Ultrasonic vocalization playback as an affective assay at both neural and behavioral levels: Implications for understanding adversity-induced emotional dysfunction

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Despite the prevalence of anxiety disorders, few translational models to study the neural correlates of anxiety exist. Playback of pre-recorded emotionally valenced rat ultrasonic vocalizations (USVs) may be a model to assess affective processing of stimuli in actively behaving rats. Here, male and female rats were exposed to USVs at 22kHz (aversive call) and 55 kHz (appetitive call) in an open field test (OFT). Brain tissue was stained for regional and cell specific activity (cFos+ cell count). Results show that adults were mildly, behaviorally affected by playback. Neural results in the PL PFC point to decreased parvalbumin-expressing (PV+) interneuron activity as an effect of playback. In a second study, juvenile (P26) or young adult (P47) animals raised in typical or early life adversity (ELA) conditions were subjected to 15 minutes of aversive 22 kHz USV playback or silence in an open field. ELA experience led to dysregulation of affective processing, particularly in juveniles. Anxiety-like behaviors for juveniles persisted though 15 minutes of playback and were more prominent during 22 kHz playback for ELA females. Young adults largely regulated behavioral output in response to playback, but ELA females exhibited novel hyperlocomotion behavior, indicating a sex-specific anxiety-like phenotype in the OFT. PV+ neuron activity in PL PFC of juvenile females was increased for ELA individuals during playback, suggesting early onset of maturation of this region supported by hypervigilant, anxiety-like behavioral output. These data suggest USV playback is an affective assay of underlying sex-specific chronic anxiety states due to ELA history.

Overall, the first study began to show altered behavioral output in response to USV playback at different ethologically relevant frequencies and the corresponding levels of neural activity in affective processing regions. Examination of PV+ interneuron activity points to the inhibitory/excitatory roles of this cell type in affective processing regions in response to these stimuli in typical adults. Results from the second study showed behavioral and neural results that suggested that adult animals are subtly affected by valenced USV playback in sex-specific and frequency-specific ways while juveniles are more acutely affected on the behavioral level following ELA. While behavioral output may be attenuated by mature and normative inhibitory processes in adult animals to prevent outward signs of distress, physiological and neural data begin to point to affective neural correlates of reactions to USV playback due to ELA experience.

Both studies described here highlighted the utility of USV playback as an affective probe at both behavioral and neural levels, particularly in animals at higher risk for affective dysfunction due to ELA exposure. In the first experiment, adult rats presented with 22 kHz or 55 kHz USV playback showed behavioral effects of playback largely in locomotive behaviors in a sex-dependent manner which faded as playback continued in the OFT. Measures of neural activity revealed the PL PFC as a sex-specific regulator of behavior with PV+ neuron activity playing a role in the adult female PL PFC. With additional consideration of ELA experience and development, a playback probe revealed that juvenile males were behaviorally affected by playback while females were influenced by combinations of adversity experience and playback exposure that largely persisted for the duration of playback. Young adult females were markedly influenced by rearing but all adults were generally less affected by playback. These results show that aversive playback can be a probe for assessing affective processing of different populations.