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Conference paper

LATE LIFE DEPRESSION AND LATE ONSET DEPRESSION: ARE THE SAME CLINICAL AND PATHOPSYSIOLOGICAL PICTURE?

Apostolos Papazacharias, Giancarlo Logroscino, Maria Rosaria Barulli & Marcello Nardini
Department of Neurological and Psychiatric Sciences, University "Aldo Moro", Bari, Italy

SUMMARY

Phenomenological differences between older patients with late- and early-onset depression may reflect differences in aetiology and neuropathological processes involved in these two types of depression. Early- onset depression has been mainly correlated to a family history of depression while late-onset depression has been principally correlated to vascular dysfunction. The same cortical and sub-cortical areas are involved in both types of depression. However, lesions in these brain areas and cognitive impairment are most pronounced in late-onset depression. Based on these observations we propose a common neuroanatomical substrate but different pathophysiological processes implicated in these two types of depression.

Key words: *late-onset depression - early-onset depression - cognitive deficits*

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Depression is one of the most prevalent psychiatric disorders in late life with devastating health consequences. It could become the second most common cause of disability by 2020 (Murray & Lopez 1996). Furthermore late-onset depression (LOD) becomes an important public health problem and leads to increased risk of morbidity, increased risk of suicide, increased risk of physical, cognitive and psychosocial impairment, all of which have been associated with increased mortality (Blazer 2003; Hamer et al. 2010). However, depression may often be overlooked and untreated in older patients (after age 60-65). Misdiagnosis and under-treatment are principally based on the existing differences between LOD and early-onset depression (EOD). These differences regard aetiology, pathophysiology and phenomenology of these two types of depression (Schweitzer et al. 2002; Rapp et al. 2005; Brodaty et al. 2001). In this article we tried to identify and briefly analyze some of these differences.

Several evidences suggest that LOD is a distinctive phenomenological entity as opposed to EOD. LOD has been associated with lower rate of family history of depression and higher prevalence of dementia suggesting a poorer impact of genes and a higher correlation with cognitive decline (Devanand et al. 2004; Alexopoulos 2003). In this regard, older adults with depression present with several signs and symptoms indicative of functional and cognitive impairment, often attributed to initial dementia. Executive function, memory, attention and processing speed seem to be the most compromised cognitive domains (Elderkin-Thomson et al. 2010, Rosenberg et al. 2010; Gangulli et al. 2006; Hermann et al. 2007; Rapp et al. 2005). Cognitive deficits have been associated with depression independently of age of onset (Bhalla et al. 2006). However, cognitive impairment is significantly greater in LOD than in EOD (Hermann et al. 2007; Naismith et al. 2003; Thomas et al. 2009). In addition, several studies have demonstrated that initially cognitive impairment in LOD is independent of dementia conditions (Bhalla et al. 2006; Gangulli et al. 2006). On the other hand LOD increases risk of mild cognitive impairment and dementia (Panza et al. 2010; Dotson et al. 2010; Saczynski et al. 2010; Barnes et al. 2006; Wilson et al. 2002). Further, Rapp et al. 2010 have demonstrated that cognitive decline in patients with dementia was further accelerated by the presence of depression. Taken together these data provide evidence for some pathophysiolocal event linking LOD, cognitive decline and dementia. Some authors suggest a common neuropathological platform based on vascular dysfunctions linking these two major geriatric pathologies (Gironi et al. 2010; de Toledo et al. 2010; Santos et al. 2009).

Novel structural and functional neuroimaging techniques are becoming increasingly important in defining the pathophysiology of psychiatric disorders, including depression. Recent studies have suggest that structural imaging changes vary substantially between LOD and EOD (Takahashi et al. 2008). LOD has been associated with more severe structural brain abnormalities and cerebrovascular pathology compared to age-matched controls and EOD patients (Lesser et al. 1996; Devanand et al. 2004). There is some evidence that patients with LOD have more pronounced atrophy in cortical and sub-cortical regions. In particular, important local and global differences have been found in prefrontal cortex and hippocampus (Ballmaier et al. 2008; Almeida et al. 2003; Hickie et al. 2005). Further, LOD has been associated with frontostriatal disruption caused by subcortical, white matter and periventricular hyperintensities (Sheline et al. 2006; Lin et al. 2006; Murphy and Alexopoloulos 2006). In particular, recent studies have demonstrated that LOD and white matter lesions are strongly related (Gunning-Dixon et al. 2008; Godin et al. 2008). Interestingly, in a longitudinal study white matter hyperintensities in LOD have also been associated with dementia (Steffens et al. 2007).

In conclusion, in our brief review we have tried to identify the main clinical and pathophysiological differences between LOD and EOD. Recent studies have suggested many neurocognitive and imaging markers distinguishing these two types of depression. A possible explanation for these neurocognitive and brain volumetric differences is the different aetiology. Indeed, EOD has been largely correlated to stress factors and genes, while LOD has been correlated principally to vascular dysfunction (Sheline et al. 2010). However, recent neuroimaging studies have established that the prefrontal cortex and hippocampus are the principle brain areas involved in both types of depression. This would suggest that the same brain areas are implicated in two different neuropathologic processes, with similar but not identical clinical pictures.

More follow-up clinical and imaging studies are needed to clarify the main phenomenological and pathophysiological characteristics of these two types of depression.

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Correspondence:
Apostolos Papazacharias, M.D.
Dipartimento di Scienze Neurologiche e Psichiatriche, Universita' degli Studi di Bari,
Piazza Giulio Cesare, 9 - 70124, Bari, Italy
E-mail: a.papazacharias@yahoo.it