

IS LATE-ONSET DEPRESSION PRODROMAL NEURODEGENERATION ? – NO

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Late-life depression (LLD) is frequently associated with cognitive impairment and increases the risk of subsequent dementia. Cerebrovascular disease, deep white matter lesions, Alzheimer disease (AD) and dementia with Lewy bodies (DLB) have all been hypothesized to contribute to this increased risk, and a host of studies have looked at the interplay between cerebrovascular disease and LLD. This has resulted in new concepts of LLD, such as "vascular depression", but despite multiple magnetic resonance imaging (MRI) studies in this field, the relationship between structural changes in human brain and LLD is still controversial. While pathological findings of suicide in some elderly persons revealed multiple lacunes, small vessel cerebrovascular disease, AD-related lesions or multiple neurodegenerative pathologies, recent autopsy data challenged the role of subcortical lacunes and white matter lesions as major morphological substrates of depressive symptoms as well as poorer executive function and memory. Most neuropathological studies, including a personal clinico-pathological study in a small cohort of elderly persons with LLD and age-matched controls confirmed that lacunes, periventricular and deep white matter demyelination as well as AD-type pathology and cerebral amyloid angiopathy that previously had been suggested to induce depression are usually unrelated to the development of LLD. In the same line, neuropathological data show that early-onset depression is not associated with an acceleration of age-related neurodegenerative changes. There is also no evidence for a loss of serotonergic neurons or neuritic pathology in the raphe nuclei of LLD patients. Very recent data on the critical role of glia-modulating neuronal dysfunction and degeneration in depression are discussed. In summary, there are no definite data to support the suggestion that depression is an essential pathogenic factor for the development of AD or other neurodegenerative disorders. It should be emphasized, however, since the published findings are not consistent and are often complicated by co-morbidities, there is limited success in demonstrating any clear cause-related relationship of many of these pathological changes.

Therefore, long-term clinico-pathologic studies in larger, well defined patient series using standardized methods are warranted to further elucidate the relations between structural and functional brain lesions and LLD.

References

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