REVIEW ARTICLE

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Ventral prefrontal cortex and emotion regulation in aging: A case for utilizing transcranial magnetic stimulation

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Objectives: The ventrolateral prefrontal cortex (vlPFC) has been speculated to play an important role in complex processes that allow emotional factors to influence human cognition. Accumulating evidence from human neuroimaging studies, in conjunction with studies of patients with lesions and animal models, shed light on the role of the vlPFC in emotion regulation (ER). This review aims to discuss and integrate recent findings related to vlPFC's role in ER in the context of aging, drawing from diverse sources, and suggest future directions for research utilizing transcranial magnetic stimulation (TMS).

Methods/Design: We summarize findings from the existing literature investigating the neural basis of frontal-lobe mediated ER and then highlight major findings from recent studies directly comparing healthy younger and older adult groups. We conclude by pointing to unaddressed questions worth pursuing in future research.

Results and Discussion: We propose future research directions utilizing TMS to answer key unaddressed questions. Moreover, we discuss the potential advantages, challenges, and limitations of using TMS as a complement to the existing neuroimaging methods in ER.

KEYWORDS
emotion regulation, neuroimaging, transcranial magnetic stimulation, ventral prefrontal cortex

1 | INTRODUCTION

This manuscript provides a brief overview of findings from the existing literature investigating the neural basis of frontal lobe-mediated emotion regulation (ER) and places these findings within the broader context of age-related differences in the behavioral and neural bases of ER. We first describe the adaptive nature of ER for mental health and well-being in the general population, as well as specifically in older adults (OA) and further discuss what is known about the ventrolateral prefrontal cortex (vlPFC)'s involvement in ER. We then highlight key findings from recent studies directly comparing healthy younger adult (YA) and OA groups and point to unaddressed questions for future research. We pay particular attention to the benefit of utilizing transcranial magnetic stimulation (TMS) as a complement to the existing neuroimaging literature.

2 | EMOTION REGULATION

Emotion regulation is defined as processes that individuals utilize to change the trajectory (eg, type, intensity, and time course) of their emotional experience.[1,2] These processes have been described as "multi-componential," with a collection of dynamic progressions transpiring over time.[3] The ER process begins with a specific psychologically relevant situation (eg, a spider is on my arm). Then, individuals devote attentional resources to assess the situation (ie, appraisal). Subsequently, initial emotional responses are engendered by one's interpretation or *appraisal* of the situation the individual experiences. After appraising a situation, ER can be employed as a functionally adaptive process that individuals utilize for the purpose of changing the intensity or the trajectory of one's emotional experience.

There are a variety of ER strategies that have been identified in the literature. As a method of ER that reframes the meaning of the situation, cognitive reappraisal is considered an *antecedent-focused* ER strategy.[1,4] This regulation strategy contrasts with *response-focused* strategies that rely on regulating outward expressions of emotional responses, such as via suppression or distraction. While distraction is thought to provide more relief from unpleasant emotion in the short term,[5] reappraisal, through increased contextualizing of emotional events, provides longer-term adaptation.[6]

Cognitive reappraisal serves as an adaptive process for one's affective functioning because it helps to regulate mood states that can be detrimental in the long term to one's mental health. In fact, faulty mood regulation and its resulting behavioral consequences are considered a hallmark feature of major psychiatric disorders such as depression and bipolar disorder.[7] Critically, these psychiatric disorders commonly exhibit abnormal mood states, both in terms of intensity and duration.[8] Furthermore, maintenance of anxiety disorders such as obsessive-compulsive disorder, post-traumatic stress disorder, and specific phobias are thought to include emotion dysregulation as a core component.[9,10] More broadly, poorly controlled, and intensified emotional distress is widely considered one of the main pillars of many, if not most, psychopathological conditions diagnosed by current clinical standards.[11,12] This common involvement of poor ER in multiple psychiatric disorders necessitates an effort to examine the core mechanism that underlies both normal and abnormal ER.

In the context of aging, ER may have even greater relevance in the maintenance of mental health and well-being. Aging is associated with loss and deteriorated physical and cognitive functioning. Thus, one's ability to down-regulate negative affect and increase positivity arguably becomes even more relevant for well-being and mental health. It is speculated that ER skills serve a critical role in abnormal aging such as in the case of OA with neuropsychiatric and neurological disorders. Importantly, being diagnosed with a neuropsychiatric condition with known emotion dysregulation component later in life confers a greater risk of developing other neurological disorders.[13] In this sense, identifying key neural components of ER and their age-related changes can help better elucidate the neurobiological mechanisms that underlie distressing mood problems and identify specific treatment targets for multiple psychopathological conditions across the life span.

3 | NEURAL BASES OF ER

Functional neuroimaging research has advanced our understanding of neural processes relevant to ER. Most of the neuroimaging studies of ER employ *reappraisal-based* ER. The vast majority of neuroimaging studies in ER have implicated ventral regions of the prefrontal cortex (PFC), and more specifically the lateral subregion of the orbitofrontal cortex (OFC)/orbitalis portion of the inferior frontal gyrus, as a key area involved in regulatory control of affective states.[14] These studies have reported that lateral OFC is heavily recruited when subjects try to engage in such reappraisal-based ER.[15] Although this specific strategy has been most commonly used in studies of reappraisal, other studies that use other types of ER, such as suppression and distraction, have also shown similar ventral prefrontal involvement.[16,17] Correlational evidence gleaned from these neuroimaging studies are also consistent with our current knowledge of bidirectional structural connection between the amygdala and the caudolateral OFC[18] as well as our knowledge of the existing cortical projection to the basolateral amygdala, specifically from the ventrolateral region of the PFC.[19]

A comprehensive review of data from neuroimaging studies points to the vlPFC as a core neural substrate underlying ER processes regardless of valence or direction of regulation.[14] Attempted

> **Key points**
>
> - Neuroimaging research suggests that vlPFC likely plays an important role in emotion regulation (ER).
> - FMRI studies comparing young adults and older adults, vlPFC has shown age-related recruitment differences during ER.
> - Further research utilizing neuromodulatory techniques such as TMS will allow testing the putative causal role of the vlPFC in reappraisal-based ER.

regulation of either positive or negative emotions commonly recruit the left lateral OFC, regardless of the valence of affect being regulated,[16] providing more weight to the idea that attempts to regulate differently valenced affect may rely on common neural underpinnings that include the lateral OFC for cognitive control of emotions.[14] This also suggests that while positive and negative valence systems have been traditionally theorized as orthogonal dimensions,[20,21] they may still share a common regulatory control implemented by the vlPFC (Figure 1).

Moreover, it has been speculated that modulation of amygdala activity, which likely reflects changes in affective salience of sensory stimuli, occurs as a function of regulatory control via activating regions of the ventral PFC. Accumulating evidence from multiple neuroimaging studies has revealed that ER is accompanied by the modulation of amygdala activity regardless of the valence of the emotion being regulated. While amygdala activity is not strictly necessary for subjective experience of emotion,[22,23] changes in the perceived salience of sensory stimuli have been associated with concomitant parametric modulation of amygdala activity.[24] Neuroanatomically, a portion of the amygdala[25] whereas more dorsal frontal areas such as dorsolateral PFC lack a direct pathway. Moreover, studies have found that the degree of ER success as measured by self-report of changes in affect magnitude was correlated with lateral OFC activity during regulation strategy deployment[26] and that tighter functional coupling between lateral OFC and amygdala activity predicted greater ER success. In other words, closer linkage between lateral OFC and amygdala activity predicted more successful ER.[27]

While greater vlPFC activity has been correlated positively with more successful ER, more recent neuroimaging data have focused on identifying a more mechanistic understanding of the regulatory process. For instance, Wager and colleagues[28] have shown some evidence using mediation analysis that the vlPFC plays an important role in affect regulation through both positive and negative reappraisals via its functional linkage to the ventral striatum and the amygdala, respectively.[28] A meta-analysis[29] that integrated data from 23 fMRI and PET imaging studies of ER similarly concluded that vlPFC serves as a critical component of regulatory process. In their heuristic model of ER, vlPFC functions as a gatekeeper of ER such that activation of the region during ER serves a dual purpose of appraising the salience of the stimuli but also feeding forward this information to other frontal areas to allow effective reappraisal when deemed necessary. These data, in addition to a wealth of existing literature,[30-32]

Left   **Front**   **Bottom**

● Amygdala   ● Periaqueductal Gray   ● Insula

● Ventral Striatum / Nucleus Accumbens   ● Dorsal Anterior Cingulate Cortex   ● Ventrolateral Prefrontal Cortex
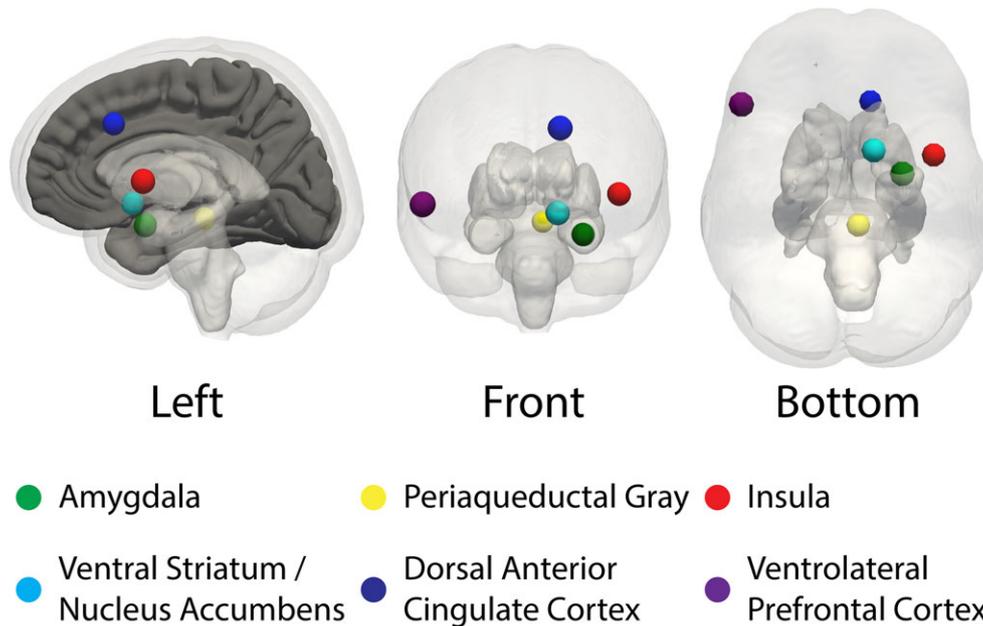
FIGURE 1 The ventrolateral PFC and subcortical regions implicated in emotion regulation [Colour figure can be viewed at wileyonlinelibrary.com]

strongly suggest that vlPFC activity is critically involved in reappraisal-based ER.

4 | EMOTION REGULATION IN AGING

There has been growing interest in the aging research community to uncover the behavioral and neural bases of ER. Indeed, there are several studies indicating possible age-related differences in neural signatures associated not only with emotion processing but also the cognitive control of emotions. At the basic level of emotion processing, it has been shown that healthy OA tend to focus more on positively valenced stimuli relative to negatively valenced stimuli.[33-35] Healthy OA are less accurate and slower in identifying facial emotions than are YA and demonstrate a bias toward categorizing and reacting quickly to emotions as positive.[36] At the same time, studies have suggested decreased negativity and enhanced ER ability in older age,[37,38] which is a potential explanation of the finding that increased life satisfaction is associated with healthy normal aging.[39] Socioemotional selectivity theory[40] postulates that OAs have a tendency to prefer positive stimuli and avoid negative stimuli. This theory proposes that a changing perception of time that comes with aging increases motivation toward positive, and away from negative stimuli. Importantly, the positivity effect in OAs is observed more often with low- and medium-arousing stimuli, and less with high-arousing stimuli, which are processed more quickly and make greater demands on executive processes than less arousing stimuli.[41,42] Behavioral studies have also demonstrated a preference for distraction among OA, relative to YA, who report using more active strategies, such as confrontation and reflection.[43,44] Importantly, choice of ER strategy is likely moderated by cognitive resources, as reappraisal requires greater resources than does distraction.[45] Consistent with this, Scheibe et al found that executive functioning (EF) measures negatively correlated with use of distraction in both YAs and OAs.[43]

In terms of neural level age-related differences in emotion processing, it has been shown that OA tend to over-recruit frontal control regions when processing positive stimuli.[46,47] It has been theorized that such biased shift towards positively valenced information combined with enhanced recruitment of frontal control regions reflect efforts to increase one's positive affect in older age by utilizing "enhanced elaboration and up-regulation of positively-valenced stimuli."[48] It has also been argued that due to frontal-lobe mediated up-regulation of positivity, individual differences in EF correlate with age-related positivity shifts. Importantly, studies have shown that individual differences in EF modulate the level of vlPFC engagement when inhibiting negative affect, and the intensity to which OA can down-regulate amygdala activity during reappraisal-based ER.[49] This further provides weight to the hypothesis that the PFC and especially the vlPFC subregion serve a critical role in ER in general and in the OA population, more specifically.

Anatomically, the inferior frontal gyrus, which overlaps with the vlPFC, is known to be affected by age-related atrophy relative to inferior temporal and cingulate regions that are less impacted by age.[50] This age-related preferential cortical thinning of this region also adds an additional burden on cognitive control of emotion in older age. Some have even suggested that normal EF decline seen in older age as evidence of anatomical deterioration of such frontal lobe regions. Indeed, anatomical deterioration of these frontal lobe regions may underlie age-related decline in EF skills, which have a disproportionate dependence on the fronto-striatal network.[51,52] Such selective vulnerability of prefrontal regions in aging has been suggested to fit the "last in, first out" hypothesis, which suggests that the brain regions such as the vlPFC that have been the newest to develop phylogenetically are likely the first to be adversely impacted by aging.[50]

While several studies have attempted to elucidate the neural bases of ER using neuroimaging methods such as functional magnetic resonance imaging (fMRI), only a handful of studies have specifically included YA and OA samples for a direct comparison of the neural

bases of ER. In a study by Winecoff and colleagues,[53] YA and OA groups performed a cognitive reappraisal task during an fMRI scan. The results indicated an age group-related activation difference, such that lower regulation-related activations in the left inferior frontal gyrus as well as left superior temporal gyrus were observed in OA relative to their younger counterpart. In this study, a separately collected measure of executive function predicted greater regulation-related reduction in amygdala activation above and beyond the effects of age alone, which suggested that the functional recruitment of the neural substrate important for ER may share the resources utilized by general cognitive control, an aspect of EF. In a subsequently published study by Opitz and colleagues,[54] YA and OA groups were compared in their neural response to reappraisal of negative emotions. In this study, OAs similarly under-recruited the left vlPFC region as well as the dorsomedial region relative to the YAs, and this activation level also tracked their worse performance on down-regulating negative affect behaviorally. More recently, Allard and Kensinger[55] utilized a film-clip based ER task during an fMRI scan, which revealed a similar finding of under activation of the lateral PFC (including the vlPFC) in OA during regulation of negative emotions. Although studies comparing the two age-groups show consistent finding of OA's showing under-recruitment of the vlPFC, this study demonstrated that the OA group show temporally delayed recruitment of the vlPFC compared with their younger counterpart, which is speculated to be evidence of OA's compensatory engagement of the region as adaptation to using a cognitively demanding reappraisal strategy.

Even though the aforementioned studies have indicated the potential age-related differences in the neural bases of ER between YA and OA, several unanswered questions remain. For instance, it is still unclear whether age-related frontal lobe anatomical changes directly mediate differences in recruitment of the vlPFC shown in older age, and also whether EF changes have a direct causal relationship with ER abilities. And if so, can ER be enhanced by improving one's executive function? Elucidating the neural basis for ER in aging serves a critical role in (1) explicating how the aging brain works to cognitively control emotions; and (2) helping to identify treatment targets for emotion dysregulation symptoms and syndromes seen in older age such as frontotemporal dementia, late life depression, and other neuropsychiatric or neurological disorders particularly vulnerable to being diagnosed in OAs.

5 | UTILIZING NEUROMODULATION TO STUDY EMOTION REGULATION

While growing evidence provides weight to the hypothesized role of the vlPFC in ER, there are at least two unaddressed key issues requiring further examination. First, data reported to date have limited explanatory power to confidently claim a causal relationship between vlPFC activities and ER processes. Most current knowledge on the emotion-regulation related functions of the human vlPFC stems from neuroimaging studies that are inherently correlational in nature. [56,57] In other words, neuroimaging data reveal brain regions are activated during a task (or cognitive operation) of interest. While activation data may be misconstrued as sufficient evidence that the ventral prefrontal lobe is where reappraisal-based ER takes place, it is still unclear whether there is indeed a causal link between ventral prefrontal lobe activity and reappraisal.

Prior neuroimaging studies of ER thus far reviewed are, to a limited extent, supplemented by additional observational clues from studies of individuals with OFC damage. These studies suggest that individuals who sustain OFC damage have measurable deficits in regulating mood and engaging in culturally appropriate behavior in social contexts, despite their generally intact ability to experience a full spectrum of emotions to a similar level as healthy normal individuals would. For instance, individuals with OFC damage have been reported to show disinhibition and behavior that indicates the individual's disregard of moral and social decorum.[58,59] It has also been reported that OFC lesion patients exhibit lower levels of self-reported as well as outwardly visible facial expressions of embarrassment.[60] One possible interpretation of these data is that subjective experience of socially relevant emotions, such as embarrassment, guilt, shame, and pride, may be associated with the OFC. One problem with this speculation is that most human OFC lesion studies report results from an aggregate of heterogeneous lesion cases that include multiple subregions within the OFC. Importantly, studies with a more homogeneous sample of OFC lesion foci have generally restricted their samples to medial OFC lesion cases and rarely include ventrolateral OFC lesions. Furthermore, samples in such studies are commonly collected from neuropathological or clinically necessitated surgical lesions that are inherently heterogeneous sites within the larger OFC,[61] making generalizable inferences more difficult.

Non-human primate lesion studies can be valuable sources to gain more precision when making inference about specific subregions of the frontal lobe and their dissociable functions in the context of affective control. Conducting laboratory-controlled lesion studies of non-human primates may be considered a viable approach to address this issue, albeit to a limited extent. For example, in one study, researchers induced excitotoxic lesion to the anterior OFC and vlPFC in marmoset monkeys. This revealed that both groups of lesioned marmosets exhibited observably increased anxious behavior and fear responses to the presence of human intruders, which is generally regarded as only mildly threatening.[62] Interestingly, lesions targeted specifically to the vlPFC, but not the anterior OFC, influenced the marmosets' use of a coping mechanism of increasing proactive vocalization of alarm calls in response to the anxiety inducing stressor. However, an added layer of complication is the difficulty of ascribing to the behaviors of non-human primate subjects such a complex cognitive process as ER, especially since reappraisal-based ER is thought to require willful control of emotional experience.

An alternative method that combines the ability to probe ER process in humans while simultaneously allowing for more precise causal inferences about brain-behavior relationships is using a neurostimulation method called TMS.[63] TMS is a neurophysiological technique that allows the induction of a current in the brain using a magnetic field to pass the scalp and the skull safely.[64] In TMS, depending on the parameters used such as frequency and pattern of pulses delivered, one can depolarize or hyperpolarize the underlying cortex of the subject's brain.[65] TMS can be applied in trains of multiple pulses within a given period of time to a targeted cortical region, known as repetitive TMS (rTMS). Depending on the stimulation parameters, rTMS is capable of changing the activity in a brain area for a brief

period of time beyond the duration of the rTMS application itself. In other words, it is possible to increase or decrease activity level in a given cortical region for extended period of time. Low-frequency rTMS (<1 Hz) has been shown to suppress cortical excitability of the targeted region for several minutes following rTMS stimulation.[65] This particular variant of TMS techniques has been used widely by researchers to transiently disrupt cortical activity within a targeted brain region, thus allowing examination of a focal cortical area's hypothesized involvement in specific cognitive functions.[66-69]

Neuromodulation techniques such as TMS methods and ER tasks can be conjunctively utilized to investigate the impact of modulated cortical excitability in specific brain regions and their impact on regulation of one's emotional response. Using this approach, one can thus transiently disrupt brain excitability in a targeted cortical area and measure its effect on cognitive processes such as ER. Because the effects of rTMS-dependent cortical excitability modulation are transient, rTMS can safely test the hypothesis that vlPFC function contributes to effective ER in healthy individuals. Directly manipulating cortical excitability using this technique provides an invaluable window of opportunity to gather crucial causal evidence where only correlation evidence currently exists.[63] More specifically, this approach could help answer questions about the causal nature of ventral prefrontal lobe activity in ER.

To date, there has not been any published TMS study that targets vlPFC to investigate its effect on ER. A handful of TMS studies that have targeted other regions of the PFC examined the effect of TMS in the broader context of mood and emotion, but not necessarily ER. One of the early TMS studies demonstrated that 5-Hz rTMS on dorsolateral regions of the frontal lobe could significantly shift mood states in healthy individuals.[70] Another study reported that repeated sessions of rapid-rate (10 Hz) rTMS over the left dorsolateral PFC could significantly alleviate depressive symptoms in patients suffering from major depression.[71] Moreover, meta-analysis studies have shown that high-frequency rTMS to the left dorsolateral PFC (DLPFC) has antidepressant effects,[72] and the effect of low-frequency right DLPFC rTMS was comparable to that of left DLPFC rTMS.[73,74]

In all of these studies, researchers have targeted the dorsal regions of the PFC, without additionally considering the effect of ventral PFC stimulation. Lack of ventral PFC rTMS studies is not surprising given that ventral prefrontal TMS stimulation may be logistically more difficult due to the region's proximity to facial nerves and the anterior visual tracts. There are, however, a few exceptions. Among existing studies, Schutter and Van Honk[75] reported that low-frequency rTMS specifically targeting the left frontopolar cortex facilitated study participants' memory for happy faces but not fearful faces. Interestingly, a relatively recent study reported that low-frequency rTMS to the cerebellum prevented stimulated individuals from suppressing negative mood.[76] However, there remains a dearth of TMS studies of ER that target the ventral frontal lobe. Even though previous functional neuroimaging data point to lateral regions of the ventral PFC as a prime candidate region associated with ER,[16,28] there is a void of data in the area of neurostimulation research that could complement the existing neuroimaging data, perhaps due to technical difficulties associated with targeting ventral regions of the frontal cortex.

In summary, although neuroimaging research has reported a significant association between vlPFC activity and successful ER using cognitive reappraisal, little research has been done to causally link vlPFC activity and effectiveness of ER. In particular, to date, there has not been a TMS study that specifically examines whether disrupting activity in ventrolateral regions of the PFC influences individuals' ability to exert conscious and effortful control over externally elicited emotions. Previous TMS studies targeting regions near the ventral PFC have rarely focused on processes relevant to ER. Therefore, TMS stimulation studies specifically designed to target the vlPFC to subsequently probe its effect on ER can greatly enhance our understanding of the frontal lobe's involvement in affective processes.

6 | LIMITATIONS AND ANTICIPATED DIFFICULTIES OF UTILIZING TMS

There are limitations to utilizing TMS that should be noted. First, TMS likely has restricted spatial coverage of the vlPFC. While the precise spatial resolution of the effect of rTMS is considered to vary somewhat by the equipment and parameter used during stimulation,[77] with currently available coil designs, it is generally believed to deliver stimulation over the target area in the order of approximately 0.5 to 1 cm in diameter. vlPFC area however covers a wide region along the lateral portion of the OFC that cannot be captured within a 1-cm diameter. Therefore, utilizing TMS-dependent focal stimulation will partially modulate the vlPFC. For a greater coverage, it is possible in the future to combine using multiple figure-8 coils.[78] Second, the method and implementation of adapting the amplitude of cortical stimulation to each participant's brain can be challenging. Motor-thresholding is a method that has been conventionally used as a reference point for adjusting the amplitude of TMS stimulation, as this indicates the level of the individual's excitatory cortical response of the primary motor cortex (M1). However, this method assumes that the excitability of M1 is comparable to the excitability of other regions being targeted by TMS, namely in our case, the vlPFC. However, further investigation is needed in order to conclude whether TMS-dependent cortical excitability can be generalized from one region to another. One way to directly address this issue is to utilize what is known as TMS-evoked potential (TEP), which is a measurement of cortical excitability directly from the TMS target. Consistent with idea of possible regional variability in cortical excitability, TEPs from different brain areas have been shown to produce different latencies and amplitudes.[79] Thus, taking into account individual differences in cortical excitability in future neurostimulation studies of ER using TEP may help maximize the power to detect the impact of experimental manipulation.

Third, TMS studies with OA samples can be particularly challenging to apply the stimulation at equivalent amplitude across individuals. Specifically, the aging brain may show varying degrees of atrophy, which is accompanied by the dilation of sulci and ventricles of the brain. This increases distance between the skull and the brain, and also increases CSF density that populates the space between the skull and the brain.[80] The distance from the TMS coil to the motor cortex is a significant predictor of motor-threshold.[81] Thus, when there is significant cortical atrophy, motor-threshold measured can be significantly increased and considerably change the TMS stimulation amplitude delivered. Furthermore, studies suggest that increased CSF volume density occupying the
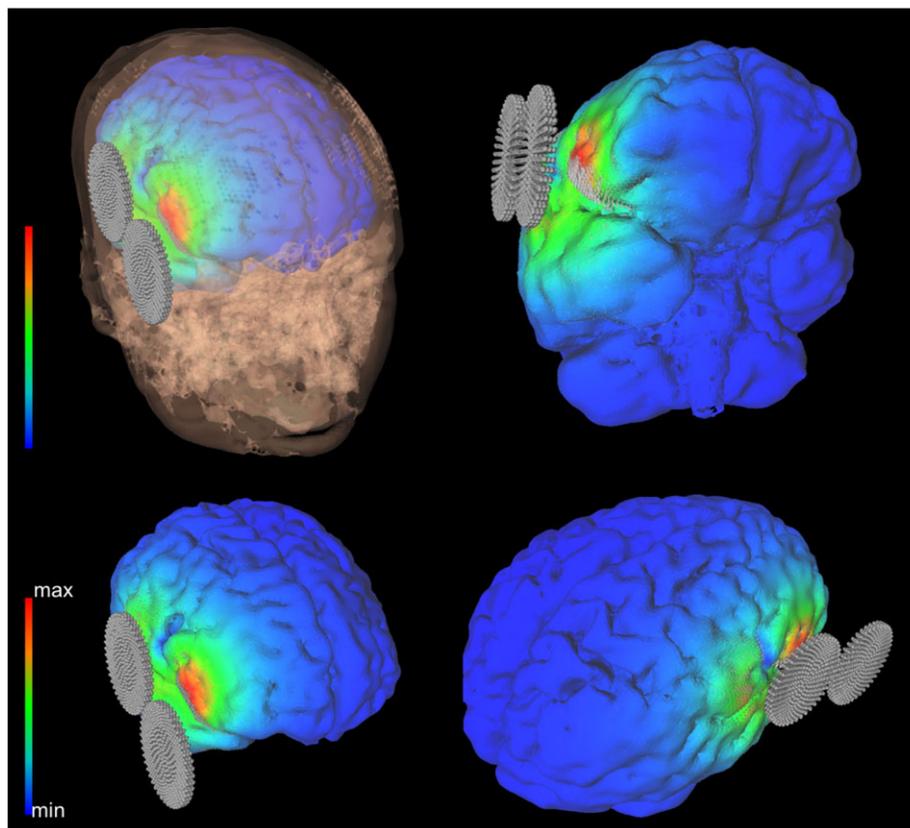
FIGURE 2   An example of visualized electrical field modeling of the vlPFC rTMS [Colour figure can be viewed at wileyonlinelibrary.com]

space between the skull and the target cortex can have a significant influence on the direction and dosage of TMS on the target area by way of shunting the current delivered through the neuromodulation technique.[82] This is known to be due to the fact that CSF has higher conductivity compared with the brain matter and skull.[83] In order to address these issues, careful measurement of anatomical individual differences and subsequent prospective electrical field modeling of the neuromodulation technique will become necessary to demonstrate equitable methodological setup across samples, especially when compared the YA and OA groups known to have age-related confounding variables such as age-related brain atrophy (Figure 2).

7 | FUTURE DIRECTIONS

Future studies should further aim to examine the impact of vlPFC structure and function on reappraisal of positive and negative emotions. Findings from such studies would provide further clarification of the role that intact vlPFC may play in successful positive and negative affect reappraisal, as well as elucidate the neural mechanisms involved in normative patterns of effective ER. Results from these studies can suggest possible differences in socio-affective experience of older individuals with frontal lobe insults, as observed in certain neurodegenerative conditions known to disproportionately affect OAs. Moreover, it will be important to not only probe the effectiveness of ER use but also examine how brain function and structure influence one's preference for and deployment of ER strategies at one's disposal. Recent studies have suggested that those who are

successful at regulating negative emotions may be more adept at choosing the adaptive regulation strategy for the situation ER is needed.[84] Thus, it will be important to learn how the vlPFC function and structure in older age contribute to one's preference for and deployment of ER strategies that fit the situation being regulated.

Future studies should also further clarify the role of subregions of the vlPFC, as the current neuroimaging literature in ER suggest the critical role that lateral OFC may play in regulating the stability of positive and negative affect. Further investigations should also address whether and how differences in appraisal and regulation of emotional experience can translate to real-world differences in functional adaptiveness. A comparative examination of the commonalities and differences in neural mechanisms underlying successful and ineffective ER in the young and old in both healthy normal and pathological sample will also enhance our overall understanding of the neural bases of ER across the life span.

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