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Frontal alpha asymmetry as a pathway to behavioural withdrawal in depression: Research findings and issues

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HIGHLIGHTS

- Depression may be conceptualised as behavioural withdrawal from stressor.
- Neurobiological pathways include asymmetry of frontal lobe activation.
- Although overall supportive, findings are inconsistent with some confounds.
- Depressive symptom profiles, gender and location of asymmetry need attention.

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ABSTRACT

Depression has been described as a process of behavioural withdrawal from overwhelming aversive stressors, and which manifests itself in the diagnostic symptomatology for Major Depressive Disorder (MDD). The underlying neurobiological pathways to that behavioural withdrawal are suggested to include greater activation in the right vs the left frontal lobes, described as frontal EEG asymmetry. However, despite a previous meta-analysis that provided overall support for this EEG asymmetry hypothesis, inconsistencies and several methodological confounds exist. The current review examines the literature on this issue, identifies inconsistencies in findings and discusses several key research issues that require addressing for this field to move towards a defensible theoretical model of depression and EEG asymmetry. In particular, the position of EEG asymmetry in the brain, measurement of severity and symptoms profiles of depression, and the effects of gender are considered as potential avenues to more accurately define the specific nature of the depression-EEG asymmetry association.

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1. Introduction

1.1. Depression and behavioural withdrawal

Depression is a major contributor to the total disease burden [1] and has greater adverse effects on personal health [2] and higher costs of care [3] than other chronic diseases. It is also associated with suicide in about 15% of all depressed patients [4] and carries a similar risk as smoking for mortality from all causes, even when blood pressure, alcohol intake, cholesterol and social status are taken into account [5]. Prevalence rates for a lifetime major depressive episode are between 13% (Europe) and 17% (USA) [6–8]. However, despite the significant burden of depression, initial treatments succeed as infrequently as one-third of the time and only improve to twice that rate with additional treatments, often with significant inter-patient variability in outcomes [9]. These data reflect a need to investigate models of depression that encompass a wider range of factors than simply the neurochemical explanations upon which pharmacological treatments are based. As recently commented by Ross et al. [10], depression is a disease of the brain and requires neurological models to understand and treat it successfully.

One of those potential neurological models concerns the pathways that underlie the behavioural withdrawal from uncontrollable and chronic aversive stressors which often initiate depressive behaviours. Conceptualised by Ferster [11] and reiterated by several authors since then [12–16], sadness, anhedonia, sleep and appetite change and cognitive disturbances may be seen as part of a "biological response pattern ... identified as the conservation-withdrawal response to excesses or deficits of stimulation" [12,p. 127] that includes low self-esteem, hopelessness and helplessness, all of which are symptoms of Major Depressive Disorder (MDD) [4]. An important aspect of the mechanism underlying this withdrawal is the conviction on the part of the depressive person that he/she has no real control or effective response (other than withdrawal) over the unpleasant experience that is occurring [17,18] and therefore is left with a single response that will reduce distress – i.e., withdrawal from the environment that includes the unpleasantness. Although such withdrawal responses may become self-defeating in the longer term, they may also have positive immediate benefits [14] and have been described as 'adaptive' [17,19–21] in that they reduce the quantum of noxious stimuli to which the person is exposed. As well as the withdrawal response from chronic aversive stressors (i.e., additional unpleasant stimuli), behaviour withdrawal may also occur as a response to decreased environmental rewards and reinforcers (i.e., fewer pleasant stimuli) [22,23].

Because some of the aversive stimuli that people seek to withdraw from may take the form of unpleasant thoughts, memories of painful events and social interactions, and negative emotions, the escape-focused behaviours that are used by people who experience these aversive stimuli may include cognitive avoidance [24] or attempts to reduce thinking about these aversive stimuli. Such cognitive and behavioural avoidance behaviours are significantly correlated with depression [25,26] and may precede the development of specific depressive symptoms, as suggested by evidence that exposure to early aversive environmental stimuli (in the form of childhood neglect) is significantly related to later adult behavioural avoidance and depression [27]. Further evidence of the avoidance-depression association comes from reports of the effect of behavioural activation on depression, in which depressed patients monitor their mood and daily activities and learn how to increase the number of pleasant interactions they have with their environments. A meta-analysis of behavioural activation across 16 studies with 780 participants showed a large effect ($d = 0.87$) between behavioural activation treatment and control groups at post-treatment [28], adding support to the role of avoidance as a causal factor in development of depression.

1.2. Neurobiological mechanisms of behavioural withdrawal in depression

These data support the behavioural withdrawal model of depression but do not attempt to explain or describe *how* the withdrawal process occurs at a neurological level. Understanding that process has the potential to lead to treatment models that incorporate more than simple behavioural strategies (i.e., as used in behavioural activation therapy) to also include the neurological mechanisms that lead from aversive stimuli to behavioural and cognitive withdrawal. Research into those neurological mechanisms is therefore a potentially valuable goal in eventually improving the current first-line success rate of only one-third efficacy for pharmacological treatments for depression reported by Rush et al. [9]. Several models of avoidance (and the opposite response of "approach") behaviour have been suggested, including a comprehensive model described by Trew [29] that includes emotions such as sadness and cheerfulness, a cognitive focus on positive and negative aspects of the environment, social support and isolation, plus potential neurobiological factors including hypoactivation of the left frontal lobes, abnormalities in the amygdala and dysregulation of the serotonin and dopamine neurotransmitter systems. Concerning these neurobiological factors, depression has been associated with amygdala neurogenesis and enlargement, which may be a function of prolonged hypercortisolaemia induced by chronic stress effects upon the Hypothalamic–Pituitary Adrenal axis [30]. Dopamine is closely related to approach behaviour, incentive motivation and expectation of reward and low levels of dopamine are consistently associated with depression [31–33]. While all these pathways represent