AN UPDATE ON BEHAVIOURAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA: PATHOPHYSIOLOGICAL AND CLINICAL ASPECTS

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Objectives
The aim of this review is to:
- provide an overview of current literature that addresses neurophysiological basis and evidence-based management strategies of Behavioural and Psychological Symptoms in Dementia (BPSD)
- explore recent research findings and clinical implications in hopes of forthcoming further understanding of pathological mechanisms and treatment approaches of these neuropsychiatric symptoms of dementia.

Methods
A MEDLINE/PubMed literature search was conducted using terms such as "behavioural and psychological symptoms", "BPSD", "neuropsychiatric symptoms", "non-cognitive symptoms", "dementia" and "Alzheimer’s Disease" that appear in titles and abstracts.

Other journal articles were selected by reviewing relevant bibliography quoted in original papers.

Introduction
With an ageing population worldwide, dementia has emerged as a highly prevalent syndrome that comprises heterogeneous presentations of both cognitive and neuropsychiatric symptoms, estimated to affect over 115 million people by 2050.

While much research has been directed toward understanding and assessing cognitive impairment arising from dementia, there is still relatively little known about how these symptoms develop and correlate with pathological mechanisms. Hence, there has been a growing awareness of the relevance of understanding pathological mechanisms and the implications in hopes of furthering newer treatment options.

BPDS are commonly found in approximately one-third of patients with mild cognitive impairment, in two-thirds of those with severe cognitive impairment, and in more than 80% of patients with dementia living in nursing homes.

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Hence, there has been a growing awareness of the relevance of BPDS in dementia treatment, as they are major sources of distress for patients and their caregivers as well as producing substantial public health and economic consequences in clinical and community settings.

Background
BPDS are key manifestations of dementia that describe a heterogeneous array of behavioural signs and psychological states such as delusions, hallucinations, agitation, aggression, depression, dysphoria, anxiety, elation, euphoria, apathy, indifference, disinhibition, irritability, liability, aberrant motor behaviour, and sleep and appetite disorders. These are classified in Cummings’ Neuropsychiatric Inventory (NPI) in 1990s and NPI is a form of neuropsychiatric assessment based on a self-report, interviewer-rated evaluation of BPDS that gathers information from an informed caregiver of the patient regarding the twelve specific symptom fields.

During the following decade, these symptoms have been demonstrated in various neuroimaging analyses that they do not exist in isolation but co-occur in clusters. In a cross-sectional study of 194 participants taken from six European Alzheimer’s Disease (EADC) centres, Patricio et al. identified four distinct behavioural clusters of BPDS known as the psychosis factor (irritability, agitation, hallucinations and anxiety), the psychomotor factor (abnormal motor behaviour and delusions), the mood liability factor (disinhibition, elation and depression), and the institutional factor (appetite, sleep and apathy).

While these studies revealed significant associations between NPI symptoms, it did not further investigate the possible aetiologies of BPDS. BPDS are likely to involve complex inter-relationships and interactions of neurobiological systems governing behavioural and psychological processes.

In the current decade, the focus of intensive research is to correlate BPDS with neuromaging and neurochemical findings in order to explain the neuropsychology behind BPDS and using this knowledge to enhance clinical intervention of dementia patients with neuropsychiatric manifestations.

Discussion
- BPDS is not a unitary concept but instead constitutes numbers of distinct and interconnecting component symptoms. This interconnecting framework, while not yet fully known, is believed to form clusters within groups of BPDS with each cluster possibly reflecting patterns of pathological features, biochemical correlates or genetic predispositions.
- At present, combination of pharmacological and non-pharmacological strategies represents the most appropriate treatment of BPDS.

Conclusions
- Recent research has suggested that BPDS, alike different phenotypes of dementia, may be strongly linked with abnormalities of protein metabolism due to protein misfolding. Neuropsychiatric symptoms may be intimately related to specific amyloidopathies, tauopathies or synucleinopathies depends on the type of dementia from which the symptoms are derived. (Cummings, 2003)
- With improved understanding of BPDS, parallels may be drawn between similar neuropsychiatric symptoms that occur in patients with dementia and those occur in patients with other psychopathologies. Neuropsychological findings from dementia patients regarding specific symptoms can shed light on the pathophysiological mechanisms behind these behavioural disturbances in general. (McKeith, 2005)
- Future revision of the NPI scale can improve its validity and reliability by incorporating clinician rating component based on interview with the patient, together with information gathered from caregivers. In addition, NPI can be further developed to reflect the current trend of research toward clustering of neuropsychiatric symptoms and examine behavioural and psychological manifestations based on grouping of NPI scores rather than the total score or individual sub-scale scores. (Hermmann, 2011)
- Instead of measuring behavioural symptoms as secondary outcomes in major studies of BPSD-related clinical trials at present, implementation of clinical trials with specific neuropsychiatric symptoms as primary outcome measures is required which centres on the behaviour-modifying effects of agents. (McKeith, 2005)

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