UNIVERSITY OF PADOVA

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Bachelor's Degree Course in Psychological Science

Final dissertation

Affective processing in dysphoria: evidence from startle probe modulation of ERPs

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ABSTRACT

Background: A core feature of depression is dysregulated affective disposition. Particularly, depression is thought to be characterized by reduced affective processing of emotional stimuli, both pleasant and unpleasant. Affective processing can be studied through startle-elicited event-related potentials (ERPs). Specifically, the N2 component reflects the early stages of stimulus identification and processing while the P3 portrays the later attention resources allocation to the stimulus. However, to date, startle-elicited ERPs have been rarely employed to explore depression and depression vulnerability.

Aim of the study: The objective of the present study was to examine affective processing in individuals with dysphoria, a vulnerability condition to develop full-blown depression, through the analysis of startle-elicited ERP components N2 and P3, during the viewing of pleasant, neutral and, unpleasant emotional pictures.

Materials and methods: 48 university students (46 females, 2 males) were divided into two groups, with and without dysphoria. Subsequently, both groups engaged in a passive viewing of emotional pictures (pleasant, neutral and, unpleasant) while a startle probe that was semi-randomly administered at 300, 1500, 3500, or 4500 ms after picture onset. The EEG data were recorded during the entire emotional picture viewing task.

Results: The analysis revealed a significant Group x Condition effect (p = .040). Particularly, individuals without dysphoria had a significantly smaller N2 amplitude to the startle probe in the pleasant condition, compared to the neutral one (p = .008). No such effect was found in the group with dysphoria (p = 1.000). Additionally, the results showed only a Condition effect of the P3, whereby greater P3 amplitude to the startle probe in the unpleasant condition relative to the neutral one (p = .040) across all participants emerged.

Conclusions: The findings on the N2 amplitude suggest that in controls, but not in dysphoria, the pleasant context inhibited the early auditory processing of the startle probe, indicating that higher early attentional resources were allocated to the pleasant content rather than the probe. Hence, the present study further supports the hypothesis of blunted affective processing of pleasant emotional stimuli in individuals with depressive symptoms and at higher risk to develop full-blown depression.

Keywords: Dysphoria, Startle probe, ERPs, Emotion, Affect

PART I

CHAPTER ONE: A COMPREHENSIVE VIEW OF DEPRESSION

1.1 Depression: clinical characteristics and epidemiology

Major Depressive Disorder (MDD) is a serious mood disorder considered one of the most common and disabling forms of psychopathology (Kessler & Bromet, 2013). The Global Burden of Disease (GBD) study states that approximately 280 million people suffer from depression which constitutes 3.8% of the population being affected by MDD (WHO, 2019). The lifetime prevalence of MDD is about 5% to 17% with the average being 12% (Bains et al., 2021), which further portrays the high pervasiveness of this psychiatric disorder. One of the most widely documented findings in psychiatric epidemiology is the higher prevalence of MDD in women, with the female-to-male risk ratio being 2:1 (Kessler et al., 2003). This gender discrepancy appears to be stable across both time and different regions of the world (Figure 1.1) and is attributed to factors including, but not limited to, hormonal differences, childbirth effects, and different psychosocial stressors in men and women (Bains et al., 2021).

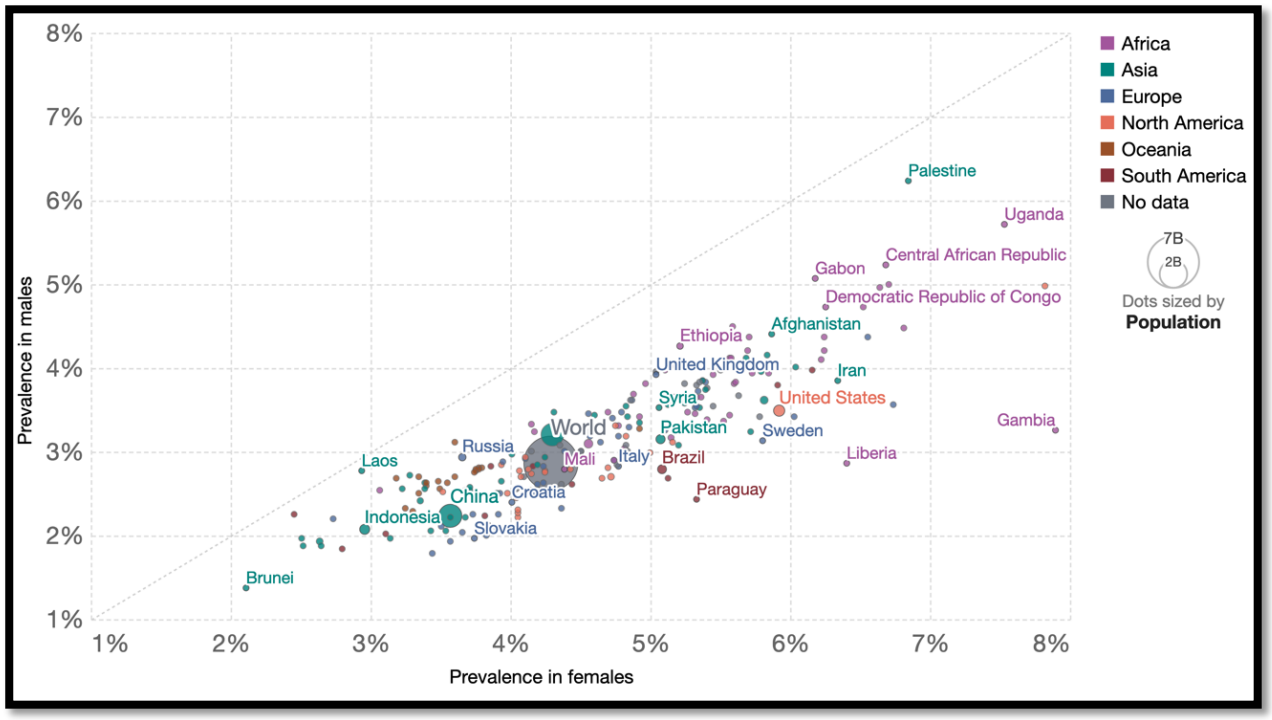

Figure 1.1 Prevalence of depression in males and females across different areas of the world, 2019. Adapted from the Institute for Health Metrics and Evaluation, The Global Burden of Disease Study, 2019.

The World Health Organization ranked MDD as the third leading cause of burden of disease worldwide in 2008 and has projected the disorder to rank first by 2030 (Malhi & Mann, 2018). The total burden of disease both in terms of years of life lost and years lived with the disorder can be measured by the Disability-Adjusted Life Year, which for depressive disorders was found to be the highest for 50 to 69-year-olds (GBD, 2019). Unlike most mental disorders the age of onset for MDD is both later, with the median typically in the early to mid-20s, and more widely distributed ranging from late adolescence up to late adulthood (Kessler & Bromet, 2013). Indeed, about 15-20% of adolescents experience major depressive disorder before the age of 18 (Lewinsohn & Essau et al., 2002). MDD is a disorder of a highly chronic and recurrent nature (Murray & Lopez, 1997) with recurrence occurring in approximately 40 to 50 percent of individuals who experience a depressive episode (Monroe & Harkness, 2011). The probability of

recurrence increases with subsequent episodes as well as with the presence of comorbid disorders (Hooley et al., 2017).

Depressive symptoms include persistent low or depressed mood, decreased interest in pleasurable activities or anhedonia, feelings of worthlessness or excessive guilt, fatigue or lack of energy, poor concentration, appetite changes, psychomotor agitation or retardation, sleep disturbances, or suicidal thoughts (Bains et al., 2021). Per the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-V) five or more of the above symptoms must be present during the same 2-week period for the MDD diagnosis to be made (American Psychiatric Association, 2013). Additionally, at least one of the symptoms must be either the presence of depressed mood or anhedonia associated with significant distress or impairment (Uher et al., 2014). For the MDD diagnosis, a history of manic or hypomanic episodes needs to be ruled out as well (APA, 2013).

One of the most profound consequences of MDD is diminished role functioning and quality of life (Kessler & Bromet, 2013). An association was found between MDD and decreased work productivity as well as work absenteeism (Broadhead et al., 1990) which combined with social dysfunction are a burden for both the patient and the patient's family. Depressive symptoms tend to disrupt family stability often leading to separation or divorce (Lépine et al., 2011). Indeed, marital dissatisfaction and depressive symptoms are found to be strongly related, with an average correlation of r =.4 (Whisman et al., 2001). However longitudinal studies revealed that the association is bidirectional (Mamun, 2009), implying that caution is needed when interpreting such findings. MDD negatively impacts physical and emotional and psychosocial functioning (Ormel et al., 1999) all contributing to a diminished quality of life. Moreover, depressed patients have a

20-fold greater mortality risk for suicide compared to the general population (Lépine et al., 2011), which makes addressing depression of paramount importance.

Depression is a complex mental disorder that calls for an interdisciplinary treatment approach which most commonly draws on pharmacological, psychotherapeutic (e.g., cognitive, behavioral), and neuroscientific (e.g., electroconvulsive therapy, transcranial magnetic stimulation) protocols (Bains et al., 2021). The post-treatment outcome is considerably favorable for many, but by no means, all diagnosed patients (Hooley et al., 2017). Moreover, the treatment-seeking rates for MDD ranged between 27.6% to 60.7% (Bristow & Patten, 2002) hardly encompassing the entire target population. Therefore, much study has been devoted to delineating barriers to recognition, diagnosis, and optimal management of depression (Goldman et al., 1999). Additionally, MDD is among the costliest disorders in Europe (Olesen et al., 2012). Substantial efforts have also been directed toward establishing prevention programs for this disorder and, although findings appear promising, there is still a need for further research (Brunwasser & Garber, 2016).

Given the tremendous psychological and physical strain of MDD, it is of utmost importance to devise strategies for early identification and treatment of this disorder (Dell'Acqua et al., 2023). The negative impacts of MDD on the individual, as well as their families, can be diminished with early detection and thus rapid intervention (Cacheda et al., 2019). Monitoring individuals at risk of MDD but who did not yet develop the disorder, is an effective prevention strategy (Dell'Acqua et al., 2023). A common risk factor for developing MDD is the parental history of MDD as parental depression has been associated with a higher child's risk for developing this disorder (Sander & McCarty, 2005). Another important marker for depression is the presence of dysphoria characterized by a generalized feeling of discontent and agitation

(American Psychological Association, 2013). Dysphoria, also known as subclinical depression, is characterized by depressive symptoms which do not meet the criteria needed for a formal diagnosis of MDD (Dell'Acqua et al., 2021). The study of dysphoria in the context of depression may be of particular interest as it allows for the study of the associated neurophysiological mechanisms, free from the influence of antidepressant medication (Dell'Acqua et al., 2021). However, the prevention and early recognition efforts might be hindered by the still limited knowledge of the early psychobiological markers that lead to depression onset (Wong & Licinio, 2001).

1.2 The Research Domain Criteria (RDoC) perspective of depression

Neuroscientific research into psychiatric disorders generally relies on disease classifications (Casey et al., 2013) however with increasing findings failing to align with the diagnostic categories (Insel et al., 2010), there has been a recent attempt to consider mental illnesses from a more dimensional standpoint. The National Institute of Mental Health (NIMH) in the aforesaid view launched the Research Domain Criteria (RDoC) project which aims to facilitate the translation of basic neuroscience research findings to clinical diagnosis and treatment of psychiatric disorders, such as depression (Casey et al., 2013). The RDoC perspective assumes that mental disorders are multidimensional disorders observable at different levels of analysis (e.g., from genetics to behavior). The RDoC framework includes a matrix in which rows represent the five functional domains: Positive Valence, Negative Valence, Arousal/Regulatory Systems, Cognitive Systems, and Systems for Social Processes (Cuthbert et al., 2014). Whereas the columns denote different units of analysis ranging from genes, molecules, cells, and circuits, to physiology, behavior, and self-reports (Insel et al., 2010). Moreover, each domain in the matrix is composed of several constructs and sub-constructs, for instance, the Positive Valence domain includes reward

responsiveness, reward learning, and reward valuation which are further divided into sub-categories. Additionally, the impact of development and environment on biological and behavioral aspects of functioning is acknowledged in the RDoC (Figure 1.2). In compliance with the self-correcting principle of science, the RDoC project is thus open to revisions in light of new scientific evidence. (Lilienfeld & Treadway, 2016).

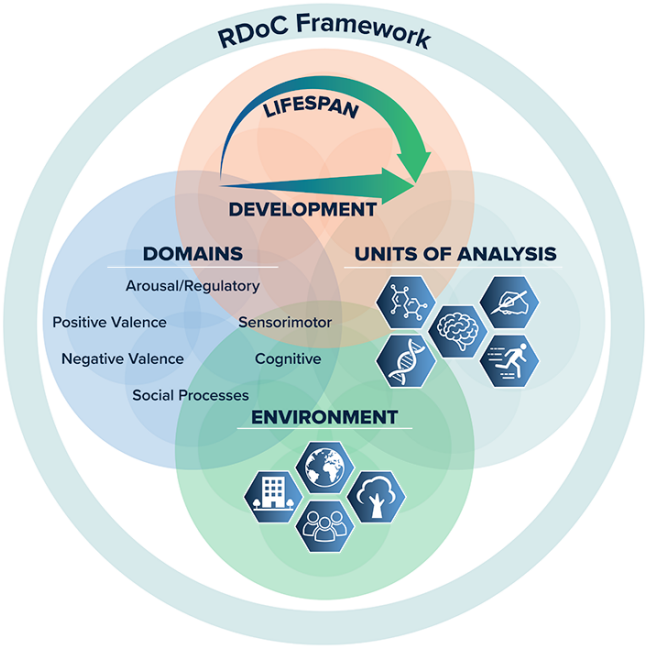

Figure 1.2 The diagram of the RDoC framework. Adapted from: www.nimh.nih.gov

Understanding depression through the prism of the RDoC framework entails implementing an integrative and well-rounded approach across multiple units of analysis, from neural correlates to behavior (Woody & Gibb, 2015). The RDoC perspective of depression can be depicted through the mapping of depressive symptomatology onto the domains of the framework.

The core symptoms of MDD involve emotional dysfunctions including anhedonia, defined as the inability to enjoy pleasurable experiences, and persistent negative mood (American Psychiatric Association, 2013; Otte et al., 2016). Both the Positive Valence System (PVS) and Negative Valence System (NVS) are responsible for the beforementioned processes, differing

however in the context of the response as well as in the brain structures they engage. The PVS regulates responses to positive situations or contexts such as responses to rewards, motivation to pursue pleasant experiences, and consummatory behavior, whereas the NVS modulate responses to unpleasant and aversive situations or contexts, such as loss and fear (Craske et al., 2016; Cuthbert & Insel, 2013). At the neural level, the PVS involves the ventral tegmental area, nucleus accumbens, and frontostriatal pathways while NVS engages the amygdala, insula, and striatum (Dillon et al, 2014). It was found that the two systems function differently in depressed and nondepressed individuals (Hamilton et al., 2012). Functional neuroimaging studies revealed lower activation of brain areas involved in PVS in depressed patients during reward tasks when compared with healthy controls (Pizzagalli, 2014). In fact, an abnormality of the PVS in depressed individuals displays a decreased behavioral response to rewards (Pizzagalli et al., 2005) which by several studies was also identified as a potential predictor of depression development (Nelson et al., 2016). Additionally, a reduced PVS is present in depression, not anxiety disorders, thereby differentiating the two (Sandre et al., 2019). On the contrary, a greater response to unpleasant stimuli in areas engaged in NVS has been found in depressed individuals as compared to the non-depressed sample (Hamilton et al., 2012). Indeed, one of the five constructs enclosed in the NVS domain, the loss construct, defined as a state of deprivation of a con-specific, object or situation, is a prominent feature of depression (NIMH, 2018). The loss construct in the RDoC framework is analyzed from the genetic and molecular up to behavioral and self-report levels (e.g., rumination) (Woody & Gibb, 2015), once again highlighting RDoC's attempt to embrace the heterogeneity of depression.

1.3 Affective models of depression

Affective models conceive emotions as action dispositions, representing individuals' readiness to act within their environment accompanied by a physiological preparatory activation (Frijda, 2007; Lang et al., 1998). According to these models, emotions are modulated by two motivational circuits in the brain, one appetitive and the other defensive, which evolved primarily to increase the adaptation and survival of individuals (Bradley et al., 2001; Lang & Bradley, 2010). The appetitive motivational system is associated with pleasant affect and is active in contexts that promote sustenance (e.g. obtaining rewards, nutrients, or sexual partner) whereas the defensive motivational system is associated with avoidance behavior and is activated in response to aversive stimuli or threatening contexts (e.g. attack, illness or injury) (Lang & Bradley, 2013). Individual differences in valence and intensity of emotional responses, which stem from the interplay of the two motivational systems, are referred to as affective style (Davidson, 1999). Affective style impacts attention allocation, perceptual processing, information intake, and arousal, all to set off context-appropriate behaviors and actions (Lang & Bradley, 2013). The behavioral patterns triggered by the defensive system include mainly fight or flight but also freezing/hiding and counter-threat displays seen in animals (Lang & Bradley, 2010). Individual differences in affective style are related to individual personality, temperament as well as vulnerability to psychopathology, including depression (Davidson, 1999). Indeed, studies have shown depression to be associated with a reduced functioning of the approach motivational system, which is in line with some depressive symptoms including anhedonia and an overall decrease in goal-directed motivation and behavior (Davidson, 1998). Therefore, the activation of the two motivational circuits is linked to specific patterns of behavioral and physiological responses.

Lang and colleagues (1998) proposed a dimensional model of emotions where emotions are seen as a tendency to react to environmental conditions through changes in behavior, physiological patterns, and language (Lang et al., 1998). In this view, an emotion is a result of three interconnected systems: the behavioral system representing the motor response to a stimulus, the physiological system regulating the nervous response, and a subjective system accounting for one's individual experience relative to the stimulus. All of the above systems play their role in establishing an emotional state (Lang et al., 1998).

MDD falls into the category of mood disorders (APA, 2013), however, the answer to the question of how exactly MDD affects emotional reactivity, remains unclear. In an attempt to further explore this proposition, a crucial distinction has to be made between the concept of mood and emotion as well as their relationship (Rottenberg & Gross, 2003). Mood can be defined as a rather constant feeling state which is weakly related to the environment (Rottenberg & Gross, 2003) while emotions are fleeting reactions arising when processing a stimulus (Ekman, 1992). Despite the two being distinct constructs, they appear to be interconnected where moods can influence emotions (Bylsma et al., 2008). In fact, the notion of mood-congruent emotion facilitation may be seen as a groundwork for the three competing models of emotional reactivity in MDD (Bylsma et al., 2008). The first hypothesis put forward was the negative potentiation hypothesis, which proposes that the persistent negative mood present in MDD potentiates/increases emotional responses to negative or unpleasant stimuli (Hill et al., 2019; Beck, 1979). This belief is rooted in Beck's cognitive schema theory of depression, yet supporting evidence appears to be limited (Rottenberg, Gross, & Gotlib, 2005). Another view is referred to as the positive attenuation hypothesis stating that individuals diagnosed with MDD experience an attenuated/reduced emotionality towards positive or pleasant stimuli, thus indicating a deficit in

the appetitive motivational system (Hill et al., 2019). This perspective is not only in line with the core MDD symptoms such as anhedonia but is also compatible with the previous hypothesis as both refer to stimuli with opposing valences (Bylsma et al, 2008). Additionally, the positive attenuation view is supported by a larger body of data in comparison to the negative potentiation hypothesis (Bylsma, 2021). The positive attenuation hypothesis has been extended to a third alternative, known as the emotional context insensitivity (ECI) hypothesis, which holds that depression is characterized by a hypoactivation of both motivational systems (Bylsma et al., 2008). The ECI proposes that depression is illustrated by a pattern of general environmental disengagement, where a blunted emotional response is present in both pleasant and unpleasant contexts (Bylsma, 2021). From an RDoC standpoint, this would indicate a reduced functioning of the Positive and Negative Valence Systems (Insel et al., 2010; Bylsma, 2021). The ECI model drawing from evolutionary theories implies a reduced activation of both motivational systems, in the direction of adaptive withdrawal (Nesse, 2000). Indeed, a meta-analysis of 19 studies (Bylsma et al., 2008) provide further empirical proof of attenuated emotional reactivity in depression, regardless of the context valence (Lawrence et al., 2004; Moses-Kolko et al., 2010, Rottenberg, 2005) (Figure 1.3). Although the empirical support for ECI theory is most profound across all three models, the heterogeneity of findings still pertains (Bylsma, 2021; Fitzgerald et al., 2008).

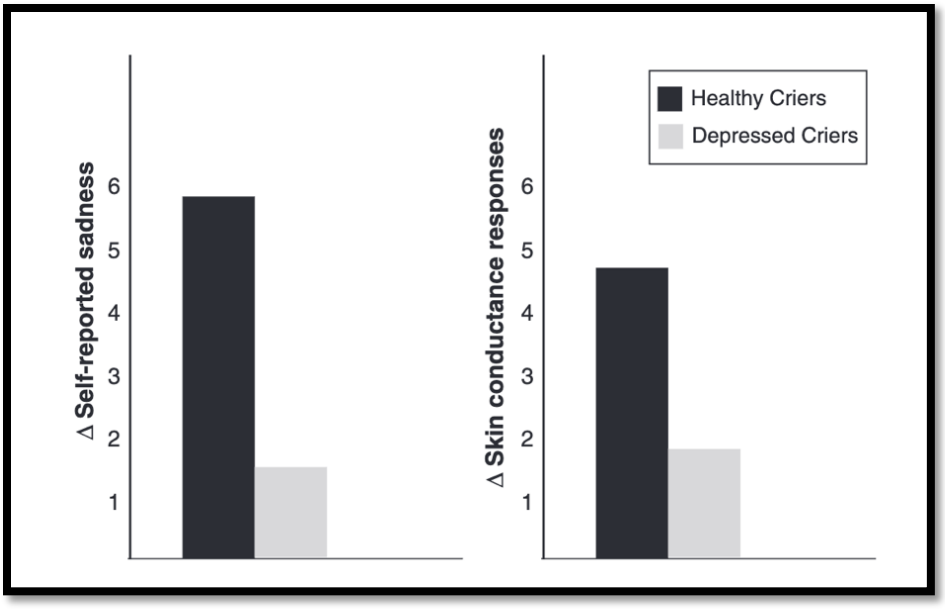

Figure 1.3 Comparison of self-reported sadness (left) and skin-conductance response rate (right) between healthy and depressed individuals who cried in response to a sad film. Adapted from Rottenberg, 2005.

CHAPTER TWO: ELECTROENCEPHALOGRAPHIC (EEG) CORRELATES OF AFFECTIVE PROCESSING

Electroencephalography (EEG) is a noninvasive method of recording the spontaneous electrical activity of the brain from the scalp (APA, 2013). Over the last century, EEG has been a vital tool to explore emotional processing and has been widely used in the field of affective neuroscience (e.g., Keil, 2013). Prior to outlining the use of electroencephalography (EEG) in the field of affective neuroscience, it is crucial to comprehend some basics of EEG signals.

2.1 Basic principles of EEG signal

The first EEG signal as well as much of what we know about EEG is credited to a German psychiatrist, Hans Berger (Kaiser, 2005). From his work, it is known that the EEG signal is a bioelectrical potential recorded with the use of electrodes placed at precisely established points on the surface of the head.

The EEG signal represents the combined activity of a myriad of postsynaptic potentials of giant cortical pyramidal neurons near the scalp (Britton et al., 2016). The reason why pyramidal neurons are thought to produce most EEG signals is due to their long apical dendrite extending towards the cortical surface as well as their well-aligned, parallel organization which allows for the production of easily detected waves (Kirschstein, & Köhling, 2009). The postsynaptic potential is generated with the release of neurotransmitters by the presynaptic cell, which activates ion channels on the postsynaptic cell membrane thus causing the flow of ions (e.g. NA+, CL-) in or out of the postsynaptic cell. Some neurotransmitters such as GABA generate an inhibitory signal (influx of negative ions) to the postsynaptic neuron called inhibitory postsynaptic potential (IPSP) which causes cell hyperpolarization whereas others such as glutamate produce an excitatory signal

(influx of positive ions), called excitatory postsynaptic potential (EPSP) causing cell depolarization (Figure 2.1). In other words, the flow of ions creates a negative or positive electrical field surrounding the neuron. The summation of IPSP and EPSP creates a separation of a positive and negative charge, also known as a dipole (Britton et al., 2016). An electric field generated by a single neuron is too weak to be detected by an EEG electrode on the scalp thus thousands of neurons need to be simultaneously active for the EEG signal to be obtained (Kirschstein & Köhling, 2009)

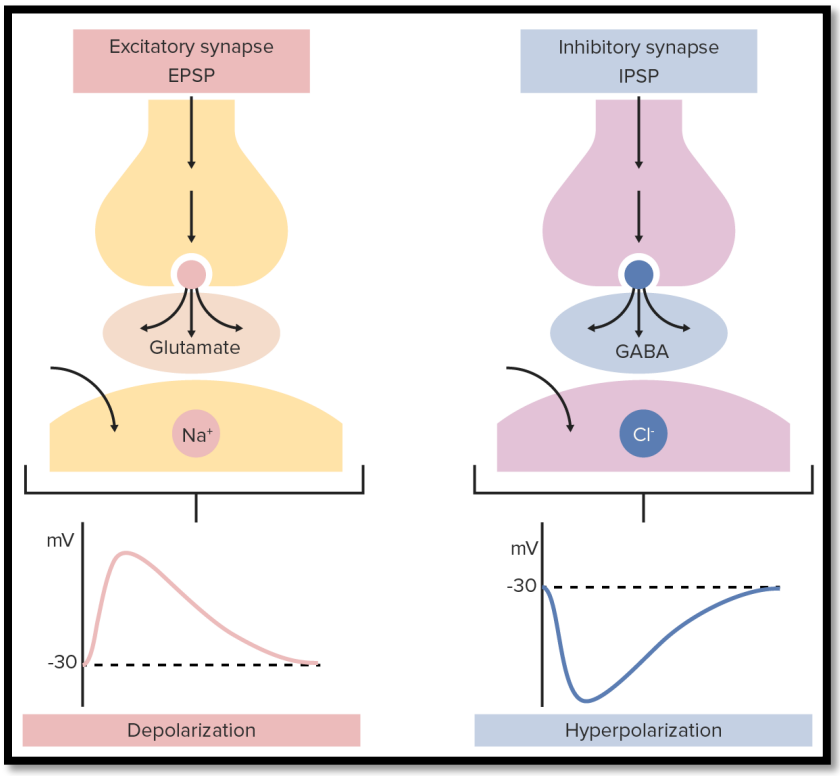

Figure 2.1 Excitatory and inhibitory synapses (2022) Adapted from: https://rb.gy/6kqe2

The EEG signal is oscillatory in nature. It has been demonstrated that specific patterns of cerebral waves are associated with particular cognitive, perceptual, and emotional processes (Cohen, 2017). Brain oscillations are marked by their characteristic morphology, frequency, and amplitude, allowing for their classification into 5 main bands, which features and roles will be

briefly mentioned in this part. The bands have been labeled with Greek letters and are as follows: delta (d) with the lowest frequency with a range up to 4Hz and highest amplitude, theta (θ) with the frequency range between 4 to 8Hz, alpha (α) with a frequency range from 8 to 12Hz, beta (β) with a frequency range from 12 to 30Hz, and gamma (γ) with the highest frequency above 30Hz and lowest amplitude (Buzsáki, 2011). The relationship between amplitude and frequency is inversely proportional, meaning an increase in frequency will lead to a decrease, by the same amount, the amplitude (Buzsáki, 2011).

The classification of neural oscillations into the five ranges is useful in further understanding how the former are associated with different stages of arousal and cognitive tasks, thus acting as functionally relevant markers of the brain (Başar et al., 2001) (Figure 2.2). Delta rhythm is typically present in deep sleep stages while theta is characteristic of lighter stages of NREM sleep and dreaming (Freberg, 2015). Higher frequency waves are more prevalent during waking with the beta being correlated with higher alertness, and concentration than alpha while gamma is particularly present during the processing of sensory input (Freberg, 2015).

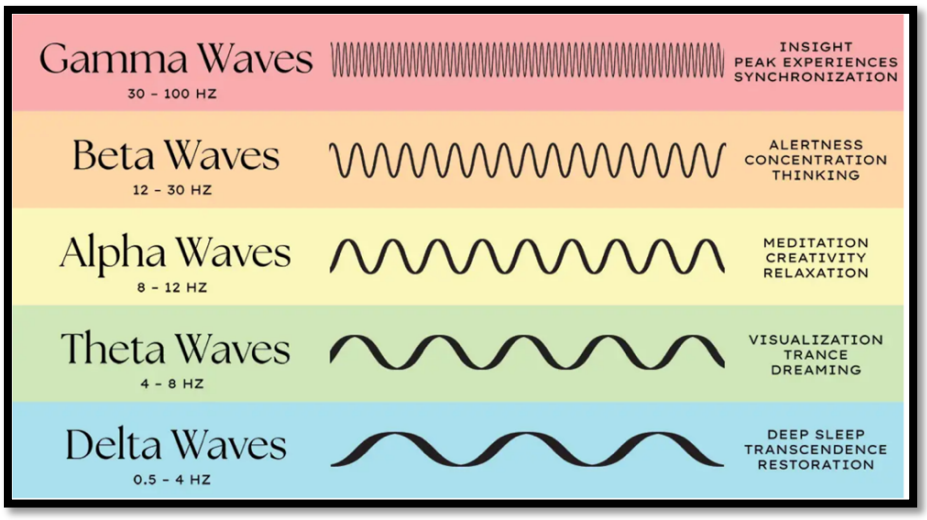

Figure 2.2 The five brain waves bands and the cognitive processes or stages they commonly accompany. Adapted from Pearce, 2022.

The recorded EEG signal is composed of a combination of frequency bands so for an in-depth analysis of frequency, the signal needs to be decomposed. The aforementioned procedure can be accomplished with the Fast Fourier Transform (FFT) which is a computational procedure of decomposing the original signal (in the time domain) into a sum of sinusoidal waves with specific frequency and amplitude (Buzsáki, 2011) (Figure 2.3). The outcome of this process is the power spectrum representing the energy incidence at each frequency (Buzsáki, 2011).

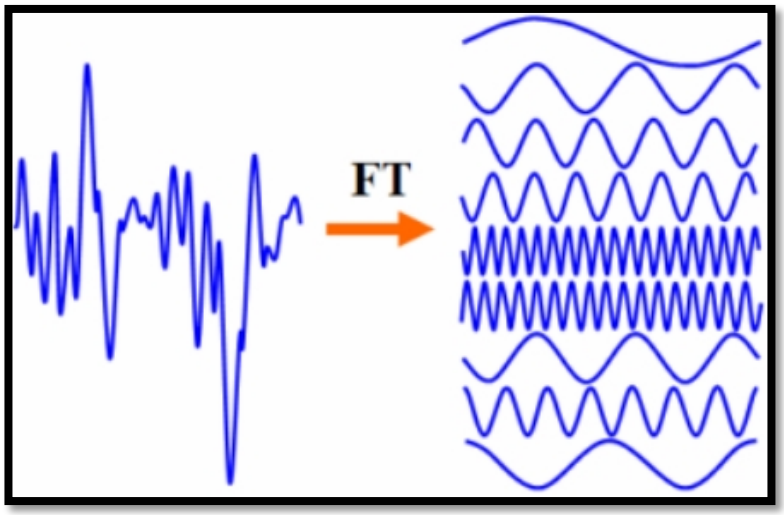

Figure 2.3 Visualization of a decomposition of a complex original signal (on the left) into a sum of simple sinusoidal waves (on the right) with the Fast Fourier Transform. Adapted from Chambers, 2014.

2.2 Event-related potentials (ERPs) in the study of affective processing

In the study of neural activity, the neural processes associated with a specific cognitive, sensory, or motor event have to be extracted from the original EEG signal (Luck, 2014). Such extractions from an EEG signal are called event-related potentials (ERPs) as they represent electrocortical activity associated with a particular stimulus or event (Luck, 2014).

In laboratory conditions, The EEG signal is often recorded during paradigms where stimulus (e.g., emotional images) are repeated across multiple trials, which are then averaged to isolate the activity related to the event, namely the event-related potential (Figure 2.4). The ERP

wave can be seen as alternating positive and negative peaks over time (Figure 2.4) (Luck & Kappenman, 2011). The ERP components are named in that the first letter of a name is based on whether the deflection in voltage is positive (P) or negative (N) and the second number on their latency (timing) in milliseconds (ms) (Luck, 2014). Therefore, the ERP component N150 describes a negativity peak at 150ms after the display of a stimulus. Some ERP components are also named based on their position (e.g. N1 – first negative peak) or the neural/psychological process they relate to (e.g. The Recognition Potential).

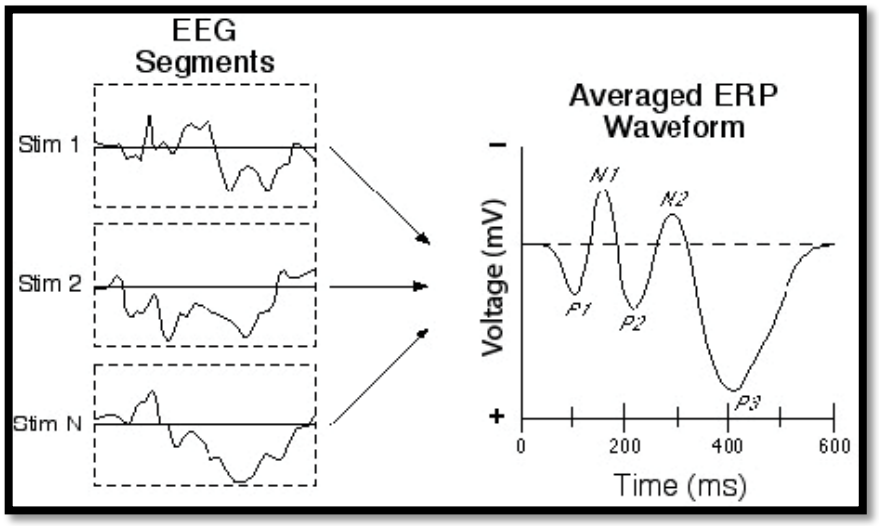

Figure 2.4 The averaging of EEG segments into the averaged ERP waveform. Adapted from Manhães & França, 2011.

The high temporal resolution of ERPs, in contrast to other neuroimaging methods like fMRI or PET, makes it a valuable tool in the study of affective processing (Olofsson et al., 2008). The ERP components with early, intermediate, and late latencies correspond to different stages of stimulus processing. The early ERP components (below 200 ms), also known as sensory ERP components, reflect the initial sensory processing of a stimulus and thus are useful in assessing attention and vigilance in healthy participants as well as in psychopathology (Luck & Kappenman, 2011). The affective valence of stimuli can modulate the short-latency ERP components. The P1

component evoked by visual stimuli may serve as an example as a larger P1 positivity was found for unpleasant pictures compared to pleasant and neutral ones (Olofsson, et al., 2008; Cacioppo et al., 1999). Such findings may suggest that unpleasantly valenced stimuli draw more attention in the early processing stages (Olofsson et al., 2008). The late ERP components (above 300ms) on the other hand are associated with the cognitive processing of a stimulus including stimulus classification and discrimination as well as explicit memory storage and retrieval (Luck, & Kappenman, 2011; Hillyard, 2009). The arousal of stimuli can influence the amplitude of late ERPs as visible in a study by Palomba et al. (1997) which recorded more positive-going ERPs in the range of 300-900ms for arousing stimuli as compared to neutral ones. From the above, it can be stated that both valence and arousal influence the amplitude of ERPs in the early and later stages of information processing (Olofsson et al., 2008).

The ERP approach can be also used to study the effects of emotional reactivity, most prominently visible in the intermediate ERP components (200-300 ms), based on the changes in arousal and valence (Olofsson et al., 2008). Considering diminished emotional reactivity and anhedonia are profound symptoms of MDD, many have been devoted to the research of neural ERP component patterns characteristic of this mood disorder. For the purpose of this thesis, most focus will be given to two middle-latency components: N2 and P3. The N2 component, also known as the Mismatch Negativity (MMN), reflects sensory encoding, memory, and attention (Fitzgerald & Todd, 2020). In laboratory conditions, the MMN component is evoked with an oddball paradigm in which a deviant (infrequent change) is placed in a repetitive sequence of identical stimuli (auditory or visual) attention (Fitzgerald & Todd, 2020). In the study where depressed individuals, were asked to respond to attended stimuli (high-frequency sound), a reduction in the amplitude of the N2 component has been recorded, which may illustrate the presence of attentional bias

variability and possible attention deficits in MDD patients (Ogura et al., 1993; El Massioui et al., 1996). Another significant ERP component in the study of depression is the P3. This endogenous potential reflects cognitive functions in response to the stimulus such as updating information in the working memory and attentional resource allocation (Bylsma, 2012). The association between the P3 component and stimulus salience is further portrayed by the oddball paradigm, in which the infrequent, deviating stimulus produces the characteristic P3 waveform, as opposed to standard, repetitive stimuli. A large body of research conducted on depressed individuals, reported a reduction in the P3 amplitude induced by the bimodal (auditory and visual) oddball task in depressed patients as opposed to controls, suggesting deficits in orienting of attention as well as evaluation of the stimulus (Nan et al., 2018; Karaaslan et al., 2003; Bruder et al., 2009). Moreover, P3 amplitude reduction during the bimodal oddball task has been negatively correlated with both the number and severity of depressive symptoms, thereby suggesting its possible role in predicting the severity of depression (Nan, et al., 2018; Santopetro et al., 2021). Recently, more research has been devoted to MDD deficits related to emotion and motivation, rather than solely cognitive dysfunctions (Proudfit et al., 2015). A study employing a recognition-memory task with positive, negative, and neutral face stimuli, reported a reduced N2 to positive facial stimuli as opposed to negative and neutral ones, in individuals with major depression (Deldin et al., 2000). Other studies, concerned with the association between stimulus valence and P3 amplitude in depression, found a larger P3 response in depressed individuals for negatively valenced words in comparison to neutral (Ilardi et al., 2007). The aforementioned findings may provide additional support for the negative attention bias present in depression (Ilardi et al., 2007).

The Late Positive Potential (LPP) is another ERP component commonly studied in depressive disorders due to its particular relevance for emotional responding (Bylsma, 2012).

Moreover, LPP is of particular interest in depression as it reflects both attention allocation processes as well as motivated attention arising from the two motivational systems: the appetitive and defensive systems (De Cesarei & Codispoti, 2011; Bylsma, 2012). In a study of affective picture viewing where both the valence (pleasant or unpleasant) as well as arousal (low, high) of images were manipulated, the largest increase in LPP was observed for highly arousing affective images, regardless of their valence (Leite et al., 2012; Bylsma, 2012). Abnormal patterns of decreased responsiveness to stimuli, as seen in LPP attenuation, are characteristic patterns present in depressive disorders (Weinberg et al., 2016). In a study by Grunewald et al. (2019), a sample of individuals with clinically diagnosed depression was presented with either emotional (sad, happy, fearful) or calm faces, and the variations of the LPP component were observed. The results showed a decreased LPP to emotional and calm faces in comparison to a group of healthy control, suggesting a reduced emotional reactivity to stimuli and an overall blunted response pattern (Grunewald et al., 2019). Additionally, an investigation of emotional processing in dysphoria revealed a smaller LPP amplitude in response to pleasant and neutral pictures in individuals with dysphoria, as opposed to non-depressed controls (Moretta et al., 2021). Such findings are consistent with the Emotional Context Insensitivity hypothesis (ECI) as an affective model of response patterns in MDD.

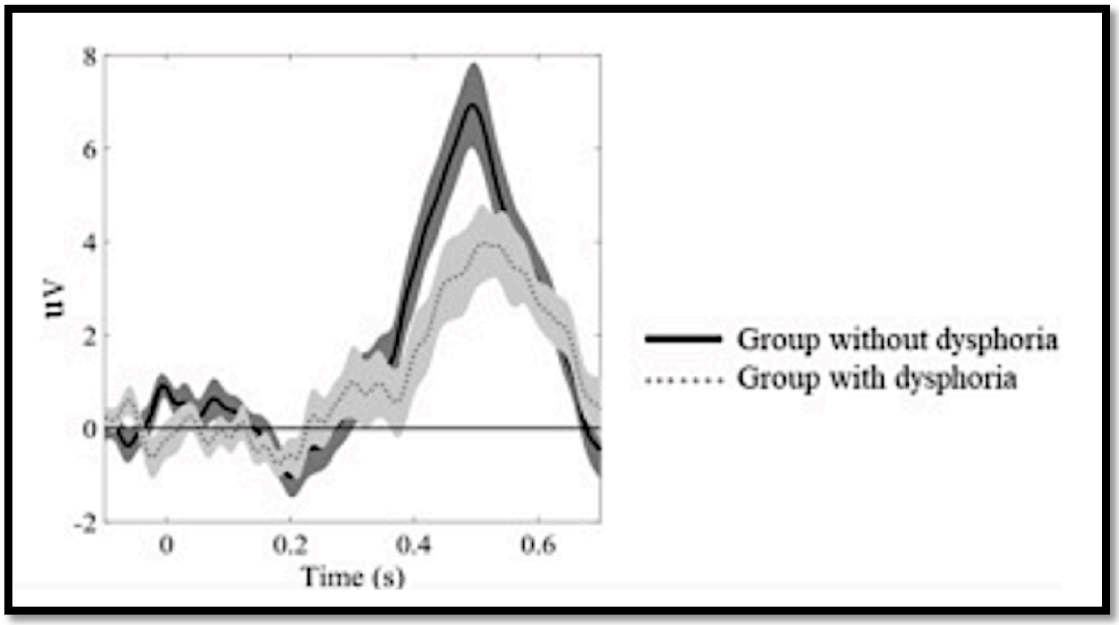

Figure 2.5 Individuals with dysphoria (dashed, light gray line) showed a smaller LPP for the pleasant condition compared to individuals without dysphoria (solid black line). Adapted from Moretta et al., 2021.

2.3. Startle modulation of ERPs in affective contexts

Another methodology utilized in the study of affective processing, besides the previously discussed oddball paradigm, is the startle response modulation. The startle response is an automatic, defensive response elicited by a stimulus with a sudden or abrupt onset (Anokhin & Golosheykin, 2010). The startle eyeblink reflex characterizes the onset of the startle response, which is studied most extensively in the acoustic modality (Filion, Dawson, & Schell, 1998). More precisely, in a laboratory setting a startle-eliciting stimulus (e.g., loud noise) is presented in a series of non-startling stimuli (Filion, Dawson, & Schell, 1998). The eyeblink reflex when the startle probe (i.e., loud noise) is presented during the exposure to affective pictures, is modulated based on the affective valence of the stimulus, in that greater eyeblinks are reported while processing unpleasant or threatening stimuli and smaller during the processing of pleasant stimuli (Bradley, Cuthbert, & Lang, 1999; Keil, et al., 2007). The progressing research suggests the two basic

motivational systems (appetitive and defensive) underlie the changes in the intensity of the startle reflex (Anokhin & Golosheykin, 2010). When the affective startle modulation has been compared in depressed relative to nondepressed individuals, the former demonstrated an abnormal pattern of startle responses (Allen, Trinder, & Brennan, 1999; Kaviani et al., 2004). Individuals with clinical depression showed a lack of startle modulation in affective stimuli, suggesting reduced reactivity not only towards pleasant but also unpleasant contexts (Kaviani et al., 2004). Other studies found a potentiated startle response to pleasant stimuli, implying that depressed individuals may view them as aversive (Allen, Trinder, & Brennan, 1999). Moreover, Mneimne, McDermut & Powers (2008) in their study on individuals with subclinical depressed symptoms (dysphoria) documented an absence of affective startle modulation, corresponding to the one found in clinical depression (Figure 2.6) Recently, the findings in dysphoria provide more support for attenuated startle modulation towards unpleasant pictures, indicating hypoactivation of the defensive motivational system (Taubitz, Robinson, & Larson, 2013; Messerotti Benvenuti et al., 2020). The data from the startle probe in preclinical depression appears to be at variance with the negative potentiation account whilst partially aligning with the Emotional context insensitivity hypothesis (ECI) (Messerotti Benvenuti et al., 2020).

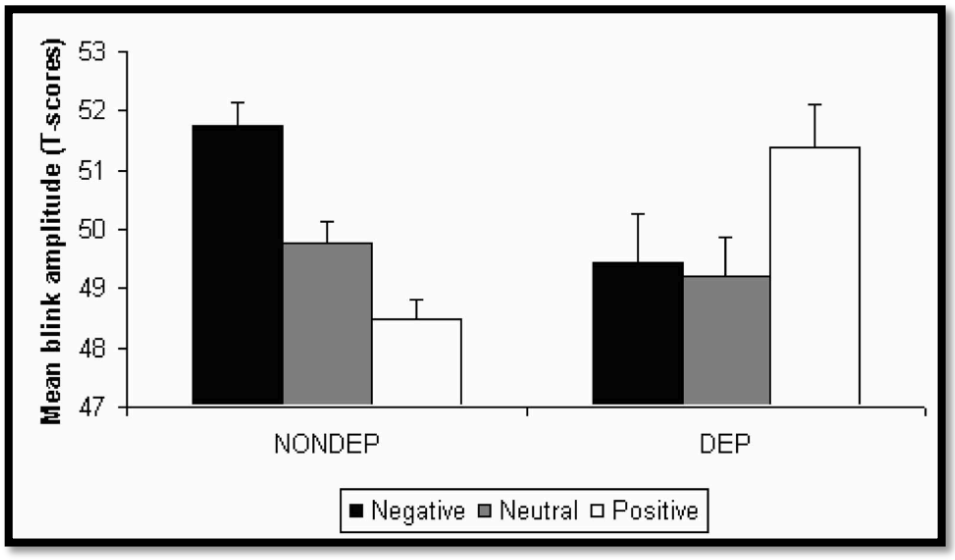

Figure 2.6 An absence of affective startle modulation in depressed (DEP) individuals as compared to the healthy controls (NONDEP) as expressed in the mean blink amplitude in negative (black), neutral (gray), and positive (white) conditions. The error bars expressed the standard errors. Adapted from Mneimne et al., 2008.

Besides producing the eyeblink reflex, the startle probe also elicits electrocortical responses such as the P3 component, which depicts the attentional processing in affective contexts (Nelson, Hajcak, & Shankman, 2015). In contrast to the eyeblink reflex magnitude being modulated by valence, the ERP amplitude to the startle probe is modulated by emotional arousal (Keil, et al., 2007). Particularly, the P3 response to the startling probe was smaller when viewing pleasant or unpleasant pictures compared to neutral ones, which can be explained through resource allocation reduction (Bradley, Cuthbert, & Lang, 1999; Keil, et al., 2007). In other words, the processing of affective pictures requires resources, thereby limiting the number of resources allocated to the processing of the startle probe (Keil, et al., 2007). Research on startle-elicited ERP as a potential brain marker of pathology found it may significantly contribute to facilitating the classification of mood disorders. (Lang et al., 2018). More precisely, the reduced amplitude of ERP evoked by a startle probe was found to be a significant predictor not only of higher levels of

depression but also of increased life dysfunction and poorer prognosis (Lang et al., 2018). Despite the promising role of startle-elicited ERPs in affective paradigms, to date, very few studies have explored ERPs components elicited by startle probes during the viewing of emotional pictures to study distinct phases of motivated attention to pleasant and unpleasant stimuli in depression or dysphoria.

PART II

CHAPTER THREE: THE STUDY

3.1 Introduction and Hypothesis

In the previous chapters, the key features of depression have been outlined. It has been described that depression is one of the most prevalent, debilitating, and costliest disorders worldwide (Kessler & Bromet, 2013; WHO, 2019; APA, 2013). Hence, identifying early psychophysiological indicators of depression has been highlighted as a core priority. The study of dysphoria, or subclinical depression, is particularly advantageous not only as it constitutes a risk for the onset of depression but also because it enables the sole analysis of depressive symptoms in the absence of confounds associated with the chronicity of MDD and the antidepressant medication (Greco et al., 2018; Messerotti Benvenuti et al., 2017, 2020).

The presence of depressive symptoms is associated with dysregulated affective disposition, determined by both the approach and defensive motivational systems functioning (Davidson, 1998). The depressive symptom of anhedonia is related to the hypoactivation of the former while persisting distress the activation of the latter motivational system (Admon & Pizzagalli, 2015). One way of studying the affective disposition of an individual is through their psychophysiological emotional responses (Lang et al.,1997; Messerotti Benvenuti et al., 2020) and, in this context, three main hypotheses have been put forward. First, 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 account is not fully supported by empirical evidence. The positive attenuation hypothesis specifies a reduced emotional responding toward pleasant and rewarding stimuli (Messerotti Benvenuti et al., 2017, 2020). The latter hypothesis has been extended to a

third one, known as Emotional Context Insensitivity (ECI), which suggests that depression is associated with an overall attenuation in response to emotional stimuli regardless of their valence (Rottenberg, 2005). A meta-analysis conducted by Bylsma et al. (2008) provided support for the positive attenuation hypothesis and Emotional Context Insensitivity account in depressed individuals. Of note, recent evidence suggests that reduced emotional reactivity to emotional stimuli might not only be a correlate of depressive symptoms but also predict the course of the disorder (Bylsma et al., 2008; Rottenberg et al., 2002).

Affective disposition related to depressive symptoms has been largely investigated with the use of event-related potentials (ERPs) (Messerotti Benvenuti et al., 2020). As described in Chapter 2, the N2 component reflects the early stages of attention processing and has also been utilized in non-emotional paradigms to study attentional processes in depression (El Massioui et al., 1996), while the P3 component represents higher-level processing related to the stimulus elaboration, including later attention resources allocation (Diner et al., 1985; Klumpp & Shankman, 2018). Both the N2 and P3 have been employed to explore emotional processing in startle paradigms. In a study of auditory ERPs in healthy individuals, a significantly reduced N2 response was found during the viewing of positively valenced pictures, in contrast to neutral and negatively valenced pictures (Surakka et al., 1998). In healthy individuals, a smaller P3 response to the startling probe has been recorded during the viewing of emotionally arousing pictures (pleasant or unpleasant) as compared to neutral ones, thereby suggesting a diminution of the resources allocated to the processing of the startle probe, in favor of the processing of affective pictures (Bradley, Cuthbert, & Lang, 1999; Keil, et al., 2007). Further research, employing the viewing of emotional and neutral pictures, found the reduced amplitude of startle-elicited P3 component (across all emotional conditions), to be a significant predictor of higher depression

scores, hence further highlighting the role of startle-elicited ERP in identification and classification of mood disorders and its risk factors (Lang et al., 2018). However, to date, startle-elicited ERPs during affective processing in depression and depression risk are largely unexplored.

In light of these considerations, the present study aimed to **investigate affective processing in individuals with dysphoria** through the analysis of startle-elicited ERPs during the viewing of pleasant, neutral and unpleasant emotional pictures and thereby attempting to seal the observed gap in the literature. Based on the previous research, this work's objective was to explore the following hypotheses:

1. Participants with dysphoria were expected to show reduced affective processing of emotional pictures, indexed by a greater amplitude of the N2 component to the startle probe when viewing pleasant and unpleasant emotional pictures relative to neutral ones and controls.
2. Participants with dysphoria were expected to show reduced affective processing of emotional pictures, indexed by a greater amplitude of the P3 component to the startle probe during the presentation of both pleasant and unpleasant emotional pictures relative to neutral ones and controls.

3.2. Materials and Methods

3.2.1. Participants

A cohort of 48 Caucasian students at the University of Padua, Italy, voluntarily took part in the research project. An ad-hoc anamnestic interview was to make sure that all included participants were medically healthy and not taking any psychotropic medication. In the sample,

participants were assigned to either a group with dysphoria or without dysphoria based on specific criteria. The module A of the Structured Clinical Interview for DSM-5 (SCID-5-CV; First et al., 2016; Italian version Fossati & Borroni, 2017) was used to assess past and present depressive symptoms and thereby identify the participants with dysphoria. Additionally, the Beck Depression Inventory-II (BDI-II, Beck et al., 1996; Ghisi et al., 2006) was utilized to assess the severity of depressive symptoms. The participants who both scored equal or greater than 12 on the BDI-II and had at least four current depressive symptoms, for a period of at least 2 weeks, without meeting the criteria for the diagnosis of major depressive disorder, persistent depressive disorder, or bipolar disorder, were assigned to the group with dysphoria (n = 24, 23 females). The participants who scored equal to or lower than 8 on the BDI-II and had no depressive symptoms or history of depression, were assigned to the group without dysphoria (i.e., controls) (n = 24, 23 females). In order to ensure a clear separation between the two groups, participants who scored in the range between 9 and 11 on the BDI-II or had only one depressive symptom were excluded from the study.

With respect to demographic variables, the two groups (with dysphoria, without dysphoria) did not differ in terms of sex (x^2 = 9.46, p = .975), age (p=.832; dysphoria group: Mean (M) = 21.9, standard deviation (SD) = 2.21, min = 19, max = 28; group without dysphoria: M = 22, SD = 1.92, min = 18, max = 27), and education (p = .523; dysphoria group: M = 16.3, SD = 1.71, min = 13, max = 20; group without dysphoria: M = 16.5, SD = 1.25, min = 14, max = 20).

3.2.2. Psychological measures

The participants in the study underwent a psychological assessment composed of both the SCID-5-CV and BDI-II. The Italian version of module A (mood episode module) of the SCID-5-

CV was administered by a trained clinical psychologist in order to assess the presence of dysphoria. Additionally, the diagnostic interview served as a tool to identify participants with major depressive disorder, persistent depressive disorder, or bipolar disorder and thereby exclude them from the study. All participants also completed the BDI-II, which is a reliable self-report measure used to assess the severity of the depressive symptoms present in the last 2 weeks. The aforementioned questionnaire is composed of 21 questions, each scored on a four-point Likert scale. The final score of the inventory ranges between 0 and 63, where more severe depressive symptoms are demonstrated with a higher score. In the Italian version of the BDI-II employed, the score of 12 was agreed to serve as a discriminant between individuals with and without depressive symptoms (Ghisi et al., 2006).

3.2.3. Experimental task

The experimental paradigm employed 24 color pictures (600 × 800 pixels) from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 2008) in each category: pleasant (e.g., erotic couples, sports), neutral (e.g., household objects, neutral faces), and unpleasant (e.g., attacking humans and animals), all of which were presented to the participants. The pleasant and unpleasant pictures were matched for normative arousal ratings which were significantly higher than for neutral pictures.

The experimental paradigm was a passive viewing task of pictures, presented for 6000 ms each, in a semi-randomized manner, meaning that no two pictures from the same condition were shown consecutively. A 3000 ms interval with a white fixation cross on a grey background (baseline), preceded each picture display. The participants were instructed to focus their gaze on the central fixation cross in order to ensure proper processing of the chosen stimuli. After each

picture presentation, an intertrial interval (ITI) with a white fixation cross (like in the baseline) was presented for a period of time that varied between 6000 and 8000 ms. The acoustic startle probe was administered randomly at one of the four time points after picture onset: 300, 1500, 3500, or 4500 ms. However, only the startle probe administered at 1500 ms or later was considered in the analysis as the primary focus of the study was on affective processing and no prior study employed startle-elicited ERPs at 300 ms. The acoustic startle stimulus, used in the paradigm, was a burst of 100 dB white noise with a duration of 50 ms (instantaneous rise time), which was conveyed to both ears through Sennheiser headphones (HD 280 Pro model). The experimental task is depicted in Figure 3.1

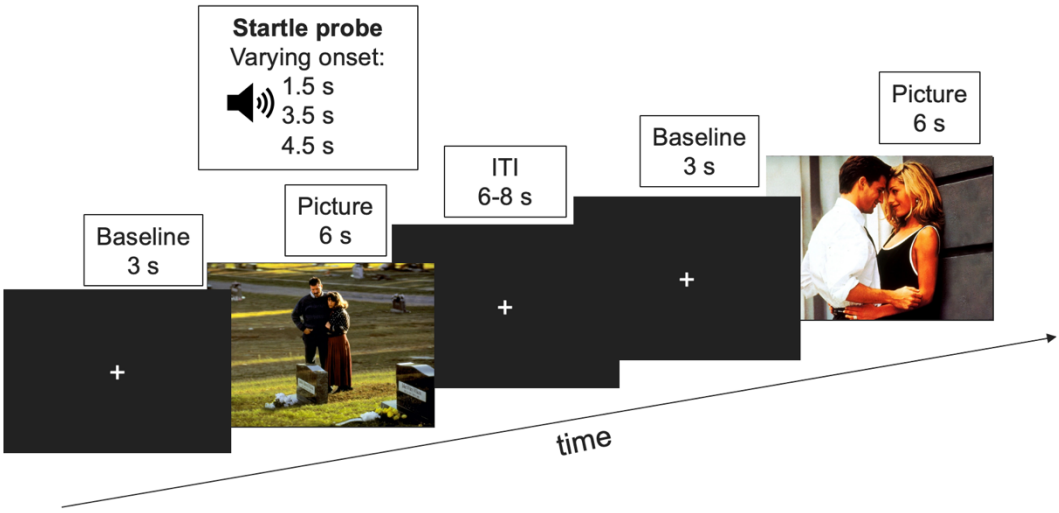

Figure 3.1 Illustration of the passive viewing task with the startle probe.

3.2.4. EEG recording and data reduction

The recording of EEG data was conducted with an elastic cap containing 32 tin electrodes arranged in a 10-20 system (Fp1, Fpz, Fp2, F7, F3, Fz, F4, F8, FC5, FC1, FC2, FC6, T7, C3, Cz, C4, T8, CP5, CP1, CP2, CP6, P7, P3, Pz, PA, P8, POz, O1, Oz, O2, and mastoids: M1, M2) and

referenced online to CPz. Eye movements and eye blinks were monitored through a bipolar montage of horizontal and vertical electrooculograms (EOG). During the EEG recording it was crucial to keep the impedance of all electrodes lower than 10 kΩ. The eego software and eego amplifier (ANT Neuro, Enschede, Netherlands) have been used for the data acquisition. Post-amplification, the EEG and EOG signals were bandpass filtered (0.3-40 Hz) and digitalized at 1000Hz.

The first stages of data reduction: re-reference and downsampling, were conducted in EEGLAB. The EEG signal was re-referenced offline to mastoids to remove the electric noise captured by the ground electrode (online reference). To reduce the computational costs the EEG signal was downsampled at 500 Hz, in accordance with the Nyquist theorem. The further stages of preprocessing were conducted in Brainstorm, including the application of a 0.3-30 Hz bandpass filter. Additionally, blink artifacts and horizontal eye movements were manually corrected using the Independent component analysis (ICA). For each trial, the EEG was epoched starting 500 ms before the startle probe and continuing for 2000 ms. The baseline for each epoch corresponded to the 200 ms recorded 50 ms prior to the onset of the startle probe. The ERPs were computed as an average activity at all three times of startle probe administration (1500, 3500, 4500 ms) since all are part of the late processing stages where affective processing occurs. The separate grand averages ERPs were calculated for each group (with dysphoria and without) and condition (pleasant, neutral, and unpleasant), producing a total of 6 different ERP averages. The N2 and P3 components were calculated as an average and peak activity at the Cz electrode, with the former measured between 200 and 300 ms post startle and the latter between 300 and 500 ms post startle.

3.2.5. Procedure

Prior to the experimental session, the participants were instructed to avoid the consumption of caffeine or alcohol on that day. Upon arriving in the laboratory each participant signed a written consent form and was later administered module A of the SCID-5-CV interview and the BDI-II. Subsequently, each individual was asked to sit comfortably in the assigned chair, positioned in a dimly lit and sound-attenuated room. After the careful attachment of electrodes and a resting state of 3 minutes, six practice trials were presented to the participants, two of each category (pleasant, neutral, and unpleasant). Afterward, the participants underwent the passive emotional viewing task while EEG was recorded. The last part of the task involved an assessment of arousal and valence of 36 pictures (12 in each category) using the Self-Assessment Manikin (SAM, Bradley & Lang, 1994). The entire procedure, including the final full debriefing of the participants, lasted a total of 90 min.

3.2.6. Statistical analyses

The three time points of the acoustic startle probe administration (1500, 3500, and 4500 ms) were averaged across and clustered into one time condition, due to the occurrence of the same hypothesized mechanism in each. Both N2 and P3 responses to the startle probe were analyzed using a repeated measure analysis of variance (ANOVA) with Group (with dysphoria and without dysphoria) as a between-subject factor and Condition (pleasant, neutral, and unpleasant) as a within-subject factor. The ANOVAs for the N2 and P3 amplitudes and peaks were conducted separately. Significant main effects and interactions ($p < .05$) were reported and a Tuckey post-hoc test was carried out to inspect significant effects.

3.3. Results

The N2 component

For the N2 amplitude, the mixed ANOVA revealed a significant Condition main effect, (F = 4.42, p= .015), no significant Group effect (F = .548, p = .463) and a significant Condition * Group interaction effect, (F = 3.95, p = .022). The post-hoc test revealed that the control group had a significantly smaller N2 amplitude to the startle probe in the pleasant condition as compared to the neutral one ($p_{Tukey} < .001$). Such a condition effect was not present in the group with dysphoria as no significant difference in response to the startle when viewing pleasant and unpleasant pictures was found ($p_{Tukey} = 1.000$). The N2 response to the startle probe in the pleasant condition did not differ between the two groups ($p_{Tukey} = .691$) which, along with the previous findings suggest a presence of a difference in each within group's pattern of responding to pleasant as compared to neutral condition (Figure 3.2 and Figure 3.3).

Similarly, the mixed ANOVA of the peak N2 amplitude also yielded no Condition effect (F = 2.22, p = .114), no Group effect (F = .801, p = .375), but a significant Condition * Group effect, (F = 3.33, p = .040). The Tukey post-hoc test further explored the Condition * Group interaction effect, revealing that the group without dysphoria showed a significant reduction in the N2 peak amplitude to the startle during the presentation of pleasant pictures in comparison to neutral ones ($p_{Tukey} = .008$). Such a reduction was absent in the group with dysphoria which showed no significant difference in N2 peak amplitude during the presentation of pleasant as compared to neutral pictures ($p_{Tukey} = 1.00$) (Figure 3.4). Additionally, no group differences emerged for the pleasant condition ($p_{Tukey} = .640$), highlighting the different response patterns to pleasant and neutral pictures within both groups.

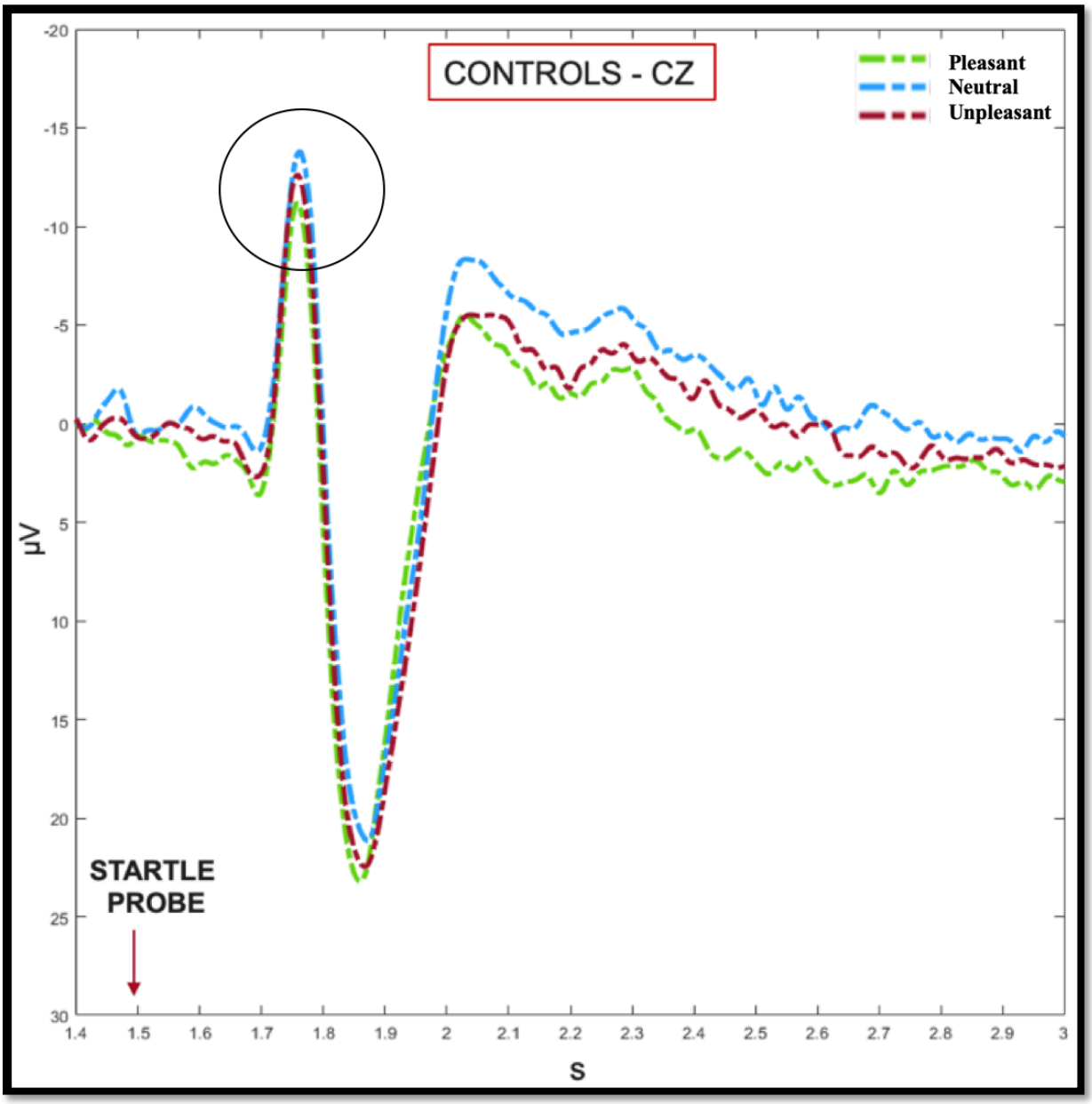

Figure 3.2 ERP amplitude (μV) to the startle probe in the group without dysphoria (controls) during pleasant (green line), neutral (blue line), and unpleasant (red line) picture processing. The N2 was highlighted with a circle.

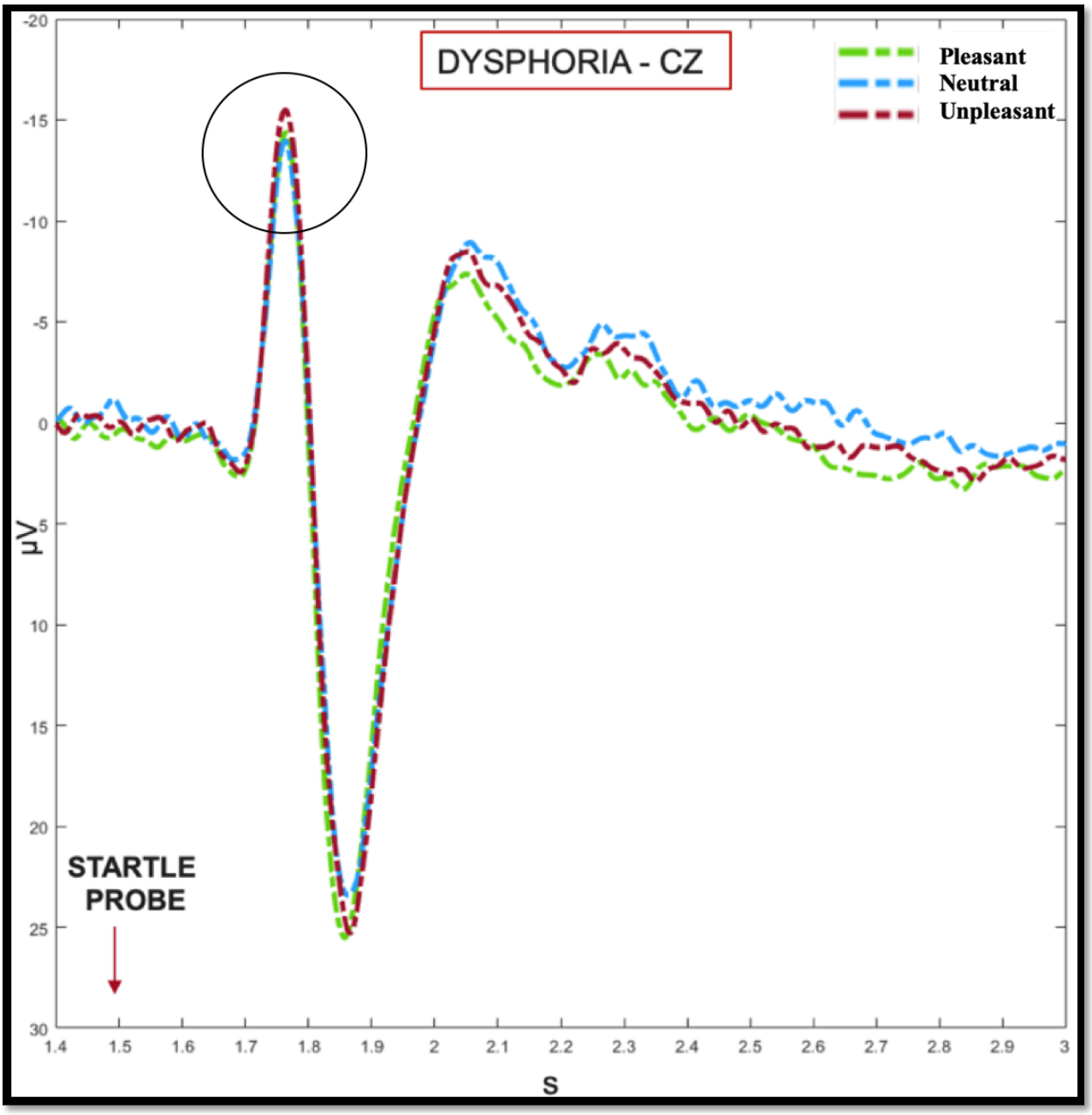

Figure 3.3 N2 amplitude (μV) to the startle probe in the group with dysphoria during pleasant (green line), neutral (blue line), and unpleasant (red line) picture processing. The N2 was highlighted with a circle.

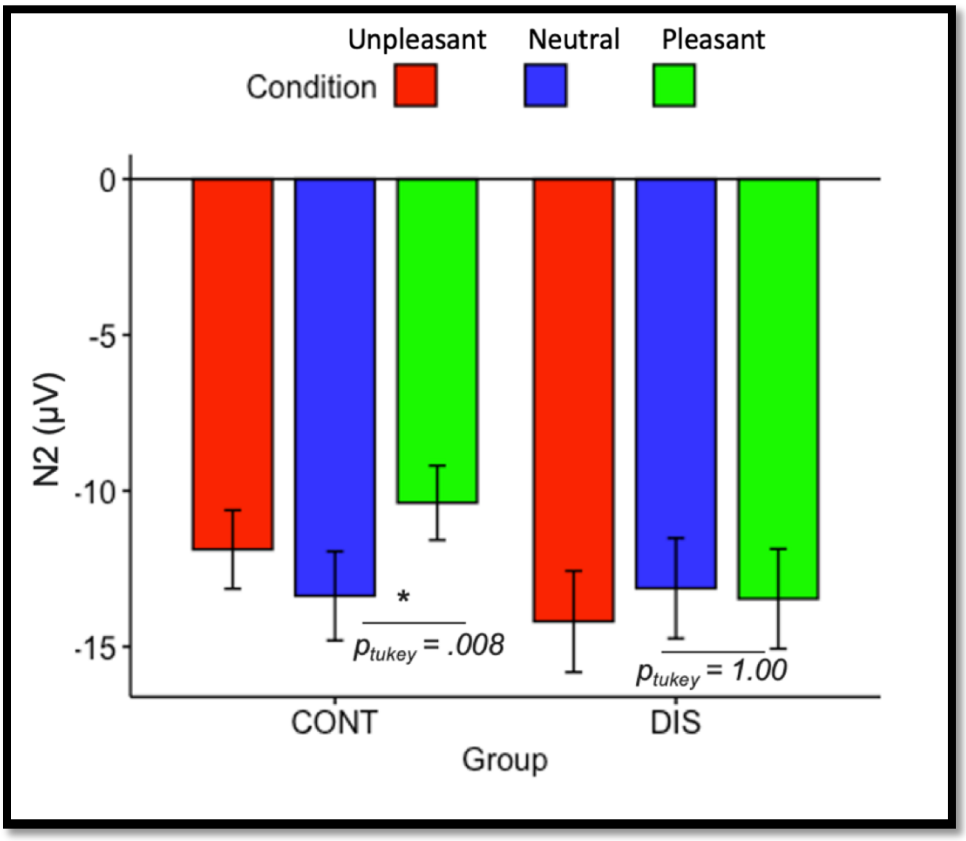

Figure 3.4 Interaction effect of condition and group on N2 peak amplitudes to the startle probe.

The P3 component

For the P3 mean amplitude, the mixed ANOVA revealed no significant Condition effect (F = 3.02, p = .054), no Group effect (F = .158, p = .693) and no Condition * Group effect (F = 1.21, p = .304).

The mixed ANOVA on the P3 peak amplitude yielded a significant Condition main effect, (F = 3.32, p = .041), but no Group effect (F = .315, p = .577) and no significant Condition * Group effect (F = .798, p = .453) for the peak P3 amplitude.

Both groups (with dysphoria and without dysphoria) had a significantly larger peak P3 response to the startle probe in the unpleasant condition as compared to the neutral condition

($p_{Tukey} = .040$). The significant within-subjects effect was found only between the unpleasant and neutral condition (Figure 3.5). No between-group difference was reported as significant.

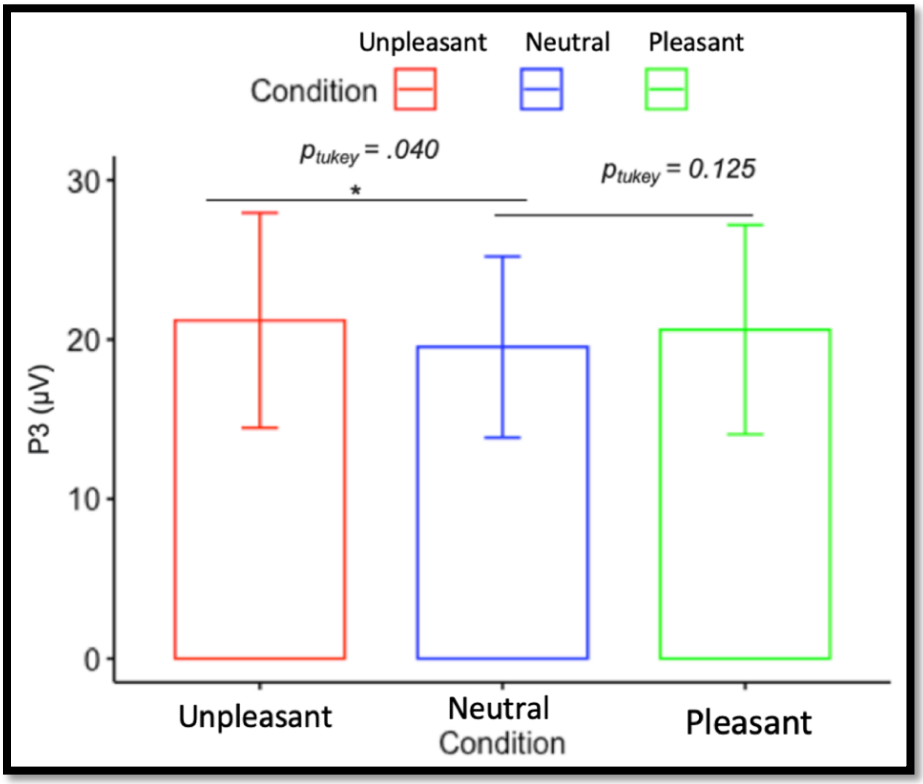

Figure 3.5 Main effect of condition on P3 amplitudes elicited by the startle probes. The unpleasant condition (red) elicited greater P3 as compared to the neutral condition (blue).

Correlations

A correlation matrix of P3 component and Self-Assessment Manikin (SAM) ratings revealed a significant correlation. Specifically, peak and mean P3 amplitude to the startle probe for each category (pleasant, neutral and unpleasant) was positively correlated with self-reported arousal for pleasant and unpleasant pictures (Table 1.1). No such correlations were found for the N2 component.

	P3_Peak_Pleasant	P3_Peak_Neutral	P3_Peak_Unpleasant
Arousal pleasant	0.405**	0.322*	0.304*
Arousal neutral	0.193	0.232	0.186
Arousal unpleasant	0.367*	0.314*	0.397**
Valence pleasant	-0.120	0.018	0.060
Valence neutral	0.131	0.310*	0.191
Valence unpleasant	-0.013	0.004	-0.164

Note. *p <.05. **p <.005

Table 1.1 Correlation matrix for the P3 peak amplitude in the three emotional conditions (pleasant, neutral, and unpleasant) and SAM ratings.

3.4. Discussion and Conclusion

This study aimed at exploring affective processing in dysphoria through the startle-elicited ERPs during the passive viewing of emotional pictures. This research was centered around the variations of both N2 and P3 amplitudes in response to the startle probe administered in an emotionally arousing context. Based on the previous literature (Benning & Ait Oumeziane, 2017; Keil et al., 2007) it was hypothesized that individuals with dysphoria would show an attenuated early affective processing of the emotional picture in both pleasant and unpleasant conditions, visible in the presumed greater N2 response. Furthermore, the second hypothesis suggested that individuals with dysphoria would have reduced late affective processing of the picture in the two contrasting emotional conditions, indexed by a larger P3 component, compared to controls.

In agreement with the first hypothesis, the pattern of larger N2 response to the startle probe in pleasant, compared to neutral emotional context, was found in the group with dysphoria and not in the control group. Particularly, the control participants showed a significant reduction of the N2

amplitude to the startle when viewing pleasant pictures, compared to neutral ones, which may suggest that they were paying more attention to the pleasant emotional stimuli thereby resulting in less detection of the auditory stimulus. On the other hand, individuals with dysphoria showed a greater N2 response, meaning they did not pay as much attention to the pleasant picture as the healthy controls, which in turn did not reduce their early detection mechanism of the auditory stimulus. Contrary to what was hypothesized, individuals with dysphoria did not show a greater N2 while viewing unpleasant pictures, which suggests that there was no significant attenuation in the affective processing of the unpleasant stimuli. These findings as a whole provide more support to the positive attenuation hypothesis. Therefore, these findings are in line with the literature showing a reduced affective processing of pleasant stimuli in individuals with a higher risk to develop depression (Bylsma et al., 2008).

Contrary to the second hypothesis, in the present study no greater amplitude of P3 to the startle probe in the pleasant and unpleasant condition relative to the neutral one and the control group emerged in the group with dysphoria. Although no group effect emerged for the P3 amplitude to the startle probe, a condition effect was found. Specifically, a larger P3 amplitude to the startle, across both groups, was present when the participants were shown unpleasant pictures. The above results may be hypothetically explained with startle probe potentiation by an unpleasant context, in that the reaction to the startle probe (an aversive stimulus) may be further strengthened in the presence of another unpleasant stimulus such as an unpleasant picture. The aforementioned interpretation is also represented by the correlation findings between the P3 component and SAM ratings. Particularly, those with higher P3 amplitudes to startle probes across all conditions also presented with greater self-reported arousal ratings for pleasant and unpleasant but not neutral

pictures. However, to fully understand the role of startle-elicited P3 during affective pictures processing, further studies are warranted.

Some limitations of this study need to be acknowledged. Firstly, the sample of participants consisted entirely of university students, which possesses some restrictions for the generalization of these findings to the general population. Additionally, due to the higher prevalence of dysphoria in the female population (Rodríguez et al., 2012), the great majority of the participants in this study belonged to the female sex, which further limits the generalizability of this work's findings to the male population. An additional need for future replication stems from the inconsistent results obtained for the P3 amplitude to startle probes in the unpleasant emotional context.

In conclusion, the results of this study demonstrated that individuals with dysphoria are characterized by greater attention to a startle probe presented during pleasant contexts, suggesting a blunted affective processing of pleasant emotional stimuli, in line with the positive attenuation hypothesis. Importantly, the paradigm of startle modulation of ERPs may serve as a valuable quantitative measure of early identification as well as prevention of full-blown clinical depression.

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