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Tell me what to do: Stress facilitates stimulus-response learning by instruction

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ABSTRACT

Learning by explicit instruction is a highly efficient way to instantaneously learn new behaviors and to overcome potentially harmful learning by trial-and-error. Despite the importance of instructed learning for education, influences on the efficacy of an instruction are currently unknown. Decades of research, however, showed that stress is a powerful modulator of learning and memory, including the acquisition of stimulus-response (S-R) associations. Moreover, brain areas critical for instructed learning are a major target of hormones and neurotransmitters released during stress. Thus, we investigated here whether acute stress affects instructed S-R learning and whether this effect differs for trial-and-error learning. To this end, healthy participants underwent a stressor (Socially Evaluated Cold Pressor Test) or a control manipulation before learning arbitrary S-R associations. For half of the stimuli, participants were explicitly instructed about the correct association, whereas the remaining associations had to be learned by trial-and-error. As expected, the instruction resulted in better performance and enhanced explicit rule knowledge compared to trial-and-error learning. Stress further boosted the beneficial effect of an explicit instruction on learning performance, while leaving trial-and-error learning unchanged. These beneficial effects of stress were directly correlated with the activity of the autonomic nervous system and the concentration of cortisol. Moreover, acute stress could override the detrimental effect of high trait anxiety levels on instructed S-R learning performance. Our findings indicate that acute stress may facilitate learning from instruction, which may represent a highly efficient way to learn how to act, without the necessity of own experience, that helps to save cognitive resources during a stressful encounter.

1. Introduction

The ability to rapidly adopt novel rules about which action results in a certain outcome is a hallmark of human goal-directed behavior (Ruge & Wolfensteller, 2010). Whereas most other animals rely heavily on learning by trial-and-error, humans can use their unique communicative skills to avoid this time-consuming and potentially dangerous way of learning (Petrides, 1997; Wolfensteller & Ruge, 2012). For instance, we do not have to try whether smoking puts us at risk for cancer, or whether managing a phone conference while driving during rush hour is dangerous. Instead, we can use instructed rules that can be rapidly implemented, leading to almost perfect performance instantaneously. Despite the importance of instructed learning in everyday life and virtually all educational settings, it is largely unclear to what extent the fundamental process of learning by instruction is shaped by characteristics of the situation and the individual.

Acute stress is very well known to alter learning and memory processes (Joëls, Pu, Wiegert, Oitzl, & Krugers, 2006; Quirarte, Roozendaal, & McGaugh, 1997; Schwabe, Joëls, Roozendaal, Wolf, & Oitzl, 2012; Smeets et al., 2009; Zoladz et al., 2011). In particular, stress is thought to enhance memory formation but to impair memory retrieval (Schwabe et al., 2012). Whereas early research focused mainly on stress-induced changes in hippocampus-dependent forms of learning and memory, more recent research shows that stress may also affect stimulus-response (S-R) learning that is supported by the dorsal striatum (Guenzel, Wolf, & Schwabe, 2013; Quirarte et al., 2009) Beyond changes in single memory systems, stress has further been shown to favor rather simple forms of 'habitual' memory over more flexible and elaborate memory processes or goal-directed behavior (Packard & Wingard, 2004; Schwabe et al., 2012; Schwabe, Tegenthoff, Höffken, & Wolf, 2013; Schwabe & Wolf, 2009, 2012, 2013; Siller-Perez, Serafin, Prado-Alcala, Roozendaal, & Quirarte, 2017; Wingard & Packard, 2008). At the neural level, these effects of stress on learning and memory are critically mediated by the amygdala interacting with the prefrontal cortex (PFC), hippocampus, and the dorsal striatum (Arnsten, 2009; Hermans, Henckens, Joels, & Fernandez, 2014; Schwabe et al.,

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2013; Schwabe & Wolf, 2012; Vogel, Fernandez, Joels, & Schwabe, 2016; Vogel et al., 2017). These structures are also of pivotal importance to instructed learning (e.g., Doll, Jacobs, Sanfey, & Frank, 2009; Ruge & Wolfensteller, 2010, 2015, 2016; Wolfensteller & Ruge, 2012). The LPFC is thought to encode and maintain relevant symbolic rule representations in a 'procedural' working memory and guide the transfer to a pragmatic rule by the posterior premotor cortex and the dorsal striatum (Ruge & Wolfensteller, 2010). Rules learned previously can be stored in episodic memory in the medial temporal lobe, and retrieval of these rules in the correct context is again guided by the LPFC (Doll et al., 2009). Further support for important roles of the LPFC and the medial temporal lobe in instructed learning comes from patients with lesions in frontal and temporal regions that are unable to learn from instruction despite normal intelligence test scores (Petrides, 1997). Although instructed learning relies on prefrontal areas that are known to be highly stress sensitive, previous research on stress-induced changes in S-R learning focused on trial-and-error learning and whether learning from instruction is affected by stress is unknown.

In addition to situational variables such as a stressful encounter, individual differences in trait anxiety or related personality traits are associated with learning and memory performance. For instance, clinical anxiety is linked to impairments in prefrontal working memory (Castaneda, 2010) and hippocampal memory (Airaksinen, Larsson, & Forsell, 2005; Thoresen et al., 2016). Also in subclinical populations, trait anxiety is associated with increased worrying which impairs working memory capacity (Eysenck & Calvo, 1992), and with attentional and memory biases towards threat signals which may reduce task performance (Bishop, 2007). At the neural level, these biases are paralleled by enhanced activity in brain regions activated in response to emotional stimuli, i.e. amygdala, insula, dorsal anterior cingulate cortex (ACC), anterior hippocampus, and superior frontal gyrus, and reduced activity in regions of the default mode network (Servaas et al., 2013; Stein, Simmons, Feinstein, & Paulus, 2007). Moreover, another study showed reduced top-down regulation of the amygdala, resulting in enhanced emotional responding (Cremers et al., 2010). However, whether (subclinical) trait anxiety may interfere with the use of an instruction in learning and whether such an effect of trait anxiety interacts with acute stress, as suggested by a recent study (Goette, Bendahan, Thoresen, Hollis, & Sandi, 2015), is currently unknown.

The current experiment was set up to answer how acute stress affects instructed S-R learning in contrast to S-R learning by trial-and-error, whether individual differences in instructed learning performance depend on individual trait anxiety levels, and whether stress and anxiety interact to affect instructed learning. To address these questions, healthy participants were exposed to a standardized laboratory stressor, the socially evaluated cold pressor test (SECPT; Schwabe, Haddad, & Schachinger, 2008), or a non-stressful control procedure before learning S-R associations. Importantly, participants were instructed about the correct response for half of the stimuli, but had to use trial-and-error learning for the remaining stimuli. Additionally, trait anxiety was assessed using a German version of the Spielberger State-Trait Anxiety Inventory (STAI; Laux, Glanzmann, Schaffner, & Spielberger, 1981). We expected that performance would be significantly enhanced by prior instruction. Given that the brain areas underlying instructed learning are highly stress sensitive, we expected that stress would alter instructed learning. The exact direction of this effect, however, was difficult to predict because on the one hand stress is known to impair prefrontal (and often hippocampal) processing (Arnsten, 2009; Hermans et al., 2014; Schwabe & Wolf, 2013; Vogel et al., 2016), suggesting that stress might impair the effectiveness of an instruction. On the other hand, stress is thought to enhance S-R learning (Guenzel, Wolf, & Schwabe, 2014; Quirarte et al., 2009; Vogel et al., 2017), which might also result in better instructed S-R learning. Moreover, we expected that high trait anxiety would be associated with impaired instructed learning.

2. Materials and methods

2.1. Participants and experimental design

Sixty-one healthy, normal-weight volunteers with normal or corrected-to-normal vision (mean body mass index [BMI] = 22.5, SD = 2.13) participated in this study. Two participants (female/stress and male/control) stopped the experiment before the instructed learning task. Thus, the final number of participants for the learning task was 59 (30 women, 29 men, mean age = 24.7 years, SD = 3.6 years). We excluded individuals with current medication intake, any medical condition potentially affecting stress reactivity, and lifetime history of any neurological or psychiatric disorder. We also excluded smokers and women taking hormonal contraceptives as both smoking and hormonal contraceptives affect the cortisol response to stress (Kirschbaum, Kudielka, Gaab, Schommer, & Hellhammer, 1999; Rohleder & Kirschbaum, 2006). Moreover, women were not tested during their menses. The study protocol was approved by the institutional review board (University of Hamburg, Vogel II). All participants provided written informed consent and received monetary compensation for participation (16.50 €, approximately 20 USD).

We used a mixed design with the between-subjects factors treatment (stress vs. control manipulation), and the within-subject factor instruction (instructed vs. not instructed learning) to investigate the effects of stress and trait anxiety on instructed S-R learning as opposed to learning by trial-and-error. Participants were pseudorandomly assigned to treatment groups in order to reach a comparable gender distribution in the two groups (stress: n = 30, 15 men; control: n = 29, 14 men). The resulting groups did not differ in age (p = .159), BMI (p = .294), depressive symptoms (p = .893), or trait anxiety (p = .551, Table 1).

Table 1
Subjective mood, ratings, and trait anxiety for both experimental groups across the experiment.

	Control group			Stress group		
	Before control procedure	After control procedure	End of experiment	Before SECPT	After SECPT	End of experiment
Subjective mood						
Low vs. elevated mood	33.86 (4.84)	33.24 (5.31)	32.55 (6.13)	35.27 (4.21)	32.17 (5.51)$^{\circ\circ\circ}$	34.27 (4.80)$^{++}$
Restlessness vs. calmness	31.28 (5.84)	31.86 (5.74)	31.52 (5.90)	33.74 (4.62)	30.97 (6.63)$^{\circ\circ}$	33.23 (5.36)$^{++}$
Sleepiness vs. Wakefulness	30.90 (4.61)	29.59 (5.41)	28.03 (6.08)$^{+}$	30.93 (5.38)	31.27 (5.51)	28.87 (6.66)$^{+}$
Rating of SECPT/control procedure						
Difficult		9.64 (23.96)***			51.67 (28.42)	
Unpleasant		7.14 (12.43)***			64.00 (23.28)	
Stressful		8.57 (17.58)***			52.33 (28.25)	
Trait anxiety	37.14 (10.88)			35.43 (10.84)		

Note: Data represent mean (SD). SECPT socially evaluated cold pressor test. $^{***}p < .001$ compared to stress group; $^{\circ\circ\circ}p < .001/^{\circ\circ}p < .01$ compared to before the experimental treatment; $^{++}p < .01/^{+}p < .05$ compared to directly after the experimental treatment.

2.2. Procedure and instructed S-R learning task

All testing took place in the afternoon (13:00–18:45) to control for the diurnal rhythm of cortisol. Upon their arrival at the laboratory and their informed consent, participants provided a baseline saliva sample (see Section 2.3) and their vital signs (blood pressure and heart rate) were assessed using a Dinamap system (Critikon). They completed German versions of the STAI (Laux et al., 1981), Beck Depression Inventory (Hautzinger, Bailer, Worall, & Keller, 1994), and a German mood questionnaire (MDBF; Steyer, Schwenkmezger, Notz, & Eid, 1994) that assesses current low vs. elevated mood, restlessness vs. calmness, and sleepiness vs. wakefulness. Sum scores per MDBF scale range from 8 to 40 and high scores represent elevated mood, calmness, and wakefulness, respectively.

Participants were then brought to a separate room where they underwent either the SECPT or a non-stressful control procedure (Schwabe et al., 2008). The SECPT is a standardized laboratory stressor for humans, known to reliably activate both the ANS and the HPA axis. Briefly, participants in the stress group had to immerse their right hand up to and including the wrist into ice water (0–2 °C) for up to three minutes (or until they could no longer tolerate it). They were monitored and evaluated by a rather cold, non-reinforcing, and unfamiliar opposite-sex experimenter and videotaped throughout the SECPT. In contrast, participants in the control group immersed their right hand in warm water (35–37 °C) and they were neither monitored nor videotaped.

To evaluate the effectiveness of the stress induction, participants' vital signs were assessed again during and after the experimental treatment. In addition, participants completed another MDBF and rated the difficulty, stressfulness, and unpleasantness of the experimental treatment on three scales from 0 to 100. After two additional saliva samples, another vital signs and mood assessment, and a short task probing planning behavior (which will be reported elsewhere), the instructed learning task started approximately 32 min (SD 3.9) after the onset of the experimental treatment, when peak cortisol responses to the SECPT could be expected (Guenzel et al., 2013; Schwabe et al., 2008).

The task began with the instruction phase in which participants were sequentially presented with eight abstract geometrical stimuli and a highlighted target button (out of four buttons) which they should press (Fig. 1). The stimuli were presented for 4 s, followed by feedback (the word 'correct' or 'incorrect' in German, 1 s) and a jittered inter-trial-interval (on average 2.25 s). The instruction phase was comprised of two blocks; all eight stimuli were presented once per block in random order. To assess the effectiveness of the instruction, participants were then asked to explicitly assign the correct target button to each stimulus on a paper-pencil questionnaire. Thereafter, the study phase started in which participants were presented with the eight instructed stimuli randomly intermixed with eight new stimuli for which they were required to learn the target button by trial-and-error. Stimuli were presented for 2.5 s, followed by feedback (1 s), and a jittered inter-trial-interval (on average 2.25 s). The assignment of the stimulus set to be instructed or not instructed was counterbalanced across participants and the assignment of stimuli to target buttons was randomized. There were ten blocks in the study phase and all stimuli were presented once per block (160 trials in total). At the end of the study phase, participants were again asked to explicitly assign the correct target buttons to all 16 stimuli (i.e., eight learned by instruction and eight by trial-and-error) on a paper-pencil questionnaire. After a final saliva sample, vital signs, and mood assessment, participants were debriefed, paid and left the laboratory.

2.3. Saliva sampling

To measure concentrations of the stress hormone cortisol, saliva samples were obtained using Salivette® collection devices (Sarstedt, Germany). At the end of the experiment, all samples were stored at −18 °C (−0.4 °F). At the end of the study, the samples were thawed for biochemical analysis, and the fraction of free cortisol was assessed using a commercially available chemiluminescence immunoassay (IBL, Tecan Trading AG, Switzerland).

2.4. Data analysis

To examine whether the stress induction was successful, subjective and physiological data were analyzed using repeated measures analyses of variance (rmANOVAs) with the between-subjects factor treatment and the within-subject factor time, followed by t-tests where indicated. T-tests were also used to investigate group differences in the ratings of the SECPT/control manipulation. Explicit rule knowledge was assessed by summing the errors in the explicit knowledge questionnaires, task performance was aggregated per instruction condition and block, and converted to percentages. RmANOVAs were used to investigate the effects of stress on instructed vs. not instructed (=trial-and-error) learning over blocks, t-tests were used to follow-up group differences and to test against chance level. To explore the association between task performance, explicit rule knowledge, and reactivity of ANS and HPA axis, we calculated the area under the curve with respect to the increase

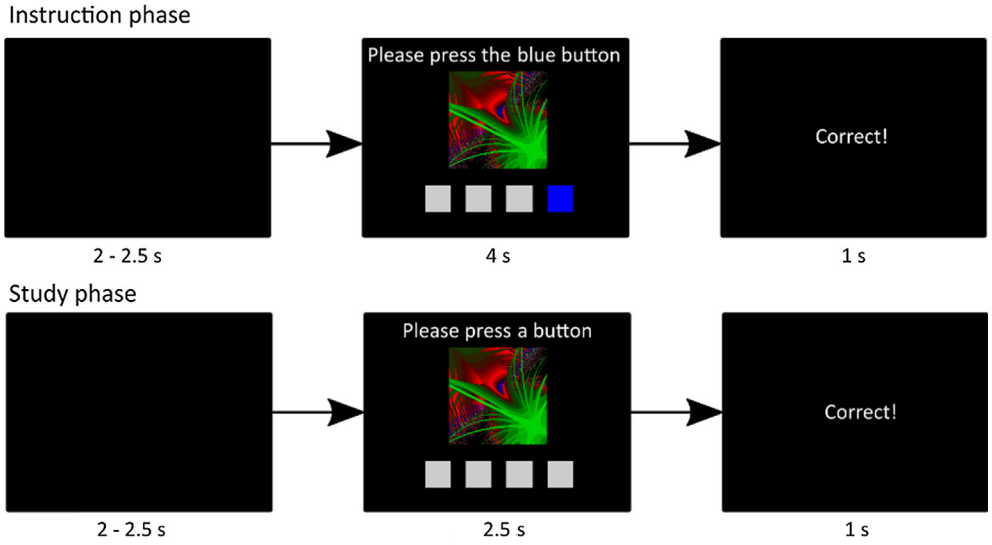

Fig. 1. Learning task. In the instruction phase, participants were presented with eight abstract geometrical stimuli (one stimulus per trial) for four seconds and told to press the target button (highlighted in blue), followed by feedback. Each stimulus was shown twice. In the study phase, participants were presented with the eight instructed stimuli and eight new stimuli for which they were told to learn the target button by trial-and-error. Each stimulus was presented ten times in the study phase; stimulus order was randomized and assignment to the 'instructed' and 'non-instructed' lists was counterbalanced across participants. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

for cortisol (Pruessner, Kirschbaum, Meinlschmid, & Hellhammer, 2003) and the increase from before to during experimental treatment (measurement 2 – measurement 1) for blood pressure as the blood pressure response is much more short-lived. Pearson's r was used to assess these associations and to investigate the link between learning and trait anxiety. The latter analysis was repeated using partial correlations correcting for state anxiety to exclude that associations were driven by current state anxiety rather than trait anxiety. Finally, we used linear regressions to predict average performance for instructed and not instructed stimuli by trait anxiety scores (mean centered), treatment group, and a treatment × trait anxiety interaction term. All analyses were conducted using IBM SPSS Statistics 24. The alpha level was set to $\alpha = 0.05$ for all analyses (two-tailed), and Greenhouse-Geisser correction was used to correct for violations of sphericity (corrected dfs reported). Data on trait anxiety was missing for one participant (female/control), and one saliva sample (female/stress) did not contain enough saliva to be analyzed. Furthermore, a technical failure during the instructed learning task resulted in performance data loss for the study phase of one male/stress participant. Thus, the respective analyses were based on a sample of 58 participants.

3. Results

3.1. Successful stress induction before learning

As expected, the SECPT was experienced as more stressful, unpleasant, and difficult than the control treatment (all $p < .001$, Table 1). Additionally, stress affected positive mood and calmness (mood: time × treatment: $F(1.8, 103.6) = 5.59$, $p = .006$, $\eta^2 = .089$, calmness: time × treatment: $F(1.9, 109.4) = 5.42$, $p = .006$, $\eta^2 = .087$, Table 1). Positive mood and calmness decreased in response to the SECPT (mood before – after: $p < .001$, calmness: $p = .009$) whereas they did not change in response to the control manipulation ($p = .277$ and $p = .336$, respectively). Sleepiness was not affected by stress (all $p > .30$).

The successful stress induction by the SECPT was further indicated by profound activations of the ANS and HPA axis (Fig. 2). In detail, diastolic and systolic blood pressure increased in response to the SECPT compared to the control condition (systolic blood pressure: time × treatment: $F(2.9, 167.0) = 15.49$, $p < .001$, $\eta^2 = .214$, treatment: $F(1, 57) = 5.52$, $p = .022$, $\eta^2 = .088$; diastolic blood pressure: time × treatment: $F(2.8, 159.7) = 28.65$, $p < .001$, $\eta^2 = .334$, treatment: $F(1, 57) = 12.90$, $p = .001$, $\eta^2 = .185$). Whereas there was a statistical trend for heightened blood pressure in the stress group already prior to treatment (systolic: $p = .081$, diastolic: $p = .061$), blood pressure was strongly elevated during the SECPT as compared to the control manipulation (systolic and diastolic: $p < .001$), an effect which remained for approximately ten minutes but wore off afterwards (systolic +8 min: $p = .025$, +28 min: $p = .502$, +53 min: $p = .318$; diastolic +8 min: $p = .036$, +28 min: $p = .051$, +53 min: $p = .303$). A similar transient increase was observed for heart rate (time × treatment: $F(3.5, 199.0) = 14.55$, $p < .001$, $\eta^2 = .203$) with the stress group showing elevated heart rates compared to the control group during the SECPT ($p = .003$), but not before ($p = .503$) or after the experimental treatment (all $p > .40$). We also found a significant cortisol response to the SECPT (time × treatment: $F(1.8, 102.0) = 10.17$, $p < .001$, $\eta^2 = .154$, treatment: $F(1, 56) = 13.48$ $p = .001$, $\eta^2 = .194$), resulting in higher cortisol levels after the SECPT (+15 min: $p = .006$) and during task performance (+28 min: $p < .001$, +53 min: $p = .004$), but not prior to the SECPT ($p = .912$). To conclude, the SECPT induced a significant subjective and physiological stress response, resulting in elevated cortisol levels throughout task performance.

3.2. Instruction improves task performance and explicit rule knowledge

Next, we assessed whether an explicit instruction indeed improved performance. As expected, task performance during the initial instruction phase was high and increased over the two instruction blocks (block 1: 88.1%, block 2: 94.8%, main effect block: $F(1, 56) = 19.17$, $p < .001$, $\eta^2 = .255$, chance was 25%, Fig. 3). Moreover, participants performed clearly above chance in the explicit rule knowledge test, making on average 3.1 (± 1.95) mistakes (chance: 6 mistakes, $t(58) = -11.27$, $p < .001$).

The beneficial effect of the initial instruction was revealed in the following study phase: As expected, task performance in this study phase was significantly better for instructed than not instructed stimuli (average performance instructed: 57.5%, not instructed: 39.9%, $F(1, 56) = 75.76$, $p < .001$, $\eta^2 = .575$; Fig. 3B). Performance in each single block was higher for instructed than not instructed stimuli (all $p < .01$), although the difference due to the instruction tended to decrease over blocks (instruction × block: $F(7.3, 407.9) = 1.92$, $p = .062$, $\eta^2 = .033$; main effect of block: $F(7.2, 403.18) = 17.10$, $p < .001$, $\eta^2 = .234$). Notably, the beneficial effect of the instruction could not be explained by merely more exposure to the stimuli, as the differences remained when comparing task performance for the instructed set in a given block with performance for the not instructed set two blocks later, thus controlling for stimulus exposure (block 1 vs. 3, 2 vs. 4, and so on, all $p < .05$). Finally, participants made fewer errors in the explicit rule test after the study phase for instructed stimuli (on average 2.3 errors) than for not instructed stimuli (3.0 errors; instruction: $F(1, 56) = 6.56$, $p = .013$, $\eta^2 = .105$, Fig. 3D). Thus, both task performance data and explicit rule knowledge indicated that instructed S-R associations were clearly better acquired than those learned by trial-and-error.

3.3. Stress boosts instructed S-R learning

Stress markedly improved the effectiveness of the initial instruction as revealed by fewer errors in the explicit rule knowledge test after the instruction phase ($t(52.7) = -2.07$, $p = .043$, Fig. 3D). This improvement was associated with both ANS and HPA axis activity across groups, with higher diastolic blood pressure and cortisol responses to treatment being associated with fewer explicit knowledge errors (diastolic blood pressure: $r = -.324$, $p = .013$; cortisol: $r = -.291$, $p = .027$, Fig. 4). Although these associations did not reach significance in the stress group alone ($r = -.270$, $p = .157$ and $r = -.284$, $p = .135$, respectively), most likely due to a lack of power in this smaller sample, they suggest that both cortisol and autonomic arousal enhance instructed S-R learning.

Task performance in the instruction phase was not affected by stress ($p = .888$), likely due to a ceiling effect considering the high average performance level overall. In the study phase, however, stressed participants showed a significantly stronger benefit of the instruction (average instructed: 60.8%, not instructed: 38.6%) compared to the control group (instructed: 54.3%, not instructed: 41.3%, instruction × treatment: $F(1, 56) = 5.15$, $p = .027$, $\eta^2 = .084$, Fig. 3B). Difference scores (instructed – not instructed) revealed that stress enhanced the instruction benefit particularly in block 1, 7, and 8 ($p = .012$, $p = .099$, and $p = .037$, respectively, Fig. 3C). Exploratory analyses testing whether stress effects might be modulated by gender revealed no treatment × gender interaction on task performance or explicit knowledge (all $p \geq .082$, all $p > .10$ for follow-up T-tests).

The beneficial effect of stress on instructed learning was further indicated by correlation analyses: Participants with a stronger diastolic blood pressure response to treatment displayed better performance for instructed stimuli across both groups ($r = .325$, $p = .013$) and in the stress group alone ($r = .390$, $p = .037$), but not in the control group ($p = .439$). Importantly, the diastolic blood pressure response was not associated with performance for the not instructed set (across groups:

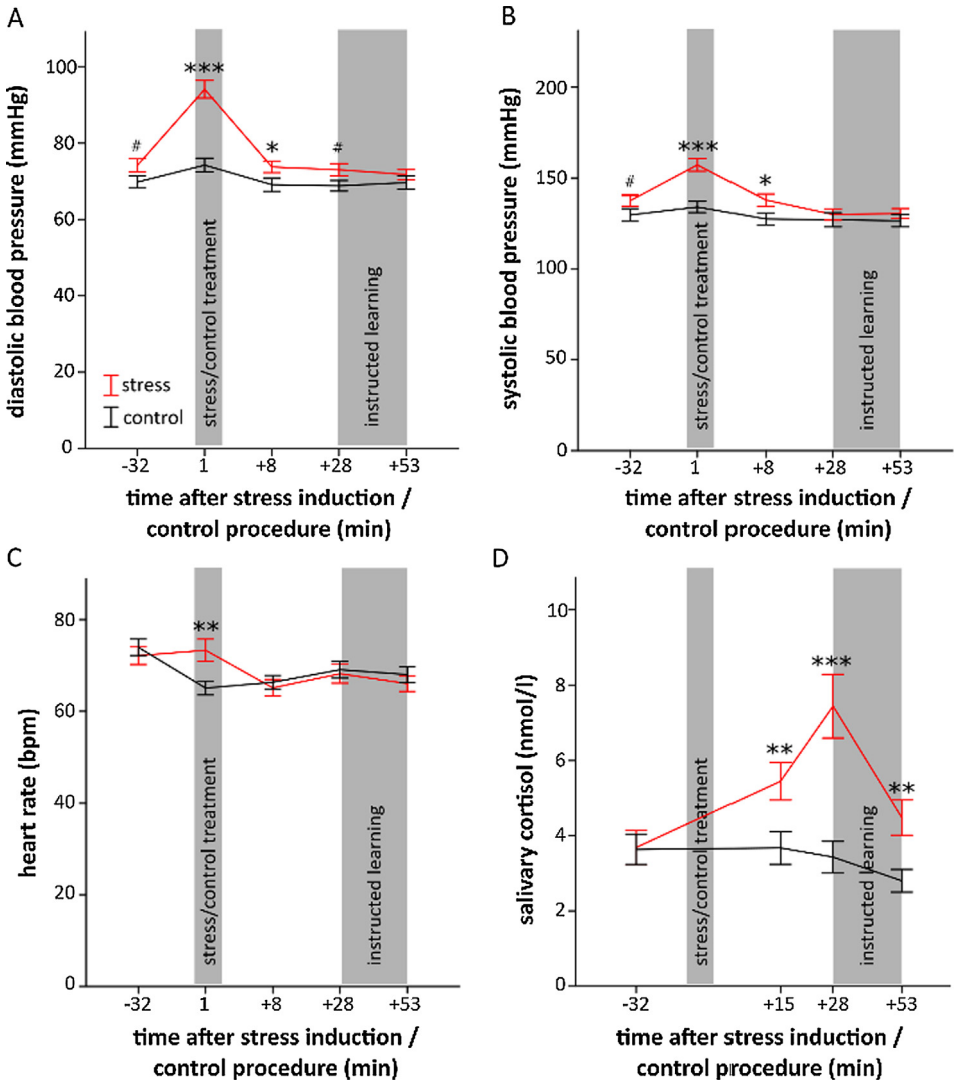

Fig. 2. Successful stress induction by the SECPT. Individuals in the stress group showed significant elevations of diastolic blood pressure (A), systolic blood pressure (B), and heart rate (C) during the experimental manipulation, indicating a pronounced activation of the autonomous nervous system. (D) Moreover, the exposure to the SECPT resulted in a significant activation of the hypothalamus-pituitaryadrenal axis leading to heightened cortisol levels during task performance. SECPT Socially Evaluated Cold Pressor Test. Data show mean ± 1 SEM, $^{***}p < .001$, $^{**}p < .01$, $^{*}p < .05$, $^{\#}p < .10$.

$p = .673$, stress group: $p = .129$), supporting that stress-induced autonomic arousal was selectively associated with enhanced learning of instructed associations. No association with the cortisol response to treatment was found (across groups: $r = .135$, $p = .314$, stress group: $r = .167$, $p = .387$).

3.4. Trait anxiety is associated with impaired instructed learning

After establishing that acute stress affects instructed learning, we set out to investigate whether trait anxiety is associated with inter-individual differences in instructed learning and whether trait anxiety may modulate the impact of acute stress. As hypothesized, individuals with higher trait anxiety scores displayed impaired performance for instructed associations. Across experimental groups, more anxious individuals made more errors in the explicit rule knowledge test after the instruction phase ($r = .287$, $p = .030$, Fig. 5), showed impaired task performance at the end of the instruction phase (block 2: $r = -.286$, $p = .031$), and displayed lower average performance during the study phase for instructed stimuli ($r = -.286$, $p = .031$). Importantly, there was no association with task performance for not instructed stimuli ($p = .128$) and partial correlations correcting for state anxiety revealed a highly similar pattern, supporting the idea that it is trait anxiety that reduces the effectiveness of an instruction.

3.5. Stress overrides anxiety-related individual differences in instructed learning

Upon investigating these associations further, we discovered that all of these correlations between trait anxiety and instructed learning were present in the control group (errors: $r = .497$, $p = .007$, block 2 performance: $r = -.359$, $p = .061$, average performance: $r = -.547$, $p = .003$) but not in the stress group (all $p > .30$). We thus performed linear regressions to test whether the effect of trait anxiety on instructed learning was altered by acute stress.

Indeed, we found that the effect of trait anxiety on average instructed learning performance in the study phase depended on treatment (treatment × trait anxiety: $\beta = -.406$, $p = .024$, whole model: $R^2 = .187$, $F(3, 53) = 4.07$, $p = .011$, Table 2). When using the performance for not instructed stimuli as outcome, the model turned insignificant ($R^2 = .082$, $F(3, 53) = 1.574$, $p = .207$, Table 2) and there was no significant trait anxiety × treatment interaction ($p = .229$), suggesting that anxiety and trait specifically affected instructed

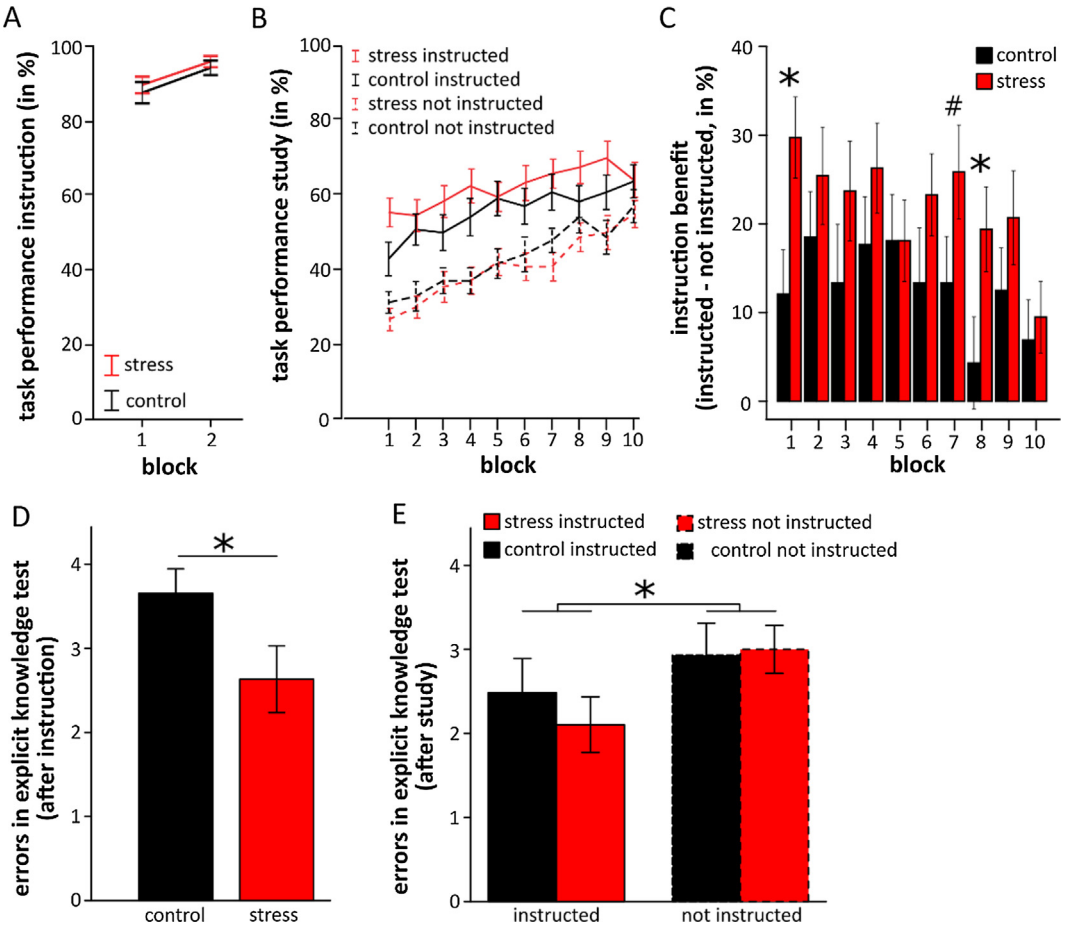

Fig. 3. Task performance and explicit task knowledge. (A) Performance during the instruction phase was high and increased from block 1 to block 2 for both groups (red: stress, black: control), and groups did not differ. (B) During the study phase, task performance was better for instructed stimuli (solid lines) compared to not instructed stimuli (dashed lines) in each block. Moreover, the benefit of the instruction was stronger in the stress group compared to the control group. (C) The enhanced instruction benefit in the stress group was particularly pronounced in block 1, 7, and 8. (D) Stressed individuals showed better explicit knowledge of instructed stimulus-response associations as revealed by fewer errors in the explicit knowledge test after the instruction phase. (E) At the end of the experiment, participants had better explicit knowledge for the instructed stimuli compared to not instructed stimuli, but no group difference was found (all $p > .30$). Data show mean ± 1 SEM, $^{*}p < .05$, $^{\#}p < .10$.

learning. Notably, the results were very similar when depressive symptoms and gender were included first in a stepwise regression model (trait anxiety × treatment: $\beta = -.479$, $p = .002$) and depressive symptoms and gender had no effect by themselves ($p = .349$ and $p = .377$, respectively).

To illustrate this interaction between acute stress and trait anxiety further and compare individuals with different trait anxiety scores, we split the sample across the median into a high trait anxiety group (trait anxiety > 35, n = 27 of which 15 from the stress group, 18 women) and a low trait anxiety group (trait anxiety ≤ 34, n = 30, 14 from stress

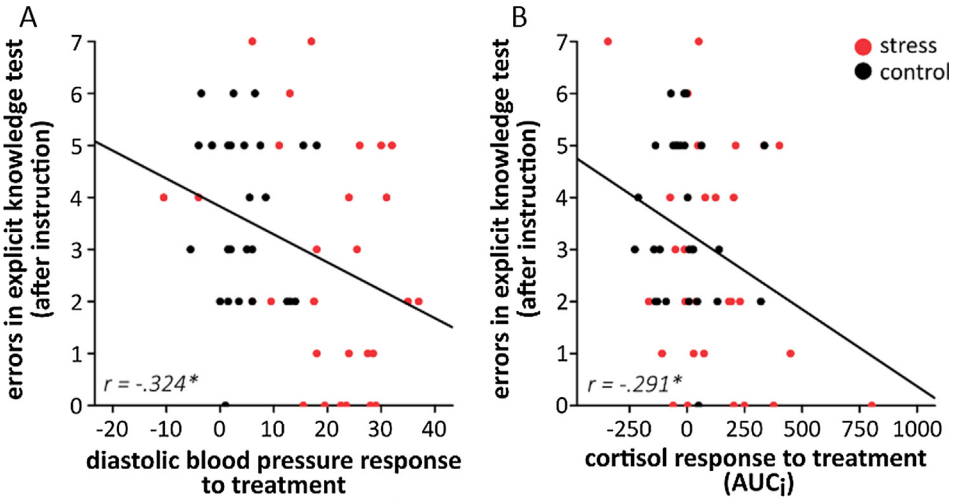

Fig. 4. Performance in the explicit rule knowledge test is correlated with the physiological stress response. Higher diastolic blood pressure responses (A) and cortisol responses (B) to the experimental manipulation were associated with fewer errors in the explicit knowledge test after the instruction phase. AUC_i Area under the curve with respect to the increase, $^{*}p < .05$.

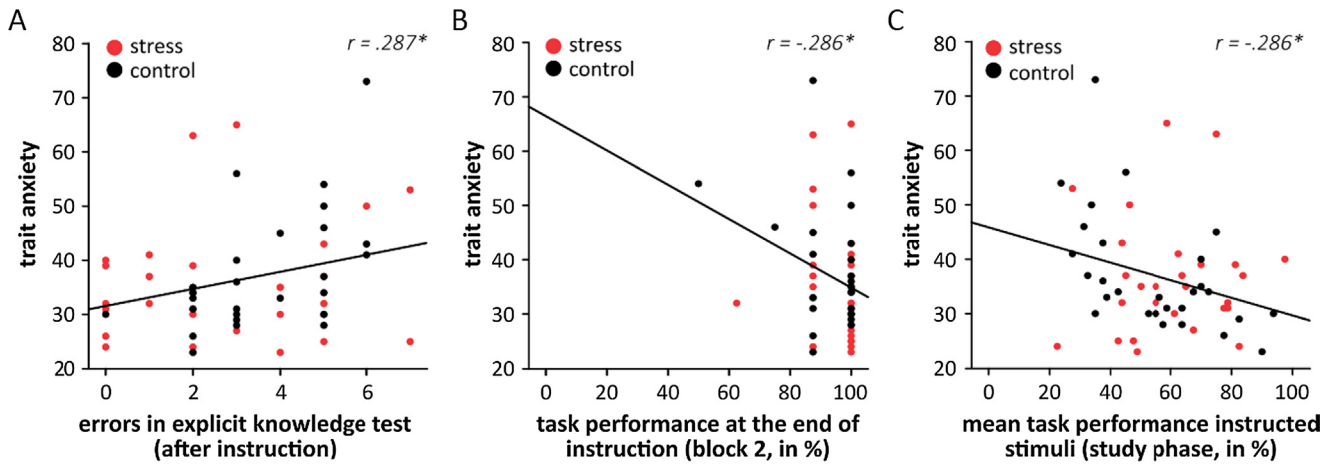

Fig. 5. Trait anxiety is associated with impaired instructed learning performance. Higher scores in trait anxiety predicted more explicit rule knowledge errors after the instruction (A), impaired task performance at the end of the instruction phase (B), and impaired performance for instructed items during the study phase (C). Please note that the association shown in Panel B holds when removing two individuals who classified as outliers based on low performance (< 3 SD from the mean). $^{*}p < .05$.

Table 2
Summary of multiple regression analyses.

Predictors	Mean performance instructed stimuli			Mean performance not instructed stimuli		
	β	t	p	β	t	p
Constant		18.65	< .001		17.43	< .001
Treatment[a]	−.152	−1.22	.227	.120	.91	.365
Trait anxiety[b]	.010	.06	.955	−.051	−.28	.785
Treatment × Trait anxiety[b]	**−.406***	**−2.32**	**.024**	−.227	−1.22	.229

Note: Mean performance instructed: $R^2 = .187$, $F(3, 53) = 4.07$, $p = .011$. Mean performance not instructed: $R^2 = .082$, $F(3, 53) = 1.574$, $p = .207$. [a]0 = stress, 1 = control; [b]mean centered. $^{*}p < .05$.

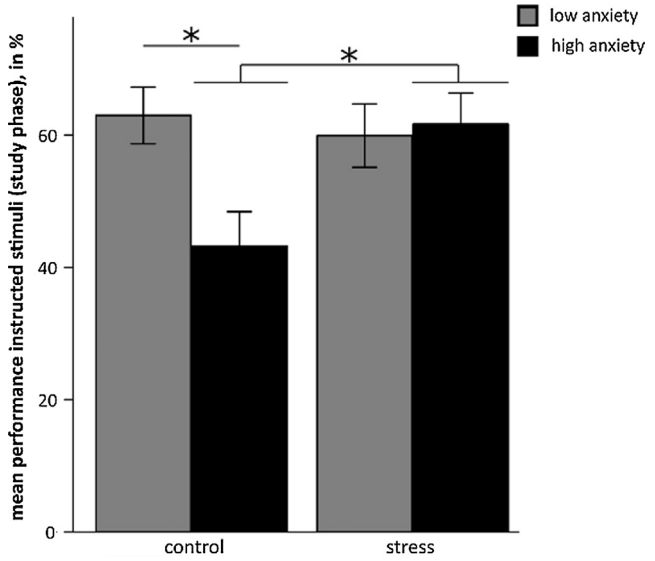

Fig. 6. Acute stress overrides individual difference due to trait anxiety. Whereas highly anxious individuals in the control group were impaired in task performance for instructed items compared to less anxious participants, this effect was abolished in the stress group. Data show mean ± 1 SEM, $^{*}p < .05$.

group, 11 women). Supporting the correlation analyses reported earlier, highly anxious individuals in the control group showed impaired performance for the instructed stimuli compared to less anxious individuals ($t(26) = 2.95$, $p = .007$, Fig. 6). In contrast, this effect was abolished in the stress group ($p = .796$, instructed stimuli: treatment × trait anxiety: $F(1, 53) = 5.136$, $p = .028$, $\eta^2 = .088$; not instructed stimuli: treatment × trait anxiety: $p = .252$, instruction × treatment × trait anxiety: $F(1, 53) = 3.026$, $p = .088$, $\eta^2 = .054$). Moreover, highly anxious individuals in the stress group outperformed highly anxious participants in the control group ($t(25) = 2.63$, $p = .014$).

4. Discussion

Whereas previous studies examined the impact of acute stress on forms of trial-and-error S-R learning (Atsak et al., 2016; Guenzel et al., 2013, 2014; Vogel et al., 2017) we tested here whether acute stress may also alter learning S-R rules from instruction, a fundamental process both in everyday life and educational contexts. In addition, we tested whether the capacity to learn by instruction is affected by individual differences in trait anxiety. Our results demonstrate that the exposure to a stressful event can boost the beneficial effect of an instruction on learning and that this effect is directly linked to the physiological stress response. In contrast, trait anxiety reduced the beneficial effect of instructions, leading to impaired instructed learning performance.

Our finding of a beneficial effect of stress on instructed S-R learning extends previous reports of an enhancing effect of stress (hormones) on the encoding of S-R associations (Atsak et al., 2016; Goodman, Leong, & Packard, 2015; Guenzel et al., 2014; Quirarte et al., 2009; Siller-Perez et al., 2017) to learning by instruction. The enhancement may be due to improved encoding of the instruction, better retrieval of the instructed rules during the study phase, or a general learning improvement. By including a condition of trial-and-error learning for which we did not obtain an influence of stress, we could demonstrate that stress did not improve learning per se but specifically instructed learning. Moreover, it has been shown previously that stress and glucocorticoids impair the retrieval of S-R associations (Atsak et al., 2016; Guenzel et al., 2013), making a stress-induced enhancement of rule retrieval during the study phase rather unlikely, although differential effects for the retrieval of instructed versus acquired S-R associations cannot be completely ruled out. Thus, our results speak strongly for the idea that stress improved the encoding of the rules during the instruction phase, as indicated by the explicit knowledge test after instruction. Moreover, our correlational analyses suggest that both HPA axis and ANS activity might mediate this beneficial effect of stress, which corresponds to previous reports showing that cortisol and noradrenaline enhance S-R learning (Goodman et al., 2015; Quirarte et al., 1997; Schwabe, Höffken,

Tegenthoff, & Wolf, 2011) and seems to hold true for instructed S-R learning as well.

However, previous reports also suggested that stress and stress mediators profoundly impair goal-directed behavior (Plessow, Kiesel, & Kirschbaum, 2012; Schwabe, Tegenthoff, Hoffken, & Wolf, 2010; Schwabe, Tegenthoff, Höffken, & Wolf, 2012; Schwabe & Wolf, 2010). At first glance, this seems to contradict a stress-induced enhancement of instructed learning, given that instructed learning is considered a hallmark of human goal-directed behavior, at least early in practice (Ruge & Wolfensteller, 2013; Wolfensteller & Ruge, 2012). Moreover, instructed learning necessitates – in addition to the dorsal striatum (Vriezen & Moscovitch, 1990) - a critical involvement of the LPFC and working memory (Petrides, 1997; Ruge & Wolfensteller, 2010, 2013, 2016), which are often impaired under stress (Arnsten, 2009; Bogdanov & Schwabe, 2016; Qin, Hermans, van Marle, Luo, & Fernández, 2009). Part of the answer might lie in the way we instructed our participants and in the complexity of the rules. Whereas previous studies on instructed learning often implemented verbal symbolic rules (e.g., Ruge & Wolfensteller, 2010), our instruction already contained motor responses, thus possibly reducing the need to translate a prefrontal symbolic rule into a striatal pragmatic rule. Moreover, S-R learning depends on the dorsal striatum, and striatal functioning is often enhanced by stress (hormones) (Guenzel et al., 2014; Vogel et al., 2017). Other instructions relying on different neural systems might thus be differentially affected by stress. Finally, the way we instructed participants did not pose a high burden on working memory. Thus, it may well be that a more stressful experience or more complex rules might result in an impairment of instructed learning when working memory capacity is exceeded. However, this remains speculative and should be investigated in future studies. To conclude, acute stress can enhance instructed S-R learning when instructed by ways of training that do not pose a high burden on working memory (Arnsten, 2009).

Beyond the influence of acute stress, we investigated how more stable interindividual differences in trait anxiety relate to the use of an instruction during learning. Our results demonstrate that anxious individuals are impaired in learning by instruction, but not in learning by trial-and-error. Importantly, these findings were not driven by state differences in anxiety, thus supporting that the stable disposition to anxious feelings and worries impairs instructed learning. This finding fits well with other studies reporting that highly anxious individuals are impaired in other cognitive processes, such as working memory (Castaneda, 2010; Eysenck & Calvo, 1992) and hippocampal memory (Airaksinen et al., 2005; Thoresen et al., 2016). Moreover, trait anxiety scores are negatively associated with self-reported attentional control (Bishop, Jenkins, & Lawrence, 2007), suggesting that highly anxious individuals might be prone to distraction, leading to a reduced effectiveness of an instruction. The detrimental effect of trait anxiety on instructed but not trial-and-error learning may thus have important implications for educational settings and explain some of the divergent findings, sometimes but not always associating trait anxiety with poor learning performance (e.g., Cassady, 2004; but see Reteguiz, 2006).

Finally, we could demonstrate an interaction between trait anxiety and stress on instructed learning. Strikingly, acute stress appeared to alleviate, or even abolish, the detrimental effect of trait anxiety on instructed learning. The underlying neural mechanism might depend on the amygdala. A previous study reported that anxious individuals displayed stronger amygdala reactivity and reduced lateral prefrontal activity to fearful face distractors indicating enhanced distractibility, but only under conditions of low perceptual load (Bishop et al., 2007). In contrast, the same study showed that individual differences due to anxiety were abolished under high perceptual load and neither low- nor high-anxious individuals displayed increased amygdala responses to distractors. These findings might relate to the current study as anxiety only reduced performance under control conditions, possibly due to enhanced distractibility or reduced attentional control. However, the stressful event may have increased attentional vigilance (Hermans et al., 2014) to the task and reduced distraction (Easterbrook, 1959), thus abolishing these interindividual differences somewhat similar to the high-load condition. An alternative account comes from a recent study showing that neuroticism, a trait closely related to trait anxiety, is associated with stronger amygdala activation to target stimuli under stressful, but not control conditions (Everaerd, Klumpers, van Wingen, Tendolkar, & Fernandez, 2015). As the amygdala in turn mediates the stress-induced shift in memory (Packard, Cahill, & McGaugh, 1994; Packard & Wingard, 2004; Schwabe et al., 2013; Vogel et al., 2015, 2017), highly anxious individuals under stress might show an additional enhancement in S-R learning, ultimately leading to the abolishment of individual differences under stress. However, future neuroimaging studies would be needed to support this explanation.

We did not see an effect of stress (or trait anxiety) on learning by trial-and-error, which is in line with previous studies from our lab showing no effect of stress on learning performance in a trial-and-error-based probabilistic classification learning task (Schwabe et al., 2013; Schwabe & Wolf, 2012; Wirz, Wacker, Felten, Reuter, & Schwabe, 2017). However, these studies showed also that stress effects on task acquisition became apparent when learning strategies or explicit task knowledge were assessed. Furthermore, fMRI revealed that the control of learning switched from the hippocampus to the dorsal striatum after stress. Whether the present S-R learning task involves also the activation of parallel learning systems is not known. Nevertheless, it is important to note that the absence of a stress effect on behavioral performance does not provide ultimate evidence that the acquisition of the S-R learning task remained completely unaffected by stress (or trait anxiety).

It is well known that several factors can influence how stress affects learning. For instance, it is often found that the emotionality of the learning material affects stress-induced memory changes (Payne et al., 2006; Schwabe, Bohringer, Chatterjee, & Schachinger, 2008; Zoladz et al., 2011). While we found that stress improved instructed learning using neutral visual stimuli, the effects may be different, and potentially stronger, for emotional learning material. Additionally, several studies have shown that stress effects depend on the timing between stress induction and task administration (Joëls et al., 2006; Quaedflieg, Schwabe, Meyer, & Smeets, 2013; Vogel & Schwabe, 2016b; Zoladz et al., 2011). The stress-induced enhancement we report here is in line with the model of enhanced memory formation in the direct aftermath of stress (Cadle & Zoladz, 2015; Schwabe et al., 2012). Similarly, a recent study from our lab followed stress-induced memory alterations continuously over two hours after stress induction and found a memory enhancement 41–65 min after stress (Vogel & Schwabe, 2016b), which overlaps with the timing in the current project. Thus, while our study is the first to show an enhancing effect of stress on instructed learning, several factors may be important moderators of stress effects, which should be investigated in future studies.

5. Conclusions

To conclude, learning by instruction is a critical process in virtually all educational settings, yet situational and personal factors that affect the efficacy of an instruction have been unknown. We demonstrate here that acute stress can boost instructed learning of S-R associations and that this effect may override detrimental effects of high trait anxiety on instructed S-R learning. In particular, the negative impact of trait anxiety on learning form instruction and its modulation of stress (or arousal) may have relevant implications for educational contexts (Vogel & Schwabe, 2016a), in which both stress and trait anxiety are frequent and highly relevant phenomena (Valizadeh, Farnam, & Rahkar Farshi, 2012). The boost of instructed learning may further be seen as part of the general cognitive adaptation to stressful events. Relying on information from others, without own, direct experience, is highly efficient and may represent a valuable heuristic to save cognitive resources which are scarce under stress. The facilitation of learning by instruction

thus fits well to other cognitive changes under stress that promote efficient responding (Schwabe, Schachinger, de Kloet, & Oitzl, 2010; Vogel et al., 2016). However, an overreliance on instruction might also have negative effects. For instance, events that are inconsistent with the instruction are processed less, leading to a bias to follow instructed rules and rule-induced rigidity (Doll et al., 2009; Hayes, 1993), an effect which may be further enhanced by stress.

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