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Trait anxiety and post-learning stress do not affect perceptual learning

Kristoffer C. Aberg [a,b,*], Aaron M. Clarke [a], Carmen Sandi [c], Michael H. Herzog [a]

[a] Laboratory of Psychophysics, Brain Mind Institute, École Polytechnique Fédérale de Lausanne (EPFL), Switzerland
[b] Laboratory for Neurology and Imaging of Cognition, Department of Neurosciences, University of Geneva, Geneva, Switzerland
[c] Laboratory of Behavioral Genetics, Brain Mind Institute, École Polytechnique Fédérale de Lausanne (EPFL), Switzerland

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ABSTRACT

While it is well established that stress can modulate declarative learning, very few studies have investigated the influence of stress on *non-declarative learning*. Here, we studied the influence of post-learning stress, which effectively modulates declarative learning, on perceptual learning of a visual texture discrimination task (TDT). On day one, participants trained for one session with TDT and were instructed that they, at any time, could be exposed to either a high stressor (ice–water; Cold Pressor Test; CPT) or a low stressor (warm water). Participants did not know when or which stressor they would be exposed to. To determine the impact of the stressor on TDT learning, all participants returned the following day to perform another TDT session. Only participants exposed to the high stressor had significantly elevated cortisol levels. However, there was no difference in TDT improvements from day one to day two between the groups. Recent studies suggested that trait anxiety modulates visual perception under anticipation of stressful events. Here, trait anxiety did neither modulate performance nor influence responsiveness to stress. These results do not support a modulatory role for stress on non-declarative perceptual learning.

1. Introduction

Stress and the corresponding release of glucocorticoids modulate declarative human memory (reviews: Het, Ramlow, & Wolf, 2005; Joels, Pu, Wiegert, Oitzl, & Krugers, 2006; Sandi & Pinelo-Nava, 2007; Shors, 2006). For example, exposure to ice-water (CPT; Cold Pressor Test) directly after presentation of pictures improved memory of the pictures when tested 1 week later (Cahill, Gorski, & Le, 2003). Pharmacologically induced elevations of cortisol levels deteriorated word learning (Kirschbaum, Wolf, May, Wippich, & Hellhammer, 1996). The influence of stress on learning and memory is heterogeneous and varies depending on the emotional content and the valence of stimuli (Buchanan & Lovallo, 2001; Cahill & Alkire, 2003; Cahill et al., 2003; Rimmele, Domes, Mathiak, & Hautzinger, 2003; Schwabe, Bohringer, Chatterjee, & Schachinger, 2008; Southwick et al., 2002), timing of stress (before the learning: Lupien et al., 2002; Maheu, Collicut, Kornik, Moszkowski, & Lupien, 2005; Schwabe et al., 2008; after the learning: Andreano & Cahill, 2006; Cahill et al., 2003), the intensity of stress (Andreano & Cahill, 2006; Maheu, Collicut, et al., 2005; Kirschbaum et al., 1996) and memory type (Kirschbaum et al., 1996; Luethi, Meier, & Sandi, 2009). Most studies addressing the influence of stress on memory used paradigms tapping into declarative memory.

In contrast, only a few studies investigated how stress modulates non-declarative memory formation (Kirschbaum et al., 1996; Luethi et al., 2009; Lupien et al., 1997). In one of these studies, participants were first exposed to a stressor and then performed a battery of memory tasks including classical conditioning with emotionally positive and negative stimuli, as well as perceptual and conceptual priming tasks (Luethi et al., 2009). Stress had no influence on the priming tasks and the only significant effect in the conditioning task was found with negative stimuli. These results indicate that stress may influence non-declarative learning to some extent, however, it is not clear which phase of learning was affected because memory recall was tested shortly after performing the tasks. Hence, little time was allowed for memory consolidation and for the stress response to decline prior to memory recall. For declarative learning, different phases of learning are influenced differently by stress (Het et al., 2005; Roozendaal, 2002). It is therefore important to systematically study the influence of stress on different phases of learning also for non-declarative learning. Furthermore, previously tested non-declarative learning tasks are rather short-term and may not depend on the post-learning phase, i.e. consolidation, which has been shown to be sensitive to the influence of stress and changes in cortisol levels (Roozendaal, 2002; Sandi, 1998; Shors, 2006). Here, we used a visual perceptual learning paradigm, known to be sensitive to post-learning manipulations (consolidation), to study how

* Corresponding author at: Laboratory for Neurology and Imaging of Cognition, Department of Neurosciences, University of Geneva, Geneva, Switzerland.
E-mail address: kc.aberg@gmail.com (K.C. Aberg).

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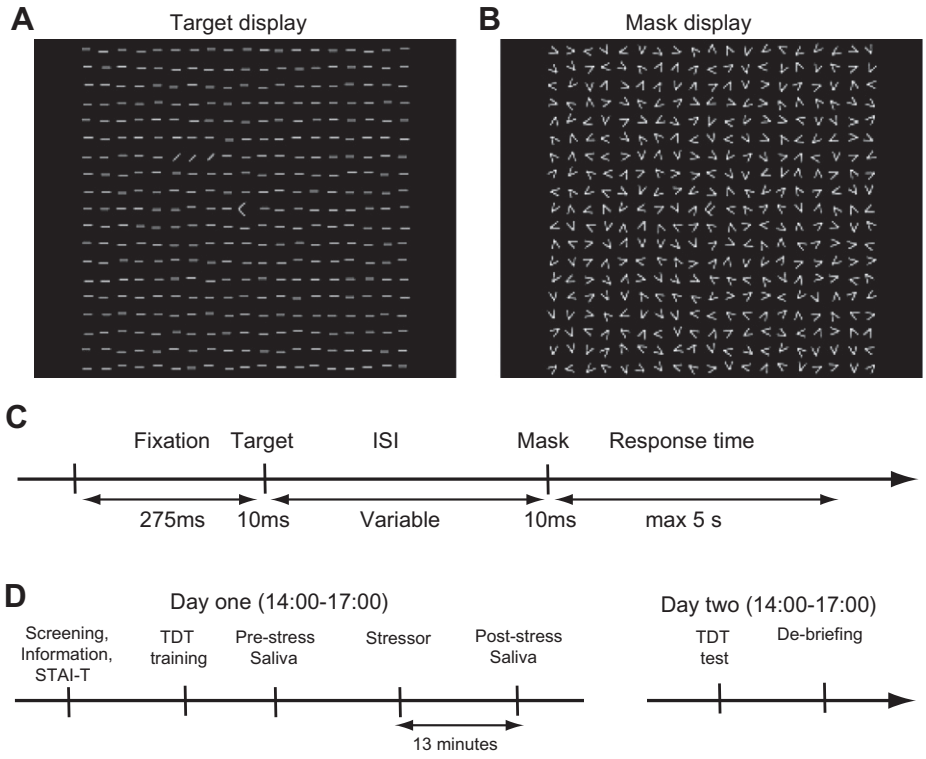

Fig. 1. TDT experiment: stimuli and procedure. (A) Three diagonal target bars were presented within a background of horizontal bars. The target texture could be either horizontal or vertical (here, a horizontal target array is shown). A rotated letter in the center served as a fixation task. This letter could be either a rotated L or a rotated T (here, a rotated L is shown). (B) The mask display consisted of randomly oriented V-shapes. In the center, a compound pattern of superimposed T's and L's was presented. (C) In each trial, a blank screen with a red fixation dot was presented for 275 ms followed by a target display presented for 10 ms. The target was followed by a blank screen for a variable amount of time (ISI) which was followed by a mask presented for 10 ms. Following the mask, a blank screen was presented for 5 s or until participants responded. (D) Experimental procedure. On the afternoon of day one, participants arrived in the lab and were tested for visual acuity, informed about the procedure, provided written consent and filled out the STAI-T questionnaire. Directly after, participants trained with the visual texture discrimination task. A saliva sample was collected immediately following training. Then, participants were exposed to a stressor which was followed 13 min later by the collection of another saliva sample. Participants returned in the afternoon the following day to perform a second session with the texture discrimination task and were de-briefed directly after.

stress influences consolidation of non-declarative perceptual learning.[1]

Perceptual learning is the ability to learn to perceive (review: Fahle & Poggio, 2002). Visual perceptual learning is a non-declarative form of learning that improves discrimination of basic visual stimulus features including vernier acuity (Crist, Kapadia, Westheimer, & Gilbert, 1997; Herzog & Fahle, 1997), contrast (Kuai, Zhang, Klein, Levi, & Yu, 2005; Yu, Klein, & Levi, 2004), motion (Ball & Sekuler, 1982; Liu & Vaina, 1998) and textures (Censor, Karni, & Sagi, 2006; Karni & Sagi, 1993; Mednick, Arman, & Boynton, 2005; Stickgold, LaTanya, & Hobson, 2000). In a texture discrimination task (TDT), participants determine the orientation of an array of target elements within distracter elements (Fig. 1A). Task difficulty is controlled by the ISI (Inter-Stimulus Interval) between the target display and a mask display (Fig. 1A). The ISI limits the temporal availability of a stimulus and reflects the time needed to obtain a workable percept. Thus, the ISI is a measure of perceptual performance and becomes potent with experience (Karni & Sagi, 1991, 1993; Karni, Tanne, Rubenstein, Askenasy, & Sagi, 1994). A short ISI indicates good performance. Importantly, consolidation and sleep are often needed to improve texture discrimination (Censor et al., 2006; Karni et al., 1994; Mednick, Nakayama, & Stickgold, 2003; Stickgold, Whidbee, Schirmer, Patel, & Hobson, 2000; Yotsumoto, Chang, Watanabe, & Sasaki, 2009). For example, performance between two sessions did not improve unless they were separated by a night (Karni & Sagi, 1993; Karni et al., 1994; Stickgold, LaTanya, et al., 2000; Stickgold, Whidbee, et al., 2000; Yotsumoto, Chang, et al., 2009). Furthermore, training another task directly after the TDT abolished performance improvements (Yotsumoto, Chang, et al., 2009) suggesting that this task is sensitive to post-learning manipulations (see also Beer, Vartak, & Greenlee, 2012). Finally, sleep deprivation increased cortisol levels (Meerlo, Sgoifo, & Suchecki, 2008) and disrupted consolidation of the TDT (Stickgold, LaTanya, et al., 2000). Accordingly, these results suggest that (1) TDT can be disrupted by post-learning manipulations and (2) these manipulations may involve stress and increased cortisol levels.

To test if stress modulates TDT learning, two groups of participants trained two sessions with the TDT on two consecutive days (Fig. 1C). After TDT training on day one, participants in the stress group immersed their arms into ice water (0–4 °C; Lovallo, 1975) while participants in a control group immersed their arms into warm water (37–40 °C). To determine whether this stress manipulation induced changes in cortisol levels, saliva was collected before and after stressor exposure. Participants returned the following day for another TDT session.

Besides studying the influence of stress on perceptual learning, we were also interested in studying the influence of trait anxiety on visual perception and learning. Laretzaki, Plainis, Argyropoulos,

[1] Following declarative learning participants have conscious recollection of the learning experience and the information learned. Declarative memory can be accessed by explicit measures, for example by asking: What did you have for breakfast this morning? Non-declarative memories cannot be verbalized and need to be accessed by implicit measures. For example, learning to ride a bike can be accomplished, even though it is impossible to verbalize how it was learned. Similarly, perceptual learning is an implicit measure used to tap into non-declarative memories.

Pallikaris, and Bitsios (2010) showed that anticipation of a stressful event (an electric shock) modulated early visual processing of Gabor stimuli (Laretzaki et al., 2010). Interestingly, this modulation was more pronounced for participants with low trait anxiety while no modulation occurred for participants with high trait anxiety. In the present study, participants anticipated a stressful event which similarly may influence visual processing. To test if trait anxiety modulated performance of the TDT task, participants filled out the State Trait Anxiety Inventory (STAI; Spielberger, 1983) prior to the start of the experiment.

We found a significant increase in cortisol levels for participants exposed to the high stressor (ice water) but not to the low stressor. However, the response to stress did not modulate TDT learning because performance improved similarly in both groups. Furthermore, trait anxiety had no influence on performance, learning, or responsiveness to stress.

2. General materials and methods

2.1. Participants

Thirty-six male, naïve participants from the École Polytechnique Fédérale de Lausanne (EPFL) joined the experiment after providing informed written consent. One participant failed to follow instructions and was excluded and another participant was excluded because one saliva sample was collected at the wrong time. In total, data from 34 participants were used in the analysis. Fourteen additional participants participated in a control experiment to verify that our procedure is able to induce stress-related changes in a declarative learning task. All participants had normal or corrected to normal vision, as measured with the Freiburg visual acuity test (Bach, 1996) and were paid for participation (20 CHF per hour). All participants reported normal sleep the night between testing sessions.

2.2. Apparatus and stimuli

Stimuli were presented on a 19″ monitor. The luminance of the stimulus (line textures) was 64 cd/m^2. The experimental room was dimly illuminated (0.5 lux).

Stimuli consisted of a target display (Fig. 1) and a patterned mask (Fig. 1B). Participants indicated whether an array of 3 diagonal bars (orientation 45°) embedded in a background of horizontal bars (19 × 19, 25.2′ (arcmin) × 1.8′ each) had a horizontal or vertical orientation (Fig. 1A). The exact position of the target array was varied from trial to trial, but was always presented within one to four segments from the center. In addition, to ensure fixation at the center of the screen, participants had to indicate whether a central, randomly rotated letter was an L or a T.

In each trial, a black screen with a red fixation dot was presented for 275 ms directly followed by a 10 ms presentation of a target display (Fig. 1C). A blank screen was then presented for a variable duration (Inter-Stimulus Interval; ISI) followed by a 10 ms presentation of a mask. Following the mask, a blank screen was presented for 5 s or until participants responded.

At the begin of training, the ISI between the target display and the mask was set, for each observer individually, to 240–300 ms to establish correct texture discrimination above 95%. For the following blocks, the ISI level was decreased in steps of 20 ms until less than 60% correct discrimination occurred in 3–4 blocks. One level of ISI was presented in one block of 50 trials for 3–4 consecutive blocks. For each session, a threshold for 80% correct responses was determined by maximum likelihood estimation of the parameters of the psychometric function.

2.3. Procedure

The first part of the experiment took place in the afternoon on day one between 14:00 and 17:00 (Fig. 1D). At arrival, participants were tested for visual acuity, received information about the experiment, provided informed written consent and filled out the State Trait Anxiety Inventory-Trait questionnaire (STAI-T; Spielberger, 1983). Importantly, participants were informed that they could be exposed to either the high or the low stressor at any time during the training. Following a period of rest (approx. 5 min), participants trained with the TDT and a saliva sample was collected immediately after. Then, participants immersed their arm (up to the elbow) in either ice water (0–4 °C; stress group) or warm water (37–40 °C, control group). Participants were told to keep their arm in the water for 3 min or until feeling major discomfort. A second saliva sample was collected 13 min following stressor exposure. Participants returned in the afternoon of the following day (14:00–17:00) to perform another TDT session which was followed by a de-briefing.

2.4. Saliva assessment

Saliva was collected using Salivette collection tubes (Sarstedt Sevelen, Switzerland). Two samples were collected; on day 1 after training with the TDT and 13 min following the stressor exposure (Fig. 1D). Samples were stored at −20 °C until assayed. Salivary cortisol was measured using the Spectria Cortisol radio immunoassay RIA kit (Orion Diagnostica, Espoo, Finland).

2.5. State Trait Anxiety Inventory

Self-report of anxiety was assessed with the Spielberger State-Trait Anxiety Inventory (STAI; Spielberger, 1983). The trait scale (STAI-T) consists of 20 statements that assess *general* anxiety levels. Scores range from 20 to 80, with lower scores indicating less anxiety and higher scores indicating a greater level of anxiety.

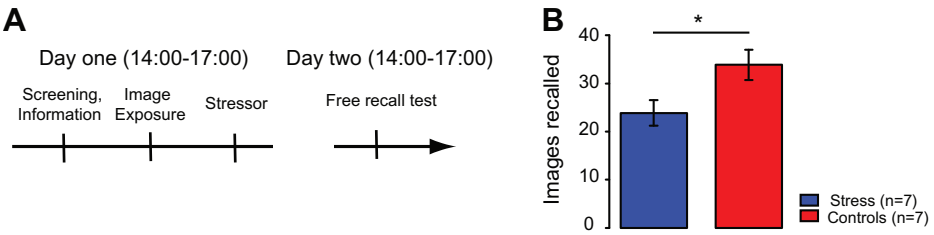

Fig. 2. Control experiment: procedure and results. (A) Experimental procedure for the control task. On the afternoon of day one, participants were exposed to 54 images presented in a sequence. Directly after, participants were exposed to a stressor. On the afternoon of day two, participants performed a surprise free recall task where they had to recall the images from the previous day. (B) Results for the control experiment. Participants in the stress group recalled less images than participants in the control group. Mean ± SEM. (*$p < .05$).

2.6. Control experiment

A separate control experiment was conducted to test whether our stressor could modulate post-learning performance in a declarative memory task.

Stimuli were presented on a 19″ monitor and consisted of images selected from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 2008) where each image has been rated independently on emotional dimensions such as arousal and valence. Based on the standardized IAPS ratings, each image was assigned to one of three arousal types (Low, Neutral, and High) and to one of three valence types (Negative, Neutral, and Positive). By combining these types, nine different categories of images were created. For each participant, six images were chosen from each of the categories such that 54 images in total were presented.

In the afternoon of day one (14:00–17:00), the images were presented sequentially to the participants who were instructed to pay close attention to the contents of the image. To make sure participants paid attention, a brief description of the image (limited to one short sentence) had to be typed in. The next image was presented following completion of the description. Directly after all images had been presented, participants were exposed to the stressor. Half of the participants were assigned to the stress group (ice cold water) and the other half were assigned to the control group (lukewarm water) as described above. Participants returned in the afternoon (14:00–17:00) the next day for a surprise free recall task and were instructed to recall the images from the previous day (Fig. 2A). The results were scored by K.C.A. and A.M.C. without knowing what scores belonged to which subject or group. Only images found to be recalled by both reviewers were considered as correctly recalled.

3. Results

3.1. TDT Experiment: the influence of the stressor on cortisol levels

A two-way mixed factors ANOVA with within-group factor Pre/Post (before and after stress), and between-group factor Group (stress and control), and salivary cortisol as dependent measure revealed a significant effect of Pre/Post [$F(1,32) = 9.60$, $p < .01$], no effect of Group [$F(1,32) = 1.27$, $p = .27$], but a significant interaction between Pre/Post × Group [$F(1,32) = 4.79$, $p < .05$]. The interaction was due to participants in the stress group having significantly elevated cortisol levels as compared to the controls. Participants in the stress group were further divided into two groups based on their individual stress response. A median split (median = 0.027 μg/dl) divided participants into a responders (change in cortisol > 0.027 μg/dl) and non-responders group (change in cortisol < 0.027 μg/dl). Cortisol levels before and after exposure to the stressor for the three groups (responders, non-responders and controls) are shown in Fig. 3A. Only participants in the responders group showed a significant increase in cortisol levels.

3.2. The influence of the stressor on performance and perceptual learning

Thresholds for the different days are shown in Fig. 3B. A two-way mixed factors ANOVA with within-group factor Day (day one and two) and between-group factor Group (responders, non-responders, and controls) with performance thresholds (ISI) as dependent measure revealed a significant effect of Day [$F(1,31) = 24.70$, $p < .001$], but no effect of Group [$F(2,31) = 0.55$, $p = .58$] and no Day × Group interaction [$F(2,31) = 0.20$, $p = .82$]. Hence, stress-induced increases in cortisol levels had no significant effect on performance or performance improvements.

3.3. The influence of trait anxiety on cortisol levels

Trait anxiety modulates responsiveness to stress, for example, high trait anxiety leads to higher cortisol levels following stress as compared to low trait anxiety (Duncko, Makatsori, Fickova, Selko, & Jezova, 2006; Jezova, Makatsori, Duncko, Moncek, & Jakubek, 2004; Schlotz, Schulz, Hellhammer, Stone, & Hellhammer, 2006; Takahashi et al., 2005). Therefore, participants in the stress group were divided into a high anxiety and a low anxiety group based on a median split of the STAI-T scores (median = 36). Cortisol levels before and after exposure to the stressor for participants with high- and low-trait anxiety are shown in Fig. 4A. A two-way mixed factors ANOVA with within-group factor Pre/Post (before and after stressor) and between-group factor Anxiety (high and low trait anxiety) with cortisol levels as a dependent measure revealed a significant effect of Pre/Post [$F(1,21) = 10.29$, $p < .01$], but no effect of Anxiety nor an interaction Pre/Post × Anxiety [Anxiety: $F(1,21) = 0.25$, $p = .62$; Anxiety × Pre/Post: $F(1,21) = 1.80$, $p = .19$]. Hence, responsiveness to stress was not significantly modulated by trait anxiety. It has been shown that high trait anxiety leads to elevated basal cortisol levels (Jezova et al., 2004; Takahashi et al., 2005; Taylor et al., 2008). However, we found no significant difference in cortisol levels before exposure to the stressor for participants with high- and low-trait anxiety scores [average difference = 0.023 μg/dl, $t(13.44) = -0.89$, $p = .39$].

3.4. The influence of trait anxiety on performance and learning

ISI's for participants with high- and low-trait anxiety for the 2 days are shown in Fig. 4B. A two-way mixed factors ANOVA with

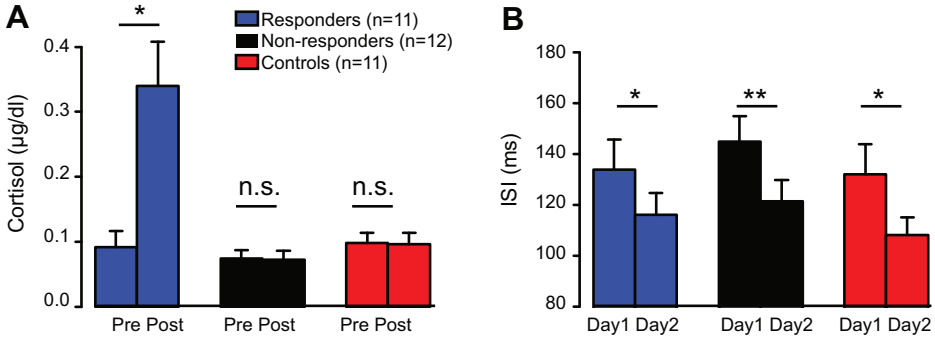

Fig. 3. Change in cortisol and ISI for responders, non-responders, and controls. (A) Cortisol as a function of Pre/Post stressor and Group. Only participants in the responder group showed a significant increase in cortisol level following stressor exposure. (B) ISI as a function of Day and Group. Performance improved significantly from day one to day two for all groups. Mean ± SEM. (*$p < .05$, **$p < .01$).

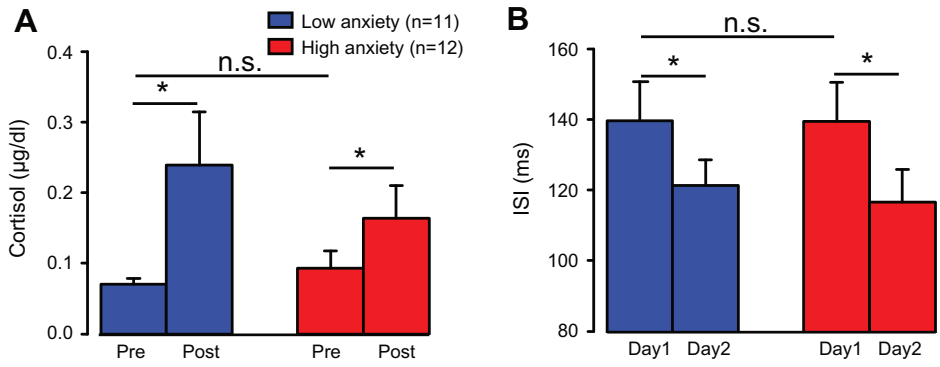

Fig. 4. Change in cortisol and ISI for high- and low-anxiety groups. (A) Cortisol as a function of Pre/Post stressor and Anxiety. Both high-anxiety and low-anxiety participants increased their cortisol levels after exposure to the stressor. Although low-anxiety participants increased their cortisol levels more, the difference was not significant. There was no difference between groups in cortisol levels before exposure to the stressor. (B) ISI as a function of Day and Anxiety. Performance improved significantly from day one to day two for both groups. There was no significant difference in initial performance levels between the two groups. Mean ± SEM. (*p<.05).

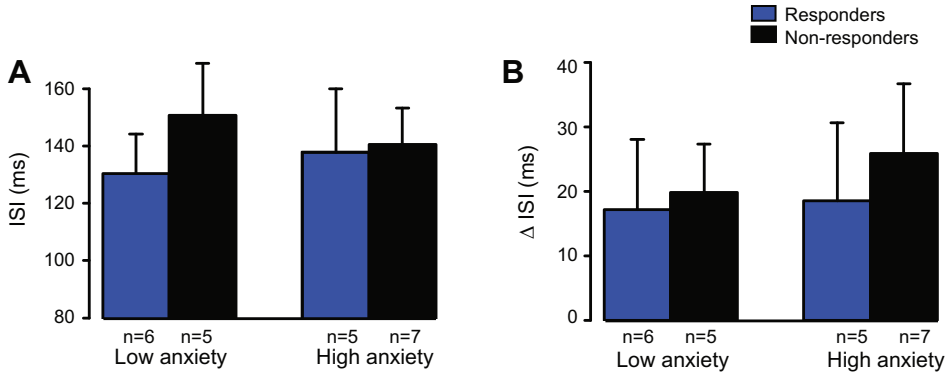

Fig. 5. Initial performance and change in performance for responders and non-responders with high- and low-trait anxiety. (A) Initial performance (ISI) as a function of Anxiety and Responsiveness. There were no significant effects. (B) Change in performance (ISI) between day 1 and day 2 as a function of Anxiety and Responsiveness. There were no significant effects. Mean ± SEM.

within-group factor Day (day one and day two) and between-group factor Anxiety (low- and high-trait anxiety) with performance threshold as dependent measure revealed a main effect of Day [$F(1,21) = 16.31$, $p < .001$] but no other effects were significant [Anxiety: $F(1,21) = 0.04$, $p = .85$; Anxiety × Day: $F(1,21) = 0.19$, $p = .67$]. Hence, in contrast to a previous study, performance levels during anticipated stress were not different between participants with high- and low-trait anxiety scores [average difference = 0.2, $t(20.98) = -0.01$, $p = .99$].

3.5. The combined influence of trait anxiety and stress responsiveness on initial performance and learning

A two-way ANOVA with factors Anxiety (low and high trait anxiety) and Responsiveness (responders and non-responders) with change in performance (ISI; from day 1 to day 2) revealed no significant effects or interactions [Fig. 5B; Anxiety: $F(1,19) = 0.18$, $p = .68$; Responsiveness: $F(1,19) = 0.22$, $p = .65$; Anxiety × Responsiveness: $F(1,19) = 0.83$, $p = .83$]. Hence, learning was not influenced by trait anxiety, responsiveness to stress, or their interaction. A two-way ANOVA with factors Anxiety (low- and high-trait anxiety) and Responsiveness (responder and non-responder) with performance thresholds on day 1 as the dependent measure revealed no significant main effects or interactions [Fig. 5A; Anxiety: $F(1,19) = 0.001$, $p = .99$; Responsiveness: $F(1,19) = 0.47$, $p = .50$; Anxiety × Responsiveness: $F(1,19) = 0.29$, $p = .60$]. Thus, initial performance was not influenced by trait anxiety, responsiveness to stress or their interaction.

3.6. Control experiment

A three-way mixed factors ANOVA with between-group factor Group (stress and control), and within-group factors Valence (negative, neutral, and positive), and Arousal (low, neutral, and high) revealed a significant effect of Group [$F(1,12) = 5.94$, $p < .05$]. This effect was due to participants in the stress group recalling less images than participants in the control group (Fig. 2B). These results are in accordance with previous studies showing reduced declarative memory performance following stress (Kirschbaum et al., 1996; Lupien et al., 1997; Maheu, Collicut, et al., 2005; Newcomer, Craft, Hershey, Askins, & Bardgett, 1994). Surprisingly, we found no significant interactions with the emotional features of the stimuli, i.e. the interaction with the *Group* factor was not significant [all $p > 0.55$].

4. Discussion

Perceptual learning is the ability to learn to perceive. Perceptual learning is non-declarative and long lasting (Fahle & Poggio, 2002). Improvements of performance were shown to last for more than a year (Karni & Sagi, 1993). Some kinds of perceptual learning need long-term consolidation (Karni & Sagi, 1993, 1994; Matarazzo, Franko, Maquet, & Vogels, 2008; Seitz et al., 2005; Stickgold, LaTanya, et al., 2000; Stickgold, Whidbee, et al., 2000) whereas others do not (Aberg & Herzog, 2010; Aberg, Tartaglia, & Herzog, 2009; Tartaglia, Aberg, & Herzog, 2009). For example, performance improvements in texture discrimination occur between sessions

and/or after sleep (Karni & Sagi, 1993; Mednick et al., 2002, 2003; Stickgold, LaTanya, et al., 2000) and can be disrupted by post-learning manipulations (Stickgold, LaTanya, et al., 2000; Yotsumoto, Chang, et al., 2009).

Consolidation of declarative learning can be modulated by stress (Cahill et al., 2003). Here, we asked the question whether also the consolidation of non-declarative perceptual learning can be modulated by stress. Our results show that performance improved equally for participants who were stressed and those who were not (Fig. 3B). Hence, stress did not affect perceptual learning even though exposure to the stressor significantly elevated cortisol levels in the stress but not the control group. In addition, we found in contrast to other studies, that trait anxiety did neither modulate visual performance under anticipated stress nor the responsiveness to stress or basal cortisol levels.

4.1. Stress does not modulate consolidation of perceptual learning

Consolidation in declarative learning can be modulated by post-learning manipulations, such as stress exposure (Sandi, 1998; Shors, 2006). Previous work has shown that also TDT learning can be disrupted by post-learning manipulations. For example, TDT learning was disrupted by subsequent training with another task (Yotsumoto, Chang, et al., 2009) and sleep deprivation the night following TDT training (Stickgold, LaTanya, et al., 2000). Sleep deprivation increases cortisol levels (Meerlo et al., 2008), suggesting a link between stress-related elevated cortisol levels and disrupted TDT learning (Stickgold, LaTanya, et al., 2000). Here, we found no disruption of TDT learning for participants with elevated cortisol levels (responders) as compared to non-responders and controls (Fig. 5B). Why is consolidation of the TDT unaffected by stress? Two reasons come to mind.

First, stress-related modulations of human memory are related to, for example, the amygdala (Buchanan & Lovallo, 2001; Buchanan, Tranel, & Adolphs, 2006; Maheu, Collicut, et al., 2005; Rimmele et al., 2003; Schwabe et al., 2008), the hippocampus (Andreano & Cahill, 2006; Cahill & Alkire, 2003; Cahill et al., 2003; Kirschbaum et al., 1996; Luethi et al., 2009), and the prefrontal cortex (PFC; Luethi et al., 2009) which have high densities of glucocorticoid receptors making them more reactive to increased levels of cortisol accompanying stress (Het et al., 2005; Joels et al., 2006; Maheu, Collicut, et al., 2005; Roozendaal, 2002; Sandi, 1998; Shors, 2004; Sandi & Pinelo-Nava, 2007). In contrast, TDT learning is usually related to early visual areas (Schwartz, Maquet, & Frith, 2002; Pourtois, Rauss, Vuilleumier, & Schwartz, 2008; Yotsumoto, Sasaki, et al., 2009b; Yotsumoto, Watanabe, & Sasaki, 2008) which have a low density of glucocorticoid receptors and thus being less reactive to stress. Accordingly, stress may not influence visual perceptual learning because this type of learning does not involve brain areas which are sensitive to glucocorticoid release. We do not suggest that non-declarative learning *per se* is unaffected by stress because it was recently shown that learning occurred in a classical conditioning task with emotional stimuli known to activate the amygdala (Luethi et al., 2009).

Second, TDT learning often requires sleep, for example, Karni and Sagi (1993) showed that no improvement occurred when the TDT was trained and tested within the same day, but there was a large leap in performance following a night of sleep. In addition, it has been shown that the amount of learning correlated with how much time was spent in slow wave sleep and REM (rapid eye movement) sleep (Karni et al., 1994; Mednick et al., 2002). Accordingly, consolidation of the TDT could not be disrupted by stress in the present study because TDT consolidation occurs during sleep and the stress response had most likely already declined at the time of sleep (stress exposure occurred in the late afternoon).

Finally, as a speculation, performing the experiment combined with the anticipation of being exposed to a high stressor could have been sufficient to induce stress before the TDT learning. Stress administered before encoding modulates declarative learning (Buchanan & Lovallo, 2001; Luethi et al., 2009; Maheu, Joober, & Lupien, 2005; Payne et al., 2007). Similarly, TDT learning may have been influenced by pre-learning stress rather than post-learning stress. As with post-learning stress, little is known how pre-learning stress influences non-declarative learning and this should be addressed in future studies. However, it is worth to mention that most (if not all) studies finding an effect of post-learning stress on declarative memory did not control for elevated cortisol levels due to being in an experimental context (Andreano & Cahill, 2006; Buchanan & Lovallo, 2001; Cahill & Alkire, 2003; Cahill et al., 2003; Luethi et al., 2009; Payne et al., 2007; Preuss & Wolf, 2009).

4.2. Trait anxiety does not modulate texture discrimination performance

It was recently shown that negative emotions facilitate contrast perception (Phelps, Ling, & Carrasco, 2006) and modulate orientation discrimination of Gabors (Bocanegra & Zeelenberg, 2009). Furthermore, contrast perception during anticipation of a stressful event (electric shock) was modulated for participants with low-, but not high-, trait anxiety scores (Laretzaki et al., 2010). We tested similarly whether trait anxiety modulated visual performance in a texture discrimination task, tapping into early visual processes, when anticipating exposure to a potent stressor (ice water). Trait anxiety did neither modulate TDT performance (Fig. 4B) nor did it depend on responsiveness to the stressor (Fig. 5A). There are several differences between ours and the study by Laretzaki et al. (2010) that may account for the discrepancies in data. First, the impact of anticipating a stressful event may depend on the event itself, for example, the threat of an electric shock may be more potent than the threat of ice water. Second, Laretzaki et al. (2010) did not use any behavioral measures, but based their conclusions on event-related electro physiological (ERP) recordings obtained while participants were exposed to different contrast stimuli. Thus, it is not clear how these measures translate into behavior. Third, other studies showed that the influence of emotion on early visual processing depends on stimulus features such as spatial frequency (Bocanegra & Zeelenberg, 2009) and contrast (Laretzaki et al., 2010; Phelps et al., 2006). Hence, our stimuli may not have tapped into a stimulus configuration that could be modulated by emotion or threat anticipation. However, our results suggest that not all early visual processes may be modulated by emotions or threat anticipation.

4.3. Trait anxiety and responsiveness to stress

Anxiety can loosely be defined as a heightened state of fear with hyper excitability of brain structures such as the amygdala and hippocampus (Rosen & Schulkin, 1998). These areas have a high concentration of glucocorticoid receptors and are strongly influenced by stress-induced elevation of cortisol levels (Het et al., 2005; Joels et al., 2006; Maheu, Collicut, et al., 2005; Roozendaal, 2002; Sandi, 1998; Sandi & Pinelo-Nava, 2007; Shors, 2004). Accordingly, high trait anxiety has been linked to elevated stress responses (Duncko et al., 2006; Hubert & de, 1992; Oswald et al., 2006; Preville, Zarit, Susman, Boulenger, & Lehoux, 2008) and increased basal cortisol levels (Jezova et al., 2004; Takahashi et al., 2005; Taylor et al., 2008). However, we found no significant relation between trait anxiety and responsiveness to stress nor between trait anxiety and basal cortisol levels (Fig. 4A). Previous studies mainly used non-physiological stressors to investigate

stress responsiveness, for example, psycho-social stressors (Oswald et al., 2006; Preville et al., 2008) or uncomfortable video clips (Hubert & de, 1992). Hence, participants with high-trait anxiety may be highly responsive to psychological stress but less responsive to physiological stress. Why there was no difference in basal cortisol levels between participants with high- and low-trait anxiety is less clear. One study reported differences in basal cortisol levels between participants with high- and low-trait anxiety in the morning, but not in the afternoon (Taylor et al., 2008). Since our experiment was conducted in the afternoon, it may explain why we did not find any difference in basal cortisol levels. However, our results are also in line with many other studies reporting no modulation of basal cortisol levels by trait anxiety (Francis, 1981; Preville et al., 2008; Schlotz et al., 2006; Singh, Petrides, Gold, & Deuster, 1999; Takai et al., 2007).

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References

Aberg, K., & Herzog, M. (2010). Does perceptual learning suffer from retrograde interference? *PLoS One, 5*, e14161.

Aberg, K. C., Tartaglia, E. M., & Herzog, M. H. (2009). Perceptual learning with chevrons requires a minimal number of trials, transfers to untrained directions, but does not require sleep. *Vision Research, 49*, 2087–2094.

Andreano, J. M., & Cahill, L. (2006). Glucocorticoid release and memory consolidation in men and women. *Psychological Science, 17*, 466–470.

Bach, M. (1996). The freiburg visual acuity test – Automatic measurement of visual acuity. *Optum Vision Science, 73*, 49–53.

Ball, K., & Sekuler, R. (1982). Specific and enduring improvement in visual motion discrimination. *Science, 218*, 697–698.

Beer, A. L., Vartak, D., & Greenlee, M. W. (2012). Nicotine facilitates memory consolidation in perceptual learning. *Neuropharmacology, 64*, 443–451.

Bocanegra, B., & Zeelenberg, R. (2009). Emotion improves and impairs early vision. *Psychological Science, 20*, 707–713.

Buchanan, T. W., & Lovallo, W. R. (2001). Enhanced memory for emotional material following stress-level cortisol treatment in humans. *Psychoneuroendocrinology, 26*, 307–317.

Buchanan, T. W., Tranel, D., & Adolphs, R. (2006). Impaired memory retrieval correlates with individual differences in cortisol response but not automatic response. *Learning & Memory, 13*, 382–387.

Cahill, L., & Alkire, M. T. (2003). Epinephrine enhancement of human memory consolidation: Interaction with arousal at encoding. *Neurobiology of Learning and Memory, 79*, 194–198.

Cahill, L., Gorski, L., & Le, K. (2003). Enhanced human memory consolidation with post-learning stress: Interaction with the degree of arousal at encoding. *Learning & Memory, 10*, 270–274.

Censor, N., Karni, A., & Sagi, D. (2006). A link between perceptual learning, adaptation and sleep. *Vision Research, 46*, 4071–4074.

Crist, R. E., Kapadia, M. K., Westheimer, G., & Gilbert, C. D. (1997). Perceptual learning of spatial localization: Specificity for orientation, position, and context. *Journal of Neurophysiology, 78*, 2889–2894.

Duncko, R., Makatsori, A., Fickova, E., Selko, D., & Jezova, D. (2006). Altered coordination of the neuroendocrine response during psychosocial stress in subjects with high trait anxiety. *Progress in Neuro-Psychopharmacology & Biological Psychiatry, 30*, 1058–1066.

Fahle, M., & Poggio, T. (Eds.). (2002). *Perceptual learning*. MIT Press.

Francis, K. (1981). The relationship between high and low trait psychological stress, serum testosterone, and serum cortisol. *Experientia, 37*, 1296–1297.

Herzog, M., & Fahle, M. (1997). The role of feedback in learning a vernier discrimination task. *Vision Research, 37*, 2133–2141.

Het, S., Ramlow, G., & Wolf, O. (2005). A meta-analytic review of the effects of acute cortisol administration on human memory. *Psychoneuroendocrinology, 30*, 771–784.

Hubert, W., & de Jong-Meyer, R. (1992). Saliva cortisol responses to unpleasant film stimuli differ between high and low trait anxious subjects. *Neuropsychobiology, 25*, 115–120.

Jezova, D., Makatsori, A., Duncko, R., Moncek, F., & Jakubek, M. (2004). High trait anxiety in healthy subjects is associated with low neuroendocrine activity during psychosocial stress. *Progress in Neuro-psychpharmacology & Biological Psychiatry, 28*, 1331–1336.

Joels, M., Pu, Z., Wiegert, O., Oitzl, M. S., & Krugers, H. J. (2006). Learning under stress: How does it work? *Trends in Cognitive Sciences, 10*, 152–158.

Karni, A., & Sagi, D. (1991). Where practice makes perfect in texture discrimination: Evidence for primary visual cortex plasticity. *Proceedings of the National Academy of Sciences, 88*, 4966–4970.

Karni, A., & Sagi, D. (1993). The time course of learning a visual skill. *Nature, 365*, 250–252.

Karni, A., Tanne, D., Rubenstein, B. S., Askenasy, J. J. M., & Sagi, D. (1994). Dependence on rem sleep of overnight improvement of a perceptual skill. *Science, 265*, 679–682.

Kirschbaum, C., Wolf, O. T., May, M., Wippich, W., & Hellhammer, D. H. (1996). Stress- and treatment-induced elevations of cortisol levels associated with impaired declarative memory in healthy adults. *Life Sciences, 58*, 1475–1483.

Kuai, S.-G., Zhang, J.-Y., Klein, S., Levi, D. M., & Yu, C. (2005). The essential role of stimulus temporal patterning in enabling perceptual learning. *Nature Neuroscience, 8*, 1497–1499.

Lang, P. J., Bradley, M. M., Cuthbert, B. N. (2008). *International affective picture system (iaps): Affective ratings of pictures and instruction manual*. Technical report a-8. Tech. rep. University of Florida, Gainesville, FL.

Laretzaki, G., Plainis, S., Argyropoulos, S., Pallikaris, I., & Bitsios, P. (2010). Threat and anxiety affect visual contrast perception. *Journal of Psychopharmacology, 24*, 667–675.

Liu, Z., & Vaina, L. M. (1998). Simultaneous learning of motion discrimination in two directions. *Cognitive Brain Research, 6*, 347–349.

Lovallo, W. (1975). The cold pressor test and autonomic function: A review and integration. *Psychophysiology, 12*, 268–282.

Luethi, M., Meier, B., & Sandi, C. (2009). Stress effects on working memory, explicit memory, and implicit memory for neutral and emotional stimuli in healthy men. *Frontiers in behavioral neuroscience, 2*, 1–9.

Lupien, S. J., Gaudreau, S., Tchiteya, B. M., Maheu, F., Sharma, S., Nair, N. P. V., Hauger, R. L., McEwen, B. S., & Meaney, M. J. (1997). Stress-induced declarative memory impairment in healthy elderly subjects: Relationship to cortisol reactivity. *Journal of Clinical Endocrinology and Metabolism, 82*, 2070–2075.

Lupien, S. J., Wilkinson, C. W., Briere, S., Menard, C., Ying King, N. M. K. N., & Nair, N. P. V. (2002). The modulatory effects of corticosteroids on cognition: Studies in young human populations. *Psychoneuroendocrinology, 27*, 401–416.

Maheu, F. S., Collicut, P., Kornik, R., Moszkowski, R., & Lupien, S. J. (2005). The perfect time to be stressed: A differential modulation of human memory by stress applied in the morning or in the afternoon. *Progress in Neuro-Psychopharmacology & Biological Psychiatry, 29*, 1281–1288.

Maheu, F. S., Joober, R., & Lupien, S. J. (2005). Declarative memory after stress in humans: Differential involvement of the beta-adrenergic and corticosteroid systems. *The Journal of Clinical Endocrinology & Metabolism, 90*, 1697–1704.

Matarazzo, L., Franko, E., Maquet, P., & Vogels, R. (2008). Offline processing of memories induced by perceptual visual learning during subsequent wakefulness and sleep: A behavioral study. *Journal of Vision, 8*, 1–9.

Mednick, S. C., Arman, A. C., & Boynton, G. M. (2005). The time course and specificity of perceptual deterioration. *Proceedings of the National Academy of Sciences, 102*, 3881–3885.

Mednick, S. C., Nakayama, K., Cantero, J. L., Atienza, M., Levin, A. A., Pathak, N., & Stickgold, R. (2002). The restorative effect of naps on perceptual deterioration. *Nature Neuroscience, 5*, 677–681.

Mednick, S. C., Nakayama, K., & Stickgold, R. (2003). Sleep-dependent learning: A nap is as good as a night. *Nature Neuroscience, 6*, 697–698.

Meerlo, P., Sgoifo, A., & Suchecki, D. (2008). Restricted and disrupted sleep: Effects on autonomic function, neuroendocrine stress systems and stress responsivity. *Sleep Medicine Reviews, 12*, 197–210.

Newcomer, J. W., Craft, S., Hershey, T., Askins, K., & Bardgett, M. E. (1994). Glucocorticoid-induced impairment in declarative memory performance in adult humans. *The Journal of Neuroscience, 14*, 2047–2053.

Oswald, L., Zandi, P., Nestadt, G., Potash, J., Kalaydjian, A., & Wand, G. (2006). Relationship between cortisol responses to stress and personality. *Neuropsychopharmacology, 31*, 1583–1591.

Payne, J. D., Jackson, E. D., Hoscheidt, S., Ryan, L., Jacobs, W. J., & Nadel, L. (2007). Stress administered prior to encoding impairs neutral but enhances emotional long-term episodic memories. *Learning & Memory, 14*, 861–868.

Phelps, E., Ling, S., & Carrasco, M. (2006). Emotion facilitates perception and potentiates the perceptual benefits of attention. *Psychological Science, 17*, 292–299.

Pourtois, G., Rauss, K., Vuilleumier, P., & Schwartz, S. (2008). Effects of perceptual learning on primary visual cortex activity in humans. *Vision Research, 48*, 55–62.

Preuss, D., & Wolf, O. T. (2009). Post-learning psychosocial stress enhances consolidation of neutral stimuli. *Neurobiology of Learning and Memory, 92*, 318–326.

Preville, M., Zarit, S., Susman, E., Boulenger, P., & Lehoux, R. (2008). Response variability of salivary cortisol among older adults under psychological stress. *Aging & Mental Health, 12*, 249–257.

Rimmele, U., Domes, G., Mathiak, K., & Hautzinger, M. (2003). Cortisol has different effects on human memory for emotional and neutral stimuli. *NeuroReport, 14*, 2485–2488.

Roozendaal, B. (2002). Stress and memory: Opposing effects of glucocorticoids on memory consolidation and memory retrieval. *Neurobiology of Learning and Memory, 78*, 578–595.

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

Sandi, C. (1998). The role and mechanisms of action of glucocorticoid involvement in memory storage. *Neural Plasticity, 6*, 41–52.

Sandi, C., & Pinelo-Nava, M. T. (2007). Stress and memory: Behavioral effects and neuribiological mechanisms. *Neural Plasticity, 2007*, 1–20.

Schlotz, W., Schulz, P., Hellhammer, J., Stone, A., & Hellhammer, D. (2006). Trait anxiety moderates the impact of performance pressure on salivary cortisol in everyday life. *Psychoneuroendocrinology, 31*, 459–472.

Schwabe, L., Bohringer, A., Chatterjee, M., & Schachinger, H. (2008). Effect of pre-learning stress on memory for neutral, positive and negative words: Different roles of cortisol and autonomic arousal. *Neurobiology of Learning and Memory, 90*, 44–53.

Schwartz, S., Maquet, P., & Frith, C. (2002). Neural correlates of perceptual learning: A functional mri study of visual texture discrimination. *Proceedings of the National Academy of Sciences of the United States of America, 99*, 17137–17142.

Seitz, A. R., Yamagishi, N., Werner, B., Goda, N., Kawato, M., & Watanabe, T. (2005). Task-specific disruption of perceptual learning. *PNAS, 102*, 14895–14900.

Shors, T. (2004). Learning during stressful times. *Learning & Memory, 11*, 137–144.

Shors, T. (2006). Stress experience and learning across the lifespan. *Annual Review of Psychology, 57*, 55–85.

Singh, A., Petrides, J., Gold, P. G. P. C., & Deuster, P. (1999). Differential hypothalamic–pituitary–adrenal axis reactivity to psychological and physical stress. *The Journal of Clinical Endocrinology % Metabolism, 84*, 1944–1948.

Southwick, S. M., Davis, M., Horner, B., Cahill, L., Morgan, C. A., III, Gold, P. E., Bremner, J. D., & Charney, D. C. (2002). Relationship of enhanced norepinephrine activity during memory consolidation to enhanced long-term memory in humans. *American Journal of Psychiatry, 159*, 1420–1422.

Spielberger, C. (1983). *Manual for the State-Trait Anxiety Inventory*. Palo Alto, CA: Consulting Psychologist Press.

Stickgold, R., LaTanya, J., & Hobson, J. A. (2000). Visual discrimination learning requires sleep after training. *Nature Neuroscience, 3*, 1237–1238.

Stickgold, R., Whidbee, D., Schirmer, B., Patel, V., & Hobson, J. A. (2000). Visual discrimination task improvement: A multi-step process occuring during sleep. *Journal of Cognitive Neuroscience, 12*, 246–254.

Takahashi, T., Ikeda, K., Ishikawa, M., Kitamura, N., Tsukasaki, T., Nakama, D., & Kameda, T. (2005). Anxiety, reactivity, and social stress-induced cortisol elevation in humans. *Neuroendocrinology Letters, 26*, 351–354.

Takai, N., Yamaguchi, M., Aragaki, T., Eto, K., Uchihashi, K., & Nishikawa, Y. (2007). Gender-specific differences in salivary biomarker responses to acute psychological stress. *Annals of the New York Academy of Sciences, 1098*, 510–515.

Tartaglia, E., Aberg, K., & Herzog, M. (2009). Perceptual learning and roving: Stimulus types and overlapping neural populations. *Vision Research, 49*, 1420–1427.

Taylor, M., Reis, J., Sausen, K., Padilla, G., Markham, A., Potterat, E., & Drummond, S. (2008). Trait anxiety an salivary cortisol during free living and military stress. *Aviation, Space, an Environmental Medicine, 79*, 129–135.

Yotsumoto, Y., Chang, L.-H., Watanabe, T., & Sasaki, Y. (2009). Interference and feature specificity in visual perceptual learning. *Vision Research, 49*, 2611–2623.

Yotsumoto, Y., Sasaki, Y., Chan, P., Vasios, C., Bonmassar, G., Ito, N., Nanez, J., Sr., Shimojo, S., & Watanabe, T. (2009b). Location-specific cortical activation changes during sleep after training for perceptual learning. *Current Biology, 19*, 1278–1282.

Yotsumoto, Y., Watanabe, T., & Sasaki, Y. (2008). Different dynamics of performance and brain activation in the time course of perceptual learning. *Neuron, 57*, 827–833.

Yu, C., Klein, S. A., & Levi, D. M. (2004). Perceptual learning in contrast discrimination and the (minimal) role of context. *Journal of Vision, 4*, 169–182.