, B., Kendall, P. C., Piacentini, J., Sherrill, J., & Walkup, J. T. Parent symptoms and treatment outcomes for anxious youth: Roles of family functioning and caregiver strain. *Journal of Consulting and Clinical Psychology* **83** 213-224 (2015).
26 Schleider, J. L., Abel, M., & Weisz, J. R. Do immediate gains predict long-term symptom change? Findings from a randomized trial of a single-session intervention for youth anxiety and depression. (Manuscript under review).
27 Schleider, J. L., Gordon, D., Conoway, L., & Bonora, M. Developing a single-session growth mindset intervention for teachers: Feasibility, acceptability, and preliminary effects. (Manuscript in preparation).
28 Schleider, J. L., & Weisz, J. R. (in press). Parent expectancies and preferences for mental health treatment: The roles of emotion mindsets and views of failure. *Journal of Clinical Child and Adolescent Psychology* (2018, in press).
29 Weisz, J. R., Kuppens, S., Ng, M. Y., Eckshtain, D., Ugueto, A. M., Vaughn-Coaxum, R., ... & Weersing, V. R. What five decades of research tells us about the effects of youth psychological therapy: A multilevel meta-analysis and implications for science and practice. *American Psychologist* **72**, 79-117 (2017).
30 Mullarkey, M., Schleider, J. L., Jones, P., & Weisz, J. R. Using network analysis to compare youth and parent reports of youth depressive symptoms. (Manuscript in preparation.)
31 Whiteford, H. A., Degenhardt, L., Rehm, J., Baxter, A. J., Ferrari, A. J., Erskine, H. E., ... & Burstein, R. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *The Lancet* **382** 1575-1586 (2013).
32 Hankin, B.L., Abramson, L.Y., Moffitt, T.E., Silva, P.A., McGee, R., & Angell, K.E. Development of depression from preadolescence to young adulthood: emerging gender differences in a 10-year longitudinal study. *Journal of Abnormal Psychology* **107** 128–40 (1998).
33 Hammen, C., Brennan, P. A., & Keenan-Miller, D. Patterns of adolescent depression to age 20: The role of maternal depression and youth interpersonal dysfunction. *Journal of Abnormal Child Psychology* **36**, 1189–1198 (2008).
34 Wilson, S., Hicks, B. M., Foster, K. T., McGue, M., & Iacono, W. G. Age of onset and course of major depressive disorder: associations with psychosocial functioning outcomes in adulthood. *Psychological Medicine* **45**, 505-514 (2015).
35 Fried, E. I., & Nesse, R. M. Depression sum-scores don't add up: why analyzing specific depression symptoms is essential. *BMC Medicine* **13**. (2015).
36 Hollon S., Garber J., & Shelton R. Treatment of depression in adolescents with cognitive behavior therapy and medications: A commentary on the TADS project. *Cognitive and Behavioral Practice* **12**, 149-155 (2005).
37 Chu, B. C., Colognori, D., Weissman, A. S., & Bannon, K. An initial description and pilot of group behavioral activation therapy for anxious and depressed youth. *Cognitive and Behavioral Practice* **16**, 408-419 (2009).
38 Kataoka, S.H., Zhang, L., & Wells, K.B. Unmet need for mental health care among U.S. children: variation by ethnicity and insurance status. *American Journal of Psychiatry* **159**, 1548–1555 (2002).
39 Harpaz-Rotem, I., Leslie, D., & Rosenheck, R. A. Treatment retention among children entering a new episode of mental health care. *Psychiatric Services* **55** 1022-1028 (2004).
40 Schleider, J. L., & Weisz, J. R. Can less be more? The promise (and perils) of single-session youth mental health interventions. *The Behavior Therapist* **40**, 256-261 (2017).
41 Pe, M. L., Kircanski, K., Thompson, R. J., Bringmann, L. F., Tuerlinckx, F., Mestdagh, M., ... & Kuppens, P. Emotion-network density in major depressive disorder. *Clinical Psychological Science* **3**, 292-300 (2015).
42 Boschloo, L., van Borkulo, C. D., Borsboom, D., & Schoevers, R. A. A prospective study on how symptoms in a network predict the onset of depression. *Psychotherapy and Psychosomatics* **85**, 183-184 (2016).
43 http://www.pnas.org/content/early/2018/06/15/1711978115.short?rss=1

44 Miu, A. S., & Yeager, D. S. Preventing symptoms of depression by teaching adolescents that people can change: Effects of a brief incremental theory of personality intervention at 9-month follow-up. *Clinical Psychological Science*, **3** 726-743 (2015).

45 Treadway, M. T., Bossaller, N. A., Shelton, R. C., & Zald, D. H. Effort-based decision-making in major depressive disorder: a translational model of motivational anhedonia. *Journal of Abnormal Psychology*, **121** 553 (2012).

46 Joiner Jr, T. E., Catanzaro, S. J., & Laurent, J. Tripartite structure of positive and negative affect, depression, and anxiety in child and adolescent psychiatric inpatients. *Journal of Abnormal Psychology*, **105** 401 (1996).

47 Rothbaum, F., Weisz, J. R., & Snyder, S. S. Changing the world and changing the self: A two-process model of perceived control. *Journal of personality and social psychology*, **42** 5 (1982).

48 Weisz, J. R., Weiss, B., Wasserman, A. A., & Rintoul, B. Control-related beliefs and depression among clinic-referred children and adolescents. *Journal of Abnormal Psychology*, **96** 58 (1987).

49 Calhoun, C. D., Franklin, J. C., Adelman, C. B., Guerry, J. D., Hastings, P. D., Nock, M. K., et al. Biological and cognitive responses to an in vivo interpersonal stressor: Longitudinal associations with adolescent depression. *International Journal of Cognitive Therapy*, **5** 283-299 (2012).

50 Prinstein, M.J., & Aikens, J.W. Cognitive moderators of the longitudinal association between peer rejection and adolescent depressive symptoms. *Journal of Abnormal Child Psychology*, **32** 147-158 (2004).

51 Dennis, M.L., Scott, C.K., Funk, R.R., & Nicholson, L. A pilot study to examine the feasibility and potential effectiveness of using smartphones to provide recovery support for adolescents. *Substance Abuse*, **36** 486-492 (2015).

52 van Roekel, E., Goossens, L., Verhagen, M., Wouters, S., Engels, R., & Scholte, R. Loneliness, affect, and adolescents' appraisals of company: an experience sampling method study. *Journal of Research on Adolescence*, **24** 350-363 (2013).

53 Rusby, J.C., Westling, E., Crowley, R., Light, J.M. Concurrent and predictive associations between early adolescent perceptions of peer affiliates and mood states collected in real time via ecological momentary assessment methodology. *Psychological Assessment*, **25** 47-60 (2013).

54 Suveg, C., Payne, M., Thomassin, K., & Jacob, M. Electronic diaries: a feasible method of assessing emotional experiences in youth? *Journal of Psychopathology and Behavioral Assessment*, 32 57-67 (2009).

55 Wen, C. K. F., Schneider, S., Stone, A. A., & Spruijt-Metz, D. Compliance With Mobile Ecological Momentary Assessment Protocols in Children and Adolescents: A Systematic Review and Meta-Analysis. *Journal of Medical Internet Research*, **19** e132 (2017)

56 Eaton, N. R. Latent variable and network models of comorbidity: Toward an empirically derived nosology. *Social Psychiatry and Psychiatric Epidemiology* **50** 854-859 (2015).

57 Kim, H., & Eaton, N. R. The hierarchical structure of common mental disorders: connecting multiple levels of analysis, bifactor models, and predictive validity. *Journal of Abnormal Psychology,* **124** 1064-1078 (2015).

58 Eaton, N. R., Krueger, R. F., Markon, K. E., Keyes, K. M., Skodol, A. E., Wall, M., Hasin, D. S., & Grant, B. F. The structure and predictive validity of the internalizing disorders. *Journal of Abnormal Psychology,* **122** 86-92 (2013).

59 Kotov, R., Krueger, R. F., Watson, D., Achenbach, T. M., Althoff, R. R., Bagby, M., … Eaton, N. R., … & Zimmerman, M. The Hierarchical Taxonomy Of Psychopathology (HiTOP): a dimensional alternative to traditional nosologies. *Journal of Abnormal Psychology* (in press).

60 Eaton, N. R. The broad importance of integration: psychopathology research and hierarchy as construct. *European Journal of Personality* (in press).

61 Eaton, N. R., Krueger, R. F., & Oltmanns, T. F. The structure and long-term stability of the internalizing spectrum of personality and psychopathology across the lifespan. *Psychology and Aging,* **26** 987-993 (2011).

62 Cyranowski, J. M., Frank, E., Young, E., & Shear, M. K. Adolescent onset of the gender difference in lifetime rates of major depression: a theoretical model. *Archives of General Psychiatry*, **57**, 21-27 (2000)

63 Kovacs, M. *Children's Depression Inventory 2:(CDI 2)*. Multi-Health Systems (2010).

64 Petersen, A. C., Crockett, L., Richards, M., & Boxer, A. A self-report measure of pubertal status: Reliability, validity, and initial norms. *Journal of youth and adolescence*, **17** 117-133 (1988).

65 Angold, A., Costello, E. J., & Worthman, C. M. Puberty and depression: the roles of age, pubertal status and pubertal timing. *Psychological Medicine*, **28** 51-61 (1998).

66 Kaufman, J., Birmaher, B., Brent, D., Rao, U. M. A., Flynn, C., Moreci, P., ... & Ryan, N. Schedule for affective disorders and schizophrenia for school-age children-present and lifetime version (K-SADS-PL): initial reliability and validity data. *Journal of the American Academy of Child & Adolescent Psychiatry*, **36** 980-988 (1997).
67 March, J. S. Manual for the Multidimensional Anxiety Scale for Children (MASC 2). North Tonawanda, NY: MHS (2012).
68 Schleider, J.L., Krause, E.D., & Gillham, J.E. Sequential comorbidity of anxiety and depression nin youth: Present knowledge and future directions. *Current Psychiatry Reviews*, **10**, 75-87 (2014).
69 Kirschbaum, C., Pirke, K.M., & Hellhammer, D.H. The 'Trier Social Stress Test'—a tool for investigating psychobiological stress responses in a laboratory setting. *Neuropsychobiology,* **28** 76-81 (1993).
70 Grossman, P., & Taylor, E.W. Toward understanding respiratory sinus arrhythmia: Relations to cardiac vagal tone, evolution and biobehavioral functions. *Biological Psychology,* **74** 263–285 (2007).
71 Grossman, P., & Taylor, E. Respiratory sinus arrhythmia, cardiac vagal tone and a critique of the polyvagal theory: Toward a theory of biobehavioral allostasis of energy exchange. *Biological Psychology*, **74**, 263-85 (2007).
72 Rømer Thomsen, K., Whybrow, P. C., & Kringelbach, M. L. Reconceptualizing anhedonia: novel perspectives on balancing the pleasure networks in the human brain. *Frontiers in Behavioral Neuroscience,* **9** (2015).
73 Snaith, R. P., Hamilton, M., Morley, S., & Humayan, A. A scale for the assessment of the hedonic tone: The Snaith-Hamilton Pleasure Scale. British Journal of Psychiatry, **167** 99–103 (1995).
74 Kanter, J. W., Mulick, P. S., Busch, A. M., Berlin, K. S., & Martell, C. R. The Behavioral Activation for Depression Scale (BADS): psychometric properties and factor structure. *Journal of Psychopathology and Behavioral Assessment*, **29** 191-202 (2007).
75 Treadway, M. T., Buckholtz, J. W., Schwartzman, A. N., Lambert, W. E., & Zald, D. H. Worth the 'EEfRT'? The effort expenditure for rewards task as an objective measure of motivation and anhedonia. *PloS One,* **4** e65 (2009).
76 Rawal, A., Collishaw, S., Thapar, A., & Rice, F. 'The risks of playing it safe': A prospective longitudinal study of response to reward in the adolescent offspring of depressed parents. *Psychological Medicine*, **43** 27–38 (2013).
77 Olino, T.M., McMakin, D.L., Morgan, J.K., Silk, J.S., Birmaher, B., Axelson, D.A., Williamson, D.E., Dahl, R.E., Ryan, N.D., & Forbes, E.E. *Developmental Cognitive Neuroscience*, **8** 55-64 (2014).
78 Whitton, A. E., Treadway, M. T., & Pizzagalli, D. A. Reward processing dysfunction in major depression, bipolar disorder and schizophrenia. *Current Opinion in Psychiatry*, **28**, 7 (2015).
79 Weisz JR, Weiss B, Wasserman AA, Rintoul B (1987) Control-related beliefs and depression among clinic-referred children and adolescents. *J Abnorm Psychol,* 96, 58–63.
80 Weisz, J.R., Southam-Gerow, M.A., & McCarty, C.A. Control-related beliefs and depressive symptoms in clinic-referred children and adolescents: Developmental differences and model specificity. *Journal of Abnormal Psychology*, 110, 97–109 (2001).
81 Weisz, J.R., Francis, S.E., & Bearman, S.K. Assessing secondary control and its association with youth depression symptoms. *Journal of Abnormal Child Psychology*, **38** 883-893 (2010).
82 Yeager, D.S., Miu, A.S., Powers, J., & Dweck, C.S. Implicit theories of personality and attributions of hostile intent: A meta-analysis, an experiment, and a longitudinal intervention. *Child Development*, **84** 1651–1657 (2013).
83 Yeager, D.S., Trzesniewski, K.H., Tirri, K., Nokelainen, P., & Dweck, C.S. Adolescents' implicit theories predict desire for vengeance after peer conflicts: Correlational and experimental evidence. *Developmental Psychology*, **47**, 1090-1107 (2011).
84 Spirito, A., Williams, C.A., Stark, L.J., & Hart, K.J. The Hopelessness Scale for Children: Psychometric properties with normal and emotionally disturbed adolescents. *Journal of Abnormal Child Psychology*, **16**, 445-458 (1988).
85 Mynard, H., & Joseph, S. Development of a multidimensional peer-victimization scale. *Aggressive Behavior*, **26**, 169-178 (2000).
86 Russell, D. W. UCLA Loneliness Scale (Version 3): Reliability, validity, and factor structure. *Journal of Personality Assessment*, **66**, 20-40 (1996).
87 Derogatis, L. R. *BSI 18, Brief Symptom Inventory 18: Administration, scoring and procedures manual*. NCS Pearson, Incorporated (2001).

88 Kroenke, K., Spitzer, R. L., & Williams, J. B. The PHQ-9: Validity of a brief depression severity measure. *Journal of Internal Medicine,* **16**, 606-613 (2001).
89 Bak, M., Drukker, M., Hasmi, L., & van Os, J. An n=1 clinical network analysis of symptoms and treatment in psychosis. *PLoS One*, **11** e0162811 (2016).
90 Bulteel, K., Mestdagh, M., Tuerlinckx, F., & Ceulemans, E. VAR(1) based models do not outpredict AR(1) models in current psychological applications. *Psychological Methods* (in press).

Resource Sharing Plan

All elements of NIH Grants Policy will be followed, and data from this project will be made available for research purposes to qualified individuals within the scientific community. Data will be released and shared in a timely manner. Data will be free of identifiers that would permit linkages to individual research subjects and variables that could lead to deductive disclosure of the identity of individual subjects. Findings from this project will be published and presented in appropriate outlets (e.g. scientific conferences; peer-reviewed journals) in a timely manner upon completion of data collection and analysis.