Effects of early-life adversity and acute stress on the experience of emotion in schizophrenia

James Waltz[1], Jacob Nudelman[1], Olivia Hutchinson[1], Eric Neutzling[1]

[1]Maryland Psychiatric Research Center, University of Maryland School of Medicine

Background

- Early-life adversity (ELA) can alter sensitivity to rewarding, stressful, and neutral events and stimuli.
- Psychosis is also associated with increased sensitivity to acute stressors, perhaps engendered by elevated rates of ELA.
- **Our overarching goal was** to examine effects of ELA on reactivity to pleasant, aversive, and neutral stimuli.
- **We also sought to determine** whether diagnosis interacted with abuse history in predicting ratings of affective pictures, as well as differences in ratings between stressed and non-stressed conditions.
- **We hypothesized that** acute and cumulative stress would increase affective reactivity to unpleasant stimuli and decrease affective reactivity to pleasant stimuli, with stress exposure interacting with diagnosis in moderating sensitivity to stimuli.

Study Schedule

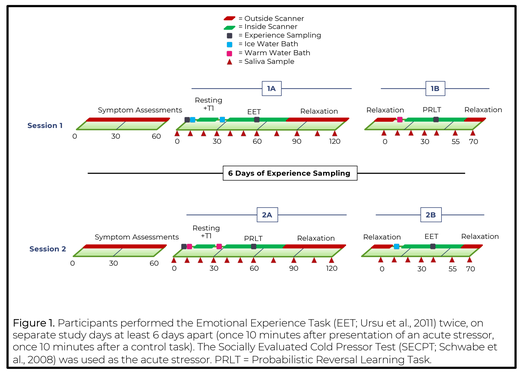

Figure 1. Participants performed the Emotional Experience Task (EET; Ursu et al., 2011) twice, on separate study days at least 6 days apart (once 10 minutes after presentation of an acute stressor, once 10 minutes after a control task). The Socially Evaluated Cold Pressor Test (SECPT; Schwabe et al., 2008) was used as the acute stressor. PRLT = Probabilistic Reversal Learning Task

Acute Stress Manipulation

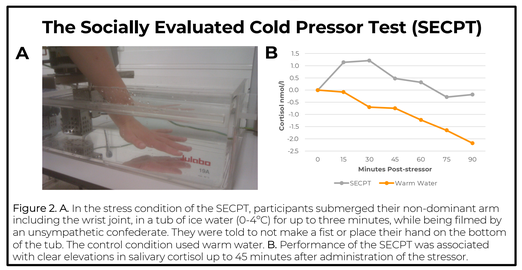

Figure 2. A. In the stress condition of the SECPT, participants submerged their non-dominant arm including the wrist joint, in a tub of ice water (0-4°C) for up to three minutes, while being filmed by an unsympathetic confederate. They were told to not make a fist or place their hand on the bottom of the tub. The control condition used warm water. **B.** Performance of the SECPT was associated with clear elevations in salivary cortisol up to 45 minutes after administration of the stressor.

Behavioral Paradigm

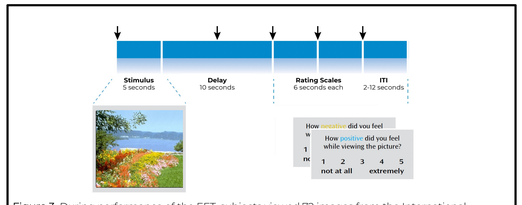

Figure 3. During performance of the EET, subjects viewed 72 images from the International Affective Pictures Set (IAPS; Lang et al., 2005; 24 pleasant, 24 unpleasant, 24 neutral) in four runs of 18 trials each. On each trial, subjects were asked to rate both the "positivity" and "negativity" of the emotion experienced, during the presentation of a picture, on a 5-point scale, by means of a three-button response unit.

Both diagnosis and abuse history impacted ratings of affective pictures.

- However, diagnosis and abuse history did not produce interacting effects on ratings of affective pictures in our study.
- Abuse history also moderated the effect of the acute stressor.

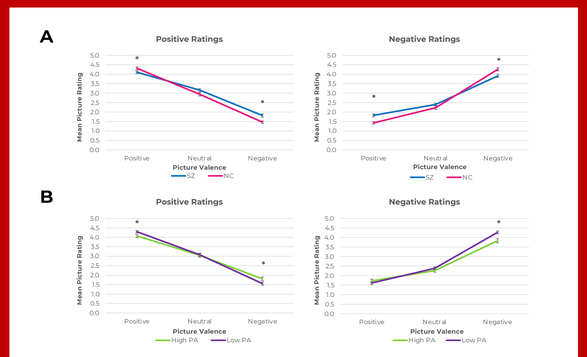

Figure 4. A. We observed an effect of diagnosis on mean picture ratings, such that SZ patients exhibited reduced dynamic range, relative to HVs, in their ratings. Specifically, we found that SZ patients, in comparison to HVs, rated positive pictures as less positive (t_{82} = 1.958; p = 0.05) and more negative (t_{82} = 3.640; p < 0.001). SZ patients also rated negative pictures as more positive (t_{82} = 2.911; p = 0.005) and less negative (t_{82} = 2.711; p = 0.008) than HVs. **B.** We also found that individuals who suffered physical abuse (High PA) as children rated positive pictures as less positive (t_{77} = 2.056; p = 0.043), in comparison to individuals who did not (Low PA). High PA individuals also rated negative pictures as more positive (t_{77} = 1.994; p = 0.05) and less negative (t_{77} = 3.424; p < 0.001) than Low PA individuals.

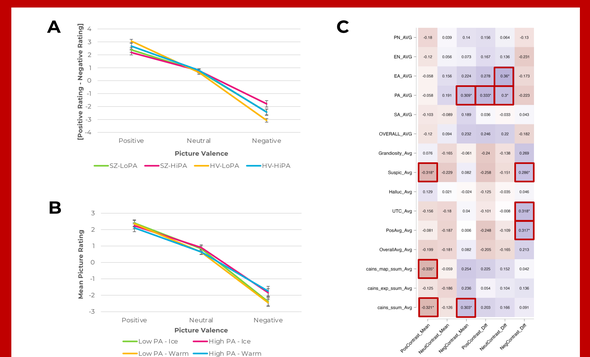

Figure 5. A. We observed no significant interactions between diagnosis and abuse history in predicting picture ratings (all F-values < 1). **B.** However, patients with higher physical abuse (PA) scores showed a greater impact of the acute stressor on picture ratings. **C.** Pearson correlation analyses revealed significant associations between PA scores and mean ratings of aversive images (r = 0.309; p = 0.035), as well as the effect of the acute stressor on ratings of positive (r = 0.333; p = 0.022) and neutral stimuli (r = 0.300; p = 0.040). Other abbreviations: PN, Physical Neglect; EN, Emotional Neglect; EA, Emotional Abuse; SA, Sexual Abuse; UTC, Unusual Thought Content; Contrast_Mean, mean of [positive rating – negative rating] contrast across sessions; Contrast_Diff, difference of [positive rating – negative rating] contrast across sessions.

Acknowledgements

- NIH Grant 1R01MH115031

Contact

- jwaltz@som.umaryland.edu

Clinical/Self-report Assessments

- The **Brief Psychiatric Rating Scale** (BPRS; Overall & Gorman, 1962) was administered to assess general psychopathology.
- To assess potential deficits in motivation, pleasure, and emotional expression, we used the **Clinical Assessment Interview for Negative Symptoms** (CAINS; Kring et al., 2013).
- To rate depressive symptoms in people with SZ, we administered the **Calgary Depression Rating Scale** for Schizophrenia (CDS; Addington et al., 1992).
- To ask about experiences of abuse, we administered the 28-item **Childhood Trauma Questionnaire** (CTQ; Bernstein, et al., 2003).

Participants

Table 1. Participant demographic information.

Domain/Measure	SZ (N=58)		HV (N=37)		Inferential Statistic	Significance
Demographics						
Age (Years)	39.28	(10.09)	42.30	(13.82)	t_{93} = 1.148	p = 0.255
Sex at Birth	18 F,	40 M	16 F,	21 M	χ^2 = 1.465	p = 0.226
Race	28 W,	30 NW	25 W,	12 NW	χ^2 = 3.409	p = 0.065
Ethnicity	1 Hispanic,	57 Non-Hisp.	7 Hispanic,	30 Non-Hisp.	χ^2 = 8.660	p = 0.003
Tobacco User	14 Yes,	44 No	5 Yes,	32 No	χ^2 = 1.594	p = 0.207
Education						
Subject Education	13.55	(2.09)	15.44	(2.02)	t_{93} = 4.326	p < 0.001
Mother's Education	14.86	(3.16)	14.46	(3.25)	t_{84} = 0.578	p = 0.565
Father's Education	15.08	(3.05)	14.63	(3.73)	t_{83} = 0.613	p = 0.542

Table 2. Antipsychotic Medications.

Medication	# of Participants
Aripiprazole	6
Cariprazine	1
Clozapine	18
Olanzapine	3
Quetiapine	1
Paliperidone	4
Risperidone	3
2 SGAs	4
1 FGA	7
2 FGAs	1
FGA + SGA	8
No APD	2

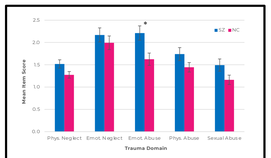

Figure 6. Trauma Domain Scores (from the CTQ) by Diagnostic Group. The two participant groups also differed significantly on total CTQ score (t_{77} = 2.108; p = 0.038).

Implications

- Future analyses will investigate whether diagnosis and abuse history exerted interacting effects on brain activity related to sensitivity to pleasant and aversive stimuli.
- A better knowledge of the processes by which ELA sensitizes susceptible individuals to the noxious effect of future stressors, is critical to our ability to reduce the severity and impact of psychotic symptoms through interventions.

References

Addington, D., Addington, J., Maticka-Tyndale, E., & Joyce, J. (1992). Reliability and validity of a depression rating scale for schizophrenics. Schizophr Res, 6, 201-208.

Bernstein, D. P., Stein, J. A., Newcomb, M. D., Walker, E., Pogge, D., Ahluvalia, T., Stokes, J., Handelsman, L., Medrano, M., Desmond, D., & Zule, W. (2003). Development and validation of a brief screening version of the Childhood Trauma Questionnaire. Child Abuse Negl, 27, 169-190.

Kring, A. M., Gur, R. E., Blanchard, J. J., Horan, W. P., & Reise, S. P. (2013). The Clinical Assessment Interview for Negative Symptoms (CAINS): final development and validation. Am J Psychiatry, 170, 165-172.

Lang, P.J., Bradley, M.M. and Cuthbert, B.N. (2005). International affective picture system (IAPS): Affective ratings of pictures and instruction manual (pp. A-8). Gainesville, FL: NIMH, Center for the Study of Emotion & Attention.

Overall, J. E., & Gorman, D. R. (1962). The Brief Psychiatric Rating Scale. Psychological Reports, 10, 799-812.

Schwabe, L., Haddad, L., & Schachinger, H. (2008). HPA axis activation by a socially evaluated cold-pressor test. Psychoneuroendocrinology, 33, 890-895.

Ursu, S., Kring, A.M., Gard, M.G., Minzenberg, M.J., Yoon, J.H., Ragland, J.D., Solomon, M. and Carter, C.S. (2011). Prefrontal cortical deficits and impaired cognition-emotion interactions in schizophrenia. American Journal of Psychiatry, 168, 276-285.