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SPECIAL ISSUE: FIFTY YEARS OF P300: WHERE ARE WE NOW?

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Significance?... Significance! Empirical, methodological, and theoretical connections between the late positive potential and P300 as neural responses to stimulus significance: An integrative review

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Abstract

Event-related potential studies of emotional processing have focused on the late positive potential (LPP), a sustained positive deflection in the ERP that is increased for emotionally arousing stimuli. A prominent theory suggests that modulation of the LPP is a response to stimulus significance, defined in terms of the activation of appetitive and aversive motivational systems. The current review incorporates experimental studies showing that manipulations that alter the significance of stimuli alter LPP amplitude. Complementing these within-person studies, also included is individual differences research on depression wherein the LPP has been used to study reduced neural sensitivity to emotional stimuli. Finally, the current review builds an existing framework that the LPP observed in studies in emotional processing and the P300 observed in classic oddball studies may reflect a common response to stimulus significance. This integrative account has implications for the functional interpretation of these ERPs, their neurobiological mechanisms, and clinical applications.

KEYWORDS

cognition, emotion, late positive potential, LPP, P300, significance

1 | HISTORICAL INTRODUCTION: EVENT-RELATED POTENTIALS AND THE STUDY OF EMOTION

There is a long history of using event-related potentials (ERPs) to study the time-course of emotional processing. Compared to neutral stimuli, emotionally evocative stimuli modulate a broad range of ERPs, beginning with early perceptual processing and continuing to later stages that involve elaborative processing and sustained attention (Hajcak, Weinberg, MacNamara, & Foti, 2012). Many studies have focused on these later stages of processing, as captured by the late positive potential (LPP). Figure 1 illustrates the prototypical LPP waveform elicited by affective stimuli (left panel). The LPP is a sustained positive deflection in the ERP waveform that typically begins within 300 ms after stimulus onset, is increased for emotionally evocative (i.e., appetitive and aversive vs. neutral) stimuli, and is maximal at centroparietal electrodes.

Basic affective neuroscience studies have utilized the LPP as a neural index of emotional reactivity and regulation (Hajcak, Dunning, Foti, & Weinberg, 2014). In these studies, changes in LPP amplitude indicate the relative degree of emotional reactivity across different stimulus types (e.g., contrasting appetitive or aversive images that differ in

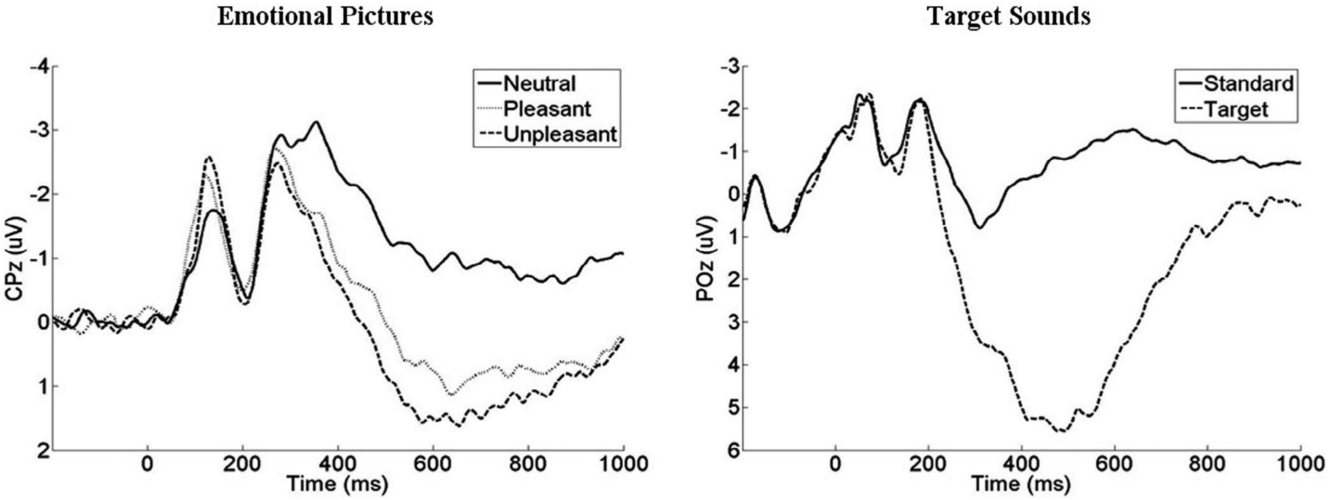

FIGURE 1 ERPs from 27 individuals who passively viewed neutral, pleasant, and unpleasant pictures (left) and responded to target compared to standard sounds (right). The LPP (left) is evident as a sustained positivity over midline central-parietal recording sites; the P300 (right) is a more transient midline positivity over parietal-occipital recording sites

semantic content) and regulation strategies (e.g., contrasting cognitive reappraisal with passive viewing). In addition, the time-course of the LPP can be used to track the dynamic allocation of attention to emotional stimuli, again as a function of stimulus type or regulation strategy. In this way, the LPP is well-suited to characterize affective chronometry within the first few hundred milliseconds—and up to several seconds—upon encountering an emotionally evocative stimulus.

Complementing this work, clinical neuroscience studies have utilized the LPP as an indicator of abnormal emotional processing in psychopathology. Nearly every psychiatric disorder is characterized by a form of dysregulated affect, and identifying disorder-specific versus transdiagnostic deficits is a challenge. The LPP provides an objective indicator of emotional reactivity that complements other measures of clinical symptoms, self-reported affective experience, and outward expressions of affect. Differences in the LPP across diagnostic groups or in relation to specific illness features can help parse complex psychopathology based on the nature of dysregulated affect in those populations (Foti, Novak, Hill, & Oumeziane, 2018; Weinberg, Perlman, Kotov, & Hajcak, 2016).

The current manuscript provides a selective review of the LPP literature on normal and abnormal emotional processing. The review includes seminal studies that have shed light on the stimulus characteristics and task parameters that shape emotional processing and, in turn, alter LPP amplitude and time course. This work is grounded within a theoretical account of the LPP as an index of stimulus *significance*, meaning the extent to which a stimulus activates appetitive or aversive motivational systems in the brain (Bradley, 2009). From this perspective, significance can be understood to vary across contexts (i.e., manipulated within an experiment) as well as across individuals (i.e., modulated in relation to a personality trait or psychological disorder). As an example of the clinical applications of this framework, the current review highlights recent studies in which the LPP amplitude has been used to characterize reduced emotional reactivity among individuals with depression. This review concludes with general comments on the way in which LPP studies of emotional processing may be directly integrated with the broader ERP literature on cognition.

2 | SEMINAL STUDIES

2.1 | Motivated attention to emotional stimuli

Decades ago, several researchers reported that emotional images elicit an enhanced positivity, commonly referred to at the time as the late positive complex (Johnston, Miller, & Burleson, 1986; Lifshitz, 1966; Radilova, 1982). Critically, this modulation of the ERP waveform was observed even when such stimuli were neither targets nor infrequent, task parameters known to also elicit an enhanced positivity. Similar results were subsequently reported using emotional adjectives (Naumann, Bartussek, Diedrich, & Laufer, 1992), faces (Allison, Puce, Spencer, & McCarthy, 1999; Cacioppo, Crites, Berntson, & G. H. Coles, 1993), and even lines conditioned to have emotional meaning (Begleiter, Porjesz, & Garozzo, 1979). These early data suggested that emotional content itself is sufficient to potentiate the ERP waveform during the first few hundred ms of stimulus processing.

More broadly, it is well-established in psychophysiological research that the processing of emotional content elicits changes across a wide range of measures, including heart rate and skin conductance (Bradley & Lang, 2000). Because of the relatively slow time-course of these peripheral measures, psychophysiological studies of emotional processing have often involved presenting stimuli for relatively long durations, as compared with cognitive studies utilizing relatively simple stimuli (e.g., geometric shapes, tones). For example, a highly influential paradigm from Cuthbert, Schupp, Bradley, Birbaumer, and Lang (2000) presented emotional images for several *seconds* while psychophysiological measures were recorded. They examined ERPs that spanned a full six seconds following the presentation of pleasant, neutral, and unpleasant pictures. Notably, they referred to the sustained positive deflection following pleasant and unpleasant stimuli as the LPP. Although they only quantified the LPP during the first 1,000 ms of picture presentation, it was evident from their figures that the increased LPP to emotional stimuli was much more protracted. Moreover, Cuthbert and colleagues (2000) found evidence of coordination between LPP amplitude, autonomic systems, and subjective affective experience: increased LPP amplitude to pleasant and unpleasant images (i.e., emotional arousal, as opposed to valence) was related to self-reported arousal ratings and skin conductance response. This study laid the groundwork for interpreting the LPP as an indicator of the sustained allocation of attention toward emotionally evocative stimuli, "reflecting activation of motivational systems in the brain that simultaneously prompt autonomic arousal, emotional facial expression, and reports of affective experience." (p. 109).

2.2 | LPP amplitude as an indicator of stimulus significance

From the perspective of affective science, emotional *content* is important because it conveys information about potential threats and opportunities that are salient to an organism's survival. Emotional content naturally captures attention—often irrespective of the goal at hand—and facilitates action tendencies to approach or avoid. That is, emotional stimuli do not need to be designated as targets or made task-relevant in order to capture attention; instead they function as natural targets. Bradley argues that the LPP is a neural response indicating that *significance* has been detected in the environment (2009). She defines significance in terms of the "activation of cortico-limbic appetitive and defensive systems that mediate the sensory and motor processes that support perception and action" (p. 9). Thus, emotional content elicits an increased LPP because it activates appetitive or aversive motivational systems. Consistent with this view, there is evidence to suggest that the LPP relates to activation in both cortical (e.g., occipital, parietal, and temporal cortices) and subcortical (e.g., amygdala, ventral striatum) neural areas involved in emotional processing as measured using fMRI (Keil et al., 2002; Liu, Huang, McGinnis-Deweese, Keil, & Ding, 2012; Sabatinelli, Keil, Frank, & Lang, 2013; Sabatinelli, Lang, Keil, & Bradley, 2006).

This framework postulates that the key stimulus dimension that modulates LPP amplitude is *significance*, and that indicators of this construct include subjective ratings of arousal, autonomic response (i.e., skin conductance, pupil dilation), and activation of specific neural circuits. It is notable that in studies of emotional processing, specific stimuli are often chosen based on normative ratings of subjective valence and arousal—but not significance per se. Hence, while significance can be expected to correlate with arousal (i.e., highly arousing stimuli, regardless of valence, will often be high in significance), they are at least somewhat separable dimensions. Although affiliative, erotic, and exciting sports images are generally rated high in emotional arousal, affiliative and erotic images strongly modulate LPP amplitude whereas exciting sports images (e.g., skydiving) do not (Weinberg & Hajcak, 2010). Indeed, other studies have shown that erotic stimuli elicit increased skin conductance (Bradley, Codispoti, Cuthbert, & Lang, 2001) and greater neural activation using fMRI (Bradley et al., 2003) as compared to exciting sports images. These data suggest that erotic and affiliative images activate appetitive motivational systems to a greater extent, on average, compared to exciting sports images—because they are more significant.

Although most neutral stimuli are low in significance, there are notable exceptions. For example, neutral images containing people elicit a larger LPP compared to neutral images that do not contain people (Ferri, Weinberg, & Hajcak 2012). Further, even when considering the neural response to people, the LPP is potentiated to faces of relatives (Grasso & Simons, 2011), faces of romantic partners (Burdwood & Simons, 2016), as well as one's own name and face (Tacikowski & Nowicka, 2010). Bradley's (2009) operationalization of significance in terms of activation of motivational systems provides a framework for understanding this variability in the LPP across stimulus types.

A direct test of the significance framework would be to select stimuli based on this dimension (e.g., ratings of significance) rather than arousal or valence and test whether this optimizes the correlation with LPP amplitude. We describe effects on LPP amplitude in relation to emotional content and strategies of emotion regulation (i.e., contrasting emotional vs. non-emotional stimuli, or contrasting regulation vs. passive viewing conditions). While these studies have explicitly been interpreted with regard to emotional processing broadly, the current review indicates how these findings can be interpreted as effects of stimulus significance.

3 | EXPERIMENTAL FINDINGS

The above sections provide an overview of the history of emotional processing studies and the LPP, as well as framework for interpreting the LPP as a neural indicator of significance. We now review several notable experimental manipulations known to alter either the time-course or amplitude of the LPP. These findings have informed the understanding of LPP time-course, which itself is sensitive to manipulations of stimulus significance.

3.1 | The time-course of the LPP

Across many studies, it is clear that emotional content robustly potentiates the LPP for the duration of picture presentation and several seconds after picture offset (Hajcak & Olvet, 2008; Pastor et al., 2008). This sustained and increased LPP to emotional content has been studied in the context of emotionally significant pictures (Cuthbert et al., 2000; Foti, Hajcak, & Dien, 2009; Pastor et al., 2008; Schupp et al., 2000), faces (Schupp et al., 2004; Smith, Weinberg, Moran, & Hajcak, 2013), words (Fischler & Bradley, 2006; Kissler, Herbert, Winkler, & Junghofer, 2009; Speed, Levinson, Gross, Kiosses, & Hajcak, in press), and hand gestures (Flaisch, Häcker, Renner, & Schupp, 2010).

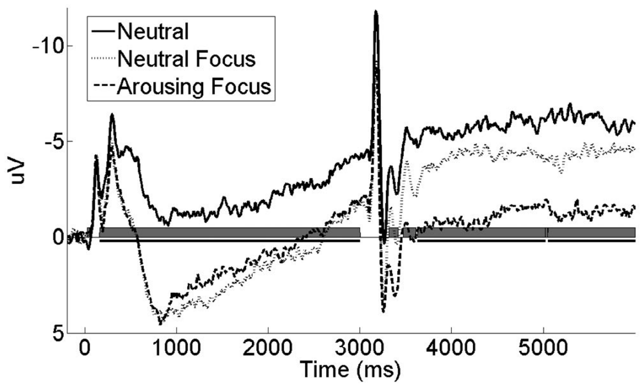

FIGURE 2 Manipulating stimulus significance through directed attention: Grand averaged ERPs at central–parietal recording sites elicited by neutral pictures (solid line) and unpleasant pictures (dotted and dashed lines). Picture onset occurred at 0 ms, and the first 3,000 ms of each trial involved passive viewing. At 3,000 ms, an instruction was presented to focus on a neutral aspect of the unpleasant picture (dotted line) or an arousing aspect of the unpleasant picture (dashed line). Neutral pictures were always associated with an instruction to focus on a neutral aspect of the picture. Shaded regions above the *x*-axis indicate significant differences ($p < .05$) between the LPP elicited by unpleasant and neutral pictures prior to the attentional instruction (0–3,000 ms) and significant reductions in the LPP following attentional instructions (3,000–6,000 ms). The presence of a solid line below the *x*-axis indicates periods of time in which the conditions differed from one another based on the number of successive significant *t* tests. Reprinted from Hajcak et al. (2009) with permission

The term LPP describes the protracted slow-wave elicited by emotional compared to neutral stimuli. This choice in nomenclature reflects the fact that the LPP appears to have a distinct time-course compared to the positivity studied in traditional cognitive tasks of attention and target detection. Figure 2 illustrates ERP data in which emotional content was shown to robustly potentiated the LPP by 160 ms after picture onset (Hajcak, Dunning, & Foti, 2009). The LPP does not *only* reflect a "late" ERP difference between emotional and neutral stimuli. Rather, the morphological difference between the canonical ERP waveform to target stimuli and the LPP is *duration*: typical ERP responses to target stimuli are relatively transient, whereas the LPP is evident as a more protracted positive potential.

We have argued that the protracted increase in the LPP reflects the relatively automatic and *sustained* engagement with emotionally significant content (Hajcak et al., 2012; Weinberg, Ferri, & Hajcak, 2013). But why does emotional content elicit such a protracted LPP? A straightforward answer is that a potential threat or opportunity continues to be significant for as long as it persists before an organism. If emotionally significant stimuli sustain engagement and attention for the duration of their presentation, this should be evident in other measurement domains. The resulting hypothesis is that the LPP reflects the *continued* activation of cortico-limbic appetitive and defensive systems *throughout the duration of stimulus presentation*.

Consistent with the view that emotional content sustains the engagement of motivational circuits, Schupp and colleagues (1997) presented an irrelevant but loud auditory probe several seconds after the presentation of emotional and neutral pictures (i.e., during the period in which the sustained LPP would be evident) and found that the target ERP response elicited by the auditory probe was reduced when participants were viewing emotional compared to neutral pictures. These data suggest that the sustained engagement with emotional picture content interferes with the processing of salient startle probes.

Other work has attempted to more directly examine the relationship between the LPP and subsequent task interference using an emotional interrupt task (Mitchell, Richell, Leonard, & Blair, 2006). Participants categorized a target that is both preceded and followed by either emotional or neutral pictures. For instance, participants might see a picture of a lamp presented for 1,000 ms, then a target such as a circle or a square presented for 400 ms, and then the lamp is presented again for 400 ms. Participants are slower to perform the categorization task when targets follow emotional compared to neutral pictures (Mitchell et al., 2006). Moreover, ERP studies using this task have found that a larger LPP to the distractor image predicted a reduced ERP response to the subsequent target stimulus—an effect that was evident both between- and within-subjects (Stange et al., in press; Weinberg & Hajcak, 2011).

Participants characterized by a larger LPP on average tended to have smaller subsequent target ERPs. Additionally, smaller target ERPs were preceded by trials with a larger LPP. There was a reciprocal relationship between the LPP to task-irrelevant stimuli and the subsequent ERP elicited by targets. Thus, a functional similarity between the LPP and other ERP indicators of attention was found, such that these components appear to rely on shared resources required to process significant stimuli.

3.2 | The amplitude of the LPP and manipulations of significance

Most work linking the LPP to variability in stimulus significance examined the LPP elicited by emotional (pleasant and unpleasant) versus neutral content or in terms of more fine-grained subtypes of emotional stimulus content. Building upon this foundational work, in a series of studies we examined whether it is possible to *manipulate* the significance of specific stimuli, and thereby alter the LPP. An initial study assessed the relatively subtle manipulation: participants were presented with emotional and neutral pictures, and participants had to either make an emotional (Is this emotional or neutral?) or non-emotional (How many people are in the picture?) decision about the picture (Hajcak, Moser, & Simons, 2006). The LPP was reduced when participants made non-emotional compared to emotional decisions, which is consistent with the possibility that drawing attention to non-emotional features might reduce the significance of picture content (Hajcak et al., 2006).

Subsequent studies tested whether participants could explicitly alter the significance of picture content based on task instructions (Moser, Hajcak, Bukay, & Simons, 2006). Figure 3 illustrates participants that were trained to do reappraisal, which is the act of reinterpreting the meaning of unpleasant picture content to reduce subjective emotional response (Hajcak & Nieuwenhuis, 2006). After seeing a picture of an automobile accident, reappraisal might involve thinking about the possibility that no one was seriously injured. Emotional content, in this case, is not less relevant to the task; rather, reappraisal involves altering the *meaning* of that content. To assess whether reappraisal could alter the LPP, participants viewed unpleasant pictures that were followed by an instruction to either "reinterpret" (reappraise picture meaning to reduce the subjective negative emotions) or "attend" (focus on natural and initial emotional responses to the picture). The original picture was then presented again, and the LPP was measured in this second presentation. Figure 3 presents the data and illustrates how the LPP was reduced following reappraisal instructions—an effect was evident throughout the duration of picture presentation (Hajcak & Nieuwenhuis, 2006). Hence, the LPP is sensitive to reappraisal of emotional content (Krompinger, Moser, & Simons, 2008; Langeslag & Sanchez, 2018; Paul, Simon, Kniesche, Kathmann, & Endrass, 2013; Thiruchselvam, Blechert, Sheppes, Rydstrom, & Gross, 2011). While these studies focused primarily on the immediate impact of reappraisal on LPP amplitude, Thiruchselvam and colleagues (2011) examined the enduring effect of reappraisal on later encounters with the images. They found that the LPP was reduced when previously reappraised pictures were viewed 30 min later. The effect of reappraisal also appears sensitive to individual differences in emotion regulation, such that effects on LPP amplitude are larger among individuals who report

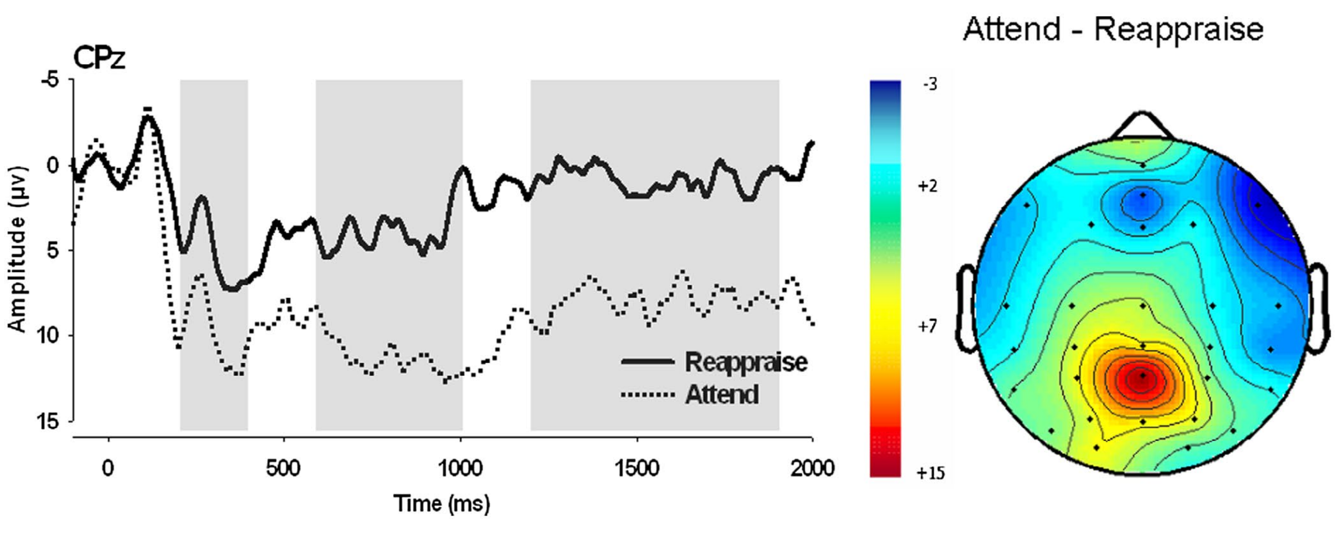

FIGURE 3 Manipulating stimulus significance through cognitive reappraisal: ERP waveforms at electrode CPz associated with unpleasant stimuli in the reappraise and attend conditions of the emotion regulation block (left). Shaded gray areas represent 100 ms windows in which the reappraise LPP differed reliably from the attend LPP. Voltage map for the attend minus reappraise comparison at 700 m (right). Reprinted from Hajcak and Nieuwenhuis (2006) with permission

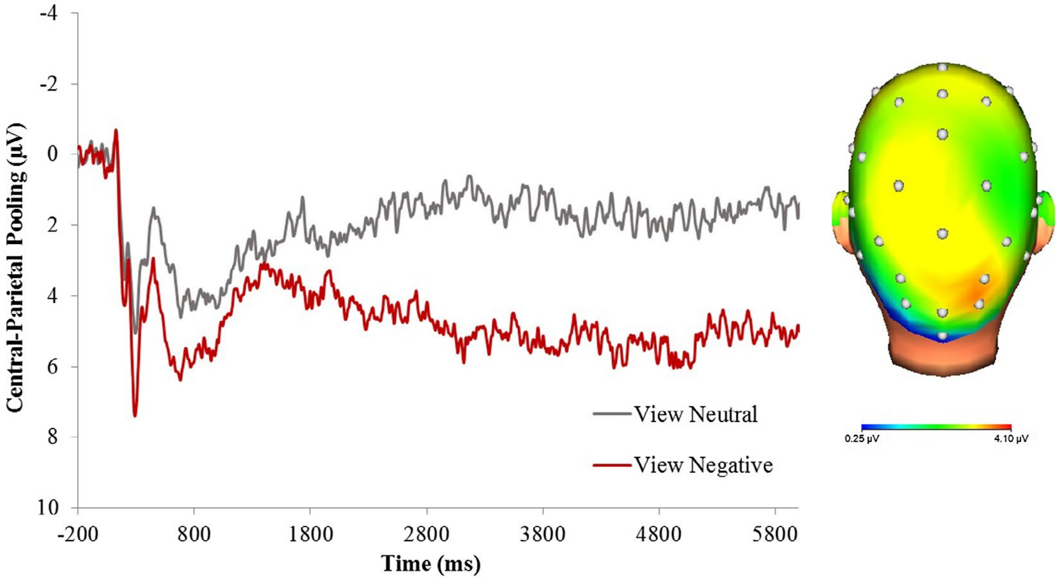

FIGURE 4 Stimulus significance of ideographic stimuli related to autobiographical memories: Grand-average ERP waveforms and head maps to negative and neutral keyword presentation during Block 1 of passive viewing in the AERT task. The LPP waveforms (left) were pooled across electrode sites Pz, Cz, CP1, and CP2. The head map (right) displays the difference between negative and neutral word presentation in Block 1. Negative keywords were associated with a sustained increase in the late positive potential. Reprinted from Speed et al. (in press) with permission

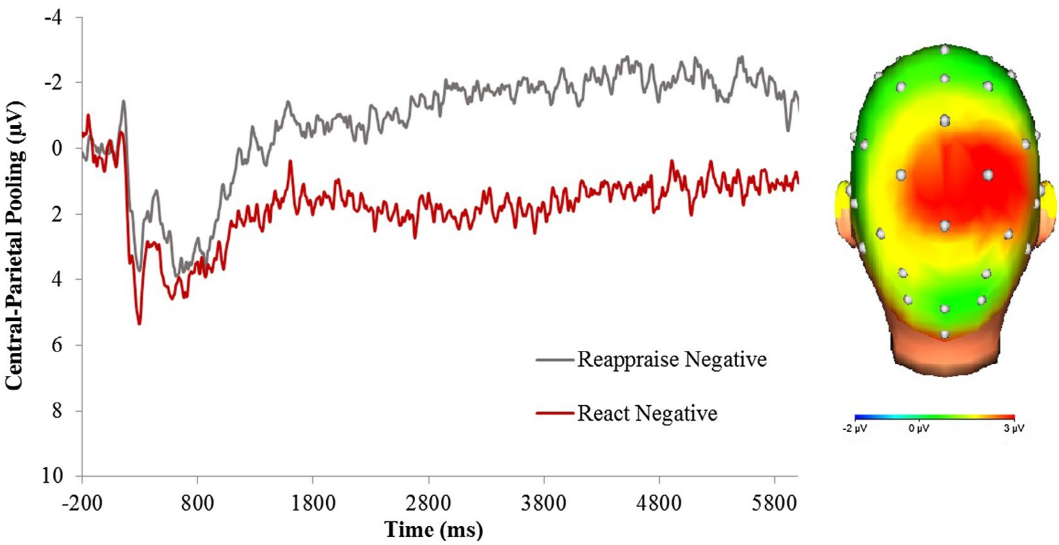

FIGURE 5 Manipulating the stimulus significance of autobiographical memories through reappraisal: Grand-average ERP waveforms and head maps to negative keyword presentation during the AERT task in react and reappraise blocks. The LPP waveforms (left) were pooled across Pz, Cz, CP1, and CP2 electrode sites. The head map (right) displays the difference between react and reappraise trials. Negative keywords presented in the reappraise condition were associated with a reduced late positive potential relative to negative keywords presented in the react condition. Reprinted from Speed et al. (in press) with permission

more frequent use of reappraisal (Moser, Hartwig, Moran, Jendrusina, & Kross, 2014).

A recent study explored reappraisal using an autobiographical emotion regulation task, with the LPP waveforms presented in Figures 4 and 5. The aim was to test whether the LPP elicited by idiographic verbal stimuli could be reduced through reappraisal (Speed et al., in press). First, participants wrote about four recent autobiographical situations: two were neutral, and two were events associated with intense negative emotions. Participants then identified 10 words that were strongly and uniquely related to each situation. As depicted in Figure 4, during an initial viewing session, words linked to a negative story elicited a potentiated LPP compared to words related to the neutral situation. Participants then were instructed to reappraise one of the situations using examples and detailed instructions. Finally, participants viewed negative words related to the reappraised situation and to words related to the other (non-reappraised) situation, in a counter-balanced order. As depicted in Figure 5, words related to the reappraised situation were associated with an attenuated LPP such that reappraising an unpleasant autobiographical memory resulted in a reduced LPP to cues related to the memory. This finding extends previous work, which focused primarily on the processing of normative emotional stimuli encountered for the first time. Therefore, reappraisal altered the significance of emotional stimuli related to autobiographical memories, showing these internal representations are also sensitive to manipulations of significance.

Across these studies, there are several potential pitfalls in interpreting reappraisal-related effects on the LPP. First, when given a general instruction to reappraise, it is not clear what participants are actually doing on each trial. The manipulation, in this case, is considered successful because LPP amplitude is reduced for reappraise versus attend conditions. Presumably, the act of reappraisal reduces the significance of the stimulus and the LPP. Other interpretations, however, also warrant consideration: Participants might be distracting themselves or even struggling to do reappraisal. In fact, reappraisal is generally more cognitively challenging than the control condition such as passive viewing, implying that reappraisal-related effects may reflect differences in task difficultly rather than a manipulation of stimulus significance per se.

Indeed, across multiple studies, the LPP has been found to be reduced under conditions of increased cognitive load. MacNamara, Ferri, and Hajcak (2011) presented participants with task-irrelevant neutral and unpleasant pictures during a working memory task. The LPP across both neutral and unpleasant pictures was reduced for high compared to low load trials (see MacNamara, Schmidt, Zelinsky, & Hajcak, 2012, for similar results using facial stimuli). These results are consistent with neuroimaging data in which increased working memory load both activates prefrontal regions and decreases activation in motivation-related neural circuits (Van Dillen, Heslenfeld, & Koole, 2009). Potential differences in task difficulty between reappraise and control conditions, therefore, might explain some between-condition variation in the LPP. Gan, Yang, Chen, Zhnag, and Yang (2017) found that high working memory load *attenuated* the impact of reappraisal on the LPP as the effects of reappraisal were only evident in only a low working memory load condition.

One way to control for the effect of task difficulty in reappraisal is to provide the relevant interpretation to participants on each trial before viewing stimuli, or preappraisals. In two initial studies, a brief audio description of the upcoming picture was presented on each trial, and the description manipulated whether unpleasant pictures were described in more or less negative terms (Foti & Hajcak, 2008; MacNamara, Foti, & Hajcak, 2009). One picture (IAPS # 6212) was preceded either by “This soldier notices the child and does not shoot” or “This child is about to be shot and killed by a soldier.” Neutral pictures were always described in neutral terms. These auditory *preappraisals* were intended to make unpleasant picture content more or less emotionally significant in a way similar to reappraisal, with two important methodological differences: First, preappraisal was not associated with task difficulty differences inherent in studies of reappraisal, and second, preappraisal was a more controlled manipulation of stimulus meaning relative to reappraisal.

In addition, the LPP elicited by unpleasant pictures was reduced when preceded by less negative descriptions (Foti & Hajcak, 2008). A subsequent report replicated this effect and also found that it was similarly possible to *increase* the LPP elicited by neutral pictures if they were preceded by more negative descriptions (e.g., “This hammer was used as a weapon in a murder.” MacNamara et al., 2009). In a final study, participants were again presented with description-picture pairs, and the LPP was measured nearly 30 min later in response to the pictures presented in isolation; no audio descriptions occurred during the second stimulus encounter. The LPP continued to be affected by the previously paired description (MacNamara, Ochsner, & Hajcak, 2010), suggesting that these preappraisal altered both how the stimuli were initially encoded as well as the response to re-encountering the stimuli.

Several studies have replicated and extended the effects of preappraisal on the LPP. Van Cauwenberge and colleagues (2017) reported evidence that preappraisal could reduce the LPP in 12 to 15 year-olds. Qi and colleagues (2016) replicated preappraisal effects, and found that the effect on LPP amplitude was smaller for trait anxious individuals. Neutral and mutilation pictures were irrelevant to the task but described beforehand to participants as either as being fictitious or real. Even though distractors in both the “real” and “fictitious” conditions were gruesome, only pictures in the “real” condition potentiated the LPP and caused behavioral interference (Mocaiber et al., 2010). Similarly, threatening information presented prior to neutral faces can potentiate the LPP (Klein, Iffland, Schindler, Wabnitz, & Neuner, 2015), as can fabricated emotional intensity ratings of neutral faces from other people (Willroth, Koban, & Hilimire, 2017). In sum, these studies indicate that the *interpretation* of picture content drives the amplitude of the LPP; stimulus significance is determined by picture meaning, which is at least partially malleable.

An extension of this framework is that meaning-based manipulations may alter the way in which unpleasant pictures are visually explored, such that a shift in meaning might cause a different pathway of stimulus exploration. Indeed, most unpleasant pictures are relatively complex stimuli that contain both emotion-laden content (a knife pressed against a person's neck), as well as relatively mundane content (a wristwatch on the arm holding said knife). Participants naturally tend to fixate first and longest on the most emotionally intense part of unpleasant pictures (Ferri, Schmidt, Hajcak, & Canli, 2013). Van Reekum and colleagues (2007) demonstrated that reappraisal instructions altered how participants *viewed* unpleasant pictures: When participants were instructed to reappraise unpleasant stimuli, they tended to fixate more on relatively neutral and non-emotional parts of unpleasant pictures. These interpretations are not mutually exclusive, since reappraisal may alter both stimulus exploration *and* meaning, and these processes may interact with one another. LPP amplitude likely reflects the combined effects of these processes: the specific content explored, as well as the derived meaning.

To examine stimulus exploration, a series of experiments examined the impact of *manipulating* visual-spatial attention *within* unpleasant pictures on the LPP (Dunning & Hajcak, 2009; Hajcak et al., 2009; Hajcak, MacNamara, Foti, Ferri, & Keil, 2013). In the first published report of this kind, participants were presented with neutral and unpleasant pictures for 6,000 ms (Dunning & Hajcak, 2009). During the first half of the trial (0–3,000 ms), attention was directed to specific areas of the picture with a blue circle; that blue circle was removed for the second half of each trial. In a second study, the structure of the trial was reversed: the initial 3,000 ms was a "free viewing" period, and attention was instead directed in the second half of each trial. In both experiments, participants were instructed to only look within the blue circle as long as it was on the screen, although they could look anywhere within the picture when there was no blue circle. Critically, attention was directed to either emotionally arousing or emotionally neutral portions of unpleasant pictures. In both studies, directing attention to non-arousing aspects of unpleasant images reduced the LPP. In fact, directing attention to non-emotional foci *eliminated* the difference between unpleasant and neutral pictures. These results indicated a prominent role for visual-spatial attention in determining LPP amplitude, such that the strength of the neural response may be driven largely by the specific content that is being attended to at a moment in time.

These findings were replicated and extended in a study that did not utilize circles to direct attention (Hajcak et al., 2009). Instead, a brief auditory stimulus (500 Hz or 1,000 Hz tone) was presented 3,000 ms after picture presentation that served as a cue to attend to more or less emotional aspects of unpleasant pictures. In contrast to circles to constrain attention, participants were free to choose the portions of the image that they found to be more or less emotionally intense. Figure 2 illustrates how the LPP was reduced following tones that directed attention to less arousing aspects of pictures, and that this reduction of the LPP was evident approximately 600 ms after the presentation of that tone. The time-course of the LPP was leveraged to quantify when in time the visual attention manipulation began to reduce the significance of the image. Thiruchselvam, Hajcak, and Gross (2012) had participants direct their visual attention to more or less arousing aspects of pictures *that were being held in working memory* rather than being viewed at the time. A similar modulation of the LPP was found: when participants directed attention to a less emotional aspect of a picture being held in working memory, the LPP was reduced compared to when participants directed attention to a more emotional aspect of a picture being held in working memory.

Across these studies, manipulations that increase or decrease stimulus significance similarly modulate the LPP. Meaning-based, attentional, and working memory load manipulations all have been shown to reduce the activation of motivational neural circuits (Ochsner & Gross, 2005). An outcome that is consistent with the notion that variability in the amplitude of the LPP reflects stimulus significance and associated activation of motivational circuits. These findings suggest that effects traditionally understood to indicate successful emotion regulation operate directly on the motivational significance of the stimuli.

4 | THEORETICAL IMPLICATIONS

The majority of studies focus on the impact of within-subjects effects on the LPP (picture content, stimulus meaning, valence) and their psychological correlates of stimulus significance. We extrapolate from this literature in two ways, drawing connections with (a) individual differences research in emotional processing as indicated by LPP amplitude, and (b) potential neurocognitive mechanisms of LPP amplitude and attentional deployment more broadly.

4.1 | Depression and the LPP

In parallel with studies on within-subjects manipulations, LPP *between*-subject variability is increasingly being used in social and clinical psychology as an individual difference measure of emotional reactivity. Studies have found the LPP has good psychometric properties, including internal and test-retest reliability (Bondy et al., 2018; Kujawa, Klein, & Proudfit, 2013; Moran, Jendrusina, & Moser, 2013), and a twin study demonstrated moderate heritability of the LPP (Weinberg, Venables, Proudfit, & Patrick, 2014). These findings indicate that the LPP is well-suited as a neural index of trait and state differences in emotional processing across individuals. Major depressive disorder (MDD) is defined by a combination of affective, cognitive, and physical symptoms. Extending this phenotype to ERP research, a large corpus of research suggests that depression is associated with reduced neural reactivity to target stimuli (Bruder, Kayser, & Tenke, 2012; Klawohn, Santopetro, Meyer, & Hajcak, 2020), which has been interpreted as a neural marker of cognitive impairment in memory and other related processes. Other studies have focused on characterizing abnormal *emotional* processing in MDD. Whereas the cardinal symptoms of MDD are low mood and reduced positive affect spanning weeks to months, there have been competing accounts about how this broader affective disturbance alters emotional reactivity per se. In the context of emotional stimuli, early studies reported that individuals with MDD were characterized by a reduced LPP to emotional words (Blackburn, Roxborough, Muir, Glabus, & Blackwood, 1990) and images of dermatological disease (Kayser, Bruder, Tenke, Stewart, & Quitkin, 2000). In addition to more general cognitive deficits, these latter data suggest that depression may also be characterized by reduced attention to emotionally evocative stimuli.

Consistent with these earlier studies, the first study to explicitly focus on abnormal LPP modulation in depression found that adults with MDD exhibited reduced LPP modulation to fearful and angry faces. The difference between fearful/angry and neutral faces was reduced in the MDD group compared to controls (Foti, Olvet, Klein, & Hajcak, 2010). Adults with MDD did not show the typical within-subjects increase in LPP for negative relative to neutral faces. This pattern of results has been replicated using complex emotionally evocative scenes (Klawohn, Burani, Bruchnak, Santopetro, & Hajcak, in press; MacNamara, Kotov, & Hajcak, 2016; Weinberg et al., 2016). For instance, in this work, MDD was associated with a reduced LPP to *both* pleasant and unpleasant pictures, and this neural deficit was most pronounced among individuals who reported early-onset MDD prior to age 18 (Weinberg et al., 2016). A reduced LPP to both pleasant and unpleasant pictures was uniquely associated with increased self-reported suicidality, even when accounting for other MDD symptoms. In a subsequent study, a reduced LPP was more related to a reported history of suicide attempts than current suicidal ideation (Weinberg, May, Klonsky, Kotov, & Hajcak, 2017).

We interpret the reduced LPP to emotional picture content in MDD as reflecting emotional disengagement that is characteristic of the disorder (Proudfit, Bress, Foti, Kujawa, & Klein, 2015). This view is consistent with a larger body of work supporting the emotion context insensitivity theory of MDD (Rottenberg & Hindash, 2015). Specifically, across self-report, expressive behavior, and peripheral psychophysiological measures, individuals with MDD are characterized by *reduced* reactions to both pleasant and unpleasant stimuli (Bylsma, Morris, & Rottenberg, 2008).

In the context of Bradley's (2009) significance framework, these studies suggest that the pathophysiology of MDD involves a disruption in appetitive and aversive motivational systems, whereby they are not activated by stimuli that would typically classified as significant. A reduced LPP may further confer specific risk for suicide insofar as capacity for suicide may reflect decreased reactivity to threat (Joiner, 2007; Klonsky & May, 2014). Current MDD individuals may evince a reduced LPP to emotional stimuli and also reflect increased *risk* for MDD. Specifically, Kujawa and colleagues (2012) reported that 6 year-old children of mothers with a history of MDD were characterized by a reduced LPP to emotional compared to neutral faces (Kayser et al., 2017; Nelson, Perlman, Hajcak, Klein, & Kotov, 2015; Weinberg, Liu, Hajcak, & Shankman, 2015). Individuals at increased risk of MDD by virtue of having a first degree relative with MDD are characterized by a reduced LPP. Personality traits linked to MDD risk also were associated with a reduced LPP in a sample of more than 500 never-depressed adolescent girls (Speed et al., 2015; Weinberg & Sandre, 2018). Finally, a recent study tested the interaction between LPP amplitude and life stress in predicting depressive symptom onset (Levinson, Speed, & Hajcak, 2018). Life stress was associated with prospective increases in depressive symptoms among adolescent girls with a blunted LPP. That is, the combination of life stress and reduced LPP uniquely predicted a worsening of symptoms. These data suggest that reduced LPP amplitude to appetite and aversive stimuli reflecting reduced engagement with significant stimuli relate both to MDD and its risk.

4.2 | LPP, significance, context updating, orienting, and LC-NE theory

The current review has focused on the LPP and has not made reference to the P300, a parietal ERP elicited by target stimuli. By reviewing a theoretical framework and empirical findings on emotional processing, this review emphasizes what is "different" about emotion research as compared to classic oddball studies common in P300 research. However, these psychophysiological phenomena may not be different. Bradley (2009) argues that stimulus significance is the common process by which target stimuli in an oddball task elicit an increased P300 *and* by which emotionally evocative scenes elicit an increased LPP. Thus, despite separate literatures, the P300 and LPP may be inextricably linked and reflect the output of a common neural generator that responds to stimulus significance.

4.2.1 | Target status and emotional content

Cognitive research often employs the oddball paradigm, in which participants are instructed to count or button press each time an infrequent target stimulus is presented; however, participants do nothing when a frequent standard stimulus is presented. Figure 1 illustrates the prototypical P300 waveform elicited in this context (right panel). Stimulus-locked ERPs elicit a positivity following targets that is maximal at midline parietal/occipital recording sites. When the frequency of target and standard stimuli are equated, target stimuli still elicit a P300. When a single-stimulus is presented, the interval between targets determines the amplitude of the P300. In describing these effects, Donchin writes "we know that events that are task-relevant and rare elicit a large P300. The larger the probability, the smaller the P300. The more important the event, the larger the P300" (Donchin, 1981, p. 504). In the classic oddball paradigm, there is nothing *inherently* significant about the target stimulus; target significance is based on frequency and task demands.

Early emotional processing studies viewed the resulting ERP response as a modulated P300, even though in these instances emotional pictures were neither targets nor infrequent (Johnston et al., 1986; Lifshitz, 1966; Radilova, 1982). These results suggested that emotional stimulus content could enhance the P300 similar to target stimuli. In a study directly contrasting the effects of target status and emotional content, a visual oddball task was employed in which target and standard stimuli could be pleasant, neutral, or unpleasant pictures (Weinberg, Hilgard, Bartholow, & Hajcak, 2012). A P300 was larger for targets compared to standards. Moreover, P300 to both target *and* standard stimuli was increased in amplitude when picture content was emotional compared to neutral. Schupp et al. (2007) found a similar enhancement of the P300 when targets were emotional pictures. Both target status and emotional content potentiated P300, even when emotional content was both frequent and irrelevant to the task. These data provide a bridge between P300 and LPP paradigms, as both target status and emotional content determine the observed ERP waveform.

4.2.2 | Time-course of the P300 and LPP

Whether the LPP is simply a more sustained version of the P300 that differs in duration but not function, it would be just as reasonable to ask if the P300 is a transient LPP. One possibility is that the difference in duration between the P300 and LPP may relate to *stimulus* presentation duration. The relatively transient P300 might reflect the fact that oddball tasks tend to present stimuli such as a tone or a letter with 200 ms duration, whereas studies of emotional processing typically present stimuli for longer durations such as 1,000 ms or more.

Rather than *just* being related to stimulus duration, the temporal characteristics of P300 may reflect how long it takes to categorize the oddball stimulus. Gable and Adams (2013) asked participants to either count the number of times a target was presented or to determine the presentation *duration* of the target. A typical and transient P300 was found in the count condition, whereas targets in the duration condition elicited a protracted P300, one that resembled the LPP commonly found in emotional viewing tasks. A subsequent study demonstrated that both duration targets and emotional content produced a similar and sustained potentiation of the P300/LPP (Gable, Adams, & Proudfit, 2015). Hence, apparent time-course differences between P300 and LPP may reflect how long it takes participants to assess targets of the oddball task. This finding is consistent with studies the relate P300 latency to decision-making response times (Donchin, 1981; Verleger, 1997). Emotional stimuli elicit a sustained LPP because they sustain attentional engagement and bottom-up processing. *Duration* targets in an oddball task can elicit a protracted P300 due to top-down task demands, an effect that resembles the LPP elicited by emotional content. Consequently, time-course differences in and of themselves may not distinguish the P300 and LPP.

4.2.3 | Context updating and LC-NE

In the 1970s and 1980s, there was a debate about the functional interpretation of the P300 (Donchin et al., 1984). One major view is that the P300 is a neural correlate of the orienting response, which describes an organism's response to novelty (Sokolov, Spinks, Näätänen, & Lyytinen, 2002). This approach may reflect responses that facilitate perception and relate to potential action, a sub-process within the broader motivational significance framework (Bradley, 2009). Donchin contrasted his view of the P300 with an orienting account: "I shall assume that the process manifested by the P300 is not elicited for the purpose of tactically responding to a given stimulus in a given trial, but rather to what I called strategic information processing….that will affect the manner in which we respond to future stimuli…undertaken for the purpose of evaluating expectancies, shifting strategies …", such that the P300 was related to "activities that affect our schemas rather than our actions" (Donchin, 1981, p. 507).

Donchin (1981) also hypothesized that the P300 is elicited when mental models or schemas are updated based on new information–what he referred to as context updating. Contrasting context updating with an orienting account, Donchin writes "The OR represents tactical actions by the organism that are undertaken in order to meet the immediate exigencies of the situation". That is, the OR represents an attempt to deal with the immediate consequences of the observed discrepancy. It is for this reason that the OR has its alerting, energy mobilizing, attributes. The detection of the discrepancy, however, leads to an additional action; an action that is taken to update the model to take account of the observed discrepancy (Donchin et al., 1984, p. 42). For a more recent account of context updating, see Polich (2007).

It is difficult to distinguish *strategic* versus *tactical* processing in the classic oddball task precisely because target stimuli typically require a response. Target stimuli may have led to context updating but also require a tactical response. To the extent that the P300 and the LPP may reflect the same process, LPP data from emotional picture viewing tasks may pose a problem for Donchin's emphasis on strategic processing and the context updating view of the P300. Donchin and Israel (1980) write that "A stimulus is task relevant to the extent that the subject is processing it so as to increase his or her potential success in performance" (p. 57). During passive emotional viewing paradigms, there is no success to be had. If an increased P300 exists in the service of better performance, and if the LPP represents a sustained P300, it is unclear why emotional stimuli would potentiate the P300. If LPP modulation by emotional stimuli represents context updating it is uncertain why novel emotional stimuli would lead to greater context updating than equally-novel neutral stimuli. Finally, even after pictures are repeated many times, emotional compared to neutral picture content continues to elicit an increased LPP, even though there is no need to update a model of the environment in such a context (Bradley, 2009; Codispoti, Ferrari, & Bradley, 2007).

In the past few years, there has been renewed effort to related to the overlap between P300 and orienting (Nieuwenhuis, De Geus, & Aston-Jones, 2011). Both the P300 and LPP may reflect orienting-type responses rooted in motivational circuits. Nieuwenhuis and colleagues (2005) have further suggested that the P300 reflects the transient activity of the locus coeruleus (LC) norepinephrine (NE) system. This work is consistent with evidence linking LC function to orienting (Sara & Bouret, 2012). The Nieuwenhuis (2005) theory of the P300 is largely consonant with Bradley (2009) and provides increased specificity regarding the motivational circuitry that produces the P300.

If the LPP also reflects LC function, then several predictions follow: First, LC activity should be similarly sustained during both duration targets and the presentation of emotional stimuli. Second, LC response should vary with specific picture content and be sensitive to manipulations that similarly affect the LPP (memory load, stimulus meaning). Third, LC activity should track visual attention to arousing versus non-arousing portions of visual stimuli, per LPP effects. Fourth, MDD and its risk should be evident in reduced LC activity. Each of these hypotheses is testable and represent important future directions that will help clarify the nature of the LPP and its relationship to the P300 as general ERP indicators of orienting and motivational significance.

Some extant evidence regarding the link between the LC-NE system function and MDD is notable. Among a group of individuals with MDD who primarily died by suicide, postmortem analyses indicated reduced NE transporter specifically in the LC (Klimek et al., 1997). These data are similar to findings of a large reduction in LPP amplitude among individuals who report previous suicide attempts (Weinberg et al., 2017). In addition, these findings suggest that LC function as reflected in the LPP may be a risk factor for suicide. Non-human animal work suggests that stress depletes NE in the LC, and this may mediate stress-induced changes in behavior (Weiss et al., 1981). Based on these data, one could hypothesize that stress-induced LPP reductions ought to predict behavioral changes characteristic of MDD. Although this has yet to be directly tested, the connections across disparate literatures suggest a way forward that could integrate findings on the P300 and LPP in a manner that may ultimately inform the understanding of MDD pathophysiology.

5 | CLOSING COMMENTS

The current review describes ERP research on the study of emotion and integrates conceptual and empirical findings on the LPP. The most parsimonious account of these literatures is that the LPP is modulated by motivational significance. By this account, emotional stimuli activate appetitive and aversive motivational systems irrespective of task instructions, yielding an LPP. *Targets* in the oddball task elicit a P300 because task relevance and frequency co-opt the same neural processes that evolved to detect and respond to emotional content. Therefore, emotional stimuli might be characterized as "natural targets" (Hajcak et al., 2012).

Bradley (2009) takes an evolutionary perspective and inverts this possibility: motivational systems that facilitate responses to novelty, threat, and reward provide the basis and infrastructure for responding to target oddball. Infrequent target stimuli activate neural systems that evolved to respond to possible opportunities and threats. The advantage of this integrative framework is that it yields testable hypotheses about shared neurobiological mechanisms that may give rise to both the P300 and LPP, perhaps from LC function, as well as a common account for individual differences in these ERPs, particularly in relation to MDD. However, all observations of a P300 "are" not emotional responses. Rather, the P300/LPP is elicited by motivationally significant stimuli, whether they are targets of the task, emotionally evocative, or idiographic for a specific individual. Thus, the P300 and LPP may reflect output from a common system that tracks the time-course of stimulus significance.

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