UNIVERSITY OF PADUA

Department of General Psychology

Master's Degree Course in Clinical Psychology

Affective processing in individuals with depressive symptoms: an ERP study

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ABSTRACT

Introduction: depression is a mood disorder characterised by negative mood and anhedonia that causes significant impairments to affected individuals. Given the significant burden of depression, identifying early indicators of the disorder has been suggested as a core priority. Altered affective processing has been identified as a potential indicator underlying the development and maintenance of the disorder. The elaboration of affective stimuli includes multiple stages (i.e., cue evaluation and engagement, anticipation, and elaboration); however, how each stage relates to depressive symptoms remains unexplored. Event-related potentials (ERPs) of the electroencephalographic (EEG) signal, thanks to their excellent temporal resolution, offer unique insights into the different stages of affective processing.

Study aims: this study aimed to investigate the anticipation and processing of affective stimuli in individuals with different levels of depressive symptoms.

Materials and methods: A sample of 42 (21 females) students from the University of Padua were recruited. An S1-S2 paradigm, a task in which an emotional picture (S2) is preceded by a cue (S1) anticipating its valence, was employed during an electroencephalographic (EEG) recording. Three ERPs reflecting different stages of emotional processing were assessed: the Cue-P300 (reflecting cue-evaluation and affective engagement), the Stimulus Preceding Negativity (SPN; reflecting outcome anticipation), and the Late Positive Potential (LPP; reflecting affective processing).

Results and conclusions: Mixed-effect models showed that higher levels of depressive symptoms predicted a reduced LPP amplitude to pleasant, but not unpleasant, pictures. No other effects emerged regarding the Cue-P300 or the SPN. These results suggest that subclinical depressive symptoms might be characterized by blunted affective elaboration, rather than the anticipation of pleasant stimuli. Taken together, the ERPs might be leveraged to enhance the early identification and the design of treatment protocols for depressive symptoms.

Keywords: ERP; Depressive symptoms; affective elaboration.

PART I

Chapter 1
DEPRESSION

1.1 Clinical overview and epidemiology

Depression, often referred to as Major Depressive Disorder (MDD), is among the most widespread mental disorders, with about 322 million individuals having the disorder worldwide (Kessler et al., 2003). MDD is a complex and disabling disorder, resulting from the interaction of multiple factors of social, psychological, and biological nature (WHO, 2012). Depression is defined by the American Psychiatric Association (APA, 2013) as a chronic and recurring affective disorder characterised by persistent sadness and significantly reduced interest or pleasure in performing normal activities (Pellegrino, 2019) along with other cognitive, physiological, somatic, and psychomotor alterations which consequently impairs the functioning of an individual and its quality of life (Kessler et al., 2003).

Clinical overview. According to the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM; 2013), MDD is characterised by the manifestation of one or more depressive episodes perduring for at least 2 weeks. The core symptoms of a depressive episode are persistent negative mood which must occur every day for most of the day, and a loss of interest or pleasure in previously enjoyed activities (i.e., anhedonia). Additionally, at least 5 or more of the following symptoms must be displayed:

- Depressed mood most of the day, nearly every day;
- Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day;
- Significant weight loss when not dieting or weight gain;
- Insomnia or hypersomnia nearly every day;
- Psychomotor agitation or retardation nearly every day;
- Fatigue or loss of energy nearly every day;
- Feelings of worthlessness or excessive or inappropriate guilt;

- Diminished ability to think or concentrate, or indecisiveness;
- Recurrent thoughts of death or recurrent suicidal ideation.

At least one of the symptoms is either a) depressed mood or b) loss of interest or pleasure. The symptoms must cause clinically significant distress or impairment in social, occupational, or other fundamental areas of functioning. It is important to establish that the episode is not attributable to the physiological effects of a substance or another medical condition. Moreover, it is imperative to exclude the present or past occurrence of a manic or hypomanic episode (sustained period of abnormally elevated mood, energy, and extreme behaviours), as otherwise, the diagnosis would qualify for bipolar disorder.

In addition, people affected by depression often experience a constellation of other symptoms, among which, excessive rumination, social withdrawal or isolation, lack of self-care and poor hygiene, and psychosomatic symptoms (e.g., recurrent back pain, headache, or gastric problems).

Affective symptoms. The low mood experienced by individuals with depression manifests as an overwhelming sense of sadness, hopelessness, and emotional turmoil. It is a pervasive state that persists throughout most of the day, impairing the quality of life of a person and the negative perception of the future. Anhedonia, along with depressed mood, is a core feature of MDD. Anhedonia manifests as a significant lack of pleasure or interest in performing daily activities previously enjoyed. It also impacts motivation and social relationships, potentially leading to social withdrawal and isolation.

Excessive guilt and feelings of worthlessness are also often reported symptoms within the affective dimension. These symptoms occur in depressed patients as strong feelings of inadequacy, helplessness, and a tendency to self-blame, which contribute to maintaining a negative self-image, and low self-esteem (Harrison et al., 2022). Other common affective symptoms linked to a depressed mood are anxiety and emotional fluctuations, such as hypersensitivity or irritability, which might cause disproportionate reactions to minor stressors and emotional upheaval.

Cognitive symptoms. Cognitive dysfunctions in depression are highly frequent in most patients and often persist even after other symptoms of the disorder have improved (Fehnel et al., 2016). These symptoms impact a wide range of neurocognitive functions spanning from executive

functions, concentration, and memory to negative automatic thoughts and maladaptive schemas. Individuals with depression often report feeling mentally foggy, a mental state associated with a reduced ability to focus, plan, and make decisions, which impairs the performance of daily tasks whether at work, school, or personal activities (Gonda et al., 2015).

Memory problems include both short-term and long-term memory recall, leading to reduced ability to retain information, and recall details and, therefore, increasing feelings of frustration. Indeed, overgeneralized autobiographic memory, that is the tendency to recall categories of events rather than specific details, has been linked to depression (Gibbs & Rude, 2004).

On a higher cognitive level, rumination, defined as a metacognitive pattern of recurrent thinking focused on one's negative mood, is another common symptom associated with increased access to negative memories and with the worsening of negative mood states (Cooney et al., 2010; Zhou et al., 2020). Moreover, rumination has been linked to enhanced cognitive biases in emotional information processing, and to deficits in mood regulation, overall reinforcing depressed states (Joormann, Dkane & Gotlib., 2006). Negative cognitive biases indeed represent another key feature of MDD, as individuals develop a distorted way of thinking about themselves, the world, and the future, leading to a pessimistic perception of reality (Nieto, Robles & Vazquez., 2020).

Psychomotor symptoms. In most cases, depression involves a series of psychomotor disturbances, encompassing observable changes in a person's physical movements and behaviour (Buyukdura, McClintock & Croarkin, 2011). For example, depressed patients might experience agitation, a state of restlessness that induces an increase in action, such as fidgety or inability to stay still. Or on the opposite, they often report psychomotor retardation, a noticeable slowing down of motor functions and speech (Schrijvers, Hulstijn & Sabbe., 2008).

Vegetative symptoms. This dimension of symptoms is characterised by dysfunctions in basic physiological functions that can manifest as opposites, including changes in sleep patterns and appetite (Baxter, 2011). The severity and manifestation of neurovegetative symptoms can vary widely among individuals with depression and can overlap with other medical conditions, so it is important to undergo a comprehensive evaluation for an accurate diagnosis (Rice et al., 2019). About 80% of depressed patients suffer from insomnia and 15–35% from hypersomnia (Steiger &

Paawlowski, 2019). Impaired sleep negatively conditions the level of energy during the day, adding to the sensation of fatigue, and is linked to more severe symptoms and difficulties in treatment (Fang et al., 2019).

Changes in appetite frequently occur as reduced or increased appetite, resulting in unintended weight loss or weight gain linked to emotional distress. Evidence suggests that these opposite manifestations might be linked to distinct depression subtypes that drive the direction of appetite changes (Simmons et al., 2020). Many individuals with MDD also experience decreased libido, that is reduced sexual desire, and sexual dysfunctions, resulting from several factors linked to depression (Phillips & Slaughter, 2000).

Epidemiology. Epidemiological data on the prevalence and incidence of depression is fundamental to gaining a better understanding of the impact of the disorder on public health and an approximate overview of how it develops and spreads across populations in terms of demographics (Stein, 1981). It was reported by the Global Burden of Disease Study (GBD collaborators., 2019) that depressive disorders, predominantly MDD, are the most prevalent mental health disorders and the primary cause of disability worldwide. It was estimated that roughly 3.8% of the global population is affected by MDD (WHO, 2023) with a prevalence twice as high in females relative to males (see Figure 1.1).

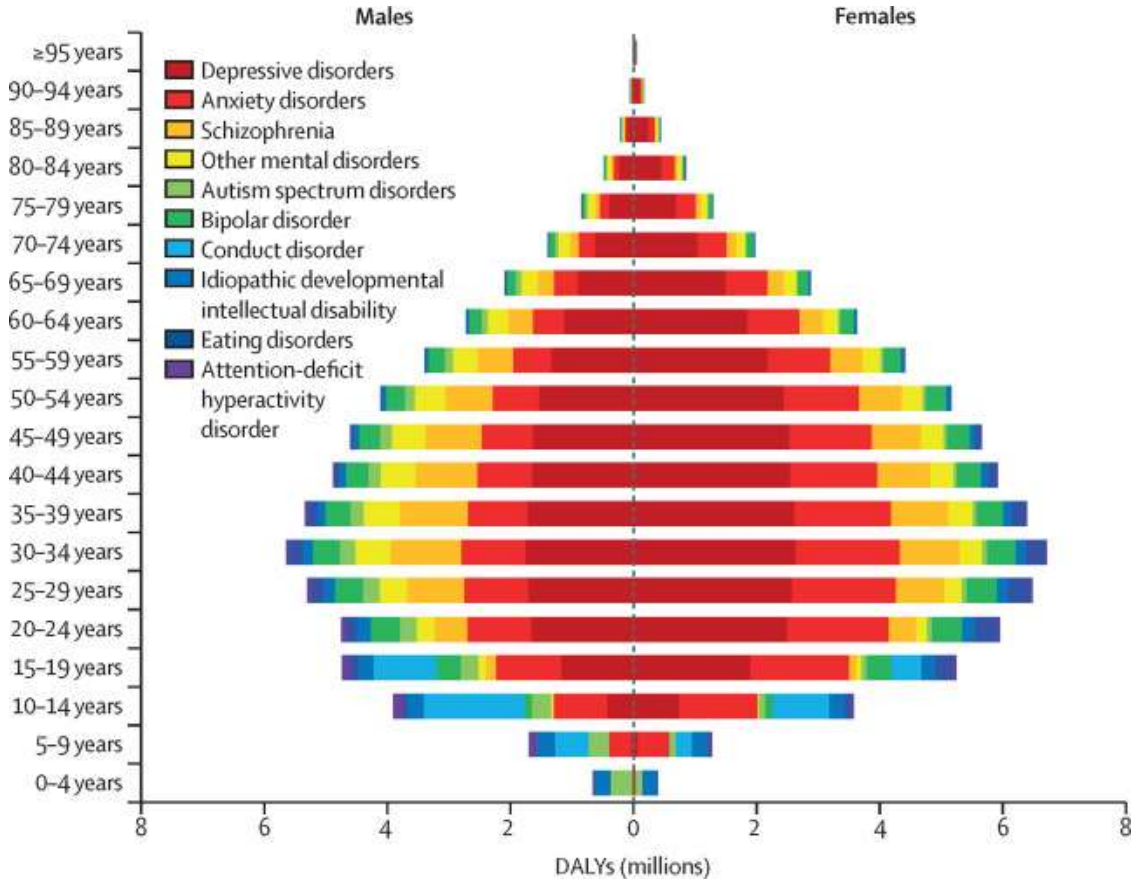

Figure 1.1 *The figure reports depressive disorders as the leading cause of DALYs (disability-adjusted life-year; lost years of life due to premature death or disability) among the most spread mental disorders, with a higher prevalence for the female sex and the age group going from adolescence to young elderly (from GBD 2019 Mental Disorders Collaborators, 2022).*

These numbers have significantly increased over the last decades as assessed in a subsequent GBD study published by Health Metrics and Evaluation (Liu et al., 2020) that recorded an incidence of 49,86% more in depressive cases diagnosed worldwide from 1990 to 2017 (Campanardi et al., 2022; Paganin et al., 2022), with an additionally increase observed in concomitance of the global pandemic COVID-19 (Hawes et al., 2022). These insights are particularly concerning as accumulating evidence from meta-analyses reported higher rates of the illness among children and adolescents (Thapar et al., 2022). Furthermore, the occurrence of an MDD episode during adolescence is associated with more severe and recurrent depression in adulthood as well as higher rates of comorbidity with other mental disorders (Liu et al., 2015; Clayborne, Varin, & Colman, 2019; Groen et al., 2020).

The lifetime likelihood of experiencing a depressive episode has been estimated to be around 15% and, despite the timing and severity of an MDD episode being variable, roughly 20%

of cases tend to become chronic, highlighting the weight of the disease on the general population (Goldman et al., 1999; Eaton et al., 2008). Epidemiological research is also relevant to estimate the direct and indirect impact of the disorder on public health from an economic point of view by measuring healthcare costs, lost productivity, and disability across countries (Mrazek et al., 2014). In line with this, cost-of-illness (COI) studies estimating yearly costs related to depression, reported higher indirect costs (i.e., workplace absenteeism) compared to the direct ones (i.e. treatment for diagnosed people) (Thilina, & Yadurshini, 2020). These results are not surprising considering that access to treatment is lacking for around 80% of people suffering from mental disorders (WHO; 2020). This evidence expands to a global extent across ages and socio-economic statuses; however, the risk of developing depression is greater for populations living with higher rates of unemployment and individuals who experienced a history of traumatic life events such as the loss of a loved one or physical diseases (WHO, 2017) (see Figure 1.2).

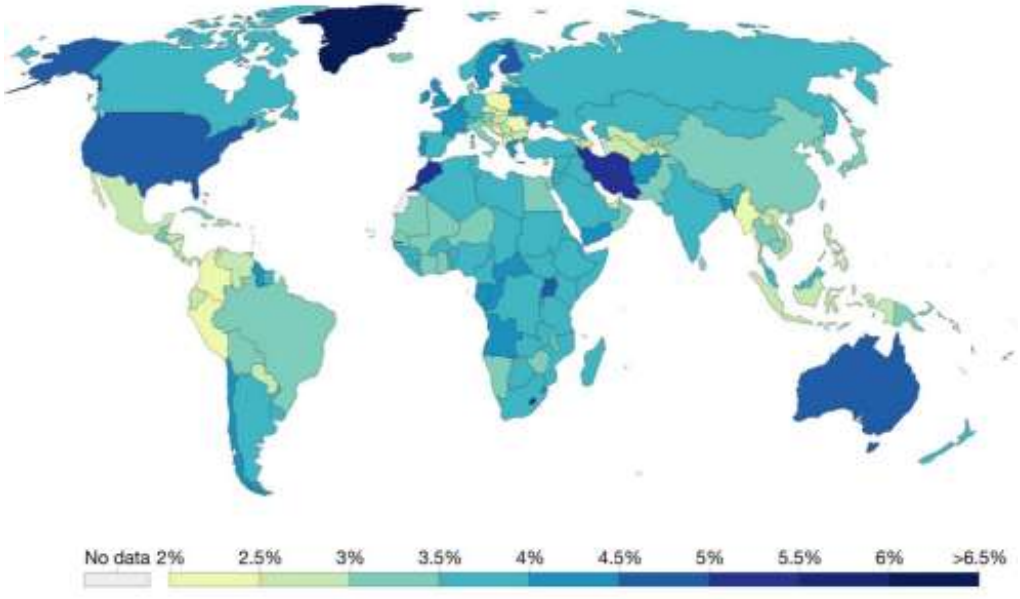

Figure 1.2 *Distribution of prevalence of MDD across countries reported by the Institute for Health Metrics and Evaluation and Global Burden of Disease Study (Our World in Data, 2017).*

1.2 Risk factors for depression

While the etiology of depression is multifaced and complex, it is increasingly recognised that a constellation of risk factors contributes to the onset and maintenance of the disorder. Understanding these mechanisms is crucial for informing prevention, early intervention strategies,

and targeted treatment approaches (Dell'Acqua et al., 2023). This is relevant considering the recurrent nature of the depressive disorder, the high probability of relapse, and the severity of symptoms associated with an early onset of MDD. Comprehensive investigations of potential risk factors revealed a diverse array of contributors including biological, psychological, and environmental domains.

At the biological level, heritability studies suggest the presence of a certain degree of genetic influence in depression vulnerability accounting for approximately 30-40% of the variance in depression risk. Twin and family studies have indeed consistently demonstrated higher rates of the condition among monozygotic twins compared to dizygotic ones, highlighting the hereditary component (Wurtman, 2005; Hamet & Tremblay, 2005). Indeed, having a family history of depression is associated with a heightened risk of developing the disorder (Parker et al., 1997; Monroe, Slavich & Gotlib, 2014) linked to both genetic and environmental factors (e.g., shared environment) (Rice, Harold & Thapar, 2002). Many studies have been conducted on the offspring of parents with a history or current depression (Hammen, 2008). For instance, a longitudinal study conducted by Weissmann and colleagues (2006) monitored the offspring of depressed and non-depressed parents for 20 years and again after 30 years (Weissman et al., 2016) and concluded that offspring of parents with a history of MDD had 3 times higher risk to develop depression and other psychopathological conditions (e.g., anxiety, substance abuse, social impairments) than those without a familial risk. Growing up in a household affected by parental depression can create a stressful and emotionally unstable environment for children (Goodman & Gotlib, 1999).

A factor well-known to increase the risk of developing clinical depression is dysphoria, or sub-clinical depression, which refers to a set of elevated depressive symptoms that do not meet the criteria for clinical MDD or persistent depressive disorder (Horwath et al., 1992). Dysphoria exhibits a set of symptoms that encompasses affective, cognitive, psychomotor, and vegetative dimensions, similar to depression, but on a sub-clinical level (Gotlib & Joormann, 2010). Subclinical levels of depression are associated with higher aberrant cognitive processes and negative mood states that over time can exacerbate depressive symptoms and lead to the full-blown condition. Moreover, the presence of dysphoria is one of the main risk factors for the development of an episode of MDD. Specifically, individuals with dysphoric mood are 4.4 times more likely, compared to non-dysphoric individuals, to experience a depressive episode during a year (Horwath et al., 1992). From a clinical perspective, dysphoria is characterized by a series of dysfunctional

symptoms relative to the affective, cognitive, psychomotor, and vegetative dimensions, qualitatively similar to depression, but quantitatively inferior, making it a sub-clinical condition (Healy, 1993).

Investigating dysphoria in the context of depression is a useful approach for the study of the associated neurophysiological mechanisms, as it allows the analysis of a sample with depressive symptoms that do not meet the criteria for the clinical condition and, therefore, is free from the influence of psychopharmacological drugs (Dell'Acqua et al., 2021). However, the limited knowledge of early psychobiological indicators of depression hinders the early recognition of the disorder, suggesting further research is needed (Wong & Licinio, 2001).

Research on individuals with sub-clinical depression and familiarity for depression has helped to highlight some key risk components. For instance, *neuroticism* is a personality trait that implies the disposition of an individual to report and experience negative emotions (Eysenck, 1967). Twin studies estimated the shared genetic correlation between neuroticism and depression and found that 35-55% of the genetic variance in depression is shared with neuroticism (Kendlar et al, 1993; Kendler et al, 2006). Indeed, neuroticism was found to consistently distinguish depressed from non-depressed individuals, and to correlate with more chronic and recurrent course, poorer treatment outcome, and more frequent hospitalizations (Mulder, 2002).

Neuroendocrine imbalance, especially related to hormones like *cortisol*, which is the most well-known stress hormone, is another contributing influence in the vulnerability for depression widely analysed as much evidence reported substantial, but variable genetic influence shared with the disorder (Riese et al., 2009). Indeed, abnormal cortisol response, specifically, higher levels of basal and reactive cortisol, have been reported in individuals with depression and also in healthy offspring of parents with depression (Klimes-Dougan et al, 2022).

Another candidate risk factor of depression is frontal asymmetry as measured by electroencephalography in the frontal regions of the scalp (Goldstein & Klein, 2014). Activity of the right frontal side is thought to reflect withdrawal behaviour and negative behaviour, whereas activity within the left region would reflect approach behaviour and positive affect. Although mixed findings have been reported relative to frontal asymmetry in depressed vs. non-depressed individuals (Goldstein & Klein, 2014), reduced left frontal activity was linked to healthy offspring of parents with a history of depression, and to the prediction of first depressive episode onset, which makes it an interesting construct to consider when investigating vulnerability to depression.

Indeed, this dysfunctional activity was linked to reduced processing of positive content and to overall reduced motivation and symptom of anhedonia.

Some cognitive biases, such as attentional biases, also play a role in the processes of vulnerability to depression. For instance, eye tracking studies reported that depressed patients attend negative stimuli longer compared to healthy individuals (Kellough et al., 2008), whereas other studies reported that individuals with depressive symptoms displayed reduced attention to positive content (Sears et al., 2010), both of which are consistent with the idea that depressed people preferentially process, or attend to, negative information about the world.

Stemming from the concept of genetic predisposition and environmental experiences, a popular explanation of the etiology of depression is the diathesis-stress model (Colodro-Conde, et al., 2018). This model postulates that stressful events may activate a diathesis, or biological vulnerability, converting the predisposition for depression into the actual psychopathology, and can overall be conceptualised as a gene by environment interaction (Colodro-Conde et al., 2018). The term "diathesis" refers to underlying vulnerabilities ranging from biological, psychological, and social factors (Colodro-Conde et al., 2018). The stress component instead refers to external events or circumstances that challenge a person's coping and adaptive resources, including major life events (e.g. loss of a loved one), chronic stress (e.g. recurrent interpersonal conflicts or financial problems), environmental factors (e.g. experiencing a trauma). When individuals with underlying diatheses encounter significant stressors, the risk for developing MDD is greater, as the level of stress exceeds an individual's coping resources. Moreover, imbalances in neurotransmitters, including noradrenaline, serotonin, and dopamine, which are strongly implicated in the regulation of mood, motivation, and emotional behaviour, might represent an influencing link between factors causing depression (e.g., psychological trauma, genetic predisposition) and the development of the mental illness (Mello et al., 2003).

Most pharmacological treatments designed to treat depression are indeed based on targeting these neurotransmitters, also called monoamines.

1.3 Neurobiology of depression

Despite significant advancements in neurobiology over the past few years and the development of psychological and biological theories on the pathogenesis of depressive disorder, the etiology of MDD remains unknown (Drevets, Price, & Furey, 2008).

Structural abnormalities. On a biological level, subjects suffering from depression exhibit alterations of the limbic and cortical structures involved in emotional regulation and perception compared to healthy individuals (Kober et al., 2008) (see Figure 1.3). Consistent with a large body of neuroimaging literature, abundant studies on brain scans of patients with MDD found significant volumetric abnormalities in some of the key areas involved in emotional experience and the production of affective states, defining an overall *ventral bottom-up network*, (hippocampus, basal ganglia, orbito-frontal cortex (OFC), ventromedial prefrontal cortex (vmPFC), anterior cingulate cortex (ACC), amygdala), and a *dorsal top-down network* implicated in emotional and behavioural regulation processes (predominantly dorsal areas of the prefrontal cortex) (Davidson et al., 2000; Lorenzetti et al., 2009; Disner et al., 2011). Particularly prominent are the alterations within the PFC, hippocampus, and amygdala reflected in reductions in structural volume (Hastings et al., 2004; Wang et al., 2020; Nolan et al., 2020). The PFC retains a fundamental role in keeping goal-oriented information and directing motivational approach-oriented actions, planning, abstract thinking, and emotional and behavioural regulation, and might underlie some of the key symptoms of MDD, respectively, difficulties in decision-making and anhedonia, impaired executive functions, and poor emotional regulation.

Another fundamental area critical for emotional response to stress and memory-related functions is the hippocampus, whose neurons are damaged by prolonged exposure to stress hormones such as cortisol (Campbell & MacQueen, 2004). The latter exerts a neurotoxic effect on hippocampus neurogenesis leading to reduced structural volume thereby influencing heightened anxiety and depressive states as well as cognitive impairments (Sheline et al., 2002).

Contrasting evidence was gathered on the volumetric changes in the amygdala (Yüksel et al., 2018), a subcortical area that is one of the centers for emotional experience, specifically elaboration of fear-related stimuli even at the unconscious level (Gainotti, 2012). Some papers reported a reduced matter size (Hastings et al., 2004), and others no difference compared to healthy individuals or even larger volume size (Hamilton et al., 2008).

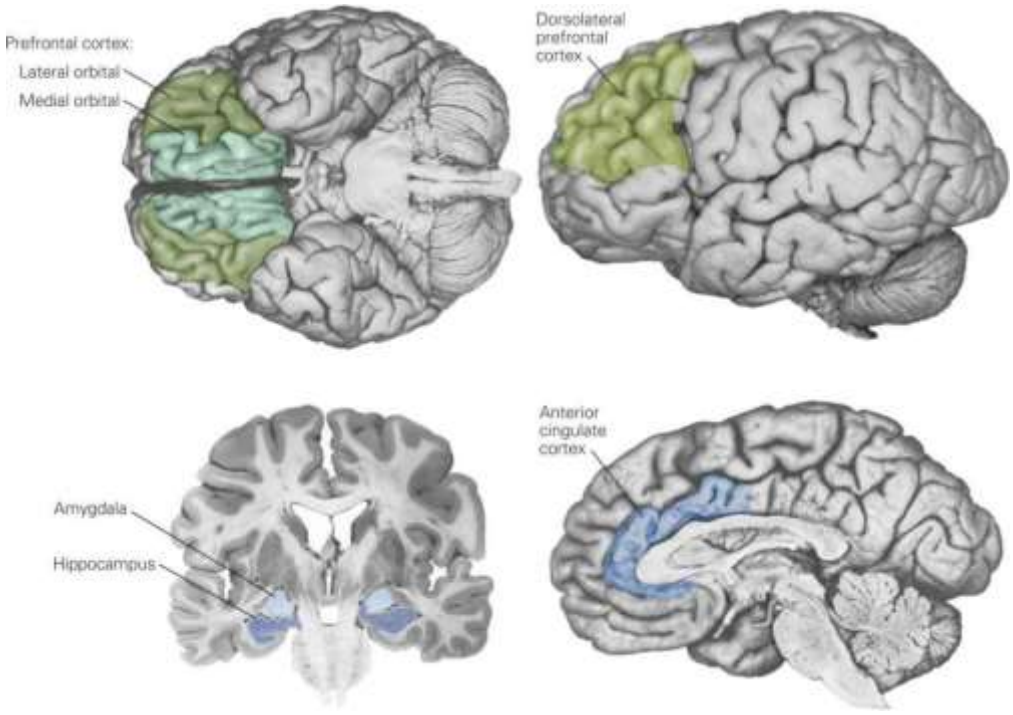

Figure 1.3 *The image shows the key brain areas central to emotional dysregulation that present abnormalities in subjects with depression. These structures form an interconnected network that plays a pivotal role in adaptive emotional, physiological, and behavioural response related to meaningful stimuli. (From Davidson, Putnam, and Larson, 2000).*

Functional abnormalities. On a functional level, neuroimaging techniques such as functional magnetic resonance imaging (fMRI), electroencephalography (EEG), or positron emission tomography (PET) (Campanella & Philippott, 2006) shed light on the most consistent abnormalities across several brain regions involved in emotional regulation, reward processing, and cognition in depression (Alexopoulos et al., 2012). Several articles reported an association between alterations in the frontal cortex and impaired emotion regulation in individuals with MDD, particularly related to abnormalities in the PFC connectivity. The most frequently reported feature of MDD is hypoactivation of prefrontal areas, especially the left PFC (Etkin et al., 2015; Kohn et al., 2014), which as previously discussed, is thought to be linked to approaching behaviours and processing of positive content (Goldstein & Klein, 2014).

By contrast, hyperactivation of some subcortical regions involved in negative emotional experience, might explain the affective symptomatology of depressed patients. The structure found to display greater activation is the amygdala, primarily implicated in the processing of negative

emotions, fear, and anxiety-related content. Accordingly, its activation resulted in a positive correlation with depression severity (Gaffrey et al., 2011).

1.4 Affective models of depression

In line with the critical data reported and the consequent growing interest in MDD, there has been a growing interest in exploring models of the vulnerability of depression (Naragon-Gainey, 2019) in relation to the affective, cognitive, and behavioural dimensions of the disorder. Depression is characterized by alterations of mood and emotions, two aspects that are interrelated but distinct, although they are often mistakenly used as interchangeably. Most studies considering these two constructs agreed on the core difference being the duration of the experience (Garrido, 2014). Emotions are transient, relatively brief experiences that arise in response to a salient stimulus (Scherer, 2000) and that, in turn, can elicit behavioural, subjective, or physiological reactions. Mood, on the other hand, is a prolonged affective state or disposition that influences the individual for a longer duration as it is enduring and pervasive, it exerts its effect on feeling states and cognition (Rottenberg, 2005). Hence, the difference between the two concepts is clear as well as the extent to which each one can impact a person. The characteristic duration and prevalence of moods rather than emotions is indeed what moderates the severity of MDD affective states. However, the two are interrelated and can influence each other, for instance, a constant low mood can generate negative emotions, and feelings of sadness or hopelessness. Likewise, while effective emotional regulation allows individuals to experience emotions adaptively, difficulties in regulating emotional responses experienced by individuals with depression, in turn, potentiates the aberrant mood state. Many studies suggest that these self-regulatory deficits emerge from the interaction of biological predisposition with environmental, and psychosocial factors (Bradley et al., 2011), with consequent anatomic-physiological and behavioural changes.

While many factors contribute to the development and maintenance of depression, affective models provide a valuable theoretical framework in the understanding of MDD, focusing on the role of emotional processes and regulation as key aspects of pathological affective states. Affective models consider emotions as guiding action and organising behaviour towards salient goals (Davidson & Irwin, 1999). These models state that emotions emerge according to two main motivational systems within the brain that, under an evolutive perspective, evolved to promote adaptation and survival of the human species: the appetitive system and the defensive systems.

The appetitive system is responsible for driving approach behaviours towards pleasant, rewarding and beneficial stimuli, whereas the defensive system motivates avoidant behaviours towards aversive stimuli, hence it activates in response to danger or stress (Lang & Bradley, 2013). The interaction between these motivational systems defines the affective style of a person, hence the individual differences in terms of valence and intensity of emotional responses. Affective styles vary at the individual level based on several factors, such as personality or vulnerability to mental disorders, and they influence how an individual process information within the environment to drive behaviour (Davidson, 2004). Indeed, reduced activation of the motivational approach system has been linked to common features of depression involving lack of motivation and pleasure in daily life (Trew, 2011).

Abundant literature reports different theoretical models on affective frameworks of depression, among which are the *negative potentiation hypothesis*, the *positive attenuation hypothesis*, and the *emotion context insensitivity.*

1.4.1 The negative potentiation hypothesis

The negative potentiation hypothesis states that negative mood tends to potentiate emotional responses to negative cues, indicating a greater activation of the defensive motivational system (Bylsma et al., 2008; Rottenberg, 2005; Messerotti Benvenuti et al., 2020). This is based on Beck's cognitive model of depression (1976, 1979), which refers to two main concepts: the cognitive triad and cognitive schemas. Cognitive schemas (mental representations of stimuli and experiences) are activated by daily internal or external stimuli and control how information is encoded, stored, and retrieved, thus driving the way an individual interprets and makes sense of information and experiences. Aversive events significantly affect internal schemas and, especially if occurring at early stages of life, they can negatively impact the development of these schemas (Disner et al., 2011), a phenomenon known as "cognitive vulnerability" (Ingram., 2003). Maladaptive schemas consequently bring about dysfunctional interpretations of environmental stimuli and lead to the tendency to attend to negative stimuli over positive ones or interpret information negatively (see Figure 1.4).

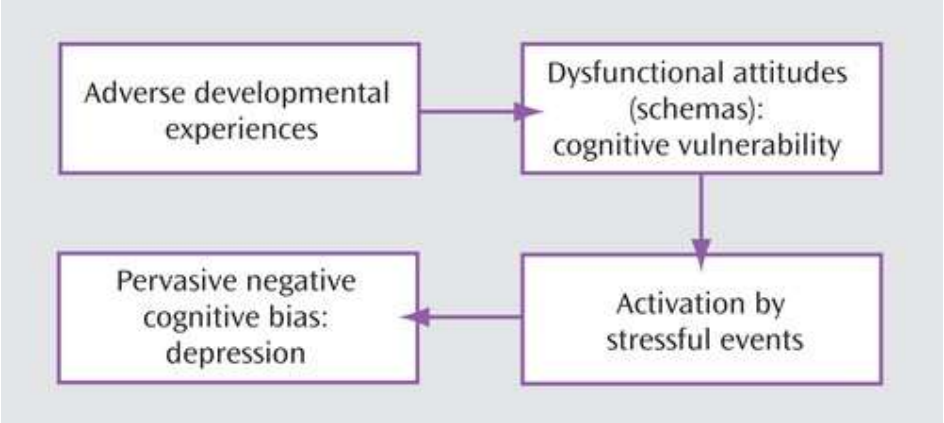

Figure 1.4 *The scheme depicts the pattern of dysfunctional cognition involved in depression (from Beck, 2008).*

The negative potentiation hypothesis states that negative moods, characteristic of MDD, contribute to potentiating negative emotional reactivity by activating aberrant cognitive schemas that consecutively produce biases towards negative content. Likewise, negative emotions do trigger depressed mood in MDD, leading to the activation of aberrant schemas and, therefore, to the negative appraisal and maintenance of cognitive distortions, generating a dysfunctional circle (Beck., 1967; 1976; 2008). In other words, negative moods and negative emotions are mutually reinforcing in MDD (Bylsma et al., 2008).

Despite the relevance attributed to the negative potentiation hypothesis and its role in informing current treatments for MDD, this hypothesis has not fully been empirically validated (Gotlib & Joormann., 2010). In this context, several psychophysiological measures (e.g., skin conductance, startle reflex) can offer insights into the functioning of the defensive motivational system (Oken, Salinsky & Elsas, 2006). However, findings are still somewhat inconsistent (Messerotti Benvenuti et al., 2015; Hill et al., 2019) For instance, a work by Rosebrock and colleagues (2017) based on the passive viewing of affective images found no difference in skin conductance responses (SCRs), an index of sympathetic activation, between participants with vs. without depression when viewing threat images. Another physiological correlate used in similar paradigms to measure emotional reactivity to affective stimuli is the startle reflex. The startle reflex is a defensive response to a sudden and intense acoustic, tactile, or visual stimulus that reflects the activation of the defensive motivational system (Boecker & Pauli., 2019), and it is measured by recording the eye blink magnitude with the electromyography (Ditcher et al., 2004). A study

conducted by Allen, Trinder, and Brennan (1999) used a passive viewing task involving the presentation of emotional pictures (pleasant, neutral, or unpleasant) accompanied by an acoustic startle probe (burst of white noise). While healthy controls displayed the typical modulation of the startle reflex (i.e., potentiated for unpleasant stimuli and attenuated for pleasant ones), the group with depression exhibited attenuated startle potentiation for unpleasant stimuli and reduced attenuation for pleasant stimuli relative to controls, overall showing an undifferentiated level of activation regardless of the affective context (see Figure 1.5).

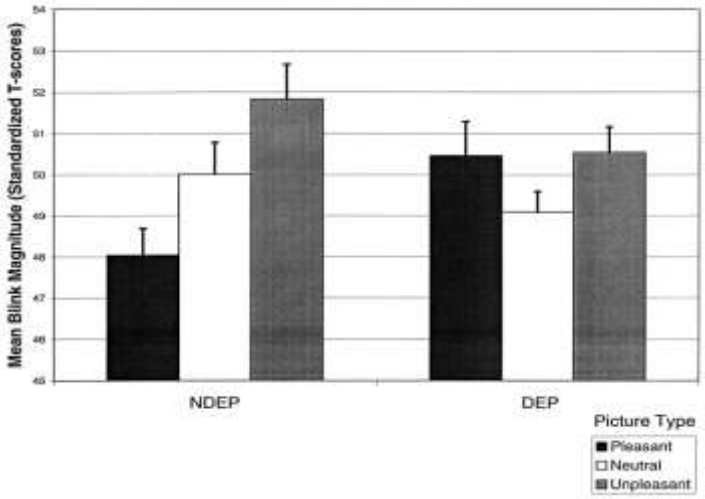

Figure 1.5 *Standardised startle modulation for depressed and non-depressed groups. Error bars indicate standard error means (From Allen, Trinder, and Brennan,1999).*

Contrarily, some neuroimaging studies collected evidence supporting the negative potentiation hypothesis. For instance, hyperactivation of the amygdala was consistently reported in MDD brain scans during tasks involving exposure to unpleasant stimuli, and abundant empirical evidence highlighted the correlation between hyperactivity of this structure and its role in mediating the potentiation of negative emotions such as fear and anxiety (Zhong et al., 2011; Boukezzi et al., 2022). Moreover, consistent with the assumption of a lateralisation of negative emotions towards a right hemispheric dominance (Manda, Tandon & Asthana, 1992; Stato & Aoki, 2006), much research found an association between depression and hyperactivity of the right hemisphere, in contrast to hypoactivation of the left side, in tasks involving the presentation of affective unpleasant images, which could explain to some degree a negative potentiation.

1.4.2. Positive attenuation hypothesis

Depression has traditionally been conceptualized as a disorder characterized by negative mood potentiation. However, emerging research suggests a role of reduced positive affect in this disorder. In this context, the positive attenuation hypothesis posits that individuals with depression may exhibit reduced activation of the appetitive motivational system, leading to reduced reactivity and processing of pleasant information, diminished positive affect, reduced motivation, and impaired reward processing (Wu et al., 2017). Indeed, this is in line with some of the main features of depression, such as anhedonia, apathy, and reduced physical activity. Psychophysiological models have supported this hypothesis, by exploring the reactivity and elaboration of pleasant and rewarding information in depression (Rottenbrg et al., 2005). As explored in the previous paragraph, the study by Allen and colleagues (1999) measured the modulation of startle reflex elicited by acoustic startle probes during the presentation of affective images (pleasant, unpleasant, or neutral) among patients with different MDD severity (Beck & Steer., 1987) vs. healthy controls. In the context of the positive attenuation hypothesis, it is interesting to note that both samples had similar reactivity to neutral and unpleasant images, but somewhat surprisingly only those with the highest BDI-II scores had potentiated startle reflex in response to pleasant stimuli (see Figure 1.6).

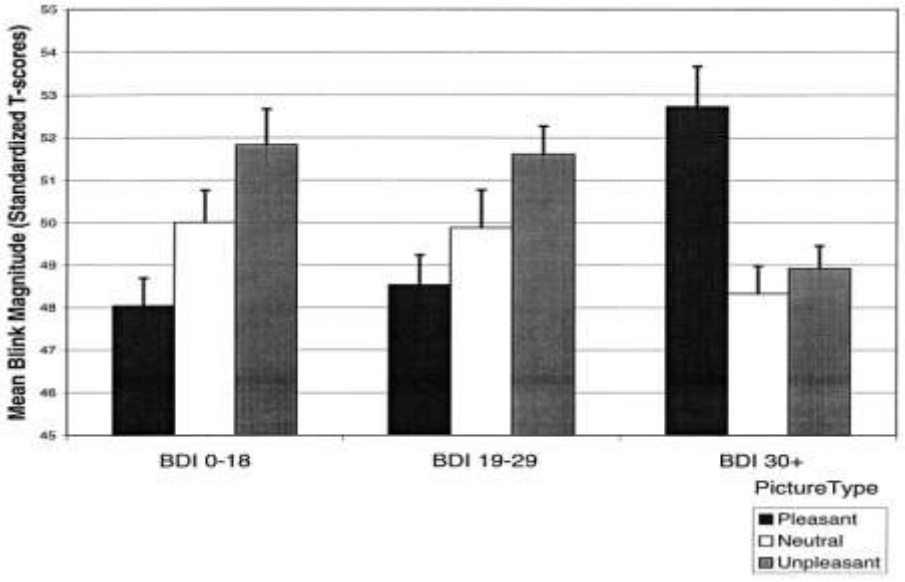

Figure 1.6 *Startle eye blink magnitudes of individuals during the viewing of affective images. The groups are sorted by BDI-II scores; the sample with severe depression (BDI-II 30+) displayed the highest startle reflex attenuation to pleasant images (From Allen and colleagues, 1999).*

Some experimental works implemented similar tasks requiring the presentation of affective clips whilst recording facial expressions assessed by electromyography (EMG) (Greden et al., 1986) and self-report measures (Sloan et al., 1997, 2001). Emotional reaction was measured by self-report psychological measures, and corrugator and zygomatic muscle activity, respectively associated with unpleasant and pleasant emotional reactions (Larsen et al., 2003). Reduced emotional response was found only towards positive stimuli in participants with depression compared to controls, as well as a discrepancy between self-report scores and facial muscle activity (see Figure 1.7).

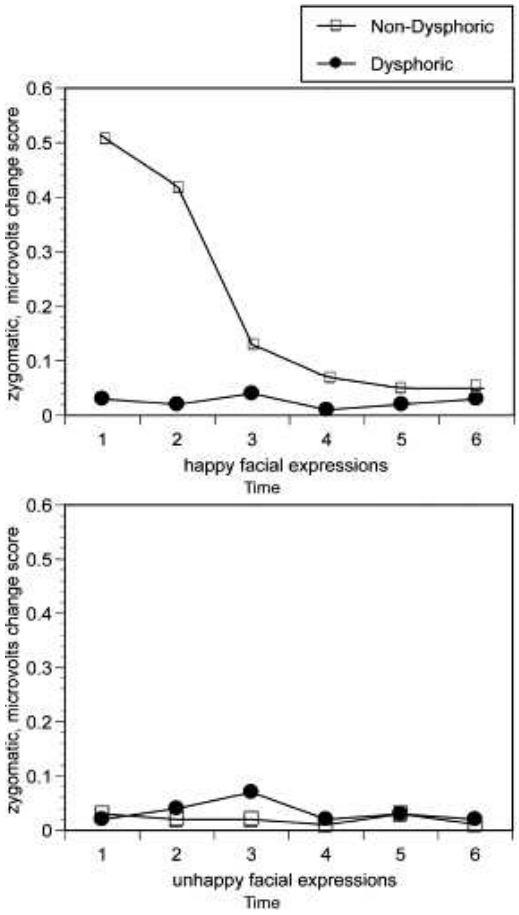

Figure 1.7 *Mean change in zygomatic facial EMG activity during picture viewing illustrating that dysphoric participants do not contract the zygomatic muscles when viewing happy facial expressions (top panel), while both groups showed a non-reactive zygomatic pattern to unhappy facial expressions (bottom panel) (from Sloan et al., 2001).*

Similarly, facial electromyography was adopted by Sloan and colleagues (2002) to record the activity of the corrugator and zygomatic muscles, in subjects with dysphoric vs. non-dysphoric

mood (BDI-II, Beck et al., 1996). The task involved the viewing of expressive faces (i.e., happy, neutral, sad, or angry) presented for 6 seconds. In line with the positive attenuation hypothesis, dysphoric subjects exhibited decreased activation of the zygomatic muscle when viewing the happy expressions compared to non-dysphoric subjects, whereas patterns of activity for negative and neutral faces did not differ.

Another useful measure in the study of emotional processing and reactivity in MDD is cardiac autonomic reactivity. Interesting evidence assessing this correlate was collected by Messerotti Benvenuti and colleagues (2015) on a sample of sub-clinically depressed (dysphoric) vs. healthy university students following a visual paradigm (narrative verbal prompt followed by emotional imaginary). Cardiac vagal withdrawal resulted to be reduced in response to pleasant but not unpleasant imagery in dysphoric vs. control individuals, supporting the hypothesis of attenuation towards positive stimuli (see Figure 1.8).

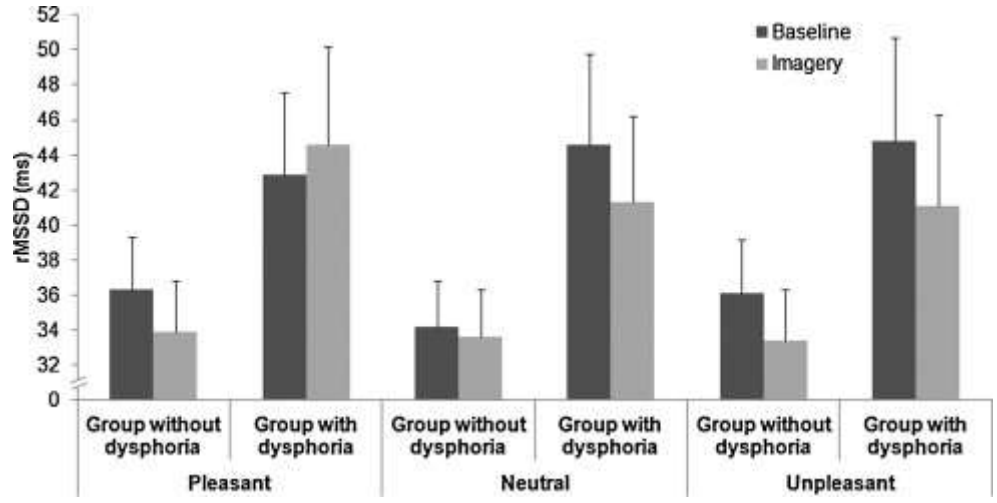

Figure 1.8 Means and standard errors of the root mean square of successive RR differences (rMSSD) (ms) of baseline vs. imagery timing, and valence (pleasant, neutral, and unpleasant) in the group with dysphoria and without dysphoria (from Messerotti Benvenuti et al., 2015).

1.4.3. Emotion context insensitivity hypothesis

More recently, the limited support for the negative potentiation hypothesis and mixed findings on the processing of unpleasant stimuli in MDD has led to the formulation of a third

alternative model following previous trajectories (Bylsma et al., 2005, Bylsma, 2021). The emotion context insensitivity (Bylsma et al., 2005, Bylsma, 2021; Rottenberg et al., 2005) suggests that individuals with depressed mood tend to experience diminished emotional responses and processing of all affective stimuli regardless of valence. Hence, it is in line with the positive attenuation hypothesis and in contrast with the negative potentiation hypothesis. These alterations in emotional reactions to positive and negative stimuli can be conceptualized in terms of positive and negative valence systems (from the National Institute of Mental Health Research Domain Criteria Framework, NIMH RDoC; Insel et al., 2010). From a clinical point of view, the disengagement with the environment assumed by this view resembles the phenomenological feature of depression, the perceptions of the world as flat, dull, and empty (Haley., 1993).

The emotion context insensitivity has received notable empirical support from psychophysiological studies (Bylsma et al., 2021). A comprehensive meta-analysis by Bylsma et al. (2008) conducted a review of MDD emotional reactivity literature utilizing evidence from subjective, behavioural, and peripheral physiological levels and concluded that, across 19 studies, there was an overall consistent reduction in emotional reactivity to both pleasant and unpleasant stimuli. Furthermore, Kaviani and colleagues (2004) examined emotional reactivity in a sample of depressed vs. healthy controls. The patients' group was further divided into low vs. high depression, low vs. high levels of anhedonia, and low vs. high anxiety. The task involved the presentation of pleasant, neutral, and unpleasant film clips, each one accompanied by the presentation of an acoustic startle probe. Reduced startle potentiation for unpleasant content and lack of attenuation for pleasant content was displayed in participants with high symptoms of depression and anhedonia compared to low, whereas subjects with anxiety symptoms showed the opposite pattern (see Figure 1.9).

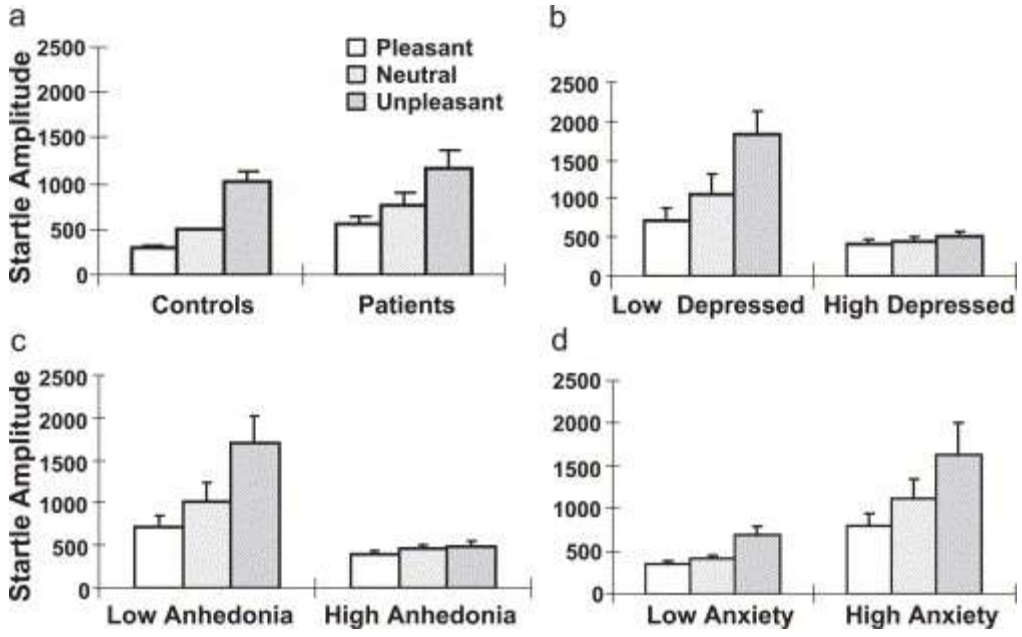

Figure 1.9 *The figure reports the startle reflex amplitude elicited by startle acoustic probe during the viewing of affective clips in a sample of healthy controls vs. patients with high and low symptoms of depression, anhedonia, and anxiety (from Kaviani and colleagues, 2004).*

This evidence is congruent with the mechanisms proposed by the emotion context insensitivity as it reports an overall disengagement with the environment across all contexts.

Analogue outcomes in terms of blunted emotional response were found by Wexler and colleagues (1993) in a task involving passive viewing of emotionally salient faces while electromiography was recorded corrugator and zygomatic muscles. Additionally, a dichotic listening paradigm (neutral vs. emotion-evoking words, directed to each ear simultaneously) was implemented to analyse the perceptual sensitivity to affective versus neutral words. As hypothesised, the sample with MDD displayed blunted facial mimicry across all contexts: corrugator muscle in patients was greater compared to controls during both happy and neutral images and showed no difference across all affective valences, meaning higher negative feelings and overall flat emotional reactivity. The zygomatic muscle was significantly reduced in the depressed group in both pleasant and neutral trials. Moreover, the patients heard fewer positive and negative words compared to neutral ones, overall supporting the emotion context insensitivity hypothesis postulates.

Some evidence in support of the emotion context insensitivity was also gathered through the use of self-reported psychological measures in a sample of clinically depressed vs. heathy controls (Rottenberg et al. 2002). Results showed that levels of self-reported sadness did not vary

as a function of the emotional valence of film clips in depressed patients compared to healthy individuals who instead reported higher levels of sadness in sad rather than neutral and pleasant film clips.

Chapter 2

EVENT-RELATED POTENTIALS IN THE STUDY OF EMOTIONAL PROCESSES

2.1 Dimensional models of emotions

Emotions are transient, relatively brief experiences that arise in response to a meaningful stimulus (Scherer., 2000) and elicit behavioural, subjective, or physiological reactions lasting for seconds or minutes (Frijda, 2007). As previously introduced, emotions developed to facilitate the adaptation to the environment based on brain systems (the appetitive and defensive motivational systems) needed for survival, that respond to either appetitive or aversive stimuli (Lang et al., 1998; Nesse, 2000; Lang & Bradley, 2009). Despite the crucial role of emotions in human behaviour and psychology, there is no commonly agreed-upon definition of emotion in any of the disciplines that study these phenomena (Mulligan & Scherer, 2012).

Emotions have initially been categorised into discrete categories such as happiness, sadness, anger, fear disgust, and surprise (Siedlecka & Denson, 2019). These categories are often referred to as basic or primary emotions (Altuwairqi et al., 2021). However, there are variations in how different theories or models of emotions categorise and define these basic emotions (Faith & Thayer, 2001). As opposed to previous views, the three-dimensional model by Lang (Lang, 1994) introduced a new perspective based on the idea that emotions can be understood following a multi-dimensional perspective rather than confined in rigid categories. In this context, Lang's dimensional model conceives emotion as a wide disposition to respond to environmental conditions with expressive language, behavioural patterns, and physiological changes.

Unlike previous models that primarily focused on valence and arousal, Lang's model acknowledges the relevance of the subjective experience and interpretation of emotions. By doing so, this model captures and highlights the role of the cognitive appraisal processes that underlie emotional phenomena (e.g. interpretation of stimuli, meaning attribution), in other words, how cognition shapes emotional reactivity and provides insight into the subjective quality of emotion. It is, therefore, proposed a three-systemic analysis of emotion, where the latter is caused by a trigger (not necessarily recognizable or physically present), and that represents the final product of the interplay between the following equally relevant systems:

- ***Subjective experience:*** this dimension refers to the individual's experience of the emotion in terms of interpretation and attribution of valence to it. It is usually expressed verbally (self-reported).
- ***Behavioural response:*** this level describes the observable behavioural manifestation of emotions, that is, it represents how emotions are communicated through behaviour. It includes variations in the tone of postural muscles; variations of facial expressions and paralinguistic indexes; fight or flight, and approach or withdrawal motor responses.
- ***Physiological arousal:*** this level represents the physiological changes, at a central and peripheric level, that emerge and accompany emotions. These responses are fundamental for the motivational modulation of an individual that manifest via activation of the endocrine, immune and autonomic nervous system.

Lang suggested that these three levels might be considered as strictly interconnected and partially independents, without any level being more significant than to the other. These levels interact dynamically to produce a common emotional response.

Emotional states can be distinguished based on the motivational direction evoked by a stimulus (appetitive vs. defensive) and the strength of the physiological arousal (Miller, 1966). These aspects of direction and intensity align with two key dimensions underlying human emotions: valence and arousal (Lang et al., 1997). Valence is critical for guiding behavioural responses along an approach/withdrawal continuum based on the perceived (un)pleasantness of stimuli. Arousal reflects the subjective sense of calmness or activation and corresponds to the intensity of the physiological response (Bradley et al., 1992).

Taken all together, these models significantly contributed to research in the field of psychology and psychopathology by facilitating the development of methodologies and paradigms for studying emotions in ecological settings. One way in which Lang's model has advanced research in psychophysiology is by defining the selection and interpretation of physiological correlates used to measure emotional responses. For instance, Lang and colleagues (1997) have developed the International Affective Picture Processing (IAPS) database, a set of pictures (over 1000 images) categorised following their dimensional model of emotions. They aimed to develop a database of standardised images available for experimental research

across the world. Images are based on different semantic categories, and each one of them has a rating along the dimensions of arousal and valence (Lang,1997) (see Figure 2.1).

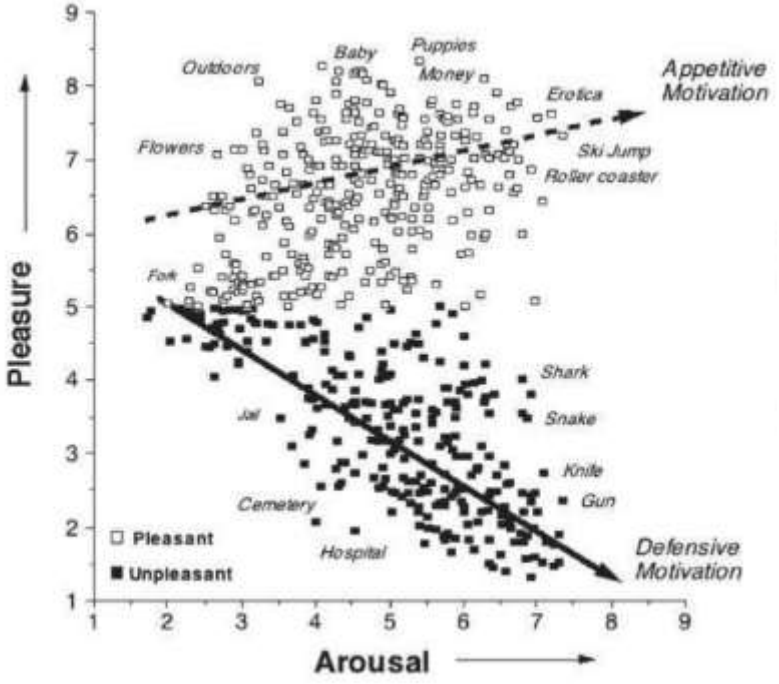

Figure 2.1 *Images from the IAPS (International Affective Picture System) distributed in the two-dimensional space defined by the dimensions of valence and arousal. The arrows in the upper and lower portions of the affective space indicate the activation of the appetitive and defensive motivational systems.*

Electroencephalography (EEG) has been employed for almost 100 years as a main non-invasive tool in the study of mental processes. EEG records the electrical activity of the brain through a set of sensors applied on the scalp, and it has long been utilised within many disciplines, such as affective neuroscience and psychophysiology, to investigate the different stages and aspects of emotional processes (Keil, 2013). Before illustrating the use of the EEG in the study of emotions, it is important to comprehend some basics of the EEG signal.

2.1 Introduction to EEG signal

The EEG detects the voltage fluctuations that result from the ionic current between the brain and the underlying pyramidal neurons (Britton et al., 2016). Considering that the electric potential monitored by a single neuron is very small, the EEG reflects the summation of the synchronous firing of a large number of pyramidal neurons present in the brain (Kaur & Kaur, 2015). These neurons communicate with each other generating electrical impulses. More

specifically, when a neuron receives signals from other neurons, neurotransmitters are released into the synaptic gap. They then bind to receptors on the post-synaptic dendrites, causing the ion channels to either open or close. Excitatory neurotransmitters will bind to receptors and allow positively charged ions to enter the neuron, making it less negative (depolarization) and reaching the threshold for action potential (firing of the neuron). Conversely, inhibitory neurotransmitters will lead to the entrance of negative ions, making the inside of the neuron more negative (hyperpolarisation). The EEG signal is the resulting bioelectrical potential acquired from the summation of this neural activity, and it is recorded with the use of electrodes located at specific points on the scalp (Britton et al., 2016).

The EEG signal's oscillations reflect numerous mental functions (i.e., cognitive, emotional, and perceptual processes) (Cohen, 2017). These waves can be organised into five main bands based on their characteristics such as frequency (pattern of oscillations repetition measured in Hertz; Hz) and amplitude (height or intensity of the oscillations measured in microvolts; μV) that are inversely proportioned: delta (δ), theta (θ), alpha (α), beta (β), and gamma (γ). This classification is used to create specific indexes associated with different stages of mental processes to allow a better analysis (Başar et al., 2001). Delta waves have the lowest frequency (i..e, 0- 4 Hz), and the highest amplitude, prominent during deep sleep; theta waves have a frequency that ranges between 4 to 8 Hz, a typical pattern observed during light sleep and daydreaming; alpha waves have a frequency range from 8 to 12 Hz, and are observed during relaxation and with closed eyes; beta waves have a frequency that ranges from 12 to 30 Hz and it reflects alertness and concentration; and gamma waves have the highest frequency above 30 Hz with the lowest amplitude, and are related to attention, focus, memory consolidation (Buzsáki, 2011).

2.2 Event-related potentials in the study of emotions

Event-related potentials (ERPs) refer to the electrocortical activity elicited in response to an internal or external stimulus. They are obtained by averaging the amplitude of the EEG epochs associated in time with the stimuli of interest from paradigms where stimuli (e.g., emotional images) are repeated across multiple trials. ERPs provide a measure of neural processing related to perceptual, cognitive and/or affective elaboration, offering insights into the timing and location of these processes. A great feature of ERPs is the excellent temporal resolution that allows the detection of neural activity occurring in milliseconds and, for this reason, this technique is widely

used to investigate processes such as attention, emotion, language, and sensory processing. ERPs are divided into *exogenous sensory components*, elicited by the physical nature of the evoking stimulus occurring within the first 200-300 ms, and *endogenous components*, reflecting the cognitive responses to the stimuli, occurring from 300 ms from the onset of the stimulus (Luck, 2012). They are further categorised into specific components based on time and polarity (negative/positive). Particularly, the ERP components are labeled with a letter (N/P) based on whether the deflection in voltage is positive (P) or negative (N), followed by a number indicating the onset of the waveform in milliseconds (see Figure 2.2). For example, the P100 is a positive peak occurring approximately 100 ms after stimulus onset that reflects early visual processing (Ibanez et al., 2012). Some ERP components are labelled with functionally descriptive names (i.e., late positive potential or LPP) (Ibanez et al., 2012).

Thanks to their excellent temporal resolution, ERPs have been extensively used in the study of emotional processing to elucidate the time course of emotional reactivity both in healthy and clinical samples (e.g., Olofsson et al., 2008; Codispoti et al., 2007). Several studies have shown that salient and emotional stimuli, compared to neutral ones, modulate the amplitude of a wide range of ERPs, starting from the initial sensorial perception to further stages of emotional processing and attention. In this context, paradigms involving the presentation of emotional faces or images are typically used while the participant's EEG is recorded (Eimer & Holmes, 2007).

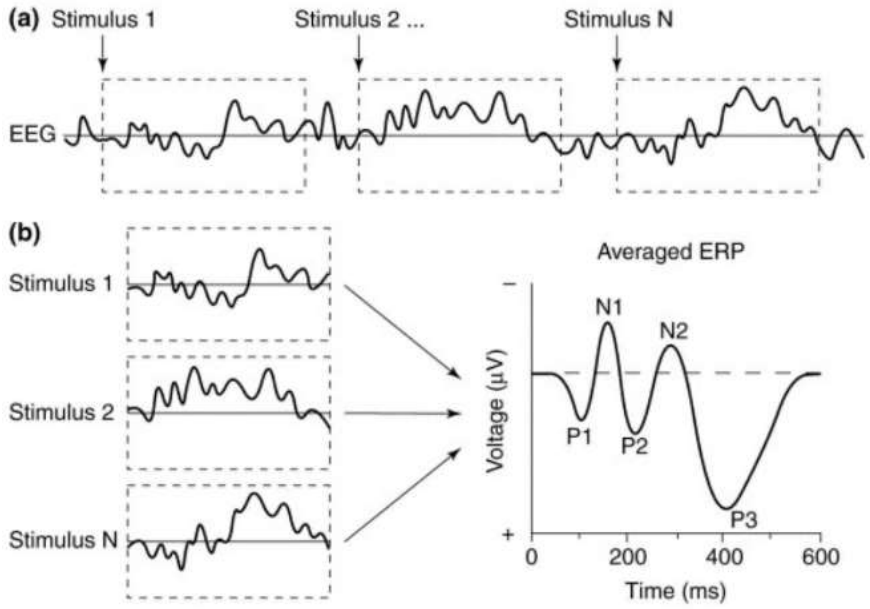

Figure 2.2 *Computation of the ERP waveform from continuous EEG data. (a) Stimuli are presented during the EEG recording, but the exact response to each stimulus is not large enough to be observable. (b) To isolate event-related activity from the continuous EEG, segments around each stimulus are extracted and averaged together to compute the averaged ERP waveform (from Luck et al., 2000).*

2.2.1 Deconstructing emotional processing: anticipation and elaboration

The ability to anticipate and process a salient stimulus enables the identification of both safe and dangerous cues in the environment, allowing us to approach or withdraw from the stimulus (Lang et al., 1998). Emotional reactivity to a stimulus involves distinct processes that can be well captured with ERPs, namely the elaboration of the cue, emotional anticipation, and emotional elaboration (Fields & Kuperberg, 2012; Brudner et al., 2018). Anticipation and elaboration are two distinct but interrelated aspects of emotional processing considering that the anticipation of an emotional upcoming event has the power to alter the elaboration of the emotional information (Sussman et al., 2016). This can lead to efficient emotion regulation (Vanderhasselt et al., 2014), or dysfunctional outcomes, such as hypervigilance and exaggerated response to threatening stimuli which, for instance, characterises anxiety and affective disorders (Sussman et al., 2016).

Anticipation within the context of emotional processing refers to the cognitive and neural processes involved in the preparation for or expectation of an emotional event or stimulus (Herwig et al., 2007). ERPs are employed to examine the distinct stages of emotional processing. To this end, paradigms involving cue-target associations where cues signal the upcoming presentation of

emotionally valenced stimuli (e.g., pleasant, unpleasant) represent an appropriate method to examine ERP components during the anticipatory phase so that researchers can examine how the brain prepares for emotional information (see Figure 2.3). *Elaboration* instead refers to the processing and evaluation of the upcoming emotional information.

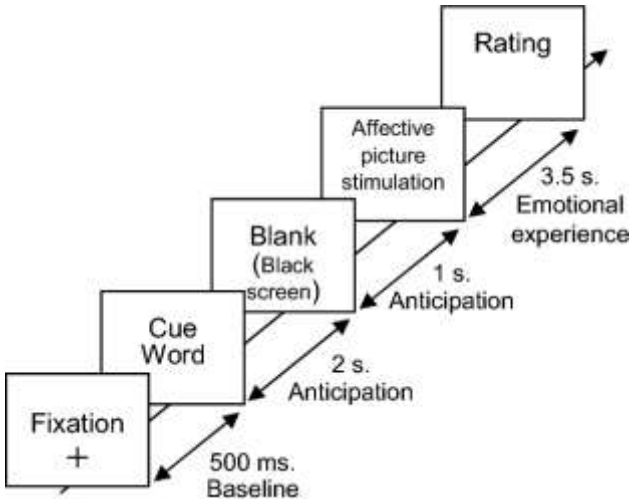

Figure 2.3 *Example of Emotional S1-S2 Paradigm (from Iwaki, 2011).*

The stimulus 1 (S1) – stimulus 2 (S2) paradigm has been shown to be a useful tool to capture the distinct emotional processes (i.e., cue elaboration, stimulus anticipation, and stimulus elaboration) (Mercado et al., 2008). The emotional S1 – S2 paradigm involves the presentation of a cue (S1) that signals the valence of the upcoming target stimulus (S2) in each trial and captures both cue engagement (to the S1), emotional anticipation (before S2) and emotional processing (to the S2).

2.2.2 *Cue-P300* and *Stimulus preceding negativity*: emotional anticipation

As for the emotional elaboration of anticipatory cues, the Cue-P300 is a suitable ERP to be analysed. Regarding emotional anticipation, the Stimulus Preceding Negativity (SPN) is employed. These potentials offer valuable insights into how the brain prepares for a salient event and how this relates to affective processes (Böcker et al., 2001; Thompson et al., 2023).

Cue-P300. The P300 complex, first reported over 60 years ago (Sutton et al., 1965), is a positive-going ERP peaking between 300-500ms after stimulus onset mainly observable within

parietal sites (Polich & Margala, 1997; 2007) that reflects the attention allocation and elaboration of a stimulus (Gray et al., 2004). The amplitude of the ERP generally increases to salient or infrequent stimuli (Pritchard, 1981). In the context of emotion anticipatory processes, the elaboration of a cue that signals the valence (e.g., pleasant, neutral, unpleasant) impending presentation of an upcoming event is captured by the Cue-P300 (Novak & Foti, 2015).

Initial evidence on this component has been gathered by adopting the *monetary incentive delay* task, a design that enables the recording of brain responses to cues signaling the opportunity for potential future gains and losses separately from gain/loss feedback, thereby disentangling the timing of expectancy for the salient event (e.g., win) from the outcomes themselves (Knutson et al., 2001) (see Figure 2.4).

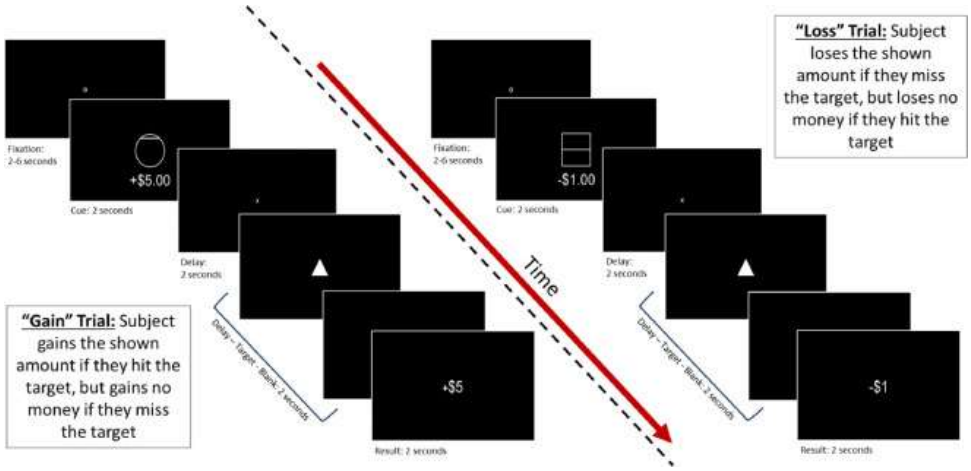

Figure 2.4 *This figure provides an overview of the monetary incentive delay task design (White et al., 2021).*

Much data implementing this design showed a greater amplitude of the Cue-P300 when allocating attention towards a symbol that indicates the presentation of upcoming emotional (e.g., win/loss) content, rather neutral (Novak & Foti, 2015; White et al., 2021), and more specifically, for reward incentives (gains) over non-reward (losses) outcomes (Flores et al., 2015).

For instance, a study conducted by Pfabigan and colleagues (2014) used mixed neuroimaging techniques (fMRI and EEG) to analyse the temporal and spatial features of anticipatory processes within an emotional context by using the monetary incentive delay task. They found a greater Cue-P300 amplitude for gains (relative to loss trials) anticipation associated with neural activation of the ventral striatum, which is a brain area linked to reward processing.

Another study by Thompson and colleagues (2023) adopted the same paradigm in a community sample of adolescents to assess whether depressive symptoms were associated with reduced reward anticipation. Congruent to expectations, depressive symptoms were associated with a reduced Cue-P300 amplitude elicited by incentive cues, supporting the role of the component as an index of anticipation in emotional contexts (see Figure 2.5).

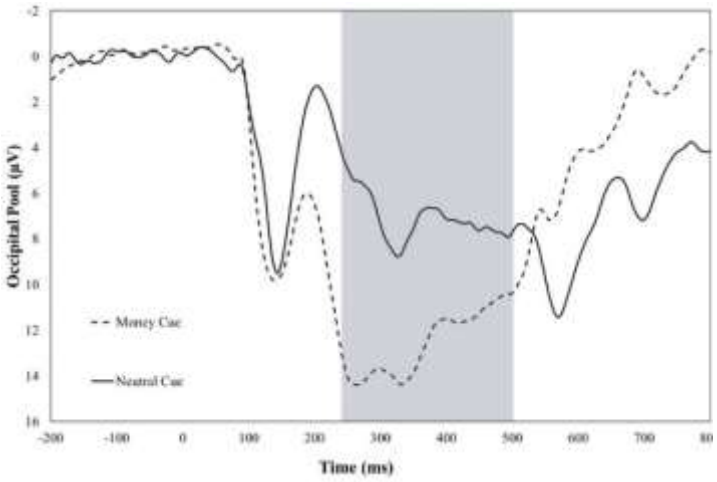

Figure 2.5 *Grand average of incentive and neutral cue-locked ERP waveforms pooled at occipital sites. The time window in which incentive and neutral Cue-P300 was scored (250–500ms) is highlighted in grey (Thompson et al., 2023).*

The modulation of the Cue-P300 by emotional valence and arousal reflects underlying mechanisms incorporating both bottom-up sensory processing and top-down cognitive control. At a sensory level, emotionally salient cues are thought to capture attention and evoke a rapid neural response further influenced by higher cognitive regions feedback. Lin and colleagues (2015) adopted a passive viewing task showing affective images (unpleasant or neutral), each one preceded by a cue that indicated the valence of the subsequent image. The indicator cue appeared in half of the trials, inducing anticipation of potential negative or neutral content, whereas the other half of the trials did not include any cue, leading to an unpredictable outcome. The amplitude of the Cue-P300 was larger in the anticipation vs. unpredictable condition, and mostly elicited by the signalling of upcoming negative stimuli compared to neutral ones.

Stimulus preceding negativity. The stimulus-preceding negativity (SPN) is a slow negative-going ERP commonly elicited a few seconds prior to the expected stimulus onset (Doe,

Smith & Johnson, 2023). It is imperative to discriminate it from other negative ERPs related to anticipation, such as the Contingent Negativity Variation (CNV), which instead indicates motor preparation for an external upcoming event or response, rather than the more cognitive, attentional processes linked to SPN that precedes task-relevant stimuli with no motor response to the S2 stimulus (Hillman et al., 2002).

The SPN is a component that reflects the anticipatory processes contributing to the preparation of upcoming events (e.g. attentional orientation, expectation of emotional stimulus) and it is visibly distributed among the frontocentral electrodes (Kotani & Aihara, 1999). Similarly to the Cue-P300, also the SPN was explored in the context of emotional anticipation in reward-related paradigms, and provided insights into how the brain prepares for emotionally significant events in the context of reward (Walentowska et al., 2018). Abundant literature found this component to be significantly elicited in reward anticipation, particularly in relation to incentives (Zhang et al., 2017). The fact that the SPN was elicited mainly by gains rather than losses, is coherent with the literature suggesting that the SPN mostly reflects approach motivation (Zhang et al., 2017; Ohgami et al., 2006).

Many studies have shown that SPN amplitude tends to be larger when participants anticipate emotionally arousing stimuli compared to neutral ones (Kitani et al., 2017). A study carried out by Van Boxtel and Böcker (2024) involved the presentation of a fear-induced cue as potentially followed by a mild electric shock. The SPN was mainly observed when participants anticipated the electric shock. Furthermore, the SPN amplitude was also tested in an emotional S1-S2 paradigm involving the presentation of affective images (Poli et al., 2007), where a sample of participants was presented with either high-arousing pictures (e.g. erotic) or low-arousing pictures (e.g. neutral objects). As hypothesised, the amplitude of the SPN was larger while anticipating high vs. low arousing pictures (Poli et al., 2007) (see Figure 2.6). Other studies adopting the same paradigm to analyse the SPN relative to the presentation of pleasant, neutral, and unpleasant pictures shed congruent results, further supporting the notion that SPN represents a neural index of anticipation of affective contexts (Takeuchi et al., 2005).

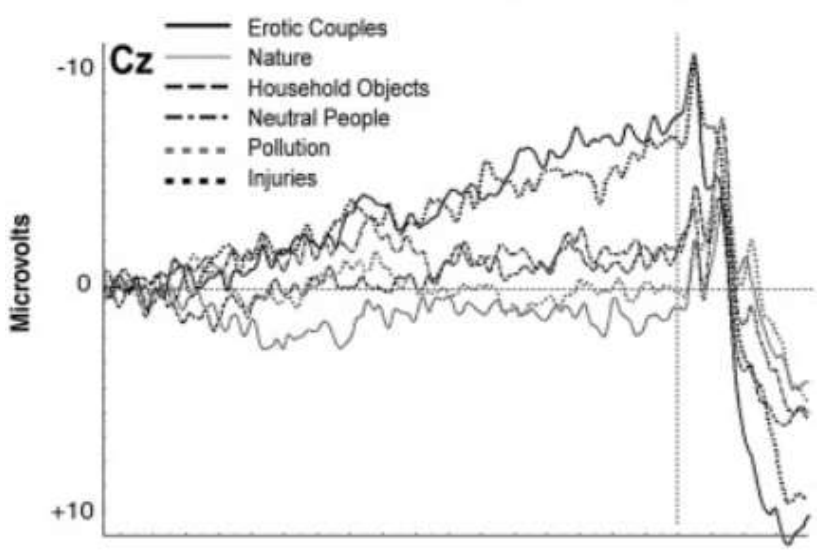

Figure 2.6 *The figure shows the SPN recorded only over the Cz site. The SPN was larger (more negative) for high arousal categories, independent of valence (erotic and injury picture) (Poli et al., 2007).*

2.2.3 *Late positive potential*: emotional processing

The late positive potential (LPP) is a late sustained positive-going component observable over midline central-parietal recording sites approximately 400 to 1000 ms following an emotional salient stimulus onset. Similarly to the SPN, the LPP is elicited by affective stimuli and represents a central measure of emotional processing and responding (Hajcak et al., 2014) (see Figure 2.7). The LPP can be regarded as part of the P300/LPP complex, as it is considered to be a prolonged continuation of the P300 component.

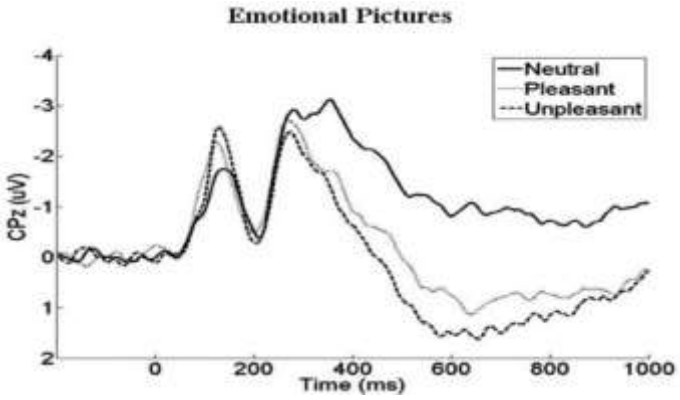

Figure 2.7 *ERPs grand averages during a passive viewing of pleasant, neutral, and unpleasant pictures. The LPP is evident as a sustained positivity over midline central-parietal recording sites. Note. negative values are plotted upward in the y-axis (from Hajcak et al., 2014).*

The LPP is generally used as a marker of sustained attention allocation towards emotionally salient stimuli, as it reflects the activation of approach and withdrawal motivational systems. Cuthbert and colleagues (2000) found evidence highlighted a coordination between the LPP, autonomic activation, and emotional subjective experience. They implemented a task involving presentation of pleasant and unpleasant images while assessing neural activity, self-reported arousal and content ratings, and skin conductance responses. They found a significant LPP increase prompted by self-rated highly arousing pictures, rather than content type, related to autonomic activation, supporting the role of the LPP as an indicator of the sustained allocation of attention towards emotionally evocative stimuli (see Figure 2.8).

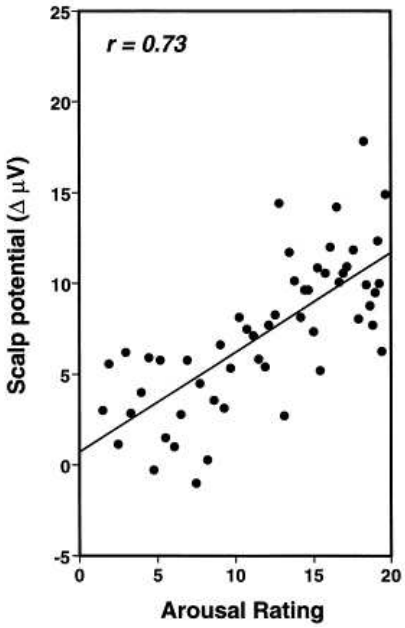

Figure 2.8 *Covariation of the judged affective arousal of individual pictures and average midline EEG amplitude in the 700-1000 ms time window (from Cuthbert et al., 2000).*

Similar results were collected by Hajcak, Dunning, and Foti (2009) in a paradigm of affective images presentation with distinct instructions. After 3000 ms of passive picture viewing, participants were instructed to focus on a neutral or arousing aspect of the unpleasant picture, whilst neutral pictures were always associated with an instruction to focus on a neutral aspect of the image. Congruent to expectations, during passive viewing, the magnitude of the LPP became reliably larger following the presentation of unpleasant pictures compared to neutral (see Figure 2.9). The LPP then reduced after participants were instructed to attend to the less arousing aspects of unpleasant pictures, hence, when individuals focused on arousing compared to non-arousing

characteristics, supporting the idea that the LPP reflects automatic attention to emotional stimuli, and arousing aspects of such information.

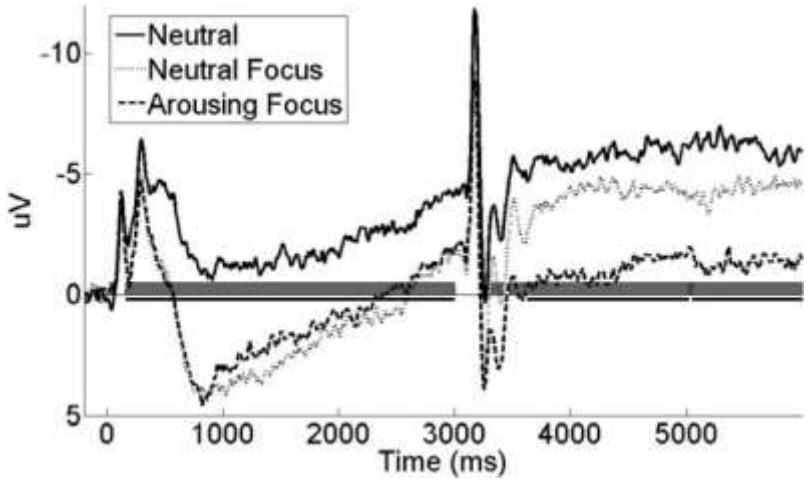

Figure 2.9 *Grand averaged ERPs at central–parietal recording sites elicited by each trial type: neutral pictures (solid line) were always associated with an instruction to focus on a neutral aspect of the picture; unpleasant pictures were followed by either an instruction to attend to a neutral (dotted line) or arousing (dashed line) portion of the image. Picture onset occurred at 0 ms and the instruction tone occurred at 3000 ms. 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 (0–3000 ms) and significant reductions in the LPP following attentional instructions (3000–6000 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 (from Hajcak, Dunning, and Foti 2009).*

In a recent review, Hajcak and Foti (2020) pointed out that arousal and significance are two similar but separate constructs: while arousal refers to the level of physiological activation experienced by an individual in response to a stimulus, significance regards the importance or relevance of a stimulus linked to a person's goals or needs. For example, they showed that the amplitude of the LPP is larger to affiliative and erotic images compared to exciting sports ones, even though they are all rated as emotionally arousing stimuli (Weinberg & Hajcak, 2010). Also, erotic images reflected greater autonomic activation as measured by SCR amplitude compared to exciting sports (Bradley, Codispoti, Cuthbert, & Lang, 2001). Similarly, greater LPP was found to be larger to familiar faces compared to unknown ones (Grasso & Simons, 2011). Taken all together these results overall highlight the role of the LPP in reflecting the processing of significant and salient affective stimuli.

2.2.4 Event-related potentials of emotional processing in depression

Event-related potentials offer a unique advantage to explore the time course of emotional processing, and, for this reason, a growing body of literature is exploring emotional processing in depression through the analysis of ERPs. Considering the affective models of the depression described in Chapter 1, assessing how individuals with depression anticipate and elaborate emotional stimuli is of particular interest to gain a better understanding of the affective and attentional processes of the disorder and its risk (Ilardi et al., 2007).

Cue-P300. A few studies have shown that depression is associated with a reduced amplitude of the Cue-P300, suggesting a reduced elaboration of the cue indicating the upcoming presentation of a reward (Thompson et al., 2023). For instance, a longitudinal study by White et al. (2021) analysed whether blunted neural responses to reward at baseline differentiate a sample of depressed compared to healthy controls, adopting the monetary incentive delay task. Participants with depression displayed significantly reduced Cue-P300 amplitude in response to cue stimuli regardless of the valence of the upcoming stimulus (win/loss) indicated by the cue, showing an overall reduced anticipation of emotional content (see Figure 2.10). Furthermore, reduced elaboration of cue stimulus correlated with poorer treatment adherence, measured on completion of 7-10 sessions of behavioural therapy, highlighting the link between altered reward

elaboration and basic features of MDD (e.g., lack of motivation) (Sherdell, Waugh & Gotlib, 2012).

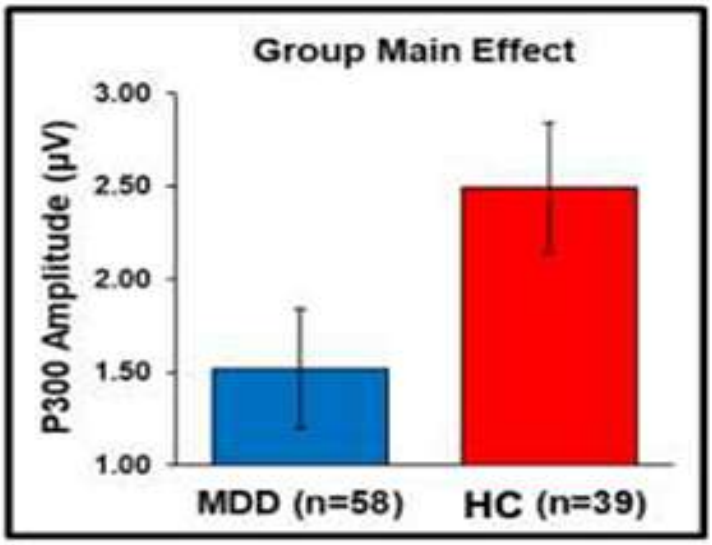

Figure 2.10 *Group main effect demonstrating that individuals with major depressive disorder (MDD) exhibit smaller P300 amplitude than healthy controls (HC). Error bars reflect ±1 standard error (from White et al., 2021).*

Further studies used similar experimental design (i.e., monetary gambling task, monetary incentive delay task) on samples of adolescents with without depression (Luckhardt et al., 2023; Thompson et al., 2023), and coherently to previous results, the participants assigned to the MDD groups exhibited significantly reduced Cue-P300 compared to controls, bringing supporting evidence on the interaction between depression and the neural component.

SPN. A few studies have reported an association between the SPN and symptoms of anhedonia, although evidence on the role of this component in relation to MDD is lacking. A recent study conducted by Sun and colleagues (2023) adopted a gambling task to investigate anticipatory and consummatory processes in depressed patients compared to healthy controls and showed blunted SPN in the MDD sample. However, inconsistent results were reported in a study that analysed anticipatory and consummatory reward processing components (Cue-P300, SPN, and Reward Positivity) in a sample of individuals with depression (Thompson et al., 2022) employing the monetary incentive delay paradigm. No significant result was noted on the SPN amplitude,

whereas Cue-P300 and RewP were both reduced relative to controls, suggesting that further research into the SPN in depression is needed.

LPP. A wealth of data also highlighted a reduced amplitude of the LPP in depression. As discussed in previous chapters, the LPP is one of the main components that reflects emotional processing of affective stimuli. Many studies found the LPP to be reduced in affective, and especially pleasant content, in individuals with depression across ages. In particular, a reduced LPP was found to predict the severity of depression in imagery tasks (Levinson et al., 2018; Grunewald et al., 2019; Whalen et al., 2020) relative to unpleasant pictures (Kayser et al., 2000), threatening content (Foti, Olvet, Klein, & Hajcak, 2010), and in tasks involving both pleasant and unpleasant images (Proudfit et al., 2015). Supporting evidence on the role of the LPP was also collected in a study by Klawohn and colleagues (2021) that investigated the neural activity related to abnormal emotional processing in a sample of depressed patients relative to healthy controls. They specifically investigated the LPP through a passive viewing paradigm of pleasant and neutral images. As hypothesised, the study showed reduced LPP amplitude to pleasant pictures compared to neutral ones in participants with depression compared to controls (see Figure 2.11).

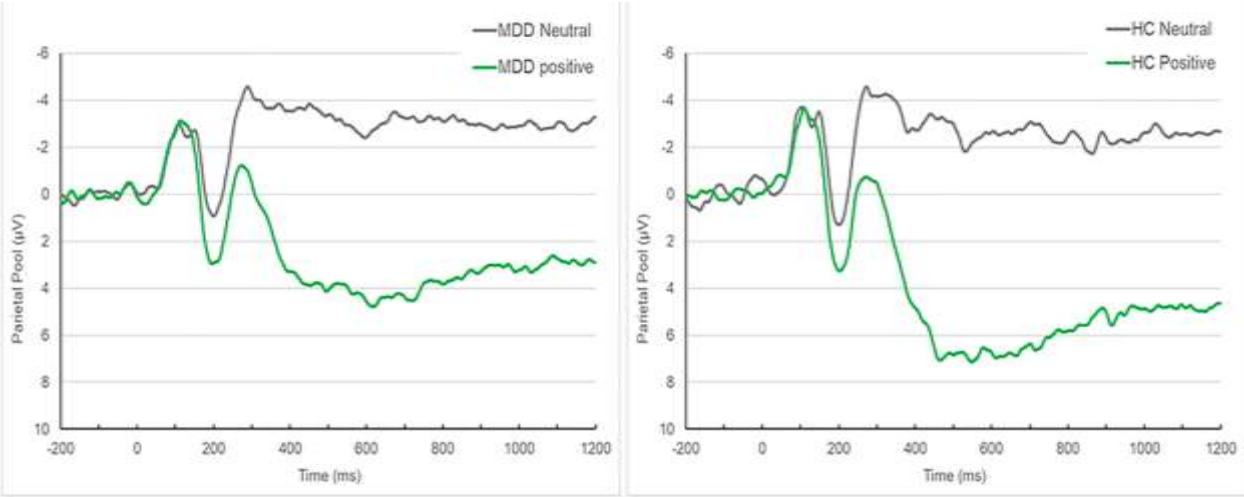

Figure 2.11 *Grand average waveforms for pleasant (left) and neutral (right) images during the time interval from 400 to 1000 ms following picture presentation in the group of participants with current depressive disorder (MDD, green line) and the healthy controls group (HC, grey line) (from Klawhon et al., 2021).*

This altered LPP response was also reported in paradigms implementing the viewing of pleasant and unpleasant images in a sample of non-depressed offspring of parents with a history

of depression, which accounts for the population at-risk, and in remittent depressed individuals (Kujawa et al., 2012; Proudfit et al., 2015).

In summary, ERPs represent an advantageous technique to examine emotional processing in depressive symptoms. As previously discussed, individuals with dysphoria represent a sample of population at-risk for developing clinical depression and some literature has already been collected on emotional processes in these samples. For instance, similarly to clinical depression, dysphoria was characterized by blunted P300/LPP complex amplitudes in response to pleasant contexts (Moretta et al., 2021) (see Figure 2.12), suggesting that deficits in approach motivation might be already present before the onset of the disorder.

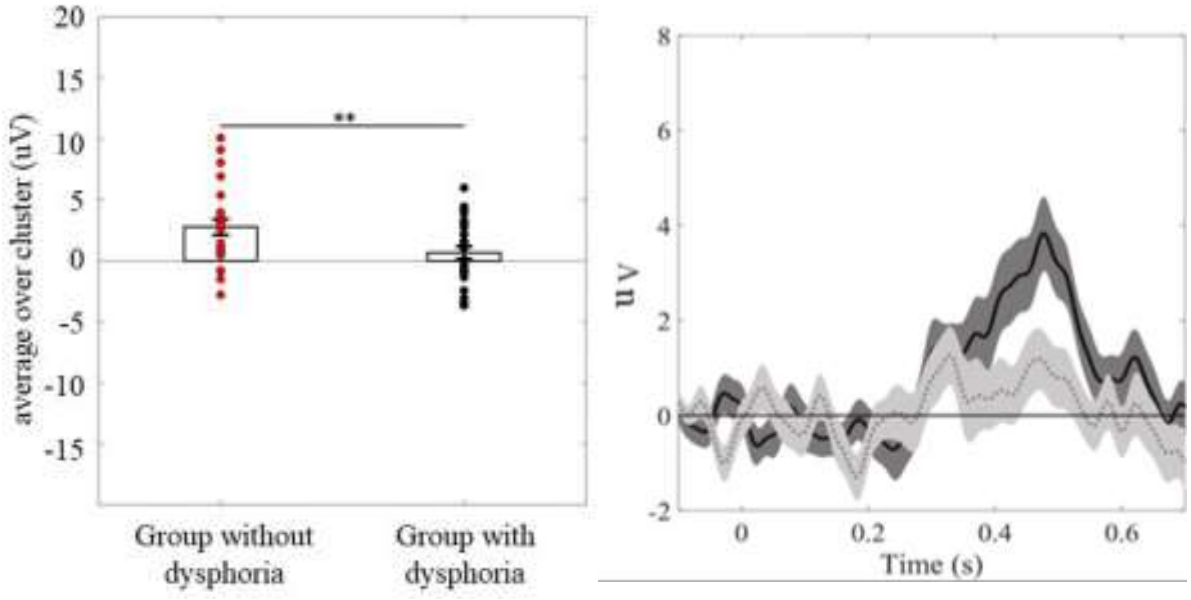

Figure 2.12 *(Left panel) Mean ERP amplitude of each participant in the group with dysphoria and the group without dysphoria averaged over the significant electrodes and time points for the neutral condition. Each circle represents one participant; the frames represent the mean ERP amplitude across all participants in the group with dysphoria and in the group without dysphoria and the solid black lines represent ± standard error of the mean (SEM). (Right panel) Time course of grand-average ERP waveforms averaged over the significant electrodes for the pleasant condition in the group with dysphoria (dashed, light grey line) and in the group without dysphoria (solid black line) (from Moretta et al., 2021).*

PART 2

Chapter 3
THE STUDY

3.1 Introduction and experimental hypothesis

The previous Chapters illustrated the core features of depression, highlighting the role of early identification and vulnerability factors of this burdensome disorder (Wahlbeck & Makinen, 2008). Depressive symptoms have been associated with a blunted emotional processing of both pleasant and unpleasant stimuli, in agreement with the Emotion Context Insensitivity (ECI) hypothesis (Bylsma et al., 2005; Bylsma 2021). In addition, a blunted emotional processing of pleasant and partly unpleasant stimuli has been suggested to represent a viable indicator of depression risk (e.g., Hajcak Proudfit, 2015; Grunewald et al., 2019; Klawohn et al., 2021; Dell'Acqua et al., 2023). However, the elaboration of affective stimuli includes multiple stages (i.e., cue evaluation and engagement, anticipation, elaboration), and how each stage relates to depression vulnerability is still unclear.

Although neuroimaging studies have reported reduced anticipation and processing of rewarding and pleasant stimuli in clinical depression (Zhang et al., 2013; Brush et al., 2018), the poor temporal resolution of these methods makes it difficult to fully explore emotional processing stages, which typically occur in the order of a few hundred milliseconds. In this context, event-related potentials (ERPs) are well-suited to distinguish and separate distinct stages of emotional processing, given their excellent temporal resolution (Luck, 2014). As detailed in Chapter 2, several ERPs reflecting different emotional processing stages can be extracted from a two-stimulus task (S1-S2), where a first stimulus (S1, or cue) indicates the occurrence of the second stimulus (S2, or imperative stimulus) (e.g., Poli et al., 2007). Three Event-Related Potentials (ERPs) reflecting different stages of emotional processing were assessed: the Cue-P300 (reflecting cue evaluation and affective engagement), the Stimulus Preceding Negativity (SPN; reflecting outcome anticipation), and the Late Positive Potential (LPP; reflecting affective processing).

As discussed, individuals with clinical depression have been shown to have a blunted LPP to pleasant – and, to a minor extent, to unpleasant – stimuli relative to healthy control groups (e.g., Klawhon et al., 2021). However, S1-S2 tasks with emotional pictures have not been thoroughly

employed in depression and findings on the Cue-P300 and SPN are lacking. However, a few studies that employed reward processing paradigms (e.g., monetary incentive delay task) have shown reduced Cue-P300 amplitudes to rewards vs. loss trials in clinically depressed individuals (e.g., Thompson et al., 2023). Furthermore, most studies have primarily focused on clinical populations, while exploring these mechanisms in subclinical levels of depression might be useful in the context of early identification and preventive efforts.

The goal of this work, hence, was to investigate distinct emotional processing stages, namely cue-evaluation and affective engagement (Cue-P300), affective anticipation (SPN), and affective processing (LPP) in relation to different levels of subclinical depressive symptoms in a sample of young adults by employing an emotional S1-S2 paradigm. Particularly, based on the previous literature (Bylsma, 2021), it was hypothesized that the LPP amplitude would be reduced when viewing pleasant and unpleasant images relative to neutral ones in individuals with higher BDI-II scores, in line with the emotion context insensitivity hypothesis. Finally, given the lack of prior research examining anticipatory ERPs (Cue-P300 and SPN) and their association with depressive symptoms, no predefined hypothesis was established regarding their association with depressive symptom levels.

3.2 Methods and materials

3.2.1 Participants

For the recruitment process, fliers with information about the study were developed and distributed around the city of Padua, predominantly across university campuses and academic libraries. A total of 40 (22 females, mean (M) age = 22.9, standard deviation (SD) = 2.97, range = 19 - 35) Italian Caucasian University students from the University of Padua (Italy) voluntarily took part in the study. The enrolled sample was medically healthy and free from psychotropic medication, as assessed with an ad-hoc anamnestic interview. Exclusion criteria included a current and past history of cardiovascular, psychiatric, and neurological diseases. Several anamnestic questions regarding exclusion criteria were administered through an online screening procedure and further assessed during the laboratory session through an ad-hoc anamnestic interview. All participants had normal or corrected-to-normal vision and were naive to the purpose of the experiment. All participants read, understood, and signed the informed consent. The study was conducted in compliance with the World Medical Association Declaration of Helsinki on research

on human subjects and was approved by the Ethical Committee of Psychological Research, Area 17, University of Padova (prot. 220-c). Participants did not receive payment or any other compensation (i.e., academic credit).

3.2.2 Psychological measures and experimental task

Psychological measures

To assess depressive symptoms, the Beck Depression Inventory-II was employed (BDI-II; Beck, Steer & Brown, 1996; Italian version by Ghisi et al., 2006). The BDI-II is a 21-items self-report questionnaire that assesses the presence and severity of depressive symptoms within the last two weeks. Responses are measured on a 4-point Likert scale (0 – 3) for each item and the final score ranges from 0 to 63, where more severe depressive symptoms are demonstrated with a higher score.

Experimental task

EEG was recorded while participants underwent an S1-S2 affective paradigm presented on a computer with a 16'' desktop positioned approximately 1 meter from the participant. E-Prime (Psychology Software Tools) was used for the presentation of the images. The paradigm included a total of 72 trials, each starting with a 500 ms baseline (a white fixation dot), followed by a symbol cue (S1) lasting 1500 ms that signaled the emotional content (a *plus* for pleasant, a *dot* for neutral, a *minus* for unpleasant) of the upcoming picture (S2), presented 4500 ms later and lasting 2000 ms. The S2 was followed by a variable intertrial interval (ITI) of 3000-4000 ms, during which a white fixation dot (identical to the baseline) was presented. Participants were asked to attend to the cue (S1) and the subsequent image (S2). Figure 3.1 illustrates the paradigm. No motor response to the second stimulus was required. The S2 included pictures selected from the International Affective Picture System (IAPS; Lang et al., 2008), a widely used database of pictures developed by the National Institute of Mental Health Center at the University of Florida, designed to provide a standardised set of images for studying emotional processing. The pleasant images included highly arousing stimuli, such as explicit erotic scenes or extreme sports. Unpleasant pictures, on the other hand, consisted of highly arousing images with threatening content, such as armed aggressions or attacking animals. Pleasant and unpleasant pictures were matched for normative arousal ratings (unpleasant, mean ± SD = 6.5 ± 0.5; pleasant, mean ± SD = 6.5 ± 0.4; p = .92),

which were significantly higher than for neutral pictures (neutral, mean ± SD = 2.9 ± 0.7; all *ps* < .001). Neutral images were low-arousing pictures showing people in neutral contexts, urban landscapes, or neutral objects. At the end of the task, 36 pictures (12 for each emotional category) were presented again, and ratings of emotional valence and arousal were obtained using a computerized version of the 9-point Valence and Arousal scales of the Self-Assessment Manikin (SAM; Bradley & Lang, 1994), illustrated in Figure 3.2.

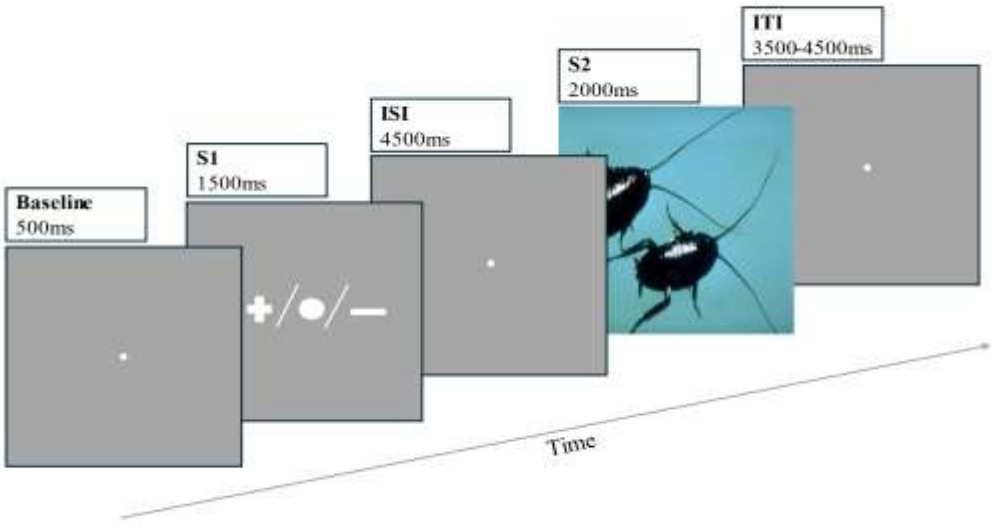

Figure 3.1 *Illustration of the S1-S2 paradigm employed in the current study.*

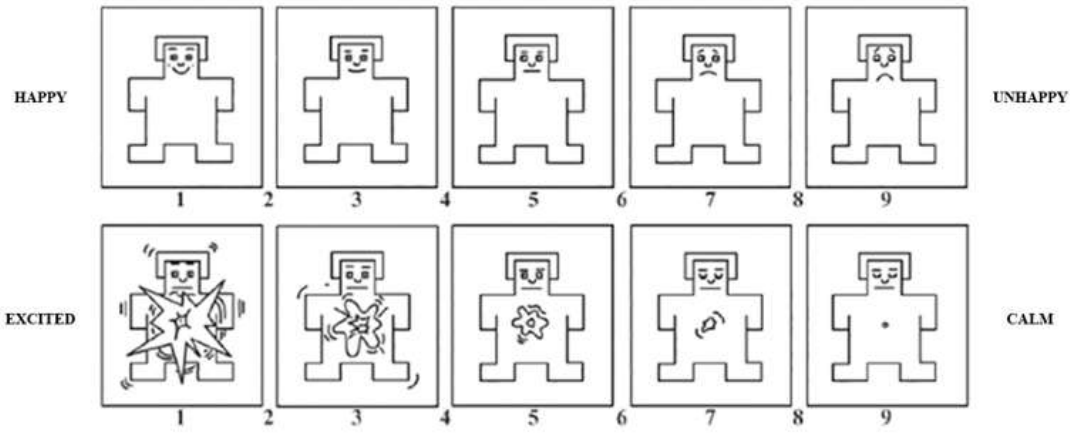

Figure 3.2 *The image shows the three dimensions assessed by the Self-Assessment Manikin (SAM) scale to rate the affective images from the IAPS, with responses measured on a 9-point Likert scale. The top row evaluates the level of pleasantness (i.e., valence) and the bottom row evaluates the level of arousal.*

3.2.3 Procedure

University students at the University of Padua completed an online survey (through Google Modules) to evaluate the inclusion criteria for the study, and then filled out the BDI-II questionnaire (Google Modules). Then, an appointment was made for a laboratory session at the Department of General Psychology of the University of Padua. The day before the agreed slot, a reminder containing the date, time, and meeting point was sent to participants via e-mail, along with some instructions (e.g., to refrain from drugs or alcohol the day before, and caffeine on the same day, and bring glasses if they had corrected eyesight problem). Upon arrival at the laboratory, after reading and signing written informed consent, participants were administered the ad-hoc anamnestic interview. Then, participants were seated on a comfortable chair in a dimly lit, sound-attenuated room. After electrode attachment and a 3-minute resting-state period, three practice trials including one pleasant, one neutral, and one unpleasant trial were provided. Then, participants underwent the S1-S2 paradigm. The entire procedure took approximately 90 min. Finally, a short debriefing was conducted to verify the emotional state of the participant.

3.2.4 EEG recording and data reduction

EEG recording. The electroencephalogram (EEG) was registered using a standard elastic pre-mounted cap (Waveguard, ANT Neuro, Enschede, Netherlands) with 32 channels (Fp1, Fpz,

Fp2, F7, F3, Fz, F4, F8, FC5, FC1, FC2, FC6, C3, Cz, C4, CP5, CP1, CPz, CP2, CP6, T7, T8, P7, P3, Pz, P4, P8, POz, O1, Oz, O2, M1, M2) in Ag/AgCl with an 8 mm diameter, positioned in accordance with the international system 10/20 (Jasper, 1958). Electrode impedance was kept below 10 kΩ. Physiological signals were sampled at 1000 Hz with filter settings from DC to 30 Hz. The electrode CPz was adopted as the online reference site. Both vertical and horizontal electrooculograms (EOGs) were recorded using a bipolar montage to monitor eye movements and eye-blinks. The electrode pairs were placed at the supra- and suborbit of the right eye and at the external canthi of the eyes, respectively.

The EEG signal was pre-processed by means of a semi-automated pipeline using EEGLab and Brainstorm (Tadel et al., 2011), two MATLAB toolboxes. The EEG signal was downsampled to 500 Hz and re-referenced offline to the linked mastoids. Data were band-pass filtered from 0.01 to 30 Hz and corrected for blink artifacts using independent component analysis (ICA). Then EEG signal was epoched into 8250 ms segments (from 250 ms before S1 until 2000 ms after S2 onset). The signal was then baseline-corrected from -250 -50 ms before S1. A semiautomatic procedure was employed to detect and reject artifacts. The criteria applied was a voltage difference of 200 μV. Visual inspection of the data was then conducted to detect and reject any remaining artifacts. Visual inspection of grand averages across all participants in the three emotional categories confirmed that the Cue-P300 and then LPP were maximal at parietal sites, consistent with previous research (Dell'Acqua et al., 2022; Novak et al., 2016; Novak & Foti, 2015; Poli et al., 2007). Therefore, the Cue-P300 and the LPP were scored by averaging peak amplitudes at electrodes P3, Pz, and P4, from 300 to 400 ms post-S1 and 400–1,000 ms post-S2, respectively (see Figure 3.3). The SPN was scored as the mean amplitude the 200 ms before the image onset (6 s) at frontal sites (F3, FZ, F4). However, from the visual inspection of grand averages, the SPN did not emerge in our data (see Figure 3.4). Hence, the SPN was not considered in further statistical analyses.

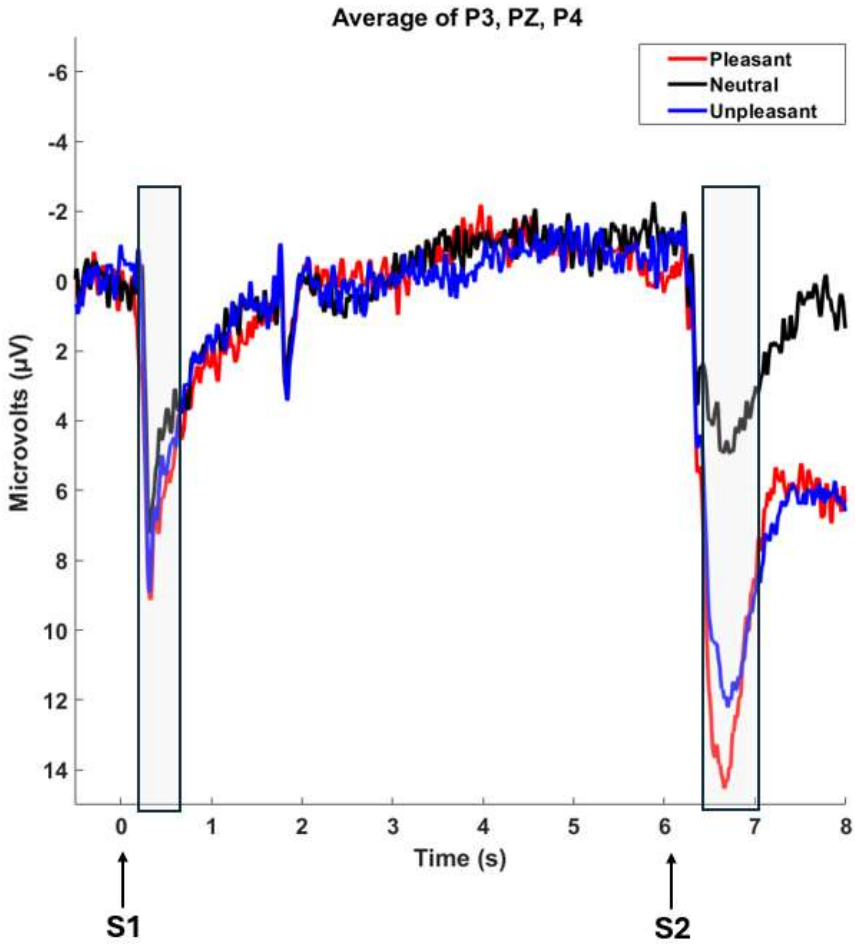

Figure 3.3 *ERP grand average to the S1-S2 emotional task, presented for parietal electrodes (P3, PZ, P4). Cue onset was at 0 seconds and image onset was at 6 seconds. The Cue-P300 was scored as the peak amplitude in the first shaded window (0.3-0.4 s). The P300/LPP complex was scored as the peak amplitude in the third shaded window (6.5 to 7 s).*

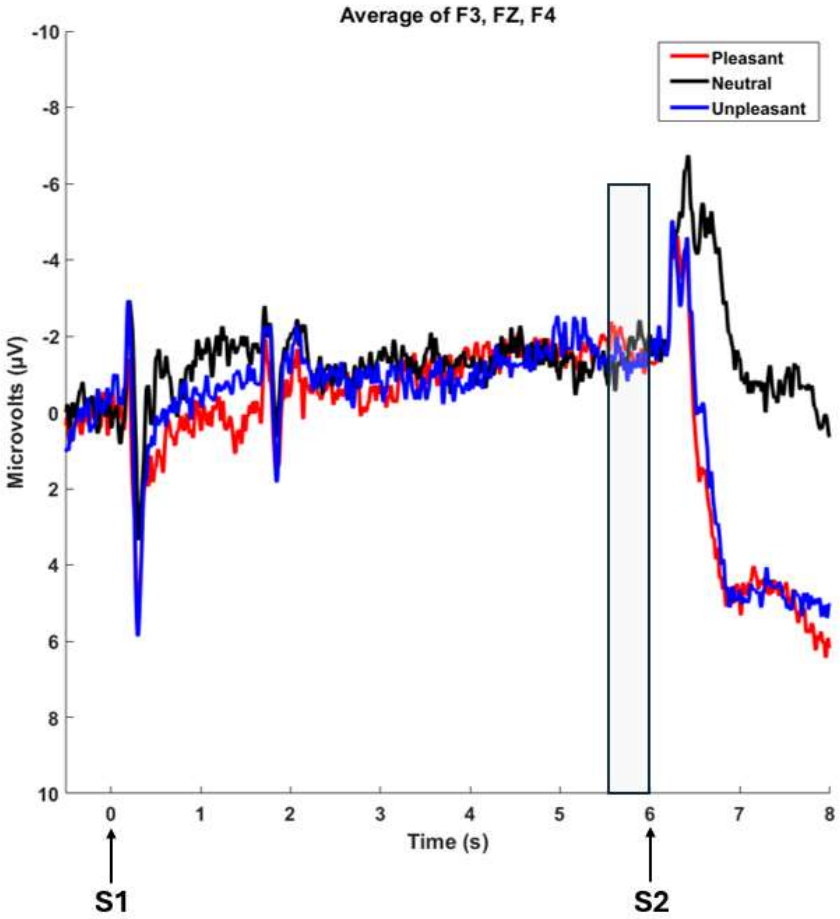

Figure 3.4 *ERP grand average to the S1-S2 emotional task, presented for parietal electrodes (F3, FZ, F4). Cue onset was at 0 seconds and image onset was at 6 seconds. The SPN did not emerge in this data and should be scored as the average activity in the second shaded window (5.8 – 6 s).*

3.2.5 Statistic analyses

The statistical analyses were performed on RStudio software (Rcore team, 2023). Descriptive statistics were reported for BDI-II scores.

To test the effect of Emotional Category, BDI-II scores, and their interaction on SAM ratings of Valence and Arousal, two mixed-effect models were computed through the *lme4* package (Bates, 2010). Both models included participant as a random intercept, while the Emotional Category and BDI-II, and their interaction were specified as fixed factors. The models were specified as follows:

*Model ← lmer(SAM rating of Valence or Arousal ~ Emotional Category * BDI-II + (1|Subject)).*

To test whether depressive symptoms predicted Cue-P300 and LPP amplitudes as a function of Emotional Category, two mixed-effect models were computed through the *lme4* package (Bates, 2010). Both models included participant as a random intercept, while the Emotional Category (differential scores of pleasant and unpleasant trials[1]) and BDI-II, and their interaction were specified as fixed factors. Differential scores of ERPs (pleasant – neutral, unpleasant – neutral) were employed to reduce the number of predictors. The models were specified as follows:

$$Model \leftarrow lmer(\Delta\ ERP\ amplitude \sim Emotional\ Category * BDI\text{-}II + (1|Subject)).$$

For the fixed effects, the estimated coefficient (*b*), standard error (SE), *t* values, and confidence intervals for each parameter included in the final model were reported. In addition, the *p*-values obtained through the Satterthwaite approximation (implemented in the lmerTest library) were reported. A *p*-value of .05 was the cut-off for statistical significance.

The collinearity was tested by calculating the Variance Inflation Factors (VIF) with the *vif* function of the car package (Fox, Weisberg, & Price, 2019). Significant categorical main effects ($p < .05$) were followed by Tukey HSD post-hoc tests to correct for multiple comparisons. Simple slopes were used to probe significant interactions with continuous variables. A *p*-value of .05 was the cut-off for significance.

3.3 Results

Psychological measures and Valence and Arousal SAM subjective

The average BDI-II score was 13.6 (SD = 9.05, range = 0 - 42).

Results of mixed-effect models on Valence and Arousal are shown in Table 3.1. The results of the mixed-effect models predicting Valence from Emotional Category, BDI-II scores, and their interaction showed a significant effect of Emotional Category, such that Unpleasant pictures were evaluated as significantly more unpleasant than neutral ($p_{Tuckey} < 0.001$) and pleasant ($p_{Tuckey} < 0.001$) pictures. Pleasant stimuli were rated as significantly more pleasant than neutral ones ($p_{Tuckey} < 0.001$). No significant effect emerged for BDI-II or the interaction between BDI-II and Emotional Category.

[1] Two mixed-effect models were conducted to confirm the spatial representation and the effect of Emotional Category of the Cue-P300 and the LPP, already inspected from the grandaverage. Both ERPs were larger for pleasant and unpleasant images relative to neutral ones (all *p*s < .001) and were most represented in parietal electrodes (P3, PZ, P4). Hence, differential scores could be computed.

The mixed-effect model on arousal ratings revealed a significant main effect for Category, such as that arousal ratings were higher for both pleasant and unpleasant pictures compared to neutral ones (all $ps_{Tuckey} < .001$). Unpleasant pictures were rated as more arousing than pleasant stimuli ($p_{Tuckey} = .05$). A significant interaction effect emerged between BDI-II scores and Emotional Category. Simple slope analyses showed that the slope of BDI-II on self-reported Arousal was significant for pleasant ($p = .02$) and unpleasant ($p < .001$), but not neutral images (see Figure 3.5).

Table 3.1 *Estimated parameters of the linear mixed-models predicting Valence and Arousal from Emotional Category, BDI-II scores and their interaction. Baseline is Neutral images. Significant effects are shown in bold.*

Predictor	B (SE)	*t*	*p*
Model predicting Valence			
CategoryPOS	**1.68 (0.43)**	**3.83**	**<.0001**
CategoryNEG	**-2.63 (0.43)**	**-5.60**	**<.0001**
BDI-II	-0.00 (0.01)	-0.21	.832
CategoryPOS × BDI-II	-0.00 (0.02)	-0.33	.738
CategoryNEG × BDI-II	0.03 (0.02)	1.25	.217
Model predicting Arousal			
CategoryPOS	**3.02 (0.35)**	**8.41**	**<.0001**
CategoryNEG	**3.94 (0.35)**	**10.10**	**<.0001**
BDI-II	-0.03 (0.02)	-1.36	.178
CategoryPOS × BDI-II	-0.02 (0.02)	-1.16	.249
CategoryNEG × BDI-II	**-0.05 (0.02)**	**-2.67**	**<.01**

Note. SE = standard error; BDI-II = Beck Depression Inventory II

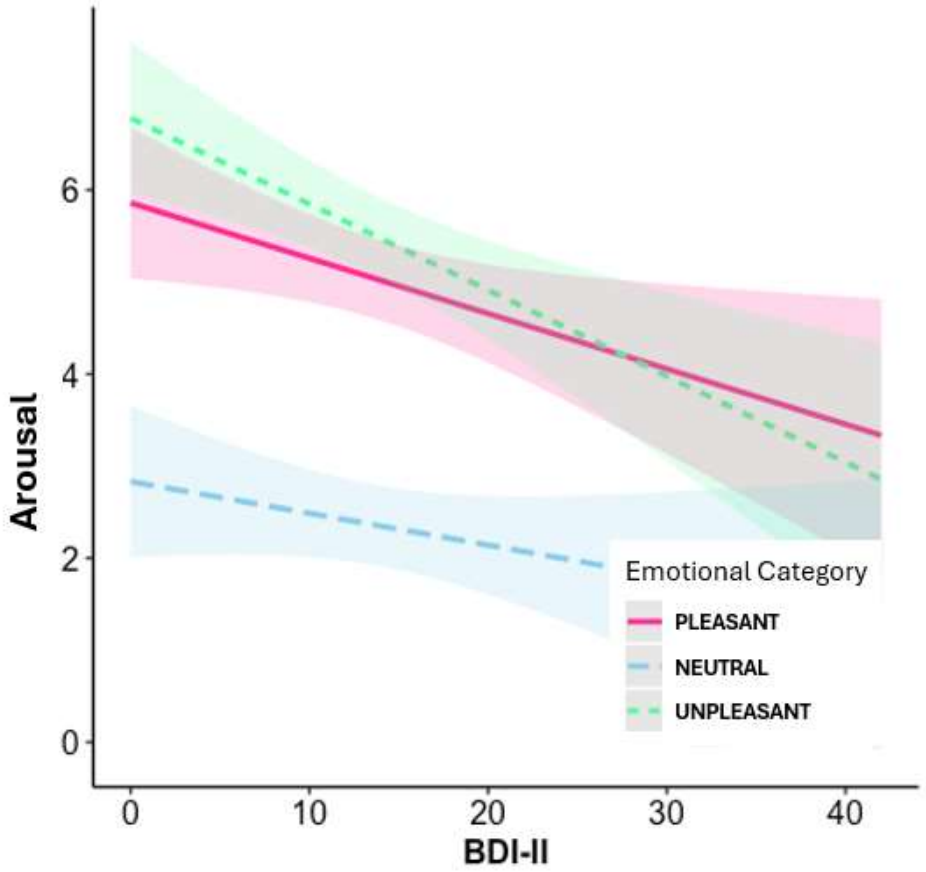

Figure 3.5 *Interaction effect of BDI-II and Emotional Category on self-reported Arousal. Ninety-five % confidence bands are presented in different colours.*

Cue-P300 and LPP

Table 3.2 illustrates the models predicting the two ERPs from Emotional Category and BDI-II scores. The results of the mixed-effect models predicting Cue-P300 amplitude from Emotional Category, and BDI-II scores did not yield any significant effect. Instead, the results of the mixed-effect models predicting the LPP amplitude from Emotional Category and BDI-II scores showed a significant effect of Emotional Category, such that pleasant images elicited a larger LPP amplitude relative to unpleasant ones (p_{Tukey} = .004). In addition, a significant interaction emerged between Emotional Category and BDI-II scores (p = .005). Specifically, simple slope analyses were used to probe this interaction and showed that the slope of BDI-II scores on P300/LPP amplitude was significant and negative when the Emotional Category was pleasant (p = .04) but not unpleasant (p = .92) (see Figure 3.6).

Table 3.2 *Estimated parameters of the linear mixed-models predicting ERPs (Cue-P300, LPP) from Emotional Category and BDI-II and their interaction. Significant effects are shown in bold.*

Predictor	B (SE)	*t*	*p*
Model predicting Cue-P300 amplitude			
Emotional Category	-0.20 (0.60)	-0.33	.739
BDI-II	-0.09 (0.06)	-1.50	.140
Emotional Category × BDI-II	-0.01 (0.03)	-0.51	.610
Model predicting LPP amplitude			
Emotional Category	**-5.552**	**-4.327**	**<.0001**
BDI-II	**-0.234**	**-2.143**	**.037**
Emotional Category × BDI-II	**0.223**	**2.869**	**<.01**

Note. SE = standard error; BDI-II = Beck Depression Inventory II; LPP = late positive potential.

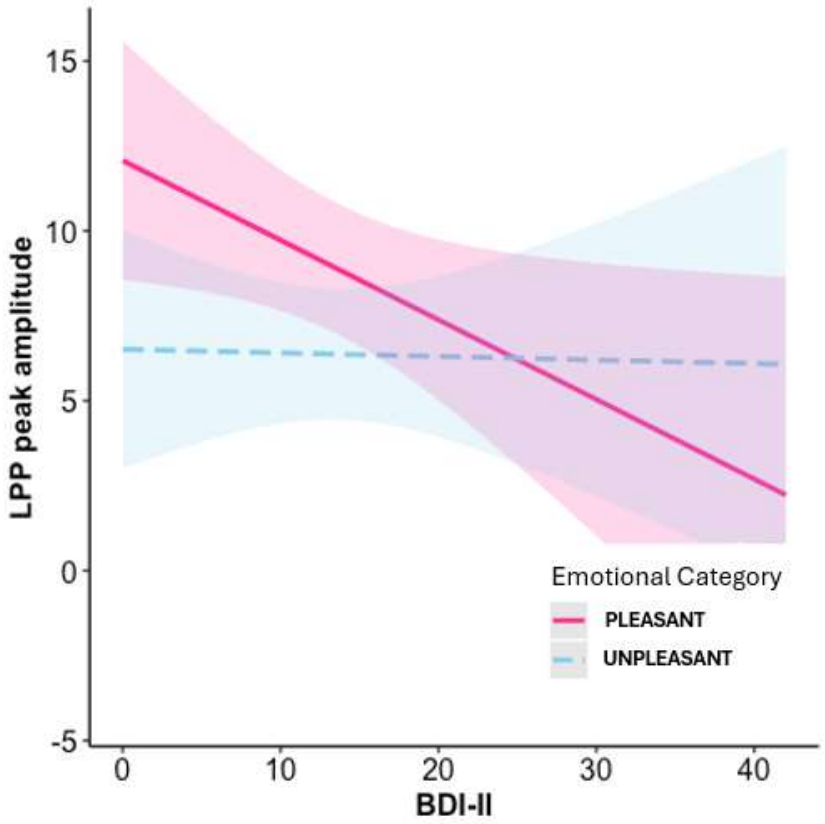

Figure 3.6 *Interaction effect of BDI-II and Emotional Category on LPP amplitudes. Ninety-five % confidence bands are presented in different colours.*

3.4 Discussion

The present study aimed to explore whether depressive symptoms would be associated with changes in different stages of emotional processing, namely affective cue engagement, emotional anticipation, and emotional processing in a sample of non-clinical university students with different levels of depressive symptoms. To do so, the EEG was recorded during an S1-S2 emotional paradigm, so that three ERPs could be extracted. Specifically, the Cue-P300, SPN, and LPP components were assessed. Based on the Emotion Context Insensitivity Hypothesis (Bylsma et al., 2008; Bylsma, 2021; Rottenberg et al., 2005), the main hypothesis was that depressive symptoms would be associated with a blunted emotional processing of emotional (pleasant and unpleasant) images relative to neutral ones, as indexed by the LPP amplitude. No specific hypotheses on the other stages of processing were formulated due to the lack of previous evidence.

The grand averages of the ERPs showed that the Cue-P300 and LPP elicited the expected pattern of response to emotional stimuli, namely a greater amplitude to pleasant and unpleasant stimuli relative to neutral ones. This is in line with previous studies (Hajcak et al., 2014; Lin et al., 2015; Nelson, Hajcak & Shankman, 2015) and confirms the sensibility of ERPs in affective processing. Moreover, the LPP amplitude was larger for pleasant than unpleasant images. However, contrary to the literature (Poli et al., 2007; Kitani et al., 2017), the SPN was not sensitive to affective stimuli. Future research might implement a version of this task with an expected motor response and assess motor preparation to affective stimuli through the Contingent Negative Variation (CNV, Hillman et al., 2002).

Of note, partly in line with the hypothesis, depressive symptoms predicted a blunted LPP to pleasant but not unpleasant pictures. Instead, depressive symptoms were not associated with changes in affective cue engagement and emotional anticipation. The result of a reduced LPP to pleasant images in individuals with higher depressive symptoms aligns with the abundant literature described in the previous chapters sustaining the positive attenuation hypothesis which posits that depression is characterised by a reduced elaboration of pleasant information (Sloan, Strauss, Wisner, 2001; Rottenberg et al., 2005; Bylsma, Morris & Rottenberg, 2008). Indeed, many studies investigating affective processing in depression using distinct psychophysiological correlates (e.g., startle reflex, cardiac activity, skin conductance, ERPs, electromyography) and employing similar paradigms, reported congruent results linking depressive symptoms to reduced positive but not negative processing (Sloan et al., 1997; 2001; 2002; Messerotti Benvenuti et al., 2015; Dell'Acqua et al., 2024). Therefore, the current results add to the previous literature supporting the positive attenuation hypothesis and highlight the role of the LPP as an early indicator of depression among sub-clinical populations.

Contrary to the emotion context insensitivity, which assumes that depression is linked to a general disengagement with the environment regardless of context (Bylsma et al., 2008), depressive symptoms were not associated with the LPP to unpleasant stimuli. Moreover, these findings also contradicted the view of a negative potentiation as there was no greater LPP amplitude during the presentation of unpleasant stimuli. It is possible to speculate that subclinical depressive symptoms may not be sufficient to elicit the blunted reactivity to unpleasant emotional stimuli that has been observed in clinically depressed individuals (Rottenberg, Gross & Gotlib, 2005). This was also suggested by previous research that assessed cardiac vagal withdrawal in

response to emotional contents in a subclinical population and found less vagal withdrawal towards pleasant but not unpleasant content (Messerotti Benvenuti et al., 2015).

This study aimed at disentangling distinct stages of emotional processing. However, in the studied sample, no effects of depressive symptoms on affective cue engagement (i.e., Cue-P300) emerged. Namely, depressive symptoms did not influence the elaboration of the cue. This is in contrast with the literature discussed in the previous Chapters that found a reduced Cue-P300 amplitude in individuals with depression (Sherdell, Waugh & Gotlib, 2012; White et al., 2021; Moretta et al., 2021; Thompson et al., 2023). However, this can be explained by different task designs. In fact, significantly reduced Cue-P300 activity in individuals with depression compared to healthy controls, was captured in previous studies that adopted paradigms such as the monetary incentive delay and the monetary gambling task (Novak & Foti, 2015; Flores et al., 2015). These methodological differences might have impacted the results of the current study as, perhaps, the chosen design may not elicit cue engagement to the same extent as incentive reward cues do and might explain the lack of difference in the current sample among different categories and depressive symptoms. In addition, the heterogeneity of the depressive disorder might have also affected the inconclusive results. Depressive symptoms manifests in several forms, to the point that several sub-categories of the disorder were proposed (Chen et al., 2000; Kessing, 2007). Indeed, many studies have pointed out how the heterogeneity of the disorder hinders the progression of research and treatment (Fried, 2017); this may be, perhaps, because diverse symptoms vary in their effects on an individual's functioning and response to specific life events, as well as the associated biological markers (Fried, 2015).

At the subjective level, the SAM ratings were in line with the literature, namely, participants indicated pleasant pictures as more pleasant than neutral and unpleasant ones. In addition, depressive symptoms did not predict self-reported valence. Moreover, contrary to the standardized rating scores of the employed pictures, unpleasant pictures were rated as more arousing than pleasant ones. This result is partly in contradiction with the LPP results in this sample, which was found to be larger for pleasant than unpleasant ones, suggest a higher motivated attention and elaboration to these stimuli. Furthermore, depressive symptoms showed an inverse relationship with arousal self-report scores only to emotional (pleasant, unpleasant) but not to neutral images. This is in line with the hypothesis of a blunted emotional responding to all kinds of emotional stimuli (i.e., ECI model; Rottenberg et al., 2005).

To summarise, the present study brings supporting evidence on the role of a blunted emotional processing of pleasant stimuli, as indexed by LPP amplitude, as an indicator of early depressive symptoms. A reduced amplitude of this ERP in response to pleasant content might reflect an attenuated elaboration of pleasant information in individuals with subclinical depressive symptoms, in line with the positive attenuation hypothesis of depression. Furthermore, although exploratory, this study suggests that depressive symptoms in non-clinical populations might not be associated with reduced affective cue engagement.

The results that emerged from this study represent novel and useful evidence that might have meaningful implications at a clinical level. The identification of early predictors of depression is essential for early prevention of the disorder. In particular, assessing depressive symptoms and LPP to emotional stimuli might be a useful target for identifying individuals who are more vulnerable to the development of clinical depression and might help the design of tailored treatments. A useful approach could address depressive symptoms through psychological interventions, such as cognitive-behavioural therapy (Franklin, Carson & Welch, 2016) in combination with specific strategies aimed at improving motivated attention towards pleasant content. For instance, *behavioural activation* is a strategy that involves the employment of activity planning, social skills training, shaping reward, and positive imagery to increase engagement in pleasant activities. A systematic review considered several articles on low-intensity behavioural activation for depression and concluded that this technique might be a viable option as a guided self-help treatment for mild to moderate depression (Chartier & Provencher, 2013). Moreover, there is initial evidence that specific emotion regulation protocols, such as savouring, increase positive emotions and the LPP to pleasant images in healthy cohorts (Wilson & Macnamara, 2021) and future studies should be focused on exploring this training in depressive symptoms.

Some limitations of the present study need to be acknowledged. Firstly, the sample size of the participants was relatively small and consisted almost entirely of university students, mainly from the same background and ethnicity, which might limit the generalisability of the findings to the general population. Furthermore, considering the absence of the SPN amplitude expected effect, a different paradigm might be considered for future research.

In conclusion, the present study provided evidence on distinct facets of affective elaboration in non-clinical levels of depression, mainly associated with a blunted emotional processing of pleasant stimuli, in line with the positive attenuation hypothesis. Importantly, the

LPP may serve as a valuable quantitative measure of early identification as well as the prevention of full-blown clinical depression.

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