abstract



Screaming is widely viewed as a common behavioural disturbance in dementia. It influences the performance in daily life of the patient, adds to the burden and embarrassment experienced by the caregiver and the frustrations encountered by the treating physician, and is a decisive factor for institutionalization. This article outlines an approach to screaming and its possible neuroanatomical substrates and neurotransmitter systems. The ultimate basis for discussion will be the strategies available for management of this challenging behaviour.

Key words: *screaming, disruptive vocalization, dementia, limbic system, frontal-subcortical circuitry*

Screaming in Dementia

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Introduction

Several behaviours have been described in dementia and they may be so varied, and in some instances so poorly defined, that their definition continues to be debated. It has been recommended that behavioural disturbances be replaced by the term behavioural and psychological symptoms of dementia (BPSD).[1] BPSD form a substantial part of the morbidity associated with dementia; they are more troublesome to the patient and caregivers than the cognitive symptoms, and should be the focus of greater clinical attention.

In a 1907 landmark single case study, Alois Alzheimer[2] described a 51-year-old woman suspicious of her husband; she also exhibited rapidly developing and increasing memory impairment, disorientation, the urge to drag objects here and there, and loud screaming. She greeted her doctor as a visitor and on occasion screamed that he wanted to cut her open. She often screamed for hours in a horrible voice and burst into loud screams each time she was approached to be examined. She was paranoid and had delusions of sexual abuse and hallucinations. Although screaming had been recorded as an integral part of dementia from the earliest times it had received little attention in its own right until more recently.

This article outlines an approach to screaming and its possible neuroanatomical substrates and neurotransmitter systems. The ultimate basis for discussion will be the strategies for its management. Such an approach may be substantiated by the fact that a better understanding of the neural substrate for behavioural disturbances could result in effective therapeutic regimes as it combines knowledge of both neuroanatomy and behaviour.

General Considerations

Types

Vocalization or noise making besides screaming can take various forms such as yelling, shouting obscenities, cursing, crying, singing, chanting, swearing, grunting, muttering, and mumbling, amongst others (Table 1). Sloane *et al.*[3] categorized these vocalizations into patients who made nonverbal noises ("screamers") and those whose predominant expressions were words ("talkers"). We included two others, namely the "mutterers" (unintelligible) and those who "sing or chant."

Causes

Heterogeneity among noise-making patients could raise the possibility of Alzheimer's disease and other causes of dementia, but may complicate a diagnosis of seizure disorder and certain psychiatric disorders such as chronic schizophrenia (patient shouting back at the voices they hear). Screaming can be erroneously attributed to depression or delirium, although behavioural manifestations may be the first sign of a major affective disorder. Some patients with affective disorder may display psychomotor activity characterized by agitation, screaming, head-banging, hand-wringing, or restlessness. Screaming and head-banging in dementia patients could be an unusual expression of depression.[4]

In many instances there is no cause for the screaming, but often screaming is associated with cognitive impairment, depressed affect, social networks of poor quality, severe functional impairment, a response to social isolation,[5] emotional reactions of nursing staff, communication difficulties, or use of psychotropic medication.[6] Restriction in the ability to communicate in dementia patients may be a determinant of the disturbed behaviour. It is well known that these patients express their frustration and anger by agitation or by "acting out" behaviours. Nagaratnam *et al.*[7] found no correlation between impaired communication and disturbed behaviour. Screaming could be secondary to physical problems (pain, infection) or activity related (to get dressed or to have a bath).

Acute delirium (acute confusional state) is a common complication of medical illnesses; it may also emerge in the course of dementia and may be the presenting symptom of dementia. Furthermore, these patients often manifest the behavioural and psychological symptoms seen in dementia. Not only is acute delirium an important cause of increased morbidity and mortality in dementia, it is often missed because of the difficulty in diagnosis.

Subsyndromes

Several investigators have proposed that behavioural disturbances such as screaming, verbal outbursts, agitation, verbal and physical aggression, and wandering are a continuum of severity of hyperactive behaviour. This is the view adopted in this article. Vocalization is associated with other disturbed behaviours. In one study of 12 dementia patients exhibiting noise making, 10 exhibited aggression.[8] There was no difference in the prevalence of aggression across the diagnostic groups (that is, dementia patients with Alzheimer's disease, multi-infarct dementia, and mixed).[9,10]

In a study of 91 dementia-related behavioural changes in 12 dementia patients, 44% of the patients had only one behavioural disturbance while 53% exhibited two or more.[10] Apart from aggression, many dementia patients have psychotic symptoms; there is considerable evidence on the cause of behavioural disturbance linking aggression to psychotic manifestations. In dementia patients, the behavioural symptoms often associated with screaming are aggression, psychosis, and depressive symptoms. Alzheimer's dementia consists of a full panoply of screaming, paranoid delusions, hallucinations, memory impairment, disorientation, and bizarre behaviour.[2] Among patients with screaming, four symptom clusters or subsyndromes emerge, namely (i) screaming with verbal aggression, (ii) screaming and motor restlessness, (iii) screaming with psychotic symptoms, and (iv) screaming with depressive symptoms. It would be more useful to consider clusters of symptoms rather than individual behaviours to correlate with the neurochemical measures, and the treatment may best be directed towards them rather than towards the individual behaviour.[11]

Table 1: Vocalization Subtypes

Screamers	Talkers	Mutterers	Singers
Screaming	Perseveration	Muttering	Singing
Yelling	Palilalia	Mumbling	Chanting
Swearing	Echolalia	Grunting	
Shouting obscenities	Incessant talking	Weird noises	
Crying	Continuous chatter		

Neuroanatomic Correlates

The frontal lobe is closely associated with human behaviour. The frontal-subcortical circuits provide a comprehensive framework for understanding the anatomy, biochemistry, and pharmacology of behaviour.[12] Alexander *et al.*[13] proposed five parallel circuits connecting discrete lesions in the frontal lobes with specific subregions of the striatum, globus pallidus, and thalamus (Figure 1). Hyperactivity, disinhibition, impulsiveness, and distractability are characteristic behaviours associated with orbital frontal lesions. Lesions of the dorsal medial nucleus of the thalamus could give rise to manifestations similar to prefrontal lesions. The frontal lobe and the frontal-subcortical circuitry play an important role in the occurrence of aggression and agitation. It is well accepted that the temporal lobe and the limbic system are closely related to a number of psychological syndromes. Delusional syndromes are known to involve the temporal lobe, especially the medial temporal-limbic structures.[14] Alexander *et al.*[13] have expanded the frontal subcortical circuitry to encompass the limbic system.

The neurogenic pathways that control mood and behaviour are associated with the neurotransmitter systems. Neurotransmitters such as serotonin, dopamine, and acetylcholine have a modulatory role. Serotonin has been associated with disturbed behaviours.[4] While there is considerable variation in the presentation of noise making patients, the clinical features seem to correspond to the functional anatomy of the brain regions affected rather than to the pathology. Noise making may be a single syndrome with different locations and with different clinical presentations.[7]

It may be asked how similar neuroanatomic changes could give rise to syndromes whose features are not uniform. According to Cummings[15] the occurrence of different psychological syndromes could be influenced by several factors, including genetic constitution, age of onset, personality characteristics, early life experiences, and exact location and extent of the lesions. Environmental

provocations might also precipitate behaviour by evoking aggressive responses in patients whose threshold for agitation is affected.[9]

Management

Screaming is widely viewed as a common behavioural disturbance in dementia that poses difficult dilemmas in management. It is difficult to envisage which neurotransmitter system is involved in noise making and it is likely there may be more than one. This may be the reason why there is no effective therapy. Despite these caveats, there are areas of interest to those interested in approaches to managing screaming. As stated above, treatment might best be directed towards syndromes rather than toward individual behaviours.[11] Agitation and aggression appear to be prominent features accompanying screaming. Aggressive behaviours are related to disordered frontal-subcortical circuitry and have been linked to the dysfunction of the serotonergic neurotransmission. Conditions that may be characterized by brain serotonergic dysfunction should benefit by the use of drugs with apparent serotonergic selectivity.[4,16]

There is no single approach that will solve the problem. Instead, a multimodal intervention is needed; nonpharmacological approaches must precede or accompany pharmacological therapies, and are often more effective.

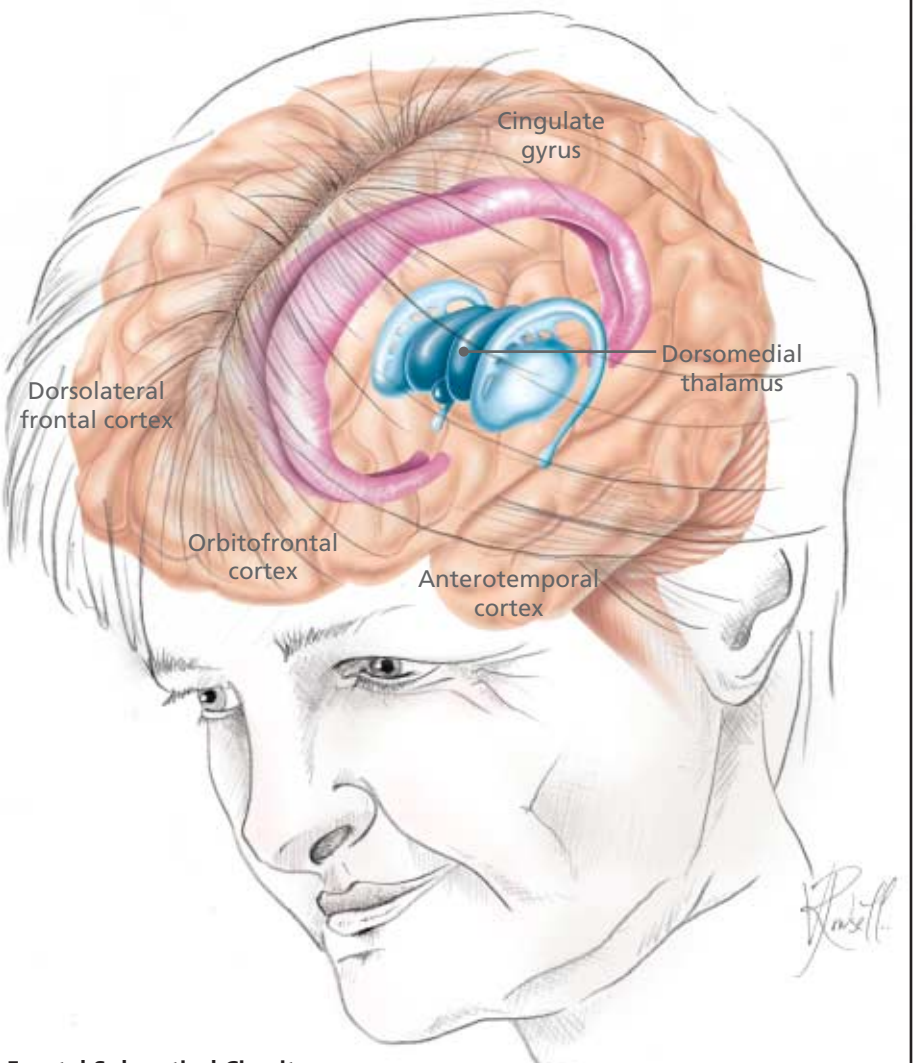
The behavioural and psychological symptoms in dementia patients could be intrinsic to the disorder or can occur across multiple diagnoses: for example, with primary psychiatric illness, chronic alcoholism, or cerebral disorder (cerebral infarction, cerebral tumour, normal pressure hydrocephalus). Figures 2a and 2b illustrate an algorithm describing the steps in recognition, diagnosis, and treatment of behavioural and psychological symptoms.

Nonpharmacological Intervention

Nonpharmacological strategies for managing these patients should include a multifaceted approach considering physical, behavioural, environmental, and social factors (Table 2). It is important to identify, minimize, and avoid stressors (for instance, physical stressors such as pain or any other medical illness); to reduce overwhelming stimulation (e.g., too many people around or other provoking situations); and avoid too little activity (e.g., when the patient needs more animation). Behavioural approaches include such strategies as avoiding arguing and confrontation; touching thoughtfully and using a gentle, calm, and reassuring voice; avoidance of physical restraints; and engaging in pleasure-related activities.

There are other adjunctive approaches such as using bright light, aromatherapy, white noise, pet therapy, and music, but none have been evaluated using group study methodology for screaming patients. However, Ballard *et al.*,[26] in a double-blind, placebo-controlled trial, demonstrated that aromatherapy with

Figure 1:
Frontal Subcortical Circuitry and the Limbic System



Frontal Subcortical Circuitry
Frontal lobe (orbitofrontal, dorsolateral, medial frontal, motor, and oculomotor), striatum, globus pallidus, substantia nigra, and thalamus

Limbic System
Paralimbic cortex (limbic system—orbitofrontal, insular and anterior temporal lobe)

lemon balm was a safe and effective treatment for dementia-related agitation. A recent controlled trial has shown that individualized music therapy reduced agitation but group classical music did not.[27]

Environmental manipulation may also be helpful. Education of the caregiver and change in the caregiver's behaviour, will in turn improve the patient's behaviour as necessary. When behavioural and environmental approaches fail, medications may be helpful as an adjunct.

Pharmacological Intervention

In treating screaming, some drug classes should be favoured for initiation in certain subsyndromes because they have evidence of benefit in particular coexisting conditions (e.g., aggression, psychotic symptoms, and depression) (Table 3). Medications are not sufficient to terminate these behaviours, but they can often reduce the severity, transitioning them from disturbed to acceptable. Older adults are particularly sensitive to side effects from neuroleptics, and those drugs with sedative effects frequently cause hypotension. It is important to review the side effect profiles of the common medications used in screaming and the general principles of prescribing them (Tables 3 and 4).

Antidepressants

Screaming can be associated with depression[5] and there is a favoured association with certain types of dementia such as vascular dementia. Depressive symptoms are common in dementia but their cause remains unclear. Selective serotonin reuptake inhibitors (SSRIs) are better tolerated in older adults than more traditional tricyclic antidepressants or monoamine oxidase inhibitors. Citalopram has been shown to be effective for depression and behavioural disturbance in dementia.[17,18]

Trazodone, a trizolopyridine derivative, inhibits the neural response of serotonin[19] and has been used in continuous and repetitive screaming patients with effect.[4,16] Pasion and Kirby[16] described an 84-year-old woman with continuous screaming who had been on a number of medications with little or no effect. They were ceased and the patient commenced on trazodone, which selectively inhibits neuronal reuptake of serotonin. The dose was increased over the next two weeks to 300mg per day with no adverse effects. Two weeks after starting tradazone the screaming stopped and verbal outbursts were limited to intermittent calls for assistance. Greenwald *et al.*[4] described an 82-year-old woman with repetitive screaming and table and head banging with moderately advanced dementia. The medications haloperidol, oxazepam, tranylcypromine, and thiothixene provoked unwanted side effects. A trial with increasing doses of trazodone up to 300mg at three weeks was without side effects. The head banging decreased, her mood improved, and screaming was no longer constant. She was then commenced on 1g/day L-trytophan as an adjunctive therapy, which was titrated to 2.5g daily, and within two weeks the screaming and echolalia almost stopped. They concluded that screaming and banging in demented patients may be a related symptom responsive to serotoninergic modifiers. Single-case studies such as these in relation to treatment success or failure are useful and contribute to an assumption that can be validated by group study.

The doses are given in Table 3. In general, it is advisable to start on a small dose and to increase it to the target dose that is likely to be effective for a typical patient.

Fluoxetine should be avoided in those with agitation and anxiety.

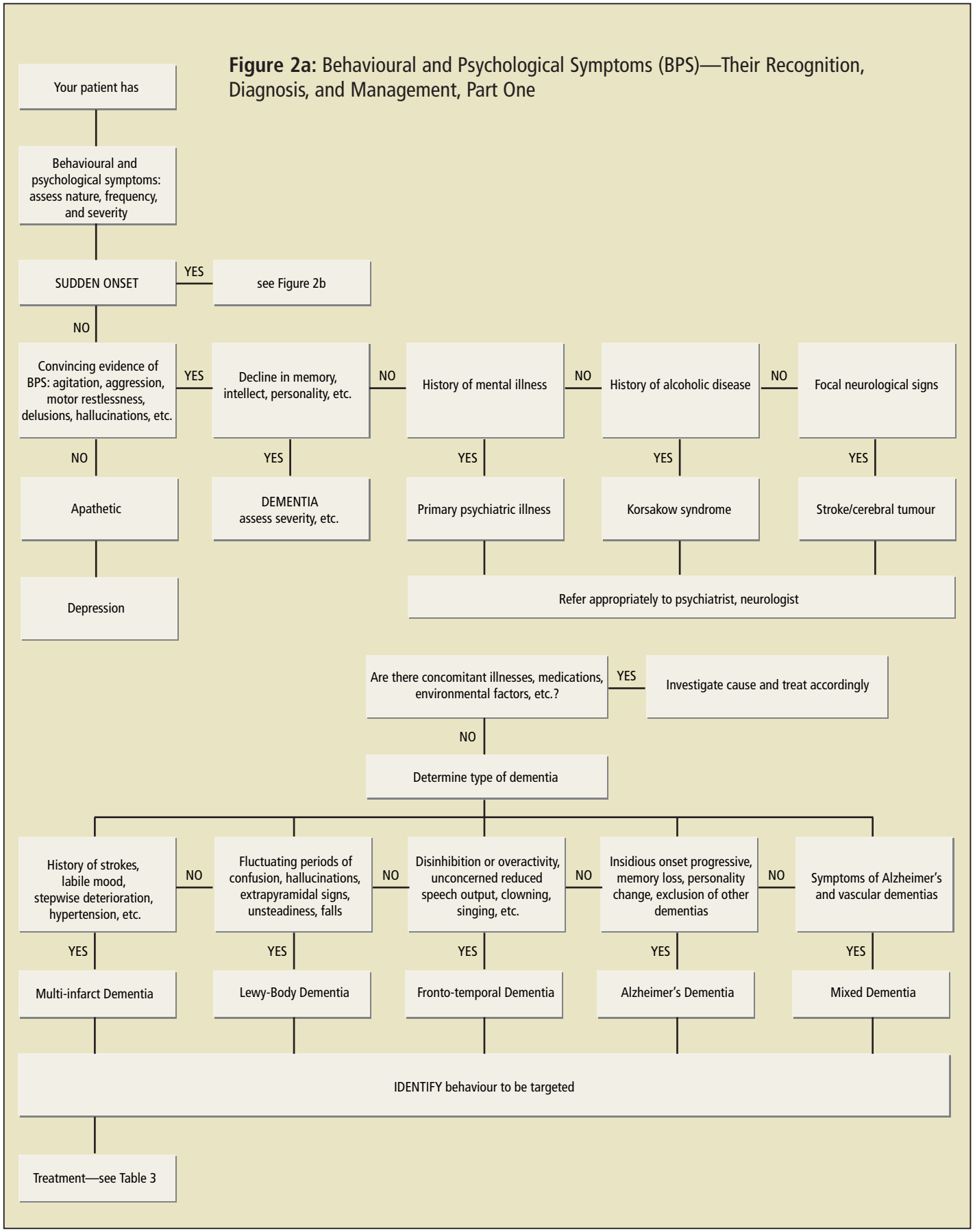
Antipsychotics

The typical antipsychotic haloperidol is commonly prescribed but has a high

Table 2: Nonpharmacological Interventions for Screaming Patients

Early Intervention	Preferably one-on-one care Frequent reassessment of physical, behavioural, and environmental causes
Physical	Treatment of comorbid illness Sensory impairment-vision/hearing corrected, and nightlights if necessary Address pain, discomfort, and fear Check and review medication effects Avoid interruptions to sleep
Behavioural	Avoid confrontation Approach calmly, touch sensibly, and converse in gentle and reassuring voice Distracting with an activity may help
Environment	Change to suit the needs of patient Establish a safe, calm, and quiet environment Avoid physical restraint Refrain from provoking individuals and situations Search for and remove triggers for behaviour (e.g., too many people around) Moving out roommate if incompatible
Social	Education of the caregiver Caregiver should receive adequate help to facilitate the above Presence of family members encouraged

Figure 2a: Behavioural and Psychological Symptoms (BPS)—Their Recognition, Diagnosis, and Management, Part One



risk of extrapyramidal symptoms (EPS), particularly in older adults. In patients with Lewy Body dementia, antipsychotics can give rise to disastrous medical consequences—such as tardive dyskinesia and possibly sudden death[34]—and therefore must be avoided altogether. There is evidence that antipsychotics have inhibitory effects on cholinergic, dopaminergic, and histaminergic neurotransmission and thus could give rise to deleterious cognitive effects in some older patients.[28]

Atypical antipsychotic medications have been used to manipulate the serotonin system and modulate vocalizations.[20] The newer atypical antipsychotics are a heterogenous group of drugs that may be associated with lower risk of EPS and are better tolerated.

Frenchman and Prince[29] reported their experience in a retrospective study of 186 patients with diagnoses of Alzheimer's dementia, senile dementia (not otherwise specified), or organic brain syndrome. In all, 60 were treated with risperidone (mean 1mg/day), 83 with haloperidol (mean 2mg/day), and 43 with thioridazone (mean 33mg/day). The target behaviours were violence (74), shouting (31), delusions (26), paranoia (19), pacing (3), and mixed behaviours (33).

Figure 2b: Behavioural and Psychological Symptoms (BPS)—Their Recognition, Diagnosis, and Management, Part Two

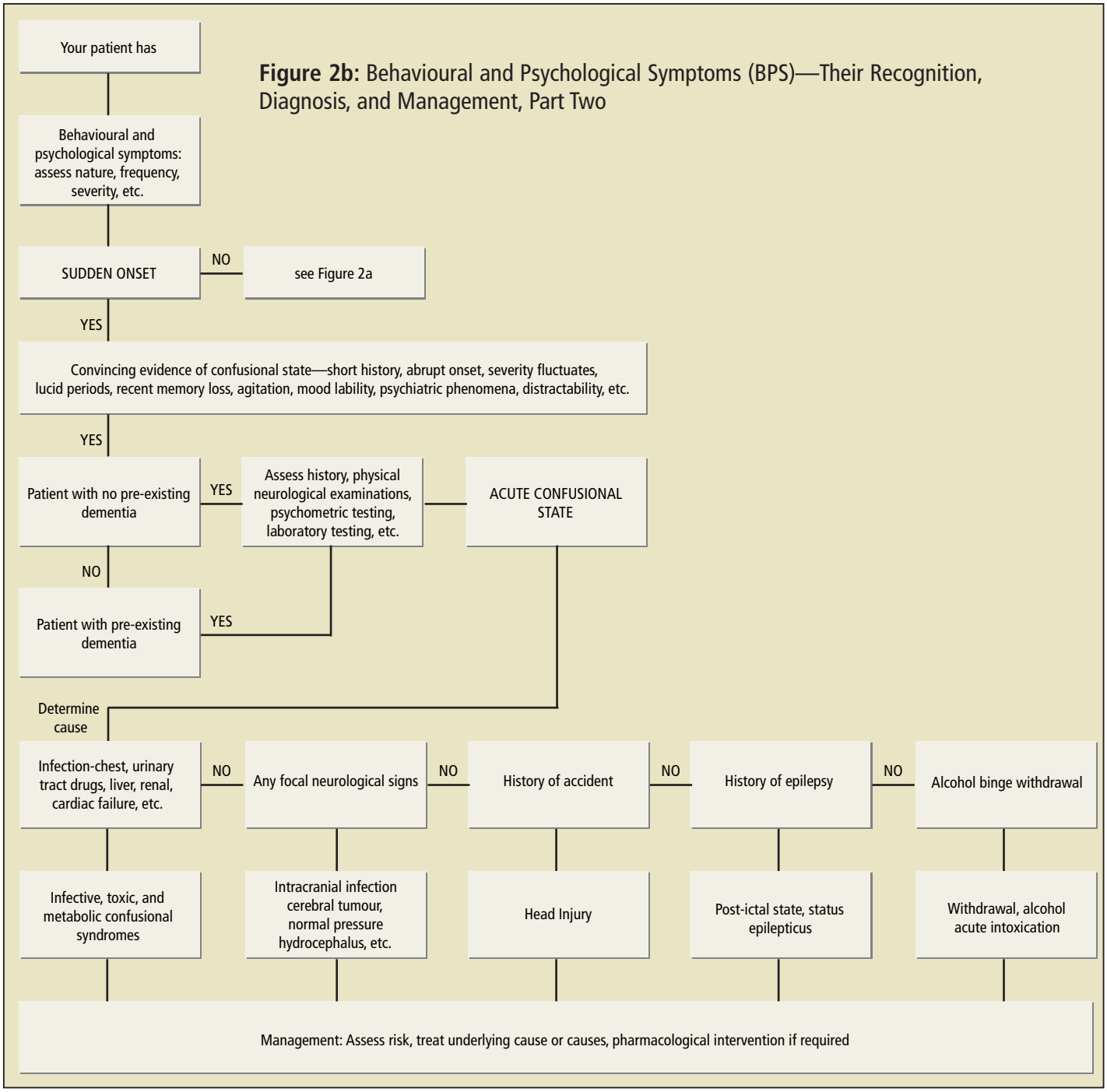


Table 3: Profile of Common Medications Used in Screaming

Drug category	Associated symptoms with screaming	Daily dose (oral) mg*	Side Effects					
			EPS	AC	Sedation	Hypotension	Weight loss	Agranulocytosis
Antidepressants								
SSRIs	Depression, agitation, aggression							
Sertraline		25–100	SSRIs are now considered first-line therapy because of their more tolerable adverse effects and relative safety in overdose. Avoid fluoxetine when anxiety and agitation are present.					
Citalopram		10–20						
Fluoxetine		10–40						
Trazodone (SARI)		50–200	0	0	++	No data	No data	0
Antipsychotics								
Atypical								
Clozepam	Psychosis	200–600	+	+++	+++	+++	+++	+++
Olanzepine	Agitation	5–20	+	++	+++	+	+++	+
Risperidone	Aggression	2–6	++	0	++	+++	++	+
Quetiapine	Violence	300–750	+	+	+++	++	++	+
Typical								
Haloperidol		2–7.5	+++	+	+	+	++	+
Anticonvulsants								
Valproic acid	Aggression	100–1,000						
Carbamazepine	Agitation, Hostility	200–600	Hepatotoxicity, sedation, drug interaction, and ataxia					
Cholinesterase Inhibitors	Behavioural							
Donepezil	Psychosis	5–10	Predominantly gastrointestinal: nausea, anorexia, cramps Nightmares					
Rivastigmine	Aggression	1.5–6 b.i.d.						
Galantamine	Depressive symptoms, activity disturbance	4–12 b.i.d.						
Other								
Beta-blocker								
Propanolol			Hypotension, bradycardia, unapparent hypoglycemia in diabetes					
Benzodiazepines			Exacerbation of cognitive impairment, risk of falls					

0-normal;+= minimal;+=mild;++=moderate;+++=severe; EPS=extrapyramidal symptoms; AC= anticholinergic; SSRI=selective serotonin reuptake inhibitors; SARI= serotonin-2 antagonists/serotonin reuptake inhibitor

* the higher dose shown is the target dose likely to be effective for a typical patient

Source: Information from Liu DD *et al*, 2000;[36] Lovestone & Gauthier, 2001;[37] Smith AG, 2004.[38]

Target behaviours improved in 94% of patients given risperidone, 65% given haloperidol, and 67% given thiordazine. Treatment failures were more frequent on patients started on haloperidol and thioridazine as compared with risperidone; extrapyramidal side effects were reported in 7% of patients taking risperidone, 22% taking haloperidol, and 18% taking thioridazine. Safe and effective doses were readily achieved with risperidone.

Anticonvulsants

Older patients with dementia and behavioural agitation improved when treated with sodium valproate, and the proposed mechanism of action was via the alteration of the gamma-aminobutyric acid (GABA) system and not the serotonergic system.[21]

The use of carbamazepine in BPSD was positive in a study of its efficacy for agitation and aggression in dementia. Carbamazepine and valproic acid are increasingly used for BPSD, particularly in patients with cerebrovascular disease and dementia.[30]

Acetylcholinesterase Inhibitors

Cholinesterase inhibitors are generally prescribed in Alzheimer's disease to slow the cognitive decline but have also been found to be effective in reducing agitation.[35] In Lewy Body dementia, the psychosis and behavioural disturbances rapidly respond to cholinesterase inhibitors.[22,23] In a single case study of a patient with Lewy Body dementia with severe visual hallucinations and behavioural problems, introduction of donepezil was associated with cognitive improvement and complete remission of behavioural symptoms.[31]

It has been postulated that cholinergic agents may have psychotropic activity through actions in the paralimbic cortex of the frontal and temporal lobes.[24] A large double-blind placebo controlled trial examined the prevalence of behavioural symptoms in moderate to severe dementia and the effect of treatment with donepezil. The common symptoms were aberrant motor behaviour (53%), depression/dysphoria (52%), agitation/aggression (45%), and apathy/indifference (67%). At the end of 24 weeks on donepezil, the behavioural symptoms had improved.[32]

Similar results were seen in another study with donepezil in which treatment had a mildly positive effect on emotional/behavioural symptoms in Alzheimer's Disease.[33] However, more evidence for this use of cholinesterase inhibitors is needed and responses thus far have been variable.

Benzodiazepines

Physicians should be cautious in prescribing benzodiazepines for older patients as they can lead to increased confusion and falls, although they are sometimes useful in managing anxiety and agitation.

Beta-Blockers

Many of the patients who exhibit noise making have features attributable to orbital-frontal cortical dysfunction and the use of beta-adrenergic blocking agents (beta-blockers) has been found to be effective. Shankle *et al.*[25] suggested low-dose propranolol in such patients.

Evidence-Based Approach to Pharmacotherapy

The decision to initiate drug therapy in dementia patients with behavioural disorders that can occur across multiple diagnoses is based on an assessment of the severity and nature of the symptoms, the type of dementia, and the failure to respond significantly to nondrug interventions. Some drug classes should be favoured for initiation in certain symptom clusters (subsyndromes) because they have evidence of benefit in coexisting conditions. The next step would be to select the individual drug within the class; this will be influenced by known efficacy and side effect profile.

Because of the multiple changes occurring with age, older adults need to be prudently treated following the admonition: "start low, go slow," with even more caution in the very old. The management algorithm and profile of the common medications used are provided in Table 3 and Figure 3. These are individualized choices based on clinical data, but may not have the support of RCTs. If the response to a drug in the class is inadequate, substitute a drug from a different class (that is, if the first drug produces intolerable side effects or adequate doses produce poor or little response).

Conclusion

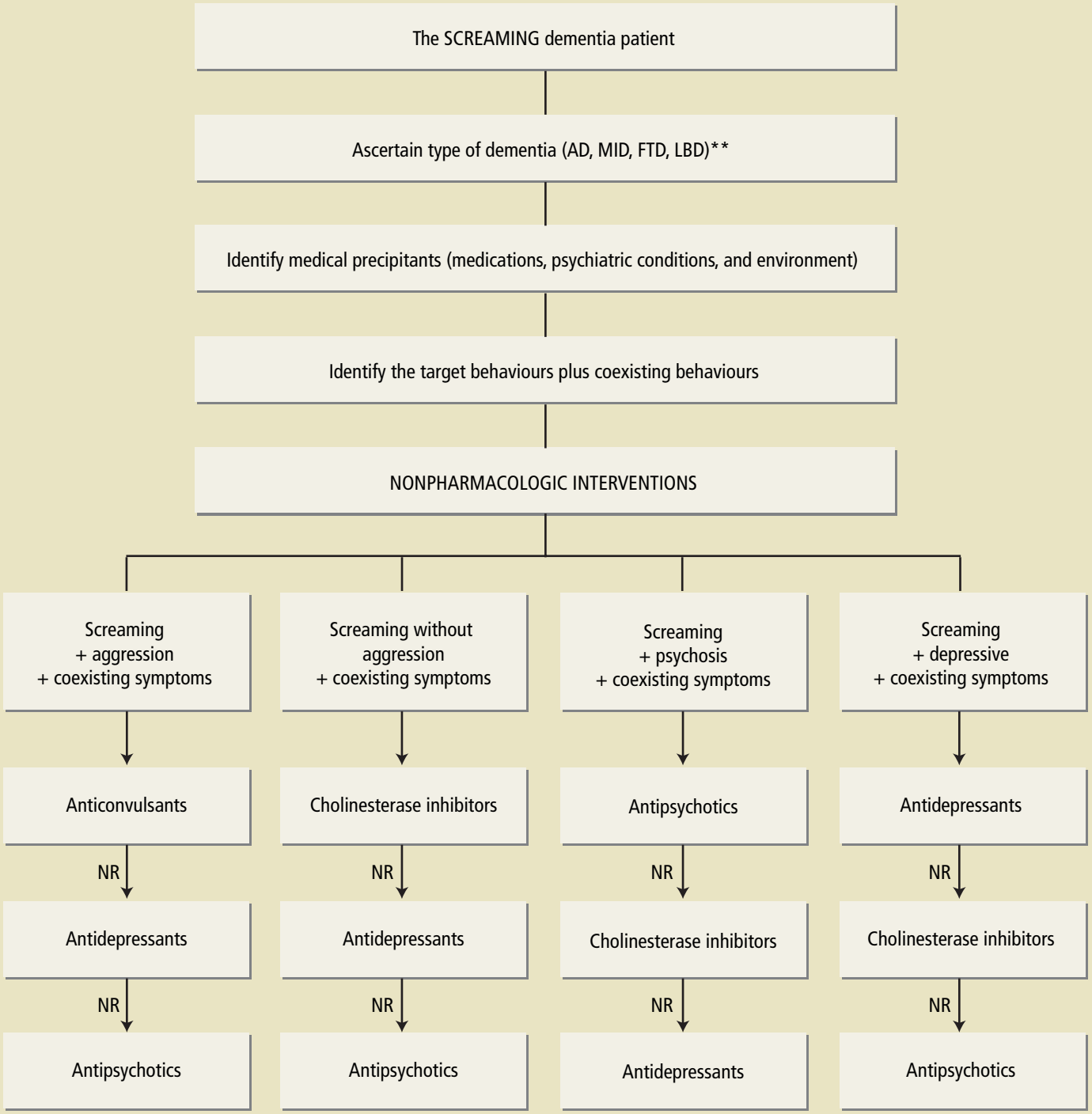
Screaming in dementia is viewed as a common behavioural disturbance pre-

Table 4: Prescribing Pointers

Start low and go slow (response may be more gradual in older patients).
Cease or change medication if no response.
One single approach rarely terminates the behaviour.
Select the agent judiciously and selectively, considering favourable effects on coexisting conditions (symptoms clusters) and potential side effects; some drug classes are favoured for initiation in certain subgroups.
Reduce initial dose in frail or older patients.
Titrate dose to lowest possible effective dose.
Monitor closely to identify side effects.
Review regularly.
Monotherapy is the preferred form.

Source: Adapted from Smith AG 2004.[38]

Figure 3: Algorithm for the Management of Screaming



NR=No response; **AD: Alzheimer's Disease; MID: Multi-infarct Dementia; LBD: Lewy Body Dementia; FTD: Frontotemporal Dementia

Preferred medications in the subsyndromes: anticonvulsants: sodium valproate/carbamazepine; antidepressants: citalopram/sertraline; antipsychotics: risperidone/olanzapine; cholinesterase inhibitors: donepezil/rivastigmine/galantamine

senting with difficulties in its management, as the neural mechanisms underlying screaming in dementia are still obscure. This article does not illuminate the issue but does indicate that screaming with verbal outbursts, agitation, aggression, and wandering is said to be a continuum of hyperactive behaviour.

Screaming is often associated with other behavioural disturbances, and the target behaviours are agitation/aggression, wandering, psychotic manifestations, and depressive symptoms. It would be useful to consider screaming as part of a symptom cluster, for treatment may thus be directed towards subsyndromes rather than towards the individual behaviour.

There is no single approach that will solve the problem. Instead, a multimodal intervention initiating in nonpharmacological and followed by pharmacological treatments is needed. The former remains the mainstay of management. Although reported as effective, it lacks the support of controlled trials. However, these nondrug interventions do improve the quality of life of patients in long-term care.

Medication is often required as an adjunct therapy. In treating screaming, certain drug classes are preferred for initiation in the different subsyndromes because there is evidence of benefit in particular coexisting symptoms. Other influencing factors are the severity of the screaming and the type of dementia. The drug classes commonly used are antidepressants, anticonvulsants, antipsychotics, and cholinesterase inhibitors. There is no single effective therapy, and treatment of screaming in dementia remains a challenge.

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