Psychometric Properties of Psychophysiological Paradigms in the NIMH RDoC: Startle and Corrugator Response in NPU, Affective Picture Viewing, and Resting State Tasks

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Study Objectives

Psychophysiology tasks are poised to become a major contributor to the National Institute of Mental Health Research Domains Criteria (RDoC) and related experimental medicine initiatives. For these tasks to meaningfully contribute to the RDoC they must possess sound psychometric properties.

We designed the current study to comprehensively evaluate key psychometric properties of **startle and corrugator response modulation** in three commonly used psychophysiology tasks that can be anchored within the RDoC Negative Valence System domain.

1) Effect size and stability: We examine the strength and stability of each focal task manipulation (e.g., unpredictable shock vs. no-shock in NPU Task, unpleasant vs. neutral pictures) by quantifying its effect size and testing for an effect of study visit (visit 1 vs. 2).
2) Internal consistency: We examine split-half reliability using Spearman-Brown corrected Pearson correlations between odd and even trials to quantify internal consistency within subjects.
3) Temporal stability: We examine temporal stability using Pearson correlations between study visit 1 and study visit 2 to quantify the stability of individual differences in responses over one week.

Methods & Measures

- Healthy participants (N=128, 64 female) completed three psychophysiology tasks at two study visits separated by one week.
- Participants first completed the Resting State Task and were then randomized to a Task Order (1st task: NPU Task or Affective Picture Viewing Task) for both study visits.
- The startle and corrugator responses are measures of negative affective reactivity that are modulated by emotional stimuli (e.g. potentiated by threat).
- EMG sensors over the orbicularis occuli and corrugator supercilii muscles measure activity associated with the eyeblink and frown, respectively. Responses are measured during shock cues in the NPU Task or pictures in the Affective Picture Viewing Task to acoustic probes for startle and cue/picture-onset for corrugator.

Quantification Approach: We quantified startle and corrugator response in two common ways:

Startle Response: 1) Raw scores (microvolt units) & 2) Standardized T-scores

Corrugator Response: 1) Raw scores (microvolt units) in time domain & 2) Power in frequency domain

- **Raw & Power scores:** Mean startle and corrugator responses for each condition during cues or pictures in the NPU and Affective Picture Viewing tasks, respectively. Raw startle calculated as peak magnitude 20-100ms post-probe onset. Corrugator response calculated during 0-3000ms post-cue/picture onset as mean magnitude in microvolts (time domain) or power in the 28-200Hz band (frequency domain).
- **Startle Standardized T-score:** For each trial we subtracted participant's mean raw startle response and divided by the standard deviation across their trials within each task. Scores were multiplied by 10, plus 50.

No Shock, Predictable Shock, Unpredictable Shock (NPU) Task

Predictable Shock Block (Acute Threat)

= Electric Shock to Fingers

Predictable shock: Shock occurs during cues only

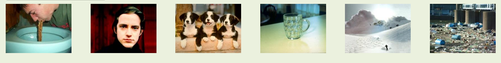
Unpredictable Shock Block (Potential Threat)

Unpredictable shock: Shock occurs at any time.

- This task manipulates participants' affect by administering mild electric shocks under predictable and unpredictable (vs. neutral, no-shock) conditions.
- Participants viewed blocks of a series of 5 second colored square cues. Both shock and no shock conditions counterbalanced within- & between-subjects.
- To control for individual differences in shock sensitivity, participant's maximum tolerated shock at 1st study visit is used during the NPU Task at both visits.
- **Startle potentiation** = shock cues minus no shock cues (not displayed)

Affective Picture Viewing Task

Picture Block



- This task manipulates participants' affect by presenting unpleasant, pleasant, and neutral pictures from the International Affective Picture System (IAPS).
- Participants viewed 36 different pictures (set) at each study visit comprising 12 pleasant, 12 unpleasant and 12 neutral pictures. Pictures were displayed for 6s each in blocks.
- Picture condition order was counterbalanced within- & between-subjects and picture set order was counter balanced between-subjects.
- **Pleasant startle modulation** = pleasant minus neutral pictures
- **Unpleasant startle modulation** = unpleasant minus neutral pictures

Table Notes

Effect size units:
- Microvolts (raw)
- T-scores (standardized)
- Power (frequency domain).

- Internal consistency and temporal stability reported as correlation coefficients.
- Confidence Intervals in brackets [95% CI].

Significant effect (p <. 05) of:

* Effect size or correlation (non-zero)

[a] Study visit for raw startle

[b] Study visit for startle standardized scores or for corrugator power in frequency domain

[c] Difference in psychometric property (i.e., internal consistency or temporal stability) between quantification methods within each measure.

NPU Task: Startle Potentiation

	Raw Scores		Standardized Scores	
Effect Size & Stability	Visit 1	Visit 2	Visit 1	Visit 2
Predictable Potentiation	36.2 [29.9, 42.5]*	37.0 [30.4, 43.7]*	9.5 [8.4, 10.5]*	10.2 [8.9, 11.4]*
Unpredictable Potentiation [b]	26.5 [21.6, 31.5]*	22.9 [18.8, 27.0]*	7.5 [6.6, 8.5]*	6.5 [5.6, 7.4]*
Internal Consistency	Visit 1		Visit 1	
Predictable Potentiation [c]	.81 [.72, .87]*		.57 [.37, .70]*	
Unpredictable Potentiation	.64 [.48, .76]		.52 [.31, .67]*	
Temporal Stability	Visit 1 to Visit 2		Visit 1 to Visit 2	
Predictable Potentiation	.71 [.60, .79]*		.58 [.44, .69]*	
Unpredictable Potentiation [c]	.71 [.60, .79]*		.49 [.33, .62]*	

NPU Task startle potentiation displayed large effect sizes across study visits and good internal consistency and temporal stability, making it a robust and reliable task-measure pairing.

NPU Task: Corrugator Potentiation

	Raw Scores in Time Domain		Power in Frequency Domain	
Effect Size & Stability	Visit 1	Visit 2	Visit 1	Visit 2
Predictable Potentiation	.15 [.02, .28]*	.18 [.06, .29]*	.015 [-.002, .031]	.020 [-.001, .040]
Unpredictable Potentiation	.17 [.07, .27]*	.18 [.08, .28]*	.023 [.007, .040]*	.020 [.002, .038]*
Internal Consistency	Visit 1		Visit 1	
Predictable Potentiation [c]	.45 [.20, .63]*		-.25 [-.49, .09]	
Unpredictable Potentiation [c]	-.18 [-.45, .17]		-.64 [-.75, .-47]	
Temporal Stability	Visit 1 to Visit 2		Visit 1 to Visit 2	
Predictable Potentiation	.51 [.35, .64]*		.35 [.17, .51]*	
Unpredictable Potentiation [c]	.27 [.09, .44]*		.00 [-.19, .19]	

NPU corrugator potentiation was significant, but smaller in size than startle. It displayed generally poor internal consistency and temporal stability, potentially limiting it's utility in this task.

Affective Picture Viewing Task: Startle Modulation

	Raw Scores		Standardized Scores	
Effect Size & Stability	Visit 1	Visit 2	Visit 1	Visit 2
Pleasant Modulation [b]	-4.7 [-6.4, -3.0]*	-1.9 [-4.3, 0.5]	-1.5 [-2.4, -0.7]*	-0.1 [-1.0, 0.7]
Unpleasant Modulation [b]	6.8 [4.9, 8.8]*	8.8 [7.0, 10.6]*	3.1 [2.3, 4.0]*	4.9 [4.0, 5.8]*
Internal Consistency	Visit 1		Visit 1	
Pleasant Modulation [c]	.16 [-.21, .41]		-.10 [-.38, .23]	
Unpleasant Modulation	.07 [-.34, .35]		.14 [-.25, .41]	
Temporal Stability	Visit 1 to Visit 2		Visit 1 to Visit 2	
Pleasant Modulation	-0.1[-.19, .18]		.08 [-.10, .26]	
Unpleasant Modulation	.50 [.35, .63]*		.40 [.24, .54]*	

Unpleasant pictures produced large startle modulation, adequate temporal stability, but poor internal consistency. Psychometric properties of pleasant pictures startle modulation were poor.

Affective Picture Viewing Task: Corrugator Modulation

	Raw Scores in Time Domain		Power in Frequency Domain	
Effect Size & Stability	Visit 1	Visit 2	Visit 1	Visit 2
Pleasant Modulation	-.01 [-.13, .11]	.04 [-.10, .19]	-.006 [-.03, .02]	.006 [-.03, .04]
Unpleasant Modulation	.73 [.54, .91]*	.83 [.60, 1.05]*	.101 [.06, .14]*	.135 [.09, .18]*
Internal Consistency	Visit 1		Visit 1	
Pleasant Modulation [c]	.21 [-.14, .45]		-.46 [-.63, -.22]	
Unpleasant Modulation	.54 [.33, .68]*		.44 [.20, .62]*	
Temporal Stability	Visit 1 to Visit 2		Visit 1 to Visit 2	
Pleasant Modulation	.20 [.02, .36]*		.30 [.12, .46]*	
Unpleasant Modulation	.56 [.42, .67]*		.54 [.39, .66]*	

Unpleasant pictures produced large corrugator modulation with adequate internal consistency and temporal stability. Corrugator response was not modulated by pleasant pictures.

Resting State Task

- This task involves a period of time characterized by the absence of other explicit manipulations or potent experimental stimuli, often conducted at "baseline".
- General startle reactivity during this task has been suggested to index individual differences in defensive reactivity within the Negative Valence System domain of the RDoC.
- Participants viewed a fixation cross while 9 startle probes were presented at random intervals. No other distracting stimuli were presented (e.g., images or shock).
- General startle reactivity was calculated as the mean raw startle response during the Resting State Task.

Resting State Task: Startle Response

	Raw Scores	
Effect Size & Stability	Visit 1	Visit 2
General Startle Reactivity [a]	.87.3 [75.7, 98.8]*	72.5 [61.5, 83.5]*
Internal Consistency	Visit 1	
General Startle Reactivity	.95 [.93, .97]*	
Temporal Stability	Visit 1 to Visit 2	
General Startle Reactivity	.89 [.85, .92]*	

Conclusions

- NPU task predictable and unpredictable startle potentiation appears well-suited for both single administration and longitudinal or other research designs with multiple administrations. Corrugator potentiation appears adequate to detect NPU threat reactivity but concerns with internal consistency and temporal stability may limit the utility of corrugator in this task.
- Affective Picture Viewing task startle modulation is very heterogeneous across trials/pictures such that effects may depend on a few key pictures. Poor internal consistency for startle modulation may also limit its sensitivity to detect effects of other manipulations and the reproducibility of these other effects across studies. Unpleasant pictures appear to produce more robust modulation of both startle and corrugator that persists over study visits relative to pleasant pictures in this task. Pleasant pictures may not be useful for situations that require repeated task administration due to small/null effects for subsequent administrations and the absence of any temporal stability across measures.
- General startle reactivity possesses admirable internal consistency and temporal stability within subjects. It is well suited for experiments that require single or repeated administration.
- Quantification as raw scores (microvolt units) in the time domain generally yields superior psychometric properties than alternative approaches for both measures across affective tasks.

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