Dear Editors,

We read the article entitled “The next frontier: Moving human fear conditioning research online” with great enthusiasm. Threat (or fear) conditioning is a fundamental learning process enabling organisms to predict and anticipate impending threats. Ney, O’Donohue, et al.’s (2023) review offers fascinating ways to advance threat conditioning research and makes an important contribution to the field. Here, we expand on this contribution by highlighting two critical challenges of moving threat conditioning online: the restricted ranges of stimuli and sensory modalities that can be tested in this setting.

A limitation of online-based threat conditioning is that the nature and intensity of the conditioned (CS) and unconditioned (US) stimuli that can be used is relatively narrow. Yet, these factors—along with the CS-US functional relationship—exert a prominent influence on learning dynamics during threat acquisition, extinction, and generalization. More intense CSs and USs produce faster and stronger learning (e.g., Rescorla & Wagner, 1972), whereas functionally-related CSs and USs generally produce more persistent learning (e.g., Garcia & Koelling, 1966). Notably, electro-tactile USs commonly used in the laboratory evoke stronger physiological conditioned responses than loud screams (Ney, Nichols, et al., 2023), which are predominant online. High-intensity USs have also been found to widen threat generalization compared to low-intensity USs (Dunsmoor et al., 2017). The difficulty of adapting high-intensity stimuli may thus impact the spectrum of threat learning processes that can be studied in an online setting. This has significant implications for research using threat conditioning as a laboratory model for understanding the etiology and maintenance of anxiety-related disorders (see Beckers et al., 2023). The emergence of these disorders—in particular posttraumatic stress disorder—is often linked to exposure to an intense negative emotional or traumatic event (Homan et al., 2019). Online threat conditioning procedures involving stimuli that are less intense than the ones used in their laboratory counterparts may therefore be further removed from the natural settings contributing to the development of anxiety-related disorders, thereby limiting their translational potential with respect to clinical research and applications.

Another notable pitfall concerns the fact that nociceptive, tactile, and chemosensory (i.e., olfaction and gustation) modalities cannot be easily translated in an online setting. In addition to being powerful elicitors of emotional responses (Delplanque et al., 2017; Rolls et al., 2003), these sensory modalities are central to avoid environmental hazards and play an important role in threat-related processes and learning (Gottfried & Dolan, 2004; Hakim et al., 2019; Wiech & Tracey, 2013). The use of nociceptive, tactile, and chemosensory stimuli has been instrumental in elucidating the elaborateness of the mechanisms underlying Pavlovian reward and threat conditioning (Prévost et al., 2013; Stussi et al., 2018, 2021). This work has contributed to demonstrating that Pavlovian learning is not a unitary process but involves several parallel associations between the CS and multiple attributes of the US, such as its sensory, temporal, spatial, hedonic, and motivational properties (Delamater & Oakeshott, 2007; Starita et al., 2023; Stussi & Pool, 2022). Specifically, US affective and sensory features elicit different classes of conditioned responses that rely on dissociable learning processes and neural substrates (Pool et al., 2023; Zhang et al., 2016). Using thermal pain as a tactile/nociceptive US and manipulating its affective and sensory features through its aversive value and location delivery (i.e., left or right arm), respectively, Zhang et al. (2016) showed that threat-related conditioned facial and autonomic responses were driven by a preparatory system tracking the US aversive value independently of its location delivery. By contrast, conditioned motor responses were dependent on a consummatory system sensitive to the lateralization of the US delivery. Consequently, the challenge of adapting nociceptive, tactile, and chemosensory stimuli might render the exploration of the multiple Pavlovian learning signals and...
representations particularly difficult to achieve online despite the importance of this research line for improving our mechanistic understanding of threat conditioning processes and their links to mental health.

In summary, moving threat conditioning online offers exciting opportunities for the collection of large-scale data and the development of new methods to measure behavioral and physiological responses online is promising. Nonetheless, caution is necessary. Considering the challenges inherent in this transition and the limitations regarding stimulus intensities and modalities is key in establishing the translational relevance, specificity, and reliability of threat conditioning phenomena that can be investigated online. These considerations are equally pivotal to determine the extent to which online experiments can capture the richness and sophistication of threat conditioning processes.

Funding
YS is supported by an ERC Starting Grant (INFORL-948671) awarded to Prof. Dr. Maël Lebreton. GC is supported by an Eccellenza Grant from the Swiss National Science Foundation (181094).

CRediT authorship contribution statement
Géraldine Coppin: Writing – review & editing, Funding acquisition, Conceptualization. Yoann Stussi: Writing – review & editing, Writing – original draft, Conceptualization.

Declaration of Generative AI and AI-assisted technologies in the writing process
The authors did not use generative AI for preparation of this work.

Declaration of Competing Interest
The authors declare no competing interests.

Data availability
No data was used for the research described in the article.

Acknowledgments
The authors would like to thank Dr. Eva R. Pool for insightful discussions and Dr. Vanessa Sennwald for her helpful comments on the manuscript.

References
Ney, L. J., Nichols, D. S., & Lipp, O. V. (2023). Fear conditioning depends on the nature of the unconditional stimulus and may be related to hair levels of endocannabinoids. Psychophysiology, 60(8), Article e14297. https://doi.org/10.1111/psyp.14297

Yoann Stussi, Géraldine Coppin

a Swiss Center for Affective Sciences, Campus Biotech, University of Geneva, Geneva, Switzerland
b Department of Psychology, FPSE, University of Geneva, Geneva, Switzerland
c UniDistance Suisse, Brig, Switzerland

*Correspondence to: Campus Biotech, CISA–University of Geneva, Chemin des Mines 9, CH-1202 Geneva, Switzerland.
E-mail address: yoann.stussi@unige.ch (Y. Stussi).