Perspective

Decoding of Processing Preferences from Language Paradigms by Means of EEG-ERP Methodology: Risk Markers of Cognitive Vulnerability for Depression and Protective Indicators of Well-Being? Cerebral Correlates and Mechanisms

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Abstract: Depression is a frequent mental affective disorder. Cognitive vulnerability models propose two major cognitive risk factors that favor the onset and severity of depressive symptoms. These include a pronounced self-focus, as well as a negative emotional processing bias. According to two-process models of cognitive vulnerability, these two risk factors are not independent from each other, but affect information processing already at an early perceptual processing level. Simultaneously, a processing advantage for self-related positive information including better memory for positive than negative information has been associated with mental health and well-being. This perspective paper introduces a research framework that discusses how EEG-ERP methodology can serve as a standardized tool for the decoding of negative and positive processing biases and their potential use as risk markers of cognitive vulnerability for depression, on the one hand, and as protective indicators of well-being, on the other hand. Previous results from EEG-ERP studies investigating the time-course of self-referential emotional processing are introduced, summarized, and discussed with respect to the specificity of depression-related processing and the importance of EEG-ERP-based experimental testing for well-being and the prevention and treatment of depressive disorders.

Keywords: cognitive vulnerability; depression; self-referential processing; emotion processing; language; event-related brain potentials

1. Introduction

Affective disorders such as depression are among the most common mental disorders in Western industrialized societies, and are on the rise worldwide. According to the WHO (World Health Organization), already more than 300 million people worldwide currently suffer from a depressive disorder [1]. The lifetime prevalence is 16–20% for both sexes [1]. The onset of major depressive disorder is early in life, starting during adolescence, and affecting emerging adults, if untreated, during their whole lifespan [2]. Due to its high prevalence, as well as due to its multifactorial negative consequences for mental and physical health, the prevention of depressive symptoms is of outstanding clinical and health economic importance [1]. Indeed, depressive disorder affects the whole person—the body, the brain, and the mind—and related affective, motivational, and cognitive processing [3].

Regarding emotional processing, depressed individuals are found to sustain attention to negative stimuli, have difficulties in the inhibition of negative information, and, compared to non-depressed individuals, recall negative information better than positive information, e.g., [4,5]. These processing biases, described in the literature as negativity bias, have been repeatedly reported in studies investigating acute or remitted depressed individuals. Moreover, the negativity bias has been confirmed in vulnerable individuals, i.e., individuals at risk of depression e.g., see [4–9]. According to cognitive vulnerability models, two major cognitive risk factors can be identified that promote the occurrence and severity of depressive symptoms and the development of depressive symptoms prior to a

clinical diagnosis of major depressive disorder [10]. These cognitive risk factors include an increased self-focus and a negative emotional processing bias [10,11]. Thus, according to cognitive vulnerability models, for the diagnostic decision of whether processing preferences for negative stimuli are specific risk markers of depressive symptoms, it is essential to determine whether these processing biases occur in reference to one's own self. Theoretically, a pronounced self-reference or self-focus, negative self-schemas, and negative attitudes towards the self are among the core characteristics of a depressive personality structure, and they are important causal disease factors characterizing depressed thinking in cognitive theories of depression [12,13]. Accordingly, cognitive vulnerability models of depression (for an overview, see [10]) assume that the aforementioned cognitive biases exist prior to the onset of depressive disorders. Moreover, it is assumed that both self-referential and emotional processing are linked in depressive disorders—specifically, it is assumed that a focus on the self, including a negative view of the self, biases information processing towards negative information [10].

In line with two-process models of information processing, cognitive vulnerability models distinguish between a fast, predominantly associative, implicit, stimulus-driven (bottom-up) processing mode and a temporally slower, reflective, and cognitively elaborate and controlled (top-down) processing mode. Both the associative and the controlled processing modes can occur during stimulus processing in a serial sequence. Any type of stimulus appraisal occurring spontaneously can be assumed to be related to the fast and associative processing level. Reflective and cognitively controlled stimulus processing, including more elaborate processing of the information, can be assumed to follow associative processing and to occur, in particular, when a task demands it, the context requires information to be elaborated and appraised in-depth, or when responses triggered by emotional stimuli have to be actively and cognitively regulated (an overview is given in [10]). As illustrated in Figure 1, according to cognitive vulnerability models, in this information processing cascade, self-reference acts as a processing filter that can bias emotion processing already at early stages of associative information processing. Moreover, it can trigger more elaborate and reflective self-related negative information processing at later stages of cognitive controlled information processing. When viewed from the perspective of information processing, according to these models, depressive vulnerability results from the interaction between self-related and emotional processing occurring at early processing stages, and the processing biases resulting from this interaction are considered the main characteristics, or risk markers, of depressive vulnerability. Therefore, individuals in whom an interaction between self-related and negative emotional processing and, consequently, a self-negativity bias can be observed should be particularly vulnerable to the experience of depressive symptoms compared to individuals not displaying self-referential negative processing. Following cognitive vulnerability models, this self-negativity bias should be best empirically observed during experimental task conditions that (a) favor self-referential associative stimulus processing (e.g., spontaneous processing or passive viewing), (b) require cognitively reflective or cognitive-controlled processing of self-related emotional content, and (c) use stimulus material that varies in emotional content and self-reference.
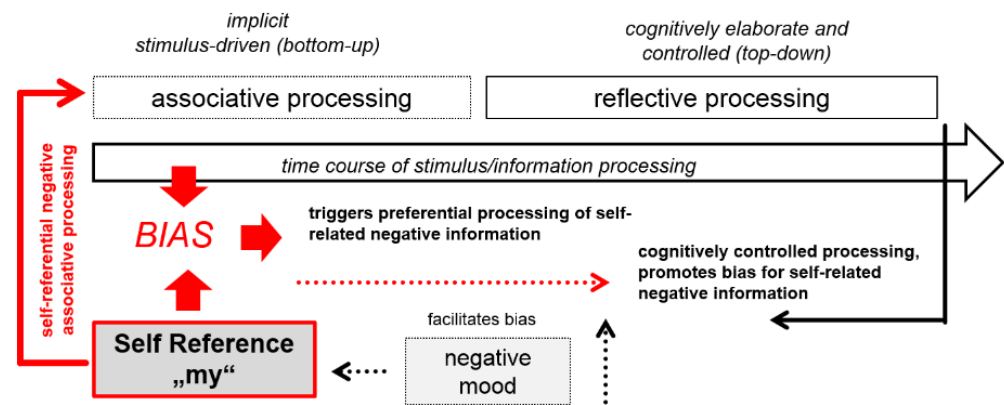
Figure 1. Information processing according to cognitive vulnerability models of depression. For further details, please see text and e.g., [10].

2. Decoding Processing Preferences by Means of EEG Methodology

Methodologically, non-invasive electroencephalography (EEG) and the analysis of event-related brain potentials (ERPs) from the electroencephalogram (EEG) are ideally suited neurophysiological techniques to unravel the processing biases of cognitive vulnerability and determine how these biases unfold over the time course of information processing. EEG methodology allows precise insights into the time course of stimulus- and information processing and their task- and mood-related changes. The latency, as well as the amplitude modulation of early and late ERPs in response to the averaged stimulus response recorded in different task contexts allow differentiated conclusions about the different stimulus and information processing stages from stimulus perception to more in-depth processing [14]. In contrast to behavioral methods, EEG methodology allows the investigation of stimulus processing and its time course even in designs in which no behavioral responses are required and no tasks are given other than to, e.g., read, watch, or listen to the stimulus presentation. EEG methods therefore might be ideally suited to study bottom-up processing without the confounding influence of task-related factors, while at the same time allowing for comparisons between spontaneous (no task) and task-related stimulus processing. Moreover, in event-related stimulus designs, a number of event-related brain potentials can be elicited that, depending on the stimulus and processing specificities, have been shown to be reliable markers of, e.g., perceptual, cognitive, semantic, sensorimotor, or affective processing [14].

Regarding emotional processing, as exemplified in Figure 2, the processing of emotional and neutral stimuli can elicit the modulation of early and late event-related brain potentials (ERPs). For example, in an EEG-ERP experiment with emotional and neutral stimuli, the amplitude amplification of early event-related potentials such as the EPN (early posterior negativity) has often been observed, irrespective of the type of stimuli presented, whether it is words or pictures of emotionally evocative scenes [15–17]. Due to its almost obligatory elicitation across many study designs (passive viewing tasks, fast stimulus presentations, or selective attentive stimulus processing), the EPN has been suggested to be a prominent neural marker of early stimulus-driven processing of high-arousing stimulus content of motivational salience [15–17]. Therefore, in the EEG, a larger EPN amplitude modulation during the processing of stimuli of negative content, compared to stimuli of positive or neutral content, would argue for a rapid, spontaneous, and bottom-up driven allocation of visual attention to negative stimulus information that, according to the two-process models mentioned above, occurs at fast—and probably still associative—levels of information processing.
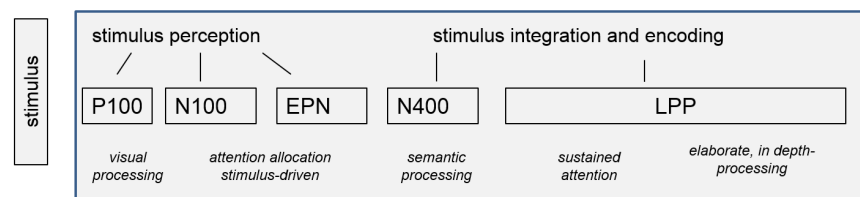
Figure 2. Temporal processing in the EEG as exemplified by the modulation of event-related brain potentials (ERPs).

In addition, the amplitude modulation of temporally later ERP components such as the N400 ERP component, typically elicited by lexical stimuli (but also found to be elicited by non-lexical stimuli such as faces), can indicate semantic processing due to facilitated lexical access [18], facilitated activation of long-term memory representation [19], or contextual integration of the stimuli [20]. Contextual integration can be established either experimentally by a sentence context [20], a specific task context, or an internal context such as the current mood and affective state of the participant [21–23]. Therefore, N400 modulation by negative or positive stimuli compared to neutral stimuli occurring approximately 400 ms after stimulus presentation during spontaneous stimulus processing tasks could suggest mood-dependent processing of negative or positive content [22], with mood acting as a context for stimulus integration and mood-incongruent stimuli being processed differently from mood-congruent stimuli under mood induction (e.g., [21]). Last, but not least, the enhanced amplitude modulations of late ERP components such as the LPP (late positive potential) have been assumed to be associated with deeper processing of the content of negative or positive stimuli (e.g., [22–24]). LPP modulation may therefore indicate a sustained attentional focus for certain information of relevance for the person. Moreover, its modulation has been shown to indicate cognitively controlled emotion processing in a number of emotion regulation studies that used implicit and explicit strategies of stimulus reappraisal or emotion suppression (e.g., [24,25]).

3. Research Gaps

Despite of the prominence of cognitive vulnerability models and the popularity of non-invasive EEG methodology, so far, the literature lacks studies that systematically investigate the time course of emotional processing and its interaction with self-referential processing in line with cognitive vulnerability models in controlled experimental laboratory settings in cognitively vulnerable individuals at risk of depression, with healthy, cognitively non-vulnerable individuals as controls. Investigating the hypothesis of cognitively vulnerable models by means of EEG-ERP methods requires appropriate experimental paradigms that allow to experimentally manipulate the self-reference and the emotionality/the emotional significance of the stimuli independently from, as well as in combination with, each other to induce and trigger self-referential as well as emotional processing at the stage of associative stimulus processing in a bottom-up fashion without any influence from higher-order, task-induced self-referential or emotional processing. This seems crucial to test the early interactions between self-reference and emotion processing postulated by cognitive vulnerability models to occur during implicit associative processing conditions compared to cognitively controlled reflective processing conditions (see Figure 1).

So far, experimental paradigms that investigated the interaction between emotion and self-referential processing in healthy controls and depressive subjects have almost exclusively induced self-referential processing explicitly via task instructions. In particular, paradigms such as the Self-Referent Encoding Task (SRET [26]) have been used, e.g., [26–29]. In this paradigm, participants are exposed to positive and negative personality traits and asked to judge which of the trait words describe them best. Afterwards, the participants are often asked to recall the words presented. The results of several studies suggest that words that have been judged to describe the self and are thus considered to be congruent with the person's own self-views are also better remembered e.g., [30], with healthy subjects

differing from depressive subjects in their performance [26–29]. Studies recording EEG-ERP parameters during the SRET in healthy individuals and in individuals suffering from current or remittent depressive disorder [31–33] have found differential processing of positive and negative trait words as a function of group (healthy participants vs. participants with current or remitted depression) during later stages of stimulus processing [31–34]. Temporally earlier processing differences in the time window of early ERPs as a function of group (healthy participants vs. participants with current or remitted depression) have been reported only occasionally in the SRET [33]. Given that in the SRET, self-reference is induced via task instructions, there is a search for tasks and paradigms that allow the independent experimental manipulation of the dimensions of self-reference and emotion based on stimuli instead of task to assess not only the reflective aspects of self-referential processing, but also the associative and stimulus-driven effects of self-referential processing on emotion processing, independent from, as well as in comparison with, task-induced affordances and cognitive demands.

Experimental paradigms that allow both, the independent experimental manipulation and the joint assessment of the effects of the self-referentiality and the emotionality elicited by a stimulus are paradigms such as the so-called 'HisMine' paradigm [for an overview see below or the Supplementary Materials]. In its non-affective form, the HisMine paradigm consists of singular and plural first-person pronouns (1PP: I, my), second-person pronouns (2PP: you, yours), and third-person pronouns (3PP: he/she, hers, his), addressing the self as the subject or object of self-experience, e.g., [35–37]. In its affective form (e.g., [38,39]), self- and/or other-referential possessive pronouns ("my"/"his/her") are combined with nouns that vary in emotionality (positive, negative, and neutral) and are matched on the two emotional dimensions of valence and arousal. In addition, the stimuli are matched on several linguistic dimensions such as word length, or word frequency, or concreteness. The nouns chosen can describe positive and negative emotions (e.g., fear, anger, or happiness), emotion-inducing objects or events (e.g., gun, failure, money, or love), or neutral states or objects rated by normative study samples as neither positive nor negative in valence and low in emotional arousal (e.g., furniture, books, etc.). The nouns can be paired with 1PP, 2PP, or 3PP possessive pronouns to make reference to the reader's own emotions or to the emotions of a third person. In addition, nouns paired with articles instead of pronouns can serve as controls, and the effects triggered by self- and other-referential pronouns on emotion processing triggered by the nouns can be compared to a control condition of non-referential emotional and neutral content. Thus, in summary and in contrast to the SRET paradigm, the stimuli used in the HisMine paradigm can capture a broad range of concepts and emotional feeling states. This may—with respect to cognitive vulnerability models—allow a comprehensive insight into depression-related emotional processing biases. Instructions in the HisMine paradigm can vary from passive viewing and reading to spontaneous emotional evaluation (to trigger associative processing) to active attentive and cognitively controlled processing of the stimuli (to trigger elaborate processing). In combination with EEG methodology, this allows a reliable investigation of the time course and the neural sources of implicit stimulus-driven and task-related explicit self-referential emotional processing. Moreover, when pronouns are paired with non-verbal stimuli (e.g., faces [25]), the specificity of self-referential processing can be explored across and between emotion modalities (verbal and non-verbal). While the HisMine paradigm is conceptualized to investigate the behavioral, subjective, and neuronal correlates of self-referential emotional processing at the word–phrase level, similar approaches for the study of self-referential and emotional processing at the sentence level have been recently suggested (e.g., [40–42]).

The approaches using pronoun–noun phrases or sentences in combination with EEG methodology might be interesting for the investigation of cognitive vulnerability. At the same time, these paradigms might have the capacity to provide insight into what characterizes "normal" and healthy information processing in terms of emotion and self-referential processing. Akin to a negativity bias, a processing advantage for self-related

positive information including better memory for positive than negative information has often been observed, especially in association with the above-mentioned SRET self-reference task [30]. The brain regions correlated with self-referential processing in the SRET are well known from several imaging studies (e.g., [43,44]). Nevertheless, the understanding of the time course of these biases as assessed by EEG methodology in combination with self-report methods of mental health and subjective well-being is still scarce. Assessing ERP correlates during pronoun–noun processing (e.g., HisMine paradigm) or at the sentence level might provide solutions to this: At the phrase or the sentence level, the temporal dynamics of processing preferences for self-referential negative and self-referential positive stimuli can be investigated in the same paradigm and, therefore, unravel the risk markers of cognitive vulnerability for depression and the predictive markers of well-being. In the following sections, the results from previous studies investigating the correlates and, specifically, the time course of self-referential emotional processing within the HisMine paradigm will be briefly reviewed, summarized, and discussed with respect to their importance for future studies investigating EEG-ERP-based experimental testing for the prevention, intervention, and treatment of depressive disorders and the promotion of well-being.

4. Exploring the Time Course of Stimulus-Driven, Self-Referential, and Emotional Processing by Means of EEG-ERPs

4.1. EEG Indicators of Healthy Self-Referential Emotional Processing

Using the methodological benefits of electroencephalography (EEG), a number of studies have already explored when, i.e., at which processing stages during reading, self-referential vs. other-referential pronouns are differentiated from each other [35–37], as well as at which processing stages self-referential and other referential pronoun–noun pairs referring to the reader's own emotions or to the emotions of a third person are distinguished from each other and from article–noun pairs having no personal reference or having a neutral meaning [38,39]. In addition, using functional magnetic imaging it was also explored whether brain regions belonging to the emotion, self, and reading networks are involved in these discriminatory processes [45]. In the studies with self-referential and other referential pronoun–noun pairs, the nouns (positive, negative, and neutral) were paired with possessive pronouns (my or his) or articles (the) (e.g., my fear vs. his fear vs. the fear, etc.). The possessive pronouns and articles were either shown together with the nouns without any temporal delay between pronouns and nouns (SOA = 0 ms) [39] or were presented, for example, as primes with a stimulus onset asynchrony (SOA) of 600 ms preceding the presentation of the nouns to investigate and control for expectancy effects induced by the presentation of the pronouns [38]. In neither of these studies was there an explicit self-referential processing task given to the readers; rather, the task in these studies was to silently read the presented words. This was followed by a spontaneous free recall task and a subjective evaluation task (rating task) in which the participants rated the words in terms of valence and emotion intensity (arousal). During reading and in the EEG, early and late event-related potentials (ERPs) were analyzed as cortical indicators of the time course of information processing, and ERP source estimations were used to explore the brain structures involved in the modulation of these ERPs [39]. In addition, changes in the activity of certain brain regions during reading were explored by functional magnetic resonance imaging using whole brain analysis [45]. In the EEG-ERP studies using the affective HisMine paradigm, an interaction of the two factors on which the word pairs could vary, namely, the "emotionality" of a word pair (carried by the nouns) and the "reference" (elicited by the pronouns vs. articles) occurred in the time window of the late positive potential (LPP). The LPP modulation was elicited approximately 500 ms after the stimulus onset and was most pronounced over the centro-parietal electrodes during passive reading of the words. Comparing the processing of self-referential pronoun–noun pairs against the processing of other referential pronoun–noun pairs or article–noun pairs without personal reference revealed a stronger cortical processing of self-referential positive words (self-positivity bias) in the time window of the LPP [38]. The source estimates of the

LPP modulation patterns revealed significant activation in the brain structures involved in autobiographical memory functions and in self-referential processing, which are part of the so-called self-referential processing network, i.e., the cortical midline structures (CMS) or the default mode network [46,47]. The stronger cortical processing of self-referential positive words coincided with a better recall performance in the subsequent memory test in which the participants recalled emotional words spontaneously and significantly better than neutral words, especially when they were self-referential and possessed a positive meaning [39]. In addition, analysis of the ratings obtained after the EEG session showed that participants rated emotional words higher in valence and arousal when during reading, the nouns were related to the own person (self-referential) than when the nouns were related to others (other referential), and rated self-referential positive nouns higher in arousal compared to when positive nouns had no person reference (article–noun pairs) [39]. This more in-depth processing of positive concepts, specifically when perceived as self-referential in healthy participants, accords well with the results from the more explicit self-referential processing tasks in the SRET studies (see Section 3 in this manuscript). This self-positivity has received proof from a number of behavioral studies in which healthy participants in the HisMine paradigm were asked to affectively judge the words as positive, negative, or neutral based on their gut feelings e.g., [48–50], for an overview see the Supplementary Materials. Across these behavioral valence–judgment studies, healthy participants had significantly more valence–congruent judgments for positive words than for negative or neutral words, specifically when these were linguistically made self-referential by the pronoun pairings. The results fit with theoretical assumptions of a self-positivity bias among healthy subjects. This self-positivity bias might stem from positive self-views and overall positive self-concepts [51,52], that in healthy subjects, even if sometimes too positive and optimistic, characterizes positive self-attribution in the service of well-being and mood-regulation. The experimentally observed self-positivity bias in the EEG studies thus suggests a spontaneously deeper encoding of self-referential emotional pronoun–noun stimuli during reading (LPP), as well as better memory-related recall and a faster valence-congruent appraisal, of these stimuli that is in line with these theoretical assumptions of positive self-attribution in the service of well-being.

The observations of differential processing of positive vs. negative self vs. other vs. no person-referential pronoun–noun stimuli as indicators of healthy and normal processing receive further support from recent EEG-ERP and fMRI studies from other laboratories investigating the interaction between self-referential and emotional information processing via sentences. In these studies, pronouns and emotional words are embedded in a sentence context e.g., [40–42].

When evaluated across studies, the findings from the EEG studies thus far support the notion that in healthy subjects, the impact of self-referential processing on the processing of emotional information first occurs at stages of information processing at which perceptual information is processed, lexical information is accessed, and information is elaborated in relation to subjective experiences stored in memory. Indeed, as graphically illustrated in Figure 3, in healthy participants, a cascade of processing steps seems to precede and occur in parallel prior to the self-positivity bias. Temporally earlier interaction effects of self-referential stimuli on the processing of emotional stimuli may, in healthy subjects, be restricted to a few occasions, including highly accessible information or top-down attentive processing. In support of a cascade of processing steps preceding the self-positivity bias, the results from an fMRI study [45] suggest that in healthy subjects, significant activity changes in at least three brain region of interests in trials in which the positive content of nouns and self-reference of first-person possessive pronouns are combined, including activity changes in the MPFC regions involved in self-referential processing, the left and right (anterior) insular cortex as a region of the salience network [53] and a relay or hub at the interface of cognition, emotion, and the body (interoception), and the amygdala as a significant emotion and relevance detector [54].
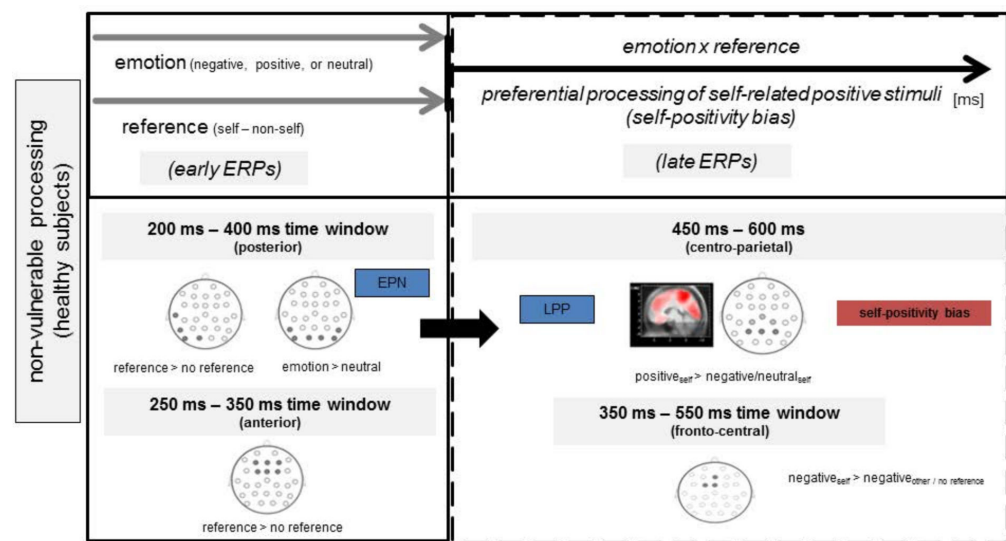
Figure 3. Cascade of processing steps preceding and underlying the self-positivity bias during reading of self-referential and other-referential pronoun-noun and non-referential article-noun pairs according to the results from [39].

4.2. EEG Indicators of Cognitive Vulnerable Self-Referential Emotional Processing

In summary, the EEG results in healthy subjects summarized in Section 4.1. provide indirect support for the assumptions that in tasks with no explicit self-referential instruction, temporally earlier interactions between self-referential and emotion processing at early stages of stimulus-driven associative processing could indeed be electrophysiological markers specific to individuals experiencing depressive symptoms or individuals prone to or at risk of or already suffering from depressive disorders. The first evidence for a self-negativity bias in the processing of pronouns and nouns as a marker of depressive symptoms was found in the EEG-ERP studies in which pronouns were used as primes for the nouns and processing of self-referential pronoun–noun pairs was compared with the processing of article noun pairs [38]. The participants' depressive symptoms were assessed via self-report standardized assessment tools, allowing assumptions about the presence of depressive symptoms and their severity of actual depressive symptoms (the BDI inventory [55]). The results showed that a deeper cortical processing (LPP) of self-referential negative rather than positive emotional words (self-negativity bias) is positively correlated with the degree of self-reported depressive symptoms. In addition, and in line with cognitive vulnerability models, this self-negativity bias started at temporally earlier processing stages—the processing of self-referential, prime- x emotional target pairs elicited a pronounced N400 potential whose amplitudes, akin to the modulation of the LPP, showed depression-congruent modulation yielding smaller N400 amplitudes for self-referential negative emotional words.

Further, though yet preliminary, evidence for even earlier temporal influences, as theoretically predicted by cognitive vulnerability models, is provided by studies investigating the EEG-ERP modulation patterns elicited during the affective HisMine paradigm in depressed and medicated individuals (with a current diagnosis of major depressive disorder) and healthy controls [56]. The HisMine paradigm was presented in multiple runs comprising passive reading/viewing conditions and conditions with instructions to pay attention to or ignore the self-referential word pairs. The first preliminary analysis of the EEG data provided in [56] suggests that depressed subjects, in contrast to the healthy control subjects, show a processing bias for negative self-referential words in the EEG which is already present during the silent reading in early time windows that started during the N100 modulation, and especially while modulating the amplitudes of the EPN Supplementary Materials [56]. In the study design, self-reference was induced by second-person possessive pronouns instead of first-person possessive pronouns. These results comple-

ment the findings from SRET studies in depressed and non-depressed participant samples, showing that besides significant group differences in the time window of elaborate processing (LPP), there are early ERP processing differences between groups. As a marker of risk of depression, more recently, early processing biases towards self-referential negative information have been shown to continue into the remission of the disorder, being still observed in remitted depressed participants [57]. The hypothesis of an early self-negativity bias in the processing of self-referential emotional content as EEG-ERP markers of depressed vulnerability is currently further evaluated and extended in a research project comprising a series of EEG-ERP studies [58]. In the studies, EEG-ERP modulation patterns are assessed in samples of healthy subjects, who, prior to study participation, were preselected into groups of depression-prone individuals vs. individuals not prone to depression, according to clinical screening and assessment tools [58].

4.3. Studying Self-Referential Emotional Processing Biases as Markers of Cognitive Vulnerability and Well-Being by Means of Language-Dependent EEG Paradigms: Potential Limitations and Advantages

The investigation of emotional and self-referential processing by means of linguistic stimuli and language paradigms might be considered a limitation or a restriction. The reservation might stem from classical theoretical definitions of emotions that define emotions from an evolutionary, biological perspective and that consider emotion processing as being largely independent from language processing; specifically, emotion perception is suggested to be primarily driven by non-linguistic physical features of stimuli that the brain, due to its biological significance, is attuned to respond to with heightened attention and the preparation of bodily preparation for fight or flight and approach or consumption (for an overview, [59,60]). While there is no doubt that emotional stimuli, be it words, pictures, or faces, can elicit similar early ERP modulation in a number of task contexts (for an overview, see [61,62]), there is also no doubt that modality- and stimulus-specific processing effects between verbal and non-verbal emotional stimuli might, nevertheless, exist. Regarding depression and its cognitive vulnerability, a particular interest in the use of language paradigms to study emotion and the self might stem from three theoretical grounds: first, to examine the theoretically assumed "errors" in cognition and self-reflection in the schemata of depressed vs. non-depressed individuals; second, to determine, in line with modern theoretical accounts of embodiment and embodied cognition, how cognitive biases are influenced by sensory and motor information among cognitively vulnerable individuals at risk of depression vs. among individuals already suffering from depressive disorders vs. healthy controls; and third, given that depression, being an affective disorder that includes mood changes, to investigate psychophysiological, neurophysiological, and neurobiological changes to determine how cognitive and bodily processes might interact while participants are construing meaning from language stimuli that might trigger feelings and subjective experience relating to one's own person.

Methodologically, an important limitation of the EEG-ERP technique with regard to its application as a diagnostic tool is its reliability and power at the individual level. However, unless the focus is on the group level, results from the EEG-ERP analysis could be used as an additional testing option, in addition to self-report diagnostic questionnaires, to distinguish between individuals at risk and those without risk of mental health conditions, specifically when EEG-ERP analysis is combined with an experimental and theoretically driven task or paradigm, such as those proposed in this perspective paper. Regarding clinical disorders, previous studies have already provided promising results for such an approach. Using EEG-ERP analysis, amongst others, in combination with more advanced preprocessing and analysis tools, or in combination with a mixed methodological analysis based on time- and frequency measures, has shown to obtain good results in, for example, attention-deficit/hyperactivity disorder (ADHD) or the prediction of Alzheimer's disease (e.g., [63,64]) or major depressive disorder, e.g., [65]. Regarding depressive disorders, EEG analyses based on time–frequency analysis and/or independent-component-based event-related synchronisation/desynchronisation analysis, as reviewed and suggested in [66],

would be interesting methodological approaches to be combined in future studies with paradigms investigating alterations in self-referential emotional processing in individuals with and without the risk of depressive disorders.

5. Questions for the Future

Depressive disorder is not one disease: all disease and disorder-related changes in mood, as well as in self-reference and affective processing can, as outlined in this manuscript, theoretically manifest as biases in the processing of self-referential positive and negative information well prior to onset of the disorder. EEG and, specifically, EEG-ERP methodology are currently pursued as means that, if combined with an experimental paradigm, could help unravel the mechanisms of processing preferences and their clinical relevance as traits or state markers of the risk of mental health conditions such as depression. Although preliminary evidence has already been accumulated, future studies should principally replicate and extend the current evidence with a focus on the following guiding questions:

(1) At which stages of stimulus processing does an interaction between self-referential and emotional processing occur? Can the preliminary findings, illustrated in this manuscript, be replicated in larger cohorts of both, cognitively vulnerable and already depressed individuals vs. healthy controls?

(2) To what degree can processing preferences for self-related negative and positive stimuli, respectively, be influenced by self-related attentive and cognitively controlled processing, and which of these influences are specific for depression and its risk?

(3) Is self-negativity bias the only marker of cognitive vulnerability, or is a self-negativity bias accompanied by a reduced self-positivity bias as well (see Figure 4)?
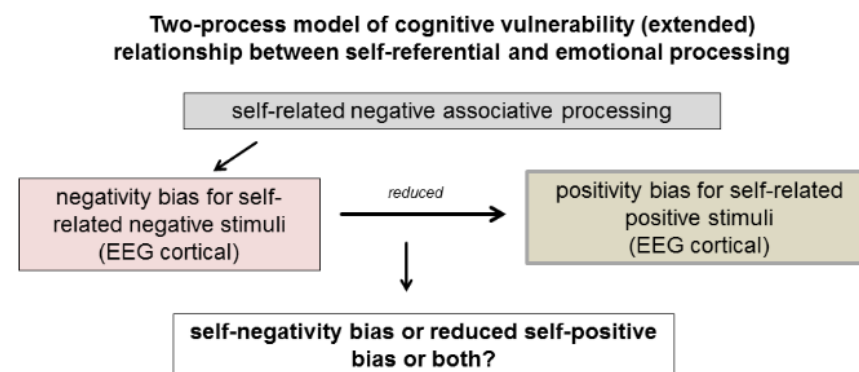

Figure 4. Extended cognitive vulnerability model (EEG cortical processing).

(4) Do the observed electrophysiological ERP correlates of the processing preferences for self-related negative or positive stimuli prove to be temporally stable markers of subjective well-being and cognitive vulnerability?

(5) Do the results vary across languages, and do they also apply to a bilingual/ multilingual context?

Importantly, question 5 is receiving increasing attention in a global society in which bilingual and multilingual psychotherapy is becoming more and more prevalent. Recent research, including EEG-ERP studies, has observed a weaker emotional reactivity to negative language content in the second language than in the first, with results being further modulated by mood, proficiency, and language use, e.g., [67,68]. Future projects and studies that focus on questions (1)–(5), respectively, will fill an important gap between the understanding of processing preferences, their electrophysiological dynamics, and their psychological and clinical significance as depressive vulnerability indicators and markers of subjective well-being. Based on this evidence, experimental tests could then be developed with which depression-associated processing biases as well as indicators of well-being could be detected by means of EEG-ERP measurements and used for depression monitor-

ing and improvement in well-being in the context of health prevention, intervention, and therapy.

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