

**Neural Correlates of Cognitive Inflexibility and Associations with Childhood Irritability**

A Dissertation Presented

By

**Ellen M. Kessel**

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in

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**Stony Brook University**  
The Graduate School

**Ellen M. Kessel**

We, the dissertation committee for the above candidate for the  
Doctor of Philosophy degree, hereby recommend  
acceptance of this dissertation.

**Daniel N. Klein, Ph.D. – Dissertation Advisor**  
**Distinguished Professor**  
**Department of Psychology**

**Kristin Bernard, Ph.D. - Chairperson of Defense**  
**Associate Professor**  
**Department of Psychology**

**Hoi-Chung Leung, Ph.D.**  
**Professor, Department of Psychology**

**Gabrielle A. Carlson, M.D.**  
**Professor**  
**Department of Psychiatry**

This dissertation is accepted by the Graduate School

Eric Wertheimer  
Dean of the Graduate School

Abstract of the Dissertation

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Irritability is the most common reason that children are referred for mental health services. However, irritability specific treatments are lacking, in part because little is known about its pathophysiology. An emerging literature suggests that impairments in cognitive flexibility may be a core mechanism underlying irritability. However, the precise mechanisms that mediate the cognitive rigidity in irritable youth have yet to be identified. The first goal of the current study was to modify and validate a novel, developmentally appropriate, version of the Wisconsin Card Sorting Task (WCST)—PokéSort— to elicit event-related potentials (ERPs)— the switch positivity (SwP), reward positivity (RewP) and the P3b— neural indices of set-shifting, reinforcement learning (RL) and working memory (WM), respectively. The second goal was to examine the associations between these neural indices and irritability in a sample of (N=58) children from Long Island, New York. Electroencephalography (EEG) was recorded while children performed the PokéSort task. Children also completed behavioral measures of set-shifting and WM and self-report questionnaires about their irritability. Parents completed

questionnaires about their children's irritability and sensitivity to reward and punishment. There were moderate correlations between the SwP, RewP and P3b and their corresponding but not noncorresponding behavioral or questionnaire measures tapping the same construct, suggesting that these ERPs are valid indicators of set-shifting, working memory and RL. Irritability was associated with poorer performance on PokéSort and with a blunted or less enhanced SwP. Results suggest that cognitive inflexibility associated with irritability is specifically associated with neural perturbations in set-shifting. These findings also point to the utility of using ERPs in conjunction with the PokéSort task to elucidate the neurocognitive processes that mediate cognitive rigidity in childhood irritability and other forms of psychopathology.

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## Introduction

Psychiatric disorders are the leading disease burden in youth and are associated with significant impairment that persists into adulthood (Copeland et al., 2014). Childhood irritability is a substantial part of this public health concern as it predicts adverse health outcomes, continued emotional distress, financial strain, social isolation, and suicide in adolescence and adulthood (Brotman et al., 2006; Copeland, Shanahan, Egger, Angold & Costello, 2014). Moreover, irritability is the primary reason that children are referred to mental health services (Stringaris & Taylor, 2015). Unfortunately, existing treatments have limited efficacy, and may induce severe adverse health effects (e.g., antipsychotic medications and cardiometabolic problems). A better understanding of the pathophysiology of irritability may lead to more effective treatment and prevent long-term impairment.

Irritability is a tendency toward negative affective states characterized by anger and temper outbursts (Leibenluft & Stoddard, 2013; Snaith & Taylor, 1985; Stringaris & Taylor, 2015). Consistent with the cross-cutting emphasis of the RDoC (Insel et al., 2010, Garvey, Avenevoli & Anderson, 2010), irritability, in severe and dysregulated forms, is a defining symptom of at least 10 disorders (e.g., major depressive disorder [MDD] in youth, disruptive mood dysregulation disorder [DMDD], generalized anxiety disorder [GAD], posttraumatic stress disorder, and oppositional defiant disorder [ODD]) (American Psychiatric Association, 2013). Irritability is also a heritable trait (Roberson-Nay, et al., 2015) that is common in community samples of youth (Copeland, Angold & Costello, 2013). Even at relatively low levels (Copeland, Brotman & Costello, 2015; Wakschlag et al., 2015), irritability is a non-specific marker of risk and predicts the development of common forms of psychopathology that span both the internalizing and externalizing spectrums (Dougherty et al., 2013; 2015; Waskchlag et al., 2015).

Despite its prevalence and public health importance, irritability is under-studied. Identifying core underlying mechanisms of irritability is crucial for both enhancing our understanding of shared and unique etiological mechanisms among childhood psychopathologies and for identifying targets for novel intervention/prevention (Garvey, Avenevoli & Anderson, 2015).

### **Irritability and Cognitive Flexibility**

Clinically, it is common for irritable individuals to have difficulty and become frustrated when needing to switch from one activity to another. An emerging literature suggests that impairments in cognitive flexibility, or the ability to appropriately adjust one's behavior to a changing environment, may be a core mechanism underlying irritability (Adleman et al., 2011; Dickstein et al., 2007; Stringaris & Taylor, 2015; Wakschlag et al., 2014). Most of this research has focused on severe mood dysregulation (SMD), a condition characterized by severe, persistent irritability in conjunction with hyperarousal symptoms that are also evident in attention deficit hyperactivity disorder (ADHD; e.g. distractibility and hyperactivity) and has examined performance on response reversal tasks (Adleman et al., 2011; Dickstein et al., 2007). In these tasks, two stimuli, A and B, are presented. Through trial and error, participants learn that selecting A but not B results in a reward. Without warning, the stimulus-reinforcement (S-R) relationship reverses, such that B but not A is the choice that produces a reward. Compared to controls, irritable youth make more errors on response reversal paradigms (Adleman et al., 2011; Dickstein et al., 2007). Reinforcement learning (RL) theory (Sutton and Barto, 1998) suggests that cognitive flexibility and adaptive learning is driven by reward prediction error (RPE) signals that are encoded by dopaminergic midbrain neurons (Schultz, 2002). These signals reflect expectation violations, in that a positive RPE will be elicited either through a phasic increase or decrease in dopaminergic firing when events are better or worse than expected, respectively.

This signal is then used to learn associations between rewards and task events. Thus, it has been posited that the link between irritability and cognitive flexibility may be due to an inability to learn from shifting reward-contingencies (Leibenluft & Stoddard, 2013; Stringaris & Taylor, 2015).

However, cognitive flexibility is impacted by a complex interplay of factors (Armbruster, Ueltzhöffer, Basten & Fiebach, 2012; Scott, 1962). A cascade of rapid, overlapping cognitive processes are required to successfully shift from one mode of processing to another to respond to the demands of a new situation. In addition to processing reinforcement signals, maintaining multiple rule representations in memory, inhibiting previously learned responses, and executing new responses are also necessary (Dajani & Uddin, 2015). Thus, reinforcement learning (RL) (Nilsson, Alsiö, Somerville & Clifton, 2015; Hauser, Iannaccone, Walitza, Brandeis & Brem, 2015; Ragozzino, 2007), working memory (WM) (Blackwell, Cepeda, & Munakata, 2009; Chevalier et al., 2012; Dick, 2014), and set-shifting (Crone, Wendelken, Donohue & Bunge, 2006, Hsieh & Wu, 2011; Manzi, Nessler, Czernochowski & Friedman, 2011; Mayr & Kliegl, 2003) all play important roles in promoting cognitive flexibility and may independently or collectively contribute to deficits in this area. Behavioral measures represent the cumulative endpoint of these processes, but do not offer insight into the temporal evolution of the processes leading up to the behavior. Neural measures, on the other hand, may provide greater precision and power in parsing these processes.

### **Neuroimaging Studies of Cognitive Flexibility**

Using metanalytic evidence from neuroimaging studies in adults, researchers have identified a distributed network of frontoparietal regions involved in cognitive flexibility. This network includes the inferior frontal junction (IFJ), ventrolateral prefrontal cortex (VL-PFC),

dorsolateral prefrontal cortex (DL-PFC), anterior cingulate, occipital cortex and subcortical structures including the caudate and the thalamus (Kim et al, 2012; Niendam et al, 2012). Dajani and Uddin (2015) theorize that cognitive flexibility emerges from the interplay of specific nodes in this network that support cognitive processes that are nonspecific to cognitive flexibility and are activated across a range of other EFs. For example, researchers postulate that DL-PFC activation during cognitive flexibility tasks support WM and the maintenance of task representations, whereas IFJ activation observed during cognitive flexibility tasks may be the site of response set updating of task rules, or the site of inhibition of the previous response set. However, the precise cognitive processes that activation in these regions support remains unknown. Dajani and Uddin (2015) speculate that temporal dynamics or internode connectivity may be important to distinguish brain activity between the various EFs underpinning cognitive flexibility.

Findings from neuroimaging studies of cognitive flexibility in adults also extend to children and adolescents, such that preschool- and school-aged children and adolescents show DL-PFC activation while shifting mental sets (Moriguchi and Hiraki, 2009; Morton et al., 2009; Wood et al., 2009). Cognitive flexibility is for the most part mature by age ten (Dick, 2014) and the age-related improvements leading up to this point are associated with increases in the recruitment of brain regions implicated in cognitive flexibility in adults (Buttelmann & Karbach, 2017).

To date, only a handful of studies have examined the neural mechanisms mediating cognitive inflexibility associated with irritability in children. Using functional Near Infrared Spectroscopy (fNIRS), Li and colleagues (2017) found that in preschoolers, individual differences in dispositional irritability were associated with greater activity in the DL-PFC but

unrelated to task performance while completing a modified Stroop task. Although the Stroop task is considered to be a measure of cognitive flexibility, it differs from traditional cognitive flexibility tasks in that it relies on a prepotent and more automatic response rather than a rule shift to elicit cognitive flexibility. Interestingly, in neuroimaging studies of younger children completing other tasks that are rigged to induce frustration and/or tap inhibitory control and attention orienting a similar pattern of heightened DL-PFC activation in irritable children has been found also in the context of intact or even enhanced behavioral performance (Fishburn et al., 2019, Perlman, Luna, Hein & Hupert, 2014; Tseng et al, 2018). The majority of these studies have examined individual differences in dispositional irritability in preschool-aged children, a developmental period in which anger and temper loss is relatively normative, it has been postulated that children with less impairing irritability may recruit increased DL-PFC activation as a compensatory inhibitory mechanism to self-regulate and/or adjust their behavior to meet task demands. Conceptualizing DL-PFC activation as a compensatory mechanism, however, suggests that perturbations in other neural processes may underpin cognitive inflexibility associated with irritability.

When neural patterns of brain activation were examined using a response reversal task in children with impairing and chronic irritability who were diagnosed with severe mood dysregulation (SMD), a different pattern of findings emerged. Using fMRI, Adleman and colleagues (2011) found that children with SMD showed both poorer performance and lower activity than healthy controls in both the caudate and inferior frontal gyrus (IFG) during incorrect (when compared to correct) trials. The IFG is believed to subservise inhibitory processes necessary for successful task-set switching (Brass & Cramon, 2004; Swainson et al., 2003), while the caudate supports feedback and reward-based learning (Packard & Knowlton, 2002). As ADHD is

associated with the same pattern of caudate activity during response reversal tasks (Durstun et al., 2003; Rubia, Smith, Brammer, Toone & Taylor, 2014; Vaidya et al., 2005), this raises the possibility that diminished caudate activity is due to the hyperarousal symptoms (e.g. distractibility, racing thoughts, intrusiveness) included in the diagnostic algorithm for SMD, rather than irritability. Indeed, more recent psychophysiological and neuroimaging evidence suggests that irritability is associated with enhanced neural reactivity to rewarding feedback and exaggerated S-R learning (Deveney et al., 2013; Kessel et al., 2016; Perlman et al., 2015, Tseng et al., 2019) which may be difficult to override in the context of changing task demands. Thus, deficits in WM or set-shifting, as opposed to or in tandem with, RL may limit the ability of irritable children to adjust their behavior to perform optimally on response-reversal and other cognitive flexibility tasks.

Taken together, these studies suggest that irritable children show aberrant neural activity – even in the absence of behavioral deficits— in brain regions implicated in cognitive flexibility. However, the specific nature and pattern of the neural processes underlying inflexible behavior characterizing irritability in children remains unclear. Furthermore, fMRI and fNIRS have poor temporal resolution and as a result cannot both simultaneously examine and disentangle the role of set-shifting, working memory and reinforcement learning in childhood irritability. This is a significant limitation as it has been speculated that temporal dynamics of these cognitive processes may distinguish brain activity between the various EFs implicated in cognitive flexibility.

### **Event-Related Potentials (ERPs) and Facets of Cognitive Flexibility**

One way to better elucidate different cognitive processes involved in cognitive flexibility is by using event-related (ERPs) potential measures. While fMRI and fNIRS offer high spatial resolution, ERPs provide superior temporal resolution. This is because electrical activity can be

sampled rapidly, capturing very early and dynamic neural processes subserving cognitive flexibility as they unfold, such as set-shifting, RL, and WM (Luck, 2014). Furthermore, ERPs have been shown to relate robustly to individual differences in EF in ways that may clarify similarities and distinctions between cognitive processes.

In older adolescents and adults, the Wisconsin Card Sorting Task (WCST), modified to elicit ERPs, has been used to disentangle the role of set-shifting, working memory, and feedback processing (Vila-Ballo et al., 2015). The WCST requires participants to flexibly adapt their behavioral responses to simple geometrical stimuli on the basis of feedback. In this task, participants have to match a target card (with a specific color, shape and number) with one of four key cards (each one with one different color, shape and number). Participants are required to infer the correct rule (color, shape, number), on the basis of the positive and negative feedback provided and maintain it, until the sorting rule changes. Cue signals indicating whether to repeat either the same sorting rule or to switch to another rule are incorporated at the beginning of each trial. Using this task, Vila-Ballo and colleagues (2015) demonstrated that cognitive inflexibility associated with physical aggression in adolescence may be specifically due to an increased reliance on external feedback and perturbations in task-set reconfiguration.

This task elicits three ERPs reflecting separable components of cognitive flexibility which include the switch positivity (SP), the reward positivity (RewP), and the P3b (Hsieh & Wu, 2011, Gajewski & Falkenstein, 2011; Swainson et al., 2006). The SwP is a posterior positivity, which is larger for switch compared to stay cues. It peaks at approximately 300–500ms after cue onset and is thought to index task-set reconfiguration processes that reflect proactive cognitive control to prepare for a shift in task and overcome S-R priming (Astle, Jackson & Swainson, 2008; Rushworth, Passingham & Nobre, 2002). A greater SwP is



associated with a greater recruitment of anticipatory control processes to shift trials in children and adults (Karayanidis, Coltheart, Michie & Murphy, 2003; Chevalier et al., 2105). An abnormal SwP has been identified in adolescent criminal offenders (Vilà-Balló et al., 2015). The RewP is elicited by positive compared to negative feedback (Proudfit, 2015). It is thought to reflect the processing of dopaminergic RL signals triggered by feedback indicating that an outcome was better or worse than expected and indexes RPEs (Holroyd & Coles, 2002). The RewP peaks 250-300ms after feedback and is observed over frontocentral recording sites. More positive RewPs are associated with greater RL (Holroyd & Coles, 2002). Perturbations in the RewP have been linked to numerous psychiatric disorders, including depression, anxiety, and substance use (Baskin-Sommers & Foti, 2015; Bress, Smith, Foti, Klein & Hajcak, 2012; Kessel, Kujawa, Proudfit & Klein, 2014). The P3b is purported to reflect elaborative post-perceptual processing that is used to update WM about task demands. The P3b peaks 300-600ms after feedback cues and shows the largest amplitude in response to the first instance of feedback after a set switch (Barcelo, Escera, Corral & Periáñez, 2006, Brydges et al., 2014; Cunillera et al., 2012; Donchin & Coles, 1998). An enhanced P3b is associated with better behavioral performance on WM tasks (Brydges et al., 2014), and a blunted P3b has been identified in most forms of psychopathology (Anokhin, Golosheykin & Heath, 2010; Gangadhar et al., 1993; Iacono, Malone & McGue, 2003; Iacono & Malone, 2011).

Although there are subtle developmental changes in the latency and topography of these ERPs, these components can all be elicited in young children (Brydges, Fox, Reid & Anderson, 2014, Kujawa, Proudfit & Klein, 2014; Manzi et al., 2014). We are unaware of any studies examining associations between the SwP and P3b, let alone several of these ERPs, and irritability in young children. In particular, it is important to use reliable and well-validated tasks

that simultaneously examine multiple neurocognitive substrates of cognitive inflexibility in order to determine which process or processes play the greatest role in irritability in youth.

### **Goals and Hypotheses**

The goal of the current study was to modify and validate a novel, developmentally appropriate, version of the Wisconsin Card Sorting Task (WCST)—PokéSort—to use in conjunction with temporally sensitive ERPs (described below) in order to simultaneously measure and disentangle neural indices of set-shifting, RL and WM, and examine their associations with irritability in a sample of children. Because the developmental trajectory of WM is not identical to, and lags behind, other cognitive processes underpinning cognitive flexibility (Hunter, 2012), we reduced the WM demands of the task to control for these developmental differences. Like most experimental paradigms, the WCST was not designed to engage the interest of children; therefore, we also incorporated a Pokémon story line and engaging graphics to make the task more engaging. Thus, our study had two main objectives: (1) demonstrate that our task would elicit dissociable electrocortical measures of set-shifting, feedback sensitivity and working memory (i.e., the SwP, RewP and P3b) and evaluate their convergent and divergent validity by examining their associations with other measures that have been related to these ERP components or the cognitive processes the ERP aims to tap; and (2) examine whether childhood irritability is associated with neural disruptions in set-shifting, working memory and/or reinforcement learning. As there is some evidence to suggest that irritability is associated with aberrant patterns of neural activation even in the absence of observed inflexible behavior (e.g. Li et al., 2017) and that this pattern may vary depending on whether behavioral perturbations are also present (Adleman et al., 2011), an exploratory aim of

the current study was to examine whether neural and behavioral indices of cognitive inflexibility interact to predict irritability.

## Method

*Participants.* Families (n=58) with a 7 to 14-year-old child whose primary caretaker speaks fluent English were recruited from Western Long Island using advertisements on social media. Exclusion criteria were a lifetime history of a distinct manic or hypomanic episode, and a significant developmental disorder or medical disability. Eight participants were excluded from the final analyses due to refusal to complete the lab visit, or poor EEG quality or technical error<sup>1</sup>. Table 1 presents demographic and sample characteristics of this report's final sample of 50 children. Consistent with an RDoC approach, the study recruited children with variability in child-reported ( $M = 2.66$ ;  $SD = 2.47$ ; Range: 0-12) and parent-reported irritability ( $M = 1.96$ ;  $SD = 2.33$ ; Range: 0-10) assessed using the Affective Reactivity Index (ARI; Stringaris et al., 2012).

The Institutional Review Board approved all study procedures. Families were compensated for their time. After written informed consent from parents and verbal assent from children were obtained, parents completed questionnaires to assess current child irritability. Children completed questionnaires to assess irritability and were administered behavioral executive functioning (EF) tasks. Next, children began the EEG portion of the visit, including a 20-minute developmentally adapted Wisconsin Card Sorting Task (WSCT), in addition to other tasks not discussed here.

## EEG Measures

*PokéSort Task.* To examine the SP, P3b, and RewP, electroencephalography (EEG) was

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<sup>1</sup> Feedback-related ERP data from an additional four participants were not included in relevant analyses due to poor data quality.

recorded while children performed the PokéSort task, a developmentally adapted Wisconsin Card Sorting task (see *Figure 1*). In order to distinguish multiple cognitive components of cognitive flexibility, PokéSort incorporates audio cues indicating task-switches that elicit the SwP as well as visual stimuli indicating performance feedback that elicit both the P3b and RewP. Stimuli were presented by Presentation software, and included images containing pokémon that differ in three dimensions: color, habitat, and type. Each card had 1 of 3 possible characteristics in each dimension (e.g., electricity, fire and grass). In each trial, participants were presented with a pokémon stimulus, and 3 targets comprised of 3 pokémon stimuli that all differed from one another in color, habitat and type. The participant was instructed to match the pokémon stimuli to one of the target pokémon, but was not told whether the match should be based on color, habitat, or type. The pokémon stimulus and 3 target pokémon remained on the screen until the participant made a selection using her/his index finger on a keyboard. After 1000ms, feedback was presented for 1000ms. A correct response was indicated by a smiley face, and an incorrect response, by a sad face. After 300ms, an auditory cue lasting 250ms signaled to participants whether or not to repeat the rule used in the previous trials (65 dB tone; 250ms duration; 2000 Hz) or to switch to another new rule (500 Hz), beginning a new block. There was a 1000-1700ms varying interval between the auditory cue and the beginning of the next trial. 150 trials were semi-randomly arranged into 30 blocks (a block begins with a rule change and is ended by the next rule change), varying in length from 4-6 trials per series, to avoid rule-switch anticipation.

*EEG Recording.* While participants completed PokéSort, continuous EEG was recorded with a 34-channel Biosemi system (32 channel cap, Iz, FCz). Electrodes were placed on the left and right mastoids and the electrooculogram were recorded from four facial electrodes. The ground electrode was formed by the Common Mode Sense active electrode and the Driven Right

Leg passive electrode. Off-line analysis was conducted using Brain Vision Analyzer software. Data was converted to a mastoid reference, filtered, corrected for eye blinks, and artifact rejected with semi-automated procedures. Auditory cue-locked and feedback-locked ERPs were averaged separately for switch trials, repeat trials, positive feedback (pFB) trials, and the first and last pFB trials of each series. Feedback-locked ERPs on the first and second negative feedback (nFB) trials were also averaged (errors on the switch trial and on trial following the switch); set-maintenance errors, i.e. errors made after acquiring the correct rule were excluded from the analyses. Averages were baseline corrected using the time window from -200-0ms prior to stimulus (cue or feedback) onset. Consistent with prior work and scalp topography, the SwP was scored as the difference in mean activity at Cz/Pz from 300-400ms after switch vs. repeat cue onset; the RewP was scored as the difference in mean activity at Fz from 290-360 ms after feedback onset on positive vs. first two negative feedback trials; and the P3b was scored as mean activity at Pz from 300-400ms after positive feedback onset on the first trial vs. the last repetition trial.

In order to isolate the variance unique to ERPs in response to switch compared to stay cues, negative compared to positive feedback, and initial vs later positive feedback after a task-switch, we also calculated residuals that reflected the difference between an individual's observed response to the outcome of interest and what would be predicted from an individual's response to the alternate outcome. These residuals were independent from the average response to the alternate outcome but correlated with the average response to the outcome of interest. In the present study, we conducted three sets of two regression models each to calculate residuals. In the first set, the first regression model included the stay positivity (StP) as the independent variable and the switch positivity (SwP) as the dependent variable (i.e., the SwP residual), and

the other with the SwP as the independent variable and the StP as the dependent variable (i.e., the StP residual). More positive SwP and StP residuals are believed to reflect greater neural activity allocated to task-set reconfiguration processes and cognitive control to prepare for a shift in task (Astle, Jackson & Swainson, 2008; Rushworth, Passingham & Nobre 2002). In the second set, the first regression included the RewP to positive feedback as the independent variable and the feedback negativity (FN) to negative feedback as the dependent variable (i.e., the FN- residual), and the second with the FN to negative feedback as the independent variable and the RewP to positive feedback as the dependent variable (i.e., the RewP-residual). A more negative FN residual indicates greater neural sensitivity to negative feedback, whereas a more a more positive RewP residual indicates greater neural reactivity to positive feedback. The last set included one regression including the P3b on the last correct trial as the independent variable and the P3b on the first correct trial as the dependent variable (i.e. the P3b-Trial 1 residual), and the second with the P3b on the first correct trial as the independent variable and the P3b on the last correct trial as the dependent variable (i.e. the P3b-Last trial residual<sup>i</sup>). A more positive P3b-residual is hypothesized to reflect greater elaborative post-perceptual processing that is used to update WM (Cunillera et al., 2012; Polich, 2007).

### **Behavioral and Questionnaire Measures**

*Set-shifting.* Participants completed the Trail Making Task (TMT; Reitan & Wolfson, 1993), paper and pencil task in which participants are first asked to draw lines between encircled numbers (TMT A). Participants are then asked to alternate between connecting encircled numbers and letters arranged on a page (TMT B) as quickly as they can, requiring them to remember the rules while also inhibiting the prepotent response to connect items of the same category. Set-shifting was calculated by regressing performance on Trails A on Trails B (i.e., the

completion time) and saving the standardized residuals. Lower scores denote better performance.

*Working memory.* Participants completed the Digit Span subtest of the WISC-III (Weschler, 1991), which include a forward (DF) and backwards (DB) component. DF required participants to repeat verbatim digits presented forward, whereas DB required participants to repeat the strings of digits in reverse order. Both subtests included two trials per number of digits ranging from 2 to 8. Factor-analytic studies have demonstrated that memory processes involved in DF and DB are distinct. Whereas DF is a task of short-term auditory memory, sequencing and simple verbal expression, DB is more sensitive to deficits in working memory (Rosenthal, Ricchio, Gsanger & Jarrett, 2006). Therefore, for the purposes of our study, only performance on DB were included in analyses. Working memory performance was calculated as the longest sequence of digits recalled on the DB. Higher scores indicate better performance.

*Feedback sensitivity.* To measure children's sensitivity to punishment and reward, parents completed the reward responsiveness (RR) and behavioral inhibition system (BIS) subscales of the BIS/Behavioral Approach System (BAS) questionnaire (Carver and White, 1994) that was modified for parent report and use with children (Vervoort et al., 2015). Questions are answered on a 4-point Likert-type scale from "strongly disagree" to "strongly agree". The RR subscale consist of five items (e.g. "When my child is successful at something, he/she continues doing it".) Higher scores indicate higher trait reward sensitivity. Although seven items comprise the BIS scale, we removed two of the items ("your child is very fearful compared to his or her friends" and "your child does not become fearful or nervous, even when something bad) due to an accumulating body of research that suggests that these items show weak and inconsistent loading on the overall BIS scale (Pagliaccio et al., 2016). Items on the BIS scale tap the degree to which children are sensitive to aversive and punishing stimuli. Higher scores on the

BIS scale indicate higher trait punishment sensitivity. Previous studies have demonstrated that these measures show meaningful relations with neurophysiological and psychophysiological markers and punishment processing (Blair, Peters & Granger, 2004; Bress & Hajcak, 2013). Coefficient  $\alpha$ s were 0.71 and 0.75 for the parent-reported BIS and RR scales, respectively.

*Child irritability.* To measure children's irritability, children and their parents completed the Affective Reactivity Index (ARI). The ARI is a 6-item self- and parent-report questionnaire that assesses irritability in children over the past 6 months. The scale has good reliability, both internally and across informants, and good convergent and discriminant validity (Stringaris et al., 2012). Coefficient  $\alpha$ s were 0.80 and 0.85 for the child- and parent-report, respectively.

## Results

### Task Effects on Accuracy and ERPs

Two single-level 2 factor (cue; switch, stay trials) rmANOVAs were calculated to demonstrate the task effect of condition (i.e. switch vs. stay) on participant's behavioral performance and the SP, respectively. With regards to accuracy, the main effects of cue on behavioral performance,  $F(1, 49)=347.62, p<.001, \eta^2_p=.88$  and the SwP,  $F(1, 49)=32.78, p<.001, \eta^2_p=.40$  were both significant. Accuracy on trials preceded by a switch cue ( $M = .39, SD = .13$ ) was lower compared to trials preceded by a stay cue ( $M = .75, SD = .13$ ). Additionally, switch cues were associated with an enhanced positivity ( $M = 3.05, SD = 7.47$ ) compared to stay cues ( $M = -2.3463, SD = 7.73$ ), and scalp distributions confirmed that this difference was maximal at centroparietal sites (see *Figure 2*). The mean switch minus stay positivity difference score ( $\Delta SP$ ) was 5.39 ( $SD = 6.66$ ).

To demonstrate a task effect of feedback valence on the RewP, a single-level 2-factor (feedback: correct, incorrect) rmANOVA was calculated. The main effect of feedback was



significant  $F(1, 45)=5.29, p<.05, \eta^2_p=.11$ , such that incorrect feedback was associated with an enhanced (i.e., more negative) FN ( $M = -1.51, SD = 6.93$ ) compared to correct feedback ( $M = -0.24, SD = 5.69$ ), and scalp distributions confirmed that this difference was maximal over frontal sites (see *Figure 3*). The mean correct minus incorrect RewP difference score ( $\Delta$ RewP) was 1.76 ( $SD = 5.18$ ).

To examine whether there was a main effect of trial order after a task switch on the P3b in response to positive feedback, we calculated a single-level 2-factor (trial order: first, last repetition) rmANOVA. The main effect of trial order was significant  $F(1, 49)=18.41, p<.001, \eta^2_p=.27$ , such that the P3b amplitude was larger in response to the first instance ( $M = 7.78, SD = 1.57$ ) of positive feedback after a task switch compared to repeated trials ( $M = 1.78, SD = 1.01$ ) (see *Figure 4*).

### **Bivariate Associations Between Major Study Variables**

Table 2 displays bivariate correlations between all study variables. There were significant associations between age and accuracy on the PokéSort task, set-shifting latency on the TMT, backwards digit span number recall, SwP, and P3b-1<sup>st</sup> trial such that older children had better performance on the TMT-B, BDS and PokéSort Task, and an enhanced SwP and P3b-1<sup>st</sup> trial. Gender was significant associated was parent-reported punishment and reward sensitivity and the SwP, such that females were rated as more sensitive to punishment and reward by their parents and had a greater SwP amplitude. There was no significant association between child- and parent-reported irritability or between parent-reported reward and punishment sensitivity. Parent- and child-reported irritability were correlated with the SwP, such that higher levels of parent-reported and child-reported irritability were significantly associated with a reduced SwP. Parent-reported, but not child-reported, irritability was significantly associated with reward

sensitivity and performance on the PokéSort Task and the TMT-B, such that higher levels of parent-reported irritability predicted reduced reward sensitivity and poorer behavioral performance on both tasks. The SwP and performance on the PokéSort task and TMT B were intercorrelated such that better performance on the PokéSort Task was associated with better performance or shorter set-shifting latencies on the TMT-B, and superior performance on both were associated with an enhanced or more positive SwP amplitude. Finally, the P3b-6<sup>th</sup> trial amplitude was significantly associated with a more positive RewP amplitude.

### **Convergent and Discriminant Validity of the SwP, RewP and P3b.**

Next, to evaluate the convergent and discriminant validity of the electrocortical measures of set-shifting, feedback sensitivity and working memory elicited by the PokéSort Task, bivariate correlations between corresponding and noncorresponding behavioral and parent-report measures of EF and neural reactivity to auditory shift (SwP) and stay cues (StP), positive (RewP) and negative feedback (FN) and P3b on the 1<sup>st</sup> pFB and last pFB trial in a series were calculated. The SwP was significantly associated with performance on a behavioral measure of set-shifting, such that youth who exhibited greater neural reactivity to switch cues had better performance or shorter set-shifting latencies on the TMT-B task. The FN was associated with parent-reported trait-punishment sensitivity, at a trend level, such that blunted FN was associated with enhanced trait punishment sensitivity. The P3b-1<sup>st</sup> trial was significantly correlated with performance on the DSB, such that as the number of digits recalled on the BDS increased, the P3b was relatively more enhanced in response to initial positive feedback following a task switch. There were no significant associations between the SwP, StP, FN and RewP and behavioral measure of working memory (DS), nor were there significant associations between FN, RewP and P3b to behavioral measures of set-shifting. Additionally, parent-report of sensitivity to reward and punishment

sensitivity was unrelated to the SwP, StP, P3b and RewP, though the absence of a significant association between trait reward sensitivity and the RewP was somewhat surprising and contrary to our prediction.<sup>2</sup>

### **Associations Between Irritability and ERP Measures of Cognitive Flexibility**

To examine whether irritability was specifically associated with neural indices of set-shifting, even when accounting for neural indices of RL and WM, we conducted multiple regression analysis. As child- and parent-reported irritability were not significantly correlated, we were unable to create a composite measure. Therefore, we conducted two separate analyses, one examining child- and the other examining parent-reported irritability as dependent variables, respectively. We entered the SwP, StP, FN, RewP, P3b-1<sup>st</sup> trial, P3b-last trial residual scores as simultaneous predictors to compare symptom variance accounted for by measures of distinct neural processes of cognitive flexibility. In both models, the SwP was associated with irritability, such that a more blunted SwP was associated with greater child- and parent-reported irritability. Neither the FN, RewP, P3b-1<sup>st</sup> trial or P3b-last trial was significantly associated with either measure of irritability, suggesting that the association between irritability and neural indices of cognitive flexibility, may be specific to set-shifting (see *Table 3 & Figure 5*).

To examine whether the SwP and behavioral measures of set-shifting interacted to predict irritability, another set of hierarchical multiple regression analyses were separately computed with child- and parent-reported irritability as the dependent variables. Behavioral performance on the PokéSort task and TMT were entered into step 1, followed by the SwP in step 2, and interactions between the SwP and performance on the PokéSort Task and TMT were entered into

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<sup>2</sup> We also conducted partial correlations to examine the possibility that age confounded the effect of the SwP on behavioral performance on the PokeSort Task. Although associations between the SwP and behavioral performance on the PokeSort Task ( $p = .13$ ) and TMT B ( $p = .18$ ) were no longer statistically significant, a similar pattern of results emerged.

step 3 (see Table 4). When simultaneously entered in the multiple regression, behavioral predictors of set-shifting explained a significant portion (14%) of the variance in parent-reported irritability, and performance on the TMT predicted parent-reported irritability at a trend level, such that children whose parents rated them as more irritable had greater set-switching latencies on the TMT B vs. A. After accounting for behavioral measures of set-shifting, the SwP was not a significant predictor of parent-reported irritability. However, there was a significant interaction between the SwP and performance on the TMT B, such that among children with worse performance or longer set-shifting latencies on the TMT B, a more blunted SwP amplitude was associated with higher levels of parent-reported irritability,  $b = -1.12$ ,  $SE = 0.42$ ,  $t(44) = -2.63$ ,  $p < 0.05$ . However, among children with better performance or shorter set-shifting latencies on the TMT B, there was no association between the SwP and parent-reported irritability,  $b = 0.38$ ,  $SE = 0.58$ ,  $t(44) = 0.65$ ,  $p = ns$ . The interaction between the SwP and behavioral performance on the PokéSort task was not significant (see Figure 6).

At entry, behavioral predictors of set-shifting did not significantly predict or explain a significant amount of variance in child-reported irritability. However, a significant association between performance on the TMT B and child-reported irritability emerged after the SwP was entered into the regression. Children who rated themselves as more irritable had better performance or shorter latencies on the TMT B. When accounting for behavioral measures of set-shifting, the SwP was a significant predictor of child-reported irritability such that a blunted or less enhanced SwP predicted greater levels of child-reported irritability. There were no

significant interactions between the SwP and performance on the TMT or PokéSort task predicting child-reported irritability<sup>3</sup>.

## Discussion

In the current study, we adapted and modified the Wisconsin Card Sorting Task, to create a novel more developmentally appropriate task, PokéSort Task. We established that the task elicits ERPs that tap a series of distinct components implicated in cognitive flexibility and captures individual differences in irritability. Using this task, in tandem with well-established measures of cognitive processes associated with cognitive flexibility in young children, we examined behavioral and neural correlates of cognitive inflexibility associated with irritability in a sample of 7 to 13-year-old children. This study is the first to find that both behavioral and electrocortical features of cognitive inflexibility observed in irritable children is specifically associated with perturbations in set-shifting. Irritability was associated with poorer performance on both our modified developmentally sensitive WCST, PokéSort, and on the TMT. Additionally, irritability was associated with a blunted or less enhanced SwP— an ERP thought to index the recruitment of anticipatory control processes to prepare for a shift in task (Astle, Jackson & Swainson, 2008; Rushworth, Passingham & Nobre, 2002).

The PokéSort task elicited the SwP, RewP and the P3b: three neural indices of set shifting, RL and working memory, respectively: auditory cues indicating a rule switch vs. stay was accompanied by a positivity that was maximal at 350 ms at centroparietal sites, and consistent with the SwP; positive versus negative feedback elicited a modest positivity maximal at 325 ms at frontal sites and consistent with the RewP; finally, a positivity maximal at 350 ms at

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<sup>3</sup> Distance statistics were used to test for multivariate normality and potential undue influence of outliers-cases with an unusual combination of scores on two or more variables. One case was identified by the value of the Cook's D statistic and analyses were repeated with this case removed.

electrode Pz that was consistent with the P3b and enhanced for initial compared to repeated positive feedback was identified.

Additionally, moderate correlations between the P3b, SP and the RewP and their corresponding but not noncorresponding behavioral or questionnaire measures tapping set-shifting, WM and RL suggest that these ERPs are valid indicators of set-shifting, working memory and RL. An enhanced SwP was associated with shorter set-shifting latencies on the TMT and more accurate performance on the PokéSort task, but unrelated to a behavioral measure of working memory (the DSB), whereas an enhanced P3b was associated with better performance on the DSB and unrelated to set-shifting latencies on the TMT. Neither of these measures were associated with parent-reported punishment or reward sensitivity. It is important to note, however, that we only found modest evidence to support the validity of the RewP as a measure of RL. Contrary to our expectations, the RewP to positive feedback was unrelated to parent-reported reward sensitivity. Additionally, a more enhanced FN to negative feedback was associated with a diminished parent-reported punishment sensitivity at a trend-level. On the surface it may seem contradictory that children with enhanced parent-reported punishment sensitivity would demonstrate diminished neural reactivity to negative outcomes. However, neither punishment nor reward sensitivity directly taps RL, and an accumulating body of research suggests that generalized fear in nonthreatening situations and chronic worry, both which have been shown to be characterized by a more activated behavioral inhibition system, results from an inability to effectively process and learn from negative outcomes. For example, deactivating the mesolimbic dopamine system causes impairment in contingency awareness to aversive events, resulting in a generalized anxiety-like phenotype in mice (Zweifel et al., 2011).

Thus, a reduced FN to negative feedback may be simultaneously indicative of impaired RL and greater punishment sensitivity.

Although it has been postulated that the link between irritability and cognitive inflexibility may be due to an inability to learn from shifting reward-contingencies (Leibenluft & Stoddard, 2013; Stringaris & Taylor, 2015), our findings suggest that neural perturbations associated with shifting set as opposed to RL may mediate behavioral and cognitive rigidity observed in irritability. In contrast to previous research (Kessel et al., 2016), there was no association between the RewP with irritability or task performance. However, the RewP elicited by PokéSort task was less robust than what is typically seen in developmental ERP studies using tasks including monetary reward: positive and negative feedback included in the PokéSort task were a smiling and frowning face indicating a correct and incorrect response, respectively. The absence of salient reward may explain the absence of an association, as the RewP is sensitive to outcome valence and magnitude, likely reflecting the motivational and emotional consequence of decision outcomes. Thus, future studies should examine the role of RL in flexible behavior in the context of more salient rewarding outcomes and how it relates to childhood irritability. In the current study, child- and parent- reported irritability were uncorrelated. While both were associated with a reduced SwP in bivariate analyses, subtle differences in behavioral and neural correlates also emerged for parent- versus child-reported irritability. Reduced parent-reported reward sensitivity and poorer PokéSort task performance and longer set-shifting latencies were associated with parent- and not child- reported irritability in bivariate analyses. This is consistent with well-known informant discrepancies in developmental psychopathology research and previous research which has demonstrated that parent-, and not child-reported irritability

form distinct factors in bifactor models of negative affectivity that show unique associations with neural activity during threat orienting (Kircanski et al., 2018).

Additionally, the SwP interacted synergistically with behavioral measures of set-shifting to predict parent- but not child-reported irritability. Only among children who exhibited inferior performance or longer set-shifting latencies on the TMT, did a blunted SwP predict parent-reported irritability. In the absence of behavioral perturbations of set-shifting, there was no association between the SwP and parent-reported irritability. While there were no interactive effects between the SwP and behavioral measures of set-shifting on child-reported irritability, we found that when behavioral and neural measures of set-shifting were examined simultaneously, both a blunted SwP and *superior* performance on the TMT predicted child-reported irritability, suggesting the possibility of a suppression effect in which correlated variables are related to the dependent measure in the opposite direction concealing bivariate associations between variables. Thus, there may be a subset of children who behaviorally demonstrate superior set-shifting behavior which is independent from neural perturbations observed during the PokéSort Task. As the SwP predicts child-reported irritability regardless of behavioral manifestation of set-shifting, our findings also raise the possibility that parent-reported irritability may reflect more observable behavioral manifestations of irritability and may not capture the full range of irritability that gives rise to more covert and internalized forms of irritability, like angry brooding and rumination, of which parents may be unaware. As increased DLPFC activation has been observed in less impairing forms of childhood irritability (Li et al., 2017), it is also possible that children who are unimpaired by or able to self-regulate and internalize their irritability compared to those who exhibit more behavioral manifestations of irritability and externalize, are able to



recruit increased DLPFC activation to somewhat compensate for their neural perturbations in set-shifting. More research, however, is needed to examine this possibility.

Cognitive flexibility rapidly increases during middle and late childhood, a developmental period characterized by heightened brain plasticity in which the brain is collecting input from the environment in order to promote development that serves to increase the biological fitness within that milieu (Del Giudice, 2014). Indeed, there is an emerging body of research suggesting that training children with task-switch paradigms can yield significant improvements in cognitive flexibility (Karback & Kray, 2016; Konen et al., 2016). In the current study, compared to younger children, older children were better at shifting their sets and also had more enhanced or more positive SwPs. Despite these differences, however, they were no less irritable than younger children. Thus, future research should examine whether improvements in cognitive flexibility, particularly shifting set, also lead to reductions irritability.

The current study is not without limitations. First, as the sample size is small and underpowered, results from the present study should be interpreted cautiously. Nonetheless, results are promising as associations between the SwP and irritability replicated across informants. Second, the age range of the participants included in the present study was relatively broad. Follow-up studies should examine developmental changes in mechanisms of cognitive inflexibility associated with irritability longitudinally. Third, some ( $n = 5$ ) participants were taking psychotropic medication. While it is possible that results would be different in unmedicated individuals, children taking psychotropic medication did not differ from those who were medication naïve on any of the behavioral or ERP measures. Fourth, it will be important to replicate these findings in clinical samples of irritable youth, as there is some evidence to suggest

that irritability assessed in the community may be qualitatively distinct from that which is observed in clinical settings (Carlson et al., 2016).

The present study is the first to simultaneously measure and disentangle neural indices of set-shifting, RL and WM in children and examine their associations with irritability in a sample of 7- to 13-year-old children. Results suggest that cognitive inflexibility associated with irritability is specifically associated with neural perturbations in set-shifting, as evidenced by a reduced SwP. These findings suggest that the SwP may be a viable target for the development of novel treatments. These findings also point to the utility of using ERPs in conjunction with the PokéSort task to elucidate the neurocognitive processes that mediate cognitive rigidity in childhood irritability and other forms of psychopathology.

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Table 1

*Demographic and clinical characteristics of the study sample*

<i>Demographic characteristics</i>	
Child mean age: years (SD)	10.50 (2.27)
Child sex: female <i>n</i> (%)	22 (44)
Child race: <i>n</i> (%)	
White	43 (86)
Black/African-American	2 (4)
Asian	4 (8)
Other	1 (2)
Child Hispanic/non-Hispanic ethnicity (%)	7 (14)
Biological parents' marital status: <i>n</i> (%)	
Married or living together	37 (74)
Divorced, separated, or widowed	12 (24)
Never married	3 (6)
Parent's education: graduated from college <i>n</i> (%)	
Mother	32 (64%)
Father	19 (38%)
Child psychotropic medication use (%)	5 (10%)
<i>Mean highest number of digits recalled on WISC-III DS (SD)</i>	
Forward	6.02 (1.41)
Backward	3.88 (1.26)
<i>Mean TMT completion time: seconds (SD)</i>	
Part A	34.95 (14.64)
Part B	97.94 (56.53)
<i>Mean child irritability symptom scale (SD)</i>	
Child-reported	2.66 (2.47)
Parent-reported	1.96 (2.33)

DS = digit span; TMT = trail making task

Table 2

*Bivariate Correlations Among Major Study Variables*

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	
1. Sex	—	.00	.14	.21	-.41***	-.25*	.06	.00	-.02	-.30*	.14	.18	.09	-.05	.20	
2. Age		—	-.15	-.15	-.11	-.21	.46**	-.36**	.54**	.34*	.16	.14	-.17	.34*	-.16	
3. Irritability (P)			—	.14	.18	-.30*	-.32*	.32*	-.05	-.34*	.10	.11	.08	-.02	.04	
4. Irritability (C)				—	-.09	-.01	-.05	-.11	-.07	-.39**	.14	-.05	-.02	-.04	-.04	
5. BIS					—	-.18	-.03	.14	.15	-.05	-.05	-.19	.28†	-.15	.08	
6. RR						—	.08	-.02	-.24	.03	-.16	-.09	.07	.14	-.16	
7. PS Accuracy							—	-.36**	.19	.34*	.03	.06	.05	.24	-.04	
8. TMT B								—	-.24	-.29*	.01	-.12	.13	-.21	-.02	
9. DSB									—	.20	.05	.07	-.06	.35*	-.22	
10. SwP										—	-.51**	.05	-.05	.17	.01	
11. StP											—	-.06	-.14	.15	-.21	
12. RewP												—	-.64**	.17	.29*	
13. FN														—	-.08	
14. P3 Trial1															—	-.48**
15. P3 Trial6																—

\*p < .05, \*\*p < .01, SwP = switch positivity; StP = stay positivity; TMT = trails making task; DSB = digit span backwards; FN = feedback negativity; RewP = reward positivity; BIS = behavioral inhibition system; RR = reward responsiveness

Table 3

*Multiple regression analyses regressing age and ERPs elicited by the PokéSort task on irritability*

Child-reported Irritability		
<i>Total Model <math>F(6,38)=1.45, R^2=.18, p=.22</math></i>		
	$\beta$	t
SwP	-.46*	-2.62*
StP	-.11	-.60
RewP	.02	0.08
FN	-.11	-.55
P3b-1 <sup>st</sup> Trial	.02	.09
P3b- Last Trial	-.06	-.31
Parent-reported Irritability		
<i>Total Model <math>F(6,43)=1.65, R^2=.19, p=.16</math></i>		
	$\beta$	t
SwP	-.38*	-2.21
StP	-.03	-.20
RewP	.35	1.58
FN	.28	1.42
P3b-1 <sup>st</sup> Trial	-.01	-.05
P3b- Last Trial	-.05	-.27

\* $p < .05$ , \*\* $p < .01$ , SwP = switch positivity; StP = stay positivity; FN = feedback negativity; RewP = reward positivity

Table 4

*Hierarchical regression analyses regressing behavioral measures of set-shifting and the SwP residual on irritability*

Child-reported Irritability			
	Entry $\beta$	Step 2 Partial $r$	Step 3 Partial $r$
<i>Step 1</i>			$F(2,44)=1.04, R^2=.05, p=.36$
TMT B	-.22	-.30*	-.24
PS	-.05	.06	.07
<i>Step 2</i>			$\Delta F(1,43)=8.34, \Delta R^2=.16, p=.006$
SwP	-.42*	-.40*	-.39*
<i>Step 3</i>			
SwP X TMT B	--	--	--
SwP X PS	--	--	--
<i>Total Model <math>F(3,43)=3.59, R^2=.20, p=.02</math></i>			
Parent-reported Irritability			
	Entry $\beta$	Step 2 Partial $r$	Step 3 Partial $r$
<i>Step 1</i>			$F(2,47)=4.47, R^2=.14, p=.02$
TMT B	.26†	.21	.09
PS	-.23	-.17	-.19
<i>Step 2</i>			$\Delta F(1,46)=2.58, \Delta R^2=.05, p=.12$
SwP	-.23	-.23	-.16
<i>Step 3</i>			$\Delta F(1,45)=4.24, \Delta R^2=.07, p=.04$
SwP X TMT B	-.37*	--	-.29*
SwP X PS	--	--	--
<i>Total Model <math>F(4,45)=4.22, R^2=.27, p=.005</math></i>			

† $p < .10$ , \* $p < .05$ , \*\* $p < .01$ , SwP = switch positivity; TMT = trails making task; PS = PokéSort

## Figure Captions

*Figure 1.* Schematic diagram of the PokéSort Task.

*Figure 2.* ERPs (negative up) at Cz/Pz following audio cues indicating trial condition and the scalp distribution depicting the switch-stay difference 300-400 ms after switch vs stay cue.

*Figure 3.* ERPs (negative up) at Fz following feedback and the scalp distribution depicting the correct-incorrect difference 290-360 ms after feedback.

*Figure 4.* ERPs (negative up) at Pz following correct feedback in trial sequence after a task switch

*Figure 5.* ERPs (negative up) at Cz/Pz following task condition cues and scalp distributions depicting the switch minus stay difference 300 to 400 ms after audio task switch and stay cues for children high and low in irritability. Note: A median split of irritability was used for illustrative purposes. Analyses used continuous measures of irritability.

*Figure 6.* Significant interaction between SwP and TMT set-shifting latencies in predicting the parent-reported childhood irritability. Slower and faster TMT set-shifting latencies are one standard deviation above and below the mean. SwP = switch positivity; TMT = trail-making task.

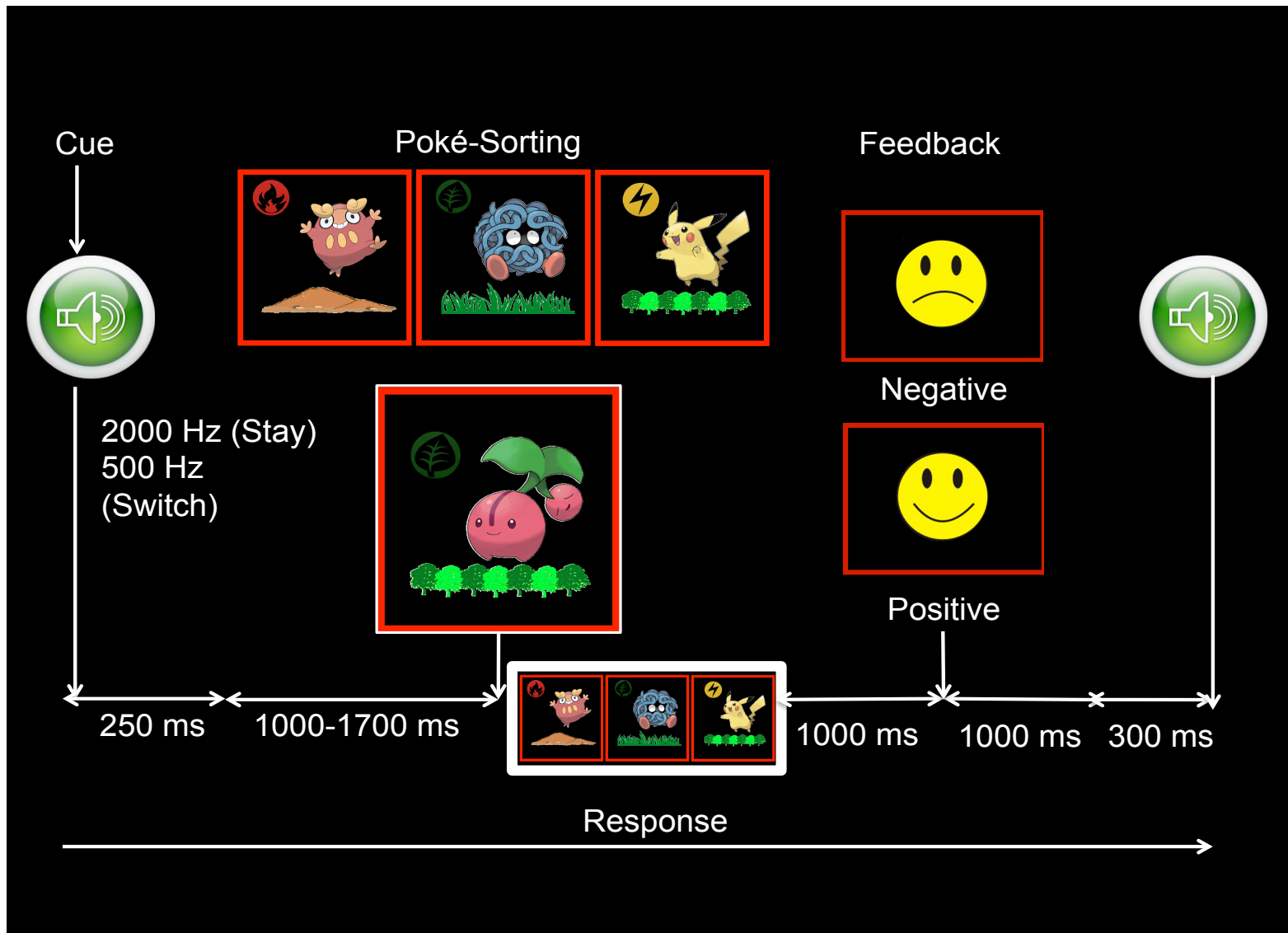
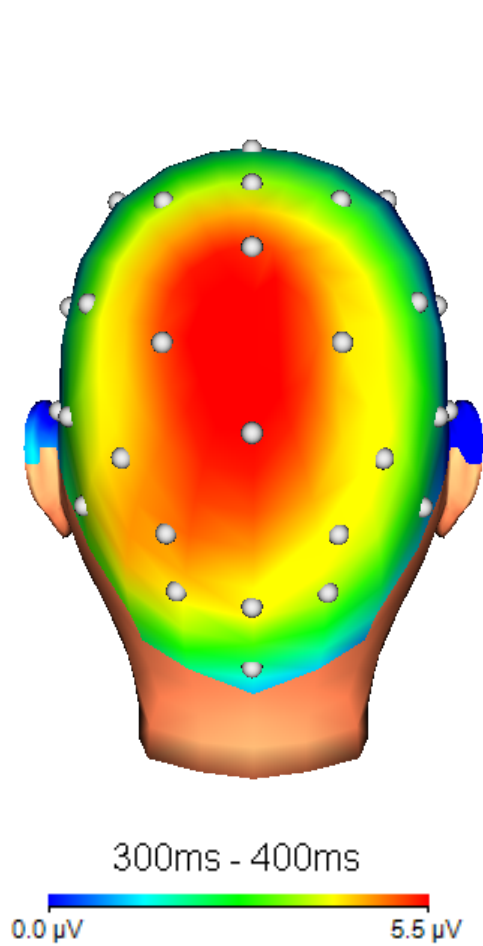


Figure 1. Schematic diagram of the PokéSort Task.



## Switch Positivity ( $\Delta\text{SP}$ )

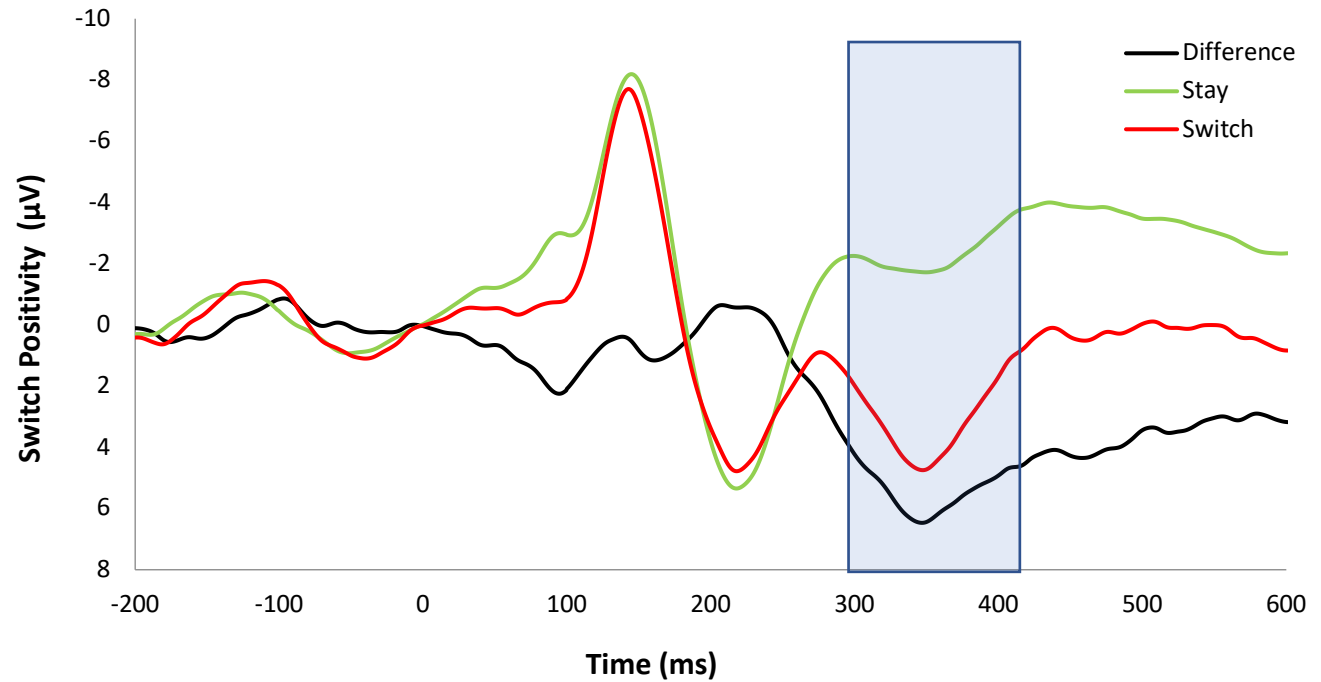
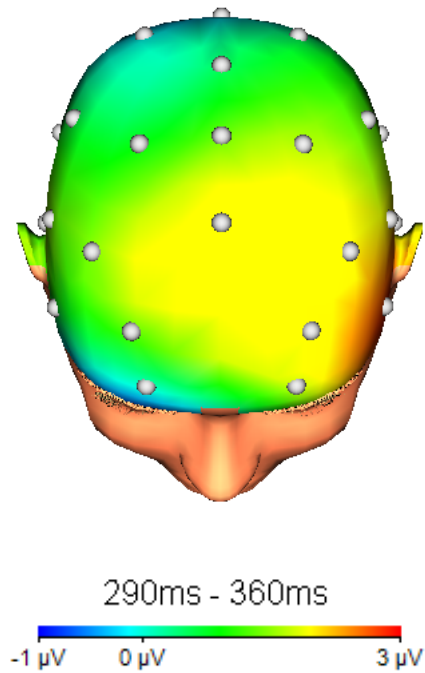


Figure 2. ERPs (negative up) at Cz/Pz following audio cues indicating trial condition and the scalp distribution depicting the switch-stay difference 300-400 ms after switch vs stay cue.





### Reward Positivity ( $\Delta$ RewP)

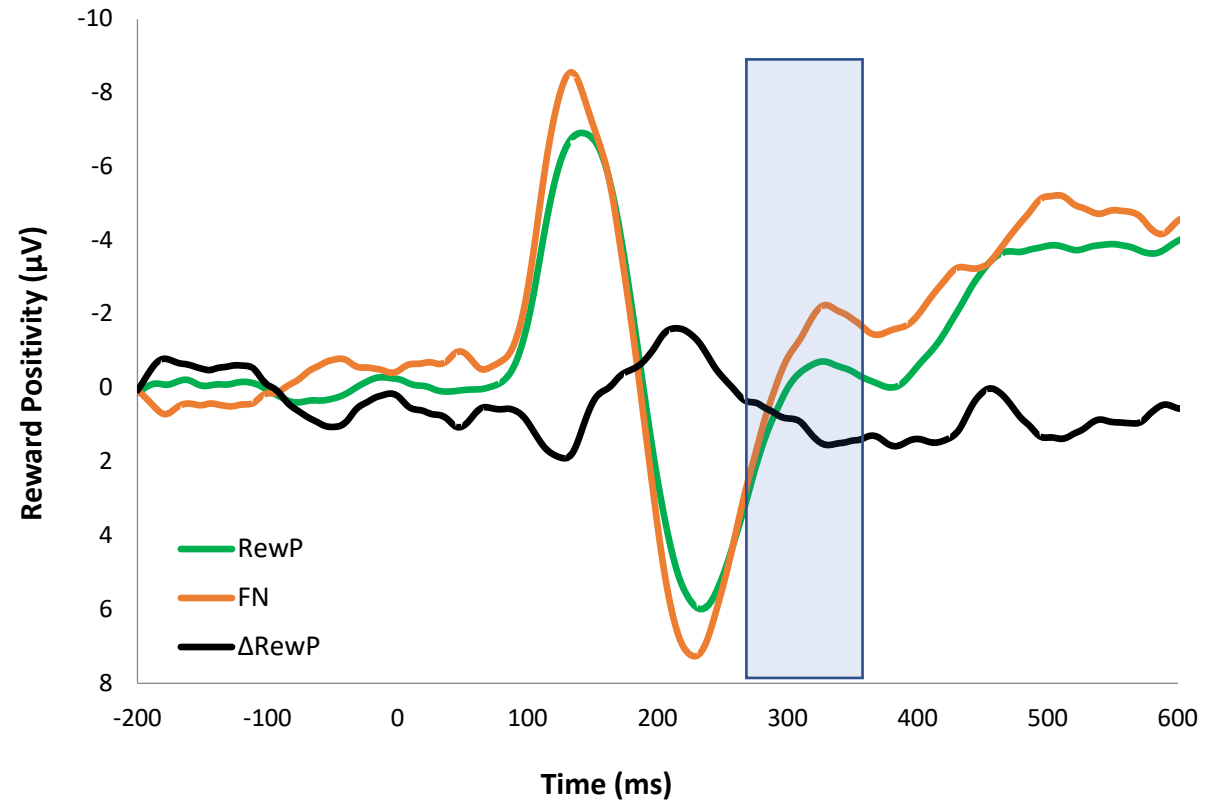


Figure 3. ERPs (negative up) at Fz following feedback and the scalp distribution depicting the correct-incorrect difference 290-360 ms after feedback.

# P3b

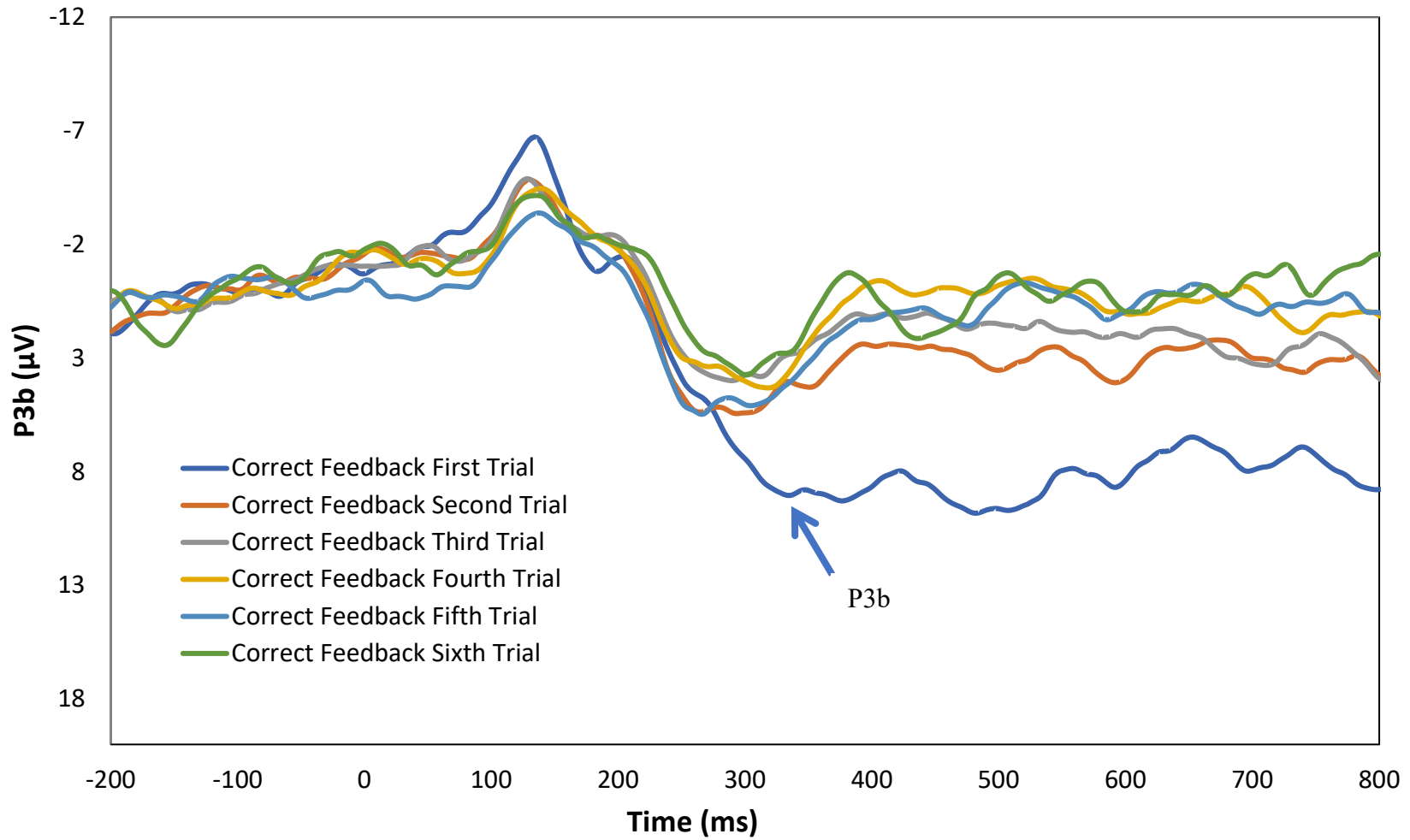
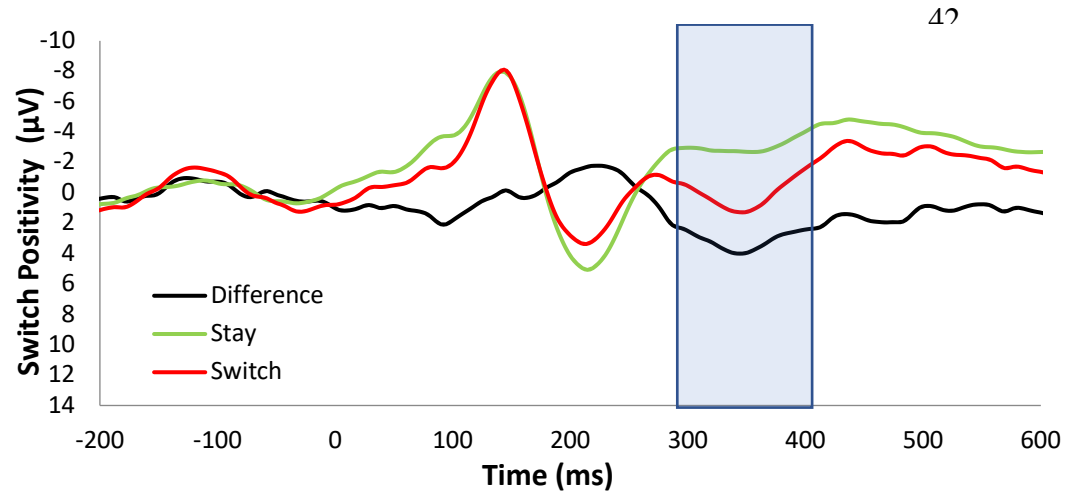
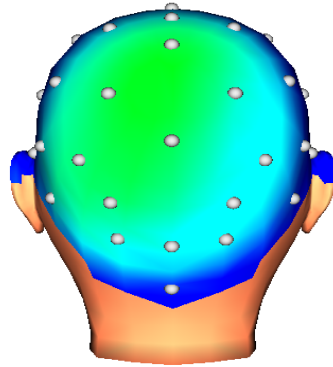


Figure 4. ERPs (negative up) at Pz following correct feedback in trial sequence after a task switch.

High Irritability



Low Irritability

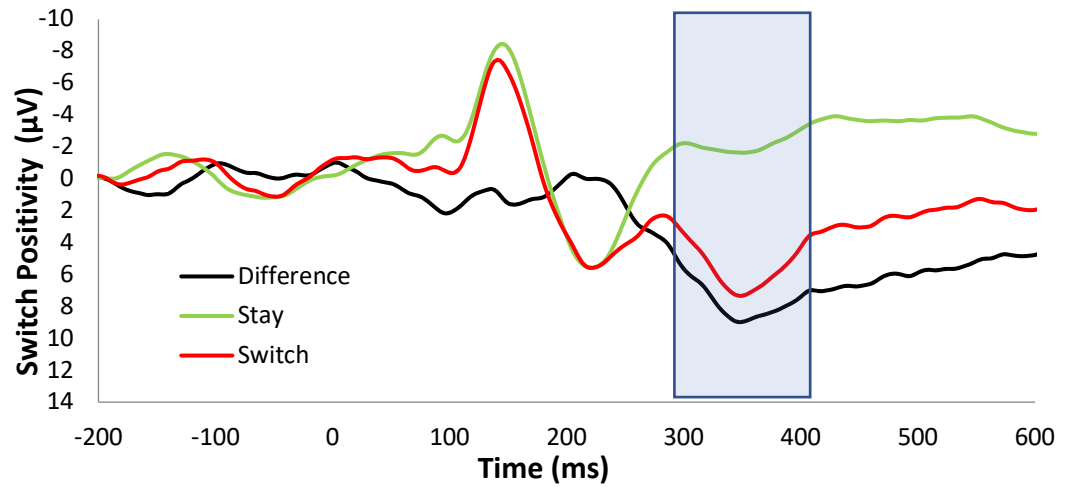
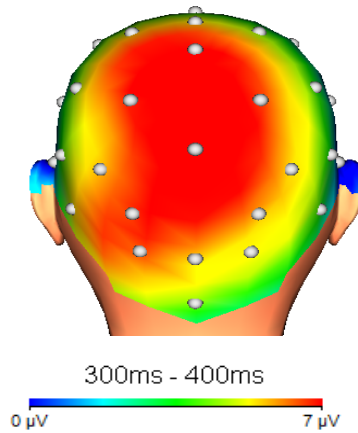
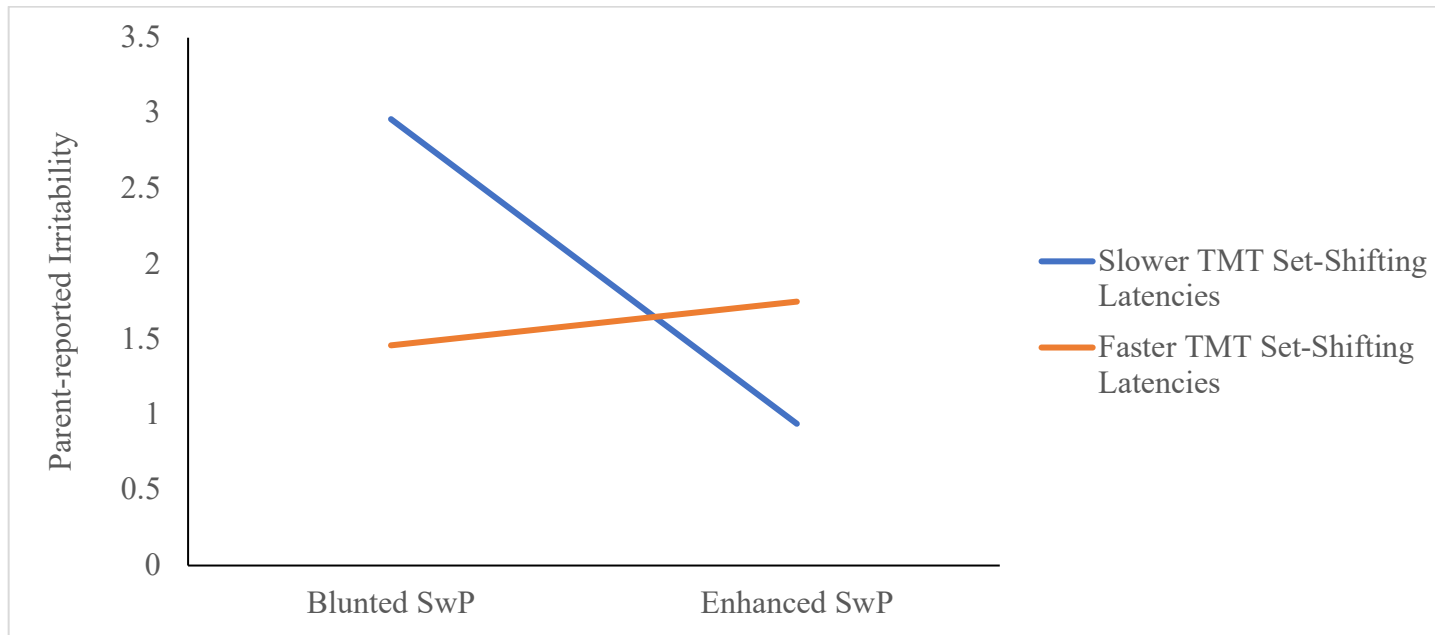


Figure 5. ERPs (negative up) at Cz/Pz following task condition cues and scalp distributions depicting the switch minus stay difference 300 to 400 ms after audio task switch and stay cues for children high and low in irritability. Note: A median split of irritability was used for illustrative purposes. Analyses used continuous measures of irritability.



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