#### ABSTRACT

Title of Thesis:	DELTA AND THETA: A TIME- FREQUENCY FRAMEWORK FOR MEASURING ERPS
	Melanie Arenson, Master of Science, 2019
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Time-frequency methodologies, which allow for the examination of spatially and temporally overlapping subprocesses, have shown that delta and theta can be used to explain the majority of variance in many traditional ERP components. Furthermore, prior work suggests that traditional ERPs likely contain separable activity associated with the salience and central executive networks, which indexed by theta amplitude and theta ICPS, respectively. The present study sought to validate a core set of measures in the theta and delta bands (amplitude, ICPS and ITPS measures) using a novelty oddball task, which allowed us to assess the separability of SN and CEN activity indexed by medial-frontal theta. Our results indicated that timefrequency amplitude, ICPS and ITPS each represent separable processes, such that delta amplitude indexes task-based elaborative processes, theta indexes relevant SNrelated information, and ICPS indexes activity associated with the CEN; therefore, all can be used to more fully characterize ERP data.

# DELTA AND THETA: A TIME-FREQUENCY FRAMEWORK FOR MEASURING ERPS

by

Melanie Arenson

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Advisory Committee: Professor Edward Bernat, Chair Professor Tracy Riggins Professor Alexander Shackman © Copyright by Melanie Arenson 2019

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## List of Abbreviations

Anterior cingulate cortex (ACC)

Central-executive network (CEN)

Default mode network (DMN

Dorsolateral prefrontal cortex (dlPFC)

Electrocorticography (ECoG)

Electroencephalogram (EEG)

Event-related potential (ERP)

Expected Value of Control theory (EVC)

Intracranial EEG (iEEG)

Inter-channel phase synchrony (ICPS)

International Affective Picture Set (IAPS)

Inter-trial interval (ITI)

Inter-trial phase synchrony (ITPS)

Prefrontal cortex (PFC)

Posterior parietal cortex (PCC)

Salience network (SN)

### Chapter 1: Introduction

Time-frequency methodologies allow EEG researchers to examine spatially and temporally overlapping subprocesses, which has resulted in a sharp increase in their application to event-related potential (ERP) data over the past two decades. This work has identified a number of processes associated with specific frequency bands, leading to a greater understanding of their unique contributions. Importantly, recent work in our lab and others has shown that delta (0-3 Hz) and theta (3-7 Hz) can be used to explain the majority of variance in many traditional ERP components (Bachman & Bernat, 2018; Bernat, Nelson, & Baskin-Sommers, 2015; Harper, Malone, & Bernat, 2014), suggesting that those time-domain components may be better understood as mixture of separable activity occurring within these bands.

There is also growing interest in the measurement of functional connectivity. First identified with fMRI, two "task positive" networks are of particular importance to the cognitive processes that underlie task completion: (1) the salience network (SN), which is responsible for identifying relevant stimuli towards which to allocate attention, and (2) the central executive network (CEN), which is responsible for higher-order cognitive processes (Menon, 2011). There is strong evidence that theta amplitude is an appropriate measure of SN activity, as it has primary sources in the anterior cingulate cortex (ACC; Holroyd & Umemoto, 2016; Tsujimoto, Shimazu, & Isomura, 2006). There is also growing evidence that the ACC plays a critical role in the cost-benefit analysis of whether or not to call for effortful CEN activation (Shenhav, Botvinick, & Cohen, 2013), suggesting that SN activation may serve a dual purpose: 1) early orienting and 2) the decision to call for effortful top-down cognitive control (e.g. the CEN) and attention. However, the ability to measure the CEN in ERPs has remained more elusive until the fairly recent application of phase dynamics. Inter-channel phase synchrony (ICPS) analyses index the degree of phase alignment between two electrode sites. Recent work has demonstrated that ICPS in the theta band (3-7 Hz) can index functional connectivity between the ACC and dorsolateral prefrontal cortex (dlPFC), a key component of the CEN (Cavanagh & Frank, 2014; Menon, 2011; Sridharan, Levitin, & Menon, 2008; Watts, Tootell, Fix, Aviyente, & Bernat, 2018).

Given the above, it is possible that theta activity during ERPs may contain separable SN and CEN activity, indexed by theta amplitude and theta ICPS, respectively. However, the primary task paradigms used to elicit theta activity (e.g. gambling feedback, go/no-go, and tasks that produce an error-related negativity) generally involve increases in the SN and CEN to the same stimuli (e.g. losses, no-go trials, and errors) and thus this hypothesis has not been closely examined.

Furthermore, inter-trial phase-synchrony (ITPS), or the amount of phase alignment from trial to trial, accounts for a significant amount of the variance in amplitude and ICPS measures, and indexes activity not represented by amplitude alone (Burwell, Malone, Bernat, & Iacono, 2014; Watts et al., 2018). Greater consistency of neural responding (as measured by ITPS) is hypothesized to play an important role in coordinating actions between distant brain areas and integrating new task information into prior knowledge (Cavanagh, Cohen, & Allen, 2009; Fries, 2005). As such, ITPS can provide important information about ERP activity.

The purpose of the present study is to validate a core set of measures in the theta and delta bands for use in the novelty oddball task. This framework includes amplitude, ICPS and ITPS measures, and was recently applied to a gambling feedback task (Watts et al., 2018). The present study applies this measurement framework to a novelty oddball task to test sensitivity to multiple key processes known to underlie ERP data from oddball tasks, providing a unique opportunity to assess the separability of SN and CEN activity indexed by medial-frontal theta.

#### Section 1: Time frequency approaches to ERPs

While EEG/ERP measurement approaches have long been focused on timedomain approaches (wherein ERP 'components' are defined by amplitude peaks and troughs over time), this approach has important drawbacks. Most notably, timedomain methods are less sensitive to temporally overlapping ERP subprocesses, particularly when occurring at different frequencies (Bernat, Williams, & Gehring, 2005). Substantial work has now demonstrated that frequency-specific subcomponents are important for indexing cognitive processes using EEG (Başar, Başar-Eroglu, Karakaş, & Schürmann, 2001; Bernat, Nelson, Holroyd, Gehring, & Patrick, 2008; Clayton, Yeung, & Cohen Kadosh, 2015; Demiralp, Ademoglu, Comerchero, & Polich, 2001; Harper et al., 2014). Time-frequency approaches address this problem, as they are sensitive to neural activity simultaneously in time and frequency, and therefore can separate components that overlap in time but differ by frequency. As a result, there has been growing interest over the past two decades in using time-frequency methodologies to elucidate temporally overlapping cognitive processes that occur at different frequencies.

In general, time-frequency analyses have focused on longstanding definitions of frequency bands: alpha (8-13 Hz), beta (13-30 Hz), gamma (30-70 Hz), theta (3-7 Hz), and delta (0-3 Hz). Research into each of these bands has implicated them in different processes (Başar et al., 2001; Clayton et al., 2015). Alpha-band activity has

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been implicated in top-down processing and memory (for reviews, see Başar & Güntekin, 2012; Bazanova, 2012; Klimesch, Sauseng, & Hanslmayr, 2007). Betaband activity has been traditionally associated with sensorimotor functions, but has also recently been implicated in a number of cognitive-functions, including working memory and decision making (for review, see Spitzer & Haegens, 2017). Gammaband oscillations are thought to underlie multiple sensory and cognitive processes, and primarily represent broader whole-brain communication in response to external stimuli (Başar, 2013; Herrmann, Fründ, & Lenz, 2010). Theta and delta band activity have been studied in the context of a variety of cognitive processes. Theta-band activity has been related to early orienting, attention and cognitive control (Cavanagh & Frank, 2014; Cooper et al., 2015; Polich, 2012). Delta-band activity has been related to broader elaborative cognitive processes, reward processing, and memory (Cavanagh, 2015; Güntekin & Başar, 2016; Harmony, 2013).

Importantly, recent work in our lab has shown that theta and delta amplitude account for the majority of the variance in several common ERP components (Bachman & Bernat, 2018; Bernat et al., 2015; Harper et al., 2014). For example, Bernat and colleagues (2015) demonstrated that the time-domain feedback negativity (FN) measure is comprised of two overlapping processes: negative-polarity theta amplitude, which is sensitive to losses, and positive polarity delta amplitude, which is sensitive to gains. Similarly, Harper and colleagues (2014) demonstrated that delta and theta index separable but overlapping processes occurring during the N2 and P300 in a go/no-go task; combined, they explain the majority of variance in those components. Their results support the view that theta is sensitive to salience-related information, and is separable from delta activity, which the authors argue may reflect

motor inhibition, cognitive inhibition, and stimulus context updating (Harper et al., 2014). As such, it is critical to consider theta and delta amplitude contributions when analyzing ERP activity.

#### Section 2: Neural networks and phase synchrony

While the above-referenced work has well-indexed amplitude in ERP components (which more often reflect activity in a single brain region), high-order cognitive functions depend on both neural and regional specialization and global integration of broad brain processes; this requires researchers to view the brain as an integrated network of systems (Fingelkurts, Fingelkurts, & Kähkönen, 2005; Friston, 2011; Tononi, 2005). Investigation into these systems using fMRI has implicated three important networks: the salience network (SN), the central-executive network (CEN), and default mode network (DMN; Bressler & Menon, 2010; Seeley et al., 2007).

The SN (comprised of the ACC, the frontoinsula, and subcortical regions including the amygdala and the substantia nigra) is responsible for identifying the most relevant stimuli in the environment towards which to allocate attention (Critchley, 2005; Menon, 2011; Seeley et al., 2007). The CEN is comprised of the dorsolateral prefrontal cortex (dIPFC) and the posterior parietal cortex (PPC); it is responsible for higher-order cognitive processes such as sustained attention, working memory, and decision making (Banich et al., 2009; Koechlin & Summerfield, 2007; Menon, 2011; Seeley et al., 2007). Finally, the DMN represents tonic levels of activity and neural communication within the brain while at rest (Raichle et al., 2001). The SN and the CEN, in particular, are critical to cognitive processes associated with task completion, and are therefore considered "task positive." In

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contrast, DMN activity decreases during goal-oriented actions requiring cognitive control and is therefore considered "task negative" (Cocchi, Zalesky, Fornito, & Mattingley, 2013; Raichle et al., 2001). The present study addresses "task positive" processes, and therefore focuses on the SN and CEN.

Results from recent studies suggest that the SN is well-indexed by midfrontal theta amplitude. Using source localization techniques, researchers have found strong evidence that the ACC (a critical component of the SN) generates midfrontal theta (Asada, Fukuda, Tsunoda, Yamaguchi, & Tonoike, 1999; Foti, Weinberg, Bernat, & Proudfit, 2015; Holroyd & Umemoto, 2016; Tsujimoto et al., 2006). Furthermore, Shenhav and colleague's Expected Value of Control theory (EVC) posits that the ACC not only orients to incoming sensory information, but also is instrumental in the cost-benefit analysis associated with the decision to recruit the effortful and resource-costly CEN. This theory has been supported by recent findings that the SN plays a role in switching between the DMN and the CEN (Bressler & Menon, 2010; Sridharan et al., 2008), and that midfrontal theta amplitude is implicated in the call for cognitive control (Cavanagh & Frank, 2014). Taken together, these findings suggest that SN activation can be measured by midfrontal theta amplitude, and likely serves a dual purpose: 1) early orienting and 2) the decision to call for costly top-down control and attention.

The ability to measure the CEN in ERP-based research has historically remained more elusive. However, recent advancements in phase synchrony approaches to analyzing ERP data have begun to change that. By examining activity that is time-locked to a specific event (as ERP data is), researchers can measure phase dynamics both within and between neural networks, nodes, and populations.

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Interchannel phase synchrony (ICPS) indexes the degree of phase alignment between two electrodes, and allows researchers to measure functional connectivity during EEG tasks (Aviyente, Bernat, Evans, & Sponheim, 2011; Cohen, 2011; Cohen, Wilmes, & van de Vijver, 2011; Watts et al., 2018). In particular, multiple studies have suggested that theta-band functional connectivity between medial-frontal (cf. ACC) and lateral-frontal (cf. dlPFC) regions indexes the CEN (Aviyente, Tootell, & Bernat, 2017; Cavanagh & Frank, 2014; Watts et al., 2018). For example, trails that require greater cognitive control result in greater medial-lateral PFC theta ICPS (Aviyente, Tootell, & Bernat, 2017; Hanslmayr et al., 2007; Smith et al., 2015), suggesting that it is an appropriate methodology with which to index the CEN using ERP data.

Additionally, growing evidence requires the consideration of intertrial phase synchrony (ITPS), which measures the amount of phase alignment from trial to trial, in measuring ERP data. Recently, researchers have demonstrated that ITPS indexes important variance above and beyond amplitude alone (Burwell et al., 2014; Watts et al., 2018). Specifically, current conceptualizations of ITPS suggest that it plays an important role in integrating new task-based information into existing knowledge and coordinating activity between distant brain regions (Burwell et al., 2014; Cavanagh & Frank, 2014; Fries, 2005). This is supported by recent research demonstrating greater ITPS in response to trials that contain important learning information (Cavanagh et al., 2009; Papenberg, Hämmerer, Müller, Lindenberger, & Li, 2013; van de Vijver, Richard Ridderinkhof, & Cohen, 2011).

In sum, current evidence suggests that traditional ERPs likely contain separable activity associated with the SN and the CEN, which can be appropriately indexed by theta amplitude and theta ICPS, respectively. Furthermore, the relationship between theta amplitude and ICPS can likely be used to elucidate the dual roles of the SN. Specifically, when the SN is calling for the CEN, there should be a stronger relationship between theta amplitude and theta ICPS. If, however the SN is simply orienting to a stimulus, and does not call for the CEN, there should be less or no relationship between theta amplitude and ICPS. Unfortunately, most ERP tasks that have been used to study the SN and CEN do not contain stimuli which differentially activate the SN. Instead, those trails that activate the SN will also require cognitive control, thereby activating the CEN (e.g. conventional gambling tasks, go/no-go tasks, and tasks eliciting the ERN). As such, the present study will use a novelty oddball task, which contains target and novel stimuli that are hypothesized to differentially activate the SN and CEN, to elucidate these processes. Furthermore, examining both delta amplitude and theta ICPS allows researchers to separate taskbased elaborative processing (e.g. task-set and memory updating) and cognitive control processes associated with the CEN, as recent work suggests they can be differentiated (Harper, Malone, Bachman, & Bernat, 2016; Zink, Stock, Colzato, & Beste, 2018). Finally, ITPS measures are critical to comprehensively indexing ERP activity not well-represented by amplitude or ICPS alone.

#### Section 3: The novelty oddball task

First published about over 50 years ago, the oddball task is one of the most extensively examined EEG paradigms. The traditional oddball task is comprised of two stimuli types: a standard stimulus (which the participant is instructed to ignore), and an infrequent target stimulus (to which the participant is asked to respond). The novelty variant of this paradigm includes a third infrequent and unexpected distractor stimulus known as a novel, which the participant is instructed to ignore (Squires, Squires, & Hillyard, 1975).

Traditionally, researchers have studied the P300 by breaking it into two 'subcomponents': (1) predominantly frontocentral theta-driven early orienting elicited by novel and to a lesser extent target stimuli, and (2) predominantly centroparietal delta-driven task-based evaluative processing elicited by target stimuli (Bledowski et al., 2004; Debener, Makeig, Delorme, & Engel, 2005; Friedman, Cycowicz, & Gaeta, 2001; Kiat, 2018; Kok, 2001; Polich, 2007; Spencer, Dien, & Donchin, 1999, 2001). Furthermore, two recent studies have shown that the oddball-elicited P300 component contains separable contributions of delta and theta-band activity (Bachman & Bernat, 2018; Harper, Malone, & Iacono, 2017).

Extensive literature has also demonstrated that the P300 behaves differently depending upon the stimulus presented. For example, P300 activity decreases (habituates) over the course of repeated presentations of a stimulus, with particular effects seen in theta amplitude for novel stimuli (Bachman & Bernat, 2018; Polich, 2007, 2012; Riggins & Polich, 2002).

Less is known about phase synchrony and coherence in a novelty oddball task. While previous studies have investigated functional networks during attention and surprise or novelty processing (Clayton et al., 2015; Soltani & Knight, 2000), there has been limited investigation of functional connectivity associated with ERPs during an oddball task (Güntekin & Başar, 2010; Harper et al., 2017; Hurtado-Rincón, Restrepo, Padilla, Torres, & Castellanos-Dominguez, 2018). Furthermore, the studies that have been conducted have used wavelet approaches to time-frequency analyses, which have a non-uniform resolution and are prone to poor temporal resolution at low frequencies and poor frequency resolution at high frequencies. Only one of those studies included a novelty stimulus in the task (Harper et al., 2017). As such, additional research is needed using approaches to time-frequency analyses with greater temporal and frequency resolution in order to elucidate the role of functional connectivity in a novelty oddball task, as well as appropriate ways to measure it. Finally, no studies to our knowledge have examined the role of ITPS in the novelty oddball task.

#### Section 4: The present study

Our lab has previously proposed a measurement framework containing amplitude, ICPS and ITPS in delta and theta bands as a way to index key processes implicated in many traditional ERP components, and tested it using a gambling task (see Watts & Bernat, 2018). The present study will validate this framework in a novelty oddball task by testing its ability to index the key processes it implicates. We hold the following aims and hypotheses:

<u>Aim 1:</u> To replicate prior findings showing that delta and theta <u>amplitude</u> will have separable contributions to the P300 and index different processes.

*Hypothesis 1a:* Delta and theta amplitude will each represent unique variance in overall time domain P300 measures.

*Hypothesis 1b:* Delta amplitude will be greater for targets than for novels and novels than for standards.

*Hypothesis 1c:* Theta amplitude will be greater for novels than for targets, and for targets than for standards.

Aim 2: To differentiate the role of the SN and CEN using ICPS.

*Hypothesis 2a:* Theta ICPS will be greater for targets than for novels and for novels than for standards.

*Hypothesis 2b:* Theta ICPS and amplitude will be correlated more strongly for targets than for novels, and for novels than for standards.

<u>Aim 3:</u> To elucidate the variance in amplitude and ICPS that is explained by <u>ITPS</u>. *Hypothesis 3a:* ITPS will account for all of the variance in amplitude measures.

*Hypothesis 3b:* ITPS and ICPS will be correlated, but ICPS will explain some unique variance relative to ITPS.

<u>Aim 4:</u> To reassess conventional condition comparisons using the proposed measurement framework.

*Hypothesis 4a:* There will be greater habituation effects for theta in novels than in targets and in targets than in standards.

*Hypothesis 4b:* The relationship between theta amplitude and ICPS will vary based on the affective content of the novel images.

### Chapter 2: Methods

#### Section 1: Participants

147 undergraduate students were recruited from Florida State University. Participants were excluded if they had any visual impairment, traumatic brain injury, or neurological conditions. 11 participants were removed from analyses due to problems with their data collection (e.g. experimenter error, technical difficulties with data collection, or incorrect trigger codes), 17 due to an excessive number of EEG artifacts (>40% of the trials rejected) and 4 because there were too few (< 3) trials available for subsampling. This left a final sample of 115 participants (65 female, *M* age: 20.13 years, SD: 3.88). All participants provided informed consent and received either course credit or \$10/hr for their participation.

#### Section 2: Procedure

All data collection occurred in a dimly lit, sound-attenuated room. Stimuli were presented on a 21-inch Dell high-definition CRT color monitor, centered at a viewing distance of 100cm from the participant. We used E-Prime version 1.1 to present stimuli, and a PST Serial Response Box (Psychology Software Tools, Inc.) to collect responses to the task.

We asked participants to complete the three-stimulus variant of the 'rotatedheads' visual oddball task (Begleiter, Porjesz, Bihari, & Kissin, 1984). This task consisted of a total of 240 trials, each presented on the screen for 100 ms, with an inter-trial interval (ITI) that varied between 1000 and 2000ms. Three types of stimuli were presented: *standard, target, and novel* (see Figure 1). *Standard:* 168 trials (70%) were standard stimuli (an oval on the screen) to which participants were instructed *not* to respond.

*Target:* 36 (15%) of the trials were target stimuli, which consisted of an oval with a nose and an ear; participants were instructed to *respond via a button press* indicating which side of the head the ear was on. For half of the target trials the nose was pointed upward, representing the "easy target" trails, while for the other half of the trails the oval was rotated 180° and the nose was pointed downward, representing the "hard target" trials.

*Novel:* 36 (15%) of the trails were novel stimuli, which consisted of pleasant, unpleasant, and neutral images taken from the International Affective Picture Set (IAPS; Lang, Bradley, & Cuthbert, 2008). Participants were instructed *not* to respond to these stimuli.

Prior to the start of the task, participants completed a short practice of the target and non-target stimuli, but data was not collected. During the ITI, participants were told to fixate on a small dot in the center of the screen.

As a part of this project, participants also completed three other tasks, none of which will be analyzed for the present study. Once data collection was complete, participants were debriefed and thanked for their time.

#### Section 3: Physiological data acquisition and preprocessing

*Data acquisition:* All EEG data were recorded using a Neuroscan 128-channel Qui-Cap (sintered Ag-Ag/Cl; non-standard layout) and a 128-channel Synamps RT amplifier (Neuroscan, Inc.). Ten electrodes near the ears were not included in data analysis due to inadequate data collection across participants, leaving 113 EEG channels for analysis. Horizonal electrooculogram activity was recorded using electrodes placed on the outer canthus of both eyes, and vertical electrooculogram activity was recorded from electrodes placed below and above the left eye. All impedances were kept below 10 k $\Omega$ . EEG signals were vertex referenced during recording, and then referenced to averaged mastoid signals offline, collected using an analog 0.05 to 200 Hz bandpass filter, and digitized at 1000 Hz using Neuroscan Acquire (Neuroscan, Inc.).

*Data cleaning:* We created epochs of 3s from 1000ms pre-stimulus to 2000ms poststimulus, with a 150ms pre-stimulus baseline, which were then re-referenced to averaged mastoid sites. This data was corrected for ocular artifacts using Semlitsch and colleagues' 1986 algorithm, and down-sampled to 128 Hz using the resample function in Matlab (Mathworks, Inc.), which applied an antialiasing filter during resampling. Visual inspection of the averaged wave-forms revealed that 1% of electrodes became disconnected during recording; the value for this electrode was replaced with the average of the nearest neighbors from the dataset. We then employed two methods of data cleaning:

- (1) If activity at F3 or F4 exceeded  $\pm 100 \ \mu V$  -1000 to -1ms pre-stimulus or 1 to 2000ms post-stimulus, those trials were rejected.
- (2) If activity at an individual electrode exceeded  $\pm 100 \ \mu V$  -1000ms to -1ms prestimulus or 1ms to 2000ms post-stimulus, those within-trail individual electrodes were rejected.

This process removed 18% of trials from analysis.

*Subsampling:* Data cleaning importantly improves the quality of the data, but removes trials, leaving an uneven number of trials across comparisons and participants. As such, we employed subsampling and bootstrapping techniques to

optimize our estimation of the averaged waveform, and to equate the number of trials across outcomes. We used full waveforms as the unit on which these processes were performed (e.g. all samples within each waveform were treated together). Through subsampling, we created 50 averages for each condition from a subset of 3 randomly selected trials; all subsampling was done with replacement. These 50 averages were then bootstrapped 500 times using the Matlab bootstrap function to produce a single average per electrode per each condition, for each participant.

#### Section 4: Data Reduction

*Comparisons:* We conducted comparisons within each stimulus type. For all habituation analyses, we separated stimuli into thirds (e.g. first third of the stimulus of interest presented, second third of the stimulus of interest presented, and last third presented of the stimulus of interest presented). We separated target stimuli into "easy" (e.g. nose pointed upward) and "hard" (e.g. nose pointed downward) response types. We separated novel stimuli by valence (e.g. pleasant, neutral, and unpleasant). *Time-domain amplitude:* We defined the time-domain P300 separately for each stimulus type, as the P300 occurs at different time points depending upon the stimulus. For standards, we defined the P300 as the maximum positive deflection occurring between 328 and 468ms post-stimulus for standards, between 328 and 547ms for targets, and between 258 and 547 for novels. We selected an electrode cluster to calculate this peak amplitude based on the clusters chosen for delta and theta time-frequency amplitude (see below) to ensure all activity was represented appropriately in time domain.

*Time-frequency amplitude:* We performed time-frequency decompositions on the averaged signals, which allowed us to use the same ERP activity studied in the time-

domain. Time-frequency transforms were produced using a binomial reduced interference distribution (RID) variant of Cohen's class of time-frequency transformations on the full waveform, using 32 time bins per second and 2 frequency bins per Hz. Time-frequency regions of interest (ROIs) were then fit to the grand average time-frequency representations. These ROIs were fit separately for delta and theta in each condition, based on visual inspection of the grand average time-domain energy representation, in order to target the peak activity in each of those frequency bands. For standards, this process indicated a window from 250-344ms and 2-3.5Hz for delta and 4-5Hz for theta. For targets, it indicated a window from 281-438ms and 1-2Hz for delta and 4.5-5Hz for theta. Finally, for novels, it indicated a window from 312-406ms and 1.5-2.5Hz for delta and 3.5-4.5Hz for theta. The values associated with bins within these windows were then extracted and averaged to create variables for regression analyses. The topographic distribution for each ROI is displayed in Figure 2.

*Time frequency ICPS:* We calculated ICPS between the medial frontal and lateral frontal regions separately for standard, target, and novel trials. ICPS between these areas was calculated by computing phase synchrony based on Cohen's class of time-frequency, which is consistent with prior work (Aviyente et al., 2011, 2017). This data was then transformed using current source density and which were then used to derive phase locking values (PLVs), which source localizes activity toward the cortical surface in order to minimize volume conduction effects. The same ROI solution used in the time-frequency amplitude approach was applied to the ICPS computation. This allowed us to extract ICPS activity directly corresponding to those measures.

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*Time-frequency ITPS:* We computed average ITPS separately for standard, target, and novel trails. To do this, we took a set of trails, computed the phase differences between each trial and the average phase across trials, and then averaged those phase differences to create a PLV across trials (Aviyente et al., 2011; Watts et al., 2018). This process was iterative, using the same subsampling and bootstrapping approach previously defined, and produced a condition average ITPS surface of the same dimensions as the amplitude measures for each electrode within each participant. The same ROI solution used in the time-frequency amplitude and ICPS approach was applied to the ITPS computation, which allowed us to extract ITPS activity directly corresponding to those measures

*Electrode clusters:* For time-domain measures, we selected an electrode cluster that maximized activity in both delta and theta, based on the electrode clusters determined for time-frequency measures (see below). To avoid bias towards delta and theta, these clusters included all electrodes selected for time frequency measures, as well as the electrodes that connected them. These clusters were selected separately for each stimulus type.

For time-frequency measures, we selected electrode clusters based upon peak activity within the window of interest separately for delta and theta, and within each stimulus type. These clusters were also applied to ITPS measures.

For ICPS measures, we averaged the phase synchrony of FCZ to [88] and FCZ to [33].

#### <u>Section 5: Data Analysis</u>

We used linear regression to evaluate the contributions of delta and theta amplitude to the P300. To evaluate the effect of stimulus type on delta and theta

processing, we ran a series of repeated measures ANOVAs separately for theta amplitude, delta amplitude, theta ICPS, and theta ITPS. To test the hypothesis that midfrontal theta amplitude is a call for greater executive control, we ran correlations to assess the association between theta amplitude and theta ICPS, and then applied a z transform to compare them. To evaluate within-stimulus comparisons, we conducted repeated measures ANOVAs or t-tests as appropriate. Finally, to assess the unique contributions of each measure, we conducted a series of linear regressions with each measure as an independent variable. Residuals from those models were then extracted and statistically compared to zero. If the residuals were greater than zero, than dependent variable explained unique variance above and beyond the contributions of the independent variable. All analyses except for round-robin regressions were conducted in the statistical package R. Round robin regressions were conducted in the statistical packages SPSS.

#### **Design** Considerations

There are several design attributes that made this task appropriate for the questions posed. Although the oddball paradigm has been extensively studied, limited prior research has investigated it from a time-frequency perspective, and particularly little has explored the contribution of delta amplitude, theta ICPS, and ITPS to the cognitive processes it implicates.

Additionally, the oddball paradigm can vary by stimulus presentation (auditory or visual), the number of stimuli type (typically two-stimulus, which *does not* include novels, or three-stimulus, which *does* include novels), and the type of novel stimuli. However, the variant used in the current project (the three-stimulus variant of the 'rotated-heads' visual oddball task; Begleiter et al., 1984), is

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particularly useful in testing the hypothesized measurement framework. Specifically, it includes multiple types of stimuli that are thought to differentially activate the processes we are measuring. Furthermore, it can be used to separate the two purposes of the SN. We are therefore uniquely able to examine the hypothesized differential contributions of delta amplitude, theta amplitude, theta ICPS, and theta ITPS to processing novel, target, and standard stimuli.

## Chapter 3: Results

#### <u>Section 1: Behavioral data</u>

For targets, the mean reaction time to a stimulus was 1079.6ms (sd 358.02ms). On average, participants were 92% accurate (median 97%, sd 15.63%).

#### Section 2: Delta and theta amplitude contributions to the P300

Standards: In simple regression, delta and theta amplitude each significantly predicted time domain P300 ( $\beta$ =0.11, r<sup>2</sup>=.57, p<.001 and  $\beta$ =0.16, r<sup>2</sup>=.18, p<.001, respectively). Furthermore, both delta and theta amplitude significantly predicted time domain P300 in a multiple regression ( $\beta$ =0.10, p<.001 and  $\beta$ =0.08, p<.001, respectively, R<sup>2</sup>=.62).

*Targets:* In simple regression, delta amplitude significantly predicted time domain P300, but theta amplitude did not ( $\beta$ =0.06, r<sup>2</sup>=.72, p<.001 and  $\beta$ =0.6, r<sup>2</sup>=.02, p=.09, respectively). Similarly, in a multiple regression, delta amplitude significantly predicted time domain P300, but theta amplitude did not. ( $\beta$ =0.06, p<.001 and  $\beta$ =0.04, p=.06, respectively, R<sup>2</sup>=.72).

*Novels:* In simple regression, delta and theta amplitude each significantly predicted time domain P300 ( $\beta$ =0.07, r<sup>2</sup>=.49, p<.001 and  $\beta$ =0.06, r<sup>2</sup>=.38, p<.001, respectively). Similarly, in a multiple regression, both delta and theta amplitude predicted time domain P300 ( $\beta$ =0.05, p<.001 and  $\beta$ =0.03, p<.001, respectively, R<sup>2</sup>=.57).

Standard Habituation: In simple regression, delta and theta amplitude each significantly predicted time domain P300 ( $\beta$ =0.11, r<sup>2</sup>=.54, p<.001 and  $\beta$ =0.13, r<sup>2</sup>=.14, p<.001, respectively). Similarly, in a multiple regression, both delta and theta

amplitude significantly predicted time domain P300 ( $\beta$ =0.10, p<.001 and  $\beta$ =0.06, p<.001, respectively, R<sup>2</sup>=.58).

*Target Habituation:* In simple regression, delta and theta amplitude each significantly predicted time domain P300 ( $\beta$ =0.05, r<sup>2</sup>=.54, p<.001 and  $\beta$ =0.08, r<sup>2</sup>=.14, p<.001, respectively). Similarly, in a multiple regression, both delta and theta amplitude significantly predicted time domain P300 ( $\beta$ =0.05, p<.001 and  $\beta$ =0.06, p<.001, respectively, R<sup>2</sup>=.61).

*Novel Habituation:* In simple regression, delta and theta amplitude each significantly predicted time domain P300 ( $\beta$ =0.06, r<sup>2</sup>=.53, p<.001 and  $\beta$ =0.05, r<sup>2</sup>=.34, p<.001, respectively). Similarly, in a multiple regression, both delta and theta amplitude significantly predicted time domain P300 ( $\beta$ =0.05, p<.001 and  $\beta$ =0.03, p<.001, respectively, R<sup>2</sup>=.52).

*Pleasant novel pictures:* In simple regressions, delta and theta amplitude each significantly predicted time domain P300 for pleasant pictures ( $\beta$ =0.07, r<sup>2</sup>=.54, p<.001 and  $\beta$ =0.07, r<sup>2</sup>=.42, p<.001, respectively). Furthermore, both delta and theta amplitude significantly predicted time domain P300 for pleasant pictures in a multiple regression ( $\beta$ =0.05, p<.001 and  $\beta$ =0.03, p<.001, respectively, multiple R<sup>2</sup>=.61).

Unpleasant novel pictures: In simple regressions, delta and theta amplitude each significantly predicted time domain P300 for unpleasant pictures ( $\beta$ =0.07, r<sup>2</sup>=.53, p<.001 and  $\beta$ =0.06, r<sup>2</sup>=.34, p<.001, respectively). Furthermore, both delta and theta amplitude significantly predicted time domain P300 for unpleasant pictures in a multiple regression ( $\beta$ =0.06, p<.001 and  $\beta$ =0.03, p<.001, respectively, multiple R<sup>2</sup>=.61). *Neutral novel pictures:* In simple regressions, delta and theta amplitude each significantly predicted time domain P300 for neutral pictures ( $\beta$ =0.07, r<sup>2</sup>=.36, p<.001 and  $\beta$ =0.05, r<sup>2</sup>=.32, p<.001, respectively). Furthermore, both delta and theta amplitude significantly predicted time domain P300 for neutral pictures in a multiple regression ( $\beta$ =0.05, p<.001 and  $\beta$ =0.03, p<.001, respectively, multiple R<sup>2</sup>=.44).

#### Section 3: Condition effects of delta and theta amplitude

*Stimulus type effects: Figure 3a* displays the results for delta amplitude across stimulus type. A repeated measure 3x2 ANOVA revealed a significant main effect of condition (f(2,113)=100.21, p<.001) on delta amplitude. Post-hoc tests using a Bonferroni correction revealed that delta amplitude was significantly larger for targets (m=134.28) than for novels (m=109.42, p<.001), and both were significantly greater than standards (m=28.83, p<.01, each).

*Figure 3b* displays the results for theta amplitude across standard, targets, and novels. A repeated measure 3x2 ANOVA revealed a significant main effect of condition (f(2,113)=129.55, p<.001) on theta amplitude. Post-hoc tests using a Bonferroni correction revealed that theta amplitude was significantly greater for novels (m=93.08) than for targets (m=16.26, p<.001), and for targets than for standards (m=5.52, p<.001).

*Habituation effects: Figure 4a* displays the results for delta amplitude standard presentation. A repeated measure 3x2 ANOVA revealed a significant main effect of presentation time (F(2,113)=70.14, p<.001) on delta amplitude for standards. Posthoc tests using a Bonferroni correction revealed that delta amplitude was significantly greater for the 1<sup>st</sup> third of standard stimuli (M=43.76) than the 2<sup>nd</sup> (M=24.42; p<.001) 3<sup>rd</sup> (M=18.02, p<.001) third of standard stimuli (M=3.41, p<.001). Delta amplitude

was also significantly greater for the  $2^{nd}$  third of standard stimuli than the  $3^{rd}$  third of standard stimuli (p=.001, see *Figure 6a*).

*Figure 4b* displays the results for theta amplitude across standard presentation. A repeated measure 3x2 ANOVA revealed a significant main effect of presentation time (F(2,113)=9.20, p=.03) on theta amplitude for standards. Post-hoc tests using a Bonferroni correction revealed that theta amplitude was not significantly greater for the 1<sup>st</sup> third of standard stimuli (M=7.83) than the 2<sup>nd</sup> third of standard stimuli (M=5.16; p=.053), but the 1<sup>st</sup> third was significantly greater than the 3<sup>rd</sup> third of standard stimuli (M=3.41, p<.001). Theta amplitude was also significantly greater for the 2<sup>nd</sup> third of standard stimuli than the 3<sup>rd</sup> third of standard stimuli (p=.023).

*Figure 4c* displays the results for delta amplitude across target presentation. A repeated measure 3x2 ANOVA revealed no significant main effect of presentation time (F(2,113)=2.26, p=.106) on delta amplitude for targets. Post-hoc tests were therefor not conducted.

*Figure 4d* displays the results for theta amplitude across target presentation. A repeated measure 3x2 ANOVA revealed a significant main effect of presentation time (F(2,113)=5.84, p=.003) on theta amplitude for targets. Post-hoc tests using a Bonferroni correction revealed that theta amplitude was not significantly different between the 1<sup>st</sup> third of target stimuli (M=14.84) than the 2<sup>nd</sup> third of target stimuli (M=18.97; p=.20), but it was significantly smaller for the 1<sup>st</sup> third of target stimuli than the 3<sup>rd</sup> third of target stimuli (M=23.52, p<.001). Theta amplitude was not significantly different for the 2<sup>nd</sup> third of target to the 3<sup>rd</sup> third of target stimuli (M=23.52, p<.001). Theta amplitude was not significantly different for the 2<sup>nd</sup> third of target stimuli as compared to the 3<sup>rd</sup> third of target stimuli (p=.216).

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*Figure 4e* displays the results for delta amplitude across novel presentation. A repeated measure 3x2 ANOVA revealed a significant main effect of presentation time (F(2,113)=3.15, p=.04) on delta amplitude for novels. However, post-hoc tests using a Bonferroni correction revealed no significant differences between the 1<sup>st</sup> (M=116.85), 2<sup>nd</sup> (M=110.58) and 3<sup>rd</sup> (M=101.93) third of novel presentations (p>.05 for all comparisons).

*Figure 4f* displays the results for delta amplitude across novel presentation A repeated measure 3x2 ANOVA revealed a significant main effect of presentation time (F(2,113)=20.71, p=.03) on theta amplitude for novels. Post-hoc tests using a Bonferroni correction revealed that theta amplitude was significantly greater for the 1<sup>st</sup> third of novel stimuli (M=120.71) than the 2<sup>nd</sup> (M=83.09; p<.001) and 3<sup>rd</sup> (M=79.08, p<.001) third of novel stimuli, but 2<sup>nd</sup> and 3<sup>rd</sup> third of novel stimuli did not differ from each other (p=1).

*Novel picture type effects: Figure 5a* displays delta habituation effects across condition type. A repeated measure 3x2 ANOVA revealed a significant main effect of condition (F(2,113)=4.25, p=.015) on delta amplitude habituation. Post-hoc tests using a Bonferroni correction revealed that delta amplitude habituation effects were significantly greater for standards (M=20.80) than for targets (M=0.73, p=.014), but did not differ between standards and novels (M=14.93, p=.38) nor novels and targets (p=.46).

*Figure 5b* displays theta habituation effects across condition type. A repeated measure 3x2 ANOVA revealed a significant main effect of condition (F(2,113)=28.79, p<.001) on theta amplitude habituation. Post-hoc tests using a Bonferroni correction revealed that theta amplitude habituation effects were

significantly greater for novels (M=41.62) than for standards (M=4.42; p<.001), and for standards than for targets (M=-9.67; p<.001).

*Figure 6a* displays delta effects across novel picture type. A repeated measure 3x2 ANOVA revealed a significant main effect of picture type (F(2,113)=3.14, p=.045) on delta amplitude for novels. However, post-hoc tests using a Bonferroni correction revealed no significant differences in delta amplitude between pleasant (M=116.17), unpleasant (M=110.66), or neutral (M=100.77) pictures (p>.05 for all comparisons).

*Figure 6b* displays theta effects across novel picture type. A repeated measure 3x2 ANOVA revealed no significant main effect of picture type (F(2,113)=.83, p=.43) on theta amplitude for novels. As such, no post-hoc tests were conducted.

#### Section 4: Condition effects of theta ICPS:

*Stimulus type effects: Figure* 7 displays the results for theta ICPS across standard, target, and novel stimuli. A repeated measure 3x2 ANOVA revealed a significant main effect of condition (F(2,113) = 6995.09, p<.001) on theta ICPS. Posthoc tests using a Bonferroni correction revealed that theta ICPS was significantly greater for novels (M=.856) than for targets (M=.545; p<.001) or for standards (M=.539), and for targets than for standards (p=.005).

*Novel picture type effects: Figure 8* displays the results for theta ICPS across novel picture type. A repeated measure 3x2 ANOVA revealed no significant main effect of picture type (F(2,113)=0.18, p=.84) on theta ICPS for novels. As such, no post-hoc tests were conducted.

#### Section 5: Condition effects of theta ITPS

*Stimulus type effects: Figure 9* displays the results for theta ITPS across standard, target, and novel stimuli. A repeated measure 3x2 ANOVA revealed a significant main effect of condition (F(2,113) = 95.37, p<.001) on theta ITPS. Posthoc tests using a Bonferroni correction revealed that theta ITPS was significantly greater for novels (M=.61) than for targets (M=.56; p<.001) or for standards (M=.55, p<.001), and for targets than for standards (p<.001).

*Novel picture type effects: Figure 10* displays the results for theta ITPS across novel picture type. A repeated measure 3x2 ANOVA revealed no significant main effect of picture type (F(2,113)=9.81, p=.38) on theta ITPS for novels. As such, no post-hoc tests were conducted.

#### Section 6: Condition differences in correlations between theta amplitude and ICPS

*Stimulus type effects:* Pearson's correlations revealed that theta amplitude and ICPS were significantly correlated for targets (r=.27, p=.003) and for novels (r=.36, p<.001), but not for standards (r=.11, p=.23). Theta amplitude and ICPS were significantly more correlated for novels than for standards (z=2.06, p=.039), but were not significantly more correlated for novels than for targets (z=0.9, p=.42) or for targets than for standards (z=1.24, p=.21).

*Novel picture type effects:* Pearson's correlations revealed that theta amplitude and ICPS were significantly correlated for pleasant (r=.30, p<.001), unpleasant (r=.41, p=.001) and neutral (r=.32, p=.007) images. However, theta amplitude and ICPS were not significantly more correlated for one image type over another (Pleasant/Unpleasant z=.91, p=.36; Pleasant/Neutral Fisher's z=-.18, p=.86; Unpleasant/Neutral Fisher's z=-1.78, p=.44). *Unique contributions of amplitude, ICPS, and ITPS:* For standards, theta amplitude did not explain significant variance above theta ICPS (t(113)=-0.02, p=.984) nor ITPS (t(113)=-0.11, p=.914). However, theta ICPS and ITPS both explained unique variance above theta amplitude (t(113)=16.89, p<.001 and t(113)=16.88, p<.001, respectively). Neither theta ICPS nor ITPS explained unique variance over one another (t(113)=0.207, p=.84 and t(113)=0.11, p=.915, respectively).

For targets, theta amplitude did not explain significant variance above theta ICPS nor ITPS (t(113)=-0.09, p=.931; t(113)=-0.26, p=.796, respectively). However, theta ICPS and ITPS both explained unique variance above theta amplitude (t(113)=10.38, p<.001 and t(113)=10.36, p<.001, respectively). Neither theta ICPS nor ITPS explained unique variance over one another (t(113)=0.46, p=.647 and t(113)=0.18, p=.859, respectively).

For novels, theta amplitude did not explain significant variance above theta ICPS nor ITPS (t(113)=-0.15, p=.881; t(113)=-0.61, p=.541, respectively). However, theta ICPS and ITPS both explained unique variance above theta amplitude (t(113)=8.77, p<.001 and t(113)=8.73, p<.001, respectively). Neither theta ICPS nor ITPS explained unique variance over one another (t(113)=0.78, p=.436 and t(113)=0.02, p=.985, respectively).

### Chapter 4: Discussion

The results described above provide support for the idea that the proposed framework indexes relevant activity in the oddball task. Specifically, delta and theta amplitude both contribute significant, separable variance to traditional time domain measures of the P300, consistent with the idea that delta indexes task-based elaborative processing and theta indexes salience-related information. Similarly, ICPS activity was consistent with CEN-related activity, and both it and ITPS contributed unique variance above amplitude measures. The most surprising result was that ICPS was greater for novels than for targets, however, consistent with hypotheses, both were greater than standards. As a post hoc interpretation, it is possible that greater regulatory processing was engaged during the novels, because greater cognitive control was engaged to appropriately ignore the novel stimuli and concentrate on the oddball task itself. These interpretations are explored in detail below.

#### Section 1: The role of delta and theta amplitude

Our hypotheses for this aim were partially supported: delta and theta amplitude each contributed unique variance to time domain measures of the P300 for standards and for novels, but not for targets. Specifically, delta and theta amplitude combined accounted for 62% and 57% of the variance in the P300 for standards and novels, respectively. Furthermore, they each contributed unique variance to most habituation time domain measures in those conditions (with the exception of the final third of standards), as well as to all types of affective pictures. These findings suggest that delta and theta each uniquely contribute to and together account for the majority of variance in the P300 time domain response to standard and target stimuli. This

supports and expands prior findings, providing additional evidence to suggest that time frequency approaches to EEG measurement are able to index multiple unique ongoing processes that may overlap in time but not in frequency (Bernat et al., 2015; Harper et al., 2014).

Within targets overall, only delta contributed unique variance to the P300, accounting for 72% of its variance. However, when looking at habituation effects, delta and theta each significantly contributed to the P300 difference scores between the first and last third of presentations, together accounting for 61% of its variance. As such, it would appear that delta and theta are each indexing important aspects of overall time-domain P300 habituation effects, but delta may be relatively more indicative of overall target processing, and theta may be more sensitive to habituation effects. This interpretation matches prior findings in our lab (Bachman & Bernat, 2018) and reflects the theory that delta represents elaborative processing associated with processes such as task updating (Harper et al., 2014). This idea is even further supported by the fact that targets had significantly greater delta amplitude than either novels or standards.

#### Section 2: The role of the SN and the CEN

Our hypotheses were only partially supported for these aims: theta ICPS was greater for novels than for targets and for targets than for standards. Furthermore, while theta ICPS and amplitude were significantly more correlated for novels than for standards, there were no other significant differences in the strength of the correlation across stimulus types. These effects are explored below.

We found that theta ICPS was greater for novels than for targets and for targets than for standards. This is contrary to our hypothesized pattern, from which we expected greater ICPS for targets than for novels. We see two potential post-hoc explanations for this unexpected finding: (1) it is possible that theta ICPS does not index the CEN; however, substantial recent work supports the idea that it does (see Watts et al., 2018; Cavanagh & Frank, 2014). We therefore believe it is more likely that (2) novels in this task required a greater amount of cognitive control than other stimuli.

Specifically, it may be that novel pictures require substantial effortful control, as they are unexpected (and therefore attention-grabbing) and comprised of some emotionally valanced and highly salient pictures (e.g. threat, mutilation, and erotica). Specifically, it is possible that participants need to use emotion regulation, or "activation of a goal to influence the emotion trajectory" (Gross, 2015, p. 5), in order to appropriately complete the required task. Broadly, emotion regulation processes related to our stimuli would require attention (noticing the picture), appraisal (determining the importance picture), and response (modulation of the emotional response). Some of these processes, specifically appraisal and response, may be accurately measured by ICPS, as current evidence suggests that are modulated by activity in brain areas such as the ACC and dlPFC (Etkin, Büchel, & Gross, 2015; Zilverstand, Parvaz, & Goldstein, 2017). Taken together, these findings support the idea that effortful control is necessary in the context of emotion regulation, and support the theory that greater ICPS in reaction to novel pictures may reflect an increased need for emotion regulation (e.g. CEN engagement) in order to complete the oddball task (e.g. respond to targets). Furthermore, they findings support the conclusion that midfrontal theta amplitude accurately indexes salience-related

information (Cooper et al., 2015; Foti et al., 2015; Harper et al., 2014), and is likely a reliable measure of the SN.

We therefore looked to fluctuations of ICPS in response to different pictures. Surprisingly, we found no differences in levels of ICPS between affective picture types. As such, it is possible that novels require cognitive regulation in response to distracting stimuli. If this is the case, we would not expect to see differences in ICPS in relation to different picture types. Future research is needed to test this potential explanation.

Finally, we looked at correlations between theta amplitude and ICPS to elucidate the relationship between the SN and the CEN. Theta amplitude and ICPS were correlated a small to moderate amount across stimulus type and affective picture content. Furthermore, this correlation was significantly stronger for novels compared to standards. While no other differences were found in the strength of the correlation among stimuli type, there were substantial effects of condition on both theta amplitude and ICPS. Furthermore, the pattern of correlation, even when not significant, followed the expected pattern of greater correlations for stimuli requiring greater ICPS (e.g. theta amplitude and ICPS were more correlated for novels than for targets and for targets than for standards). Interestingly, there was no difference in the strength of the correlation between affective picture types.

Importantly, because displayed the greatest (rather than the hypothesized least) amount of CEN-related activity, we were unable to differentiate the proposed dual role of the SN. Specifically, we expected that novels would require early orienting/attention, but *not* a call for the CEN. As such, we were not able to test this

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hypothesis, and additional research using less emotionally salient and distracting novel stimuli (e.g. a blue square as a novel, rather than IAPS pictures) is needed.

### Section 3: Relative contributions of amplitude, ICPS, and ITPS

As hypothesized, theta ICPS and ITPS explained unique variance above theta amplitude for all stimuli types. However, neither ICPS nor ITPS explained unique variance over one another. These findings match prior findings in our lab (Tootell & Bernat, n.d.), and support the argument that ICPS and ITPS index meaningful variance in an EEG signal, above traditional measurement methods.

### Section 4: Conventional comparisons and the measurement framework

As hypothesized, there were greater theta habituation effects in novels than in targets or standards, while targets and standard did not significantly differ from one another. Contrary to our hypotheses, the relationship between theta amplitude and ICPS did not vary based on the affective content of the novel images. These findings and their interpretation are discussed in detail above; briefly, the habituation effects suggest that processing in this oddball task mirror prior findings, and that novel stimuli habituate to a greater extent than targets or standards. While the finding regarding affective picture content was surprising, the correlations were not uniform, suggesting some variability in SN-CEN processing across picture type. Further investigation of this phenomena is warranted.

### Section 5: Limitations

This study has several important limitations. First, it was conducted on an undergraduate population, all of whom attended the same institution in the Southeastern United States. As such, these results may not be reflective of the general population. Second, the ROI approach we employed can be somewhat rigid, and not optimally characterize the underlying data. However, alternative approaches (for example, PCA) were not reliable representations of the data when conditions were combined, as they were heavily influenced by novel stimuli. As such, all efforts were made to optimally fit the ROIs, by relying upon the information provided by the grand average time-domain energy representations. Finally, there were very few presentations of novel stimuli (only 8 in each category), reducing the number of trials from which to create the averages we used in subsequent analyses. As such, outlier values would have a greater impact on those averages. Future studies should be conducted using a similar task with a greater number of trials.

### Section 6: Conclusions

Overall, these results support the idea that time-frequency amplitude, ICPS and ITPS each represent separable information and processes, enhancing the accurate measurement of traditional ERP components. In particular, each of these components index specific processes that underlie a traditional ERP signal (e.g. delta amplitude indexes task-based elaborative processes, theta indexes relevant SN-related information, and ICPS indexes the CEN); therefore, all are important in order to more fully characterize ERP data. While some of the results in this paradigm were unexpected, this framework remains intact, and requires further research to validate is applicability across EEG tasks.

# Figures

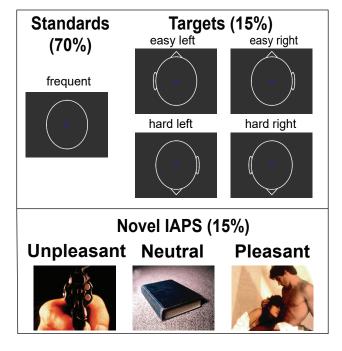
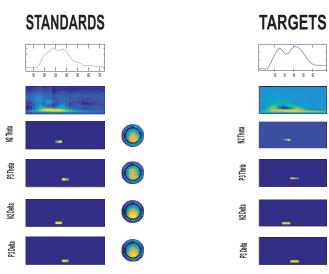
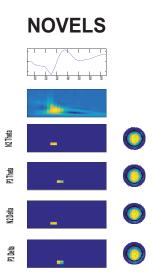


Figure 1: Sample standard, target, and novel stimuli

Figure 2: Topographic maps for ROIs





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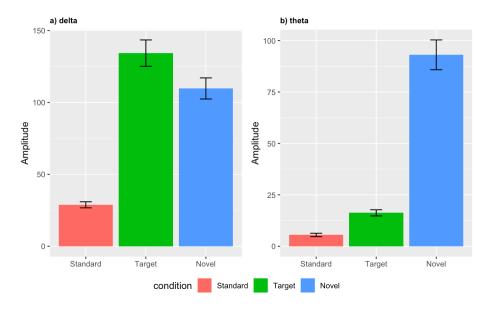
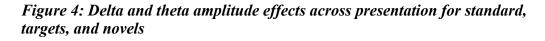


Figure 3: Delta and theta amplitude effects by stimulus type



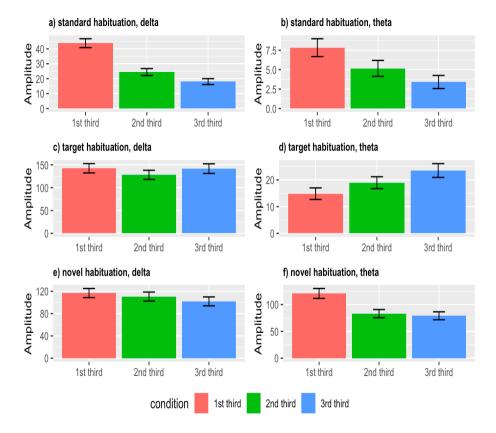


Figure 5: Delta and theta amplitude habituation effects

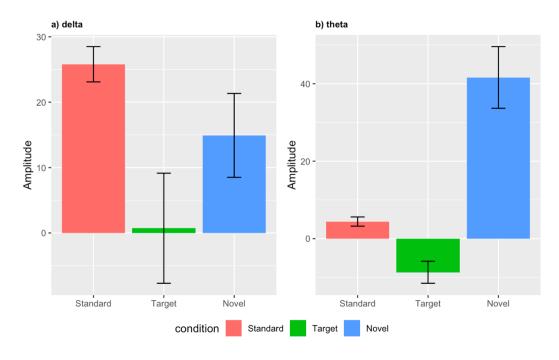


Figure 6: Delta and theta amplitude effects by affective picture type

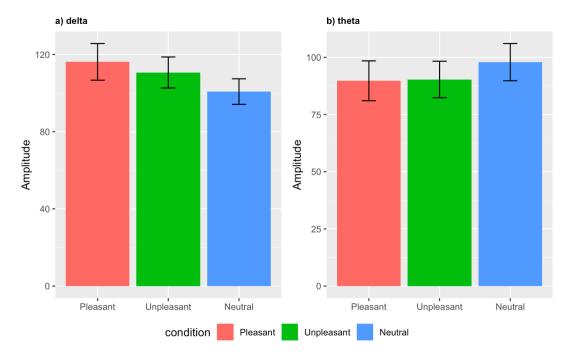


Figure 7: Theta ICPS by stimulus type

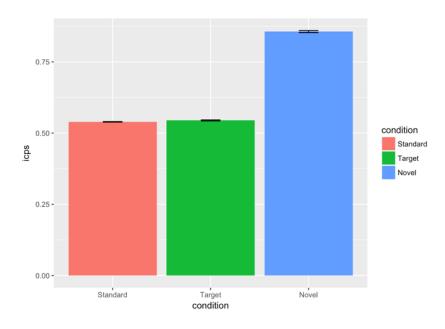


Figure 8: Theta ICPS by affective picture type

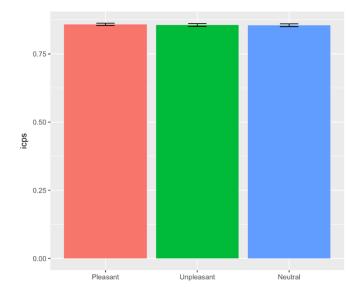


Figure 9: Theta ITPS by stimulus type

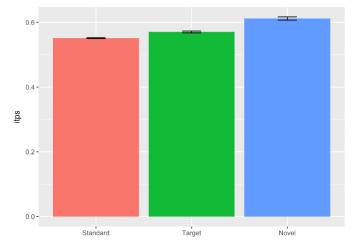
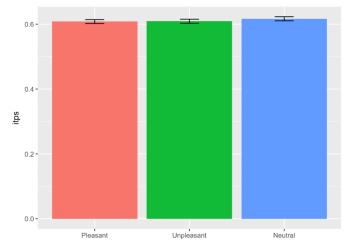


Figure 10: Theta ITPS by affective picture type



## Appendices

#### **Appendix A: Evidence from Intracranial Recordings**

Much of the support for the proposed measurement framework has relied upon findings using scalp-reported EEG and functional imaging techniques. However, it should be noted that these findings are supported by those relying upon intracranial techniques such as electrocorticography (ECoG; recorded from the cortex) and intracranial EEG (iEEG, recorded using depth electrodes) as well. Specifically, these studies suggest multiple overlapping processes during the oddball task (Citherlet et al., 2019; Kam et al., 2018). For example, Citherlet and colleagues (2019) showed that target stimuli were processed in the anterior insula only some of the time (approximately 1/3), and that novels frequently elicited greater P300 amplitude, supporting the idea that anterior insula may be involved in salience, attention, and task-relevant processing. This reflects the idea that the ACC is involved in *both* salience and control processing, such that it responds to salient information and is instrumental in the decision to call (or not) for effortful control. Recent work with depth electrodes also suggests that oddball task targets multiple processes, as evidenced by variability in activity both temporally and spatial in response to different types of stimuli (El Karoui et al., 2015; Kam et al., 2018; Wang, 2005). While these studies are limited by low sample sized and are restricted exclusively to patients with pre-existing medical conditions, their results consistently support those proposed and tested by this study.

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