



# Appetitive and aversive motivation in dysphoria: A time-domain and time-frequency study of response inhibition



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## ABSTRACT

The study of emotional response inhibition could provide novel insight into dysphoria-related deficits in appetitive and aversive motivational systems. Therefore, dysphoric ( $N = 21$ ) and nondysphoric ( $N = 21$ ) participants completed an emotional Go/Nogo paradigm, including the presentation of pleasant, neutral and unpleasant pictures. Behavioral measures [reaction times (RTs), accuracy to Go and Nogo stimuli] and neural correlates (Go/Nogo-N2 and Go/Nogo-P3) of response inhibition were compared between the two groups. Time-frequency analysis was also used as a novel approach to disentangle the multiple processes underlying time-domain ERP data. A reduced Go/Nogo effect for P3 and oscillatory delta activity was found in response to pleasant and neutral, but not unpleasant, stimuli in dysphoric relative to nondysphoric individuals. These findings showed that dysphoric individuals need a reduced and/or less effortful response inhibition to pleasant stimuli, suggesting that dysphoria is characterized by under-engagement of appetitive rather than over-engagement of aversive motivational system.

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## 1. Introduction

Subsyndromal depressive symptoms (i.e., hereinafter referred to as dysphoria), defined as two or more depressive symptoms beneath the diagnostic threshold of dysthymia or major depression (Judd, Akiskal, & Paulus, 1997), has been found to be a highly prevalent condition (Horwath, Johnson, Klerman, & Weissman, 1992), with a considerable impact on the quality of life of patients (Preisig, Merikangas, & Angst, 2001). More strikingly, the presence of dysphoria is one of the most important risk factors for developing a diagnosable episode of depression (e.g., Cuijpers & Smit, 2004; Lewinsohn, Hoberman, & Rosenbaum, 1988). Specifically, dysphoric individuals have been reported to be 4.4 times more likely than nondysphoric individuals to develop a first-onset major depression during a 1-year period (Horwath et al., 1992). Consistent with these findings, the presence of dysphoria has emerged as the strongest risk factor for major depression onset and the best single screening measure in a sample of female adolescents across a 4-year follow-up (Seeley, Stice, & Rohde, 2009).

From a clinical perspective, individuals with dysphoria are characterized by negative affectivity and exhibit sadness or depressed mood, which have been considered as the core symptoms of dys-

phoria (Fowles, 1988). These symptoms are indicative of increased activation of the withdrawal-related motivational system, which is primarily activated in contexts that involve threat, with a basic behavioral repertoire of withdrawal, escape, and attack (Bradley, Codispoti, Cuthbert, & Lang, 2001). However, dysphoric individuals are also characterized by anhedonia, psychomotor retardation, apathy and/or inability to respond to reward (Fowles, 1988). In turn, these symptoms are indicative of underactivation of the approach-related motivational system, which results in under-engagement with environment and may increase the propensity for withdrawal-related action tendencies (Bradley et al., 2001).

Dysphoria-related motivational dysregulation has been hypothesized to alter emotional responding, which is defined as a multicomponential and coordinated process, including affective experiences, expressive behaviors, and physiological adjustments, that has evolved to mediate transactions in the environment that promote an organism's survival and adaptation (Lang, Bradley, & Cuthbert, 1997). In particular, dysphoria-related motivational dysregulation has been proposed to attenuate emotional responding to pleasant stimuli and/or to potentiate emotional responding to unpleasant stimuli, respectively (e.g.; Golin, Hartman, Klatt, Munz, & Wolfgang, 1977; Lewinsohn, Lobitz, & Wilson, 1973; Messerotti Benvenuti, Mennella, Buodo, & Palomba, 2015). Importantly, the reduced activation of approach-related motivational system has been found to predict the onset of major depressive episode in never-depressed adolescent girls (Bress, Foti, Kotov, Klein, & Hajcak, 2013), as well as impair recovery in depressed

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patients (Kasch, Rottenberg, Arnow, & Gotlib, 2002; Rottenberg, Kasch, Gross, & Gotlib, 2002). Therefore, studying motivational dysregulation in dysphoria is critical because it may determine the persistent anhedonia and/or negative mood that, in turn, may put a dysphoric individual at risk for full-blown depressive episode (Beevers & Carver, 2003). Accordingly, it is important to examine whether motivational dysregulation may be associated with dysphoria, rather than being a mere correlate of clinical depression only (Pizzagalli, 2011). To date, however, inconsistent findings have been reported on the influence of dysphoria on activation of the appetitive and aversive motivational systems (e.g., Golin et al., 1977; Lewinsohn et al., 1973; Messerotti Benvenuti, Mennella et al., 2015).

Approach- and withdrawal-related motivational systems are intimately connected with emotions, which have been viewed as action dispositions, or motivationally tuned states of readiness (see Frijda, Kuipers, & Ter Schure, 1989; Lang, 1995) that prepare the organism to respond adaptively to environmental stimuli. Emotional perceptual stimuli employed in experimental contexts (e.g., affective pictures) can match “real” objects or events to such an extent as to activate a disposition towards action, thus evoking prepotent response tendencies reflected in a pattern of somatic, autonomic, and cortical changes similar to that prompted by the “real” stimuli (Bradley & Lang, 2000; Lang, Greenwald, Bradley, & Hamm, 1993). On these grounds, investigating how pleasant and unpleasant stimuli affect the active suppression of prepotent motor responses provides a way to test approach- and withdrawal-related action readiness, respectively. More specifically, action dispositions associated with emotional stimuli are reflected in the degree of difficulty inhibiting prepotent responses, so that the greater the activation of a motivational system, the greater the difficulty withholding an action (e.g., Messerotti Benvenuti, Sarlo, Buodo, Mento, & Palomba, 2015).

In this context, a useful task is the emotional Go/Nogo paradigm. In the classic Go/Nogo task (Falkenstein, Hoormann, & Hohnsbein, 1999), a continuous series of stimuli is presented, including Go cues, to which subjects are required to respond as quickly and accurately as possible, and Nogo stimuli, to which subjects have to withhold responding. The high frequency of Go cues ( $\geq 70\%$ ) determines a prepotent tendency to respond, that must be inhibited upon occurrence of infrequent Nogo stimuli. In the emotional variant of the Go/Nogo task, affective stimuli (e.g., emotional pictures or words) are used in place of standard nonemotional stimuli, thus providing a reliable measure of the emotional modulation of response inhibition (Schulz et al., 2007). The Go/Nogo task is among the most well-characterized paradigms of response inhibition to perceptual stimuli (e.g., Dillon & Pizzagalli, 2007), and has been widely used in neuroscientific studies of response inhibition (Aron, Robbins, & Poldrack, 2004). The Go/Nogo task has high clinical utility and construct validity when assessing such constructs as impulsivity (e.g., Berwid et al., 2005), and motivation/reward neural pathways (e.g., Albert, López-Martín, & Carretié, 2010; Zhang & Lu, 2012). Accordingly, the Go/Nogo paradigm has been widely used to assess impulsivity in patients with attention deficit hyperactivity disorder or in patients with borderline personality disorder and to assess motivational deficits in patients with depression (e.g., Durston et al., 2003; Ruchow, Groen, Kiefer, Beschoner et al., 2008; Ruchow, Groen, Kiefer, Buchheim et al., 2008). Related to this, affectively salient stimuli have been included into Go/Nogo paradigms as they evoke prepotent response tendencies compared to irrelevant (neutral) stimuli. In turn, a more prepotent tendency to respond to emotion-laden stimuli makes response inhibition to these stimuli more difficult and/or effortful compared to neutral stimuli (Chiu, Holmes, & Pizzagalli, 2008; Zhang & Lu, 2012). Thus, affective stimuli have been incorporated into Go/Nogo tasks

to examine both approach- and withdrawal-related motivational systems (Albert et al., 2010).

Two components of the event-related potentials ERP have been consistently found to be related to response inhibition: the Nogo-N2 and the Nogo-P3. The Nogo-N2 is a negative deflection occurring 250–350 ms following Nogo stimuli, with maximum amplitude over frontocentral scalp locations. It is considered as a robust index of response inhibition across several tasks (e.g., Go/Nogo, anti-saccade, stop-signal) and stimulus modalities (e.g., Falkenstein et al., 1999; Kok, Ramautar, De Ruiter, Band, & Ridderinkhof, 2004). The Nogo-P3 is a large positive deflection occurring 300–600 ms following Nogo stimuli, with maximum amplitude over frontocentral scalp sites similar to the P3a distribution (e.g., Kiefer, Marzinzik, Weisbrod, Scherg, & Spitzer, 1998). In addition to the Nogo-P3, a parietal P3 (identified as P3b) has been observed in response to Go trials. However, differently from the frontocentral Nogo-P3 component, the parietal P3 in response to Go trials has been proposed to reflect attention to relevant target stimuli rather than response inhibition (Tekok-Kilic, Shucard, & Shucard, 2001). It has been proposed that the Nogo-N2 and the Nogo-P3 reflect different processes that characterize response inhibition. Specifically, the Nogo-N2 has been suggested to mirror a variety of cognitive control processes that underlie response inhibition, the most important being conflict monitoring (e.g., Donkers & van Boxtel, 2004). The conflict monitoring process is a central function of cognitive control, which is implicated not only in tasks requiring individuals to choose between multiple alternatives (e.g., Barch, Braver, Sabb, & Noll, 2000), or to make error-detection responses (e.g., Carter et al., 1998), but also in tasks requiring participants to inhibit an incorrect but prepotent response (e.g., Botvinick, Nystrom, Fissell, Carter, & Cohen, 1999). By contrast, the Nogo-P3 has been proposed to primarily reflect the inhibitory process itself (e.g., Smith, Jamadar, Provost, & Michie, 2013). Consistent with these findings, studies using source-localization algorithms have shown that the anterior cingulate cortex (ACC) and the right lateral orbitofrontal cortex are involved in the generation of the Nogo-N2 (e.g., Bekker, Kenemans, & Verbaten, 2005; Bokura, Yamaguchi, & Kobayashi, 2001). Conversely, the Nogo-P3 has been associated with the activity of the left lateral orbitofrontal cortex and motor regions, including left inferior frontal gyrus, the primary motor cortex contralateral to the hand used for Go responses, the left supplementary motor areas, and the bilateral thalamus (Bokura et al., 2001; Smith et al., 2013).

A number of studies have examined the emotional modulation of the behavioral responses [i.e., reaction times (RTs), and performance accuracy to Go and Nogo stimuli] and the Go/Nogo effect for N2 and P3 (i.e., larger N2 and P3 amplitudes in response to Nogo than Go stimuli) in healthy individuals during an emotional Go/Nogo task. At the behavioral level, RTs have been reported to be faster in response to pleasant and unpleasant than neutral Go stimuli, whereas RTs to pleasant and unpleasant Go stimuli were found to be comparable (e.g., Chiu et al., 2008; Zhang & Lu, 2012). However, it should be noted that some studies have reported faster RTs to pleasant than unpleasant Go stimuli (Albert et al., 2010; Fonseka, Jaworska, Courtright, MacMaster, & MacQueen, 2016). There is also evidence that accuracy to Go trials is higher in response to pleasant and unpleasant than neutral conditions (Chiu et al., 2008; Zhang & Lu, 2012; but see also Albert et al., 2010). By contrast, findings regarding the emotional modulation of Nogo trials have been mixed due to methodological differences (Albert et al., 2010; Chiu et al., 2008; Zhang & Lu, 2012). At the neural level, there is evidence that the amplitude of the Nogo-N2 appears not to be modulated by the emotional valence of stimuli. Specifically, no differences in Nogo-N2 amplitudes between emotional and neutral stimuli have been observed (e.g., Chiu et al., 2008; Zhang & Lu, 2012). By contrast, the Nogo-P3 has been shown to be larger in response to emotionally arousing than neutral stimuli, suggesting that the more prepotent

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