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Title

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Permalink

<https://escholarship.org/uc/item/5mr141qc>

Journal

Current Neurology and Neuroscience Reports, 16(2)

ISSN

1528-4042

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Publication Date

2016-02-01

DOI

10.1007/s11910-015-0618-1

Peer reviewed



HHS Public Access

Author manuscript

Curr Neurol Neurosci Rep. Author manuscript; available in PMC 2017 February 01.

Published in final edited form as:

Curr Neurol Neurosci Rep. 2016 February ; 16(2): 14. doi:10.1007/s11910-015-0618-1.

Non-pharmacological Management of Behavioral Symptoms in Frontotemporal and Other Dementias

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Abstract

Worldwide prevalence of dementia is predicted to double every 20 years. The most common cause in individuals over 65 is Alzheimer's disease (AD), but in those under 65, frontotemporal dementia (FTD) is as frequent. The physical and cognitive decline that characterizes these diseases is commonly accompanied by troublesome behavioral symptoms. These behavioral symptoms contribute to significant morbidity and mortality among both patients and caregivers. Medications have been largely ineffective in managing these symptoms and carry significant adverse effects. Non-pharmacological interventions have been recommended to precede the utilization of pharmacological treatments. This article reviews the research about these interventions with special attention to the variations by etiology, especially FTD. The authors offer recommendations for improving utilization of these strategies and future research recommendations.

Keywords

Dementia; Alzheimer's disease; Frontotemporal dementia; Neuropsychiatric symptoms; Behavioral and psychological symptoms; Non-pharmacological

Introduction

In 2010, the worldwide prevalence of dementia was estimated to be 35.6 million with a doubling predicted every 20 years [1]. The most common cause for dementia in individuals over 65 is Alzheimer's disease (AD), but for those less than 65, frontotemporal dementia (FTD) is as frequent as AD [2, 3]. The physical and cognitive decline that characterizes these diseases is accompanied by symptoms that affect behavior and personality, occurring in 61–98 % of those with dementia sometime during the trajectory of their illness. [4–6]. In

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This article is part of the Topical Collection on *Behavior*

Compliance with Ethical Standards

Conflict of Interest Cynthia Barton, Robin Ketelle, and Jennifer Merrilees each declare no potential conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

FTD, these behavioral symptoms are often the presenting symptom and a hallmark of the disease [7, 8]. Referred to as neuropsychiatric symptoms (NPS) or Behavioral and Psychological Symptoms of Dementia (BPSD), they include sleep disruption, irritability, apathy, and mood and psychotic symptoms. There is increasing evidence that prevalence of these behaviors varies with the type of dementia although the specific profiles are inconsistent across studies [4, 9–12]. Research has linked the specific anatomical and chemical changes associated with differing pathologies to specific behaviors.

Regardless of etiology, behavioral symptoms are challenging for family caregivers and result in considerable consequences including caregiver burden and stress [13, 14] increased risk for placement [15–17] and significant cost to the health care system [18, 19]. Some data report that caregivers of people with FTD and dementia with Lewy bodies (DLB) are particularly burdened by behavioral symptoms [20, 21]. FTD caregivers specifically report a loss of emotional attachment leading to isolation and anger due to behavioral symptoms [22]. Medication therapies have not proven effective in managing these symptoms and in fact, have significant adverse effects and risks [23–25]. Non-pharmacological strategies include interventions that target environmental adaptations, behavioral strategies, caregiver training, and education and have been recommended to precede consideration of pharmacological therapies [26, 27]. A meta-analysis suggested that interventions that use a non-pharmacological approach were more likely to be effective in managing these behavioral symptoms [28]. A more recent meta-analysis of 23 trials concluded significant benefits for interventions targeting both patient and caregiver that suggest they are comparable in efficacy to the use of antipsychotics with fewer risks [29••]. However, attention to specific etiologies has not been well studied, and in fact, only case studies and small series have been published in FTD. The purpose of this paper is to review the current literature regarding these symptoms and management strategies in community dwelling individuals with attention particularly to FTD.

Causes and Etiology

Anatomy

Neuropsychiatric symptoms in the dementia syndromes reflect the changes in the diseased brain. Anatomical changes related to neurodegeneration, pathology burden, hypometabolism and changes in neurotransmitters are all responsible for the observed clinical symptoms. A table of affected regions and corresponding symptoms in various syndromes are listed in Table 1. In general, disease in the left hemisphere (dominant) may produce more awareness of deficits, depression, and anxiety. Changes in the right hemisphere are associated with poorer insight into symptoms. The changes in behavior and personality seen in dementia are often associated with loss of function among various structures in the frontal and temporal lobes. Four behaviors: apathy, disinhibition, eating disorders, and aberrant motor behavior have been correlated with tissue loss in specific regions in the right frontal lobe [30].

In addition to anatomical substrates, disruptions in the serotonergic and cholinergic systems (5HT dysfunction) are linked to behavioral changes in AD along with a variety of other neurotransmitter systems including noradrenergic, dopaminergic, and glutamatergic [31]. The monoaminergic and glutamatergic systems have also been proposed to play a role in the

modulation of behaviors in dementia patients [32•]. In FTD, pre- and postsynaptic changes in serotonin occur, and these changes may play a role in the behavioral disorders of this disease [33]. Although many symptoms may be anatomically specific, the disruption of circuits and networks in the brains of affected patients may produce behavioral symptoms associated with regions far from the areas of tissue loss [34]. These circuits include the dorsolateral circuit (which mediates aspects of executive function), the prefrontal basal ganglia (responsible for motivation), and the orbitofrontal circuit (inhibition and social appropriateness) [32•].

Recent advances regarding the genetics of FTD have further expanded knowledge in the field, particularly genetic forms of the disease. Delusions as a presenting neuropsychiatric manifestation were more common in FTD patients who were C9ORF72 (C9) gene carriers [35]. In addition to psychosis, other psychiatric manifestations at onset of disease are seen in C9 carriers and also carriers of the granulin (GRN) gene, including bipolar presentations and compulsive disorders [36•]. While some symptoms may directly correlate to a specific brain region, the behavioral manifestations of dementia syndromes remain a complex of patient factors, environmental influences, and caregiver adaptation.

Theoretical Models

Theoretical models have been used to guide the understanding of dementia-related behaviors. These models provide a rationale for why behaviors occur and have been used to direct clinical care, caregiver training, and research in a variety of settings (nursing home, day program, and home). The Unmet Needs Model proposes that problematic behaviors result when the environment and/or the caregiver are not supportive of the person's changing functional deficits and diminished ability to communicate [37]. For example, agitation occurs when the person is bored and cannot communicate his or her need for activity. Repetitive vocalizations may represent pain and discomfort in a patient that can no longer express the sensation of pain via typical speech [38]. The Progressively Lowered Stress Threshold (PLST) model suggests that dementia-related behaviors arise when cognitive deficits disrupt the person's interpretation of the environment [39]. Thus, when environmental demands exceed the person's cognitive abilities, stress manifests as behaviors such as agitation, nighttime sleep disruption, and combativeness. The PLST promotes the need for coherence between environmental demands and patient's abilities [40]. A comprehensive, conceptual model encompassing the interaction of these factors and how they relate to symptoms and approach has recently been proposed and will be discussed in greater detail below [27].

Assessment

Tools

Formal tools have been validated to assess behavioral symptoms in dementia and can be helpful in ensuring that a comprehensive inventory of behaviors is obtained in a consistent manner. The Neuropsychiatric Inventory (NPI) uses an informant interview to determine the presence of 12 common behavioral symptoms in dementia and includes frequency, severity, and level of distress to the caregiver [41]. A shortened version has been validated, and there

have been modifications for use in a nursing home, self-completion by a caregiver, and recently, one by clinician assessment without caregiver interview [42–44]. The BEHAVE—AD scale is another well-validated tool which specifically targets the behavioral symptoms associated with AD [45, 46]. Because these tools were developed to focus on symptoms associated with memory deficits, they have been modified to better reflect the changes characteristic in FTD and include the modified Clinical Dementia Rating (CDR) scale [47] and the FTD rating scale [48]. There are also tools that target a particular behavior such as agitation or apathy and can be helpful in developing a logical and targeted approach to a very specific symptom. A recent meta-analysis can be used to identify well-validated general and targeted measures according to behavior, setting, and time [49].

Framework

Once a behavioral symptom is identified, the use of a standardized framework allows the assessment and management plan to be comprehensive and targeted to the patient's individual situation. The ABC model first described by Buckwalter [50] has been the most commonly used. This model focuses on the identification of trigger(s) or events thought to be causing the behavior and the consequences or responses that may improve or worsen the symptoms. It has been used to guide the development of protocols to train caregivers to manage the NPS associated with dementia [51] and is recommended in FTD [52]. This approach has been further refined with the DICE model (Describe, Investigate, Create, and Evaluate) and reflects consensus by an expert panel, of the approach once a problematic behavior has been identified [27]. The steps include a description of the behavior (D) that includes timing, location, people involved, and detailed characteristics of the behavior. Investigation of causes (I) addresses the patient, caregiver, and environmental factors involved and includes medical sources that should be ruled out especially in an acute onset where they are commonly implicated [53, 54]. Creating a plan (C) involves development of targeted strategies to address the behavior and underlying causes. Finally, evaluation of efficacy (E) is ongoing and includes being mindful to set realistic goals, perhaps reducing rather than eliminating some behaviors.

Non-pharmacological Strategies

The overall aim of using non-pharmacological strategies includes prevention of problematic behaviors, behavior symptom relief, and a lessening of caregiver distress [55]. Several professional organizations have suggested that drug therapy should be used only after the failure of non-pharmacological strategies or in cases of grave danger or distress [26, 54, 56] and that these strategies should be specifically targeted to stage of dementia [57]. For the purpose of discussion, we have divided these strategies into categories of environmental, caregiver, and behavioral approaches.

Environmental Approaches

These strategies target the etiology of behaviors as patients struggle to accurately interpret, understand, and react to their environment in the setting of the pathological processes in their brain and emphasize increasing activity and simplifying the environment and activities of the individual with dementia [32•]. Deficits in information processing related to temporal/parietal dysfunction may produce limited ability for comprehension and can lead to

irritability, aggression, and anxiety when an individual is distracted or overwhelmed. In FTD, the impaired ability to accurately interpret and respond to subtle emotional cues may make attention to the environment especially important [58]. Reducing noise and stimulation, lessening clutter, turning off music, or simplifying social situations can help these patients to accurately focus on a designated task or response. Removing access to problematic items (credit cards, mail) or modifying public outings to reduce the opportunity for inappropriate interactions are examples of FTD-specific environmental manipulations [52].

There are other behavioral modifications that have been studied in dementia that have potential application to FTD. A meta-analysis of activities suggested that a supportive environment with normal lighting, moderate sound, and small number of people and appropriate cueing were more likely to decrease behavioral symptoms in dementia [59]. Anecdotal reports and case studies of changing mealtime routines, including playing music, suggested positive results but have not been replicated in trials [60]. Certainly, addressing sensory needs that may not be able to be verbally communicated—hearing, vision, warmth, satiety, and comfort—is encouraged to avoid the expression of an unmet need through a behavioral symptom. Implementation of hearing aids in a community dwelling cohort demonstrated improved behavioral symptoms in all enrolled participants [61]. Research has identified evidence suggesting music therapy may be beneficial in managing and treating behavioral symptoms perhaps meeting an unmet need for stimulation although most research has been done in facility settings [62, 63].

Modification of activities to accommodate functional changes has been suggested to reduce agitation by reducing activation of the PLST [64]. The Tailored Activities Program (TAP) identified strengths and deficits and recommended adjustments in the physical environment to accommodate these, resulting in a significant reduction in agitation [65–67]. Case reports identify success in FTD using this approach as well [68]. Introducing old hobbies and games was successful in reducing disinhibition and inappropriate behaviors in FTD [69]. An apathy trial showed structured occupational therapy activities were more effective than “free time” in mixed group of AD, DLB, and vascular dementia patients, and music was felt to be most helpful [70]. A small but significant improvement in behavioral symptoms has been reported in a meta-analysis of occupational therapy trials using sensory stimulation [71].

Exercise has been suggested to reduce behavioral symptoms [72, 73] although a recent Cochrane review of 17 trials found no evidence of benefit of exercise on neuropsychiatric symptoms [74]. Increased daytime walking coupled with exposure to bright light did result in fewer nighttime awakenings and less time awake in the NITE-AD study [75]; however, a recent review found insufficient evidence to recommend the use of light therapy for sleep or behavioral symptoms in dementia [76]. Aberrant motor behavior may respond to physical activity, and anecdotal reports have found that environments that encourage safe wandering and ambulation may reduce attempts to exit but evidence is inconsistent [63].

Strategies for psychotic symptoms are not well studied. Confronting delusions or hallucinations using logic often results in more agitation; reassurance and distraction can be more successful. Environmental modifications such as removing mirrors or increasing

lighting that may reduce the propensity for misinterpretation may be effective according to the anecdotal reports [63].

Caregiver Approaches

In the caregiver literature, there is strong evidence for the benefits of using non-pharmacological strategies. The promotion of more effective communication and pursuing ways to appropriately match the activity and environmental demands to patient abilities through education, support, and coaching has shown effectiveness in minimizing the negative outcomes associated with behavioral symptoms [29••, 77, 78]. Courses on home safety, problem solving, stress reduction, and health promotion lessened the impact of behavioral symptoms while protecting caregiver health in the NIH Resources for Enhancing Alzheimer's Caregiver Health (REACH) program [79]. Coaching via phone calls regarding caregiver stress and finding ways to create a better match between the person with dementia and their environment helped caregivers cope with behaviors [80]. Among FTD caregivers, the provision of disease education and access to support groups was reported to facilitate acceptance of the disease and an exchange of problem-solving strategies [81].

In one study, a specialty clinic focused on providing objective data relating to patient's cognitive and functional abilities to the caregiver [82]. A reduction in behavioral symptoms and improved caregiver outcomes resulted from caregiver training using the ABC strategy for behavior management [51, 80]. Programs such as the SAVVY Caregiver have shown similar results in promoting caregiver mastery regarding behavior management and reduced caregiver stress [83–85]. The Savvy Caregiver has been adopted by some organizations for ongoing education including some chapters of the Alzheimer's Association, allowing easy replication and transfer of proven strategies.

Behavioral Approaches

The literature on behavioral modification in FTD is sparse and consists mostly of case studies and anecdotal reports [86••]. Clinicians have focused on lack of motivation or apathy, and compulsive behaviors, when targeting challenging behaviors. Interventions for these behaviors have included using dietary or monetary rewards for desired behaviors such as showering or grooming. The use of cognitive behavioral therapy (CBT) has been mentioned as a potential strategy for dealing with mood and behavior issues in dementia [26, 87]. In one RCT for anxiety in dementia, CBT was found to be feasible but there was no measureable impact on anxiety [88]. More investigation of this type of therapy is needed, including feasibility and efficacy in different types and severities of dementia.

Substitutions for compulsive activities, especially when out in public, might consist of offering a squeeze ball to hold, instead of touching strangers, or offering a lollipop to diminish repetitive and compulsive vocalizations [89, 90]. One case study reports the effectiveness in treating uncontrollable sexual behavior by substituting a large stuffed Pink Panther for the patient to touch and fondle [91]. These types of interventions require careful observation, and creative and individualized approaches are encouraged [90].

Conclusion

Behavioral symptoms are significant and can be disruptive to the patient, caregiver, and family. Non-pharmacological approaches to managing these symptoms with randomized, controlled trials are inconclusive; however, there is increasing evidence that these strategies when targeted and individualized with caregiver education and support exceed the benefits of pharmacological interventions and have very limited adverse effects [29••, 92]. Despite the success reported with these individualized treatments, reviews continue to provide only weak evidence for recommending these interventions on a consistent basis [63, 90].

Significant limitations around study design are evident, and only mild efficacy is suggested in the literature. Although there are behavioral profiles that represent different etiologies, it is possible that the unique individual reason for the behavior may limit measurement by traditional approaches. It may not be possible to study large numbers of patients with the same behavior who respond to the same intervention because the trigger or cause may be different. It is also possible that we are measuring the wrong outcome when we look at reduction of behavioral symptoms. It may be that accommodating the behavior in a safe environment while supporting the caregiver to reduce distress is more important than actually extinguishing the behavior. The literature is particularly robust around the efficacy of education and support on caregiver outcomes and may more accurately reflect the goal of management [32•].

It has been suggested that the non-pharmacological management of these symptoms will require multiple approaches that are individualized in the home with adequate follow-up regarding outcomes [29••]. The development of these strategies requires expertise and time, something that primary care providers do not always have. Educating providers about an approach to assessment and then identifying community resources and experts to assist in managing these symptoms will be essential, especially in syndromes such as FTD [58]. Occupational therapists have been successful developing individualized regimens incorporating environmental and behavioral strategies [66, 93]. The role of creative thinking in developing individualized approaches cannot be minimized, and publication of these anecdotal reports and case studies should be encouraged [89, 91]. These represent thoughtful interventions targeted to specific individuals but may inform others managing similar challenging behaviors. Recognition of this expertise, providing opportunities for training for professionals and non-professionals along with attempts to provide adequate reimbursement for these services may increase their availability and accessibility.

Very little attention in studies of NPS has been paid to pathologically confirmed dementia syndromes. It may be that different strategies work for different pathologies and this may be important in designing interventions and measuring efficacy. In FTD, the significant behavioral changes are particularly isolating and contribute to significant disability in both the patient and family, and yet, there are only non-systematic trials of non-pharmacological interventions in this population [86••]. The cognitive profile requires different strategies from the traditional interventions that are effective with amnesic patients. Even with promising disease modifying trials underway, the number of patients who develop dementia and suffer from these symptoms will be significant. It is imperative that we identify and

communicate effective, individualized strategies to manage these debilitating symptoms according to the cognitive and behavioral profile of their disease.

Acknowledgments

Bruce Miller receives grant support from the NIH/NIA and the Centers for Medicare & Medicaid Services (CMS) as grants for the Memory and Aging Center. As an additional disclosure, Dr. Miller serves as Medical Director for the John Douglas French Foundation; Scientific Director for the Tau Consortium; Director/Medical Advisory Board of the Larry L. Hillblom Foundation; and Scientific Advisory Board Member for the National Institute for Health Research Cambridge Biomedical Research Centre and its subunit, the Biomedical Research Unit in Dementia (UK).

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Table 1

Behavioral symptoms and anatomical correlate (legend below)

Delusions	Noradrenergic, dopaminergic, and glutamatergic systems ^a
Hallucinations	Anterior temporal lobes and amygdala ^{b, c, d}
Agitation/irritability	Bilateral superior parietal, left fronto-insular; serotonergic/cholinergic systems ^e
Depression/dysphoria	Left frontal atrophy; locus ceruleus; dorsal raphe ^{f, g}
Anxiety	Medial pre-frontal cortex; amygdala; hypothalamus ^h
Euphoria/elation	Anterior insula; ventromedial pre-frontal cortex; anterior cingulate cortex ^h
Apathy/indifference	Right medial superior frontal gyrus; anterior cingulate; right temporal ^{i, j}
Disinhibition	Ventromedial frontal cortex ⁱ
Aberrant motor behavior	Dorsal anterior cingulate cortex; precentral sulcus; orbitofrontal, caudate, and temporal atrophy; striatal atrophy ^{i, k}
Nighttime behavior	Complex: possible amyloid burden in AD; hypothalamic changes; neurotransmitter disruption ^l
Appetite/eating disorder	Orbitofrontal; right insula and striatum ^m

^aChen et al., J Alzheimers Disease, 2011^bBallard, CG Am J Psychiatry, 2004^cHarding, AJ Brain, 2002^dMori, Neurology, 2006^eGarcia-Alloza, Neuropsychologia, 2005^fLyketsos, Biological Psychiatry, 2002^gForstl, Psychological Medicine, 1992^hLevenson, Sturm and Haase, Annu Rev Clin Psychol, 2014ⁱRosen, Brain, 2005^jRankin, Brain, 2006^kAmes, D, J Neuropsych Clin Neurosci, 1994^lDeschenes and McCurry, Current Psychiatry Reports, 2009^mWooley, Neurology, 2007