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Authors

Lebares, Carter C

Coaston, Troy N

Delucchi, Kevin L

et al.

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Enhanced Stress Resilience Training in Surgeons:

Iterative Adaptation and Biopsychosocial Effects in 2 Small Randomized Trials

Carter C. Lebares, MD[*], Troy N. Coaston, BS[*], Kevin L. Delucchi, PhD[†], Ekaterina V. Guvva, BS[*], Wen T. Shen, MD[*], Adam M. Staffaroni, PhD[‡], Joel H. Kramer, PsyD[‡], Elissa S. Epel, PhD[†,¶], Frederick M. Hecht, MD[§,¶], Nancy L. Ascher, MD, PhD[*], Hobart W. Harris, MD, MPH[*], Steven W. Cole, PhD[||]

[*]Department of Surgery, University of California San Francisco, San Francisco, California;

[†]Department of Psychiatry, University of California San Francisco, San Francisco, California;

[‡]Department of Neurology, Weill Institute for Neurosciences, University of California San Francisco, San Francisco, California;

[§]Department of Internal Medicine, University of California San Francisco, San Francisco, California;

[¶]Osher Center for Integrated Medicine, University of California San Francisco, San Francisco, California;

[||]Department of Psychiatry & Biobehavioral Sciences, and Department of Medicine, University of California, Los Angeles.

Abstract

Objective: To determine the effects of ESRT (an iteratively adapted and tailored MBI) on perceived stress, executive cognitive function, psychosocial well-being (ie, burnout, mindfulness), and pro-inflammatory gene expression in surgical (ESRT-1) and mixed specialty (ESRT-2) PGY-1 volunteers.

Summary of Background and Data: Tailored MBIs have proven beneficial in multiple high-stress and high-performance populations. in surgeons, tailored MBIs have been shown to be feasible and potentially beneficial, but whether mindfulness-based cognitive training can improve perceived stress, executive function, well-being or physiological distress in surgical and nonsurgical trainees is unknown.

Methods: In 2 small single-institution randomized clinical trials, ESRT, a tailored mindfulness-based cognitive training program, was administered and iteratively adapted for first-year surgical

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Carter.Lebares@ucsf.edu.
Author Contributions
Study conception and design: Lebares.
Acquisition of data: Lebares, Guvva, Shen.
Analysis and interpretation of data: Lebares, Cole, Delucchi, Guvva, Staffaroni, Coaston.
Drafting of manuscript: Lebares, Cole, Coaston, Staffaroni, Epel.
Critical revision: Lebares, Harris, Ascher, Delucchi, Epel, Hecht, Cole.

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The authors report no conflicts of interest.

(ESRT-1, 8 weekly, 2-hour classes, n = 44) and mixed specialty (ESRT-2, 6 weekly, 90-minute classes, n = 45) resident trainees. Primary and secondary outcomes were, respectively, perceived stress and executive function. other prespecified outcomes were burnout (assessed via Maslach Burnout Inventory), mindfulness (assessed via Cognitive Affective Mindfulness Scale - Revised), and pro-inflammatory gene expression (assessed through the leukocyte transcriptome profile “conserved transcriptional response to adversity”).

Results: Neither version of ESRT appeared to affect perceived stress. Higher executive function and mindfulness scores were seen in ESRT-1, and lower emotional exhaustion and depersonalization scores in ESRT-2, at pre-/post-intervention and/or 50-week follow-up (ESRT-1) or at 32-week follow-up (ESRT-2), compared to controls. Pooled analysis of both trials found ESRT-treated participants had reduced pro-inflammatory RNA expression compared to controls.

Conclusions: This pilot work suggests ESRT can variably benefit executive function, burnout, and physiologic distress in PGY-1 trainees, with potential for tailoring to optimize effects.

Keywords

burnout; cognitive training; mindfulness; performance enhancement; stress resilience; surgery; wellbeing

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Stress is inherent to the practice of medicine, yet formal skills for managing stress are absent from medical training. Among physicians, overwhelming stress has been linked to burnout,[1–4] which is strongly associated with physician depression and alcohol abuse,[4–6] and suboptimal performance, patient outcomes, and healthcare economics.[7–11] Growing international consensus recognizes that the antidote to burnout depends equally on institutional, systemic, and individual factors,[12,13] framing this as a critical issue that requires intervention on multiple levels. Almost 40% of general surgery residents report high burnout,[4] with increased risk of depression, suicidal ideation, anxiety, and alcohol abuse.[1,3,4] Chronic stress potentiates these risks,[1–4] and in multiple populations is linked to detrimental effects on learning, decision making, and performance.[7,8,14,15]

Mindfulness-based interventions (MBIs) are individually-based and promising in terms of benefits to well-being and performance in other high-stress populations.[16–20] In surgeons, tailored MBIs have been shown to be feasible[21] and potentially beneficial,[21–23] but more definitive data are needed to justify wider recommendation and the commitment of resources.

To address this gap, we iteratively modified Mindfulness-Based Stress Reduction (MBSR),[24] the most scientifically-studied MBI to date, enhancing its feasibility and acceptability in the context of graduate medical education.[21] The resultant curriculum, enhanced stress resilience training (ESRT) reflects cultural and logistical tailoring to optimize effectiveness and sustainable implementation.[25] In 2 exploratory randomized trials of post-graduate year-1 (PGY-1) residents, ESRT-1 (2016–2017) and ESRT-2 (2018) were tested against active controls. Here we report our findings in regard to effects on perceived stress, executive cognitive function, measures of psychological well-being, and pro-inflammatory gene expression.

METHODS

Trial Overview

In 2016 and 2017, we conducted a partially-blinded, pilot, parallel group randomized trial (NCT#03141190) with 1:1 allocation of PGY-1 residents to ESRT-1 (n = 23) versus active Control-1 (n = 21). ESRT-1 participants (100% surgical) were categorical, preliminary, and designated subspecialty surgical residents all assigned to PGY-1 training in General Surgery. In 2018, we repeated this trial design (NCT#03518359) with 1:1 allocation of PGY-1 residents to ESRT-2 (n = 23) versus active Control-2 (n = 22, Fig. 1). ESRT-2 participants (57% surgical) included nonsurgical PGY-1s to explore generalizable acceptability of the intervention. In both trials, eligible participants were PGY-1 residents at University California San Francisco, without current daily mindfulness meditation practice, who volunteered, provided informed consent and were blinded as to assignment: both arms were told they would receive an intervention designed at our institution to help them manage stress (Table 1). They received no financial compensation. All data were collected at the UCSF Sandler Neurosciences Center and analysis was done on de-identified data.

Interventions

ESRT-1 comprised 8 weekly 2-hour classes, focused on the development of mindfulness meditation skills using culturally acceptable language. ESRT-2 comprised 6 weekly 90-minute classes, focused on similar skills but more explicitly applied to surgery, hospital-based work, and challenges of maintaining well-being during demanding training.

Both interventions occurred during protected time and were centered on the development of 3 key cognitive skills: interoception (ie, moment-to-moment awareness of thoughts, emotions, and sensations),[26] emotional regulation (ie, development of nonreactivity in response to these stimuli),[27] and meta-cognition (ie, conscious awareness of these cognitive control processes).[28] These skills were taught through experiential training in various contemplative practices (breathing, body-scan, qi gong), and scaffolded onto a conceptual framework explaining their relationship to cognitive training and behavior change for the purpose of enhancing stress resilience in physicians. Both interventions involved a voluntary off-site weekend “retreat hike,” after week 4, and 20 minutes of prescribed daily skills practice (contemplative practice for ESRT-1 and −2 and any relaxing activity for both Controls) outside of class.

ESRT-1 and −2 differed with respect to intervention frequency and duration, greater emphasis on formal (ie, dedicated) practice time in ESRT-1, greater emphasis on informal (ie, “throughout the day”) practice time in ESRT-2, and explicit contextualization of ESRT-2 to the personal and professional circumstances of physicians and surgeons (Table 2).

Both interventions employed the same instructor, formally trained in the delivery of MBSR, with >10 years’ experience teaching MBSR and >10,000 hours of personal contemplative practice. Iterative modifications to increase feasibility and acceptability were derived from past participant focus groups and narrative feedback, and interviews with surgical and nonsurgical residency program directors. Modifications were then reviewed against the literature and discussed with MBI experts, to ensure maintenance of effective elements and essential philosophical underpinnings. Finalized modifications were practiced outside of class before being delivered to study participants. No subsequent sessions were offered between course completion and follow-up.

Controls

For surgeons, Control-1 and Control-2 (described else-where),[21] were of equal length and duration as the intervention, held during protected time, and involved group reading and discussion of lay articles pertaining to stressful and challenging aspects of surgical/medical training, led by a senior surgical faculty facilitator (W.S.). For nonsurgeons, Control-2 sessions were of equal length and duration as the intervention, held during protected time, and involved flipped classroom learning of work-related topics, in a relaxed environment with various dedicated faculty.

Outcomes

The primary and secondary outcomes were, respectively, the difference in perceived stress and difference in executive function between treatment conditions immediately after the intervention and at follow-up. Additional prespecified outcomes were differences in burnout, mindfulness, and pro-inflammatory gene expression between treatment conditions immediately after the intervention and at follow-up. Outcomes were assessed at baseline (T1, before the start of intern year), immediately postintervention (T2), and at follow-up (T3; 50-weeks for ESRT-1 and 32-weeks for ESRT-2).

Perceived Stress, Executive Cognitive Function, Psychosocial Well-being—To evaluate effects on perceived stress, we administered Cohen's Perceived Stress Scale-10 perceived stress scale-10,[33] a reliable, published questionnaire used in our prior work,[1,22] scored according to published methods. To evaluate effects on executive cognitive function, we used the computer- and paper-based NIH EXAMINER (Executive Abilities: Measures and Instruments for Neurobehavioral Evaluation and Research),[22,35] which comprises tasks targeting 4 cognitive domains (working memory, inhibition, set shifting, fluency) that subserve higher-order cognitive functions such as problem-solving and complex technical procedures. A global Executive Composite score was calculated using item response theory, according to established procedures.[35] EXAMINER was developed to avoid ceiling effects, maintain validity within multiple demographic groups, and be suitable for repeat administration in clinical trials.

To evaluate effects on measures of psychosocial well-being, participants completed an online survey which included the Cognitive Affective Mindfulness Scale-Revised (CAMS-R),[32] and the abbreviated (9-item) Maslach Burnout Inventory-Human Service Survey (ESRT-1)[3] or a validated 2-item screen for high emotional exhaustion and high depersonalization (ESRT-2),[34] all reliable and published questionnaires used in our prior work.[1,22]

Pro-inflammatory Gene Expression—To quantify the physiological impact of ESRT, we analyzed pre- to post-intervention change in activity of stress-induced pro-inflammatory molecular signaling pathways (NF-κB and AP-1), stress-inhibited Type I interferon signaling pathway (ISRE), and the cAMP response element binding protein (CREB) beta-adrenergic signaling pathway, which comprise the well-defined stress-related RNA profile known as the conserved transcriptional response to adversity (CTRA).[29,30] Using TELiS promoter-based bioinformatic analysis of genome-wide RNA transcriptional profiles of circulating blood samples,[30,31] we were able to quantify intra-individual change over time in activity of CREB, NF-κB, and AP-1, and ISRE.

Whole blood samples (PAXgene RNA tubes) from ESRT-1 and −2 were stored at −80C and shipped in a single batch to the UCLA Social Genomics Core Laboratory for RNA extraction (Qia-gen RNeasy), verification of suitable RNA mass (Thermo-Fisher Quant-it Ribo Green) and quality (Agilent TapeStation capillary electrophoresis), and genome-wide transcriptional profiling using a high-efficiency 3 mRNA-targeted transcript counting assay (Lexogen QuantSeq 3’ FWD) with multiplex cDNA sequencing on an Illumina HiSeq 4000 instrument in the UCLA Neuroscience Genomics Core Laboratory, all following the manufacturers’ standard protocols.

Sequencing targeted >10 million single-stranded 65 nt sequencing reads for each sample (achieved mean 18.2 million), mapped to the hg38 reference human transcriptome sequence using the STAR aligner[31] (achieved mean mapping rate 94.8%). Gene expression was quantified as transcripts per million mapped reads, floored at 1 to suppress spurious low-range variability, and log2-transformed to stabilize variance.

All genes showing a point estimate of> 1.5-fold differential change over time (difference: T2-T1) across groups served as input into bioinformatic analyses conducted as previously described[31] using JASPAR c-REL, JASPAR c-FOS, TRANSFAC V$ISRE_01, and TRANSFAC V$CREB_02 position-specific weight matrices. Point estimates were adjusted for any potential effects of differential leukocyte subset prevalence by including in the linear statistical model parallel measures of change in expression of 8 mRNAs encoding major leukocyte subset indicators (*CD3E, CD3D, CD19, CD4, CD8A, CD16/FCGR3A, CD56/NCAM1, CD14*). All analyses were conducted over 9 parametric combinations of core promoter length (−300, −600, and −1000 to +200 nucleotides relative to the RefSeq gene transcription start site) and transcription factor-binding motif detection stringency (TRANSFAC mat_sim values of 0.80, 0.90, and 0.96), with the average (log2) transcription factor-binding motif ratio for >1.5-fold up- versus downregulated promoters tested for statistically significant difference from 0 using standard errors derived from bootstrap resampling of linear model residual vectors (which controls for dependence across genes).

This gene expression analysis plan was prespecified to focus solely on the pooled ESRT-1 and −2 cohort because we hypothesized that ESRT would have generally positive effects on inflammatory signaling (due to reduction in stress biology) based on studies of other MBIs in stressed populations.[29,30] We did not attempt to analyze the ESRT-1 and −2 cohorts separately because such analyses would lack statistical power due to reduced sample size in each separate analysis, based on our prior work.[29–31]

Data Analysis

Sample size was based on practical limits of time and participant availability. The annual number of incoming surgery or nonsurgery PGY-1s at a single institution is fixed and created the pool from which we could recruit. Thus, for this pilot work (guided by the advice of K.D., a senior faculty biostatistician), we did not conduct a statistical power analysis as this would not have changed the design of the study and the estimated detectable effect size would not be meaningful without some context. With those caveats, we enrolled all available participants (volunteers, within designated specialties, meeting inclusion criteria). Because participants were randomized to treatment condition, we compared outcomes using t-tests at end of treatment (T2) and follow-up (T3). As a check on the influence of baseline variation, we repeated comparisons using ANCOVA with the baseline value of the outcome as a covariate. To check on the influence of nonsurgical participants (ESRT-2) and the inclusion of drop-outs (ESRT-1 and −2), statistical models were re-estimated with and without their inclusion. Data are summarized as mean and standard deviation, unless otherwise specified. All calculations were done using SAS Version 9.4 (SAS Institute Inc, Cary, NC).

RESULTS

Participants

In 2016 and 2017, 44 surgery PGY-1s were allocated using computer-generated randomization,[36] blocking for sex and surgical sub-specialty, to ESRT-1 or Control-1. Two residents were withdrawn in 2016 and 2 in 2017 by their (same) parent program due to perceived conflict with other obligations. In 2016, withdrawal occurred after allocation and baseline assessment. In 2017, withdrawal occurred after allocation, but before baseline assessments. None of the 4 withdrawals attended any intervention or control classes. One female allocated to Control-1 mistakenly attended the first week of ESRT-1 and was allowed to continue in the intervention arm. Thus, analysis included 22 ESRT-1 and 18 Control-1 participants (Table 1 and Fig. 1).

In 2018, an identical process was followed for 45 PGY-1s, with additional blocking by nonsurgical specialty, before computer-generated randomization[36] to ESRT-2 or Control-2. After T1 assessment and attending 1 of 6 classes, 2 intervention females (both nonsurgical) dropped out. No participants were withdrawn. One male control mistakenly attended the first week of ESRT-2 and was allowed to continue in the intervention arm. Thus, analysis included 22 ESRT-2 and 21 Control-2 participants (Table 1 and Fig. 1).

Attendance, Attrition, and Adherence

Total absences were minimal (≤10%) across all trials, populations, and conditions; 80% were attributable to scheduled vacations or emergent patient situations. The remainder were attributable to over-sleeping. Attrition was limited to 2 female participants (both nonsurgical), who dropped from ESRT-2 (intervention arm) due to disinterest in performing home practice and feeling “overloaded” by additional obligations.

Practice data was reported via daily (ESRT-1) or twice-weekly (ESRT-2) participant texts. For both studies, intervention and control arms differed significantly in home practice days per week [ESRT-1: 4.9 (0.64) vs 5.3 (0.35) days, $P = 0.04$, ESRT-2: 4.0 (0.14) vs 5.2 (0.35) days, $P = 0.03$] and minutes per day [ESRT-1: 13.6 (3.2) vs 26.3 (6.3) minutes, $P < 0.001$, ESRT-2: 9.2 (0.59) vs 24.3 (1.5) minutes, $P < 0.001$].

The ESRT-1 and −2 intervention arms differed significantly in home practice days per week [ESRT-1 = 4.9 (0.64) days vs ESRT-2 = 3.9 (1.17) days, $P = 0.015$] and minutes per day [ESRT-1 = 13.6 (3.2) minutes vs ESRT-2 = 9.2 (0.59) minutes; $P < 0.001$].

Within the ESRT-2 intervention cohort, surgical versus nonsurgical participants also differed significantly in home practice days per week [3.5 (0.18) vs 4.6 (0.2) days, $P < 0.001$] and minutes per days [respectively, 8.1 (0.67) vs 11.5 (0.83) minutes, $P < 0.001$].

Perceived Stress, Executive Cognitive Function, and Psychological Well-being

Perceived stress did not differ significantly between intervention and control arms in either trial (Table 3). In ESRT-1, compared to Control-1, executive cognitive function (Executive Composite score) was significantly higher at T3 (Cohen $d = 0.89$), whereas mindfulness (CAMS-R) was significantly higher at T2 and T3 (Cohen $d = 1.03$ and 0.78, respectively). Burnout (EE and DP) did not differ significantly (Table 3). In ESRT-2, compared to Control-2, executive cognitive function (executive composite score) was not significantly different at T2 or T3, and neither was mindfulness (CAMS-R), but emotional exhaustion (EE) was significantly lower at T2 and T3 (Cohen $d = 0.67$ and 0.81, respectively), as was depersonalization (DP) at T3 (Cohen $d = 0.69$, Table 3).

Additional comparisons using ANCOVA analysis with baseline score as covariate, or including drop-outs, resulted in no substantive changes; patterns of effect, significance, and/or strong effect sizes were the same (data not shown).

Pro-inflammatory Gene Expression

The results of bioinformatic analysis of genome-wide RNA sequencing of circulating blood samples showed that in pooled Controls, AP-1 activity was significantly upregulated from T1 to T2 [1.78-fold, 95% confidence interval (1.07, 2.95), $P = 0.028$] but there was no significant change in NF-κB, ISRE, or CREB activity [0.67-fold (0.38, 1.17), $P = 0.157$, 1.00-fold (0.43, 2.30), and 1.60-fold (0.80, 3.21), respectively]. Compared to Controls, pooled ESRT participants showed a significant relative reduction in activity of all 3 stress-stimulated signaling pathways from T1 to T2 [NF-κB: 0.74-fold (0.56, 0.99), $P = 0.043$; AP-1: 0.73-fold (0.54, 0.97), $P = 0.031$; CREB: 0.63-fold (0.40, 0.99), $P = 0.048$; Fig. 2]. Type I interferon signaling showed the expected relative increase, but that difference was not statistically significant [1.40-fold (0.74, 2.63), $P = 0.304$].

DISCUSSION

The results of our 2 pilot trials of ESRT versus control show that in surgical and nonsurgical PGY-1 residents, neither ESRT-1 nor −2 benefit perceived stress, but ESRT-1 does benefit executive cognitive function. The former finding may represent a lack of sensitivity on the part of our stress measure, a lack of statistical power, or the inability of ESRT/MBIs to impact the magnitude of stress associated with PGY-1 training. The latter finding is supported by our observation that Executive Composite scores in ESRT-1 intervention participants were significantly higher than controls, appearing to evolve over time (at T3). These results echo our prior work,[25] and improvements in executive function seen with the use of MBIs in predeployment military cohorts and Marines.[43,44] They are particularly striking as executive cognitive function is widely acknowledged as being critical to problem-solving and the execution of complex procedures - skills clearly essential for surgeons.

Our study also shows that ESRT-1 benefits mindfulness, as supported by our observation of significantly higher mindfulness scores (at T2 and T3) in the ESRT-1 intervention group versus controls. Similar effects were shown in small trials of primary care and internal medicine physicians undergoing MBIs[17,37,38] and higher mindfulness scores have been shown to correlate with greater resilience, better coping, and less implicit bias in nonsurgical residents and allied health profesionals.[39–42] The decrements observed in intervention mindfulness scores between T2 and T3 may reflect the presence of on-going stressors in the absence of any further formal intervention. Notably, this change does not negate net increases over baseline.

ESRT-2 was found to mitigate the development of burnout, as evidenced by significantly lower scores for emotional exhaustion (at T2 and T3) and depersonalization (at T3) in ESRT-2 intervention versus controls. Both arms showed steady increases in emotional exhaustion scores over 32-weeks of follow-up, with the most prominent increase occurring in controls between T1 and T2. This effect was dramatically curtailed in the intervention, suggesting that emotional exhaustion may be especially potent early in training and that ESRT-2 may be particularly beneficial at this time. Depersonalization showed a similar pattern of steady increase in both arms over 32-weeks, with ESRT-2 showing benefits that only become statistically significant at T3. The reasons for this delayed benefit are unclear, although longitudinal studies of large mixed-specialty physician cohorts in the Netherlands[45,46] suggest that depersonalization develops after emotional exhaustion by a process not yet fully understood. Like the effect of ESRT-1 on executive cognitive function, the effect of ESRT-2 on depersonalization seems to evolve over time.

Finally, our results show that ESRT ameliorates physiologic distress, as evidenced by a 30%–40% relative reduction in the CTRA gene expression signature relative to controls. We assessed the CTRA using bioinformatic analyses of signaling pathway activity for 2 pro-inflammatory signaling pathways that are upregulated by SNS activity (NF-kB and AP-1), the Type I interferon signaling pathway that is downregulated by SNS activity (ISRE), and the CREB signaling pathway that mediates sympathetic neurotransmitter signaling through beta-adrenergic receptors.[29] All of these pathways showed directional changes consistent with a relative reduction in SNS signaling in ESRT-exposed interns, and these effects were statistically significant in 3 of the 4 analyzed pathways. Previous randomized controlled experiments in both healthy and disease-affected populations found that MBIs can simultaneously reduce measures of psychological distress and reduce the *CTRA* gene expression profile,[29] suggesting a similar process may be at work here. The health significance of the observed reductions in CTRA gene expression remain to be clarified in future research, although the CTRA has been shown to be prognostic of poor health outcomes in other populations.[29]

The differential effects of ESRT-1 and −2 seen here may be attributable to differences in home practice time, course duration, or class content. The finding of greater home practice among controls (assigned "any non-work-related activity") is expected, as intervention home practice was, in contrast, effortful. The finding of greater home practice among ESRT-1 versus ESRT-2 intervention participants may be due to greater in-class exposure to skills and techniques in ESRT-1 (thereby creating a stronger foundation for new habits), or may reflect the fact that ESRT-2 had greater emphasis on "informal" (ie, "throughout the day") practice which was not explicitly recorded/collected. Finally, the finding of greater home practice among nonsurgeons is also not surprising in light of the widely recognized extreme workload of surgery residents, nearly obliterating discretionary time. Interestingly, the majority (90%) of surgical intervention participants in both trials still managed to practice consistently for the entire course.

Whether practice differences translate to differences in outcomes is unclear, as our trials were not designed to answer this. Nevertheless, a recent well-designed RCT showed dose and delivery effects on executive function in Marines undergoing a tailored MBI,[43] which supports the interpretation that the higher "dose" of mindfulness training in ESRT-1 (greater number of classes and longer class duration) may be responsible for the differential effects seen in improvements to executive function between ESRT-1 and ESRT-2 cohorts. Whether such as effect would be seen with ESRT-2, if followed for 50- rather than just 32-weeks, is unknown.

The course content of ESRT-2 was much more explicitly focused than ESRT-1 on applying skills to the physical, temporal, and emotional challenges of surgical training, professional interactions, and the cultivation of well-being during a demanding residency. Perhaps this difference explains the greater effect on burnout (which is defined as a work-related syndrome) in ESRT-2 versus ESRT-1. We used different scales to evaluate burnout in ESRT-1 (9-item abbreviated MBI) and ESRT-2 (2-item validated screen for high emotional exhaustion and high depersonalization). Nevertheless, the 2-item screen has been rigorously evaluated for concurrent validity as compared to the MBI, specifically in practicing surgeons,[34] supporting our interpretation of the 2 measures as being equivalent.

Study limitations include the small sample size, which limited our ability to explore the effects of dose and delivery and interaction effects due to specialty or sex, which we suspect are important factors. The generalizability of our findings is limited by the use of a resident population that was homogeneous in terms of training level (all PGY-1s), execution at a single institution, and the use of the same instructor for both trials (although prudent for work not designed to explore instructor effects). Although a mixed population (surgeon and nonsurgeon) was used in ESRT-2 to explore feasibility across specialties, the small sample size limits any definitive conclusions in this regard. Although participants were blinded to assignment and asked not to discuss class content between arms, communication was certainly possible and should be considered in evaluating our results. Additional limitations include the use of volunteers, and not accounting for informal practice (a potential source of extra-curricular mindfulness practice), which are current issues in the field of MBI research as a whole. The control experience differed somewhat for surgery and nonsurgery control cohorts in ESRT-2, introducing an unaccounted-for element with an unknown impact on outcomes. It must be noted that the gene expression differences reported here are not highly statistically significant (based on confidence intervals). We report them because they resulted from preplanned analyses and thus shed light on the potential for physiological impact of ESRT. Either omitting them or over interpreting them would be biased, and in the context of a small pilot study we feel they are promising. Nevertheless, it will be important to replicate these findings in future research to assess their statistical reliability and generalizability.

Finally, the effects of ESRT are derived from a single course of intervention (whether ESRT-1 or ESRT-2), without subsequent "boosters." This begs the question of what might be possible with additional training, either reinforcing ESRT fundamentals through regular practice sessions, or extrapolating on them to address specifically challenging aspects of surgery and medicine (such as complications, conflict, or emergencies).

In conclusion, this pilot work suggests ESRT can benefit executive cognitive function, mindfulness, burnout, and pro-inflammatory gene expression in PGY-1 surgical and nonsurgical trainees, with potential for optimization of effects based on adaptations to content and delivery. These highly promising results provide critical guidance for further study of MBIs in surgery and graduate medical education, and provide strong support for the value of pursuing tailored MBIs as an individually-based component of the fight against burnout. Recognizing the benefits of an individually-based intervention should not be confused with assigning the onus of burnout to individual physicians. On the contrary, providing individual-based tools to enhance resilience is a means of re-aligning surgeons to the joys and priorities of our vocation, re-engaging us in demands for institutional and systemic reform that are much more patient-centered, powerful, and compelling.

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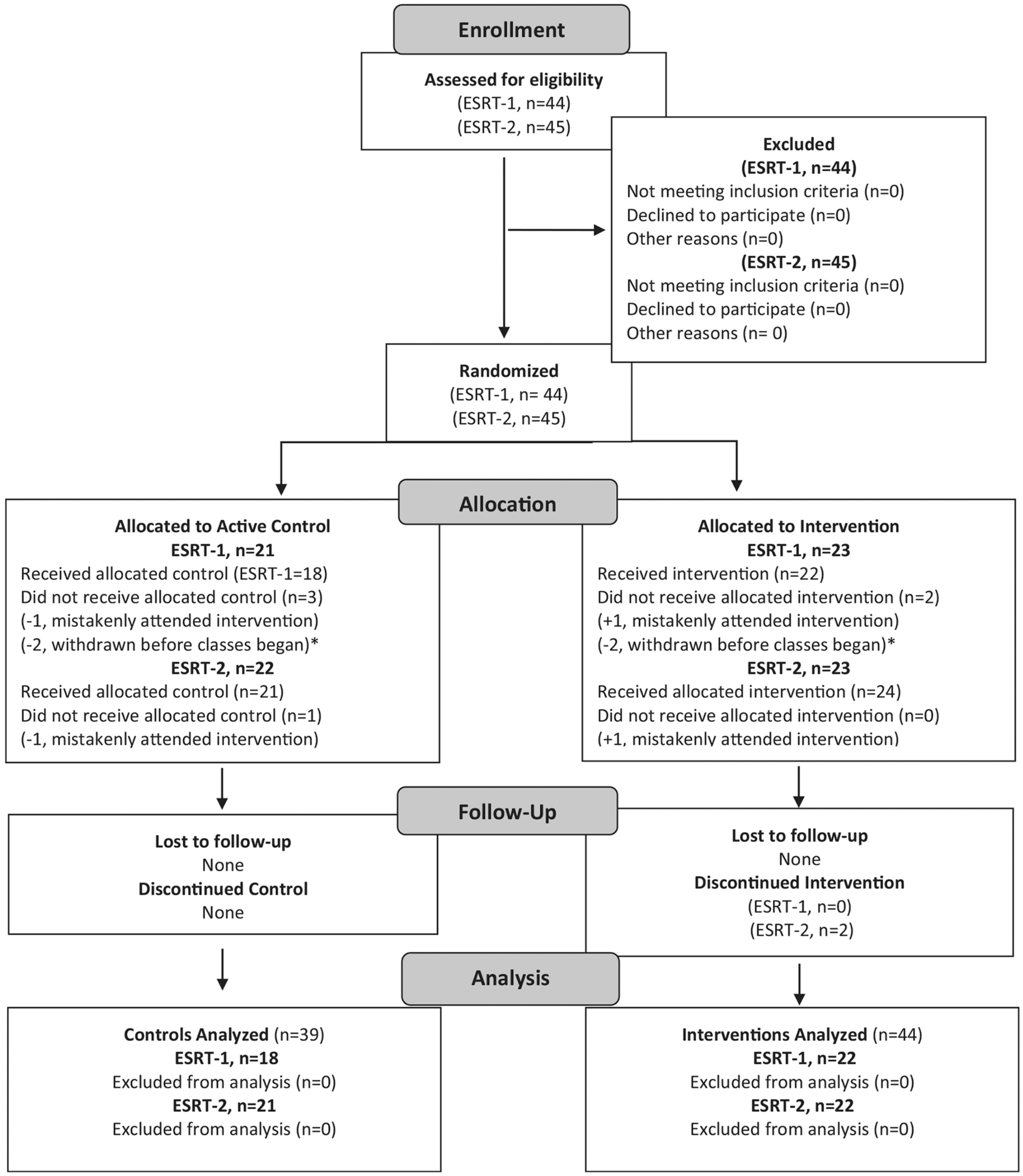

FIGURE 1.

ESRT-1 and −2 CONSORT flow diagram. [a]ESRT-1/Control-1 = 8 weekly, 2-h classes. [b]ESRT-2/Control-2 = 6 weekly, 90-min classes. ESRT indicates Enhanced Stress Resilience Training.

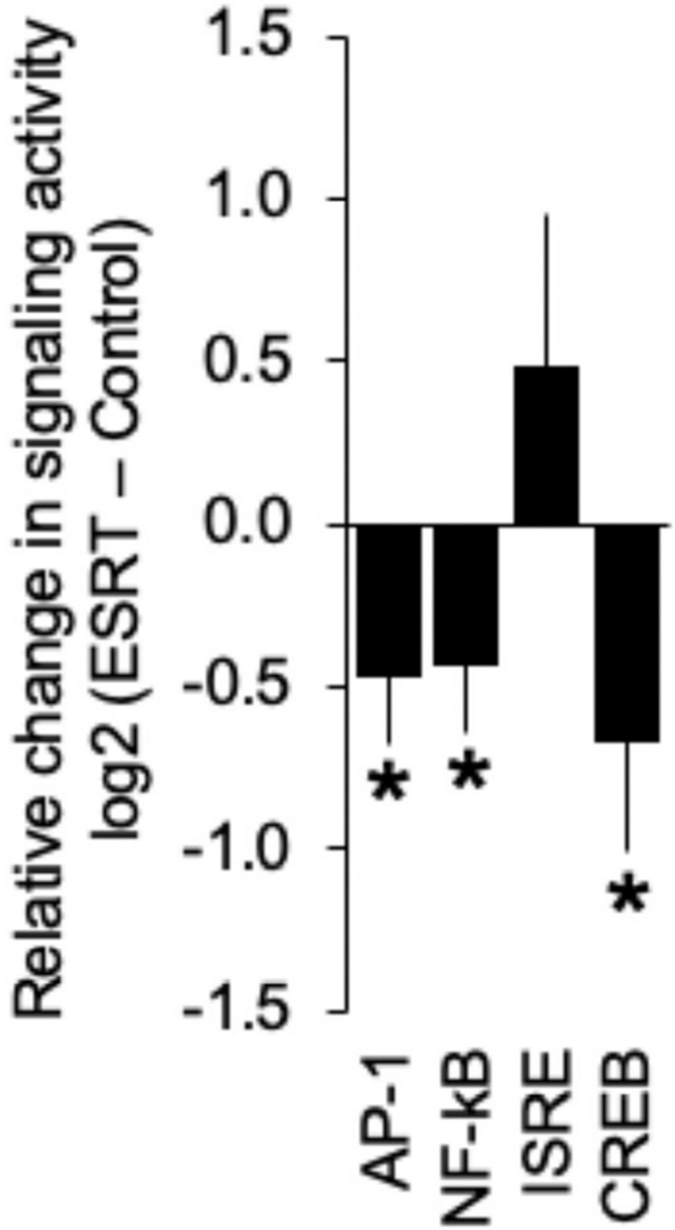

FIGURE 2.

ESRT effect on *CTRA* gene regulation. Relative difference (ESRT - Control) in change from baseline to postintervention follow-up activity of transcription factors upregulated in CTRA (AP-1, NF-κB), downregulated in CTRA (ISRE), or mediating CTRA induction via beta-adrenergic signaling (CREB). $^*P < 0.05$. CTRA indicates conserved transcriptional response to adversity; ESRT, enhanced stress resilience training.

TABLE 1.

Demographic Characteristics of Analyzed Study Samples

Characteristic	Control-1* n = 18 (%)	ESRT-1* n = 22 (%)	Control-2† n = 21 (%)	ESRT-2† n = 22 (%)
Age, mean (SD)	28.6 (2.7)	27.4 (2.1)	28.7 (2.2)	28.8 (2.4)
Sex				
Male	12 (67)	8 (36)	12 (57)	11 (50)
Female	6 (33)	14 (64)	9 (43)	11 (50)
Race/ethnicity				
White	11 (61)	16 (73)	11 (52)	14 (64)
Black	1 (6)	1 (5)	3 (14)	4 (18)
Asian American	6 (33)	4 (18)	6 (29)	3 (14)
Hispanic	—	1 (5)	1 (5)	1 (5)
Subspecialty				
General surgery				
Categorical	2 (11)	6 (27)	4 (19)	3 (14)
Preliminary	4 (22)	3 (14)	1 (5)	3 (14)
Urology	2 (11)	2 (9)	—	—
Otolaryngology	1 (5.5)	1 (4.5)	—	—
Neurosurgery	—	1 (4.5)	—	1 (4.5)
OMFS‡	2 (11)	2 (9)	—	—
Plastic Surgery	1 (5.5)	—	1 (5)	1 (4.5)
Ophthalmology	2 (11)	1 (4.5)	3 (11)	2 (9)
Orthopedics	3 (17)	4 (18)	2 (7)	2 (9)
Radiology	1 (5.5)	2 (4.5)	1 (5)	1 (4.5)
Family Practice	—	—	3 (11)	2 (9)
Emergency Medicine	—	—	6 (29)	6 (27)
OB-Gyn§	—	—	—	1 (4.5)

*ESRT-1/Control-1 = 8 weekly, 2-h classes.

†ESRT-2/Control-2 = 6 weekly, 90-min classes.

‡OMFS = oromaxillofacial surgery.

[§]OB-Gyn = obstetrics and gynecology.

TABLE 2.

Practical and Conceptual Differences Between Traditional MBSR*, ESRT-1,† and ESRT-2‡

Modification	Traditional MBSR	ESRT-1†	Purpose of Modification	ESRT-2‡	Purpose of Modification
Practical					
Class number	9 wk Intro session + 8 wks	8 wk	(L) To utilize 8 wk summer gap in didactics	6 wk	(C) Further minimize clinical disruption
Class duration	2.5 h Emergent, metaphorical, breaks, didactics	2 h Focused discussions and didactics, no break	(L) Provide protected time, while preserving 80 h work-week, educational and OR time	1.5 h Explicit, short video-based conceptual content	(L, C) To enhance acceptability and accessibility
Retreat	8 h silent sitting retreat, off-site meditation center	3 h “Medi Hike,” local nature preserve	(C) Request for fresh air and exercise	No change	
Assigned daily practice time	45 min daily	20 min daily	(C) Responsive to time-compressed surgical lifestyle	Goal is consistency, ideal is 20 min, encourage informal practice	(C) “Failing” at 20 min, added to participant stress (*Type A personality*)
Conceptual					
Class content	1.5 h - Meditation 1 h - sharing, stories, meandering approach	1.5 h - Meditation 30 min - Less sharing, more focused approach	(L) Preserve experiential focus, shorten class time	1 h - Meditation 30 min - Explicit concepts	(C) Capitalize on culture of skills training, fast learners
Emphasis	Insight, life-long learning about self, world. Broad health enhancement.	Skill set for stress resilience, in general	(C) Application to life, relationships, training, career longevity	Resilience skill set, specific work application, cognitive training.	(C) Growing distress and burnout, modeling ESRT in work, life.
Contextualization	Broad application of concepts, awareness to all interactions	Application to personal and professional situations	(C) Skills applied to surgeons’ life and work	Emphasize applied techniques, all day, various scenarios	(C) Explicit skills for explicit situations, clear mental model
Expectation	Committed formal practice	Daily practice mostly formal, less informal	(C) Reinforce “some is better than none at all”	Train formally, but “Live your practice.” Informal practice, anywhere, all day	(C) Capitalize on natural tendency for repetition and ritual

*MBSR = mindfulness-based stress reduction.

†ESRT-1 = enhanced stress resilience training-1, 8 weekly, 2-h classes, 20 min/d prescribed home practice.

‡ESRT-2 = enhanced stress resilience training-2, 6 weekly, 90-min classes, 20 min/d prescribed home practice.

(C) indicates cultural modification; (L), logistical modification.

TABLE 3.

Perceived Stress, Executive Function, and Burnout Effects of ESRT-1 and ESRT-2 Versus Controls

ESRT-1 Versus Control-1									
Measure	**Time Point**[†]	**Control-1**[‡]	**Mean (n = 18)**	**SD**[§]	**ESRT-1**[‡]	**Mean (n = 22)**	**SD**	***P*-value**	**Cohen *d***
PSS-10[//]	Baseline	17.9		3.47	17.3		4.32	—	—
	Post		18.6	2.75		18.1	3.96	0.61	0.16
	50-wk		17.2	3.70		17.0	4.65	0.84	0.07
Executive Composite[¶]	Baseline		1.52	0.48		1.67	0.44	—	—
	Post		1.69	0.42		1.80	0.40	0.37	0.29
	50-wk		1.71	0.37		2.03	0.35	0.01[*]	**0.89**
CAMS-R[#]	Baseline		25.7	4.07		28.0	5.04	—	—
	Post		25.3	5.10		30.2	4.46	0.003[*]	**1.03**
	50-wk		25.9	4.58		29.5	4.54	0.02[*]	**0.78**
ESRT-2 Versus Control-2									
Measure	**Time Point**[†]	**Control-2**[**]	**Mean (n = 22)**	**SD**[§]	**ESRT-2**[**]	**Mean (n = 22)**	**SD**	***P*-value**	**Cohen *d***
PSS-10[//]	Baseline		14.0	4.90		13.4	5.27	—	—
	Post		17.9	6.06		15.9	4.29	0.22	0.38
	32-wk		16.5	5.66		15.4	5.19	0.32	0.20
EE[††]	Baseline		7.05	5.12		6.1	3.64	—	—
	Post		9.2	4.88		6.4	3.47	0.03[*]	**0.67**
	32-wk		10.9	4.36		7.7	3.32	0.01[*]	**0.81**
DP[‡‡]	Baseline		3.4	3.20		3.1	2.84	—	—
	Post		5.8	5.81		4.3	3.59	0.24	0.37
	32-wk		7.9	4.52		5.1	3.63	0.03[*]	**0.69**

Bold = Cohen *d*, medium (d>/ = 0.5) and large (d>/ = 0.8) effect sizes.

[*] Statistically significant *P*-value.

[†] T1 = baseline score, before start of PGY-1, T2 = postintervention.

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[‡] ESRT-1/Control-1 = 8 weekly, 2-h classes.

[§] SD = standard deviation.

[//] PSS-10 = Cohen perceived stress scale-10 item, higher score is worse, meaning higher perceived stress.

[¶] Executive composite = executive function composite score, higher score is better, meaning greater executive function ability.

[#] CAMS-R = cognitive affective mindfulness scale-revised, higher score is better, meaning greater mindfulness.

[**] ESRT-2/Control-2 = 6 weekly, 90-mi classes.

[††] EE = emotional exhaustion, higher score is worse, meaning more burnout.

[‡‡] DP = depersonalization, higher score is worse, meaning more burnout.