


# Repetitive and Stereotypic Phenomena and Dementia

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Gabriele Cipriani, MD<sup>1</sup>, Marcella Vedovello, MD<sup>1</sup>,  
Martina Ulivi, MD<sup>1</sup>, Angelo Nuti, MD<sup>1</sup>, and Claudio Lucetti, PhD<sup>1</sup>

## Abstract

**Background:** Behavioral disturbances of dementia, such as repetitive and stereotypic phenomena, can be distressing to caregivers and may lead to early institutionalization of the patient. **Objective:** The purpose of this article is to examine the phenomenon of repetitive phenomena in patients with dementia. **Methods:** We searched the PubMed electronic databases for original research and review articles on repetitive phenomena in patients with dementia using the search terms “repetitive behavior, stereotypic behavior, dementia, Alzheimer’s disease, Frontotemporal dementia.” **Results:** Repetitive and stereotypic phenomena are common problems in dementia, which may reflect a disruption of coordinated function within the basal ganglia or corticostriatal structures. **Conclusions:** There are no systematic studies concerning repetitive phenomena in patients with dementia, and very little is known about the treatment. Further studies are needed to determine the specific phenomena.

## Keywords

repetitive behavior, stereotypic behavior, dementia, Alzheimer’s disease, frontotemporal dementia

## Introduction

Dementia is a syndrome, a pattern of symptoms, which can be caused by a great number of cerebral and extracerebral diseases. It has protean manifestations that comprise cognitive dysfunctions and behavioral changes, including repetitive and stereotypic phenomena.

## Phenomenology of RBs

Stereotypies are purposeless, simple, or complex involuntary/unvoluntary behaviors accomplished without apparent conscious control despite normal consciousness; they are performed the same way each time.<sup>1</sup> *Diagnostic and Statistical Manual of Mental Disorders*<sup>2</sup> defines stereotypies as a repetitive and nonfunctional behavior lasting for 4 or more weeks; it also emphasizes that the behavior interferes with normal activity or may lead to self injury.

When describing a movement, frequently used descriptors include involuntary, bizarre, repetitive, rhythmic, coordinated, patterned, and predictable (form, amplitude, and location), but purposeless.<sup>3</sup> To correctly diagnose, the stereotypical movements must be differentiated from other repetitive motor activities like tics and compulsions, mannerisms, and paroxysmal dyskinesias. Although both stereotypies and tics are purposeless movements, stereotypies are usually less abrupt than tics and lack an irresistible urge to execute the movement and a transient relief afterward.<sup>4</sup> Stereotypical movements are further distinguishable from compulsions, which are purposeful behav-

iors that are performed in response to an obsession or to eliminate discomfort.<sup>1</sup>

The term repetitive behaviors (RBs) refers to broad and often disparate classes of responses characterized by their repetition, rigidity or inflexibility, frequent lack of obvious function, and inappropriateness.<sup>5,6</sup> These phenomena may include simple motor movements such as patting, rubbing, scratching, picking, placing nonfood items in the mouth, or verbalizations that can include counting or repetitive sounds.<sup>7</sup> Impulse control disorders (pathological gambling, intermittent explosive disorder, pyromania, kleptomania, trichotillomania, etc) are not considered as stereotypic behavior because they constitute a pattern of voluntary behaviors. The RBs are described in individuals with autism spectrum disorders, and they are a common feature of a number of other neurodevelopmental disorders (eg, Rett, Fragile X, and Prader–Willi syndromes). Moreover, RBs are also part of the phenotype of other central nervous system disorders including obsessive–compulsive disorder, Tourette syndrome, schizophrenia, fronto-temporal dementia (FTD), and Alzheimer’s disease (AD)<sup>8–11</sup>

<sup>1</sup> Neurology Unit, Versilia Hospital, Lido di Camaiore (Lu), Italy

## Corresponding Author:

Gabriele Cipriani, Ospedale della Versilia, via Aurelia, 55043, Lido di Camaiore, Lucca (Lu), Italy.  
Email: cprgrl@gmail.com

## Neurobiology and Neurophysiopathology of RBs

The brain control of behavior includes 2 systems. The first selects and sequences individual responses on the basis of external and internal stimuli that are immediately present. The second system selects and sequences goals, plans, and attention to salient features in the environment on the basis of internal abstract information that is not cued by stimuli.<sup>12</sup> Environmental factors are generally of relevance in patients with dementia diagnosed with RBs. High level of stimulation (noise, temperature, etc) and also understimulation plays an important role, for example, in repetitive vocalizations, particularly in the isolated patient who may also have visual or auditory impairments and who becomes bored and cries out in a form of self-stimulation. However, in the course of dementia, RBs may be secondary to "internal factors." Thus, an accompanying memory or other cognitive impairment, for example, memory impairment might explain repetitive questioning as well as focal brain dysfunction, can induce the abnormal behavior. \*\*\*\*The underlying biologic mechanism for RBS is not clearly understood.

Observations both in humans and in experimental animals have pointed to abnormalities in corticobasal ganglia circuits as primary neural correlates of motor and cognitive repetitiveness.<sup>13</sup> The basal ganglia are the largest subcortical structures in the human forebrain, and they are placed in a key position to influence motor behavior, emotions, and cognition.<sup>14</sup> The corticostriatal circuits are multiple, parallel, segregated feedback circuits with outputs from striatum targeting primary motor areas, and specific premotor and prefrontal cortical areas. The RBs can result from the disruption of any of these circuits.<sup>15,16</sup> When striatal feedback to frontocortical areas becomes dysfunctional, it results in an inappropriate repetition of a behavior set, an inability to switch to other behavior, or the facilitation of inappropriate behavioral sets.<sup>17</sup> Because the basal ganglia modulate the release or inhibition of movements, injury to the frontal-striatal circuits that traverse the caudate nuclei may result in an inability to inhibit existing urges to perform repetitive movements or to prevent stimulus-driven behavior.<sup>1</sup>

The majority of neurons in the basal ganglia use  $\gamma$ -aminobutyric acid (GABA) and glutamate as neurotransmitters, whereas dopamine and serotonin, especially, have important modulatory effects on corticostriatal circuitry, thereby affecting the development of RBs. Pharmacological studies have established the importance of the nigrostriatal dopamine pathway in the mediation of stereotypies.<sup>18</sup> Administration of indirect and direct acting dopamine agonists or repeated administration of a potent and selective dopamine uptake inhibitor has been shown to induce stereotypic behaviors.<sup>19</sup> In rodent models, repetitive sequences of behaviors, such as sniffing, chewing, rearing, or grooming, can be induced in response to low doses of stimulants (release dopamine) and cocaine (block dopamine reuptake).<sup>20-22</sup> However, some clinical observations suggest the involvement of acetylcholine in the arrest of motor stereotypies, and restoration of cholinergic transmission in the prefrontal territory of the dorsal striatum may play a key role in the arrest of motor stereotypy.<sup>23</sup>

## The RBs in Dementia

The RBs are highly prevalent in patients with dementia and may be one of the earliest predictor of cognitive impairment.<sup>24,25</sup> They are considered the most burdensome of the behavioral and psychological symptoms of dementia<sup>26</sup> being correlated with a reduced caregiver quality of life. These behaviors may irritate or agitate others in a facility setting (eg, constant patting on a table causing unending noise) or become overwhelming to caregivers. We try to provide insights into the structure of the aforementioned behavioral disturbances in different types of dementia.

## Frontotemporal Dementia

Among patients with FTD, 90% manifest neuropsychiatric features,<sup>27</sup> and approximately 80% of these patients have RBs.<sup>28</sup> Considering the high prevalence of RBs in FTD, some authors have suggested that the presence of such features may have discriminatory power in the diagnosis of this type of dementia.<sup>29-31</sup> The RBs and other behavioral symptoms are more prominent and disruptive than memory or other cognitive deficits<sup>32</sup> in the early stage of FTD; clinicians frequently miss these behavioral symptoms early in the course of the disorder.<sup>33,34</sup> There are no differences between sporadic and genetic causes of FTD in producing stereotypies and ritualistic behavior.<sup>35,36</sup> According to Nyatsanza et al,<sup>9</sup> the severity of stereotypic behaviors in patients with frontovariant of FTD does not correlate with the level of dementia as assessed by either cognitive measures Mini-Mental State Examination (MMSE) suggesting that stereotypic and ritualistic behaviors occur early in the course of illness reflecting specific disruption of neural circuitry. In semantic dementia (a clinical variant of FTD that presents with a progressive fluent aphasia secondary to a breakdown in semantic knowledge and with preservation of speech output skills, perceptual and visuospatial functions, and episodic memory), there is a clearer association between the total Neuropsychiatric Inventory score and disease severity, suggesting that changes in behavior reflect advancing disease.<sup>9</sup> In frontotemporal lobar degeneration, RBs correlate with right frontal involvement and complex compulsions with temporal involvement.

Positron emission tomography studies showed that RBs correlate with hypometabolism in the right orbitofrontal region, an area that regulates stimulus reinforcement associated with learning aberrant motor behavior.<sup>37</sup> Joseph et al., using the technique of voxel-based morphometry, demonstrated that the patients with stereotypies show a greater volume of striatal to cortical loss than those without stereotypies.<sup>38</sup>

Repetitive phrases seem to be discriminating in FTD in which 2 contrasting subsyndromes have been described, one of disinhibition and distractibility (FTD-D), the other of apathy, inertia, and loss of volition (FTD-A). Verbal stereotypies, constituting repetition of a single word or phrase, are common in FTD-D and differentiated this group from the FTD-A group.<sup>39</sup>

## Alzheimer Disease (AD)

Patients with AD present with repetitive phenomena classified into verbal (repeated questions and excessive speech with stereotyped phrases or repeated requests) and behavioral categories (searching, buying objects, bathing, brushing teeth, telephoning, putting on and talking off clothes, opening and closing doors, counting money, and moving objects). The RBs are reported in 60% of the patients with AD and were not associated with gender, age of onset, or MMSE score.<sup>40</sup> Verbal repetition is a common complaint in AD and can include repeating phrases, words, questions or actions, and telling the story multiple times in the same conversation.<sup>41</sup> There are 3 phenomenologically distinct types of verbal repetition above the single word or morpheme level: repetitive questions, stories or perseverative narratives, and statements.<sup>42</sup> The prevalence of repetitive questions ranges from 31%<sup>31</sup> to 67.4%,<sup>32</sup> 90%,<sup>43</sup> and 91%.<sup>26</sup> Cullen et al<sup>44</sup> performed a finding in which 87% of the persons having AD presented with RBs: questions were the most common, occurring in 68.5% of the sample, with statements/stories almost as frequent at 61.1%. According to these authors, repetitive questions were predicted by higher MMSE score, poorer immediate recall on word list learning, and female gender, while repetitive statements/stories were predicted by more severe dysexecutiveness and younger age. Repetitive speech is hypothesized to be a result of compromised memory or executive function.<sup>45</sup> Those who have poor immediate recall are more likely to repeat questions, whereas patients with more advanced executive dysfunctions are more likely to repeat statements and stories.<sup>46</sup> However, while memory impairment is present in all patients with AD, repetitive questioning behavior is not. Kishimoto et al<sup>47</sup> found that patients with AD with higher score of repetitive questioning tend to show higher relative cerebral blood flow in the left pericallosal region; no sex differences were detected. Repetitive questioning may also be related to prefrontal cortical dysfunction as well as reflecting impaired hippocampal function associated with the episodic amnesic pattern characteristic of AD.<sup>48,49</sup>

## Dementia and Parkinsonism

No data on the presence and severity of RBs in degenerative parkinsonisms with dementia have been reported; this may be due to the fact that it is sometimes difficult to differentiate complex stereotypies from levodopa-induced hyperkinesia and tardive dyskinesia induced by neuroleptic treatment. Moreover, there is the problem of differentiating complex stereotypies from a wide range of compulsive/impulsive behaviors, such as gambling, excessive shopping, binge eating, and so on, recently recognized in patients with Parkinson's disease (PD) treated with dopamine agonists.<sup>50</sup> This has been linked to dopamine dysregulation syndrome<sup>51</sup> related to aberrant or excessive dopamine receptor stimulation. Most patients with parkinsonism with dementia are unaware of their elementary motor stereotypies (gestures and sounds); when they admit them they

tended to give banal justifications for them or are unable to give any explanation at all.<sup>50</sup>

## Management of RBs

Currently, very little is known about the treatment of RBs in dementia. It is essential to adopt a multifactorial strategy for both understanding and intervening in them, based on the approaches of particular circumstances of each individual.

Nonpharmacological management should always be considered as the first option. It has been proposed that the environment provides sensory input to persons that either understimulate or overload the nervous system, resulting in behavioral abnormalities. Management of environmental overstimulation generally involves reducing or eliminating excessive or troubling stimuli (eg, replacing daytime television with selected videotapes; serving one food item at a time; using one staff member rather than several for caregiving).<sup>52</sup> About the repetitive disruptive vocalizations (RDV), it was suggested that altering the environment with the needs of the patient with dementia in mind is a possible method for the treatment that can minimize the need for medication.<sup>53</sup> Sensory deprivation responds to sensory stimulation either through improvement in hearing and vision or through the introduction of pleasant stimuli; the use of music to alter the environment has gained attention primarily because of its demonstrated physical and psychological effects. Casby and Holm<sup>54</sup> supported the theory that altering the environment through music can be a viable method for decreasing RDV in residents diagnosed with AD. Cohen-Mansfield and Werner<sup>55</sup> compared 3 types of intervention for people with abnormal vocalizations (exposure to music, exposure to a family-generated videotape, and one-to-one social interaction) and found that music therapy significantly reduced the behavior.

When nonpharmacological treatment is unsuccessful in reducing distress, pharmacological intervention should be used. Trappler and Vinuela<sup>56</sup> described the effects of treatment with the selective serotonin reuptake inhibitor fluvoxamine in 3 patients with advanced dementia who developed a stereotypic movement disorder; two patients showed complete resolution of their stereotypic behaviors, and the third patient showed noticeable improvement with some residual movements after 8 weeks of treatment. Helvink and Holroyd<sup>7</sup> observed 5 cases of elderly patients with cognitive impairment (2 patients with AD, 2 with vascular dementia, and 1 with dementia due to alcoholism) exhibiting repetitive and stereotypic behaviors who were treated successfully with buspirone. It is possible that, as a 5-HT<sub>1A</sub> antagonist, buspirone works through a serotonergic mechanism to decrease these behaviors. It is interesting that treatment studies of stereotypies in people with FTD have shown that trazodone, an antidepressant, is effective in reducing such behavior, particularly in patients with clinical symptoms of depression.<sup>44</sup> Whether the association between depressive symptoms and repetitive actions is causal or coincident remains to be clarified. Rockwood et al<sup>57</sup> reported reduction in verbal repetition in patients with AD after treatment

with galantamine. In another study, it was found that verbal repetition often improved in patients with AD treated with donepezil and that improvement usually occurred in people who also improved in other domains.<sup>58</sup>

## Conclusion

Behavior change is a widespread consequence of neurodegenerative diseases. Among the clinical features of dementia described in the literature, repetitive and stereotypic behaviors are common; these symptoms correlate with a reduced caregiver quality of life, thereby affecting the care of elderly persons manifesting them. The neural substrates involved remain unclear, but traditionally, the basal ganglia and the frontal-striatal circuits have been a candidate for explaining RBs. Stereotypic behavior is more common in FTD than in AD. Currently, very little is known about treatment; a number of questions remain unresolved and further studies are needed to determine the specific phenomena.

## Declaration of Conflicting Interests

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