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THE BIOLOGICAL BASIS OF BEHAVIORAL SYMPTOMS IN DEMENTIA

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Abstract

This article describes the pathophysiology of dementia and differentiates between cognitive and noncognitive symptoms that characterize this devastating illness. Relationships between brain anatomic and neurochemical systems and behavioral symptoms of dementia are discussed. An overview of the etiologies and neuropathologies of dementia are presented as they relate to impairments in memory and intellectual abilities, personality changes, and behavioral symptoms. Recent genetic and molecular discoveries that have advanced our understanding of this complex spectrum of disorders and their treatment(s) are also highlighted.

More than 70 diseases/disorders are associated with the progressive loss of memory and intellectual function known as dementia, although Alzheimer's disease (AD) is by far the most common cause. Current estimates suggest that more than four million Americans suffer from AD (Advisory Panel on Alzheimer's Disease, 1995). Although the diagnosis of dementia focuses on the clinical presentation of cognitive deficits, complex disturbances of behavior and emotion have been recognized as part of the disorder since Alois Alzheimer's original case report in 1907 describing the cerebral cortex and abnormal behaviors of a 55-year-old woman (Alzheimer, 1987). In contrast to the cognitive symptoms, which usually follow a well-described course of progressive decline, the occurrence and course of the noncognitive symptoms in dementia are less predictable (Tariot, 1994), developing at any stage during the disease process (Eisdorfer et al., 1992).

There is a discrepancy between the labeling of symptoms by health care professionals and complaints by family members about their loved one's behavior. For example, dementia is generally defined by clinicians as progressive deterioration of cognitive abilities, however families of dementia patients often define the stages of illness with behavioral (noncognitive) markers. In fact, behavioral complications are a leading cause of institutionalization in persons with dementia (Knopman, Kitto, Deinard, & Heiring, 1988; Steele, Rovner, Chase, & Folstein, 1990).

Disease progression is not measured simply by declining scores on the Mini-Mental State Exam or other clinical rating scales, but rather includes such symptoms as the amount of sleeplessness at night, the person's degree of agitation or psychosis, and the level of depressed mood. A key unanswered scientific question is how central these noncognitive behavioral symptoms are to

the heterogeneous biological process called dementia. Are the behavioral disturbances associated with dementia complications of progressive cognitive impairment or a primary manifestation of brain disease?

Dementia presents a unique opportunity for psychiatric nurses to appreciate the interaction between biology and behavior, as noted below:

The very fabric of which the human brain is built is the substrate of cognition, emotion, and all of our faculties and, therefore, is also the substrate of the cognitive changes that occur in aging and in AD (Burns & Buckwalter, 1988, p. 23).

This article explores the relationship between brain anatomic and neurochemical systems and noncognitive (behavioral) symptoms in dementia. An overview of the etiologies and neuropathologies of dementia is presented as they relate to impairments of memory and intellectual abilities, personality changes, and behavioral symptoms that characterize this devastating illness. Some of the more recent genetic and molecular discoveries that have advanced our understanding of this complex spectrum of disorders and their treatment(s) also are highlighted. In order to provide background information for psychiatric nurses, the following section briefly describes dementia pathophysiology and differentiates between cognitive and noncognitive symptoms.

OVERVIEW OF DEMENTIA PATHOPHYSIOLOGY

Definition

Dementia is a term applied to a syndrome characterized by loss of intellectual capacity in multiple domains (Cummings & Benson, 1992). These include learning and memory, receptive and expressive language abilities, reading and writing, praxis, the ability to interpret the environment, and appreciation and manipulation of visuospatial information. Behavioral disturbances similar to discrete psychiatric disorders (affective, anxiety, and psychotic disorders) are common (Tariot & Blazina, 1993). Those affected eventually lose the ability to perform necessary activities for daily living (ADL). In later stages, basic biologic functions such as swallowing and visual interpretation are disturbed, all language abilities are lost, and a host of neurologic abnormalities develop, such as abnormal reflexes and seizures (Tariot, 1994).

Cognitive Versus Noncognitive Symptoms

Cognitive symptoms primarily reflect impairments in language, praxis, judgment, visuospatial function, and related mental activities. In studies of the relationship between functional ability and mental status scores, patients with AD have shown a remarkably orderly deterioration over time in terms of abilities and symptoms (Vitaliano, Russo, Breen, Vitiello, & Prinz, 1986). Moreover, a substantial body of research has supported the relationship between intellectual decline and impairment in activities of daily living and the presence of myoclonus and extrapyramidal signs in persons with AD (Ditter & Mirra, 1987). To date, research linking functional ability to cognitive status has been published largely in the occupational therapy literature and focuses on task performance, problem solving, and social interaction.

Noncognitive symptoms are defined as disturbances in behavior, mood, belief (delusions), and experience (hallucinations). The term “behavior” is a neutral term. The definition of “problem,” “disturbed,” or “disordered” behavior depends upon the perception of the person describing the behavior. Nonetheless, many care providers and investigators report a high prevalence of “problematic behaviors” in persons with dementia. Thus, disturbed behaviors are common in dementia and they lead to distress in the patient, family, and/or care provider. Certain behaviors such as physical aggression are particularly distressing and difficult to manage (Advisory Panel

on Alzheimer's Disease, 1995). For purposes of this article, the term "noncognitive symptoms" of dementia will be used interchangeably with the term "behavior."

Neurotransmitter Pathology

Despite the prevalence and clinical importance of the behavioral features of dementia, their underlying neurobiology has received much less attention than the neurobiologic abnormalities underlying memory loss and other cognitive deficits. In the 1970s and 1980s, a body of data relevant to the noncognitive features of dementia began to accumulate from studies in postmortem brain tissue and from neurochemical and psychopharmacologic treatment outcome studies in patients with AD.

As summarized in Table 1, the brain's cholinergic, noradrenergic, serotonergic, and dopaminergic neurotransmitters are neurobiologic systems for which abnormalities have been convincingly demonstrated in dementia and that have implications for manifestation of behaviors (Raskind & Peskind, 1994). The cells of these neurotransmitter systems contain neurofibrillary tangles which may partially account for the altered production of neurotransmitters in dementia.

Currently, the best-established neurotransmitter deficit in Alzheimer's disease is in the cholinergic system, manifested by neuronal loss and atrophy of the forebrain and decreased concentrations of choline acetyltransferase in the hippocampus and neocortex (Davis & Haroutunian, 1993). Acetylcholine appears to be important for maintaining cognitive functions related to attention, learning, and maintaining the sleep-wake cycle.

Studies of norepinephrine (NE) and its metabolite (MHPG) show mixed results, with normal, enhanced, and depleted levels of noradrenergic functioning in persons with dementia (Raskind & Peskind, 1994). CNS noradrenergic systems are complex and it is possible that both reduced and increased noradrenergic activity occur at different times and in different parts of the CNS in dementia. Norepinephrine may be an important neurotransmitter for modulating an individual's mood and response to stress.

Data relevant to the serotonergic system in dementia are more consistent than those pertaining to the noradrenergic system. Studies of postmortem brain tissue and cerebral spinal fluid (CSF) in living patients suggest decreased serotonergic activity in AD. Deficient serotonergic activity has been implicated in the pathophysiology of major depressive disorder and impulsive/aggressive behavior in persons without depression (Raskind & Peskind, 1994). Additionally, serotonin is important in the regulation of body temperature and the cardiovascular and respiratory systems.

Changes in the dopaminergic systems have been implicated in the etiology of depressive and motor symptoms associated with dementia, but not psychotic symptoms. Persons with AD and major depression demonstrate greater pathology in the substantia nigra, even though their dopamine levels are not significantly different than AD patients without depression (Zubenko, Moossy, & Kopp, 1990). With regard to motor symptoms, it has been theorized that dopaminergic systems play a role in the development of parkinsonian-type symptoms that are seen in some persons with dementia. In support of this hypothesis, a significant negative association was demonstrated between CSF dopamine metabolite (HVA) levels and impaired motor function in persons with dementia (Brane, Gottfries, & Blennow, 1989; Kaye, 1988).

Genetic Factors in Dementia

There are two types of AD: the type found in particular families (familial AD or FAD) which demonstrates an autosomal dominant pattern of transmission, and sporadic AD (genetic ties, but no clear pattern of inheritance identified). Recent research has implicated several genes in

the onset of both familial and sporadic types of Alzheimer's disease. AD is often referred to as early-onset, before age 65 (FAD), and late-onset (sporadic), after age 65. Importantly for psychiatric nurses, evidence suggests that behavioral symptoms are often more pronounced and cognitive symptoms decline faster in early-onset, rather than the more common late-onset type of AD.

Investigations have implicated three chromosomes (1, 14, 21) in early-onset AD. Mutations on the APP gene have been noted on chromosome 21. The defective gene in chromosome 14 has been labeled presenilin 1, and the defective gene in chromosome 1 is called presenilin 2. In these familial forms of AD, inheriting the genetic mutation almost always results in the person getting AD. Together, presenilins 1 and 2 account for approximately 50% of FAD (Alzheimer's Disease Education and Referral, ADEAR, 1997). Investigators also have explored connections between Down's syndrome and AD since they lead to similar pathology in the brain. Down's syndrome is caused by an extra copy of chromosome 21. Because the gene for APP has been mapped to chromosome 21, there is reason to believe that AD is related to over-expression of APP (ADEAR, 1997).

One of the most exciting recent genetic findings related to late-onset dementia was the discovery of the apolipoprotein E alleles (apoE2, apoE3, and apoE4) on chromosome 19. ApoE is a normal protein that helps transport blood cholesterol throughout the body. Although apoE is found in neurons of both affected and nonaffected individuals, it is associated with amyloid plaques and neurofibrillary tangles in persons with dementia. It is thought that apoE2 is protective against AD, apoE3 (the most common apoE allele found in the general population) plays a neutral role in AD, and apoE4 increases an individual's risk for developing the disease, although the precise mechanism is not yet known (ADEAR, 1997).

A blood test has been developed to identify which combination of apoE alleles (i.e., E3/E4, E2/E3, E4/E4, etc.) a person has inherited. This has important implications for disease vulnerability (risk). It must be stressed that the inheritance of an apoE4 gene does not predict AD; apoE4 is only a risk factor gene. Currently, no predictive test for AD exists (ADEAR, 1997).

Research is underway to identify the relationships between apoE4, tau, beta-amyloid build-up, and APP regulation, as well as how apoE affects the manner in which cells repair themselves after damage. Changes in the brains of apoE4 homozygotes in late middle age have been demonstrated using PET scans. Work is continuing to identify preclinical signs of AD correlating PET scan findings with comprehensive neuropsychological, linguistic, and functional measures (Caselli, Jack, Petersen, Wahner, & Yanagihara, 1992). Investigations of genetic links to behavior symptoms in dementia are in their infancy, although scientists have suggested that persons with the highest genetic vulnerability should be the first patients included in clinical trials of promising treatments.

Brain Changes in Dementia

Neuropathology—The diagnosis of AD requires a clinical diagnosis of dementia syndrome and postmortem neuropathologic confirmation (seldom done) of a requisite number of amyloid-containing neuritic plaques and neurofibrillary tangles in specific locations throughout the cerebral cortex and hippocampus (Mirra, Heyman, & McKeel, 1991). A plaque is a spherical structure outside the neuron containing a central amyloid core surrounded by abnormal dendrites and axons. The term "tangles" refers to bundles of filaments that are found in cell bodies, axons, and dendrites. The loss of neurons of association cortices and in several nuclei, and loss of synapses have been reported to correlate with cognitive impairment in dementia (Terry, Masliah, & Salmon, 1991). Overall cerebral atrophy is commonly found

postmortem in brains of persons with AD, but it is not uniformly seen in dementia syndromes and can occur in nondemented persons as well (Tariot, 1994).

Molecular Pathology—The major molecular component of plaques is amyloid proteins. Alzheimer amyloid protein (B/A4) is a small protein derived from cleavage of a larger peptide, the amyloid precursor protein (APP). The genetic apparatus that controls the APP has been described in detail, but its purpose remains unknown (Tariot, 1994). It is speculated that APP is either crucial to the development and maintenance of the central nervous system (CNS) or that it is neurotoxic. Tariot (1994) asserts that amyloid accumulation may be sufficient to cause certain neuropathologic features of AD but is not sufficient to cause the entire syndrome.

Neurofibrillary tangles consist of both paired helical and straight filaments found inside nerve cells. These structures are found in a variety of neurodegenerative disorders but not in normal brains (Blass, 1993; Katzman & Jackson, 1991). Several specific proteins associated with these filaments have been identified—in particular abnormal tau proteins that prevent proper microtubule assembly. In healthy neurons, tau protein promotes microtubule formation within nerve cells to allow transport of chemicals from the cell body to the end of the axons. In dementia, the microtubules collapse, resulting in a loss of communication between and within neurons (ADEAR, 1997). Table 2 summarizes hypothesized relationships between areas of brain pathology, function and behavioral symptoms in dementia.

Frontal Lobe Dementia—The frontal lobe dementias (FLDs), such as Pick's Disease and Creutzfeldt-Jakob (or C-J) Disease, affect approximately 10–15% of persons with dementia, and are most commonly misdiagnosed as late life psychiatric disorders. Hemispheric degeneration (dominant or nondominant) is usually asymmetric in the earlier stages of FLDs, leading to differences in presentation. FLDs are often characterized by extreme, marked changes in personality and behavioral disturbances, as the frontal lobes affect mood, personality, judgment, and creativity. These dementias present with unique pathological features such as Pick bodies, motor neuron disease, and atrophy of the temporal lobe, often not identified until autopsy. Onset is typically before age 65, and patients with FLDs often act childish, show impairments in judgment, are socially inappropriate, and disinhibited, which can be extremely embarrassing and burdensome to their caregivers. Emotional states are often dramatically altered, including manifestations of depression, anxiety, and obsessive behaviors. FLDs also are associated with hyperorality (excessive eating and drinking) and incontinence. Over time, patients with FLDs tend to become apathetic, and develop a blunted affect. Interestingly, memory can remain remarkably intact until the later stages of this disorder, although this is highly variable.

In persons with FLD, Magnetic Resonance Imaging (MRI) examination reveals atrophy of the frontal lobes and anterior portion of the temporal lobes. Positron Emission Tomography (PET) shows changes in brain metabolism and blood flow that are distinguishable from psychiatric disorders. The cause of FLDs is still unknown although recent studies suggest a link to a gene on chromosome 17. Treatment is focused on reducing distress and managing the psychiatric-like symptoms (i.e., depression) associated with the disorder (ADEAR, 1997). Some of the most challenging and complex patients that psychiatric nurses will encounter likely suffer from “mixed types” of dementia; that is, are experiencing small vessel ischemia, Pick's disease, and AD all at the same time.

ASSESSMENT OF BEHAVIORAL SYMPTOMS IN DEMENTIA

Because AD involves changes in three domains—behavior, cognition, and functional status—assessment in each area is important. Although a number of instruments exist to measure cognitive, functional, global deterioration, and caregiver perceptions of change in dementia,

until recently it was difficult to assess aspects of behavior and mood alterations in AD. In part, this was because many existing tools are self-report in nature, and cognitive impairments associated with dementia make them invalid with this population.

There are newer developments in tests, including: 1) the Pleasant Events Schedule-AD [PES-AD] (Teri & Logsdon, 1991), 2) the Behavioral Pathology in Alzheimer's Disease rating scale [BEHAVE-AD] (Reisberg et al., 1987; Reisberg, Franssen, & Sclan, 1987); 3) the Behavior Rating Scale for Dementia [BRSD] (Tariot, 1996); 4) the Cornell Scale for Depression in Dementia (Alexopoulos, Abrams, Young, & Shamoian, 1988); and the Revised Memory and Behavior Problems Checklist [MBPC-Revised] (Teri et al., 1992). These tests will enable psychiatric nurses to better evaluate noncognitive symptoms in AD and monitor the impact of interventions in this population. For a more extensive list and discussion of valid instruments for measuring behavioral manifestations of dementia, the reader is referred to a review by Little and colleagues (Little, Molcan, Cantillon, & Sunderlan, 1995).

PHARMACOLOGICAL TREATMENTS FOR DEMENTIA

Cholinergic Therapies

In 1993, the Food and Drug Administration (FDA) approved the drug, tacrine (Cognex or THA) and in 1996, the drug donepezil hydrochloride (Aricept or E2020) for the treatment of mild to moderate symptoms of AD (ADEAR, 1997). Both Aricept and Cognex are acetylcholinesterase inhibitors that slow the breakdown of acetylcholine, a key neurotransmitter in cognitive functioning, thus increasing the amount of available acetylcholine in the brain. However, neither drug stops or reverses the progression of AD (Buckwalter, 1997a). Indeed, even in patients who experience a reduction in symptoms of cognitive loss, behavioral problems may be either enhanced or worsened as patient awareness improves.

Approximately 20% of patients prescribed tacrine (Cognex/THA) are unable to tolerate the cholinergic side effects, especially gastrointestinal upset and liver toxicity (Schneider, 1993). Donepezil (Aricept/E2020) has greater selectivity for acetylcholinesterase, has longer action, and fewer side effects than tacrine. In general, research suggests that shortterm treatment with the current FDA approved cholinergic therapies results in modest improvements in memory, attention, cognitive abilities, and possibly some positive impact on behavioral symptoms in approximately 30% of patients with dementia (Tariot, 1997).

Physostigmine is another drug that also blocks the breakdown of acetylcholine and improves the way that acetylcholine directs messages to synapses. It helps improve working memory in people without dementia by shortening the amount of time needed to react to tasks and enhancing activity in specific parts of the brain (ADEAR, 1997). This drug is not FDA approved for treatment of dementia. Scientists are currently evaluating this drug's effectiveness in AD patients, even though it requires frequent dosing (Buckwalter, 1997a).

The drugs Aricept, Cognex, and physostigmine only temporarily reverse cognitive losses and do not prevent AD from continuing to kill the nerve cells that normally produce acetylcholine. Therefore, researchers are looking for other drugs to slow or prevent AD and to help vital acetylcholine-producing cells survive longer.

Estrogen

The search for more effective ways to treat and prevent AD has led researchers to notice that women on estrogen replacement therapy during and after menopause showed a reduced incidence (number of new cases) of AD. The hormone estrogen shows promise as a treatment for cognition, mood, behavior, and motor disturbances associated with dementia (Buckwalter,

1997b). It is thought that estrogen either aids the metabolism of APP, preventing it from forming beta-amyloid fibers, or has antioxidant effects that are protective to nerve cells in the limbic system, cerebral cortex, and hippocampus regions of the brain (ADEAR, 1997). It is interesting to note that the neuroprotective properties of estrogen are not related to its feminizing effects. Estrogen protects neurons and may interact with nerve growth factor to help neuronal development and survival. In the future, estrogen, or estrogen-like therapies, may be administered in low doses over many years to individuals at risk for AD, Parkinson's disease, and other neurodegenerative disorders (ADEAR, 1997). Although these findings show promise, clinical trials are needed before women can take estrogen to prevent or delay onset of dementia. Not only will clinical trials demonstrate if, in fact, estrogen prevents the onset of AD, they will also determine the necessary (and safe) dose and duration needed to produce these effects (ADEAR, 1997).

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

Scientific evidence is accumulating to suggest a link between inflammation and dementia. It is thought that the anti-inflammatory drugs change the cerebral inflammatory response to amyloid protein deposits, thereby reducing the risk of developing AD or slowing the progression of symptoms (Buckwalter, 1997b). In support of a possible relationship, investigators are finding that persons who regularly used non-steroidal anti-inflammatory drugs (NSAIDs) have a lower risk of developing AD, or demonstrating cognitive decline, than those who took acetaminophen (or Tylenol which has no anti-inflammatory properties) or no painkillers at all (ADEAR, 1997). Furthermore, researchers have noted that AD is less common in patients with arthritis. It may be that this finding is associated with the high rate of NSAID use by arthritis patients. These findings do not mean that taking NSAIDs can prevent cognitive decline or development of AD (ADEAR, 1997). In fact, scientists advise against taking NSAIDs to prevent AD at this point in time since they have potentially serious side effects (stomach irritation and ulceration). As with estrogen, the only way to determine if there is a cause-and-effect relationship is through randomized clinical trials (Buckwalter, 1997b).

Antioxidants

Antioxidants, such as selegiline (L-deprenyl or Eldepryl) and alphatocopherol (vitamin E), are being evaluated for their possible use in preventing or treating AD since oxidative changes are seen in the brains of persons with dementia (ADEAR, 1997). Selegiline is a monamine oxidase inhibitor that is approved for treatment of motor dysfunction associated with Parkinson's disease. Support for the use of antioxidants to treat or prevent AD is based on an oxidative stress model that suggests that free radicals, generated through oxidative mechanisms, can play a role in the development of chronic illnesses such as AD and cancer (Buckwalter, 1995). It is important to note that selegiline can have potentially dangerous side effects and can produce negative reactions when taken with other medication or certain foods. Also, Vitamin E is associated with increased risk of hemorrhage in some individuals. As with the pharmacologic treatments discussed above, further research is needed to determine cause-and-effect relationships, as well as optimal dosages and durations for either the treatment or prevention of AD.

IMPLICATIONS FOR PSYCHIATRIC NURSING

Behaviors associated with dementia are often the end-point of a complex sequence of interacting environmental, biochemical, and physiological events. Thus, caring for persons with dementia presents a complex clinical challenge for psychiatric/mental health nurses as these patients manifest a variety of both cognitive and behavioral symptoms. Certain general principles, however, underlie therapeutic goals: 1) the goal of treatment should depend on the severity of the disease; 2) therapeutic goals belong to no single scientific or health care

discipline; and 3) patient and patient-advocate valued outcomes are key considerations (Whitehouse, 1996). Burgener and Chiverton (1992) have argued persuasively for psychological well-being as an appropriate framework for guiding knowledge development in the care of cognitively impaired elders. Indeed, quality of life (QOL) is emerging as a dominant concept in the assessment of therapeutic interventions in dementia. The focus of QOL as an outcome of intervention is congruent with biopsychosocial models of care that view disease as both biological and cultural in nature. Increasingly, preservation of life without quality and function is viewed as a tragedy.

Much of the early nursing intervention research in dementia was largely atheoretical (Burgener & Chiverton, 1992). More recently, a number of conceptual frameworks have been used to guide intervention research on persons with cognitive impairment. These include, for example, Meddaugh's (1990) work using the theory of reactance, which emphasizes the importance of personal freedom and control in a restrictive environment; the concept of resistance found in research by Mahoney and colleagues (1999); Boettcher's (1983) basic need model, which identifies nine biopsychosocial needs that, when thwarted, can lead to disruptive behaviors; and several studies that use behavioral theories or behavioral therapy approaches (Whall & Boehm, 1991). Nelson (1995) proposed a model to summarize the person-environment interface observed in a study of disruptive behaviors in a care facility. The model synthesizes elements of the Progressively Lowered Stress Threshold Model (Hall & Buckwalter, 1987), reactance theory, and basic need theory. The concepts of Person-Environment Fit and Person-Environment Interaction (Lawton, 1975) have also been used extensively in research related to environmental interventions, and are logical frameworks for understanding behavioral and functional changes in persons with dementia.

The general aim of most nursing interventions is to promote optimum quality of life for both care recipients and caregivers and to manage the behavioral problems that are frequently seen in this population.

The desired outcomes at all levels of care are to maximize the potential for safe function by controlling for excess disability and providing appropriate levels of assistance; encourage participation in activities as desired by the client; minimize discomfort caused from physical and emotional stressors; and maximize expressions of comfort (Hall & Buckwalter, 1991, p. 41).

Historically, persons with dementia who displayed disruptive behaviors were managed with restraints and psychotropic medications. This approach proved only moderately effective. A meta-analysis that examined the efficacy of pharmacotherapy with AD patients found that only 20% of the patients responded favorably (Schneider, Pollock, & Lynes, 1990), whereas the adverse side effects included sedation, tardive dyskinesia, and memory impairment. More recently, behavioral and environmental interventions and staff training have been recommended as alternative approaches to managing disruptive behaviors (Burgio & Bourgeois, 1992). Ideally, nursing interventions for persons with dementia should be conceptually based and provide specific compensations for the individual's deficits secondary to the disease process. Interventions also should be based on the individual's remaining capacities, and be supportive rather than curative, over a changing and unpredictable clinical course. Many well designed interventions use a variety of combined or multimodal approaches to care, for example Cohen-Mansfield, Werner, and Marx's (1990) strategy to manage vocally disruptive behaviors, which includes music, videotapes or relatives, social interaction, and a medical exam to rule out pain. Similarly, Beck and Baldwin (1992) developed a nursing home intervention to diminish disruptive behavior that involves both an ADL intervention to increase self care and a psychosocial intervention to increase social interaction. For a comprehensive overview of effective nursing interventions for behavioral disturbances such as aggression and

agitation, the reader is referred to the Cronin-Stubbs (1997) chapter in the *Annual Review of Nursing Research*.

Currently, biomedical research is progressing at an unprecedented rate, and advances in basic, epidemiologic, clinical, and pharmacologic research have direct application to the care and treatment of persons with dementia. Animal models (transgenic mice) are being developed that enable scientists to study the etiology of cognitive symptoms (such as memory and spatial learning) associated with dementia. It follows that these animal models may someday provide a mechanism by which to understand more about the relationship among selected mutations, brain changes, and abnormal behaviors in AD (Advisory Panel on Alzheimer's Disease, 1995). Because dementia represents an integration between biology and behavior, psychiatric nurses must understand the dynamic interplay between both of these scientific fields if state of the art assessment and treatment strategies are to be implemented.

REFERENCES

- Advisory Panel on Alzheimer's Disease. Alzheimer's Disease and related dementias: Biomedical update, 1995. Washington, DC: Supt. of Docs., U.S. Govt. Print. Office; 1995. NIH Pub. No. 95-4002
- Alexopoulos GS, Abrams RC, Young RC, Shamoian CA. Cornell scale for depression in dementia. *Biological Psychiatry* 1988;23:271–284. [PubMed: 3337862]
- Alzheimer A. About a peculiar disease of the cerebral cortex (1907 article translated by L. Jarvik & H. Greenson). *Alzheimer's Disease and Associated Disorders* 1987;1:7–8.
- Alzheimer's Disease Education and Referral [ADEAR] Center. Progress Report on Alzheimer's Disease. Author; Silver Springs, MD: 1997.
- Beck C, Baldwin B. Decreasing disruptive behaviors in cognitively impaired elderly. Grant proposal funded by the National Institute on Aging. 1992
- Blass JP. Pathophysiology of the Alzheimer's syndrome. *Neurology* 1993;43(Suppl. 4):S25–S38.
- Boettcher EG. Preventing violent behavior: An integrated theoretical model for nursing. *Perspectives in Psychiatric Care* 1983;21(2):54–58. [PubMed: 6553823]
- Brane G, Gottfries CG, Blennow K. Monamine metabolites in cerebrospinal fluid and behavioral ratings in patients with early and late onset of Alzheimer's disease. *Alzheimer's Disease and Associated Disorders* 1989;3:148–156.
- Buckwalter KC. "Free radicals" are not a 60s rock group. *Journal of Gerontological Nursing* 1995;21(10):3–4. [PubMed: 7594247]
- Buckwalter KC. What's hot, what's not, in dementia drugs. Part I: Cholinergic Therapies. *Journal of Gerontological Nursing* 1997a;23(9):52–54. [PubMed: 9355485]
- Buckwalter KC. What's hot, what's not, in dementia drugs: Part II. *Journal of Gerontological Nursing* 1997b;32(12):46–47.
- Burgener S, Chiverton P. Conceptualizing psychological well-being in cognitively-impaired older persons. *Image: Journal of Nursing Scholarship* 1992;24(3):209–214.
- Burgio LD, Bourgeois M. Treating severe behavioral disorders in geriatric residential settings. *Behavioral Residential Treatment* 1992;1:145–168.
- Burns EM, Buckwalter KC. Pathophysiology and etiology of Alzheimer's disease. *Nursing Clinics of North America* 1988;23(1):11–29. [PubMed: 3279404]
- Caselli R, Jack C, Petersen R, Wahner H, Yanagihara T. Asymmetric cortical degenerative syndromes: Clinical and radiologic correlations. *Neurology* 1992;42:1462–1468. [PubMed: 1641136]
- Cohen-Mansfield J, Werner P, Marx M. Screaming in nursing home residents. *Journal of the American Geriatric Society* 1990;38(7):785–792.
- Cronin-Stubbs D. Interventions for cognitive impairment and neurobehavioral disturbances of older adults. *Annual Review of Nursing Research* 1997;15:35–56.
- Cummings, JL.; Benson, DF. *Dementia: A clinical approach*. 2nd ed. Butterworths; Boston: 1992.

- Davis KL, Haroutunian V. Strategies for the treatment of Alzheimer's disease. *Neurology* 1993;43(Suppl. 4):S52–S55.
- Ditter SM, Mirra SS. Neuropathological and clinical features of Parkinson's disease in Alzheimer's disease patients. *Neurology* 1987;37:754–760. [PubMed: 3033544]
- Eisdorfer C, Cohen D, Paveza GJ, Ashford JW, Luchins DJ, Gorelick PB, Hirschman RS, Freels SA, Semla TP. An empirical evaluation of the Global Deterioration Scale for staging Alzheimer's disease. *American Journal of Psychiatry* 1992;149(8):190–194. [PubMed: 1734738]
- Hall G, Buckwalter KC. Progressively lowered stress threshold: A model for care of adults with Alzheimer's disease. *Archives of Psychiatric Nursing* 1987;1(6):339–406.
- Hall G, Buckwalter KC. Clinical outlook—whole disease care planning: Fitting the program to the client with Alzheimer's disease. *Journal of Gerontological Nursing* 1991;17(3):38–41.
- Katzman R, Jackson JE. Alzheimer's disease: Basic and clinical advances. *Journal of the American Geriatrics Society* 1991;39:516–525. [PubMed: 1673693]
- Kaye J. Neurochemical aspects of motor impairment, in Alzheimer's disease: Clinical and biological heterogeneity. *Annals of Internal Medicine* 1988;109:307–308.
- Knopman DS, Kitto J, Deinard S, Heiring J. Longitudinal study of death and institutionalization in patients with primary degenerative dementia. *Journal of the American Geriatrics Society* 1988;36:108–112. [PubMed: 3339214]
- Lawlor, BA. Possible neurobiological basis for behavioral symptoms. In: Lawlor, BA., editor. *Behavioral complications in Alzheimer's Disease*. American Psychiatric Press; Washington, DC: 1995. p. 91–101.
- Lawton, MP. Competence, environmental press and the adaptation of older people. In: Windley, P.; Byrerts, T.; Ernst, F., editors. *Theory development in environment and aging*. Gerontological Society; Washington, DC: 1975. p. 13–83.
- Little, JT.; Molchan, SE.; Cantillon, M.; Sunderland, T. Measurement of behavioral changes. In: Lawlor, BA., editor. *Behavioral complications in Alzheimer's Disease*. American Psychiatric Press; Washington, DC: 1995. p. 103–127.
- Mahoney EK, Hurley AC, Volicer L, Bell M, Gianotis P, Hartshorn M, Lane P, Lesperance R, MacDonald S, Novakoff L, Rheume Y, Timms R, Warden V. Development and testing of the Resistiveness to Care Scale. *Research in Nursing & Health* 1999;22(1):27–38. [PubMed: 9928961]
- Meddaugh D. Reactance: Understanding aggressive behavior in long term care. *Journal of Psychosocial Nursing and Mental Health Services* 1990;28(4):28–33. [PubMed: 2110250]
- Mirra SS, Heyman A, McKeel D. The consortium to establish a registry for Alzheimer's disease (CERAD). Part II: Standardization of the neuropathological assessment of Alzheimer's disease. *Neurology* 1991;41:459–466.
- Nelson J. The influence of environmental factors in incidents of disruptive behavior. *Journal of Gerontological Nursing* 1995;21(5):19–24. [PubMed: 7759791]
- Raskind MA, Peskind ER. Neurobiological bases of noncognitive behavioral problems in Alzheimer's disease. *Alzheimer's Disease and Associated Disorders* 1994;8(Suppl. 3):54–60.
- Reisberg B, Borenstein J, Salob SP, Ferris SH, Franssen E, Georgotas A. Behavioral symptoms in Alzheimer's disease: Phenomenology and treatment. *Journal of Clinical Psychiatry* 1987;49:9–15. [PubMed: 3553166]
- Reisberg, B.; Franssen, E.; Sclan, SG. BEHAVE-AD: A clinical rating scale for the assessment of pharmacologically remediable behavioral symptomatology in Alzheimer's disease. In: Altman, HJ., editor. *Alzheimer's Disease: Problems, prospects, and perspectives*. Plenum; New York: 1987. p. 1–16.
- Schneider L. Clinical pharmacology of aminoacridines in Alzheimer's disease. *Neurology* 1993;43(Suppl. 14):S64–S79.
- Schneider L, Pollock VE, Lynes SA. Meta-analysis of controlled trials of neuroleptics in dementia. *Journal of the American Geriatrics Society* 1990;38:553–563. [PubMed: 1970586]
- Steele C, Rovner B, Chase GA, Folstein M. Psychiatric symptoms and nursing home placement of patients with Alzheimer's disease. *American Journal of Psychiatry* 1990;147:1049–1051. [PubMed: 2375439]

- Tariot PN. Alzheimer's disease: An overview. *Alzheimer's Disease and Associated Disorders* 1994;8 (Suppl. 2):S4–S11.
- Tariot PN. CERAD behavioral rating scale for dementia. *International Psychogeriatrics* 1996;8(Suppl. 3):317–320. [PubMed: 9154581]
- Tariot, PN. Treating Alzheimer's Disease; Paper presented at the Geriatric Psychiatry Alliance; Washington, DC. January 3–4; 1997.
- Tariot, PN.; Blazina, L. The psychopathology of dementia. In: Morris, J., editor. *Handbook of dementing illness*. Marcel Decker; New York: 1993. p. 461–475.
- Teri L, Logsdon R. Identifying pleasant activities for individuals with Alzheimer's disease. *The Gerontologist* 1991;31:124–127. [PubMed: 2007468]
- Teri L, Traux P, Logsdon R, Uomoto J, Zarit S, Vitaliano PP. Assessment of behavioral problems in dementia: Revised memory and behavioral problems checklist. *Psychology and Aging* 1992;7:622–631. [PubMed: 1466831]
- Terry RD, Masliah E, Salmon DP. Physical basis of cognitive alterations in Alzheimer's disease: Synapse loss is the major correlate of cognitive impairment. *Annals of Neurology* 1991;30:572–580. [PubMed: 1789684]
- Vitaliano P, Russo J, Breen A, Vitiello MV, Prinz P. Functional decline in the early stages of Alzheimer's disease. *Psychology and Aging* 1986;1(1):41–46. [PubMed: 3267378]
- Whall, A.; Boehm, S. A behavioral approach to the assaultive behavior in dementia; Paper presented at the Midwest Nursing Research Society Conference; Oklahoma City, OK. Apr. 1991
- Whitehouse, P. Conceptual framework of therapeutic goals in Alzheimer's disease; Paper presented at the Department of Health and Human Services Advisory Panel on Alzheimer's disease meeting; Washington, DC. Feb. 1996
- Whitehouse, P.; Tabaton, M.; Lanska, D. Pathological and chemical correlates of dementia. In: Corkin, F., editor. *Handbook of neuropsychology of aging*. Vol. 5. Elsevier Science Publisher B.V.; Amsterdam: 1991. p. 29–37.
- Zubenko GS, Moosy J, Kopp U. Neurochemical correlates of major depression in primary dementia. *Archives of Neurology* 1990;47:209–214. [PubMed: 1689144]

TABLE 1

Relationship Between Neurotransmitters and Behavior in Dementia

Neurotransmitter system/ neurotransmitter	Anatomical origin	Function	Dysfunction & behavior
Cholinergic/ Acetylcholine (Ach)	Synthesized by choline acetyltransferase in the nucleus basalis of Meynert of the basal forebrain.	Promotes proper hippocampal and cerebral cortex function. Necessary for selective attention, learning memory, and sleep-wake cycle.	Diminished levels of Ach leads to amnesia, agitation, and psychotic symptoms. Possible direct relationship to disease severity.
Noradrenergic/ Norepinephrine (NE)	The locus ceruleus (LC) located in the rostral pons of the brain (brain stem).	Modulates mood and stress response. Produces psychotic symptoms.	High levels of NE leads to hypervigilance, decreased appetite, insomnia, anxiety, agitation & psychosis. Low levels of NE leads to depressed mood.
Serotonergic/ Serotonin	The raphe nuclei in the brain stem.	Regulation of body temperature, cardiovascular system, respiratory system, sleep/alertness, mood, aggression, sensory perception, sexual behavior, and feeding behavior.	Low levels of Serotonin leads to anxiety, agitation, psychomotor activity, insomnia, psychosis, and depressed mood.
Dopaminergic/ Dopamine	The substantia nigra in the brain stem with projections directly communicating with the frontal lobe, limbic system, and motor areas.	Regulates emotional responses (limbic system), executive functions (frontal lobe), and complex movements (motor striatum).	Decreased levels of dopamine leads to difficulty initiating movement, rigidity, postural abnormalities, parkinsonian tremor (akinesia or bradykinesia), blunted affect, & apathy.

Adapted from Lawlor, 1995.

TABLE 2**Association of Areas of Brain Pathology to Behavioral Changes in Dementia**

Anatomical structure	Function	Dysfunction
Occipital lobe	Visual processing	Blindness, loss of depth perception, color agnosia (lack of recognition), & persistent after images.
Frontal lobe	Organize words into fluent speech.	Difficulty using "little words" (e.g., in, on, he, she, or). Changes in personality, judgment, and behavior.
Parietal lobe	Association area for integrating sensory input.	Alexia (inability to read), agraphia (inability to write), neglect syndrome, inability to perceive pain, agnosia, apraxia, aphasia, visual-spatial disturbances, loss of executive functions, psychosis.
Temporal lobe	Recognition and comprehension of sensory input, hearing, memory consolidation, association of memory, thought, perception, and emotion.	Agnosia, apraxia, aphasia, visual-spatial disturbances, loss of executive functions, disorientation in space and time, psychosis.
Limbic system	Emotions	Memory dysfunction, no affective dimension to memory, apathy, unstable affect, and personality changes.
Hippocampus	Storage of short-term memory	Poor learning ability, memory loss.

Adapted from Whitehouse, Tabaton & Lanska, 1991.