Impact of early life adversity on EMG stress reactivity of the trapezius muscle

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Abstract

Human and animal research indicates that exposure to early life adversity increases stress sensitivity later in life. While behavioral markers of adversity-induced stress sensitivity have been suggested, physiological markers remain to be elucidated. It is known that trapezius muscle activity increases during stressful situations. The present study examined to what degree early life adverse events experienced during early childhood (0–11 years) and adolescence (12–17 years) moderate experimentally induced electromyographic (EMG) stress activity of the trapezius muscles, in an experimental setting. In a general population sample (n = 115), an anticipatory stress effect was generated by presenting a single unpredictable and uncontrollable electrical painful stimulus at t = 3 minutes. Subjects were unaware of the precise moment of stimulus delivery and its intensity level. Linear and nonlinear time courses in EMG activity were modeled using multilevel analysis. The study protocol included 2 experimental sessions (t = 0 and t = 6 months) allowing for examination of reliability.

Results show that EMG stress reactivity during the stress paradigm was consistently stronger in people with higher levels of early life adverse events; early childhood adversity had a stronger moderating effect than adolescent adversity. The impact of early life adversity on EMG stress reactivity may represent a reliable facet that can be used in both clinical and nonclinical studies.

Abbreviations: ACE = adverse childhood experience, Ag/AgCl = silver/silver chloride, ECG = electrocardiography, EMG activity = electromyographic activity, HPA axis = hypothalamic–pituitary–adrenal axis, LTM = left trapezius muscle, RTM = right trapezius muscle.

Keywords: adverse childhood events, childhood adversity, EMG (electromyography), psychophysiology, stress

1. Introduction

Exposure to early life adversity (also called adverse childhood experiences (ACEs), both terms are used interchangeably) is a risk factor for developing affective and psychotic disorders later in life\textsuperscript{[1–4]} and is similarly associated with functional somatic syndromes including pain.\textsuperscript{[5,6]} Exposure to ACEs increases stress sensitivity later in life.\textsuperscript{[7–9]} A stress sensitization model has been hypothesized, which postulates that early life adversity increases vulnerability to mental disorders following adult stressful life events.\textsuperscript{[7–9]} In addition, several studies have demonstrated that ACEs have a lasting impact on adult physiology, including neurobiological processes, immunological processes and autonomous, endocrine and metabolic systems.\textsuperscript{[10–16]} Hamer et al.\textsuperscript{[17]} suggest that (psycho)physiological reactivity to mental stress can be viewed as a robust characteristic, indicating that stress-induced responses do not habituate over (a short period of) time.

Stressors experienced during childhood can be highly variable, including neglect or sexual abuse, but also parental separation or divorce. The literature indicates that significant early life adversity is not rare in western societies.\textsuperscript{[18–20]} Dong et al. demonstrated that different ACEs were significantly interrelated, and that the influence of ACEs on behavior, physical health, and mental disorders is cumulative.\textsuperscript{[9,21]} Age at the time of traumatization also may influence the effects in later life, earlier exposure being associated with more harmful effects.\textsuperscript{[22,23]}

While behavioral markers of trauma-induced stress sensitivity have been suggested,\textsuperscript{[7–9]} physiological markers of trauma-induced stress sensitivity remain to be elucidated. Electromyographic (EMG) stress reactivity may be an interesting candidate physiological marker in relation to early life adversity. It is known that muscle activity increases during stressful situations.\textsuperscript{[24–26]} In particular, trapezius muscle activity can be influenced by stress.\textsuperscript{[24,27–30]} Hamer et al.\textsuperscript{[17]} generated a model in which the trapezius muscle is a possible candidate for examining the impact of early life adversity on a physiological stress-related outcome.

In the present study, we examined the relationship between ACEs and muscle activity in a recently developed stress experiment.\textsuperscript{[26]} In this paradigm, an anticipatory stress effect is generated by inducing both a distinct cognitive stressor and a...
physical painful stimulus. The anticipatory stress effect is mediated by an increase in electromyographic activity (EMG activity) of the trapezius muscle during the prestimulus phase.[26]

The first objective was to investigate the association between ACEs, experienced during early childhood and adolescence, and stress-related trapezius muscle activity. The second objective was to examine the reliability of any influence of ACEs on EMG stress reactivity. A stress experiment was applied, in which a single unpredictable and uncontrollable electrical painful stimulus was presented. Given the relatively high rate of ACEs in the general population,[31,32] a general population sample was included. In order to investigate the reliability of the influence of ACEs on EMG stress reactivity, the study protocol included 2 experimental sessions for each participant. The first took place at the moment of inclusion, the second 6 months later. The protocol was identical across the 2 experimental sessions.

Measuring EMG over time implicates a hierarchical structure of the data, in which consecutive time elements are nested within subjects. This hierarchical structure needs to be taken into account. Consequently, multilevel random regression was used.[13] In addition, it has been shown that EMG activity measured during a stress experiment comprises nonlinear time effects,[26] which can be modeled by multilevel regression. In order to approach the naturalistic effects expected to be present in anticipatory muscle activity, it was decided to include a linear, exponential, and quadratic time effect in the analyses. A linear increase in muscle activity was expected, since the anticipatory stress phase is associated with an increase in tension, resulting in heightened muscle activity. Additionally, nonlinear time effects were also expected. A quadratic time effect could be expected: a parabola opening upwards or downwards, representing either an initial relaxation and a consecutive increase of tension, or an initial building up of muscle activity, followed by a relative relaxation afterwards. In addition to the quadratic time effect, an exponential effect may be present, representing a relatively stable muscle activity during the first part of the anticipation phase, followed by a growth in tension in which the growth is proportional to the current level of tension.

It was hypothesized that exposure to early life adversity, particularly those occurring during early childhood, would be associated with increased trapezius muscle activity during the anticipatory phase of the stress task.

2. Methods

2.1. Ethics statement

The study was conducted according to the principles of the Declaration of Helsinki and approved by the medical ethics committee of the Maastricht University Medical Centre and Maastricht University (NL40284.068.12/METC 12-3-015). Subjects provided written informed consent before the start of the experiment.

2.2. Subjects

The experiment is part of a larger study. Participants consisted of a general population sample residing in the city of Maastricht, the Netherlands, and had responded to flyers. Between June 2012 and April 2015, 115 right-handed subjects (74 females and 41 males), aged 18 to 65 years, participated in the study. Exclusion criteria were use of alcoholic beverages in excess of 10 units per day and structural use of antidepressants, antiepileptics, antipsychotics, or anxiolytics during the past year. Subjects were asked to not use alcohol-containing consumptions the evening before and caffeine-containing consumptions 3 hours before the experiment. Recompense for time spent was 50 Euros.

2.3. Electroshocker and stimuli

An electroshocker (type Shocko-100-AA-20, developed by Maastricht Instruments BV and approved for use in experimental studies) was used to deliver electrical stimuli (see also Vossen et al.[34]). Stimuli were electrical pulses of 10 milliseconds duration, administered intracutaneously on the top of the middle finger of the nondominant left hand, as described by Bromm and Meier.[15] The sensation and pain threshold were determined for all subjects, starting at zero intensity, followed by a gradual increase in stimulus intensity. The first intensity that was consciously experienced was defined as the sensation threshold. The pain threshold was defined as the first intensity experienced as painful. The procedure of determining these personal thresholds was repeated 3 times in order to attain reliable estimates. The intensity of the electrical stimulus applied during the experiment was calculated for each subject separately. This intensity level was experienced as painful by all subjects, but still acceptable.[13] The intensity of the stress stimulus that was delivered during the experiment was calculated as follows:

\[
\text{Stimulus} = \text{pain threshold} + 0.25 \times (\text{pain threshold} - \text{sensation threshold}).
\]

2.4. Procedure

EMG- and electrocardiography (ECG) electrodes, as well as the shock electrode, were attached. EMG-electrodes were placed on the skin above the left and right trapezius muscle (LTM and RTM, respectively). After determination of the individual pain threshold, subjects were instructed that they would receive a single electrical shock at some time during a 5-minute period. The experimenter pointed out that the intensity level of the electrical stimulus and the precise time of delivery would be determined by a personal computer. Additionally, subjects were told that stimulus intensity might vary between the sensation threshold and a level clearly above the pain threshold. Subjects were instructed to keep both hands on the table, palms down, and to not close their eyes during the entire measurement period. All subjects received the experimental stimulus at exactly \(t = 3\) minutes. The procedure was controlled by the software program “Presentation 0.71” (Neurobehavioral Systems, Berkeley, California, USA).

The study protocol included 2 experimental sessions for each participant. The first took place at the moment of inclusion, the second 6 months later. The protocol was identical across the 2 experimental sessions.

2.5. Psychophysiological recordings

All recordings were conducted in an electrically and sound-shielded cubic (7.1 m³). EMG activity was recorded from the left and right upper trapezius muscle. Electrodes were centered on a point 2 cm lateral to the midpoint between the acromion process and spinous process of the seventh cervical vertebra,[136] using silver/silver chloride (Ag/AgCl) electrodes. A reference electrode was placed over the spinous process of the seventh cervical vertebra. Cardiac activity was recorded with a standard 3-lead ECG. All electrodes were
fixed using conductive paste. Brainvision BrainAmp Research Amplifier was used for all recordings. ECG and EMG were sampled with 1000 Hz.

2.6. Psychological measurements

Early life adversity was assessed at the moment of inclusion, with a questionnaire developed within the context of the FP7 EU-GEI project (European Network of National Schizophrenia Networks Studying Gene-Environment Interactions).[37] The Childhood Experiences of Care and Abuse questionnaire comprises 15 questions on adverse childhood events, like the divorce of parents, the presence of financial problems, the occurrence of sexual abuse, and so on.

The questionnaire covers 2 age categories: the first category includes ACEs between 0 and 11 years (early childhood), the second category ACEs between 12 and 17 years (adolescence). Cronbach alpha coefficient was 0.68 and 0.64 for the 2 respective age categories. The maximum score in each age category was 15, the maximum score for the entire questionnaire was 30. The sum of scored events for both categories together ranged from 0 to 13 (mean 3.1, SD 3.0). For the exposure category of 0 to 11 years, the sum of scored events ranged from 0 to 8 (mean 1.6, SD 1.8), whereas for the exposure category of 12 to 17 years, the sum of scored events ranged from 0 to 7 (mean 1.4, SD 1.6).

2.7. Offline data processing

EMG data were filtered offline (low pass 0.5 Hz, high pass 250 Hz, 50 Hz notch filter) and segmented into epochs of 512 milliseconds. Raw data were visually inspected for artifacts which, if encountered, were excluded from the analyses. The EMG activity of the trapezius muscle was corrected for cardiac activity: the variance due to ECG activity was removed from the uncorrected EMG variable, using regression analysis. Next, since the number of epochs was restricted due to hardware memory limitations, 3 consecutive epochs were merged, resulting in a total of 117 analyzable consecutive epochs. For each 1536 milliseconds epoch, the root mean square value was calculated followed by a logarithmic transformation, in order to preserve a normal distribution.

2.8. Statistical analysis

Given the hierarchical structure of the EMG dataset, consisting of epochs (level 1), nested within experimental sessions (level 2), that are clustered within individuals (level 3), multilevel random regression analyses were performed (see Appendix for model, http://links.lww.com/MD/B299). Although no conclusive evidence is provided in the literature on differences between left and right muscle activity during experimental stress, some studies do report differences.[38–41] Thus, EMG activity of the LTM and RTM served as the dependent variable in all models. In order to obtain normality, the dependent variables were log-transformed. Epoch number was included in order to investigate the linear effect over time. In addition to the linear time effect, a quadratic (epoch²) and exponential (eepoch) time effect were added. Associations of interest were interactions between the time variables and the linear ACE-score. Additionally, the interactions between the time variables and the 2 age subcategories of ACE exposure (early childhood and adolescence) were examined. Analyses were adjusted for age and sex.

Additional analyses were carried out in order to examine the reliability of the influence of ACEs on the time course of EMG activity. Experimental session was included as predictor, both as main effect as well as interaction term. Three third-order interaction terms were modeled: epoch × ACE-score × session, epoch² × ACE-score × session, and eepoch × ACE-score × session.

In order to examine which covariance structure yielded the best fit for the dataset, various covariance structures were tested. The −2 log likelihood of different models was calculated in order to determine which statistical model would fit best. An autoregression (AR1) structure showed the best fit (lowest −2 log likelihood). As the dataset has a multilevel structure, consisting of consecutive epochs, each epoch is correlated with the previous epoch, which makes an autoregression model suitable. The AR1 structure was therefore used for all statistical analyses.

All models were tested with a random intercept and random slope for the linear effect of time. All statistical analyses were performed using SPSS 22.0. Two-sided P values <0.05 were considered statistically significant.

3. Results

Ten subjects were excluded from the analyses due to protocol violations (movements, not following instructions), leaving n = 103 analyzable participants (67 females, 38 males). Ages ranged from 18 to 65 years, with a mean age of 38.6 years (SD 17.1).

3.1. Influence of ACEs on EMG stress reactivity

ACE-score was included as a continuous variable in the models. Table 1 shows the T- and P values of all time effects included in the model, that is, linear, quadratic, and exponential time. When examining this table, it can be seen that for both left and right trapezius muscles, the effects are comparable. For the linear time × ACE interaction, a positive T value is present for both LTM and RTM (T = 3.676 and T = 3.070, respectively), indicating a relatively higher increase in EMG activity over time for higher ACE-scores: the higher the score, the more increase in muscle activity. Second, the quadratic time × ACE interaction shows us a negative T value (T = −4.879 for the LTM, T =

| Table 1 | Interactions between total ACE-score on EMG time effects. |
|---------|---------------------------------------------------------|
|          | Left trapezius muscle                                   | Right trapezius muscle                        |
| Time × ACE | T = 3.475<sup>**</sup> P = 0.001<sup>**</sup>         | T = 3.015<sup>**</sup> P = 0.003<sup>**</sup>        |
| Time<sup>2</sup> × ACE | T = −4.549<sup>**</sup> P < 0.001<sup>**</sup> | T = −2.780<sup>**</sup> P = 0.005<sup>**</sup>        |
| e<sup>epoch2</sup> × ACE | T = 3.066<sup>**</sup> P < 0.001<sup>**</sup> | T = 2.107<sup>**</sup> P = 0.035<sup>**</sup>        |

Values shown are T values, indexing time × linear ACE-score interaction effects. Three-level regression models were used including level of EMG response, experimental session, and subject. EMG activity of the RTM and the LTM served as the dependent variables. Linear, quadratic, and exponential time as well as their interactions with ACE-score served as the fixed effects of main interest. Results are marked with 1 asterisk (*), if P < 0.05 and 2 (*), if P < 0.01. Corresponding fitted time course of EMG activity is illustrated in Fig. 1.

ACE = adverse childhood experience, EMG activity = electromyographic activity, LTM = left trapezius muscle, RTM = right trapezius muscle.
Values shown are $T$-values and $P$-values, indexing time $\times$ ACE-score interactions. Three-level regression models were used including level of EMG response, experimental session, and subject. EMG activity of the RTM and the LTM served as the dependent variables. Linear, quadratic, and exponential time as well as their interactions with ACE-score served as the fixed effects of main interest. Results are marked with 1 asterisk (*) if $P<0.05$ and 2 asterisks (**) if $P<0.01$. For the interaction between time and ACE-score during early childhood (0 to 11 years), corresponding fitted time course of EMG activity is illustrated in Fig. 2. ACE = adverse childhood experience, EMG activity = electromyographic activity, LTM = left trapezius muscle, RTM = right trapezius muscle.

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--2.879 for the RTM), representing a parabola with a downward opening. Based on the data depicted in the table, it can be concluded that for higher scores on the ACE questionnaire, a higher maximum in muscle activity will be reached (i.e., the top of the parabola). The exact course of the EMG activity should be calculated for each score separately. Finally, the exponential time $\times$ ACE interaction has a positive $T$ value for both trapezius muscles ($T=3.847$ and $T=2.185$). These results mean that, from a certain point during the anticipatory stress phase, muscle activity builds up before the imminent painful stimulus. The exponential building of tension is more apparent for higher ACE-scores. All ACE $\times$ time interactions, both left and right, were significant. The effects on the right trapezius muscle were somewhat smaller than on the LTM.

For illustrative purposes, it was decided to depict the nonlinear EMG time course (predicted by the multilevel model) during the anticipatory stress phase for 2 relatively extreme ACE-scores: a score of 0 (representing no ACEs) and a score of 13 (maximum observed score in this sample). In order to obtain a predicted EMG time course, the scores of 0 and 13 were inserted in the regression model, respectively (see Appendix, http://links.lww.com/MD/B299). Figure 1 shows the predicted time courses for the 2 ACE-score extremes observed in this sample.

### 3.2. Influence of early life adversity on EMG stress reactivity across different ACE-exposure age categories

We investigated whether different EMG time interaction effects for the 2 age subcategories of the ACE questionnaire, early childhood and adolescence, could be demonstrated. The number of ACEs in the age category of 0 to 11 years is associated with increased muscle activity during the anticipatory phase for both the LTM and the RTM. The results, as shown in Table 2, show similar $T$- and $P$-values as described above: a positive linear time $\times$ ACE interaction, a negative quadratic time $\times$ ACE interaction and a positive exponential time $\times$ ACE interaction. For the ACE-exposure age category of 12 to 17 years, however, a less prominent interaction effect between EMG time course and the number of ACEs experienced was observed. A significant interaction between EMG time course and ACE-score was only apparent for the LTM.

Similarly as for the overall effects, for both ACE-exposure age categories, the extreme scores were inserted into the computed multilevel models. For illustrative purposes, Fig. 2 shows the predicted time courses for the 2 ACE-score extremes observed in this sample: a minimum score of 0 events, a maximum of 8 events.

In all models, age was associated with left and right trapezius muscle activity ($P=0.077$ and $P=0.003$, respectively). An association between sex and muscle activity could not be demonstrated (both $P\geq 0.836$). Finally, all models showed a significant random intercept and a random slope for linear time (all $P<0.001$).

### 3.3. Reliability of the impact of ACEs on EMG stress reactivity

In order to examine the reliability of the influence of ACEs on time course of EMG activity, additional analyses were carried out, including experimental session as predictor variable in the model. Three third-order interaction terms were modeled: epoch $\times$ ACE-score $\times$ session, epoch$^2$ $\times$ ACE-score $\times$ session, and epoch$^3$ $\times$ ACE-score $\times$ session. Since it was hypothesized that the influence of childhood adversity on EMG stress reactivity would be stable over time, no difference in ACE-effect

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**Table 2**

The effect of ACE-score on EMG time effects, per age category.

| Left trapezius muscle | Right trapezius muscle |
|-----------------------|------------------------|
| **Age 0–11 y**       | **Age 12–17 y**       |
| Time $\times$ ACE     | $T=4.482^{**}$  $P<0.001^{**}$ | $T=1.542$  $P=0.124$ |
| Time$^2$ $\times$ ACE | $T=-4.542^{**}$ $P<0.001^{**}$ | $T=-2.376^{*}$  $P=0.017^{*}$ |
| Time$^3$ $\times$ ACE | $T=4.224^{**}$  $P<0.001^{**}$ | $T=2.195^{*}$  $P=0.026^{*}$ |
| **Age 12–17 y**      | **Age 12–17 y**      |
| Time $\times$ ACE     | $T=3.576^{**}$  $P<0.001^{**}$ | $T=1.684$  $P=0.093$ |
| Time$^2$ $\times$ ACE | $T=-3.442^{**}$ $P<0.001^{**}$ | $T=-1.407$  $P=0.160$ |
| Time$^3$ $\times$ ACE | $T=2.604^{**}$  $P<0.001^{**}$ | $T=0.955$  $P=0.339$ |

Values shown are $T$-values and $P$-values, indexing time $\times$ ACE-score interactions. Three-level regression models were used including level of EMG response, experimental session, and subject. EMG activity of the RTM and the LTM served as the dependent variables. Linear, quadratic, and exponential time as well as their interactions with ACE-score served as the fixed effects of main interest. Results are marked with 1 asterisk (*) if $P<0.05$ and 2 asterisks (**) if $P<0.01$. For the interaction between time and ACE-score during early childhood (0–11 years), corresponding fitted time course of EMG activity is illustrated in Fig. 2. ACE = adverse childhood experience, EMG activity = electromyographic activity, LTM = left trapezius muscle, RTM = right trapezius muscle.
between both experimental sessions was expected. Table 3 shows the T- and P values of these third-order interaction effects. No significant results were apparent (all P ≥ 0.175).

4. Discussion

We investigated the relationship between early life adversity and EMG stress reactivity in adulthood. Although several adult stress-related outcomes are moderated by ACEs,[10–12] no previous studies reported on the influence of ACEs on EMG reactivity as a psychophysiological stress response. An association between ACEs and altered EMG reactivity was found, particularly for ACEs in early childhood. The association was reliable over time. This was conform the a priori hypotheses.

A higher ACE-score was accompanied by increased muscle activity in both trapezius muscles during the anticipatory stress phase. Early life adversities can lead to higher levels of stress sensitivity in adulthood, possibly caused by dysregulation or hyperactivity of the hypothalamic–pituitary–adrenal axis (HPA axis). This could result in long-lasting effects on psychophysiological activity.[10–12,17] The exponential time course of the EMG reactivity effect, marked by a sharp increase at the end of the anticipatory phase for high ACE-scores, is instructive. This effect may be related to uncertainty about the exact timing of the painful stimulus. It indicates that subjects who have experienced more early life adversity tend to become tense as the stressor (i.e., the unpredictably painful stimulus) is approaching. An interrelationship between ACEs, inadequate or immature coping and stress-related symptoms has been described in previous research.[42,43] Inadequate coping, associated with early life adversity, may lead to increased stress sensitivity/vulnerability for mental disorders later in life.

Early childhood ACEs (occurred between 0 and 11 years) were associated with increased EMG stress reactivity, for both trapezius muscles. For ACEs that occurred during adolescence (12–17 years) this was less prominent and apparent only for the LTM. These results are in line with previous research,[22,23] showing more enhanced effects on adult mental health outcomes associated with exposure to adversity at a younger age.

A left–right difference in interaction with EMG reactivity was observed throughout the analyses, the LTM showing greater reactivity than the right. This difference may be explained by the fact that the stimulus was applied to the left hand. Second, since it was assumed that the variables age and sex could impact stress reactivity, these variables were included as covariates. The significant main effect of age demonstrated a negative association with the degree of muscle activity. No influence of sex emerged.

Finally, invariability of EMG stress responsivity across measurement occasion was demonstrated. No intervisit (t = 0 and t = 6 months) difference was observed, suggesting a reliable influence of ACEs on psychophysiological activity. The invariability confirms the robustness of the demonstrated anticipatory stress effects. Furthermore, it increases the plausibility that altered stress reactivity plays a role in the development of stress-related health problems.

Naturalistic stress responses may not likely be solely linear. Both exponential and quadratic time effects were demonstrated, which affirms this assumption. One of the strengths of multilevel regression techniques is that random time effects can be modeled. In the present study, a highly significant random intercept as well as random linear time effect were demonstrated. The significant random intercept, indicating different EMG levels between persons, was expected since EMG is influenced by many other factors like posture and body morphology (see Wijsman et al.[28]).

The significant random time effect has to be interpreted as the existence of different slopes of linear time courses across subjects. Stated otherwise, every subject reacts differently to the stressor, a phenomenon for which the main effects are corrected. Traditional ANOVA techniques do not permit estimation of random effects.

4.1. Limitations of the study

An experimental painful stimulus was used, which can be viewed as a minor variant of an extensive collection of daily stressors. In daily life, stressors rapidly alternate. The question is to what degree the results of the present experimental study can be extended to daily life situations.

5. Conclusion

This is, to our knowledge, the first study to investigate the influence of early life adversity on EMG stress reactivity of the trapezius muscles. In sum, results showed robust alterations in EMG stress reactivity for subjects with a history of ACEs. Examining clinical populations may be productive in further unraveling the mechanisms underlying the stress–response and its relation to mental health problems.

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