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Personality Predicts Individual Variation in Fear Learning: A Multilevel Growth Modeling Approach

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Abstract

Although fear-learning research has tended to focus on typical responses, there is substantial individual variation in response to threat. Here, we investigated how personality is related to variability in associative fear learning. We used multilevel growth curve modeling to examine the unique and interactive effects of Stress Reaction (SR) and Harmavoidance (HA; Multidimensional Personality Questionnaire scales) and their corresponding higher-order factors on differential fear conditioning (n = 225) and extinction (n = 109; 24–48 hr later). Fear was indexed by fear potentiation of the eyeblink startle reflex. Our findings demonstrated weaker discrimination between threat and safety with high levels of SR. Subsequently, both retention of differential fear acquisition and extinction were weaker with high levels of SR and HA, thereby indicating maladaptive fear learning, whereas they were stronger with low levels of SR and high levels of HA, which suggests efficient fear learning. These findings illustrate how specific personality traits may operate to confer vulnerability or resilience for anxiety disorders.

Keywords

fear conditioning, extinction, individual differences, personality, multilevel growth curve modeling, startle response, Multidimensional Personality Questionnaire

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Research into mental processes has generally focused on the average response and treated individual variability as noise (cf. Plomin & Kosslyn, 2001). The application of this method to fear learning has yielded general principles that indicate fear conditioning in most people when a stimulus is followed by an aversive event as well as fear extinction over time when this threat ceases (e.g., Mineka & Oehlberg, 2008). However, researchers have recognized that such a mean learning pattern can reflect an artifact of group averaging and is unlikely to represent the response pattern of any given individual (e.g., Kristjansson, Kircher, & Webb, 2007; Pamir et al., 2011). Individual differences may be especially pertinent to understanding pathological fear learning, given that psychopathology, by definition, reflects a deviation from the mean. Researchers have advocated that to understand mechanisms of abnormal (fear) learning, it is necessary to relate naturally occurring variation in individual dispositions (e.g., traits) to variation in learning (e.g., Kosslyn et al., 2002). Accordingly, our aim in the present study was to examine how selected individual differences in personality are related to variability in fear learning.

Cronbach's (1957) classic article on the two disciplines of scientific psychology invited researchers to purposefully seek Aptitude (i.e., personality characteristics) × Treatment (i.e., fear-learning phase) interactions. In line with this call, most notably Eysenck (1965) and several

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other researchers (Mineka & Oehlberg, 2008) have pursued the notion that personality characteristics may be systematically related to individual variation in abnormal associative fear learning and, in turn, to the pathogenesis of anxiety disorders. Studies on discriminative fear conditioning in which groups "at risk" for anxiety (scoring high on certain personality risk traits) were compared with control participants have yielded mixed findings. Previous studies did not provide support for the long-standing hypothesis (e.g., Eysenck, 1979) that at-risk groups are characterized by enhanced fear responding to the threat cue during fear conditioning but, rather, demonstrated elevated fear to the safety cue, as well as impairments in extinction learning (e.g., Craske et al., 2008; Gazendam, Kamphuis, & Kindt, 2012; Grillon & Ameli, 2001; Liberman, Lipp, Spence, & March, 2006; see for review Lissek et al., 2005; but see Kindt & Soeter, 2014). Yet other studies have shown no differences between at-risk and control groups (e.g., for null findings, Fredrikson & Georgiades, 1992; Otto et al., 2007; Pineles, Vogt, & Orr, 2009; Torrents-Rodas et al., 2012).

In sum, strong evidence for the relation between personality and fear learning is lacking. These inconsistent findings may indicate that there is no strong relation between personality and fear learning or, alternatively, that previous studies did not exploit the data to their full potential to detect abnormal fear-learning patterns. Therefore, in the present study, we addressed a number of issues to improve the analysis of individual differences in fear learning. In this study, variation in fear learning was modeled with high fidelity to the nature of the data: Our analyses included not one but two predictors, which are continuous in nature (i.e., trait scores), and we analyzed the entire curve of acquisition and the entire curve of extinction learning.

An important difference between the current approach and extant body of evidence involves our method of testing trait effects on fear learning. We included dimensional ratings of personality as predictors, given that it is well recognized that dichotomizing (e.g., converting data into two categories) is associated with loss of information and a reduced probability to detect real relationships (Royston, Altman, & Sauerbrei, 2006). In addition, we suggest that inconclusive results of previous studies in which one trait (e.g., neuroticism) was assessed in isolation may reflect both that broad trait effects are mediated by specific traits and that traits act in concert with one another. In anxiety research, one important distinction concerns trait differences in "anxiety" and "fearfulness" (e.g., Depue & Lenzenweger, 2001). *Anxiety* can be defined as an apprehensive emotion, a response to a nonspecific threat. *Fear*, in contrast, is an emotional response to a known or definite physical threat, which results in active avoidance. A number of theoretical accounts as well as (more recently) accumulated data have linked anxiety and fear to distinct psychobiological structures in the brain (see, e.g., Depue & Lenzenweger, 2001; Gray & McNaughton, 2000; for review, see Walker, Toufexis, & Davis, 2003; White & Depue, 1999).

In this respect, the personality model based on the Multidimensional Personality Questionnaire (MPQ; Tellegen & Waller, 2008) is of particular interest because it explicitly distinguishes between anxiety and fearfulness. In the MPQ model, individual trait differences in anxiety form the key component of the Stress Reaction (SR) scale, and fearfulness is a key aspect of the Harmavoidance (HA) scale. We therefore focus on these specific SR and HA scales. In addition, to promote comparison with previous research, we included the corresponding higher-order traits, that is, negative emotionality (NEM; akin to neuroticism) and constraint (CON; nonaffective reversed impulsivity). NEM is widely assessed in personality and anxiety research, and NEM and CON constitute important risk factors in the development of fear-related disorders (Miller, 2003; Miller, Kaloupek, Dillon, & Keane, 2004; e.g., Miller, Greif, & Smith, 2003).

Several lines of research support the relevance of testing both the unique and the interactive effects of SR (NEM) and HA (CON) on different phases of fear learning. More specifically, a review of prospective studies revealed that high NEM forms a primary risk factor for posttraumatic stress disorder and, when combined with either low CON or high CON, produces qualitatively distinct forms of posttraumatic stress reactions (Miller, 2003). These findings illustrate how the interaction of NEM and CON can lead to different outcomes. In addition, because SR (NEM) is associated with another emotional system than HA (CON), it is likely that the effects of these traits differ. Moreover, these trait effects can vary for the fear-conditioning and extinction phases. Given that distinct (neural) processes underlie fear conditioning and extinction (Davis, Falls, & Gewirtz, 2000), SR and HA can, in turn, be related to normalities and abnormalities in either phase. Therefore, fear development can be further clarified by mapping how the (interactive) effects of SR and HA are associated with variation in the separate phases of conditioning and extinction.

Furthermore, in the present study, we comprehensively modeled variation in fear learning by analyzing the entire curve of both acquisition and extinction. In many studies to date, conditioning has been operationalized as a count (number of responses) or an average of multiple trials. These scores represent conditioning as an "end state," whereas, in reality, conditioning is understood to reflect the dynamic learning process over trials (similarly argued in Pineles et al., 2009). To analyze these trial-by-trial learning curves, we used multilevel modeling (Blackwell, Mendes de Leon, & Miller, 2006; Kristjansson et al., 2007).

Clear advantages of multilevel modeling are that all trial-by-trial data points can be analyzed and are adjusted for the correlation of these data points within individuals (Bagiella, Sloan, & Heitjan, 2000; Kristjansson et al., 2007). For these reasons, multilevel modeling is supposed to yield more reliable effect estimates (Blackwell et al., 2006). Together, this precise analysis may decipher more subtle differences in response patterns.

In sum, the present study presents a fine-grained analysis of how personality traits (SR, HA; NEM, CON) may affect fear conditioning and extinction (24 or 48 hr later). Fear was measured by startle potentiation, a validated and widely used physiological index of defensive reactivity (e.g., Davis, 2006). This measure especially suited our study, given that startle potentiation has been shown to systematically covary with individual differences in fearfulness and anxiety in many experimental paradigms (for reviews, see Kramer, Patrick, Krueger, & Gasperi, 2012; Vaidyanathan, Patrick, & Cuthbert, 2009). Because associative theories of conditioning (Rescorla & Wagner, 1972) predict an incremental learning curve (Morris & Bouton, 2006), the first growth curve model tested for linear and quadratic effects of trials on fear responses. This model also tested for random effects that is, for individual differences in the slope and curvature of participants' growth curves. A second growth curve model tested whether personality traits and their interaction accounted for variance in the midpoints, slopes, and curvatures of fear conditioning and extinction. That is, we tested how individual differences in SR (NEM), HA (CON), and the SR-HA (NEM-CON) interaction relate to variation in associative fear learning. Specifically, we investigated (a) whether SR and HA showed unique associations with fear conditioning and extinction and (b) whether the interactive effects of SR and HA are better predictors for fear-learning parameters than either trait in isolation.

Method and Materials

Participants

This study included 236 healthy students from the University of Amsterdam who participated in one of several differential fear-conditioning studies conducted in our lab and who had completed the Dutch brief form version of the MPQ (MPQ-BF-NL; Eigenhuis, Kamphuis, & Noordhof, 2013; Tellegen & Waller, 2008) in an independent mass testing session that was part of their 1st-year course requirements. Specifically, we merged the highly similar control (or no active medication) conditions of 11 differential fear-conditioning studies. All studies included a separate fear-conditioning phase followed by an extinction phase 24 to 48 hr later to ensure consolidation of fear conditioning. For a complete description of these studies, the reader is referred to the original studies (Bos, Beckers, & Kindt, 2012; Gazendam et al., 2012; Gazendam & Kindt, 2012; Kindt & Soeter, 2013; Kindt, Soeter, & Vervliet, 2009; Sevenster, Beckers, & Kindt, 2012a, 2012b; Soeter & Kindt, 2010, 2011a, 2011b, 2012).[1] Eleven participants were excluded from this composite sample because of excessive inconsistent responding as indexed by the MPQ Variable Response Inconsistency and True Response Inconsistency scales (Eigenhuis et al., 2013). The final fear-conditioning sample consisted of 225 participants (65 males, 160 females). The fear-extinction sample comprised 109 participants (41 males, 68 females).[2] The majority of participants were of Caucasian descent (89.9%). Participants were free from any previous or current medical or psychiatric condition on the basis of self-report (see the original studies for screening details). Participants received either partial course credits or a small payment (7–35 euros) for their participation. All participants provided written informed consent, and this study had full ethical approval.

Personality assessment

The MPQ (Tellegen & Waller, 2008) assesses normal personality variation and provides coverage of a range of traits that encompass the domains of temperament, interpersonal and imaginative style, and behavioral regulation. The MPQ consists of binary, mostly true-false, items that cohere into 11 lower-order factors, which in turn coalesce into three higher-order factors that have clear temperamental and proposed psychobiological referents (Depue & Lenzenweger, 2001). The three-factor solution consists of NEM, positive emotionality, and CON. We used the recently developed 132-item MPQ-BF-NL (Eigenhuis et al., 2013) that has shown strong convergence with its U.S. counterpart brief form (Patrick, Curtin, & Tellegen, 2002). On the basis of previous theoretical and empirical work, we selected SR and HA as lower-order personality variables of interest, as well as their corresponding higher-order factors NEM and CON, respectively (see Table 1 for descriptions of low and high scorers for the selected scales and factors).

Fear-conditioning task

Participants performed a discriminative fear-conditioning procedure (for additional information, see the Supplementary Methods and Materials section of the Supplemental Material available online). After attachment of all electrodes, unconditioned-stimulus (UCS) intensity was individually calibrated (see the Stimuli section). Next, participants were instructed about the conditioning procedure; that is, they were told that one of two figures

Table 1. Description of Low and High Scorers for the Selected MPQ Scales and Their Corresponding Higher-Order Factors

Factor/scale	Low scorer	High scorer
Factor		
Negative emotionality	Has a high threshold for negative emotional responses and a less adversarial interpersonal outlook.	Experiences elevated levels of negative emotions, such as fear, anxiety, and anger; antagonistic.
Constraint	Is impulsive, seeks danger, and rejects conventional and traditional behavioral strictures.	Endorses social norms; acts in a cautious and restrained manner; avoids thrills.
Scale		
Stress Reaction	Can put fears and worries out of her or his mind; quickly gets over upsetting experiences; is not troubled by emotional turmoil or guilt feelings.	Is tense and nervous; is sensitive, feels vulnerable; is prone to worry and feel anxious; is irritable and easily upset.
Harmavoidance	Does or would enjoy dangerous and exciting experiences and activities.	Avoids excitement and danger; prefers safe activities even if they are tedious.

Note: MPQ = Multidimensional Personality Questionnaire (Tellegen & Waller, 2008; Dutch version, Eigenhuis, Kamphuis, & Noordhof, 2013).

would sometimes be followed by an electric stimulus, whereas the other figure would never be followed by an electric stimulus. In the *habituation* phase, acoustic startle probes (8 or 10, depending on the study) were delivered to stabilize baseline startle reactivity (Bradley, Lang, & Cuthbert, 1993). In the *fear-conditioning* phase, partial reinforcement of the threat stimulus ($CS1^+$; between 75% and 87.5% reinforcement schedule) was implemented to delay the onset of extinction (LaBar, Gatenby, Gore, LeDoux, & Phelps, 1998). $CS1^+$ and the safety stimulus ($CS2^-$) were both presented semirandomly with the restriction of no more than two consecutive presentations of either $CS1^+$ or $CS2^-$. Both stimuli were presented for 8 s, the startle probe was delivered 7 s after stimulus onset, and for $CS1^+$ trials, the UCS was delivered at 7.5 s. The intertrial intervals varied between 15 s and 29 s, during which startle probes (noise-alone, NA, trials) were delivered (5 to 8 times).[3] After 24 or 48 hr, in the subsequent *extinction* phase, the unreinforced $CS1^-$ (no UCS), $CS2^-$, and NA trials were again presented randomly (10 to 16 times; see Fig. 1a for a schematic illustration of the procedure).

Stimuli

CS. The CS1 and CS2 presented during fear conditioning and extinction comprised either geometric shapes, faces, or spider pictures.

UCS. The UCS was a 2-ms electric stimulus produced by a Digitimer DS7A constant-current stimulator (Digitimer Ltd., Hertfordshire, England). The UCS was administered to the left wrist via a pair of standard Ag/AgCl electrodes filled with electrolyte gel. UCS intensity level was determined by gradually increasing the shock intensity level until the participant indicated the shock to be "highly annoying but not painful."

Data collection: Startle response

The eyeblink component of the startle response was measured by activity electromyogram (EMG) of the orbicularis oculi. The acoustic startle probe consisted of a 40-ms duration, 104-dB burst of white noise with a near instantaneous rise time presented binaurally by headphones. *Startle magnitude* was defined as the amplitude (measurement unit: μV) of the first peak within a 20- to 200-ms interval after the startle-probe onset.

Data reduction

Personality traits. All scores were *z*-transformed to allow for a better comparison of the regression coefficients (βs) associated with each predictor.

Startle EMG. Startle measurements that showed recording artifacts or excessive baseline activity were discarded, and outliers (more than 3 *SD*s above or below the mean) were removed (0.4%; see the Data Reduction section of the Supplemental Material). To reduce interindividual variation in baseline EMG activity, we converted raw EMG data to proportional change scores [(X – baseline) / baseline] (e.g., Tabachnick & Fidell, 2000; Walker & Davis, 2002). Baseline was determined as the average startle reactivity of an individual's final two habituation trials.[4] Next, to assess differential fear potentiation, we calculated differential conditioned responses by subtracting the startle response to the safety stimulus (CS2) from the startle response to the threat stimulus (CS1; use of differential conditioned

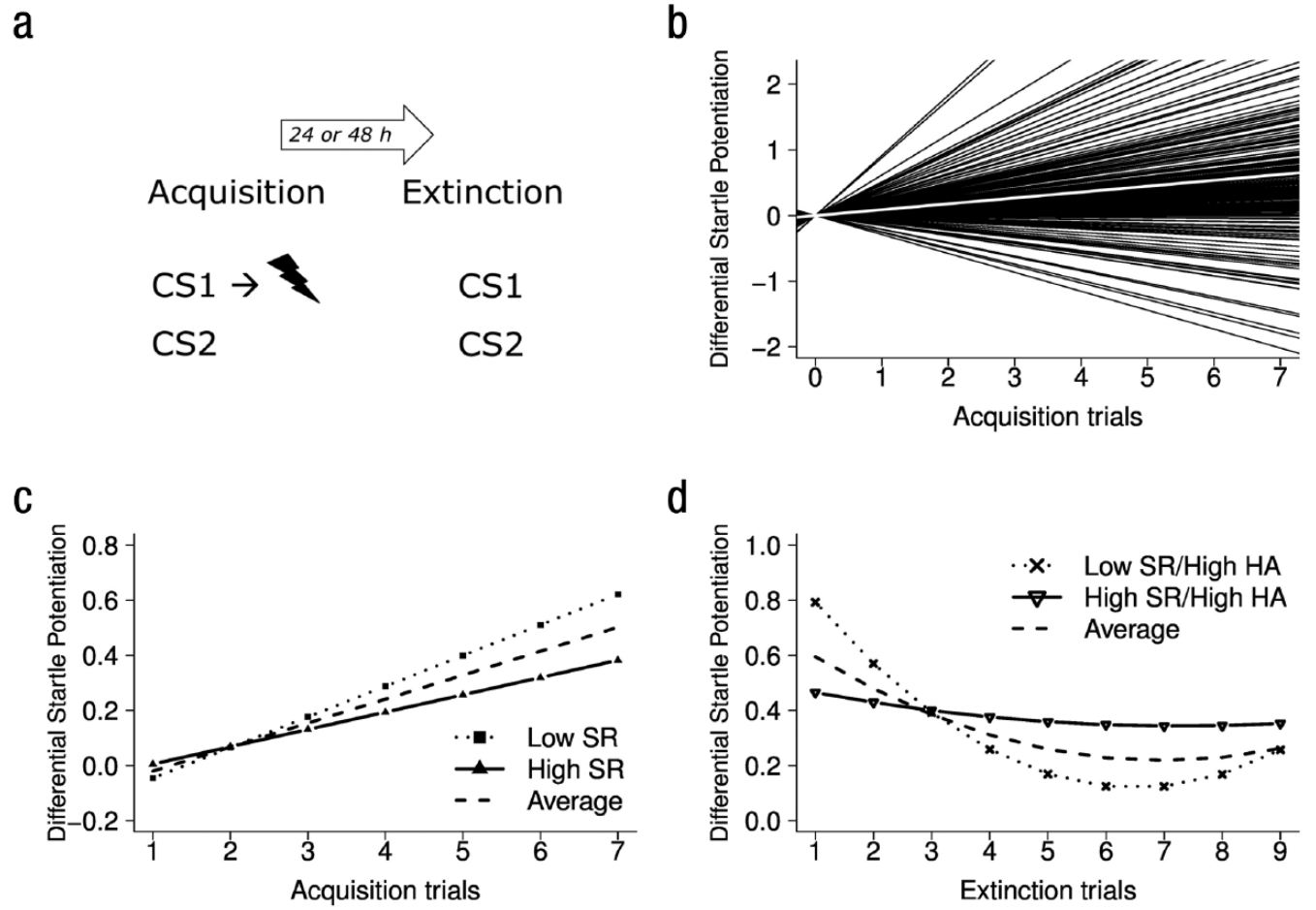

Fig. 1. Schematic illustration of general experimental procedure and growth curve results. The schematic (a) shows stimuli used in acquisition, extinction, and the experimental procedure (see the Method and Materials section). The uniform analyses contained seven fear-conditioning trials and nine extinction trials. CS1 = threat stimulus, followed by a shock during fear acquisition (partial reinforcement); CS2 = safety stimulus, never followed by a shock; flash symbol = shock (electric stimulus). The graph in (b) shows individual differences in growth curves. Differential startle acquisition slopes of each individual are shown (intercepts are set to 0; $n = 225$). The thick white line represents the average slope. Fear was indexed by a proportional change measure of fear-potentiated startle. Differential = CS1 vs. CS2. The graph in (c) shows predicted fear-acquisition growth curves as a function of individuals' level of Stress Reaction (SR). High SR (1 *SD* above the mean), low SR (1 *SD* below the mean), and average trajectories are shown. Note that the graph illustrates the effect of SR on the acquisition slope (Harmavoidance, HA, is set to 0). The fear-acquisition model of differential startle reactivity is defined by the following equation: 0.24 + **–0.05 (SR*j*)** + –0.00 (HA*j*) + **0.07 (SR*j* HA*j*)** + u0*j* + **0.09 (Trial)** + **–0.02 (SR*j* Trial)** + 0.02 (HA*j* Trial) + 0.00 (SR*j* HA*j* Trial) + u1*j* Trial + e*ij*. The graph in (d) shows predicted fear-extinction growth curves as a function of individuals' level of SR and HA. High SR and high HA (1 *SD* above the mean), low SR and high HA, and average trajectories are shown. The extinction model of differential startle reactivity is defined by the following equation: **0.26** + 0.06 (SR*j*) + 0.0 (HA*j*) + 0.03 (SR*j* HA*j*) + u0*j* + **–0.04 (Trial)** + **0.01 (Quadratic)** + 0.01 (SR*j* Trial) + –0.01 (SR*j* Quadratic) + 0.00 (HA*j* Trial) + 0.00 (HA*j* Quadratic) + **0.02 (SR*j* HA*j* Trial)** + 0.00 (SR*j* HA*j* Quadratic) + u1*j* Trial + u2*j* Quadratic + e*ij*. Equation terms in boldface represent significant effects ($ps < .06$).

responses is similar to procedures used by, e.g., Otto et al., 2007; Pineles et al., 2009).[5] To conduct uniform analyses, we analyzed the same number of trials for each participant (irrespective of the total trial number of the particular study). The conditioning phase consisted of (the first) seven $CS1^+$ and seven $CS2^-$ trials, and the extinction phase consisted of (the first) nine $CS1^-$ and nine $CS2^-$ trials. We analyzed differential (CS1 minus CS2) startle reactivity. Moreover, to independently test fear and safety learning, we analyzed startle reactivity to the threat stimulus (CS1 minus NA) and to the safety stimulus (CS2 minus NA) separately.

Data analyses

The data analyses required multilevel growth curve modeling because the study design yielded repeated measurements of the startle response, which were nested within individuals and within studies (see Fig. 2; Snijders & Bosker, 1999). Therefore we analyzed the data with growth curve modeling as implemented in the lme library of R (version 14.0, R Development Core Team, 2010; Pinheiro & Bates, 2000; Pinheiro, Bates, DebRoy, & Sarkar, 2011; see also Bliese & Ployhart, 2002). In all analyses, trial was treated as a within-individual (Level 1)

Level 1:

$$y(ijk) = \beta_{0j} + \beta_{1j} \times t(i) + \beta_{2j} \times t(i)^2 + e_{ij}$$

Level 2:

$$\beta_{0j} = \lambda_{00k} + \lambda_{01k} X_1 + \lambda_{02k} X_2 + \lambda_{0(1,2)k} X_1 \times X_2 + u_{0j}$$

$$\beta_{1j} = \lambda_{10k} + \lambda_{11k} X_1 + \lambda_{12k} X_2 + \lambda_{1(1,2)k} X_1 \times X_2 + u_{1j}$$

$$\beta_{2j} = \lambda_{20k} + \lambda_{21k} X_1 + \lambda_{22k} X_2 + \lambda_{2(1,2)k} X_1 \times X_2 + u_{2j}$$

Level 3:

$$\phi_{00k} = \lambda_{000} + w_{0k} \qquad \phi_{01k} = \lambda_{010} \qquad \phi_{11k} = \lambda_{110}$$

$$\phi_{10k} = \lambda_{100} + w_{1k} \qquad \phi_{02k} = \lambda_{020} \qquad \phi_{12k} = \lambda_{120}$$

$$\phi_{20k} = \lambda_{200} + w_{2k} \qquad \phi_{0(1,2)k} = \lambda_{0(1,2)0} \qquad \phi_{1(1,2)k} = \lambda_{1(1,2)0}$$

Fig. 2. Multilevel growth curve modeling: trial (Level 1), within-person (Level 2), within-study (Level 3). Analyses include two continuous predictors—trial (t) and trait scores (*X*). In the equations, *i* represents trial, *j* represents participant, *k* represents study, t(*i*) represents trial, t(*i*)^2 represents quadratic trial component, e_{ij} represents residual and *X* represents trait scores. The Level 1 equation consists of participant-specific intercepts (β_{0j}), linear trial effects (β_{1j}), and quadratic trial effects (β_{2j}), which are further modeled at Levels 2 and 3. The intercept can be interpreted as the midpoint of a phase because the trial vector was centered by placing its 0 point at the midpoint (Kristjansson, Kircher, & Webb, 2007). The linear trial effect can be interpreted as the rate of increase or decrease in learning. The quadratic trial effect has the following interpretation: For a positive linear slope, a positive quadratic effect indicates an acceleration and a negative quadratic effect indicates a deceleration, whereas for a negative linear slope, a positive quadratic effect indicates a deceleration and a negative quadratic effect is indicative of an acceleration of the growth curve.

variable (*t*), (standardized) scores on MPQ personality domains were included as between-individuals (Level 2) variables (*X*), and startle fear responses served as the outcome variable. We analyzed trial effects with both a linear and a curvilinear (linear plus quadratic) function (e.g., Biesanz, Deeb-Sossa, Papadakis, Bollen, & Curran, 2004) and selected the best-fitting function by means of model selection (cf. later discussion). Given that time was centered, the intercept denoted the midpoint of the growth curve (see also Kristjansson et al., 2007).

To account for the dependencies of observations over trials, we incorporated a first-order autoregressive covariance structure (Pinheiro & Bates, 2000). As recommended by Twisk (2006), a random participant intercept was included in all models. We also allowed for random participant trial (linear and quadratic) effects and random study intercepts, but we did so only if a model-selection procedure indicated that these random effects were necessary (cf. later discussion).[6] Backward model selection was performed by contrasting the deviance of a complex model with that of a simple model using a log likelihood test (e.g., Bliese & Ployhart, 2002; Pinheiro & Bates, 2000).[7] If the complex model fitted the data significantly better than did the simple model, we retained the complex model (for results on each model fit, see Table 2 and Tables S1 and S2 in the Supplemental Material). Using this approach, with all random effects and both Level 2 predictors and their interaction included in the analysis, we first determined whether the linear or curvilinear trial effect fitted the data best. We then determined whether random study intercepts were required and subsequently assessed whether the random trial effects were necessary to improve model fit.[8] With the final model thus obtained, we tested whether individuals' intercepts and trial effects were associated with personality traits or their interaction. To understand the nature of observed interactions, we inferred the growth curves for individuals scoring low

Table 2. Multilevel Growth Curve Models of Differential (CS1 vs. CS2) Startle Fear Responses During Fear Acquisition and Extinction Predicted by Stress Reaction and Harmavoidance

		Acquisition model	Extinction model
Fixed effect	Predictor	β	β
ϕ_{00}[a]	MID	**0.24**** (0.04)	**0.26**** (0.05)
ϕ_{01}	SR	**–0.05*** (0.03)	0.06 (0.05)
ϕ_{02}	HA	–0.00 (0.03)	0.00 (0.05)
$\phi_{0(1,2)}$	SR × HA	**0.07*** (0.03)	0.03 (0.05)
ϕ_{10}	TIME (T)	**0.09**** (0.02)	**–0.04**** (0.01)
ϕ_{11}	SR × T	**–0.02** (0.01)	0.01 (0.01)
ϕ_{12}	HA × T	0.02 (0.01)	0.00 (0.01)
$\phi_{1(1,2)}$	SR × HA × T	0.00 (0.01)	**0.02*** (0.01)
ϕ_{20}	QUAD (Q)	—	**0.01**** (0.00)
ϕ_{21}	SR × Q	—	–0.01 (0.00)
ϕ_{22}	HA × Q	—	0.00 (0.00)
$\phi_{2(1,2)}$	SR × HA × Q	—	0.00 (0.00)
	Intercept/start extinction[b]		***0.58**** (*0.08*)
	SR		*–0.03* (*0.08*)
	HA		*0.03* (*0.09*)
	SR × HA		***–0.15**** (*0.08*)

Note: The acquisition sample consisted of 225 participants, and the extinction sample consisted of 109 participants. Standard errors are shown in parentheses. TIME = Acquisition: Trial 1–7, Extinction: Trial 1–9; QUAD = quadratic time component (TIME^2; curvature of the growth curve); SR = Stress Reaction; HA = Harmavoidance; CS1 = threat stimulus, followed by a shock during acquisition; CS2 = safety stimulus, never followed by a shock. Effect estimates in boldface represent significant effects.

[a]For both linear models and curvilinear models, intercept reflects midpoint of the curve (MID).

[b]Separate analyses yielded effect estimates (in italics) reflecting initial reactivity at the first extinction trial (24 or 48 hr later; see the Method section). Startle potentiation was calculated as a proportional change score (*100 = percent, see also Data Analyses).

*$p < .06$. **$p < .0001$.

or high on SR or HA by (a) inserting low (1 *SD* below the mean) or high (1 *SD* above the mean) scores in the model equation and (b) analyzing contrast (group) comparisons within the multilevel model. To perform these group comparisons, we first categorized individuals as "high" or "low" on SR (NEM) and high or low on HA (CON) on the basis of a median split, which resulted in four subgroups (e.g., high SR/high HA; for details, see the Data Analyses section of the Supplemental Material). If contrast analyses indicated that one or more subgroups deviated from the total, these results were reported.

In addition, to clarify retention of fear learning after consolidation (24 or 48 hr later), we performed an additional analysis (based on Trials 1 and 2 of the extinction phase) to test whether initial startle reactivity (the intercept, i.e., extinction Trial 1) on the next day was related to the personality traits. All reported p values are two-sided.

Results

Given that results for the lower order (SR, HA) and higher order (NEM, CON) personality model were highly similar, and that the present study's primary focus was on SR and HA, we report only the lower-order model results (see Table 2). The higher-order model results are reported in Tables S1 and S2 and in the Supplementary Results section of the Supplemental Material. Furthermore, the overall course of fear learning is always reported. For the predictors, we report only significant or nearly significant effects ($p < .06$), and if there are significant main effects and interactions, we interpret only interactions (Tabachnick & Fidell, 2000). Our main focus is on the effects of SR and HA on the individuals' trial effects (i.e., linear slope and curvature). For completeness, the effects of SR and HA on individuals' intercept (midpoint of a phase) are also described. The obtained parameter estimates (βs) associated with each (standardized) predictor can be interpreted as effect sizes: "Effect sizes (ESs) can be reported in original units (e.g., milliseconds or score units) or in some standardized or units-free measure (e.g., Cohen's d, β, η_p^2 or a proportion of variance)" (Cumming, 2014, p. 15). This means that for 1 *SD* increase or decrease on SR or HA, the intercept or trial effects increase or decrease with the value of the regression coefficient. Given that startle potentiation is indexed by proportional change scores, which reflects the proportion increase or decrease from baseline, a regression coefficient associated with the main trial effect of 0.10 indicates a 10% increase in startle potentiation per trial. For this reason, the parameter estimates (βs) in each model can be similarly interpreted (e.g., Schielzeth, 2010).

Individual differences in growth curves

Before the associations between traits and trajectories of fear learning are examined, it is important to test for the presence of individual differences. First, when we included random study intercepts and slopes, it did not improve model fit except for in one model, thereby suggesting no systematic study effects. Crucially, by comparing models with and without random participant slopes (see model-selection discussion later), we established that random slopes were needed, which indicated that the strength of the linear and curvilinear relationships varied between individuals. The variability among participants' growth curves (Kristjansson et al., 2007) was further illustrated by the following observations. The fear-conditioning (acquisition) slopes of approximately 20% of the participants were negative, thereby indicating that these participants' differential fear reactivity did not increase (see Fig. 1b). Likewise, the retention of differential fear conditioning (24 or 48 hr later) of approximately 16% of the participants was 0 or negative, indicating no (or reversed) discrimination between threat and safety. For extinction, linear slopes of approximately 26% of the participants were positive, which suggested that these participants' differential fear reactivity did not decrease. Taken together, these results indicate substantial variation between individuals in fear-conditioning and extinction performance.

Fear conditioning

Differential (CS1$^+$ vs. CS2$^-$) fear conditioning. The model-selection procedure resulted in a model with a linear trial effect, random participant intercepts and trial effects, and random study intercepts and trial effects. Overall, the differential fear-conditioning data showed a significant increase over trials (0.09; cf. Table 2). This parameter estimate (trial effect $\lambda_{10} = 0.09$) reflects the linear increase in mean differential startle potentiation across trials (i.e., a 9% increase per trial). Differential startle at the midpoint was affected by SR (parameter estimate of –0.05), and this effect was qualified by a significant interaction between SR and HA (0.07). Given that contrast (group) comparisons were not significant, substitution of 1 *SD* above/below the mean (+1/−1) for the predictor effects suggested that differential startle reactivity at the midpoint tended to be stronger for low SR/low HA individuals and weaker for high SR/low HA individuals. Crucially, differential startle slope was affected by SR (–0.02). This finding indicated that individuals characterized by more SR demonstrated weakened differential (CS1$^+$ vs. CS2$^-$) fear conditioning over trials. More specifically, this

parameter estimate (Trial × SR interaction λ_{11} = –0.02) reflects the effect of SR on the change in differential startle potentiation across trials: For individuals scoring 1 *SD* above the mean on SR, there was a linear increase of 7% (i.e., main trial effect of 0.09 plus a Trial × SR interaction effect of –0.02), whereas for individuals scoring 1 *SD* below the mean on SR, the increase was 11% per trial (i.e., main trial effect of 0.09 plus a Trial × SR interaction effect of –0.02). In sum, enhanced SR resulted in a weaker differentiation between the threat ($CS1^+$) and the safety ($CS2^-$) stimulus over the course of fear conditioning (see Fig. 1c for predicted fear-acquisition growth curves as a function of individuals' level of SR).

Conditioning to the threat ($CS1^+$) and safety ($CS2^-$) stimuli alone. For the $CS1^+$, the model-selection procedure resulted in a model with a curvilinear (i.e., linear and quadratic) trial effect and random participant intercepts and trial effects. Overall, the $CS1^+$ data showed a significant increase over trials (0.04), yet the quadratic trial effect was nonsignificant. Startle to the $CS1^+$ at the midpoint was affected by the interaction between SR and HA (0.10). Given that contrast (group) comparisons were not significant, substituting 1 *SD* above/below the mean for the predictor effects suggested that startle reactivity to the $CS1^+$ at the midpoint tended to be higher in high SR/high HA individuals, whereas it was lower for high SR/low HA individuals. No significant effects of SR and HA were found on slope and curvature (all *t*s < 1.9). In sum, results revealed only a tendency for individuals who were both high on SR and high on HA to show elevated fear to the threat stimulus ($CS1^+$) at the midpoint of conditioning (see Table S2 in the Supplemental Material).

For the $CS2^-$, the model-selection procedure resulted in a model with a curvilinear (i.e., linear and quadratic) trial effect and random participant intercepts and trial effects. Overall, $CS2^-$ conditioning data showed a significant linear decrease over trials (–0.04), whereas quadratic trial effects were nonsignificant. Both the midpoint (0.06) and the linear slope (0.02; trend effect) of startle to the $CS2^-$ were positively affected by SR, thereby indicating that individuals who show more SR demonstrated a larger startle response at the midpoint and tended to show a weaker decrease in startle to the safety stimulus ($CS2^-$) across trials. We found no effects of SR and HA on the curvature (all *t*s < 1.8). These results indicated that individuals who show more SR demonstrated less reduction of fear to the safety stimulus ($CS2^-$).

Summary fear conditioning (Day 1). Together, our main fear-conditioning results indicated that enhanced SR resulted in a weaker differentiation between the threat ($CS1^+$) and the safety ($CS2^-$) stimulus over the course of fear conditioning. This weakened differential conditioning was due to a diminished reduction of startle responding to the safety stimulus ($CS2^-$) in individuals who show more SR.

Extinction (24 or 48 hr later)

Differential ($CS1^-$ vs. $CS2^-$) extinction. The model-selection procedure resulted in a model with a curvilinear (linear and quadratic) trial effect and random participant intercepts and trial effects. The additional analysis on initial differential (threat vs. safety cue) startle reactivity at the first extinction trial demonstrated that the overall effect was significant (0.58), which indicated a retention of what the participants had learned 24 or 48 hr earlier. Next, the analysis indicated that initial reactivity of differential startle responding was affected by the interaction between SR and HA (–0.15). Given that contrast (group) comparisons were not significant, substituting 1 *SD* above/below the mean for the predictor effects suggested that initial differential fear reactivity tended to be stronger in individuals low on SR and high on HA and weaker in individuals high on SR and high on HA.

No significant effects of SR and HA were observed on differential startle at the midpoint (*t*s < 1.3). Over trials (slope effects), differential startle reactivity demonstrated a decelerating negative slope (linear: –0.04; quadratic: 0.01), thereby suggesting a rapid reduction followed by a more gradual reduction in later extinction trials (cf. Table 2). It is important that the linear slope of extinction was affected by the interaction between SR and HA (0.02). Contrast comparisons suggested that, compared with everyone else, high SR/high HA subgroup tended to show the weakest extinction, $\varphi = 0.04$, $SE = 0.02$, $t(817) = 1.79$, $p = .07$, whereas the low SR/high HA subgroup tended to display the strongest extinction, $\varphi = -0.04$, $SE = 0.02$, $t(817) = -1.83$, $p = .07$. The curvature was not significantly affected by SR or HA, all $t(817)$s < 1.5 (cf. Table 2). Together, these results indicated that differential extinction learning tended to be weaker for persons who show both more SR and more HA, whereas it tended to be stronger for low SR and high HA persons (see Fig. 1d for predicted fear-extinction growth curves as a function of individuals' level of SR and HA).

Extinction of the threat ($CS1^-$) and safety ($CS2^-$) stimuli alone. For the $CS1^-$, the model-selection procedure resulted in a model with a linear trial effect and random participant intercepts and trial effects. Initial reactivity to $CS1^-$ was significant (0.71), and over extinction trials, startle reactivity to $CS1^-$ decreased (–0.05). The initial reactivity, midpoint, and linear slope of startle reactivity to the $CS1^-$ during extinction were not significantly affected by SR and HA (all *t*s < 1.6; cf. Table S2 in the Supplemental Material). These results indicate that SR

and HA did not predict fear reduction to the threat stimulus during extinction learning.

For the CS2⁻, the model-selection procedure resulted in a model with a curvilinear (linear and quadratic) trial effect and random participant intercepts and trial effects. The additional analysis indicated that initial reactivity was not significant. Initial reactivity to CS2⁻ was affected by the interaction between SR and HA (0.19). Contrast comparisons indicated that, compared with everyone else, the high SR/high HA subgroup demonstrated larger initial startle reactivity to CS2⁻, $\varphi = 0.50$, $SE = 0.18$, $t(105) = 2.79$, $p = .01$.

Over extinction trials, data showed a negative linear slope (–0.04), whereas quadratic effects were nonsignificant (cf. Table S2 in the Supplemental Material). The midpoint was not significantly affected by SR and HA (all ts < 1.6). The linear slope was affected by a trend interaction between SR and HA (0.02). Contrast comparisons indicated that, compared with everyone else, the high SR/high HA subgroup showed more decrease in reactivity over trials, $\varphi = –0.06$, $SE = 0.02$, $t(847) = 2.66$, $p < .01$. Finally, the curvature was positively affected by SR (0.01), which indicated that individuals who show more SR demonstrated an initial decrease followed by a slowing in reduction rate of fear reactivity to the CS2⁻ over extinction trials (see Table S2 in the Supplemental Material). In summary, for individuals with high levels of both SR and HA, elevated initial fear reactivity to the safety stimulus was observed, which subsequently decreased over the course of extinction.

Summary extinction (Day 2). In sum, our results showed that after consolidation of fear learning, in individuals who show more SR and more HA, the discrimination between threat and safety tended to be weaker as a result of elevated initial startle reactivity to the safety stimulus (CS2⁻). Thereafter, these high SR and high HA individuals demonstrated weaker differential extinction learning. Conversely, initial startle discrimination between threat and safety tended to be stronger for individuals characterized by low SR and high HA, and these individuals also tended to show stronger extinction learning.

Discussion

The present study shows that individual differences in personality explain variability in associative fear learning, as measured by the startle fear response. Using multilevel growth modeling, we examined the unique and interactive effects of SR and HA and their corresponding higher-order factors, NEM and CON (Tellegen & Waller, 2008), on fear conditioning and extinction. Our findings demonstrate that SR[9] predicted fear conditioning and SR interacted with HA to predict retention of differential fear conditioning (24 to 48 hr later) and extinction learning. During fear conditioning, individuals with high levels of SR showed weaker discrimination between threat and safety due to elevated fear responding to the safety stimulus (CS2⁻). After consolidation of fear conditioning and during extinction, the combination of high or low SR with either high or low HA (i.e., the interaction) yielded different outcomes.

The present data revealed that individual differences in SR and HA predicted distinct fear-learning curves and can be best described in the following four patterns. In persons scoring high on both SR and HA, a pattern characterized by weak differential fear learning was observed. Weakened discriminative fear conditioning, due to an initial increased fear to both the threat and the safety stimulus and a persistence of fear to the safety stimulus, was followed by weakened retention of fear discrimination and reduced extinction learning. These individuals high on both HA and SR are strongly motivated to prevent future threat and are highly prone to experience anxiety when believed to be in danger (e.g., in uncertain situations; Depue & Lenzenweger, 2001; Tellegen & Waller, 2008). Under (anxious) conditions of uncertainty, biased attention toward threat impedes a fine-grained analysis of environmental cues, which makes it difficult to identify safety signals (Grupe & Nitschke, 2013). Together, this may explain the observed elevated initial fear reactivity and the elevated fear to stimuli that did not signal threat (CS2⁻) or no longer signaled threat (CS1⁻).

A second pattern was evident in individuals high on SR but low on HA. Their pattern of fear learning was characterized by reduced discriminative fear conditioning due to elevated fear to the safety stimulus, which evolved into average retention of differential fear conditioning and average extinction learning. Individuals with this configuration of trait standings (i.e., who are highly stress reactive yet seek stimulation and novelty) are low in prevalence, and their behavior in this experimental context is difficult to explain.[10] Future research in different experimental contexts may focus on this group, especially in view of the clinical observation that the corresponding configuration at the higher-order level of traits (i.e., high NEM, low CON) describes a specific form of posttraumatic stress reactions (e.g., Miller, 2003).

A third pattern was observed in individuals low on both SR and HA. This fear-learning pattern was characterized by successful (rapid) differential fear conditioning and normal extinction performance. Finally, individuals low on SR and high on HA were characterized by highly efficient fear learning as evidenced by strong differential fear conditioning and strong extinction learning. This efficient learning capacity may have resulted from these individuals' high motivation to prevent future threat (high HA) under (optimal) conditions of low stress and anxiety

(low SR). Note that these latter findings of adaptive fear learning in individuals low on SR (and high or low on HA) can be viewed as consistent with the observation that individuals low on NEM, the higher-order factor of SR, have been shown to be at decreased risk for the development of posttraumatic stress symptoms (e.g., Miller, 2003).

The current results show that the study of individual variation is useful to understand different mechanisms of fear learning (Kosslyn et al., 2002). First, individual differences in learning trajectories were illustrated by the observation that a considerable proportion of the participants (16%–26%) did not show the expected fear conditioning and extinction learning; they displayed no learning or an opposite learning pattern. These results substantiate the notion that an average growth curve is unlikely to represent the response pattern of a given individual (Kristjansson et al., 2007; Pamir et al., 2011). Second, we showed that personality characteristics partly account for these individual differences, with SR and HA explaining interindividual differences in fear learning as evidenced by effects on midpoints and linear and curvilinear slopes of individual learning. In addition, we conclude that the present multilevel growth curve analysis of the interactive effects of SR and HA has provided more information than could have been obtained in a study comparing two group means. More specifically, a control versus "high-anxious" group comparison could have yielded no differences, given that our current (extinction) data show that the effects of one trait (e.g., SR) may be balanced out by the effects of another relevant trait (e.g., HA).

Our findings elucidate how personality traits may operate to confer risk or resilience for anxiety. For example, among individuals low on SR and high on HA, the observed pattern of strong discriminative fear conditioning and strong extinction indicates flexible learning and unlearning that may reflect adaptive fear behavior. Conversely, in individuals high on both SR and HA, the observed weak discrimination between threat and safety stimuli, together with deficient extinction learning, may reflect maladaptive fear learning. Deficient safety learning is considered an important maladaptive response to threat (uncertainty; e.g., Grupe & Nitschke, 2013; Seligman & Binik, 1977), and the ability to inhibit fear in the absence of predictors of threat (e.g., Davis et al., 2000) is likewise considered an important mechanism in reducing chronic anxiety. This means that SR may exert its risk for anxiety disorders by slowing down the differential threat appraisal. Together, although previous findings have shown that anxiety development can be predicted from individual differences in NEM and CON (e.g., Miller, 2003), the individual differences in fear learning observed in the present study reveal how these traits may increase (or decrease) risk for anxiety.

Some limitations of our study deserve comment. First, the current results have been obtained within this specific fear-conditioning paradigm (e.g., involving a mild and predictable aversive event). Another experimental set up may provide more opportunity for the expression of individual differences in SR (NEM) and HA (CON) to yield differential patterns of fear learning. In addition, it should be noted that we combined participants of different experiments; however, with one exception, the inclusion of the random study effect did not improve model fit, thereby suggesting no systematic study effects. We also acknowledge that a large number of tests were conducted, which leads to an increased risk of inflated Type I error. Furthermore, it deserves mentioning that although personality traits explained significant variance in the individual fear-learning growth curves, the associated effect sizes were small. Of course, many other factors codetermine how trait dispositions become expressed in fear-learning parameters, such as baseline reactivity, attention, and shock intensity or various nonspecific physiological factors. Small effects are not uncommon in experimental research (e.g., Cohen, 1992), and small effects have previously pointed to meaningful intermediate phenotypes (Caspi & Moffit, 2006).

To recap, several studies have demonstrated meaningful associations between various personality traits and anxiety disorders. The present study extends this literature by showing that SR, HA, and their interaction exert reliable effects on fear learning. These findings derive their meaning from their potential to clarify the mechanisms governing vulnerability for developing anxiety disorders. For the examination of intermediate phenotypes (Caspi & Moffitt, 2006) of anxiety disorders, the fear-conditioning model has been proffered as a well-controlled and fine-grained research platform, but this claim may be in need of reconsideration. It is notable that the traditional fear-conditioning paradigm was originally designed to unveil general principles of fear learning and unlearning in the average organism; it was not designed to be sensitive to how specific personality traits come to expression in fear learning. Indeed, the effects of fear-conditioning procedures tend to be quite strong, which leaves relatively little room for the detection of individual differences. Moreover, the traditional fear-conditioning paradigm typically models normal fear learning rather than pathological fear learning. The transition from normal fear to pathological anxiety (Rosen & Schulkin, 1998) is characterized by maladaptive *generalization* of specific fear learning to other classes of stimuli or contexts that are intrinsically safe but somehow related to the original fear learning and *persistence* of fear responses while the threat is no longer present.

In view of these observations, we hold that a next major step to advance the field would be to modify the

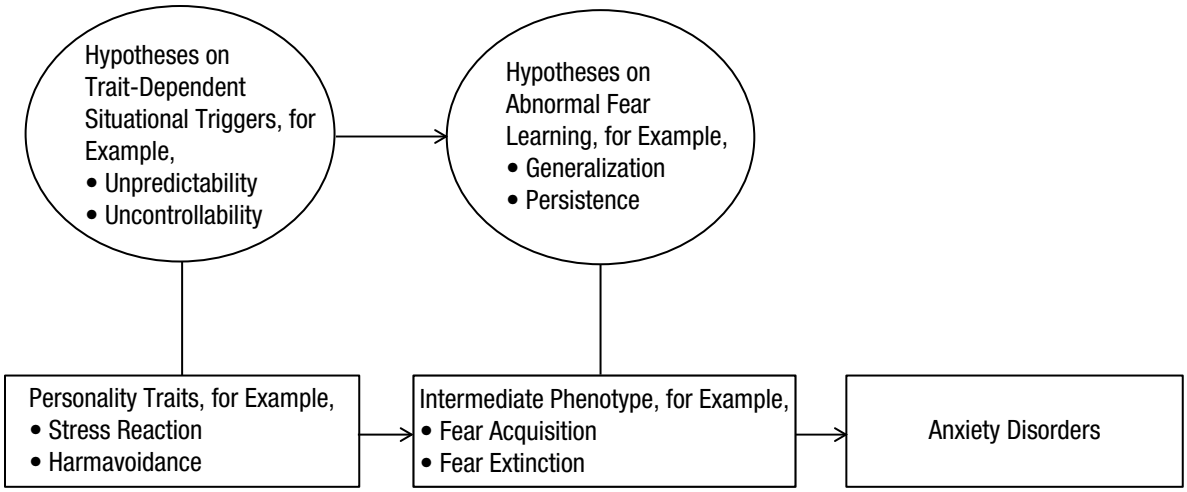

Fig. 3. Conceptual map for designing experiments crossing individual differences and fear learning.

fear-learning paradigm in ways that promote the study of fear learning as an intermediate phenotype of anxiety disorders by (a) optimizing the procedures such that the candidate traits for anxiety disorders can be optimally expressed and (b) modeling the abnormal processes of fear learning (i.e., generalization and persistence of fear). On the basis of our (and other researchers', e.g., Foa, Zinbarg, & Rothbaum, 1992; Grupe & Nitschke, 2013) review of the literature, we posit that such experimental procedures should incorporate elements that allow for the assessment of predictability/unpredictability and controllability/uncontrollability, given that unpredictability of threat lies at the root of fear generalization (i.e., less fear discrimination) and uncontrollability lies at the root of avoidance or safety behavior precluding the experience of corrective information and, thus, the persistence of fear (i.e., impaired fear extinction). Moreover, we hold that traits that are more proximal to the fear-learning parameters (such as SR and HA) are more promising to reveal their working mechanisms than are distal, atheoretical traits (such as trait anxiety and neuroticism).

To illustrate this line of reasoning, and in view of the observed modest but specific effects of SR and HA, we propose the following specific hypotheses regarding SR and HA in relation to fear-learning parameters (see Fig. 3 for a conceptual map). Individuals high on SR tend to expect, perceive, and experience/reexperience catastrophe (Tellegen & Waller, 2008), which may be best expressed in a fear-learning paradigm that incorporates the predictability/unpredictability of threat (i.e., of UCS; the proxy for catastrophe). The subjectively experienced unpredictability has differential salience for different individuals, and we conjecture that individuals with extreme SR standings will thereby exhibit overgeneralized fear responding. Predictability refers to either the onset or the termination of the UCS, given the presence or absence of a given signal (CS) or the intensity of the experienced UCS. Procedurally, a study targeting the expression of SR in fear learning might involve variable contingency schedules, variable timing of UCS administration, and variable UCS intensity. To optimize the likelihood of detecting the individual differences in fear generalization, the researcher should invest in the (iterative) fine-tuning of the experimental parameters.

HA individuals, in contrast, are characterized by the tendency to fear physical danger and by the associated avoidance of it (Tellegen & Waller, 2008), which may best be expressed in a learning paradigm that incorporates controllability/uncontrollability of threat. *Controllability* is defined in terms of the probability that a given response will prevent or terminate the UCS. The classical fear-learning paradigm (used in the present study) offers no opportunity for avoiding or controlling the administration of threat (UCS). We conjecture that individuals high on HA will have more persistent fear responding because the subjectively potentiated salience of uncontrollability will motivate avoidance and safety behaviors that, in turn, preclude disconfirmation of threat. With regard to procedure, one might manipulate the uncontrollability by instrumental fear-conditioning procedures (e.g., escape or avoidance training that involves the administration of controllable UCS; e.g., Grillon, Baas, Cornwell, & Johnson, 2006; Krypotos, Effting, Arnaudova, Kindt, & Beckers, 2013).

It warrants emphasis that this current exposition into SR and HA mainly serves as an illustration of the more general template of trait-by-fear-learning research we advocate. To complicate matters, it should be recognized that the processes of predictability and controllability are not fully independent or distinct (Foa et al., 1992); moreover, the traits are likely interactive in their effects. Accordingly, one may ultimately need to design

experiments that allow for the joint manifestation of traits. Experimental procedures that allow for the manifestation of both traits (the presumed underlying processes) may involve the combination of predictability/unpredictability and controllability/uncontrollability by manipulating the perceived rather than the actual controllability (see, e.g., Sanderson, Rapee, & Barlow, 1989). We hold that these modifications to the traditional fear-learning paradigm will contribute to its heuristic utility in terms of clarifying theory-driven intermediate phenotypes of anxiety disorders, which ultimately will help answer the fundamental question of why and how people differ in their dispositional vulnerability to develop anxiety disorders.

Author Contributions

F. J. Gazendam, J. H. Kamphuis, A. Eigenhuis, and M. Kindt developed the study concept and study design. F. J. Gazendam, M. Soeter, M. G. N. Bos, and D. Sevenster performed the testing and collected the data. F. J. Gazendam and A. Eigenhuis analyzed and interpreted the data under the supervision of J. H. Kamphuis, H. M. H. Huizenga, and M. Kindt. F. J. Gazendam drafted the manuscript, and J. H. Kamphuis, A. Eigenhuis, H. M. H. Huizenga, M. G. N. Bos, D. Sevenster, and M. Kindt provided critical revisions. All authors approved the final version of the manuscript for submission.

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The authors declared that they had no conflicts of interest with respect to their authorship or the publication of this article.

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Supplemental Material

Additional supporting information may be found at http://cpx.sagepub.com/content/by/supplemental-data

Notes

1. In several studies, other response domains were measured (electrodermal responding, UCS, expectancy or distress ratings). For this study, we did not include these responses because the subsample with complete and valid data on both the MPQ and these response measures was too small for analyses. Furthermore, all included participants were aware of the conditioned stimulus–UCS contingencies (i.e., they had learned which conditioned stimulus predicted the occurrence or nonoccurrence of the shock).
2. Fear-conditioning results remained the same when analyses were performed on the (smaller) extinction sample.
3. Given that a proportion of participants did not receive a sixth or seventh fear-conditioning trial (n = 19), we reanalyzed the results without these participants. Results were comparable and, therefore, results on the entire sample are reported.
4. We used this specific baseline for several reasons: (a) startle reactivity during habituation cannot be influenced by the experimental procedure, (b) startle reactivity is stabilized at the end of habituation, and (c) our analyses revealed that habituation was not affected by the predictors, all ts(1560) < 1.2.
5. Note that analysis of difference scores (CS1 minus CS2) is also consistent with testing the differences between groups for two stimuli (CS1 vs. CS2), as in the usual repeated measures analyses of variance performed in conditioning studies.
6. Results of all models are available from the first author.
7. The deviance test is the likelihood ratio test to compare models; the –2*log likelihood of one model is compared with that of another model. The difference has a chi-square distribution with degrees of freedom equal to the difference in the number of parameters estimated in the models compared. For the deviance tests to compare models with and without random trial effects, p values below .10 indicate that a more complex model is to be preferred over the simple model (Berkhof & Snijders, 2001).
8. Note that with 11 studies included, the power to detect between-study variances is low and, therefore, tests may indicate that between-study variance is absent, whereas it actually is present (Maas & Hox, 2005). Therefore, we reanalyzed all models with the random study intercepts included. Results were essentially the same for all models, and we report on the original model selection.
9. For the sake of brevity, we use the terms SR and HA when also referring to their corresponding factors, NEM and CON. Note that the results for the lower-order (SR, HA) and higher-order (NEM, CON) personality model were largely comparable.
10. In a sample comprising 987 students, 6.5% of students can be considered high SR/low HA (SR above the median and HA below the median). When we consider high SR as median score plus 1 and low HA as median score minus 1, then only 3% of the students fall in this category. In other words, the frequency of individuals rapidly decreases when SR scores increase and HA scores decrease (for specifics on the sample, see Eigenhuis et al., 2013).

References

Bagiella, E., Sloan, R. P., & Heitjan, D. F. (2000). Mixed-effects models in psychophysiology. *Psychophysiology*, *37*, 13–20.

Berkhof, J., & Snijders, T. A. (2001). Variance component testing in multilevel models. *Journal of Educational and Behavioral Statistics*, *26*, 133–152.

Biesanz, J. C., Deeb-Sossa, N., Papadakis, A. A., Bollen, K. A., & Curran, P. J. (2004). The role of coding time in estimating and interpreting growth curve models. *Psychological Methods*, *9*, 30–52.

Blackwell, E., Mendes de Leon, C. F., & Miller, G. E. (2006). Applying mixed regression models to the analysis of repeated-measures data in psychosomatic medicine. *Psychosomatic Medicine*, *68*, 870–878.

Bliese, P. D., & Ployhart, R. E. (2002). Growth modeling using random coefficient models: Model building, testing, and illustrations. *Organizational Research Methods*, *5*, 362–387.

Bos, M. G., Beckers, T., & Kindt, M. (2012). The effects of noradrenergic blockade on extinction in humans. *Biological Psychology*, *89*, 598–605.

Bradley, M. M., Lang, P. J., & Cuthbert, B. N. (1993). Emotion, novelty, and the startle reflex: Habituation in humans. *Behavioral Neuroscience*, *107*, 970–980.

Caspi, A., & Moffitt, T. E. (2006). Gene-environment interactions in psychiatry: Joining forces with neuroscience. *Nature Reviews Neuroscience*, *7*, 583–590.

Cohen, J. (1992). A power primer. *Psychological Bulletin*, *112*, 155–159.

Craske, M. G., Waters, A. M., Lindsey Bergman, R., Naliboff, B., Lipp, O. V., Negoro, H., & Ornitz, E. M. (2008). Is aversive learning a marker of risk for anxiety disorders in children? *Behaviour Research and Therapy*, *46*, 954–967.

Cronbach, L. J. (1957). The two disciplines of scientific psychology. *American Psychologist*, *12*, 671–684.

Cumming, G. (2014). The new statistics: Why and how. *Psychological Science*, *25*, 7–29. doi:10.1177/0956797613504966

Davis, M. (2006). Neural systems involved in fear and anxiety measured with fear-potentiated startle. *American Psychologist*, *61*, 741–756.

Davis, M., Falls, W. A., & Gewirtz, J. (2000). Neural systems involved in fear inhibition: Extinction and conditioned inhibition. In M. S. Myslobodsky & I. Weiner (Eds.), *Contemporary issues in modeling psychopathology* (pp. 113–141). New York, NY: Springer.

Depue, R. A., & Lenzenweger, M. F. (2001). A neurobehavioral dimensional model. In W. J. Livesly (Ed.), *Handbook of personality disorders: Theory, research, and treatment* (pp. 136–176). New York, NY: Guilford Press.

Eigenhuis, A., Kamphuis, J. H., & Noordhof, A. (2013). Development and validation of the Dutch brief form of the Multidimensional Personality Questionnaire (MPQ-BF-NL). *Assessment*, *20*, 565–575.

Eysenck, H. J. (1965). Extraversion and the acquisition of eyeblink and GSR conditioned responses. *Psychological Bulletin*, *63*, 258–270.

Eysenck, H. J. (1979). The conditioning theory of neurosis: Criticisms considered. *Behavioral & Brain Sciences*, *2*, 188–199.

Foa, E. B., Zinbarg, R., & Rothbaum, B. O. (1992). Uncontrollability and unpredictability in post-traumatic stress disorder: An animal model. *Psychological Bulletin*, *112*, 218–238.

Fredrikson, M., & Georgiades, A. (1992). Personality dimensions and classical conditioning of autonomic nervous system reactions. *Personality and Individual Differences*, *13*, 1013–1020.

Gazendam, F. J., Kamphuis, J. H., & Kindt, M. (2012). Deficient safety learning characterizes high trait anxious individuals. *Biological Psychology*, *92*, 342–352.

Gazendam, F. J., & Kindt, M. (2012). Worrying affects associative fear learning: A startle fear conditioning study. *PloS ONE*, *7*(4), e34882. Retrieved from http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0034882

Gray, J. A., & McNaughton, N. (Eds.). (2000). *The neuropsychology of anxiety: An enquiry into the functions of the septo-hippocampal system* (2nd ed.). Oxford, England: Oxford University Press.

Grillon, C., & Ameli, R. (2001). Conditioned inhibition of fear-potentiated startle and skin conductance in humans. *Psychophysiology*, *38*, 807–815.

Grillon, C., Baas, J. M., Cornwell, B., & Johnson, L. (2006). Context conditioning and behavioral avoidance in a virtual reality environment: Effect of predictability. *Biological Psychiatry*, *60*, 752–759.

Grupe, D. W., & Nitschke, J. B. (2013). Uncertainty and anticipation in anxiety: An integrated neurobiological and psychological perspective. *Nature Reviews Neuroscience*, *14*, 488–501.

Kindt, M., & Soeter, M. (2013). Reconsolidation in a human fear conditioning study: A test of extinction as updating mechanism. *Biological Psychology*, *92*, 43–60.

Kindt, M., & Soeter, M. (2014). Fear inhibition in high trait anxiety. *PloS ONE*, *9*(1), e86462. Retrieved from http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0086462

Kindt, M., Soeter, M., & Vervliet, B. (2009). Beyond extinction: Erasing human fear responses and preventing the return of fear. *Nature Neuroscience*, *12*, 256–258.

Kosslyn, S. M., Cacioppo, J. T., Davidson, R. J., Hugdahl, K., Lovallo, W. R., Spiegel, D., & Rose, R. (2002). Bridging psychology and biology: The analysis of individuals in groups. *American Psychologist*, *57*, 341–351.

Kramer, M., Patrick, C., Krueger, R., & Gasperi, M. (2012). Delineating physiologic defensive reactivity in the domain of self-report: Phenotypic and etiologic structure of dispositional fear. *Psychological Medicine*, *42*, 1305–1320.

Kristjansson, S. D., Kircher, J. C., & Webb, A. K. (2007). Multilevel models for repeated measures research designs in psychophysiology: An introduction to growth curve modeling. *Psychophysiology*, *44*, 728–736.

Krypotos, A., Effting, M., Arnaudova, I., Kindt, M., & Beckers, T. (2013). Avoided by association: Acquisition, extinction, and renewal of avoidance tendencies toward conditioned fear stimuli. *Clinical Psychological Science*, *2*, 336–343. doi:10.1177/2167702613503139

LaBar, K. S., Gatenby, J. C., Gore, J. C., LeDoux, J. E., & Phelps, E. A. (1998). Human amygdala activation during conditioned fear acquisition and extinction: A mixed-trial fMRI study. *Neuron*, *20*, 937–945.

Liberman, L. C., Lipp, O. V., Spence, S. H., & March, S. (2006). Evidence for retarded extinction of aversive learning in anxious children. *Behaviour Research and Therapy*, *44*, 1491–1502.

Lissek, S., Powers, A. S., McClure, E. B., Phelps, E. A., Woldehawariat, G., Grillon, C., & Pine, D. S. (2005). Classical fear conditioning in the anxiety disorders: A meta-analysis. *Behaviour Research and Therapy*, *43*, 1391–1424.

Maas, C. J., & Hox, J. J. (2005). Sufficient sample sizes for multilevel modeling. *Methodology: European Journal of Research Methods for the Behavioral and Social Sciences*, *1*, 86–92.

Miller, M. W. (2003). Personality and the etiology and expression of PTSD: A three-factor model perspective. *Clinical Psychology: Science and Practice*, *10*, 373–393.

Miller, M. W., Greif, J. L., & Smith, A. A. (2003). Multidimensional Personality Questionnaire profiles of veterans with traumatic combat exposure: Externalizing and internalizing subtypes. *Psychological Assessment*, *15*, 205–215.

Miller, M. W., Kaloupek, D. G., Dillon, A. L., & Keane, T. M. (2004). Externalizing and internalizing subtypes of combat-related PTSD: A replication and extension using the PSY-5 scales. *Journal of Abnormal Psychology*, *113*, 636–645.

Mineka, S., & Oehlberg, K. (2008). The relevance of recent developments in classical conditioning to understanding the etiology and maintenance of anxiety disorders. *Acta Psychologica*, *127*, 567–580.

Morris, R. W., & Bouton, M. E. (2006). Effect of unconditioned stimulus magnitude on the emergence of conditioned responding. *Journal of Experimental Psychology: Animal Behavior Processes*, *32*, 371–385.

Otto, M. W., Leyro, T. M., Christian, K., Deveney, C. M., Reese, H., Pollack, M. H., & Orr, S. P. (2007). Prediction of "fear" acquisition in healthy control participants in a de novo fear-conditioning paradigm. *Behavior Modification*, *31*, 32–51.

Pamir, E., Chakroborty, N. K., Stollhoff, N., Gehring, K. B., Antemann, V., Morgenstern, L., . . . Nawrot, M. P. (2011). Average group behavior does not represent individual behavior in classical conditioning of the honeybee. *Learning & Memory*, *18*, 733–741.

Patrick, C. J., Curtin, J. J., & Tellegen, A. (2002). Development and validation of a brief form of the Multidimensional Personality Questionnaire. *Psychological Assessment*, *14*, 150–163.

Pineles, S. L., Vogt, D. S., & Orr, S. P. (2009). Personality and fear responses during conditioning: Beyond extraversion. *Personality and Individual Differences*, *46*, 48–53.

Pinheiro, J. C., & Bates, D. M. (2000). *Linear mixed-effects models: Basic concepts and examples*. New York, NY: Springer.

Pinheiro, J., Bates, D., DebRoy, S., & Sarkar, D. (2011). R Development Core Team. 2010. nlme: linear and nonlinear mixed effects models. R package version 3.1-97. R Foundation for Statistical Computing, Vienna.

Plomin, R., & Kosslyn, S. M. (2001). Genes, brain and cognition. *Nature Neuroscience*, *4*, 1153–1154.

Rescorla, R. A., & Wagner, A. R. (1972). A theory of Pavlovian conditioning: Variations in the effectiveness of reinforcement and nonreinforcement. In A. H. Black & W. F. Prokasy (Eds.), *Classical conditioning II: Current theory and research* (pp. 64–99). New York, NY: Appleton-Century-Crofts.

Rosen, J. B., & Schulkin, J. (1998). From normal fear to pathological anxiety. *Psychological Review*, *105*, 325–350.

Royston, P., Altman, D. G., & Sauerbrei, W. (2006). Dichotomizing continuous predictors in multiple regression: A bad idea. *Statistics in Medicine*, *25*, 127–141.

Sanderson, W. C., Rapee, R. M., & Barlow, D. H. (1989). The influence of an illusion of control on panic attacks induced via inhalation of 5.5% carbon dioxide-enriched air. *Archives of General Psychiatry*, *46*, 157–162.

Schielzeth, H. (2010). Simple means to improve the interpretability of regression coefficients. *Methods in Ecology and Evolution*, *1*, 103–113.

Seligman, M. E. P., & Binik, Y. M. (1977). The safety signal hypothesis. In H. Davis & H. M. B. Hurwitz (Eds.), *Operant-Pavlovian interactions* (pp. 165–180). Hillsdale, NJ: Erlbaum.

Sevenster, D., Beckers, T., & Kindt, M. (2012a). Instructed extinction differentially affects the emotional and cognitive expression of associative fear memory. *Psychophysiology*, *49*, 1426–1435.

Sevenster, D., Beckers, T., & Kindt, M. (2012b). Retrieval per se is not sufficient to trigger reconsolidation of human fear memory. *Neurobiology of Learning and Memory*, *97*, 338–345.

Snijders, T. A. B., & Bosker, R. J. (1999). *Multilevel analysis: An introduction to multilevel modeling*. London, England: Sage.

Soeter, M., & Kindt, M. (2010). Dissociating response systems: Erasing fear from memory. *Neurobiology of Learning and Memory*, *94*, 30–41.

Soeter, M., & Kindt, M. (2011a). Disrupting reconsolidation: Pharmacological and behavioral manipulations. *Learning & Memory*, *18*, 357–366.

Soeter, M., & Kindt, M. (2011b). Noradrenergic enhancement of associative fear memory in humans. *Neurobiology of Learning and Memory*, *96*, 263–271.

Soeter, M., & Kindt, M. (2012). Stimulation of the noradrenergic system during memory formation impairs extinction learning but not the disruption of reconsolidation. *Neuropsychopharmacology*, *37*, 1204–1215.

Tabachnick, B. G., & Fidell, L. S. (2000). *Using multivariate statistics* (5th ed.). New York, NY: HarperCollins.

Tellegen, A., & Waller, N. G. (2008). Exploring personality through test construction: Development of the Multidimensional Personality Questionnaire. In G. J. Boyle, G. Matthews, & D. H. Saklofske (Eds.), *The SAGE handbook of personality theory and assessment* (Vol. 2, pp. 261–292). Thousand Oaks, CA: Sage.

Torrents-Rodas, D., Fullana, M. A., Bonillo, A., Caseras, X., Andión, Ó., & Torrubia, R. (2012). No effect of trait anxiety on differential fear conditioning or fear generalization. *Biological Psychology*, *92*, 185–190.

Twisk, J. W. R. (2006). *Applied multilevel analysis: A practical guide*. New York, NY: Cambridge University Press.

Vaidyanathan, U., Patrick, C. J., & Cuthbert, B. N. (2009). Linking dimensional models of internalizing psychopathology to neurobiological systems: Affect-modulated startle as an indicator of fear and distress disorders and affiliated traits. *Psychological Bulletin*, *135*, 909–942.

Walker, D. L., & Davis, M. (2002). Quantifying fear potentiated startle using absolute versus proportional increase scoring methods: Implications for the neurocircuitry of fear and anxiety. *Psychopharmacology*, *164*, 318–328.

Walker, D. L., Toufexis, D. J., & Davis, M. (2003). Role of the bed nucleus of the stria terminalis versus the amygdala in fear, stress, and anxiety. *European Journal of Pharmacology*, *463*, 199–216.

White, T. L., & Depue, R. A. (1999). Differential association of traits of fear and anxiety with norepinephrine- and dark-induced pupil reactivity. *Journal of Personality and Social Psychology*, *77*, 863–877.