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Does US expectancy mediate the additive effects of CS-US pairings on contingency instructions? Results from subjective, psychophysiological and neural measures

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ABSTRACT

Verbal instructions are a powerful pathway to learn new fear relations, and an important question has been what fear experience can still add to the effect of such instructions. Therefore, in previous studies, we investigated the effects of pairings between conditioned stimuli (CS) and unconditioned stimuli (US) after CS-US contingency instructions. Although these studies found that CS-US pairings do indeed add to the effects of contingency instructions on subjective, psychophysiological and neural measures of conditioned fear, they also produce increases in US expectancy ratings. In the current report we address whether these enhanced US expectancy ratings can account for the additive effects of CS-US pairings as suggested by expectancy models of fear conditioning. To address this question we made use of pathway models to investigate mediation in within-subjects designs. Our results demonstrate that US *expectancy* ratings do not mediate the effects of CS-US pairings on fear ratings, the startle reflex or amygdala activation pattern similarity. Additional exploratory analyses, however, revealed that subjective *fear* ratings do explain the effects of CS-US pairings on the other measures. We discuss how these results relate to expectancy models of fear conditioning and what they implicate for the validity of US expectancy and fear ratings.

Does US expectancy mediate the additive effects of CS-US pairings to contingency instructions? Results from subjective, psychophysiological and neural measures.

Humans display the adaptive ability to quickly learn to fear and avoid stimuli that predict possible harmful events. We are capable of learning this contingency not only through the pairing of initially neutral conditioned stimuli (CSs) and aversive unconditioned stimuli (US; i.e., fear conditioning), but also through verbal instructions and social observation. Although the delineation of these different pathways has been described at least 40 years ago (Rachman, 1977), the interaction between the different pathways is still not well understood.

In recent studies we have addressed this interaction between the verbal and experiential pathway (Braem et al., 2017; Mertens, Kuhn, et al., 2016; Mertens, Raes, & De Houwer, 2016; Raes, De Houwer, De Schryver, Brass, & Kalisch, 2014). Specifically, these studies investigated whether CS-US pairings (i.e., conditioning trials) add to the effect of clear and believable verbal contingency instructions. Therefore, participants first went through a conditioning phase in which one CS (CS + P) was paired with a US (a mild electric shock) while another CS (CS + U) was not paired (or: unpaired) with the US. Importantly, participants were told at the outset of the experiment that the CS + U would not be followed by the US in the first phase, but would be followed by the US in the second test phase, and participants were reminded of these instructions in between phases. In reality, however, none of the CSs were followed by the US in the test phase, which ensured that the conditioned response for the CS + U was purely based on instructions. Across all four studies, we found clear evidence that the CS + P elicited slightly larger fear responses than the CS + U (i.e., subjective fear ratings, potentiated startle response and amygdala activation pattern similarity; but not skin conductance responses), suggesting that CS-US pairings add to the effect of verbal instructions (Braem et al., 2017; Mertens, Kuhn, et al., 2016; Mertens, Raes, et al., 2016; Raes et al., 2014).

Our studies also showed that CS-US pairings did not only influence

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fear responses, but also increased participants' expectancy ratings for the CS + P. An unaddressed question in our previous studies is whether these increased expectancies could account for the increased fear responses. This would be expected on the basis of several important theories of fear conditioning. Specifically, according to Davey's expectancy model of fear conditioning (Davey, 1992), conditioned fear responses reflect participants' expectancy and evaluation of the US. Similar models have been proposed by Reiss (1980), Lovibond (2011) and Dawson and Furedy (1976). Hence, according to these models one may predict that the increased expectancy ratings due to CS-US pairings mediate the effects of CS-US pairings on the fear responses. Alternatively, other models of fear conditioning have argued that CS-US pairings can install memory associations that are independent of language and expectancies (LeDoux, 2014; Olsson & Phelps, 2007; Öhman & Mineka, 2001). According to these latter theories, CS-US pairings may increase fearful responses without necessarily altering expectancy ratings (e.g., Mineka & Öhman, 2002a,b).

In order to address these competing predictions regarding the mediating role of US expectancies for explaining the additive effects of CS-US pairings, we have re-analyzed data from our prior studies using recent methods for performing mediation analyses for within-subjects designs (see Montoya & Hayes, 2017). If the additive effects of CS-US pairings on fear measures (fear ratings, fear potentiated startle and amygdala activation pattern similarity) are explained by increases in US expectancy ratings, mediation analysis should indicate that US expectancy ratings significantly mediate the effects of CS-US pairings on these measures. Alternatively, if US expectancy ratings do not explain the additive effects of CS-US pairings on fear measures, the effects of CS-US pairings on fear measures should remain present even when partialling out the variance related to US expectancy ratings.

1. Method

1.1. Participants

To address the hypotheses stated above, we have re-analyzed the data of the four previous studies that have investigated the additive effects of CS-US pairings to contingency instructions (Braem et al., 2017; Mertens, Kuhn, et al., 2016; Mertens, Raes, et al., 2016; Raes et al., 2014). These samples consisted of healthy university students (Braem et al.: N = 20; Mertens, Kuhn, et al.: N = 36; Mertens, Raes, et al.: N = 36; Raes et al. N = 31[1]).

1.2. Materials and procedure

The procedure of these studies has been extensively described in the original studies. In brief, participants took part in a single session fear conditioning experiment. In a first phase, participants were informed about the contingency between pictures of snow fractals (or pictures of fear-relevant and fear-irrelevant animals, see Mertens, Raes, et al., 2016, Experiment 2) and an electric stimulation via instructions on the computer screen. They were told that two of these snow fractals would sometimes be followed by an electric stimulation during the experiment, whereas a third fractal would never be followed by the stimulation. Furthermore, participants were informed that in the first part of the experiment, some of the electric stimulations would be replaced by a picture of a lightning bolt in order not to expose them to too many electric stimulation. During this first phase, the snow fractals were presented on the computer screen for 8 s. One of the fractals was sometimes (i.e., on 33% of the trials) followed at offset by an electric stimulation (CS + P), whereas another fractal was sometimes (also on 33% of the trials) followed by a picture of a lightning bolt (CS + U). A third fractal was never paired with the stimulation or with the picture of the lightning bolt (CS-).

Following this first phase, participants were told that in the next phase no more replacements would be presented (i.e., the picture of a lightning bolt), and that the two fractals (referred to in the instructions in the first phase) would now actually be followed by the electrical stimulation. They were further informed that the third fractal would still not be followed by the stimulation. The procedure of this second phase (i.e., the crucial test phase) was identical to the previous phase with the exception that the electrical stimulation and the picture of the lightning bolt were never presented.

Each phase was interrupted three times by a ratings block in which participants had to rate their subjective fear levels (“How much fear did you experience while looking at this figure?”) and US expectancy (“To what extent did you expect an electro-tactile stimulation while seeing this figure?”) for the three different snow fractals on 9-point Likert scales (as further explained in Braem et al., 2017, not all ratings were assessed in the first subjects of that study, resulting in a slightly smaller sample for some of the analyses below). Besides these subjective ratings, we have also collected skin conductance responses (SCRs; Mertens, Kuhn, et al., 2016; Mertens, Raes, et al., 2016; Raes et al., 2014), potentiation of the startle reflex (Mertens, Kuhn, et al., 2016) and the fMRI BOLD signal (Braem et al., 2017) during the fractal presentations. The crucial comparison was during the test phase, between the fractal that had been paired with the stimulation (CS + P) and the fractal that was only paired with the picture of a lightning bolt (CS + U). More specifically, the analyses zoomed in on fear responses during the first three trials of the test phase, given that we expect the effects of prior CS-US pairings to be most pronounced during these first few trials because they are less affected by extinction due to non-reinforcement of the CSs during the test phase. Furthermore, also the believability of the contingency instructions (i.e., that CS + U will now also be followed by electrical stimulations) is unlikely affected by the non-reinforcement of the CSs during these first three trials of the test phase.

1.3. Data preprocessing and analysis

1.3.1. Preprocessing of the fear responses

Scoring of the psychophysiological responses has been extensively described in the previous reports. In brief, startle responses (or: fear potentiated startle, FPS) were scored by taking the maximum amplitude in the 20–120 ms time window after the startle probe onset (Mertens, Kuhn, et al., 2016). Amygdala activation pattern similarity was calculated as the similarity in voxel pattern activation between CS + P presentation during the training phase, and CS + P or CS + U presentation during the testing phase (Multi-Voxel Pattern Analysis; see Braem et al., 2017 for an extensive description of this approach). Finally, skin conductance was also measured but will not be considered here because no effects of CS-US pairings were found for this measure in any of our studies (Mertens, Kuhn, et al., 2016; Mertens, Raes, et al., 2016; Raes et al., 2014).

1.3.2. Statistical analyses

To investigate mediation of the additive effects of CS-US pairings by US expectancy ratings, we have performed mediational analyses using the MEMORE syntax developed by Montoya and Hayes (2017) in SPSS (version 24.0). This code provides the pathway coefficients, the standard error and the 95% confidence interval for the direct (i.e., the effect of a factor when controlled for the shared variance with the mediator) and the indirect (i.e., the mediation effect) pathways in a mediation model. Mediation is established in the path analytic framework when the confidence interval for the pathway coefficient of the indirect pathway does not include zero (Montoya & Hayes, 2017; Preacher & Hayes, 2004). Particularly, we investigated whether the effect of CS type (CS + P versus CS + U) during the first block of the test phase on the different fear measures (i.e., the direct effect of CS type) could be accounted by US expectancy ratings (i.e., the indirect effect of CS type through US expectancy). Pathways were estimated using 10,000 bootstrap samples. A table containing the correlations between the different

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