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Assessment of Skin Conductance in African American and Non-African American Participants in Studies of Conditioned Fear

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Abstract

Skin conductance (SC) is a psychophysiological measure of sympathetic nervous system activity that is commonly used in research to assess conditioned fear responses. A portion of individuals evidence very low or unmeasurable SC levels (SCL) and/or response (SCR) during fear conditioning, which precludes the use of their SC data. The reason that some individuals do not produce measurable SCL and/or SCR is not clear; some early research suggested that race may be an influencing factor. In the current manuscript, archival data from five fear conditioning samples collected from four different laboratories were examined to explore SCL and SCR magnitude in African American (AA) and non-African American (non-AA) participants. Across studies, the aggregate group difference for exclusion due to unmeasurable SCL or no measurable SCR to an unconditioned stimulus reflected a significant medium effect size (d = 0.54). Furthermore, 24.3% (range: 0 - 48.3%) of AA participants met SC exclusion criteria versus 14.3% (range: 4.3 - 24.2%) of non-AA participants. AA participants also displayed significantly lower SCL during habituation (d = 0.58). The low SC levels and responses in AA individuals and the consequent exclusion of their contributions to fear conditioning study results impacts the generalizability of findings across races. Given higher rates of PTSD and chronic anxiety in AA individuals, it is important that AA individuals not be excluded from fear conditioning research, which informs the treatment of anxiety and PTSD. Examination of the basis of very low SCL and/or SCR is a potentially informative direction for future research.

Keywords

skin conductance; race; psychophysiology; fear conditioning; African American

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Skin conductance (SC) has long been used as a physiological measure of emotional arousal and has been employed across a range of psychological research domains. This measure of emotional reactivity reflects activity of the sympathetic nervous system and is often used as the primary outcome measure in fear conditioning studies. For example, in a meta-analysis of classical fear conditioning studies conducted in individuals with anxiety disorders, SC response was identified as the most common dependent variable (Lissek et al., 2005). Fear conditioning research has played a central role in understanding the etiology, maintenance, and treatment of anxiety and traumatic stress disorders for decades (Milad, Rosenbaum, & Simon, 2014). The acquisition phase of a fear conditioning procedure provides a potential model for the etiology of anxiety. During this phase, a neutral stimulus (e.g., a colored shape) is paired with a naturally aversive stimulus (e.g., an electric shock). Over multiple presentations, the neutral stimulus will become capable of producing a fear response, as can be measured from a change in SC activity. Fear conditioning procedures are also used to examine methods whereby the acquired fear response can be weakened or eliminated. One common method for weakening the fear response is by extinction, which involves the repeated presentation of the conditioned stimulus without the aversive consequence. Extinction forms the basis for exposure therapy, an effective treatment for clinical anxiety/fear.

One challenge in fear conditioning research that relies on SC as the primary measure and that is not frequently discussed is that some individuals do not produce a measurable SC level, i.e., their SC level is very low or undetectable. Furthermore, other individuals do not show a detectable change in SC level in response to an unconditioned stimulus (UCS, e.g., shock) that would normally elicit an unconditioned response. Consequently, individuals with an unmeasurable SC level or who fail to show a measurable SC response to an UCS would be excluded from analyses in fear conditioning studies (e.g., Otto et al., 2014; Schiller et al., 2010). Furthermore, in studies using SC that examine extinction learning, individuals who fail to display differential conditioned SC responses during acquisition, are often excluded from analyses of extinction (e.g., Otto et al., 2014; Schiller et al., 2010). Such exclusions may reduce statistical power and limit the generalizability of a study's findings.

Although research has examined factors such as age, gender and education that may influence the magnitude of conditioned SC responses (e.g., Rosenbaum et al., 2015), the reason that some individuals fail to show measurable SC levels and/or an unconditioned response is less clear. There is evidence connecting certain trait factors and diagnoses, specifically psychopathy (e.g., Lorber, 2004) and schizophrenia (e.g., Holt et al., 2009; Öhman, 1981), with reduced electrodermal activity. There is also some early research suggesting that resting SC level may vary by race; for example, African American (AA) participants have been found to have significantly lower SC levels than Caucasian participants (Johnson & Landon, 1965; Lieblich, Kugelmass, & Ben-Shakhar, 1973). In the only recent study examining the effect of ethnicity on SC, Martínez, Franco-Chaves, Milad, and Quirk (2014) found baseline SC level to be significantly higher in Hispanic, compared to non-Hispanic, participants. However, there was no difference between Hispanic and non-Hispanic individuals in the magnitude of their SC response to an unconditioned stimulus (i.e., shock). In an interesting application of skin resistance measurement, Batson, Young

and Shepard (1962) studied children with and without cystic fibrosis using a standard ohmmeter to determine whether children with the disorder had lower skin resistance (higher SC) levels. The investigators also measured sweat chloride concentration. Upon examining their data, Batson and colleagues observed that the AA children in their control group had higher skin resistance levels than the Caucasian control children and that the chloride level tended to be lower in the AA children. These findings suggest that lower sweat chloride concentration may be associated with lower SC level. However, more recent studies have not observed chloride level differences between Caucasian and AA individuals (Dill, Yousef, Goldman, Hillyard, & Davis, 1983; Hamosh et al., 1998).

In order to assess whether or not SC level and response magnitude might differ as a function of being AA or non-African American (non-AA), we examined archival fear conditioning data from five samples collected by four independent research laboratories that measured SC. Given past research indicating lower SC levels in AA participants, and anecdotal reports from researchers who use SC measures, we hypothesized that AA participants would have a higher rate of unmeasurable SC level and undetectable unconditioned SC responses. In addition, we also compared the magnitude and rates of conditioned SC responses between AA and non-AA participants.

Method

Participants

Five cohorts of participants were separately examined: because there are significant differences in participant characteristics and study designs, we did not combine the samples. Patients with schizophrenia and individuals who identified their ethnicity as Hispanic or Latino were excluded from all samples given prior research indicating variations in SC levels and/or responses in these specific subpopulations (e.g., Holt et al., 2009; Martínez et al., 2014; Öhman, 1981). Baseline characteristics are presented for each sample in Table 1.

Sample 1—Sample 1 (AA, $n = 19$; non-AA, $n = 150$) consists of data from a study conducted at Boston University and Massachusetts General Hospital that examined fear conditioning in individuals who were psychiatrically healthy or were diagnosed with one of several affective disorders (Table 1; Otto et al., 2014). The non-AA participants identified as White (95%, $n = 143$), Asian (4%, $n = 6$), and Other (1%, $n = 1$). Although the study from which Sample 1 was derived did not exclude individuals based on medication, we excluded individuals on anticholinergic medications for the current analyses. About one fifth (20%) of individuals in Sample 1 were taking non-anticholinergic psychiatric medications and 7% of the individuals were taking benzodiazepines. Because the results of analyses did not differ when individuals on benzodiazepines were taken out of the sample, these participants were retained in the present analyses in order to maximize power.

Sample 2—Sample 2 (AA, $n = 29$; non-AA, $n = 31$) consists of data from a study conducted at the VA Boston Healthcare System examining fear conditioning in female patients with PTSD and healthy controls at different stages of the menstrual cycle (Pineles et al., 2016). The non-AA participants identified as White (61%, $n = 19$), Asian (23%, $n = 7$),

American Indian (3%, *n* = 1), and Other (13%, *n* = 4). The study from which Sample 2 was obtained excluded individuals taking psychotropic or anticholinergic medications.

Sample 3—Sample 3 (AA, *n* = 20; non-AA, *n* = 98) consists of data from a study conducted at the San Francisco VA Medical Center that examined fear conditioning in male and female patients with full or subsyndromal PTSD or trauma-exposed controls (Inslicht et al., 2013). The non-AA participants identified as White (66%, *n* = 65), Asian (17%, *n* = 17), and Multiracial (10%, *n* = 10), and 6% did not indicate a race and were coded as unknown or other (*n* = 6). The study from which Sample 3 was obtained excluded individuals taking alpha and beta-adrenergic agents, antipsychotics, benzodiazepines, mood stabilizers, anticonvulsants, antihypertensives, sympathomimetics, and steroids. Individuals taking an anticholinergic medication were excluded from the current analyses. Eleven percent of individuals in the sample were taking psychiatric medications.

Samples 4a and 4b—Sample 4a (AA, *n* = 14; non-AA, *n* = 28) and 4b (AA, *n* = 13; non-AA, *n* = 26) consists of group data from multiple studies conducted by Milad and colleagues that examined fear conditioning in a range of clinical and healthy populations (Holt, Coombs, Zeidan, Goff, & Milad, 2012; Holt et al., 2009; Hwang et al., 2015; Linnman et al., 2012; Linnman, Zeidan, Pitman, & Milad, 2012; Marin et al., 2016; 2017; Milad et al., 2008; 2009; 2010; 2013). Given that the sensor diameter of SC recording electrodes may influence SC level (SC levels recorded by larger sensor diameters typically will be higher than those recorded by smaller sensor diameters), participants who were studied using a Coulbourn system and 8-mm SC electrodes (Coulbourn Instruments, 2016) and those studied using a Biopac system and 11-mm SC electrodes (Biopac Systems, Inc., 2016) were examined separately and comprised Samples 4a and 4b, respectively. Samples 1-3 and 4a were all studied using a Coulbourn system and all used the same size electrode. Given the large size of the initial 4a and 4b samples, we were able to restrict and match the comparison groups. For Samples 4a and 4b, all AA participants who underwent the conditioning procedure were included in the analyses; non-AA participants were selected and matched on age, gender, education, diagnostic status, and UCS intensity. Non-AA participants were only included if they specifically identified as White. In order to maximize the power within this sample we selected twice as many non-AA White participants as AA participants.

The medication inclusion/exclusion criteria for Samples 4a and 4b varied given that participants were included from multiple studies. For Sample 4a, the majority of the participants were healthy controls not on medication or from studies that did not permit medication (64%, *n* = 27). A portion of the participants in Sample 4a were from a study that allowed participants to be on a stable medication regimen or medication free for greater than or equal to 8 weeks and benzodiazepine free for at least 2 weeks (29%, *n* = 12) and a small number of participants in Sample 4a (7%, *n* = 3) were involved in a study that had no medication exclusion criteria. For Sample 4b, the majority of participants (90%, *n* = 35) came from a study that allowed participants to be on a stable medication regimen or medication free for greater than or equal to 8 weeks and benzodiazepines free for at least 2 weeks. The remaining participants in Sample 4b (10%, *n* = 4) were from a study that did not permit medication use.

Procedures

All studies were reviewed by their respective Institutional Review Boards and all participants provided written informed consent. Fear conditioning procedures varied somewhat across studies and will be described in detail below. All studies used an electric stimulus as the UCS, set at a level the participant determined to be "highly annoying but not painful."

Samples 1-3—A differential fear-conditioning paradigm that included one CS+ and one CS− was used for Sample 1, 2, and 3. All three samples viewed colored shapes as the conditioned stimuli (CSs). Participants completed a 5-min baseline recording period during which SC level was continuously recorded while the participant sat alone in the laboratory with no stimuli being presented. This was followed by a Habituation phase, which consisted of five CS+ and five CS− presentations, none of which were reinforced by the UCS (i.e., shock). The Habituation phase was followed by an Acquisition phase, which consisted of five CS+ and five CS− presentations, with all CS+ presentations immediately followed by the UCS (100% reinforcement schedule). The CS duration was 8 s, the inter-trial interval was 20 +/− 5 s, and the UCS duration was 500 ms.

Sample 4a and 4b—A differential fear-conditioning paradigm with context manipulation (Milad, Orr, Pitman, & Rauch, 2005) was used for these samples. Contexts consisted of images of two different rooms (i.e., a library and an office) and conditioned stimuli were represented by a lamp located in both rooms, with three different colors of the lit lampshade constituting two CS+s and one CS−. One CS+ would later be extinguished (CS+E) and one CS+ would not be extinguished (CS+U). The selection of the two CS+ and CS− colors was randomly determined and counterbalanced across participants. The Milad et al. procedures took place inside an fMRI scanner. Participants first completed a baseline recording period of at least 7 min during which SC level was continuously recorded while participants were lying down in the fMRI scanner with no stimuli being presented. This was followed by a Habituation phase which consisted of two CS+E, two CS+U, and two CS− presentations in a counterbalanced manner presented in both the to-be conditioned context (CX+) or the to-be extinction context (CX-). This was followed by an Acquisition phase, which consisted of eight CS+E and eight CS+U and sixteen CS− trials, all presented within CX+. A partial reinforcement schedule was used; 62.5% of the CS+E and CS+U presentations were immediately followed by the UCS (i.e., shock). For each trial, the context picture was presented for 9 s; 3 s alone followed by 6 s in combination with the CS+E, CS+U, or CS−. The inter-trial interval was 15 +/− 3 s and the UCS duration was 500 ms.

Skin Conductance Measurement

All studies collected SC as a psychophysiological outcome measure using standard electrode application procedures. After attaching SC electrodes to each participant, study experimenters checked to ensure that SC levels were responsive to an anxiety producing challenge test (e.g., counting backwards by sevens). If SC levels were not responsive, SC electrodes were replaced to ensure that lack of responsivity was not due to a faulty electrode or application of the electrodes. In scoring the SC data, a distinction is made between SC level (SCL) and SC response (SCR). SCL represents the average SC level across a specified

duration, whereas SCR represents the change in SCL during the presentation of a stimulus. SCR for each CS presentation was calculated by subtracting the mean SCL during the end of the pre-stimulus period (2 s) from the peak SCL during the stimulus presentation. The equipment and collection methods used in the respective studies are described in detail below.

Samples 1-3—The Coulbourn Isolated Skin Conductance coupler of the Coulbourn Lablinc V, Human Measurement Modular Instrument System (Coulbourn Instruments, 2016) was used to measure SCL in studies 1-3. Samples 1 and 2 measured SCL through two DOCXS Ag/AgCl 8-mm electrodes and Sample 3 measured SCL through two Coulbourn Ag/AgCl 8-mm electrodes. Electrodes were filled with isotonic paste and placed on the hypothenar surface of the non-dominant hand in accordance with published guidelines (Fowles et al., 1981). The UCS was a generated by a Coulbourn Transcutaneous Aversive Finger Stimulator and delivered to the middle and index finger of the participant's dominant hand.

Sample 4a and 4b—For Sample 4a, the Coulbourn Isolated Skin Conductance coupler was also used to measure SCL through two 8-mm DOCXS Ag/AgCl electrodes filled with isotonic paste and placed on the hypothenar surface of the left palm. The UCS was a generated by a Coulbourn Transcutaneous Aversive Finger Stimulator and delivered to the middle and index finger of the participant's right hand. For Sample 4b, a Biopac System (Biopac Systems, Inc., 2016) was used with two 11-mm Biopac Ag/AgCl electrodes filled with isotonic paste.

Outcomes

Baseline characteristics—AA and non-AA participants were compared on the demographic variables of age, gender, ethnicity, and education, as well as diagnostic status and medication usage. In all studies, participants were allowed to select their own level of electric stimulation, which was used throughout the course of the experiment. Average UCS intensity selection levels were compared between AA and non-AA groups, with the exception of Sample 4a and 4b participants for whom the UCS level was matched between AA and non-AA participants.

Primary outcome—In order to test our primary hypothesis, we examined how many individuals would have been excluded from analyses due to an unmeasurable SCL or inadequate response to the UCS as defined below.

Unmeasurable SCL: For some individuals, SCL is so low, and usually unchanging, that it is difficult to obtain a measurement; in such instances, SC is considered to be “unmeasurable.” Unmeasurable SCL was defined as a mean SCL of less than 0.5 μS during the 2-s pre-stimulus period across CS+ trials during acquisition. Acquisition was selected over habituation, because SCL would likely be highest during the phase of the experiment when the UCS is being presented. Thus, racial differences in SCL, if they exist, ought to be most evident and convincing when observed during the acquisition phase. For simplicity, we only included CS+ trials in this determination; given that CS+ and CS− trials were randomly

interspersed, it is unlikely that pre-stimulus SCL varied for CS+ and CS− trials. A cutoff of 0.5 μS was selected to be well below the average range of SCL (2-16 μS) reported in published guidelines (Braithwaite, Watson, Jones, & Rowe, 2013).

SCR non-responder status: For other individuals, although they evidence a measureable SCL, they do not produce a measurable response to the UCS (i.e., shock). For the purpose of our examination, the unconditioned SCR was defined as the mean SCR to the UCS across all reinforced acquisition trials (i.e., acquisition trials that were paired with the UCS). SCR to the UCS was calculated by subtracting the mean SCL during the last 2 s of the CS+ interval from the peak SCL during the 6 s following the CS+ offset (e.g., Orr et al., 2000). Consistent with prior research (Basden, Orr, & Otto, 2016; Bui et al., 2013; Pineles et al., 2016), individuals with a mean unconditioned SCR of less than 0.1 μS were considered to be "SCR non-responders." As it is not possible to measure SCR if an individual does not have a measurable SCL, individuals with unmeasurable SCLs were not included in the examinations of SCR non-responders.

Secondary outcomes—For individuals who had measurable SCLs and produced responses to the UCS (i.e., individuals who would not be excluded from analyses per above) the following variables were also examined. These variables allow for examining whether AA participants who have measurable SCLs and SCRs may have lower SCLs and smaller SCRs, compared to non-AA participants. In addition, we examined the differential SCR (CS + minus CS−) to assess whether AA, compared to non-AA, status is associated with differences in the acquisition of a conditioned, differential SCR and whether AA participants are more likely to be excluded from analyses of extinction learning due to the absence of a differential SCR.

Habituation SCL: Habituation SCL was defined as the average SCL for the 2-s pre-stimulus period across all CS+ trials during the Habituation phase. Raw SCL data for all CS + habituation trials were not available in the archival database for Samples 4a and 4b, so the average SCL during the 2-s pre-stimulus period for the first CS trial of the Habituation phase was used. Given that the conditioning paradigm used for Sample 4a and 4b involved the presentation of a context for 3 s prior to presentation of the CS, the 2-s pre-context period for the first CS trial of the Habituation phase was used.

Unconditioned SCR: The unconditioned SCR was defined as the average SCR to the UCS, scored as above, across all reinforced acquisition trials.

SCR to CS+: The SCR to the CS+ was defined as the average SCR across all CS+ acquisition trials.

Differential SCR: The differential SCR was defined as the difference between the average SCR to CS+ trials and average SCR to the CS− trials.

Differential SCR non-responder status: For individuals with measurable SCLs who produced responses to the UCS, we also examined responder status for the differential SCR. An individual was considered to be a differential SCR Responder if their differential SCR

was greater than 0.1 μS. This cutoff was obtained from published studies examining extinction learning (e.g., Otto et al., 2014; Schiller et al., 2010), in which individuals were excluded from analyses of extinction learning if they did not display a differential SCR during acquisition above the cutoff value.

Statistical Analyses

Participants were coded as AA if they self-identified on demographic questionnaires as "African American" or "Black." Participants were coded as non-AA if they identified with any racial group besides AA, except for in Sample 4a and 4b in which the non-AA group consisted solely of individuals who identified as "Caucasian" or "White." T-tests, Fisher's exact tests, and chi-squared tests were used to compare demographic variables and UCS intensity selection levels between AA and non-AA participants.

Rates of unmeasurable versus measurable SCL were compared between AA and non-AA participants. After removing individuals with unmeasurable SCL, rates of SCR responder versus non-responder status were compared between AA and non-AA participants. Lastly, total numbers of excluded participants, due to unmeasurable SCL or SCR non-responder status, were compared between AA and non-AA participants. Chi-squared tests were used when the sample cell sizes were ≥ 5; Fischer's exact tests were used when individual sample cell sizes were < 5.

Lastly, individuals with unmeasurable SCL or classified as SCR non-responders were removed from the datasets in order to examine the secondary variables of interest for individuals in whom SC could be measured. Square-root-transformed SCR data were analyzed for all samples except Sample 1. For Sample 1, only the mean SCRs, which had been previously calculated from untransformed SCR data, were available for the present analyses. For all samples, untransformed SCR data were used when examining the UCR to establish SCR responder versus non-responder status, per above. For Samples 2-4b, transformed SCR data, and for Sample 1 untransformed SCR data, were used when examining the differential SCR to establish differential SCR responder status, per above. T-tests were used to compare Habituation SCL, Unconditioned SCR and SCR to CS+ in AA and non-AA participants. Fisher's exact tests and chi-squared tests were used to compare rates of differential SCR responder versus non-responder status between AA and non-AA participants. A within-subject factor of stimulus (SCR CS+, SCR CS−) by group (AA, non-AA) interaction was examined to determine whether the differential SCR differed between groups during the Habituation and Acquisition phases. In Sample 3, analyses of secondary outcomes were conducted while covarying for UCS intensity, due to group differences on this variable (see below). Comprehensive meta-analysis (Biostat, 2016) software was used to calculate individual sample effect sizes and estimate aggregate effect sizes for all samples run using the Coulbourn equipment and 8-mm SC electrodes (Samples 1-3 and Sample 4a).

Results

Baseline Characteristics

As can be seen in Table 1, there were no significant baseline differences for age, diagnostic status, or psychiatric medication use between AA and non-AA participants in Samples 1-3. For Sample 1 only, there was a significant difference between AA and non-AA participants in gender ($p < .05$), with a larger percentage of female AA participants. For Sample 2 only, there was a significant difference between AA and non-AA participants in education ($p < .05$), with more non-AA having completed college than AA participants. For Sample 3 only, there was a trend-level difference between AA and non-AA participants for UCS intensity selection ($p = .06$), with AA participants selecting lower UCS intensity levels. For Samples 4a and 4b, participants were matched on baseline demographic characteristics, diagnostic status, and UCS intensity; thus, there were no significant differences between AA and non-AA participants for these variables. Individual participants' psychiatric medication use data were not available for Samples 4a and 4b.

Primary Outcome

Results of analyses examining percentages of individuals who would be excluded due to unmeasurable SCL or SCR non-response to the UCS for each of the samples are presented in Table 2. Overall, significantly more AA participants than non-AA participants would be excluded for Samples 1 and 3 (Sample 1, $d = 0.64$; Sample 3, $d = 0.92$; $ps < .05$) and a similar, but trend-level, effect was observed for Sample 2 (Sample 2: $d = 0.54$ $p = .07$). There were significantly higher rates of unmeasurable SCL in Samples 2 and 3 ($ps < .05$) and higher rates of SCR non-responder status in Sample 1 ($p < .05$) in AA, compared to non-AA, participants. There were no significant differences between AA and non-AA participants in rates of unmeasurable SCL, SCR non-responder status, or combined (total rates of unmeasurable SCL or SCR non-responder status) for Samples 4a and 4b (Sample 4a, $d = -0.70$[1]; Sample 4b, $d = -0.26$; $ps > .18$). The aggregate effect size for the total numbers of AA, compared to non-AA, participants excluded due to unmeasurable SCL or SCR non-responder status across all studies was medium and significant ($d = 0.54$; $p < .05$). The average percentage of AA participants that would be excluded on the basis of SC activity across all five samples was 24.3% (range: 0 - 48.3%) versus 14.4% (range: 4.3 - 24.2%) of non-AA participants.

Secondary Outcomes

Results of analyses examining Habituation phase SCL, Unconditioned SCR, SCR to CS+, and Differential SCR for each of the five samples are presented in Table 3. Habituation phase SCL was significantly lower in AA participants, compared to non-AA, participants across three of the five samples (Sample 1, $d = 0.86$; Sample 2, $d = 0.67$; Sample 4b, $d = 1.16$; $ps < .05$). For Sample 3, Habituation SCL was lower in AA participants, compared to non-AA participants at a trend level ($d = 0.60$, $p = .08$). For Sample 4a, Habituation SCL did not differ for AA and non-AA participants ($d = 0.25$; $p = .51$). The aggregate effect size for Habituation phase SCL across all samples was medium and significant ($d = 0.58$; $p < .001$).

[1]Although this would be considered a large effect size, due to the sample size, this effect was not significant ($p = .24$).

The unconditioned SCR was significantly smaller in AA, compared to non-AA, participants for Samples 1, 2 and 4b, as reflected by medium-to-large effect sizes (Sample 1, $d = 0.66$; Sample 2, $d = 0.95$; Sample 4b, $d = 0.77$; $ps < .05$), but not for Sample 3 ($d = 0.23$; $p = 0.46$) or Sample 4a ($d = -0.11$; $p = 0.75$). The aggregate effect size for the unconditioned SCR across all samples was medium and significant ($d = 0.44$, $p < .05$). The SCR to CS+ was significantly smaller in AA, compared to non-AA, participants for Samples 1 and 4b (Sample 1, $d = 0.76$; Sample 4b, $d = 1.01$; $ps < .05$), but not Samples 2, 3 or 4a (Sample 2, $d = 0.37$; Sample 3, $d = -0.08$; Sample 4a, $d = 0.28$; $ps > .19$). The aggregate effect size for SCR to CS+ across all studies was small and at a trend level ($d = 0.35$; $p = .06$).

Results of analyses of the stimulus × group interaction effect revealed a significantly smaller differential SCR during the Acquisition phase for AA, compared to non-AA, participants for Sample 1 ($F(1, 147) = 4.87$, $p = .03$; $d = 0.63$), Sample 4a ($F(1, 33) = 7.80$, $p = .009$; $d = 0.99$), and Sample 4b ($F(1, 36) = 7.79$, $p = .008$; $d = 0.98$). The stimulus × group analysis was not significant for Samples 2 and 3 (Sample 2, $d = 0.36$; Sample 3, $d = -0.52$; $ps > .16$). The aggregate effect size for differential SCR was small and non-significant ($d = 0.35$; $p = 0.27$). Results for differential SCR are likely not due to pre-existing differences in responsivity to CS+ and CS−, as there was no evidence of a differential SCR during the Habituation phase (Sample 1: $F(1, 147) < 1$, $p =$ ns; Sample 2: $F(1, 35) < 1$, $p =$ ns; Sample 3: $F(1, 96) < 1$, $p =$ ns; Sample 4a: $F(1, 31) <1$, $p =$ ns) or a stimulus × group interaction during the Habituation phase (Sample 1: $F(1, 147) < 1$, $p =$ ns; Sample 2: $F(1, 35) < 1$, $p =$ ns; Sample 3: $F(1, 36) < 1$, $p =$ ns; Sample 4a: $F(1, 31) = 1.73$, $p =$ ns) for Samples 1-3 and 4a. Although, there was a significant effect for stimulus type during the Habituation phase for Sample 4b ($F(1, 34) = 9.43$, $p = .004$), it was in the opposite direction (CS− > CS+), and there was no interaction with group ($F(1, 34) = 2.44$, $p = .13$). There were significantly higher rates of differential SCR non-responders in Samples 1 and 4b (Sample 1, $d = 0.73$; Sample 4b, $d = 0.97$; $ps < .05$) in AA, compared to non-AA, participants. There were no significant differences between AA and non-AA participants in rates of differential SCR non-responders for Samples 2, 3, or 4a; however, in Samples 2 and 4a, rates trended in the direction of more non-responders in the AA groups (Sample 2, $d = 0.24$; Sample 3, $d = -0.29$; Sample 4a, $d = 0.59$; $ps > .15$). The aggregate effect size for the total numbers of AA, compared to non-AA, excluded due to differential SCR non-responder status across all studies was small and non-significant ($d = 0.31$; $p = 0.19$).

Discussion

Across four independent research sites, we found supporting evidence for increased difficulty measuring SC activity, as well as lower SC levels and smaller SC responses, in AA, compared to non-AA, participants. First, for two out of the five samples, a greater number of AA participants were likely to be excluded from analyses due to low, unmeasurable SCL, and for a third sample, more AA participants were likely to be excluded from analyses for producing a very small SCR to the unconditioned stimulus (i.e., shock). In combining the results across the five samples, these effects were represented by a significant aggregate medium effect size. Second, for AA participants who displayed measurable SCL and unconditioned SCR, and thereby were included in subsequent analyses, AA participants demonstrated significantly lower SCL during habituation in three of the five samples (and a

fourth at a trend level), as represented by a significant aggregate medium effect size. This supports that SCL of AA individuals is lower than that observed in non-AA individuals. The group differences for unconditioned and conditioned SCRs were less consistent. For three of the five samples, AA participants displayed less SC responsivity to unconditioned stimuli as represented by a small-to-medium significant aggregate effect size. In two of the five samples, AA participants displayed smaller SCRs to CS+ and smaller differential SCRs; however, the aggregate effect sizes for these variables were small and non-significant. In two of the five samples, AA participants were more likely to be excluded from analyses of extinction learning due to an inadequate differential SCR during acquisition represented by a small and non-significant aggregate effect size.

A strength of the present comparison of SC activity in AA and non-AA individuals rests with our ability to examine data from four independent laboratories and five different samples, thereby reducing the likelihood that findings reflect unique aspects of a particular site or sample. Although, statistical power was somewhat limited when comparing separate samples, we were able to estimate aggregate effect sizes. The reason for inconsistencies across samples (Samples 4a and 4b) is not clear, but might reflect differences in sampling or procedures (e.g., data collected while in an fMRI scanner). Nonetheless, SC results for the secondary outcomes for Samples 4a and 4b were similar to those of the other samples and still indicative of lower SCLs and smaller SCRs in AA, compared to non-AA, participants. In addition, significantly more AA participants displayed smaller differential SCRs in Samples 4a and 4b, and in Sample 4b, more AA participants than non-AA participants would be excluded from SCR analyses of extinction learning due to not having acquired a differential SCR during conditioning.

A limitation of the current study is our inability to access all trial-specific data for Samples 1, 4a, and 4b. This limited analyses of Habituation SCL for Sample 1 to only a portion of the participants and Samples 4a and 4b to a single trial. This also resulted in the use of averages, rather than trial-specific data, for certain outcomes. For example, for SCR non-responder status, the average SCR to the UCS was used, rather than the maximum SCR to any single UCS trial. Although, some participants within Studies 2-4 who were deemed “SCR non-responders” demonstrated a SCR greater than our cutoff to an individual UCS presentation, analysis of Samples 2-4 data using the maximum SCR to UCS instead of the average SCR to the UCS, did not significantly impact results. We were also unable to access participant medication-use data for Samples 4a and 4b and, therefore, could not determine whether individuals on anticholinergic medications were excluded from those samples. Although, individuals using other medications that have been shown to influence SC (i.e., benzodiazepines) were excluded from Sample 4a and 4b, we were unable to rule out the possibility that other medication usage may have influenced the results for these samples. Lastly, we chose to examine individuals who self-identified as AA, compared to those who did not. We suggest that a more nuanced examination of how race and ethnicity impact SC activity, how SC activity may vary between or within racial and ethnic groups, and examination of potential factors that might influence SC activity (e.g., skin pigmentation; Korol, Bergfeld, Goldman, & McLaughlin, 1977) is warranted.

SC is often the primary measure used in fear conditioning research. Given our findings, researchers are encouraged to examine and report whether AA participants are being disproportionately excluded from SC data analyses. In addition, alternative assessment methods should be considered in order to ensure that AA individuals are not disproportionately excluded from study results. Potential alternative psychophysiological assessment methods include fear potentiated startle (Davis, 2006), electromyography (EMG; Orr, 2000), heart rate (Orr, 2000), and pupil dilation (Korn, Staib, Tzovara, Castegnetti, & Bach, 2016). Although one study demonstrated lower heart rate in black, compared to white participants (Morell, Myers, Shapiro, Goldstein, & Armstrong, 1988), another found no differences (Korol et al., 1977). To our knowledge, there is no evidence of difficulties with these alternative psychophysiological measures in AA individuals. However, it is not clear that these other measures necessarily represent the same underlying process as SC activity. For example, corrugator EMG is responsive to dislike and disgust as well as fear (Neta, Norris, & Whalen, 2009). In fear conditioning research, there has been an increase in the use of startle response to measure fear given that it is an automatic defensive reaction and some research suggests that it may not require awareness of the contingency (CS+ and UCS association; Sevenster, Beckers, & Kindt, 2014). Similarly, research suggests that pupil dilation can occur in the absence of voluntary, conscious processes (Laeng, Sirois, & Gredebäck, 2012); however, this measure has been less used in fear conditioning research. Given these factors and that it has not been shown to vary across race, fear potentiated startle assessed by EMG may be a useful secondary psychophysiological measure in studies of fear conditioning. In addition, the use of neuroimaging, such as fMRI, or the use of measures directly related to SC activity, such as pore openings (e.g., Familoni et al., 2016; Krzywicki, Bernston, & O'Kane, 2014), should be encouraged in fear conditioning research.

Lastly, research examining the basis of lower SCL and smaller SCRs in AA individuals may suggest directions for SC assessment that would facilitate the use of this measure. A better understanding of the biological basis of smaller SCRs may provide additional insight into the neural basis of fear acquisition across racial groups. For example, differences in sweat gland physiology, melanin content, chloride concentration, or other biological aspects of skin may affect the measurement of skin conductance (e.g., Berardesca & Maibach, 2003; Johnson & Landon, 1965). Alternatively, there may be a more central explanation, such as differences in activation of the central nervous system. For example, research suggests that regions of the fear circuit of the brain may be differentially activated in individuals who do not display differential conditioned responses (MacNamara et al., 2015; van Well, Visser, Scholte, & Kindt, 2012). These possibilities are yet to be systematically examined across specific racial groups. It is also possible that SCR differences between AA and non-AA individuals may have to do with varying dimensions of anxiety, as there is evidence in the literature that individuals with anxiety display higher SCL and larger SCRs than non-anxious individuals (Bond, James, & Lader, 1974; Lissek et al., 2005). However, as all the samples in our comparisons were mixed clinical and non-clinical samples, and there were no differences in rates of clinical and non-clinical participants in AA and non-AA subgroups, potential differences in anxiety level seem unlikely to explain our findings.

Nonetheless, lower SCL and smaller SCRs may make it more difficult to assess conditioned fear in AA participants in studies that rely on SC as the primary outcome measure. At the

extreme end, this leads to the possibility that SC data for AA participants will be disproportionately excluded from studies of fear conditioning, as suggested by our findings. In the case of differential SCR, a smaller differential SCR could indicate that: (1) the participant is not displaying an increase in SC to either the CS+ or the CS−, or (2) the participant is displaying an increase in SC to both the CS+ and CS−. In the current studies, AA participants displayed smaller SCRs to both the CS+ and CS−; thereby, resulting in a small differential SCR. It may be that AA participants are not acquiring a fear response to the CS+ or, and seemingly more likely, that AA participants are acquiring a fear response to the CS+, but that it is not being detected by SC assessment.

Fear conditioning research is central to our understanding of the etiology, maintenance, and treatment of anxiety and traumatic stress disorders (e.g., Milad et al., 2014). In particular, gold-standard exposure-based treatments for anxiety and PTSD are based on fear extinction research and theory. Furthermore, many studies explore methods to enhance extinction learning in the laboratory through fear conditioning, prior to translating such work to the clinic (Milad et al., 2014). Although, our findings should be viewed as tentative given that the studies and data analyzed were not designed to examine racial differences in SCL and SCR, the implications of our findings warrant further exploration as this could impact the relevance of fear conditioning research findings based on SC assessment to AA individuals. This is of particular importance given that rates of PTSD are higher in AA than non-AA individuals (Dursa, Reinhard, Barth, & Schneiderman, 2014; Roberts, Gilman, Breslau, Breslau, & Koenen, 2011) and, when diagnosed with anxiety, AA individuals are more likely to display a chronic course (Breslau, Kendler, Su, Aguilar-Gaxiola, & Kessler, 2005) than non-AA individuals. Furthermore, AA individuals with anxiety or PTSD are less likely to seek out and be retained in treatment (Roberts et al., 2011) and there is evidence that they are less likely to receive quality care than Caucasians (Schraufnagel, Wagner, Miranda, & Roy-Byrne, 2006). Consistent with recommendations of others (Fairchild, 1991), we caution against over-interpretation or misinterpretation of the current findings. Our goal in this paper is to highlight the public health importance of ensuring that AA individuals are not inadvertently excluded from a field of research that is highly relevant to the treatment of anxiety and PTSD. Furthermore, we hope to encourage research to better understand the SC differences evident in our analyses, with the goal of improving our ability to accurately measure threat responding across all racial groups.

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References

Basden SL, Orr SP, Otto MW. Impaired de novo fear conditioning in opiate-dependent outpatients. Cognitive Therapy and Research. 2016; 40(6):824–830. DOI: 10.1007/s10608-016-9786-9

Batson R, Young WC, Shepard FM. Observations on skin resistance to electricity and sweat chloride content: A preliminary report. The Journal of Pediatrics. 1962; 60(5):716–720. DOI: 10.1016/S0022-3476(62)80098-5 [PubMed: 13865770]

Berardesca E, Maibach H. Ethnic skin: Overview of structure and function. Journal of the American Academy of Dermatology. 2003; 48(6):S139–S142. DOI: 10.1067/mjd.2003.273 [PubMed: 12789167]

Biopac Systems, Inc. 2016. Available from https://www.biopac.com

Biostat. Comprehensive Meta-Analysis (Version 3). software. 2016. Available from https://www.meta-analysis.com

Bond AJ, James DC, Lader MH. Physiological and psychological measures in anxious patients. Psychological Medicine. 1974; 4(04):364–373. DOI: 10.1017/S0033291700045803 [PubMed: 4456431]

Braithwaite, JJ., Watson, DG., Jones, R., Rowe, M. A guide for analysing electrodermal activity (EDA) & skin conductance responses (SCRs) for psychological experiments. 2013. Retrieved from https://www.biopac.com/wp-content/uploads/EDA-SCR-Analysis.pdf

Breslau J, Kendler KS, Su M, Aguilar-Gaxiola S, Kessler RC. Lifetime risk and persistence of psychiatric disorders across ethnic groups in the United States. Psychological Medicine. 2005; 35(3):317–327. DOI: 10.1017/S0033291704003514 [PubMed: 15841868]

Bui E, Orr SP, Jacoby RJ, Keshaviah A, LeBlanc NJ, Milad MR, et al. Simon NM. Two weeks of pretreatment with escitalopram facilitates extinction learning in healthy individuals. Human Psychopharmacology: Clinical and Experimental. 2013; 28(5):447–456. DOI: 10.1002/hup.2330 [PubMed: 23776033]

Coulbourn Instruments. A Harvard Apparatus Company. 2016. Available from http://www.coulbourn.com

Davis M. Neural systems involved in fear and anxiety measured with fear-potentiated startle. American Psychologist. 2006; 61(8):741–756. DOI: 10.1037/0003-066X.61.8.741 [PubMed: 17115806]

Dill DB, Yousef MK, Goldman A, Hillyard SD, Davis TP. Volume and composition of hand sweat of white and black men and women in desert walks. American Journal of Physical Anthropology. 1983; 61(1):67–73. DOI: 10.1002/ajpa.1330610107 [PubMed: 6869514]

Dursa EK, Reinhard MJ, Barth SK, Schneiderman AI. Prevalence of a positive screen for PTSD among OEF/OIF and OEF/OIF-era veterans in a large population-based cohort. Journal of Traumatic Stress. 2014; 27(5):542–549. DOI: 10.1002/jts.21956 [PubMed: 25267288]

Fairchild HH. Scientific racism: The cloak of objectivity. Journal of Social Issues. 1991; 47(3):101–115. DOI: 10.1111/j.1540-4560.1991.tb01825.x

Familoni BO, Gregor KL, Dodson TS, Krzywicki AT, Lowery BN, Orr SP, et al. Rasmusson AM. Sweat pore reactivity as a surrogate measure of sympathetic nervous system activity in trauma-exposed individuals with and without posttraumatic stress disorder. Psychophysiology. 2016; 53(9):1417–28. DOI: 10.1111/psyp.12681 [PubMed: 27286885]

Fowles DC, Christie MJ, Edelberg R, Grings WW, Lykken DT, Venables PH. Publication recommendations for electrodermal measurements. Psychophysiology. 1981; 18(3):232–239. DOI: 10.1111/j.1469-8986.1981.tb03024.x [PubMed: 7291438]

Hamosh A, FitzSimmons SC, Macek M, Knowles MR, Rosenstein BJ, Cutting GR. Comparison of the clinical manifestations of cystic fibrosis in black and white patients. The Journal of Pediatrics. 1998; 132(2):255–259. DOI: 10.1016/S0022-3476(98)70441-X [PubMed: 9506637]

Holt DJ, Lebron-Milad K, Milad MR, Rauch SL, Pitman RK, Orr SP, et al. Goff DC. Extinction memory is impaired in schizophrenia. Biological Psychiatry. 2009; 65(6):455–463. DOI: 10.1016/j.biopsych.2008.09.017 [PubMed: 18986648]

Holt DJ, Coombs G, Zeidan MA, Goff DC, Milad MR. Failure of neural responses to safety cues in schizophrenia. Archives of General Psychiatry. 2012; 69(9):893–903. DOI: 10.1001/archgenpsychiatry.2011.2310 [PubMed: 22945619]

Hwang MJ, Zsido RG, Song H, Pace-Schott EF, Miller KK, Lebron-Milad K, et al. Milad MR. Contribution of estradiol levels and hormonal contraceptives to sex differences within the fear network during fear conditioning and extinction. BMC Psychiatry. 2015; 15(1):295.doi: 10.1186/s12888-015-0673-9 [PubMed: 26581193]

Inslicht SS, Metzler TJ, Garcia NM, Pineles SL, Milad MR, Orr SP, et al. Neylan TC. Sex differences in fear conditioning in posttraumatic stress disorder. Journal of Psychiatric Research. 2013; 47(1):64–71. DOI: 10.1016/j.jpsychires.2012.08.027 [PubMed: 23107307]

Johnson LC, Landon MM. Eccrine sweat gland activity and racial differences in resting skin conductance. Psychophysiology. 1965; 1(4):322–329. DOI: 10.1111/j.1469-8986.1965.tb03264.x [PubMed: 5828005]

Korn CW, Staib M, Tzovara A, Castegnetti G, Bach DR. A pupil size response model to assess fear learning. Psychophysiology. 2016; 54(3):330–343. DOI: 10.1111/psyp.12801 [PubMed: 27925650]

Korol B, Bergfeld GR, Goldman H, McLaughlin LJ. Use of the Pigmentometer, a new device for measuring skin albedo: Relating skin color with a series of physiological measures. The Pavlovian Journal of Biological Science. 1977; 12(1):19–31. DOI: 10.1007/bf03001796 [PubMed: 857232]

Krzywicki AT, Berntson GG, O'Kane BL. A non-contact technique for measuring eccrine sweat gland activity using passive thermal imaging. International Journal of Psychophysiology. 2014; 94(1):25–34. DOI: 10.1016/j.ijpsycho.2014.06.011 [PubMed: 24956027]

Laeng B, Sirois S, Gredebäck G. Pupillometry a window to the preconscious? Perspectives on Psychological Science. 2012; 7(1):18–27. DOI: 10.1177/1745691611427305 [PubMed: 26168419]

Lieblich I, Kugelmass S, Ben-Shakhar G. Psychophysiological baselines as a function of race and ethnic origin. Psychophysiology. 1973; 10(4):426–430. DOI: 10.1111/j.1469-8986.1973.tb00800.x [PubMed: 4719485]

Linnman C, Zeidan MA, Furtak SC, Pitman RK, Quirk GJ, Milad MR. Resting amygdala and medial prefrontal metabolism predicts functional activation of the fear extinction circuit. American Journal of Psychiatry. 2012; 169(4):415–423. DOI: 10.1176/appi.ajp.2011.10121780 [PubMed: 22318762]

Linnman C, Zeidan MA, Pitman RK, Milad MR. Resting cerebral metabolism correlates with skin conductance and functional brain activation during fear conditioning. Biological Psychology. 2012; 89(2):450–459. DOI: 10.1016/j.biopsycho.2011.12.012 [PubMed: 22207247]

Lissek S, Powers AS, McClure EB, Phelps EA, Woldehawariat G, Grillon C, Pine DS. Classical fear conditioning in the anxiety disorders: A meta-analysis. Behaviour Research and Therapy. 2005; 43(11):1391–1424. DOI: 10.1016/j.brat.2004.10.007 [PubMed: 15885654]

Lorber MF. Psychophysiology of aggression, psychopathy, and conduct problems: A meta-analysis. Psychological Bulletin. 2004; 130(4):531–552. DOI: 10.1037/0033-2909.130.4.531 [PubMed: 15250812]

MacNamara A, Rabinak CA, Fitzgerald DA, Zhou XJ, Shankman SA, Milad MR, Phan KL. Neural correlates of individual differences in fear learning. Behavioural Brain Research. 2015; 287:34–41. DOI: 10.1016/j.bbr.2015.03.035 [PubMed: 25819422]

Marin MF, Song H, VanElzakker MB, Staples-Bradley LK, Linnman C, Pace-Schott EF, et al. Milad MR. Association of resting metabolism in the rear neural network with extinction recall activations and clinical measures in trauma-exposed individuals. American Journal of Psychiatry. 2016; 173(9):930–938. DOI: 10.1176/appi.ajp.2015.14111460 [PubMed: 26917165]

Marin MF, Zsido RG, Song H, Lasko NB, Killgore WD, Rauch SL, et al. Milad MR. Skin conductance responses and neural activations during fear conditioning and extinction recall across anxiety disorders. JAMA Psychiatry. 2017; Advance online publication. doi: 10.1001/jamapsychiatry.2017.0329

Martínez KG, Franco-Chaves JA, Milad MR, Quirk GJ. Ethnic differences in physiological responses to fear conditioned stimuli. PloS One. 2014; 9(12):e114977.doi: 10.1371/journal.pone.0114977 [PubMed: 25501365]

Milad MR, Furtak SC, Greenberg JL, Keshaviah A, Im JJ, Falkenstein MJ, et al. Wilhelm S. Deficits in conditioned fear extinction in obsessive-compulsive disorder and neurobiological changes in the fear circuit. JAMA Psychiatry. 2013; 70(6):608–618. DOI: 10.1001/jamapsychiatry.2013.914 [PubMed: 23740049]

Milad MR, Orr SP, Lasko NB, Chang Y, Rauch SL, Pitman RK. Presence and acquired origin of reduced recall for fear extinction in PTSD: Results of a twin study. Journal of Psychiatric Research. 2008; 42(7):515–520. DOI: 10.1016/j.jpsychires.2008.01.017 [PubMed: 18313695]

Milad MR, Orr SP, Pitman RK, Rauch SL. Context modulation of memory for fear extinction in humans. Psychophysiology. 2005; 42(4):456–464. DOI: 10.1111/j.1469-8986.2005.00302.x [PubMed: 16008774]

Milad MR, Pitman RK, Ellis CB, Gold AL, Shin LM, Lasko NB, et al. Rauch SL. Neurobiological basis of failure to recall extinction memory in posttraumatic stress disorder. Biological Psychiatry. 2009; 66(12):1075–1082. DOI: 10.1016/j.biopsych.2009.06.026 [PubMed: 19748076]

Milad MR, Rosenbaum BL, Simon NM. Neuroscience of fear extinction: Implications for assessment and treatment of fear-based and anxiety related disorders. Behaviour Research and Therapy. 2014; 62:17–23. DOI: 10.1016/j.brat.2014.08.006 [PubMed: 25204715]

Milad MR, Zeidan MA, Contero A, Pitman RK, Klibanski A, Rauch SL, Goldstein JM. The influence of gonadal hormones on conditioned fear extinction in healthy humans. Neuroscience. 2010; 168(3):652–658. DOI: 10.1016/j.neuroscience.2010.04.030 [PubMed: 20412837]

Morell MA, Myers HF, Shapiro D, Goldstein I, Armstrong M. Psychophysiological reactivity to mental arithmetic stress in black and white normotensive men. Health Psychology. 1988; 7(5):479.doi: 10.1037/0278-6133.7.5.479 [PubMed: 3215158]

Neta M, Norris CJ, Whalen PJ. Corrugator muscle responses are associated with individual differences in positivity-negativity bias. Emotion. 2009; 9(5):640.doi: 10.1037/a0016819 [PubMed: 19803586]

Öhman A. Electrodermal activity and vulnerability to schizophrenia: A review. Biological Psychology. 1981; 12(2):87–145. DOI: 10.1016/0301-0511(81)90008-9 [PubMed: 7332775]

Orr SP, Metzger LJ, Lasko NB, Macklin ML, Peri T, Pitman RK. De novo conditioning in trauma-exposed individuals with and without posttraumatic stress disorder. Journal of Abnormal Psychology. 2000; 109(2):290.doi: 10.1037//0021-843X.109.2.290 [PubMed: 10895567]

Otto MW, Moshier SJ, Kinner DG, Simon NM, Pollack MH, Orr SP. De novo fear conditioning across diagnostic groups in the affective disorders: Evidence for learning impairments. Behavior Therapy. 2014; 45(5):619–629. DOI: 10.1016/j.beth.2013.12.012 [PubMed: 25022773]

Pineles SL, Nillni YI, King MW, Patton SC, Bauer MR, Mostoufi SM, et al. Orr SP. Extinction retention and the menstrual cycle: Different associations for women with posttraumatic stress disorder. Journal of Abnormal Psychology. 2016; 125(3):349–355. DOI: 10.1037/abn0000138 [PubMed: 26866677]

Roberts AL, Gilman SE, Breslau J, Breslau N, Koenen KC. Race/ethnic differences in exposure to traumatic events, development of post-traumatic stress disorder, and treatment-seeking for post-traumatic stress disorder in the United States. Psychological Medicine. 2011; 41(01):71–83. DOI: 10.1017/S0033291710000401 [PubMed: 20346193]

Rosenbaum BL, Bui E, Marin MF, Holt DJ, Lasko NB, Pitman RK, et al. Milad MR. Demographic factors predict magnitude of conditioned fear. International Journal of Psychophysiology. 2015; 98(1):59–64. DOI: 10.1016/j.ijpsycho.2015.06.010 [PubMed: 26151498]

Schiller D, Monfils MH, Raio CM, Johnson DC, LeDoux JE, Phelps EA. Preventing the return of fear in humans using reconsolidation update mechanisms. Nature. 2010; 463(7277):49–53. DOI: 10.1038/nature08637 [PubMed: 20010606]

Schraufnagel TJ, Wagner AW, Miranda J, Roy-Byrne PP. Treating minority patients with depression and anxiety: What does the evidence tell us? General Hospital Psychiatry. 2006; 28(1):27–36. DOI: 10.1016/j.genhosppsych.2005.07.002 [PubMed: 16377362]

Sevenster D, Beckers T, Kindt M. Fear conditioning of SCR but not the startle reflex requires conscious discrimination of threat and safety. Frontiers in Behavioral Neuroscience. 2014; 8:32.doi: 10.3389/fnbeh.2014.00032 [PubMed: 24616672]

van Well S, Visser RM, Scholte HS, Kindt M. Neural substrates of individual differences in human fear learning: Evidence from concurrent fMRI, fear-potentiated startle, and US-expectancy data. Cognitive, Affective, & Behavioral Neuroscience. 2012; 12(3):499–512. DOI: 10.3758/s13415-012-0089-7

Table 1

Baseline Participant and Study Characteristics

Participant Characteristics	Sample 1	Sample 2	Sample 3	Sample 4a	Sample 4b
Sample Size					
AA	19	29	20	14	13
non-AA	150	31	98	28	26
Age {Mean (*SD*), years}					
AA	34.7(11.0)	33.6(9.6)	38.4(12.3)	39.7(16.2)	31.4(13.4)
non-AA	33.9(12.5)	32.2(9.0)	39.68(13.0)	35.6(13.4)	33.2(14.1)
Gender (% female, *n*)					
AA	73.7%, *n* = 14	100%, *n* = 29	70.0%, *n* = 14	57.1%, *n* = 8	61.5%, n = 8
non-AA	48.7%, *n* = 73*	100%, *n* = 33	55.1%, *n* = 54	75.0%, *n* = 21	57.7%, n = 15
Education (% completed college, *n*)					
AA	unknown	24.1%, *n* = 7	45.0%, *n* = 9	35.7%, *n* = 5	30.8%, n = 4
non-AA	unknown	54.8%, *n* = 17*	54.1.%, *n* = 53	46.4%, *n* = 13	42.3%, n = 11
Diagnostic Status (% clinical diagnosis, *n*)					
AA	52.6%, *n* = 10	44.8%, *n* = 13	85.0%, *n* = 17	57.1%, *n* = 8	76.9%, n = 10
non-AA	42.0%, *n* = 63	51.6%, *n* = 16	74.5%, *n* = 73	50.0%, *n* = 14	80.8%, n = 21
Unconditioned Stimulus Intensity {Mean(*SD*) mA}					
AA	1.76(0.73)	2.28(1.22)	1.88(1.47)	1.59(0.47)	1.90(0.69)
non-AA	2.03(0.99)	2.16(1.01)	2.65(1.73)†	1.92(0.80)	1.91(0.84)
Psychiatric Medication Use (% on medication, *n*)					
AA	10.5%, *n* = 2	0%, *n* = 0	10.0%, *n* = 2	unknown	unknown
non-AA	20.1%, *n* = 31	0%, *n* = 0	11.2%, *n* = 11	unknown	unknown

Study Characteristics	Sample 1	Sample 2	Sample 3	Sample 4a	Sample 4b
Diagnoses	healthy (57%), PTSD (15%), PD (12%), MDD (8%), past PD, currently healthy (9%)	healthy (52%), PTSD (48%)	trauma-exposed healthy (24%), full or subsyndromal PTSD (76%)	healthy (33%), trauma-exposed healthy (14%), GAD (2%), SAD (5%), SP (5%), OCD (17%), PTSD (24%)	healthy (20%) PD (15%), GAD (23%), SAD (21%), SP (21%)
Conditioning stimuli	Colored shapes	Colored shapes	Colored shapes	Colored lamps within contexts	Colored lamps within contexts
Equipment type	Coulbourn	Coulbourn	Coulbourn	Coulbourn	Biopac
Electrode type/size	DOCXS 8mm	DOCXS 8mm	Coulbourn 8mm	DOCXS 8mm	Biopac 11mm
fMRI	No	No	No	Yes	Yes

Note.

† $p < .08$

* $p < .05$ Significant difference between AA and non-AA groups. PTSD = posttraumatic stress disorder, PD = panic disorder, MDD = major depressive disorder, GAD = generalized anxiety disorder, SAD = social anxiety disorder, SP = specific phobia, OCD = obsessive compulsive disorder.

Table 2

Dichotomous Outcomes for Samples 1-4

	Sample 1		Sample 2		Sample 3		Sample 4a (Coulbourn)		Sample 4b (Biopac)	
	AA	Non-AA	AA	Non-AA	AA	Non-AA	AA	Non-AA	AA	Non-AA
Primary Outcomes										
Unmeasurable SCL	0% (0/8)[a]	0% (0/77)[a]	37.9% (11/29)	12.9% (4/31)	25.0% (5/20)	5.1% (5/98)	0% (0/14)	14.3% (4/28)	0% (0/13)	0% (0/26)
	-		Fisher's exact $p = .04$		$\chi^2(1, n = 118) = 8.48$ $p = .004$		Fisher's exact $p = .18$		-	
SCR Non-Responder Status	26.3% (5/19)	10.0% (15/150)	16.7% (3/18)	14.8% (4/27)	20.0% (3/15)	6.5% (6/93)	7.1% (1/14)	8.3% (2/24)	0% (0/13)	4.3% (1/26)
	$\chi^2(1, n = 169) = 4.30$ $p = .04$		Fisher's exact $p = 1.00$		Fisher's exact $p = .11$		Fisher's exact $p = .70$		Fisher's exact $p = .67$	
Total	26.3% (5/19)	10.4% (15/150)	48.3% (14/29)	24.2% (8/31)	40.0% (8/20)	11.2% (11/98)	7.1% (1/14)	21.4% (6/28)	0% (0/13)	4.3% (1/26)
	$\chi^2(1, n = 169) = 4.30$ $p = .04$		$\chi^2(1, n = 60) = 3.26$ $p = .07$		$\chi^2(1, n = 118) = 10.18$ $p = .001$		Fisher's exact $p = .24$		Fisher's exact $p = .67$	
Secondary Outcomes										
Differential Non-Responder Status	71.4% (10/14)	40.0% (54/135)	66.6% (10/15)	56.5% (13/23)	33.3% (4/12)	46.0% (40/87)	46.2% (6/13)	22.7% (5/22)	69.2% (9/13)	28.0% (7/25)
	Fisher's exact $p = .04$		$\chi^2(1, n = 38) = 0.39$ $p = .53$		Fisher's exact $p = .54$		$\chi^2(1, n = 35) = 2.08$ $p = .15$		Fisher's exact $p = .02$	

Notes. AA = African American, Non-AA = Non-African American, SCL = skin conductance level, SCR = skin conductance response

[a]In this sample, this variable was only available for some participants ($n = 85$).

Table 3

Continuous Secondary Outcomes for Samples 1-4

Outcome	Sample 1		Sample 2		Sample 3		Sample 4a (Coulbourn)		Sample 4b (Biopac)	
	AA (*n* = 14)	Non-AA (*n* = 135)	AA (*n* = 15)	Non-AA (*n* = 23)	AA (*n* = 12)	Non-AA (*n* = 87)	AA (*n* = 13)	Non-AA (*n* = 22)	AA (*n* = 13)	Non-AA
Habituation SCL	2.94(3.20)[a]	7.41(5.33)[a*]	2.19(1.27)	4.73(4.73)*	1.93(1.37)	3.57(2.85)[t]	2.28(1.22)	3.17(4.36)	3.45(3.34)	10.19(6.74)**
Unconditioned	0.96(0.86)	1.67(1.10)*	0.94(0.81)	1.75(0.88)**	1.05(0.80)	1.34(1.28)	1.96(3.02)	1.62(2.96)	1.47(0.69)	3.12(2.57)*
SCR SCR to CS+	0.24(0.17)[b]	0.82(0.80)[b***]	0.25(0.16)	0.38(0.43)	0.52(0.36)	0.49(0.37)	0.41(0.21)	0.34(0.27)	0.23(0.18)	0.63(0.47)***
Differential SCR	0.02(0.14)[b]	0.40(0.63)[b*]	0.02(0.18)	0.12(0.33)	0.30(0.32)	0.17(0.24)	0.08(0.09)	0.24(0.19)**	0.10(0.20)	0.38(0.32)**

Notes.

[t] $p < .08$

[*] $p < .05$

[**] $p < .01$

[***] $p < .001$

AA = African American, Non-AA = Non-African American, SCL = skin conductance level, SCR = skin conductance response

[a] Due to the age of the sample, this variable was only available for some participants ($n = 82$).

[b] Square-rooted data not available; raw data was used.