IRB Study Number: 20190760
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Title: Expressing Personal Recollections in English or Spanish to Alleviate Traumatic Emotions (Exprésate)

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PI Name: Roger McIntosh, Ph.D.

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1) Protocol Title

Expressing Personal Recollections in English or Spanish to Alleviate Traumatic Emotions (Exprésate)

2) IRB Review History

This study protocol has not been previously submitted for review by an external IRB.

3) Study Objectives

Participants will be recruited from the greater Miami-Dade area via flyer and chain referral. This study aims to recruit 36 Latinas with a history of trauma into one of 3 separate arms of an augmented 4-week written emotional disclosure (WED) intervention: (1) Spanish-only, (2) English-only, and (3) non-trauma daily event writing in Spanish). This study seeks to test the hypothesis that WED regarding traumatic experience in one's primary, i.e., Spanish, language will be associated with more positive health outcomes than English WED or non-trauma related writing in Spanish. Collected prior to and after this intervention will be biomarkers, neurocognitive, psychiatric, sociocultural, and neuroimaging data to address the following study objectives:

To determine whether in Latinas with or without HIV exposure to an expressive writing intervention in Spanish will have an effect on primary study outcomes, i.e., changes in verbal learning & memory as well as symptoms of post-traumatic stress.

To determine whether exposure to an expressive writing intervention, delivered in either English vs. Spanish will have an effect on secondary study outcome biomarkers that are linked to cognitive and emotional functioning, i.e., changes in task and resting state functional brain activity and connectivity and stress hormone reactivity.

To explore whether intervention-related changes in primary and secondary outcomes is associated with changes in gene expression of transcription factors associated with brain glucocorticoid as well as peripheral inflammation-immune activation.

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4) Outcome Measures

a) Primary Outcome(s)

Title: Change in PTSD symptoms as assessed by the Impact of Event Scale
Description: 22-item self-report instrument that corresponds to DSM-IV symptoms of PTSD over last 7 days on a scale from 0 (not at all) to 4 (extremely).
Time Frame: Pre-intervention (Session 1) and at post-intervention (Session 6)

Title: Change in verbal learning as assessed by Hopkins Verbal Learning Task
Description: Measures verbal learning and memory function. (Three immediate recall trials) (0 no words recalled - 12 all words recalled).
Time Frame: at post-intervention (Session 6)

b) Secondary Outcome(s)

Title: Change in functional connectivity of the Default Mode Network (DMN).
Description: DMN is a large scale network of interacting brain regions implicated in emotion and memory. Activity/connectivity indexed by Fisher's Z or Beta wt.
Time Frame: Pre-intervention (Session 1) and at post-intervention (Session 6)

Title: Change in salivary measures of stress reactivity.
Description: 200 μL of saliva will be used for immunosorbent assay of alpha amylase (sAA) and adrenal corticotrophin releasing hormone (ACTH).
Time Frame: Pre-intervention (Session 1) and at post-intervention (Session 6)

c) Exploratory Outcome(s)

Title: Change in gene expression of inflammatory immune function.
Description: A peripheral blood sample will be used for immunosorbent assay of NF-κB p65 which is a transcription factor for a gene that controls inflammatory cytokine expression in peripheral white blood cells.
Time Frame: Pre-intervention (Session 1) and at post-intervention (Session 6)

Title: Change in gene expression of glucocorticoid activity.
Description: A peripheral blood sample will be used for immunosorbent assay of FKBP5 which is a transcription factor for a gene that controls co-chaperone that modulates glucocorticoid receptor activity in response to stress in brain & body.
Time Frame: Pre-intervention (Session 1) and at post-intervention (Session 6)

5) Background

Trauma and neurocognitive function. Post-traumatic stress disorder (PTSD) and its symptoms of emotional numbing, intrusion, avoidance, and hyperarousal is three to

five times more likely to be experienced in women living with HIV (WLHIV) compared to their HIV-negative counterparts (1-4). Intrusive thoughts of traumatic events are vigilantly avoided in PTSD and attention divided or shared between task-relevant and task-irrelevant thoughts. This places excessive demands of attentional and inhibitory cognitive resources, thus depleting cognitive task performance (5, 6). Amongst HIV+ women PTSD accelerates the rate of neurocognitive decline (7, 8). Hispanics/Latinos not only show higher rates of learning and memory impairment than non-Hispanic Whites (9-13), but these impairments are more pronounced in older adult Latinas (11). This accelerated cognitive decline may be attributed to the gambit of issues facing Hispanic/Latina or low SES WLHIV such as substance abuse, violence, and HIV/AIDS (SAVA) (14-17). Although HIV+ women show deficits in multiple cognitive domains, decrements in verbal learning and memory are particularly sensitive to traumatic stress associated with violence or sexual abuse (7, 18-20). Functional magnetic resonance imaging (fMRI) has recently begun elucidating the syndemic effects of SAVA on encoding and recognition phases of a verbal learning and memory. In a high-stressed cohort of HIV+ women greater levels of PTSD not only predicted poorer verbal memory performance but greater deactivation of the medial prefrontal cortex (MPFC) and posterior cingulate cortex during episodic memory retrieval suggesting less efficient strategic retrieval (21).

Trauma and neuroendocrine function. Response of the hypothalamic-pituitary-adrenal (HPA)-axis varies considerably in traumatized women due to sex-endocrine changes and glucocorticoid sensitivity (22-25). Nevertheless, it is clear that HPA activity enhances the consolidation of fear learning extinction similar to its effect on episodic memory retrieval (26). In a most recent study a single dose of hydrocortisone was found to enhance learning and memory performance in a high-stressed group of HIV+ women (27). Moreover, when exposed to stress, cortisol responders show greater memory retrieval of everyday information (28). In tandem with HPA activity plasma and salivary cortisol levels have been linked to amygdala (29) and medial prefrontal cortex brain metabolism (30, 31). In a study of veterans with and without PTSD our group and collaborators observed that individuals with attenuated adrenal corticotophic hormone (ACTH) responses to trauma recall showed greater activity in the MPFC compared to high ACTH responders to stress (32). Recently, greater expression of FKBP5, a gene that regulates glucocorticoid receptor sensitivity reducing the affinity of cortisol and the nuclear translocation of the receptor, was found to predict higher activity, larger volume and increased coupling of the left hippocampus with the medial prefrontal cortex in individuals with a history of childhood adversity (33). In the absence of FKBP5 gene expression there is an increase in sensitivity of the hypothalamic-pituitary axis to negative glucocorticoid feedback thus leading to lower cortisol level after acute stress observed in PTSD (34-36).

Inflammation**.** Although the $CD4^+$ T-helper cell is established as a subclinical marker of HIV disease progression, studies have failed to establish a stable relationship between either CD4 or peripheral viral load RNA and rate of mood disturbance and neurodegeneration. Our group has reviewed literature surrounding

the effect of pro-inflammatory monocyte expansion on cognitive, emotional, cardiovascular and immune outcomes in persons living with HIV//AIDS (37). A particular class of non-typical monocyte, i.e., $CD16^{++}$, are implicated in the cellular signaling, trafficking, proliferation, and apoptosis associated with neurocognitive dysfunction (38). Once trafficked to the brain by the monocytes, pro-inflammatory cytokines IL-6 and TNF-alpha are released from the HIV gp120 envelope and consequentially disrupt subcortical and cortical networks (39-42). Conceivably, these neurotrophic processes may alter connectivity of limbic networks. Inversely, HPA axis dysregulation attributed to functional brain changes has implications for inflammatory-immune regulation in PLWH. For example, medial prefrontal cortex (MPFC) MPFC-mediated regulation of the HPA-axis normally increases cortisol output and binding to glucocorticoid receptors on monocytes to halt expression of pro-inflammatory cytokines (43, 44). Although hypocortisolemia may contribute to the pro-inflammatory state in PTSD and HIV, glucocorticoid resistance on peripheral monocytes is widely noted (45-47). Under normal circumstances the binding of peripheral glucocorticoid receptors suppresses Th1 activity hence down-regulating gene expression of pro-inflammatory cytokines in monocytes (48-50). Traumatized women show reduced levels of serum and plasma cortisol and higher levels of pro-inflammatory cytokines (51-56). Moreover, recovery from trauma is associated with a decrease in inflammatory cytokine levels (57). A recent study amongst virally-suppressed HIV+ women found that markers of monocyte activation predicted worse verbal learning and memory performance and global cognitive function (58, 59).

Trauma and therapeutic response. Our group has previously reported large gender-based effects for reductions in PTS symptomology following 1-month following an expressive writing intervention for a sample of 96 predominately African-American HIV+ women living in Miami (60). Hispanic/Latina women were largely underrepresented in this sample. There is a scarcity of MRI studies examining the effects of expressive writing interventions, however a 12-week cognitive behavioural therapy intervention in adults with PTSD was not only shown to increase hippocampal volume but also expression of FKBP5 suggesting greater efficacy of cortisol on brain following a trauma intervention (61, 62). Moreover, increased DNA methylation at promotor regions for FKBP5 expression have been linked to reduction in symptom severity following exposure therapy in persons with anxiety disorders (63).

6) Recruitment of Sample

Study-Wide Recruitment Methods. Thirty-six Hispanic/Latina women with a history of trauma, (i.e., childhood abuse, intimate partner, domestic violence), over the age of 21 will be recruited from the greater Miami-Dade area. Potential subjects will be identified through the use of advertisements placed at local HIV outpatient clinics throughout the greater South Florida area.

The Miami Center for AIDS Research (CFAR) Behavioral/ Social Science & Community Outreach Core (Core E) provides CFAR investigators with consultation and resources to expand behavioral clinical studies. The underlying goals are to enhance recruitment and retention of community and clinic-based study participants with attention to "hard to reach populations." Core E offers CFAR investigators the services of an Outreach Coordinator who can oversee the study recruitment and assessment activities of research projects. The Outreach Coordinator can also determine the best recruitment strategy, conduct participant outreach, recruitment, assessment and site coordination. Participants may be recruited through the outpatient referral service of the CFAR, advertisement at outpatient treatment centers and chain-referral. The initial (pre-screening) will take place via phone, in-person at the CFAR outreach center or electronic via survey link. The collection of this information is intended to elucidate whether the individual meets the inclusion criteria for participating in the study (see Screening section of procedures below).
Provided inclusion criteria are met, referrals will be scheduled for a telephone follow-up and scheduling for the first study. Individuals meeting eligibility criteria will be then be invited to the Coral Gables campus for an in-person COVID-19 and urine toxicology screening, prior to enrollment.

This study will actively recruit participants through the Community Outreach Core and Clinic Registry Project for the Center for HIV and research in Mental Health (CHARM) (IRB#20160911) of the University of Miami Center for AIDS Research. This mechanism allows IRB-approved study investigators the ability to search and identify potential willing research participants who meet study criteria. Upon contact, patients will verify their identity before being informed about the study and moving forward with the screening process. Patients will also be informed they have the right to change their consent in order to decline to be contacted for future studies.

Participants will also be recruited from the Miami MWCCS E-Prost Protocol No. 20210476, a study of men and women living with HIV in the US. The MWCCS has approved a concept sheet to refer MWCCS participants to this study. MWCCS participants who meet inclusion criteria will be asked by the MWCCS team, for willingness to participate in this study. Those interested participants will be given the contact information to contact the study directly, or if they prefer, their contact will be shared with study staff to contact them and provide information about the study.

Exclusion criteria. Following initial referral, participants will be assessed for PTSD over the phone through the primary care PTSD screen for DSM-5 (PC-PTSD-5) (64). After the participant has consented an in-house screener will also be used to assess substance dependency, suicidal ideation, history or treatment for schizophrenia or bipolar disorder, as well as severe dementia indexed by the Mini-Mental State Examination (MMSE) (65). Additional exclusion criteria include the following: 1) Left-handedness or ambidextrous; 2) Inability to tolerate the scanning procedures (e.g., claustrophobia); 3) Metal in body or prior history working with metal fragments (e.g., as a machinist); 4) Any other contraindications for MRI examination (e.g., metallic implants such as pacemakers, surgical aneurysm clips, or

known metal fragments embedded in the body); 5) currently pregnant or could be pregnant ; 6) Heavy alcohol intake (> 3 drinks) within 12 hours prior to participation in fMRI ; 7) Evidence from health history of neurological or systemic disorder which can cause cognitive impairment; 8) Self-reported current diagnosis of psychiatric disorder or psychoactive substance abuse or dependence; 9) Recent history (within two years) of myocardial infarction; 10) Severe cardiovascular disease, or currently active cardiovascular disease (e.g., angina, cardiomyopathy); 11) Uncontrolled hypertension or hypotension; 12) History of closed trauma with loss of consciousness; 13) Space occupying lesions (e.g., mass lesions, tumors); 14) CNS infection; 15) CNS vasculitis; 16) CNS demyelinating disease (e.g., multiple sclerosis); 17) Congenital CNS abnormality (e.g., cerebral palsy); 18) Seizure disorders; 19) History of cerebrovascular disease (e.g., stroke, TIA's)

Inclusion criteria**.** 1) Age ≥ 21 years; 2) Elevated PTSD symptoms as assessed by the PCL-5 using a cut-off of 34 or above. This measure has been validated using the gold standard against the goal standard for PTSD, i.e., Clinician-administered PTSD scale for DSM-5 (CAPS-5) (66, 67). Although the current gold-standard, i.e., DSM-5 has not been translated to Spanish, if this is not available at the time of study we will revert back to the Spanish version of the PCL-C adapted for DSM-IV (68). The Davidson Trauma Scale (DTS) will be used as a back-up to identify DSM-IV symptoms for post-traumatic stress disorder (PTSD); 3) on a stable anti-retroviral therapy regimen for > 6 months as assessed with the Adult AIDS Clinical Trial Group structured interview (69); 4) Spanish-English bilingual as measured by the Brief Acculturation Scale for Hispanics (cut-off of 3), Spanish speaker or English speaker 5) Participant is willing and able to sign ICF; 6) self-report as Latina (i.e. self-reported); 7) HIV positive serostatus as determined by medical record within the last 12 months; 8) born female.

7) Study Design

a) Primary purpose

To determine whether in (LLWH) exposure to an expressive writing intervention in Spanish will have an effect on primary and secondary study outcomes.

b) Interventional study model

Randomized control trial with participants randomized to either the augmented trauma-writing intervention in English, the augmented trauma-writing intervention in Spanish or the daily-event-writing control in English/Spanish. Both experimental and control participants will visit the study on four occasions during a 4-week period so that they could write for 30 min in a private office.

8) Procedures

General overview. Upon meeting all eligibility criteria individuals will be consented into the study. Full participation in the study will involve 6 separate session. The first

and sixth sessions will last approximately 4-5 hours. On the evening prior to these sessions participants will perform an overnight fast and told to avoid drugs, alcohol and exercise. On the mornings of session 1 and 6 participants will report to the Cox Neuroscience Annex (CNA). Participants will be compensated $80 each for the pre- and post-intervention sessions. Participants will also receive $20 for attending each online writing session. Each participant will be compensated using the Zelle ™ mobile banking application.

Screening. Prior to informed consent individuals will undergo screening using the 5-item PTSD checklist (PC-PTSD-5) in order to determine their eligibility to participate in the study. This is required given trauma interventions can potentially have adverse effects on asymptomatic individuals. . After the initial screening, referrals will be instructed to bring a copy of their most recent HIV labs (drawn within the last 6 months) for their in-person screening session, if they are HIV+. Labs will not be requested for the HIV- participants. After obtaining informed consent, we will make a copy of those labs, remove any identifiable information, and return the original copy to the research participant.

Pre- and post-intervention Sessions 1a and 6a (intake)**.** After adhering to overnight fasting protocols on both days participants will report to the Neuroimaging Suite (NIS) located on the second floor of the University of Miami Neuroscience Building (Cox Neuroscience Annex (CNA)) at 5151 San Amaro Drive, Coral Gables, FL 33146. Participants will be asked to wear comfortable clothing. Participants will undergo a series of screenings prior to being admitted entry into the NIS, including an fMRI metal screening and (see CNA standard operating procedures). After completion of the ICF the initial procedures will involve a clinical intake wherein participants will have their height, weight, waist and hip girth measured along with a standard information regarding medical history and pre-scan mood state, They will then have their time point 1 bloods drawn through an intravenous (IV) Teflon-based catheter inserted antecubital by an experienced phlebotomist. Three 10-15ml vials will be drawn in (2) heparin and (1) EDTA containers of blood will be drawn from all participants at time point 1.

Pre- and post-intervention Sessions 1b and 6b (MRI). Following the blood draw, the participant will have a 10-minute mock scan to allow the them to become acclimated to the MR environment and the cognitive task. Following the mock scan participants will need to complete an fMRI metal screening and be interviewed by the MR tech to ensure there are no potential hazards during scanning. Prior to the scan, and after the scan participants will be asked to provide a saliva sample. We will collect a small amount of saliva, using a disposable salivette to measure stress hormones and inflammation. During the scan, simultaneous recording of pulse, respiratory rate, and blood pressure will take place to monitor physiological arousal levels. Immediately, following the scan, the IV line will be flushed. At the conclusion of the real MRI session (time point 2) an additional (2) 20ml vials of blood will be drawn in heparinized tubes.

Pre- and post-intervention Sessions 1b and 6b (post-scan assessments). Following the blood draw (T2), participants will be escorted to a separate room. Within this room, they will be fitted with electrodes for measurement of heart rate, respiratory rate and blood pressure during the completion of a behavioral self-compassion task. This task will take approximately 30 minutes to complete. Following completion of this task a third blood draw (T3) will be performed and (2) 20ml tubes will collected for immediate processing. Following the compassion task a battery of psychosocial and neurocognitive measures will be administered lasting approximately 90 – 120 minutes. The estimated time of completion for all Session 1a & 6a activities is 4 hours per session. Participants will compete a psychosocial battery of self-report questionnaires using a laptop or personal computer (See Table 1). Following the surveys participants will engage in an exit interview.

Sessions 2-5: Arms and Interventions.

Arms 1 & 2 (Intervention). Twenty-four women will be randomized to the 2 arms of the intervention involving written emotional disclosure in English or Spanish. During the 4 writing days, participants will be asked to write about the most traumatic or upsetting experiences of their entire life. In their writing, they will be asked to "really let go" and explore their "very deepest emotions and thoughts." Subjects will be told that it is best to write about a major trauma and encouraged to write about the same experience on all 4 days. However, they will also be told it is okay if they write about current conflicts. Subjects will be encouraged to write about traumas or conflicts they have not discussed in great detail with others. They will be told to write continuously for 20 min. These instructions were developed by Dr. Gail Ironson and based upon those used in previous studies (70, 71), that were adopted along with a writing probe to assess the effect of WED on post-traumatic, depressive and disease related outcomes amongst HIV+ women (60). Scripts and instructions will be delivered exclusively in Spanish for the S-WED group and exclusively in English for the E-WED groups. When the 20-min writing session is complete, subjects will be asked to write for an additional 10 min and given the following instructions (processing probes) for each session, respectively. Session 1: How you have tried to understand and make sense of the traumatic experience(s)?; Session 2: How does the traumatic experience affect your feelings about yourself, your self-worth, and your self-esteem?; Session 3: How does the traumatic experience affect your ability to solve problems, to meet future challenges, or to deal with day-to-day stress?; and Session 4: How have you tried to understand the trauma and make sense of it?

Arm 3 (Daily event writing). Twelve women will be randomly assigned to the daily event writing condition will be asked to write a description about what they did "yesterday from the time [they] got up until the time [they] went to bed" for 20 min continuously. We will counterbalance the language used by these women to journal about their daily events. They will be told to "avoid writing about [their] emotions or opinions" but to try to be as "accurate and objective as possible." The 20-min writing period will be followed by 10 more min of describing in writing what they

have done "today from the time [they] woke in the morning." These instructions will be modified slightly for three subsequent writing sessions to reflect descriptions of what they did on different days or what they planned to do on future days.

9) Study Timeline

The timeline will begin once the participant has signed the informed consent. Upon acquiring informed consent data will be collected during 6 separate time points. After the baseline session (1a & 1b) participants returned for the second study visit where they will be randomized to either the English trauma-writing intervention, the Spanish trauma-writing intervention or the daily-event-writing control. Experimental and control participants will be asked to visit their study based on their randomized assignment for a total of four occasions over a 4-week period so that they can engage in an online expressive writing exercise for 30 min. After each writing session, the writings will be submitted online to the researcher staff. All writings will be de-identified before being stored on secured UM servers and analyzed by study staff. Questionnaires, interviews, blood draws, neurocognitive assessments and neuroimaging data collected during session 1 were again administered 1 months after the end of each participant's writing intervention. Upon completion of the session 6 participants involvement with the current study be complete and there will be no other study requirements.

10) Data Collection

Blood Assays**.** Approximately 50 ml of blood will be drawn from all participants, once at the first time point and up to 2 times (before and after neuroimaging session) at all subsequent time points. HIV-1 viral load and CD4 count will be recorded from each participant based upon the last labs drawn. Because menstrual cycle phase influence PTSD symptom presentation profile and psychophysiology (72, 73) data collection for all pre-menopause women will take place in the luteal phase and blood banked for ovarian steroid hormones, (e.g., estradiol). A salivary ACTH kit will be used to measure HPA-axis activity pre-scan and again following trauma recall. Peripheral GC sensitivity was tested by measuring in-vitro stimulated production of interleukin-6 (IL-6) in whole blood before and after cortisol vs. placebo application. Salivary cortisol will be analyzed using an Elisa plate reader at the Diabetes Research Institute under the supervision of Armando Mendez, Ph.D.

Flow Cytometry**.** Absolute counts of individual monocyte subsets and EPCs (cells/µl) will be calculated using total monocyte count obtained with hematoanalyser and proportions of individual monocyte subsets determined by flow cytometry. Due to their pro-inflammatory phenotype, ease of transmigration, and vulnerability to viral infection, anti-CD16 Alexa Fluor 488 and anti-CD14-PE antibodies will also be used to define monocyte subsets. Monocyte subsets will also be defined as CD14++CD16– cells, CD14++CD16+ cells, and CD14+CD16+ cells. The percent of the CD14+ HLA-DR+ cell subpopulation that was positive for TNF (‘‘% TNF+ monocytes) will

be analyzed based upon their expression upon incubation with lipopolysaccharide (LPS) solution and LPS+DEX in 3 final concentrations of 10−8, 10−9, and 10−10 M.

ELISA. The micro ELISA plate provided in this kit has been pre-coated with an antibody specific to Human NF-κB p65. Standards or samples are added to the micro ELISA plate wells and combined with the specific antibody. Then a biotinylated detection antibody specific for Human NF-κB p65 and Avidin-Horseradish Peroxidase (HRP) conjugate are added successively to each micro plate well and incubated. Free components are washed away. The substrate solution is added to each well. Only those wells that contain Human NF-κB p65, biotinylated detection antibody and Avidin-HRP conjugate will appear blue in color. The ELISA kit from Aviva Systems Biology FKBP5 ELISA Kit (Human) (OKCD08676) is based on standard sandwich enzyme-linked immuno-sorbent assay technology. An antibody specific for FKBP5 has been pre-coated onto a 96-well plate (12 x 8 Well Strips) and blocked. Standards or test samples are added to the wells, incubated and removed. A biotinylated detector antibody specific for FKBP5 is added, incubated and followed by washing. Avidin-Peroxidase Conjugate is then added, incubated and unbound conjugate is washed away. An enzymatic reaction is produced through the addition of TMB substrate which is catalyzed by HRP generating a blue color product that changes to yellow after adding acidic stop solution. The density of yellow coloration read by absorbance at 450 nm is quantitatively proportional to the amount of sample FKBP5 captured in the well. For Cortisol/ACTH a competitive immunoassay kit will be used. Cortisol/ACTH in standards and samples compete with cortisol conjugated to horseradish peroxidase for the antibody binding sites on a microtitre plate. After incubation, unbound components are washed away. Bound cortisol enzyme conjugate is measured by the reaction of the horseradish peroxidase enzyme to the substrate tetramethylbenzidine (TMB). This reaction produces a blue color. A yellow color is formed after stopping the reaction with an acidic solution. The optical density is read on a standard plate reader at 450 nm. The amount of cortisol enzyme conjugate detected is inversely proportional to the amount of cortisol present, in the sample.

Anthropometrics. Height, weight, waist girth (umbilicus), and hip girth (greater trochanters) measures will be obtained. The seated subject will undergo casual blood pressure assessment (mean of last 2 of 3 readings, taken 3 min apart).

Saliva. A small amount of saliva will be collected using a disposable salivette just before and immediately after the MRI. This saliva will be analyzed within our lab for the stress hormones ACTH and alpha-amylase as well and may also include inflammatory cytokines including IL-6, IL-1a, and TNF-alpha.

Neuropsychological assessment Participants will be assessed with an acculturation scale (bidimensional acculturation scale (BAS) and Brief Acculturation Scale for Hispanic (BASH). There will be a language portion assessment with the scale Civilian Spanish-English version PCL-C as well as an assessment for PTSD

with the scale Treatment Outcome PTSD Scale (TOP-8) and PTSD checklist for DSM-5 (PCL-5).
An abbreviated 15-item profile of mood states (POMS) questionnaire will be adapted to Spanish based on norms and factor structure reported in Hispanic/Latino populations (74) at the conclusion of each trauma session to assess levels of distress. Subjects will also complete a battery of self-report measures of PTSD symptom severity, subject Unit of Distress ,(impact of events scale—revised, IES-R (75), anxiety (the Spielberger State and Trait Anxiety Scales and Anxiety Sensitivity Index (ASI) (76), depression (Beck Depression Inventory, (BDI-II) (77), alexithymia (Toronto Alexithymia Scale-20, TAS-20 (78), multidimensional interoceptive awareness Scale, and dissociation using the Dissociative Experiences Scale -2 (DES-II) (79), early trauma (Early Trauma Inventory, (ETI) (80), Perceived Support Network Inventory, and Brief COPE. Surveys that have been translated and are archived by CLaRO will also be included, such as measures of psychological symptomology (Brief Symptoms Inventory (BSI) (81) depression (The Center for Epidemiological Studies Depression Scale (CESD) (82) anxiety (General Anxiety Disorder Scale (GAD-7) (83)) and intimate partner violence (HITS Tool for Intimate Partner Violence Screening (HITS) (84). The Physical Symptoms Questionnaire (PHQ-15), Pittsburgh Sleep Quality Index (PSQI) and Patient Health Questionnaire (PHQ) will also be administered. To assess HIV-associated neurocognitive dysfunction a neurocognitive battery will be administered and performance compared with published age- and education-adjusted normative data to calculate z scores (NPZ), within several cognitive domains. These domains include global functioning (Trail Making Test (TMT), Hopkins Verbal Learning Task, Brief Visual Memory Test, WAIS-R Digit symbol substitution, WAIS-R Digit Span, WAIS-R letter number sequencing, WAIS-R Design Block Test, COWAT (Spanish), Paced Auditory Serial Addition Test, Rey Complex Figure Test, Verbal Fluency Task, Stroop Color-Word Interference Test, Grooved Pegboard, and Iowa Gambling Task. Anti-retroviral regimen will be assessed with the Adult (ACTG) structured interview (69). Health Markers for Review of Systems, Basic Demographic Questionnaire, Pittsburgh Sleep Quality Index, and Physical Health Questionnaire. Individuals randomized to the S-WED group will be prompted to self-report in Spanish i.e., (anger or "enojo", anxiety or "ansiedad" and depression or "tristeza". Note: "arrepentido por cosas hechas"= regret about things done, desanimado= unmotivated, inútil= helpless, aterrorizado= terrorized, and culpable= guilty". Pronoun use will also be quantified from their responses, as research suggests that trauma victims that use more first person singular pronouns (e.g. I/mine, "yo/mio") in trauma narratives have worse, long-term symptom severity(86)), which extend to broader use of singular pronoun use (87). A similar pattern was observed in depressed and negative mood individuals (84).

Cardio-autonomic Function**.** In addition to understanding vascular mechanisms this research is also based upon autonomic mechanisms. Parasympathetic and sympathetic function will indexed by heart rate variability (HRV). Because of the variation in measure and interpretation of HRV we will use methodology recommended by the Task Force of the European Society of Cardiology for both

time and frequency domain (88). These values will be derived by in-house software made available by Bipoac™ that record and transform HRV from the R-R intervals gathered from spontaneously measured heart rate within 2 to 5 minute intervals. Overall 5 domains of HRV will be measured in the study (see Table 1) indexing relative levels of sympathetic and parasympathetic cardiac input.

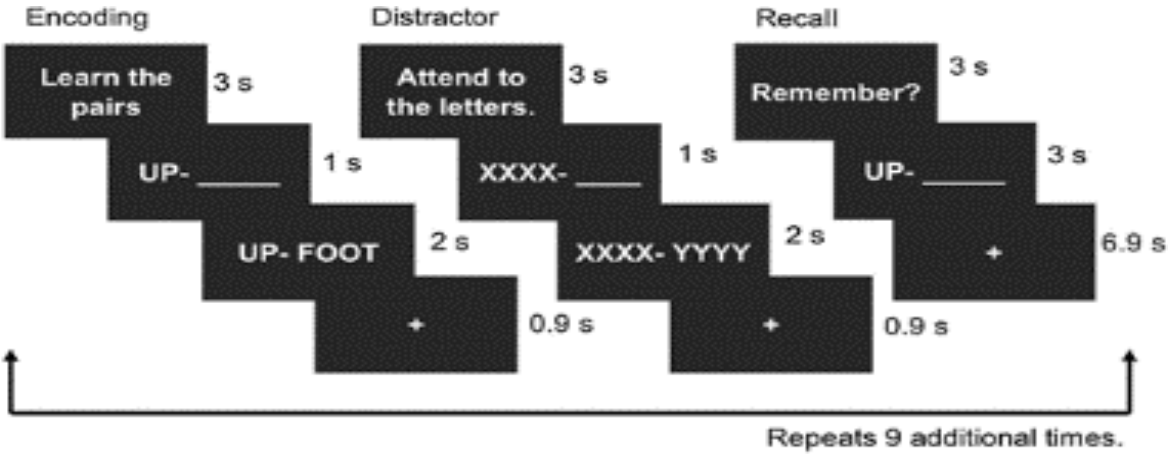
Neuroimaging Protocol**.** Functional and structural brain scans will be performed on a GE MR750 3.0-Tesla scanner during a 30-minute session. The protocol will consist of 1. Resting-state functional scan (5 minutes), 2. Functional scan during a verbal learning and memory task (12 minutes), 3. Structural/anatomical MRI scan (5 minutes) 4. Trauma recall (5-minutes).

Trauma Recall in fMRI. The 5 minutes allocated to trauma recall within the scanner will be facilitated by an "autobiographical script-driven imagery" protocol adapted for the fMRI environment (89, 90). During the protocol participants will listen to recordings of personal trauma episodes (recorded during session 1a) and will be asked to focus on the evoked mental images and feelings. Recordings and prompts to recall the trauma in primary (Spanish) or secondary (English) language will be matched to the intervention group to which the participant was randomized. During the protocol four 40-second scripts will be constructed for each subject from personal interviews, describing either aversive (e.g., sexual or childhood trauma) or neutral events. Two traumatic and two neutral conditions will be selected and played during scanning counter-balancing for valence. Participants will be instructed to focus on scripts and maintain the evoked images and states. Participants will also rate their evoked emotional states after each scan using a modified version of the Positive and Negative Affect Schedule (PANAS) (91). "Participants will be scanned at baseline and after the 4 WED sessions writing about trauma in English or Spanish or the 4 sessions of writing about daily activities (for the control group). Three salivary cortisol samples will be collected. The first sample will be collected just prior to beginning the 30-minute scan. The second and third collections being 5 minutes and 10 minutes after conclusion of the scan. Salivary ACTH will be assayed using a radioimmunoassay kit and analyzed at the DRI.

Verbal Learning & Memory in fMRI. The test for verbal learning and memory was adapted from a previous study (92). Briefly, there are three parts to this task (i.e. encoding, distractor, and recall) that repeat in the same order a total of 10 times (Fig. 1). During the encoding epochs, participants view pairs of words (e.g., UP and FOOT) and are instructed to remember that the two words went together. This occurred a total of 10 times, each epoch lasting 19.5 s. There are a total of 10 word-pairs in the paradigm. Each encoding epoch contains five of the word-pairs. All words are presented in white on a black screen. Initially, the first word of the word-pair was presented alone (1 s) and then accompanied by the second word of the word-pair (2 s). Participants pressed a button on the response pad with their right index finger when they saw the second word of the word-pair appear on screen to validate that they were attending to the stimuli. This also served to control for motor activity in other conditions. A black screen (0.9 s) followed each word-pair. The

five word-pairs in each encoding epoch are pseudo-randomly selected in a pre-determined manner such that all of the words are presented one time during epochs 1 + 2, one time during epochs 3 + 4, etc. Therefore, each of the 10 word-pairs are presented a total of five times. The word-pairs were presented in a fixed order across participants. The list will contain 6 two-syllable words and 14 one-syllable words, randomly combined into 10 pairs. Thirteen of the 20 words in the list will be nouns and 7 will be adjectives. No word in the list will have a common associate of any other word in the list, based on word association norms (Nelson, McEvoy, & Schreiber, 2004).

Each encoding block is followed by a distracter epoch (19.5 s), where participants attend to a series of letters (i.e., "XXXXX—YYYYY") to mimic the active stimulus. This is included to discourage rehearsal. Participants pressed with their right index finger when they saw the letters to control for motor activity in the other conditions. Immediately after each distracter epoch was a 19.5 s recall epoch, during which participants saw the first word of each pair from the encoding epoch that preceded it (e.g., UP - ___), attempted to recall the second word silently (3 s), and viewed a black screen (0.9 s). Subjects indicate perceived success at recalling the second word with a right index finger response and perceived failure with a left index finger response. After each recall epoch, participants focused on a crosshair (6 s) to allow for brain activity to return to its baseline. The sequence of encoding epoch, distractor epoch, and recall epoch repeated ten times. Before each new epoch began, there was a 3 s prompt to inform the participant which task they would need to perform. The full presentation of the task will last 12 m and 24 s.



The following neuropsychological tests and surveys will be administered during session 1 and 2. All forms are submitted and approved by IRB. Each assessment takes between 5 and 15 minutes to complete.

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Version: 10 Date: 06/06/2022

Table 1. Schedule of Assessments

Domain	Measure	T0 screen	T1 pre	T2 write	T3 write	T4 write	T5 write	T6 post
Cognitive	Mini-mental State Exam screener		X					
Psychiatric	Mini-International Neuropsychiatric Interview		X					
	Treatment Outcome PTSD Scale (TOP-8)		X					X
	PTSD Checklist for DSM-5 (PCL-5)		X					
	Civilian Spanish-English version PCL-C		X					
Acculturation	Brief Acculturation Scale For Hispanics (BASH)		X					
	Bidimensional Acculturation Scale (BAS)		X					
Psychosocial	Subjective Unit of Distress		X	X	X	X	X	X
	Impact of events scale—revised		X					X
	Spielberger State-Trait Anxiety Scales		X					X
	Anxiety Sensitivity Index		X					X
	Beck Depression Inventory		X					X
	Toronto Alexithymia Scale		X					X
	Multidimensional Interoceptive Awareness Scale		X					X
	Dissociative Experiences Scale		X					X
	Early Trauma Inventory		X					X
	Perceived Support Network Inventory		X					X
	Brief COPE		X					X
	*Brief Symptoms Inventory		X					X

	*Center Epi- Studies Depression Scale		X					X
	*Self/other-compassion scales		X					X
	External and Internal Shame Scale (EISS)		X					X
	*HITS Intimate Partner Violence Screening Tool		X					X
	Religion & Spirituality Questionnaire		X					X
	Profile of Mood States		X	X	X	X	X	X
Neurocognitive	Trail Making Test		X					X
	Hopkins Verbal Learning Task		X					X
	Brief Visual Memory Test		X					X
	WAIS-R Digit Symbol Substitution		X					X
	WAIS-R Digit Span		X					X
	WAIS-R Letter Number Sequencing		X					X
	WAIS-R Block Design Test		X					X
	COWAT		X					X
			X					X
	Paced Auditory Serial Addition Test		X					X
	Rey Complex Figure Test		X					X
	Verbal Fluency Task		X					X
	Color-Word Interference test		X					X
	Grooved Pegboard		X					X
	Iowa Gambling Task		X					X
Behavioral	Adult (ACTG) structured interview		X					X
	Self-compassion task		X					X
Biomarker	Saliva for CORT or ACTH & sAA via ELISA		X					X
	Serum and plasma for NFkB & FBPK5		X					X
	Serum and plasma aliquots for storage		X					X

Health Markers								
	Review of systems		X					X
	Basic Demographic Questionnaire		X					X
	Pittsburgh Sleep Quality Index		X					X
	Physical Health Questionnaire		X					X

11) **Specimen Banking***

Participants will be asked to abstain from illicit recreational substances, caffeinated and decaffeinated substances, aspirin and other medications, alcohol and strenuous exercise, and to fast from 10 pm on the night before arrival to the Behavioral Medical Research Center (BMRC) between 8 and 10 am before each visit. Participants will be advised to consult their physician before beginning the fast if the schedule varies from normal eating patterns. On the first visit, a urine toxicology screen (i.e., alcohol, barbiturates, benzodiazepines, LSD, PCP, THC, morphine, and amphetamines) will be performed. Urine samples will not be stored after analysis.

A blood draw sample in the amount of ~20 ml will be coded with a laboratory number and processed and plated within 2 hours of collection for endothelial cell assay. Once all the testing has been completed for that visit, the blood samples will be stored frozen for cytokine and neuroendocrine assays in a -80 degree freezer located on the 7th floor of the BMRC. Based on enrollment, those samples will be assayed within 45 days and the remainder saved for future research. Participants are informed that if they do not want their blood samples stored for future research samples to contact the study PI and coordinator and their samples will be destroyed at the end of end of this study. The remainder specimens will be stored up to 5 years and then destroyed. During that time, access to those specimens will only be provided by Roger McIntosh, Ph.D.

12) **Data Management***

For participants participating in the MWCCS study (E-Prost Protocol No. 20210476, see recruitment section), deidentified data will be shared with the MWCCS investigators following the MWCCS data sharing agreement as per the MWCCS approved concept sheet. There is an existing data sharing agreement with the University of Miami and other MWCCS sites.
Data Analytical Approach: Standard behavioral and neuroimaging analysis will be completed on all psychometric and survey data. Linear mixed models will be used to

analyze the effect of intervention exposure on psycho-neurocognitive-immune outcomes. The changes with functional brain activations attributed to intervention exposure will be evaluated by testing interaction effects (e.g., Group x time) using appropriate statistical thresholds, e.g., FWE-correction.

Several different types of MRI scans will be performed using standard sequence parameters. Functional scans will be performed to test our main study hypotheses. For example, functional scans may be acquired using a 64 x 64 matrix with echoplanar single shot gradient echo T2* weighting (TR=2000 msec; TE=40 msec; FOV=200mm; 64 x 64 matrix, 3.125 mm voxels) to facilitate an event-related analysis, based on stochastic methods. Resting state connectivity scans may be collected using similar parameters. Anatomical scans, a high-resolution T1-weighted volumetric scan of the whole brain, will be acquired for co-registration and morphometry. In addition, we may acquire magnetic resonance spectroscopy (MRS) to measure ratios of brain metabolite concentrations.

13) Data Storage

MRI scans obtained at the UM Cox Annex MRI facility will be de-identified and housed at the University of Miami in a secure data server for large imaging files. The Department of Psychology at the University of Miami also maintains a secure server where de-identified data can be stored under a subject ID. Access to this server is password protected and data is encrypted. Data will be uploaded to the secure server, whereby only the PI will have direct access. After uploading data to the secure server hard-copies of forms with all subject data is kept under lock and key in a secured cabinet, inside a limited access door (NIS Room 101-C) and will only be available to study personnel. All data will de-identified and stored, used and transmitted entirely separate from other participant data. Informed consent forms will be kept under lock and key in room 1520 of the CRB with card access available into the room by PI only.

Study Research Coordinator will be responsible for ensuring quality control of all data. Specimen data collected from the second blood draw at time point 2 will be processed and plated on the third floor of the NIS building. After preparing the sample for endothelial cell assay using flow cytometry, the sample will be frozen and stored on the third floor of the NIS building and then later transferred in a secured medical courier container, to the 7th floor of the BMRC. Flow cytometry will be conducted in conjunction with the Flow Cytometry Core of the Diabetes Research Institute, under the direction of Armando Mendez, Ph.D. The Research Coordinator will have received and provided proof of updated training in the responsible conduct of research.

14) Provisions to Monitor the Data to Ensure the Safety of Subjects*

Based upon the querying of traumatic events, participants will be closely monitored for suicidal ideation (SI). Upon endorsement of survey items indicative of SI or

reporting SI during interview or trauma recall the following steps will take place in conjunction with the suicide risk packet.

(1) Participant discloses suicidal ideation verbally or through administration of a study instrument.
(2) Assess the risk and severity of suicidal ideation using the HPAC Suicide Assessment (see measures).
(3) Based on the suicide assessment outcome and consultation with the postdoctoral fellow and/or supervisor, determine whether the participant is at low, moderate, severe, or extreme risk of suicide.
(4) Decide on next steps depending on risk level (in consultation with postdoctoral clinical fellow, who will then consult with primary or backup supervisor as indicated in the Suicide Risk Assessment Packet.

Participants will also be monitored for elevated levels of psychological distress throughout the course of the study. Specifically, participants will be queried regarding their distress levels before and after each session using the SUDS as well as the POMS. These measures will be scored immediately following each session. If levels of distress are elevated, we will go over ways of reducing distress via coping and stress management strategies in conjunction with the distress packet:

(1) Things I can do to help cope (e.g., exercise, playing music, relaxation exercises, hot shower, journaling, etc.).
(2) People I can contact to distract and/or support me (e.g., friend, therapist, mentor, relative, religious leader, etc.)
(3) Three positive things I can focus on right now (e.g., something good in my life, something positive that happened, ab beautiful sunset, people who care about me, an inspirational thought, a nice memory, etc.

Access to participant records will be limited to the study staff. All records are kept using a study ID number. Participant number and name will appear together only on one form. That form will be kept in a separate locked cabinet to which only the lead Study Coordinator will have access. All other forms will contain only study ID number. Participant name or other identifiable information will not appear when we present this study or publish its results. Any staff with access to identifying information will be required to sign a confidentiality pledge, which prevents them from sharing any personal information with anyone else. The signed informed/consent form will stay with PI. Only coded information will be shared with researchers and other doctors that are part of this study.

Participants will be informed that they have the right to have their data (specimen, neuroimaging, psychometric) destroyed at any time following completion of the study.

All MRIs will be reviewed by a neuroradiologist in the Division of Radiology at the Miller School of Medicine. The research team would provide de-identified images of the MRI scan and limited information (age and gender) to help the radiologist examine the images. The radiologist would generate an MRI Summary Report for

each MRI that is performed. The principal investigator would communicate any results of clinical significance to the research participant. A copy of the written report will be provided to allow the participant to communicate with his/her medical doctor. The participant may also request a copy of the scans. After obtaining written permission, a copy of scans will be given to the participant.

A plan for ensuring safety of the participant will be establishing a data monitoring committee and a plan for reporting findings to the IRB. The data monitoring committee will consist of two components. Progress and issues associated with the collection of specimens will reported to Michael Kolber M.D. Ph.D., Director of the Comprehensive AIDS Program, Clinical Director of the Adult HIV Section for Infectious Diseases and Professor of Medicine at the University of Miami Miller School of Medicine. Periodically, the PI will evaluate data collected in order to make sure participant data remains safely acquired and stored. This will include review of a daily log of all interactions with participant that will be provided by the Study Coordinator. Once per week an existing subject ID will be selected at random by the PI. The research coordinator will then need to provide a report on the location and secured state of the data collected, including but not limited to assessment forms, specimen sample & assay banks, encrypted data on server, along with any logs collected via direct or indirect communication with the participant

Adverse Event

In the event of any untoward events or conditions that endanger the participant's health, safety, and rights, suspension of the research will occur barring a full report of the event to the University of Miami IRB. In the case of an adverse event, i.e., unanticipated problem associated with the study, a report will be made indicating: 1) type related to psychological/mental or physical events; 2) severity related to the degree to which psychiatric or medical intervention is required; 3) scope of the event related to the impact it had on the participant's ability to complete all study requirements; 4) consequence of the overall event; and 5) if applicable, frequency of the problem. This report will be forward to the HRSO office within 10 days of the study team becoming aware of the adverse event. A section of our psychosocial surveys do address suicidal ideation. In order to minimize risk to the participant we have added language to the confidentiality section regarding our intention to intervene if suicidal ideation is derived from survey items. Screening data from the MINI psychiatric interview will be reviewed to determine if it meets criteria for moderate to high potential suicide risk, based upon recommended guidelines. In addition, high suicide risk may be assessed by an individual item on the Beck's Depression Inventory-2. The study PI is qualified to complete the evaluation. If the screens are positive and the participant is believed to be at risk, study team members will work with the participant contact their doctor, a trusted family member, or a therapist to discuss their thought. In more critical situations the study staff may work with the individual on a plan that might include getting them safely to a hospital environment. This data will not be reported as a part of the analysis.

15) Provisions to Protect Subjects

Dr. Gail lronson, M.D., Ph.D., will supervise and oversee of all mental health aspects of the study pertaining to treatment. Dr. Ironson has over 20 years of experience in trauma assessment and counseling. To ensure protection of the participant procedures will be adopted from the mentor's initial study on WED in trauma survivors. Participants will answer a few survey items that let us know how they are doing both before and after the writing (or trauma recall sessions). These include the POMS (Profile of Mood States, short form), a SUDS (subjective unit of distress) question, and a question about "How upset are you about the topic you wrote/spoke about today? A fluent Spanish-English bilingual trauma therapist will be designated for monitoring these responses and will do a brief check-in (about 2 minutes) with each participant, paying particular attention to those whose scores indicate distress for the safety check. Dr. Ironson has followed this protocol in trials using trauma writing and very few people (less than 5%) need extra counseling time. It should be noted that compared to 12-week cognitive behavioral therapy interventions, short expressive writing interventions such as the one proposed are shown to be non-inferior in terms of reducing post-traumatic stress (Sloan, Marx, Lee and Resick, 2018). As we have previously mentioned we will screen for such psychiatric comorbidity that would be deemed of risk to the participant's safety following traumatic recall, i.e., (a) exclusion for substance dependency as recall may exacerbate symptoms, (b) exclusion for recent or current suicidal ideation, and (c) current treatment of major depression and other neuropsychiatric conditions involving mood disturbance. To protect the participant's privacy all written samples will be de-identified. Furthermore, during the fMRI task there will be no oral or written record of the experience so as to preserve the participants right to confidentiality. The participant will be reminded that participation is voluntary, and they have the choice to participate or to withdraw from the study at any point.

Additionally, there will be a distress management plan. In the event a participant becomes distressed due to study procedures, the coordinator will ask the participant if he or she would like to withdraw from the study, and the research personnel will consult and refer the participant to the appropriate services if necessary. If necessary, participants will be referred to local service providers where they can receive treatment. Participants may feel uncomfortable about some of the questions that they are being asked about their traumatic experience, but will do so under the supervision of a trained trauma therapist. Finally, participants will be debriefed after each trauma recall exposure as it is important that those affected by traumatic events or their recall be provided practical, pragmatic psychological support and information about possible reactions and about how to help themselves access support from around them. Furthermore, participants will be contacted by the study coordinator within 24-72 hours of their writing session to ensure they are not experiencing elevated levels of distress in response to the writing probe.

We will take every precaution to ensure the participant does not experience a burdensome amount of distress associated with fMRI paradigm. Prior to the actual

scan the participants will go through a simulation in a "mock scanner" where they will be introduced to the task and the ambient sounds (MRI noise) they will be hearing during the actual scan. During the actual scan participants will have constant interaction with the researcher and MRI technician. Participants will be provided with an emergency squeeze ball that they may engage at any time to stop the procedure. Furthermore, we will continuously monitor heart rate, respiratory rate, and blood pressure so that we can ascertain whether the participant is experiencing excessive psychophysiological distress. We will take all available precautions to make the participant comfortable, e.g., allow time for acclimation, practice using a mock scanner, provision of blankets and ear protection, etc.).

We will make sure that every participant feels comfortable to let us know if they feel any discomfort, and most importantly, to let us know if they want to stop the study. Participants will be informed that the best way to minimize these events is to not clasp one's hands together and not cross one's legs during scanning. Should discomfort arise, participants may stop the scan at any time and for any reason. We will stop the study as soon as a participant communicates to us that he/she wants to stop the study. Subjects will be monitored throughout the entire experiment. They are reminded that the experimenters can see and hear them at all times to address any problems that they are having. We also interview each subject who completes our MRI studies following the study. Subjects will be reminded before the experiment that their participation is completely voluntary and they may stop the experiment at any time and for any reason without penalty. If, in the opinion of the study staff, PI, subject, or participant's family, the procedures or study participation will be discontinued if they are adversely affecting the subject's emotional well-being. This may happen even if the participant does not request stopping. At this point, subjects will be interviewed and staff will determine what additional steps should be taken.

With regards to incidental findings resulting from the fMRI scan, the imaging facility is a research facility, not a medical facility. The MRI scans obtained at the imaging facility are research scans, to be used for scientific purposes. The scientists who review the scans are not physicians and they have no competence in evaluating the scans for medical or therapeutic purposes. These scans are not meant to provide clinical information although all research scans will be read by a radiologist. If any results of clinical significance are found, we will communicate this information to the participant. This consultation will not result in an additional charge to the subject in question. Based on the radiologist's assessment, we may recommend that participants seek advice from your primary physician or a specialist. The University of Miami will not be responsible for any costs relating to standard medical care. Participants will be responsible for such costs, in such an event.

With regards to the sensitive nature of the surveys participants may choose not to answer any question that they do not want to answer. Subjects may become frustrated when performing tasks. During the consent

process, subjects will be told that they should do their best. It should be noted that compared to 12-week cognitive behavioral therapy interventions, short expressive writing interventions such as the one proposed are shown to be non-inferior in terms of reducing post-traumatic stress (Sloan, Marx, Lee and Resick, 2018). As we have previously mentioned we will screen for such psychiatric comorbidity that would be deemed of risk to the participant's safety following traumatic recall, i.e., (a) exclusion for substance dependency as recall may exacerbate symptoms, (b) exclusion for recent or current suicidal ideation, and (c) current treatment of major depression and other neuropsychiatric conditions involving mood disturbance.
Participants name and other personal identifiable information will not be released to other parties not mentioned in the Informed Consent, i.e. study personnel, unless written specific permission is given by the study participant themselves. Response to survey items will be stored in REDCap, i.e., secure web application for building and managing online surveys and databases.

16) Withdrawal of Subjects*

An anticipated circumstance under which subjects will be withdrawn from the research without their consent, is in the event that non-removable metal objects were not initially reported but detected upon arrival at the MRI facility. At that time, participants will be reminded of the dangers of conducting MRI with metal and their participation in the study will be immediately terminated. The participant may withdraw from the study at any time. Upon withdrawal the participant will be compensated for their participation up to that time point.

Subject initiated withdrawal from the study may occur at any time during participation in the study. Participants may also refuse to answer survey questions or take part in particular assessments and still be compensated for their time. Participants will be in weekly contact with project staff so that if any issues associated with the intervention warranting withdrawal were to arise, they could be dealt with immediately. Also, upon early withdrawal from the study, participants will have the option of having their data immediately destroyed without affecting compensation for their time.

17) Risks to Subjects*

The research does pose greater than minimal risk to subjects due to recall of severe trauma. Participants may feel uncomfortable about some of the questions that they are being asked. They may choose not to answer any question that they do not want to answer. Subjects may become frustrated when performing tasks. During the consent process, subjects will be told that they should do their best. The procedures may be long and boring. These procedures will be completed with interspersed breaks to reduce any fatigue or discomfort.

As a part of the phlebotomy protocol participant's heart rate and blood pressure will be taken prior to blood draw. If elevated blood pressure indicative of Stage 2 hypertension (160/100), any heart rhythm problems or evidence of underlying heart disease are found, we will inform the subject promptly, stop the test and refer the participant to see a cardiologist.

Bruising, bleeding, and rarely infection could occur at the site where the needle enters the vein. To reduce these risks, blood samples are taken in a sterile manner and lines will be routinely checked during the experiment by an experienced phlebotomist and registered nurse. Uncommonly, fainting might occur.

It is not uncommon that participants with a chronic illness such as HIV infection may tire easily during the neurocognitive battery or imaging scans. We have scheduled intermittent breaks throughout both days of the study where the participant will be provided access to food and refreshments. There is a minimum amount of walking (approximately 10 minutes) from the university shuttle service to the NIS building. Upon arrival on the Coral Gables campus each participant will be accompanied by a research assistant. There will not be any special provisions made for individuals with physical limitations a shuttle can be arranged from the CRB to Civic Center metro-rail station and from the University metro-rail station directly to the NIS (Cox Annex) building.

The subject's skin may become irritated during cleaning of the skin prior to attachment of electrodes for heart rate and skin conductance. The cleaning procedures involve using an exfoliant and alcohol wipes used routinely. Subjects will be monitored throughout the experiment for any signs of irritation. Electrodes and gels will be removed if any irritation occurs.

Subjects will be reminded before the experiment that their participation is completely voluntary and they may stop the experiment at any time and for any reason without penalty.

MRI Risks: Functional brain uses MRI to observe activity-related, hemodynamic changes with high spatial and temporal resolution. The most promising method, as is used in the current protocol, examines changes in blood oxygenation. Because of the different magnetic properties of oxy- and deoxyhemoglobin, increased levels of blood oxygenation are associated with increased signal for some MR imaging methods, including T2*-weighted gradient echo imaging and echo-planar imaging. Increased neural activity is associated with this increased signal, presumably because local, activity-related increases in blood flow are greater than increases in oxygen extraction, resulting in higher ratios of oxy- to deoxyhemoglobin. Because the change in signal is due to properties inherent in normal blood constituents, injection of contrast agents or tracers and sampling of plasma are unnecessary. MRIs will not use contrast. MRI is widely regarded as a safe, noninvasive procedure for visualization of brain tissue in both adults and children. The risks involved with MRI or DTI are the same as those involved in standard anatomic MRI, since these procedures rely on

the same physical properties of brain tissue. There are no known long-term risks of MRI scans.

As noted above, this study will be performed on an FDA approved 3T scanner. FDA standards for minimal risk MRI require that four criteria be met: 1) a static magnetic field no greater than 4T; 2) specific absorption rates a) no greater than 4W/kg for the entire body for 15 minutes, b) no greater than 3W/kg over the head for 10 minutes, and c) no greater than 8W/kg in any gram of tissue in the head or torso or 12W/kg in any gram of tissue in the extremities for five minutes; 3) a time rate of change in the field that does not produce physical discomfort or painful nerve stimulation; and 4) a peak sound pressure level that does not exceed 140 dB or A-weighted R.M.S. pressure level that does not exceed 99dBA with hearing protection. Each of these guidelines will be monitored throughout the study to insure that none are exceeded.

MRI at 3 Tesla is used on occasion for clinical scanning but is widely used for research. This includes studies with children. The gradients for the GE 3 T scanner are higher performance, in terms of gradient strength and slew rate, with a maximum gradient strength of 4 G/cm. No studies have documented any detrimental effects of gradient magnitude. The maximum slew rate, the maximum rate at which the gradients change in magnitude, of the gradients on the 3T scanner is 150 mT/m/sec. A higher maximum slew rate allows for faster imaging which is generally better because the shorter time to collect an image causes images to be less contaminated by susceptibility or motion artifacts. It is well known that if the gradients are switched too rapidly, peripheral nerve stimulation can take place. The 3T scanner has standard safeguards such as a maximal allowable slew rate that is 66% of the FDA limit. Lastly, because of the higher radio frequencies associated with the 3T scanner, larger amounts of energy are deposited into the tissue during scanning at 3T than at lower field strengths. Tissue heating becomes a concern for certain pulse sequences at higher field strength. Again, the operating system for the scanner has built-in safeguards that only allow scanning with specific absorption rates (SAR) of radio frequency that are well below guidelines established by the Bureau of Radiological Health, FDA. The operating system limits radio frequency deposition in the head to an average rate of 10 watts, < 4 w/kg, which has been shown to raise the average core temperature approximately 0.3 deg. C.92 These temperature changes are within the normal diurnal rhythms (±1oC) found in human core temperatures or a change associated with a brisk 20-minute walk (+1oC).

During a scan the subject hears a loud rhythmic tapping or banging sound. This noise is caused by the switching of the gradient coils that is necessary to produce the image. Subjects are warned of this prior to scanning, and most do not find it to be objectionable. Protective earphones or earplugs are provided.

Some people may experience physical discomfort during scanning, including brief periods of muscle twitching, eye discomfort, dizziness, mild nausea, headache, or a sensation of flashing lights. We will make sure that every participant feels comfortable to let us know if they feel any discomfort, and most importantly, to let

us know if they want to stop the study. Participants will be informed that the best way to minimize these events is to not clasp one's hands together and not cross one's legs during scanning. Should discomfort arise, participants may stop the scan at any time and for any reason. We will stop the study as soon as a participant communicates to us that he/she wants to stop the study.

Subjects will be monitored throughout the entire experiment. They are reminded that the experimenters can see and hear them at all times to address any problems that they are having.

We also interview each subject who completes our MRI studies following the study. Subjects will be reminded before the experiment that their participation is completely voluntary and they may stop the experiment at any time and for any reason without penalty.

If, in the opinion of the study staff, PI, subject, or his/her family, the procedures or study participation will be discontinued if they are adversely affecting the subject's emotional well-being. This may happen even if the participant does not request stopping. At this point, subjects will be interviewed, and staff will determine what additional steps should be taken.

The imaging facility is a research facility, not a medical facility. The MRI scans obtained at the imaging facility are research scans, to be used for scientific purposes. The scientists who review the scans are not physicians and they have no competence in evaluating the scans for medical or therapeutic purposes. These scans are not meant to provide clinical information. All research scans may be read by a radiologist. If any results of clinical significance are found, we will communicate this information to the participant. This consultation will not result in an additional charge to the subject in question. Based on the radiologist's assessment, we may recommend that participants seek advice from your primary physician or a specialist. The University of Miami will not be responsible for any costs relating to standard medical care. Participants will be responsible for such costs, in such an event.

Receiving medical information may cause some individuals distress.

18) Potential Benefits to Subjects*

One potential benefit of this study is the development of tailored interventions for Latino subgroups who represent pockets of vulnerability, e.g., HIV/AIDS and trauma, and require precise and specialized interventions that optimize access to and impact of interventions. Another potential benefits of the project to the participant is that the participant may acquire and practice expressive writing techniques and that this will facilitate management of post-traumatic stress symptomology. It is unknown whether this intervention will also facilitate improvements in cognitive function, reductions in inflammation and stress hormone reactivity. The minimal risks of the proposed research to participants, and the potential benefit, both directly to

participants and indirectly to the field, the benefits of the research appear to outweigh the risks.

19) Vulnerable Populations*

The research does not include vulnerable populations.

20) Sharing of Results with Subjects*

The imaging facility is a research facility, not a medical facility. The MRI scans obtained at the imaging facility are research scans, to be used for scientific purposes. The scientists w ho review the scans are not physicians and they have no competence in evaluating the scans for medical or therapeutic purposes. These scans are not meant to provide clinical or diagnostic information. Moreover, the facility has no medical staff to provide clinical information or advice.

Upon request, a disc copy of the anatomical scan may be provided to the participant. The psychometric and cardio-autonomic data is recorded for research purposes. There will not be any trained medical professionals available or able to diagnose this data as it was not recorded for clinical purposes, however copies of assessments may he provided upon request.

21) Setting

The study will either take place at the BMRC on the 7th floor of the Don Soffer Clinical Research Building located at 1120 N.W. 14th Street, Miami, FL 33136 or at the University of Miami (main campus) Neuroscience Building (Cox Annex) located at 5151 San Amaro Drive, Coral Gables, FL 33146. HIV positive participants will be recruited, by flyer, from UM outpatient clinics in conjunction with the Community & Outreach ore of the Center for AIDS research.

22) Resources Available

Personnel.

Roger McIntosh, Ph.D., an Assistant Professor in the Department of Psychology, is Principal Investigator of the study and has over 10 years of experience conducting neuropsychological and psychophysiological research in persons living with HIV.

Gail Ironson, M.D., Ph.D. is a Co-investigator. Dr. Ironson has over 25 years of research on uncovering psychological and biological factors that protect the health of people with HIV. She has conducted several randomized clinical trials for both trauma treatment and stress management interventions, as well as a longitudinal study examining psychological factors in coping with HIV. Dr. Ironson is primary founder

of the trauma treatment program at UM and has 20 years of expertise in assessment of and treatments for trauma.

Dr. Jennifer Britton, an Associate Professor in the Department of Psychology, has a Ph.D. in Neuroscience. She has been conducting clinical research for 12+ years with a particular emphasis on anxiety disorders in both adults and children. Dr. Britton will oversee research of this protocol.

Available Resources

The Miami Center for AIDS Research (CFAR) Behavioral/ Social Science & Community Outreach Core (Core E) provides CFAR investigators with consultation and resources to expand behavioral clinical studies. The underlying goals are to enhance recruitment and retention of community and clinic-based study participants with attention to "hard to reach populations." Core E offers CFAR investigators the services of an Outreach Coordinator who can oversee the study recruitment and assessment activities of research projects. The Outreach Coordinator can also determine the best recruitment strategy, conduct participant outreach, recruitment, assessment and site coordination.

Facilities.

The Behavioral Medicine Research Center (BMRC), directed by Neil Schneiderman, Ph.D., is located in the Clinical Research Building (CRB) on the University of Miami Miller School of Medicine campus. The BMRC is a multidisciplinary unit of faculty and staff who have worked together for 10-15 years, collaborating on NIH- and privately-funded research. The CRB building has 24-hour security with service/reception area that is staffed to greet and direct participants within the strict guidelines of privacy prescribed for clinical research protocols. Adequate parking is available on site and the building is within close proximity of public transportation (Metrorail, buses and taxis). The BMRC is contained on two floors and divided by function, with the Administrative unit on the 15th floor and the Clinical unit on the 7th floor. Located in the Clinical unit are the: 1) Behavioral Medicine and Echocardiography Laboratory; 2) Biochemical Assessment Laboratory; and 3) Hispanic Community Health Study/Study of Latinos field center. Of note, adjacent to the BMRC on the 7th floor in the CRB, is the university's Clinical Research Center (CRC) of the Clinical and Translational Science Institute.

The Bioassay Clinical Laboratory has 2 locations that have been efficiently integrated to provide bioassay services for BMRC, Diabetes Research Institute (DRI) and other investigators. Some processing of biological samples occurs at the BMRC Biochemical Assessment Laboratory that occupies 600 sq ft on the 7th floor of the CRB. This lab is on the same floor as the Behavioral Medicine and Clinical Physiology Laboratory, where patient samples are collected during the screening session. Some manual ELISA and radioimmunoassay tests are performed in this location. Other sample analysis is performed at the DRI Clinical Research

Laboratory, a CLIA and Florida State licensed facility, located on the 3rd floor of the DRI building and one block from the BMRC. Chemistry assays in this lab are performed in a room (280 sq ft), containing the automated chemistry equipment. ELISA and radioimmunoassays are performed in the adjacent laboratory (600 sq ft). A custom Laboratory Information System (LIMS) is used for sample log-in, work-flow tracking and generation of reports in both hard and electronic formats. The software is connected directly to the automated analyzers for data collection. The data may be electronically exported to the Data Management and Biostatistics laboratory using previously established protocols.

The DRI laboratory has a Roche-Cobas 6000 analyzer that incorporates automated chemistry and immunoassay capabilities. In addition, hemoglobin A1c testing is performed on the BioRad Variant analyzer. These instruments are directly connected to the laboratory LIMS system for bidirectional communication of sample test requests and data reporting. Both bioassay laboratories have all the pertinent equipment needed for performing ELISA based assays including 2 microplate spectrophotometers, a microplate fluorometer and microplate luminometer, and 3 automated microplate washers. For radioimmunoassays, the DRI has a shared gamma and beta scintillation counter, adjacent to the main DRI labs. In addition, there are 5 dedicated, refrigerated centrifuges used for sample processing, 4 ultrafreezers (-80°C) at the DRI lab and 4 ultrafreezers at the BMRC lab, housed directly adjacent to the labs and available for sample storage. The imaging lab is equipped with a Zeiss LSM510 inverted microscope, immunofluorescence and live cell imaging; a station for fluorescence microscopy (Widefield/Apotome); a Leica SP5 motorized stage confocal inverted microscope, a Leica MP/SP5/FLIM/FCS fixed stage multiphoton/confocal upright microscope enabling live imaging deep into tissue and organs; a BD Pathway High Throughput Imaging system; a CompuCyte iCys Laser Scanning Cytometry; a Leica Laser Capture Microdissection station; a conventional Leica inverted microscope with digital camera; dedicated analysis software such as the MetaMorph Imaging System is available to core users. Confocal imaging needs of the current project will rely mostly on the LSM-510 instrument that has 8 laser lines and four fluorescence photomultiplier tubes (PMTs) for detecting UV, visible and near-infrared emission, one transmitted light PMT, and can detect up to eight channels. Up to four fluorescent channels can be acquired simultaneously.

Cox neuroscience Annex is a The 1200 square foot MRI facility is housed on the first floor of the three-floor, 37,700 square foot Neuroscience building adjacent to the Cox Science Building on the University of Miami Coral Gables Campus. The facility encompasses a MR scanner suite with associated reception and waiting areas, dressing rooms and a MR simulator/mock scanner suite. The Neuroimaging Suite has a state-of-the-art GE®MR750 3.0T MR scanner and 32-channel head coil capable of performing structural and functional scans in human subjects. The MR suite is equipped to deliver visual, auditory, and tactile stimuli. In addition, behavioral and physiological responses and eye movements can be recorded. The remaining 11,000 square feet on the first floor of the building includes shared space including a large

conference/multipurpose room, kitchen, restrooms, behavioral testing rooms, a central server room, a phlebotomy room, and an assay lab. Equipment includes: Psychology Software Tools, Inc. Hyperion MRI Digital Projection System, PST-100984; Current Designs 932 fORP Response Devices (4-button diamond, 4-button inline, 5-button Pyka, Trackball2); Biopac Physiological Recording (Heart rate, respiration, skin conductance response, electrocardiography, electromyography, blood pressure); Avotec, Inc. Silent Scan SS-3300 Hearing Protection, Communication and Music System; Resonance Technology Eye-tracking (used with 8-ch head coil); Midwest Composite Technologies MRI System Simulator; Psychology Software Tools, Inc. Motrak Head Motion Tracking System, PST-100722; and Video camera monitoring.

All research staff will have to participate in a regularly scheduled MRI safety training session. This session will ensure that all research staff are aware of the potential dangers of MRI testing and assure the safety of the participant at all times.

23) Prior Approvals

Upon approval by UM IRB, the project will be submitted for review by an independent committee at the Cox Neuroimaging Facility. This committee will determine whether the protocol may need to be further modified in order to ensure patient safety.

24) Local Number of Subjects

The total number of subjects to be accrued locally will be 36.

25) Confidentiality

After samples are collected all biological specimens are coded and stored frozen. Samples will be assayed on the 3rd floor of the Cox Neuroscience Annex or at the Diabetes Research Institute. Once all the testing has been completed and the study is over, remaining blood and salivary samples will be stored frozen on the 7th floor BMRC located at the Clinical Research Building for future research to better understand HIV infection.

Subjects are asked by written consent to indicate in writing if they give permission to store any remaining samples for later use in approved studies.

Access to participant records will be limited to the study staff. All records are kept using a study ID number. Participant number and name will appear together only on one form. That form will be kept in a separate locked cabinet to which only the lead Study Coordinator will have access. All other forms will contain only study ID number.

Participant name or other identifiable information will not appear when we present this study or publish its results. Any staff with access to identifying information will be required to sign a confidentiality pledge, which prevents them from sharing any personal information with anyone else. The signed informed/consent form will stay with the local physician contractor/investigators. Only coded information will be shared with researchers and other doctors that are part of this study. Specimen samples will be stored on ice at -80 degrees for up to 5 years.

Choose the statements below that are applicable to this research:

25(a). ☐ Data will be collected from the EMR or subjects at UHealth or JHS. *If checked, answer the following:*

☐ Research Subjects will sign a HIPAA Authorization before the research will collect this data.

☐ Research Subjects will not sign a HIPAA Authorization for this data collection and the research is requesting a waiver of HIPAA authorization from the IRB. (Complete Section 17 below)

25(b). Data collected:

☒ Will not include Protected Health information or Personally Identifiable Information

☐ Will include Protected Health information or Personally Identifiable Information

25(c). How will the research store the data?

☒ On a University of Miami electronic device (e.g. encrypted, password-protected computer)
☐ On a cloud-based storage system that is approved by the University of Miami
☐ Other, specify: Click here to enter text.

Biospecimens

☐ Not applicable. No biospecimens will be collected

☐ *Bio*-Specimens obtained for this research will be stored without any direct or indirect identifiers.

☒ *Bio*-Specimens obtained for this research will be stored in a de-identified coded manner.

☐ When required to transport data or bio-specimens for this research, the research team will transport the data and bio-specimens in a de-identified (or anonymous) manner with a link to the individual subject's identity maintain separately from the data and/or bio-specimen.

26) Waiver of Authorization for Use and Disclosure of Protected Health Information (HIPAA)

☒ This section is not applicable, we are not requesting a waiver of authorization.

If the research team will access patient medical records or other identifiable health information for this research without or prior to obtaining a signed HIPAA authorization from the subject or the subject's legally authorized representative (LAR), you must obtain a waiver of the requirement for written authorization from the patients to access their medical records.

Confirm that you will destroy the Protected Health Information (PHI) you and/or your Study Team acquire receive from JHS and/or UHealth at the earliest opportunity.

☐ ***I confirm***

Confirm that the Protected Health Inform (PHI) you acquire from JHS and/or UHealth will not be re-used or disclosed to any other person or entity, except as required by law or for authorized oversight of the research study or for other research for which the use or disclosure of PHI is permissible.

☐ ***I confirm***

27) Compensation for Research-Related Injury

There will not be any formal compensation provided for research-related injury. The language pertaining to this within the informed consent is provided here: "Although injury is unlikely, if injury should occur, treatment will in most cases be available. If you have insurance, your insurance company may or may not pay for these costs. If you do not have insurance, or if your insurance company refuses to pay, you will be expected to pay. Funds to compensate for pain, expenses, lost wages and other damages caused by injury are not routinely available."

28) Economic Burden to Subjects

Upon arrival at the University of Miami Downton and Coral Gables locations there will be no additional costs for which the participants will be responsible. In addition, participants will be offered water and light snacks throughout the two sessions.

29) Consent Process

This study will follow the UM standard operating procedure for the Informed Consent Process for Research (HRP-090). The consent process will take place on the 7th floor of the BMRC located at the Clinical Research Building in downtown Miami. The research coordinator will describe the study to the participants and will go over the consent forms to make sure there are no additional questions that were not answered. Participants will be asked to sign one copy of the consent form and be provided with a signed copy. This consent form will cover participation at during both sessions 1 and 2. Approximately 20 – 30 minutes will be devoted towards going over the consent and an unlimited time will be provided for questions and answers prior to signing the consent. Participants will also be informed that they are able to refer to primary care physicians and/or loved ones before providing consent to participate in the study. In addition, study referrals will be verbally consented in order to complete the pre-screening process using

Cognitively Impaired Adults

Prior to participation in session 1 of the study, at the pre-screening, our group will administer the Montreal Cognitive Assessment or Mini-Mental State Exam. Individuals scoring at levels indicative of gross cognitive dysfunction or dementia will be excluded from the study. Each assessment takes approximately 5 minutes to administer.

30) Process to Document Consent in Writing

Standard operating procedures will be followed in order to attain written documentation of consent in conjunction with (HRP-091).

31) Drugs or Devices

None

References

1. Kessler RC, Petukhova M, Sampson NA, Zaslavsky AM, Wittchen HU. Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood disorders in the United States. International journal of methods in psychiatric research. 2012;21(3):169-84.
2. Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB. Posttraumatic stress disorder in the National Comorbidity Survey. Archives of general psychiatry. 1995;52(12):1048-60.
3. Breslau N, Kessler RC, Chilcoat HD, Schultz LR, Davis GC, Andreski P. Trauma and posttraumatic stress disorder in the community: the 1996 Detroit Area Survey of Trauma. Archives of general psychiatry. 1998;55(7):626-32.
4. Machtinger E, Wilson T, Haberer JE, Weiss D. Psychological trauma and PTSD in HIV-positive women: a meta-analysis. AIDS and Behavior. 2012;16(8):2091-100.
5. Wegner DM. Ironic processes of mental control. Psychological review. 1994;101(1):34.
6. Teasdale JD, Proctor L, Lloyd CA, Baddeley AD. Working memory and stimulus-independent thought: Effects of memory load and presentation rate. European Journal of Cognitive Psychology. 1993;5(4):417-33.

7. Vance DE, Rubin LH, Valcour V, Waldrop-Valverde D, Maki PM. Aging and neurocognitive functioning in HIV-infected women: a review of the literature involving the Women's Interagency HIV Study. Current HIV/AIDS Reports. 2016;13(6):399-411.
8. Maki PM, Rubin LH, Valcour V, Martin E, Crystal H, Young M, et al. Cognitive function in women with HIV Findings from the Women's Interagency HIV Study. Neurology. 2015;84(3):231-40.
9. Dufour CA, Marquine MJ, Fazeli PL, Umlauf A, Henry BL, Zlatar Z, et al. A longitudinal analysis of the impact of physical activity on neurocognitive functioning among hiv-infected adults. AIDS and Behavior. 2018;22(5):1562-72.
10. Heaton RK, Franklin DR, Ellis RJ, McCutchan JA, Letendre SL, LeBlanc S, et al. HIV-associated neurocognitive disorders before and during the era of combination antiretroviral therapy: differences in rates, nature, and predictors. Journal of neurovirology. 2011;17(1):3-16.
11. Mindt MR, Miranda C, Arentoft A, Byrd D, Monzones J, Fuentes A, et al. Aging and HIV/AIDS: neurocognitive implications for older HIV-positive Latina/o adults. Behavioral Medicine. 2014;40(3):116-23.
12. Durvasula RS, Miller EN, Myers HF, Wyatt GE. Predictors of neuropsychological performance in HIV positive women. Journal of Clinical and Experimental Neuropsychology. 2001;23(2):149-63.
13. Friedman MJ, Resick PA, Bryant RA, Brewin CR. Considering PTSD for DSM-5. Depression and anxiety. 2011;28(9):750-69.
14. González-Guarda RM, Florom-Smith AL, Thomas T. A syndemic model of substance abuse, intimate partner violence, HIV infection, and mental health among Hispanics. Public Health Nursing. 2011;28(4):366-78.
15. González-Guarda RM, McCabe BE, Florom-Smith A, Cianelli R, Peragallo N. Substance abuse, violence, HIV, and depression: An underlying syndemic factor among Latinas. Nursing research. 2011;60(3):182.
16. Willie TC, Overstreet NM, Sullivan TP, Sikkema KJ, Hansen NB. Barriers to HIV medication adherence: examining distinct anxiety and depression symptoms among women living with HIV who experienced childhood sexual abuse. Behavioral Medicine. 2016;42(2):120-7.
17. Spies G, Seedat S. Depression and resilience in women with HIV and early life stress: does trauma play a mediating role? A cross-sectional study. BMJ open. 2014;4(2):e004200.
18. Rubin LH, Pyra M, Cook JA, Weber KM, Cohen MH, Martin E, et al. Post-traumatic stress is associated with verbal learning, memory, and psychomotor speed in HIV-infected and HIV-uninfected women. Journal of neurovirology. 2016;22(2):159-69.
19. Rubin LH, Cook JA, Springer G, Weber KM, Cohen MH, Martin EM, et al. Perceived and posttraumatic stress is associated with decreased learning, memory, and fluency in HIV-infected women. Aids. 2017;31(17):2393-401.
20. Rubin LH, Cook JA, Weber KM, Cohen MH, Martin E, Valcour V, et al. The association of perceived stress and verbal memory is greater in HIV-infected versus HIV-uninfected women. Journal of neurovirology. 2015;21(4):422-32.
21. Rubin LH, Wu M, Sundermann EE, Meyer VJ, Smith R, Weber KM, et al. Elevated stress is associated with prefrontal cortex dysfunction during a verbal memory task in women with HIV. Journal of neurovirology. 2016;22(6):840-51.

22. Heim C, Newport DJ, Wagner D, Wilcox MM, Miller AH, Nemeroff CB. The role of early adverse experience and adulthood stress in the prediction of neuroendocrine stress reactivity in women: a multiple regression analysis. Depression and anxiety. 2002;15(3):117-25.
23. Ganzel BL, Eckenrode JJ, Kim P, Wethington E, Horowitz E, Temple E. Salivary cortisol levels and mood vary by lifetime trauma exposure in a sample of healthy women. Journal of traumatic stress. 2007;20(5):689-99.
24. Griffin MG, Resick PA, Yehuda R. Enhanced cortisol suppression following dexamethasone administration in domestic violence survivors. American Journal of Psychiatry. 2005;162(6):1192-9.
25. Altemus M, Cloitre M, Dhabhar FS. Enhanced cellular immune response in women with PTSD related to childhood abuse. American Journal of Psychiatry. 2003;160(9):1705-7.
26. Merz CJ, Wolf OT. Sex differences in stress effects on emotional learning. Journal of neuroscience research. 2017;95(1-2):93-105.
27. Rubin LH, Phan KL, Keating SM, Maki PM. A single low dose of hydrocortisone enhances cognitive functioning in HIV-infected women. AIDS. 2018;32(14):1983-93.
28. Stock L-M, Merz CJ. Memory retrieval of everyday information under stress. Neurobiology of learning and memory. 2018;152:32-8.
29. Drevets WC, Price JL, Bardgett ME, Reich T, Todd RD, Raichle ME. Glucose metabolism in the amygdala in depression: relationship to diagnostic subtype and plasma cortisol levels. Pharmacology Biochemistry and Behavior. 2002;71(3):431-47.
30. Bonne O, Gilboa A, Louzoun Y, Brandes D, Yona I, Lester H, et al. Resting regional cerebral perfusion in recent posttraumatic stress disorder. Biological psychiatry. 2003;54(10):1077-86.
31. Urry HL, Van Reekum CM, Johnstone T, Kalin NH, Thurow ME, Schaefer HS, et al. Amygdala and ventromedial prefrontal cortex are inversely coupled during regulation of negative affect and predict the diurnal pattern of cortisol secretion among older adults. Journal of Neuroscience. 2006;26(16):4415-25.
32. King AP, Abelson JL, Britton JC, Phan KL, Taylor SF, Liberzon I. Medial prefrontal cortex and right insula activity predict plasma ACTH response to trauma recall. Neuroimage. 2009;47(3):872-80.
33. Holz NE, Buchmann AF, Boecker R, Blomeyer D, Baumeister S, Wolf I, et al. Role of FKBP5 in emotion processing: results on amygdala activity, connectivity and volume. Brain Structure and Function. 2015;220(3):1355-68.
34. Touma C, Gassen NC, Herrmann L, Cheung-Flynn J, Büll DR, Ionescu IA, et al. FK506 binding protein 5 shapes stress responsiveness: modulation of neuroendocrine reactivity and coping behavior. Biological psychiatry. 2011;70(10):928-36.
35. Skelton K, Ressler KJ, Norrholm SD, Jovanovic T, Bradley-Davino B. PTSD and gene variants: new pathways and new thinking. Neuropharmacology. 2012;62(2):628-37.
36. Binder EB, Bradley RG, Liu W, Epstein MP, Deveau TC, Mercer KB, et al. Association of FKBP5 polymorphisms and childhood abuse with risk of posttraumatic stress disorder symptoms in adults. Jama. 2008;299(11):1291-305.
37. McIntosh RC, Rosselli M, Uddin LQ, Antoni M. Neuropathological sequelae of human immunodeficiency virus and apathy: a review of neuropsychological and neuroimaging studies. Neuroscience & Biobehavioral Reviews. 2015;55:147-64.

38. McIntosh RC, Rosselli, M., Uddin, L., Antoni, M. Apathy and the Neuropathological Sequelae of Human Immunodeficiency Virus: A Review of Neuropsychological and Neuroimaging Studies. Journal for Neuroscience and Biobehavioral Reviews. 2015;In press.
39. Yeung MC, Pulliam L, Lau AS. The HIV envelope protein gp120 is toxic to human brain-cell cultures through the induction of interleukin-6 and tumor necrosis factor-[alpha]. Aids. 1995;9(2):137&hyhen.
40. Poli G, Bressler P, Kinter A, Duh E, Timmer WC, Rabson A, et al. Interleukin 6 induces human immunodeficiency virus expression in infected monocytic cells alone and in synergy with tumor necrosis factor alpha by transcriptional and post-transcriptional mechanisms. The Journal of experimental medicine. 1990;172(1):151-8.
41. Fiala M, Looney DJ, Stins M, Way DD, Zhang L, Gan X, et al. TNF-alpha opens a paracellular route for HIV-1 invasion across the blood-brain barrier. Molecular Medicine. 1997;3(8):553.
42. Norris PJ, Pappalardo BL, Custer B, Spotts G, Hecht FM, Busch MP. Elevations in IL-10, TNF-α, and IFN-γ from the earliest point of HIV type 1 infection. AIDS Research & Human Retroviruses. 2006;22(8):757-62.
43. Petrillo MG, Bortner CD, Cidlowski JA. Glucocorticoids: Inflammation and Immunity. The Hypothalamic-Pituitary-Adrenal Axis in Health and Disease: Springer; 2017. p. 43-63.
44. Kim Y-K, Na K-S, Myint A-M, Leonard BE. The role of pro-inflammatory cytokines in neuroinflammation, neurogenesis and the neuroendocrine system in major depression. Progress in Neuro-Psychopharmacology and Biological Psychiatry. 2016;64:277-84.
45. Bauer ME, Wieck A, Lopes RP, Teixeira AL, Grassi-Oliveira R. Interplay between neuroimmunoendocrine systems during post-traumatic stress disorder: a minireview. Neuroimmunomodulation. 2010;17(3):192-5.
46. Rohleder N, Joksimovic L, Wolf JM, Kirschbaum C. Hypocortisolism and increased glucocorticoid sensitivity of pro-Inflammatory cytokine production in Bosnian war refugees with posttraumatic stress disorder. Biological psychiatry. 2004;55(7):745-51.
47. Pace TW, Hu F, Miller AH. Cytokine-effects on glucocorticoid receptor function: relevance to glucocorticoid resistance and the pathophysiology and treatment of major depression. Brain, behavior, and immunity. 2007;21(1):9-19.
48. Baschant U, Tuckermann J. The role of the glucocorticoid receptor in inflammation and immunity. The Journal of steroid biochemistry and molecular biology. 2010;120(2-3):69-75.
49. Liberman AC, Druker J, Perone MJ, Arzt E. Glucocorticoids in the regulation of transcription factors that control cytokine synthesis. Cytokine & growth factor reviews. 2007;18(1-2):45-56.
50. Elenkov IJ. Glucocorticoids and the Th1/Th2 balance. Annals of the New York Academy of Sciences. 2004;1024(1):138-46.
51. Maes M, Lin A-h, Delmeire L, Van Gastel A, Kenis G, De Jongh R, et al. Elevated serum interleukin-6 (IL-6) and IL-6 receptor concentrations in posttraumatic stress disorder following accidental man-made traumatic events. Biological psychiatry. 1999;45(7):833-9.

52. Spivak B, Shohat B, Mester R, Avraham S, Gil-Ad I, Bleich A, et al. Elevated levels of serum interleukin-1β in combat-related posttraumatic stress disorder. Biological psychiatry. 1997;42(5):345-8.
53. Smith AK, Conneely KN, Kilaru V, Mercer KB, Weiss TE, Bradley B, et al. Differential immune system DNA methylation and cytokine regulation in post-traumatic stress disorder. American Journal of Medical Genetics Part B: Neuropsychiatric Genetics. 2011;156(6):700-8.
54. von Känel R, Hepp U, Kraemer B, Traber R, Keel M, Mica L, et al. Evidence for low-grade systemic proinflammatory activity in patients with posttraumatic stress disorder. Journal of psychiatric research. 2007;41(9):744-52.
55. Meewisse M-L, Reitsma JB, De Vries G-J, Gersons BP, Olff M. Cortisol and post-traumatic stress disorder in adults: systematic review and meta-analysis. The British Journal of Psychiatry. 2007;191(5):387-92.
56. Gola H, Engler H, Sommershof A, Adenauer H, Kolassa S, Schedlowski M, et al. Posttraumatic stress disorder is associated with an enhanced spontaneous production of pro-inflammatory cytokines by peripheral blood mononuclear cells. BMC psychiatry. 2013;13(1):40.
57. Gill JM, Saligan L, Lee H, Rotolo S, Szanton S. Women in recovery from PTSD have similar inflammation and quality of life as non-traumatized controls. Journal of psychosomatic research. 2013;74(4):301-6.
58. Imp BM, Rubin LH, Tien PC, Plankey MW, Golub ET, French AL, et al. Monocyte activation is associated with worse cognitive performance in virologically suppressed HIV-infected women. The Journal of infectious diseases. 2016:jiw506.
59. Rubin LH, Benning L, Keating SM, Norris PJ, Burke-Miller J, Savarese A, et al. Variability in C-reactive protein is associated with cognitive impairment in women living with and without HIV: a longitudinal study. Journal of neurovirology. 2018;24(1):41-51.
60. Ironson G, O'cleirigh C, Leserman J, Stuetzle R, Fordiani J, Fletcher M, et al. Gender-specific effects of an augmented written emotional disclosure intervention on posttraumatic, depressive, and HIV-disease-related outcomes: a randomized, controlled trial. Journal of consulting and clinical psychology. 2013;81(2):284.
61. Moustafa AA. Increased hippocampal volume and gene expression following cognitive behavioral therapy in PTSD. Frontiers in human neuroscience. 2013;7:747.
62. Levy-Gigi E, Szabó C, Kelemen O, Kéri S. Association among clinical response, hippocampal volume, and FKBP5 gene expression in individuals with posttraumatic stress disorder receiving cognitive behavioral therapy. Biological psychiatry. 2013;74(11):793-800.
63. Roberts S, Keers R, Breen G, Coleman JR, Jöhren P, Kepa A, et al. DNA methylation of FKBP5 and response to exposure-based psychological therapy. American Journal of Medical Genetics Part B: Neuropsychiatric Genetics. 2018.
64. Prins A, Bovin MJ, Smolenski DJ, Marx BP, Kimerling R, Jenkins-Guarnieri MA, et al. The primary care PTSD screen for DSM-5 (PC-PTSD-5): development and evaluation within a veteran primary care sample. Journal of General Internal Medicine. 2016;31(10):1206-11.
65. Castanho TC, Amorim L, Zihl J, Palha JA, Sousa N, Santos NC. Telephone-based screening tools for mild cognitive impairment and dementia in aging studies: a review of validated instruments. Frontiers in aging neuroscience. 2014;6:16.

66. Blake DD, Weathers FW, Nagy LM, Kaloupek DG, Gusman FD, Charney DS, et al. The development of a clinician-administered PTSD scale. Journal of traumatic stress. 1995;8(1):75-90.
67. Murphy D, Ross J, Ashwick R, Armour C, Busuttil W. Exploring optimum cut-off scores to screen for probable posttraumatic stress disorder within a sample of UK treatment-seeking veterans. European Journal of Psychotraumatology. 2017;8(1):1398001.
68. Miles JN, Marshall GN, Schell TL. Spanish and English versions of the PTSD Checklist–Civilian version (PCL-C): Testing for differential item functioning. Journal of Traumatic Stress. 2008;21(4):369-76.
69. Chesney MA, Ickovics J, Chambers D, Gifford A, Neidig J, Zwickl B, et al. Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: the AACTG adherence instruments. AIDS care. 2000;12(3):255-66.
70. Pennebaker JW, Barger SD, Tiebout J. Disclosure of traumas and health among Holocaust survivors. Psychosomatic medicine. 1989.
71. Pennebaker JW, Susman JR. Disclosure of traumas and psychosomatic processes. Social Science & Medicine. 1988;26(3):327-32.
72. Bryant RA, Felmingham KL, Silove D, Creamer M, O'Donnell M, McFarlane AC. The association between menstrual cycle and traumatic memories. Journal of affective disorders. 2011;131(1):398-401.
73. Glover EM, Mercer KB, Norrholm SD, Davis M, Duncan E, Bradley B, et al. Inhibition of fear is differentially associated with cycling estrogen levels in women. Journal of psychiatry & neuroscience: JPN. 2013;38(5):341.
74. Andrade E, Arce C, Torrado J, Garrido J, De Francisco C, Arce I. Factor structure and invariance of the POMS mood state questionnaire in Spanish. The Spanish Journal of Psychology. 2010;13(1):444-52.
75. Creamer M, Bell R, Failla S. Psychometric properties of the impact of event scale—revised. Behaviour research and therapy. 2003;41(12):1489-96.
76. Oei TP, Evans L, Crook GM. Utility and validity of the STAI with anxiety disorder patients. British Journal of Clinical Psychology. 1990;29(4):429-32.
77. Beck AT, Steer RA, Brown GK. Beck depression inventory-II. San Antonio. 1996;78(2):490-8.
78. Taylor GJ, Bagby RM, Parker JD. The 20-Item Toronto Alexithymia Scale: IV. Reliability and factorial validity in different languages and cultures. Journal of psychosomatic research. 2003;55(3):277-83.
79. Frischholz EJ, Braun BG, Sachs RG, Schwartz DR, Lewis J, Shaeffer D, et al. Construct validity of the Dissociative Experiences Scale: II. Its relationship to hypnotizability. American Journal of Clinical Hypnosis. 1992;35(2):145-52.
80. Bremner JD, Vermetten E, Mazure CM. Development and preliminary psychometric properties of an instrument for the measurement of childhood trauma: the Early Trauma Inventory. Depression and anxiety. 2000;12(1):1-12.
81. Derogatis LR, Melisaratos N. The brief symptom inventory: an introductory report. Psychological medicine. 1983;13(3):595-605.
82. Eaton WW, Smith C, Ybarra M, Muntaner C, Tien A. Center for Epidemiologic Studies Depression Scale: review and revision (CESD and CESD-R). 2004.

83. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Archives of internal medicine. 2006;166(10):1092-7.
84. Tackman AM, Sbarra DA, Carey AL, Donnellan MB, Horn AB, Holtzman NS, et al. Depression, negative emotionality, and self-referential language: A multi-lab, multi-measure, and multi-language-task research synthesis. Journal of personality and social psychology. 2018.
85. Ndhlovu LC, Umaki T, Chew GM, Chow DC, Agsalda M, Kallianpur KJ, et al. Treatment intensification with maraviroc (CCR5 antagonist) leads to declines in CD16-expressing monocytes in cART-suppressed chronic HIV-infected subjects and is associated with improvements in neurocognitive test performance: implications for HIV-associated neurocognitive disease (HAND). Journal of neurovirology. 2014;20(6):571-82.
86. Kleim B, Horn AB, Kraehenmann R, Mehl MR, Ehlers A. Early linguistic markers of trauma-specific processing predict post-trauma adjustment. Frontiers in psychiatry. 2018;9.
87. Papini S, Yoon P, Rubin M, Lopez-Castro T, Hien DA. Linguistic characteristics in a non-trauma-related narrative task are associated with PTSD diagnosis and symptom severity. Psychological Trauma: Theory, Research, Practice, and Policy. 2015;7(3):295.
88. Cardiology TFotESo, Cardiology TFotESo. the North American Society of Pacing and Electrophysiology. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Circulation. 1996;93(5):1043-65.
89. Pitman RK, Orr SP, Forgue DF, de Jong JB, Claiborn JM. Psychophysiologic assessment of posttraumatic stress disorder imagery in Vietnam combat veterans. Archives of General Psychiatry. 1987;44(11):970-5.
90. Britton JC, Phan KL, Taylor SF, Fig LM, Liberzon I. Corticolimbic blood flow in posttraumatic stress disorder during script-driven imagery. Biological psychiatry. 2005;57(8):832-40.
91. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. Journal of personality and social psychology. 1988;54(6):1063.
92. Terry DP, Adams TE, Ferrara MS, Miller LS. FMRI hypoactivation during verbal learning and memory in former high school football players with multiple concussions. Archives of clinical neuropsychology. 2015;30(4):341-55.