

Mutism in older adults is not uncommon. It is often confused with severe depression, locked-in syndrome, and persistent vegetative state, but it is important to distinguish among them as the management and prognosis are different. The family physician is the most consulted professional and so is the most helpful in making this distinction. Mutism is a neuropsychological disorder with marked heterogeneity among patients, raising the possibility of conditions such as advanced Alzheimer's disease, Jacob-Creutzfeldt disease, frontotemporal dementias, and certain psychiatric and psychological conditions. It is both a symptom and a syndrome, and is often associated with akinesia when the term akinetic mutism is used. Akinetic mutism has a number of causes with varied pathology and is characterized by a marked reduction in motor function, including facial expression, gestures, and speech output, with awareness being preserved. All of the disease manifestations can be explained by damage to the frontal lobe or interruption of the complex frontal subcortical circuits and the frontal diencephalic brain stem system by focal lesions or diffuse brain damage.

**Key words:** mutism, akinetic mutism, frontal-subcortical circuitry, locked-in-syndrome, persistent vegetative state

## Mutism in the Older Adult

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### Introduction

By definition, mutism is the state or condition of being speechless. If speech occurs it is restricted to terse responses or monosyllables. Mutism is not uncommon in the older population. Since it is often caused by brain damage, mutism is considered a neurological disorder. However, it is also a psychological disorder and so can be more accurately termed a neuropsychological disorder. Mutism can be congenital or acquired when, as a result of damage to a part of the brain, the normally functioning psychological capability is altered. In mutism there is impairment of speech function and it is an articulatory disorder as opposed to aphasia, a disorder of linguistic processing (Figure 1).

The primary care physician must have a high degree of awareness or suspicion in patients presenting with varied clinical conditions that are often associated with mutism, and often erroneously diagnosed as depression, delirium, and locked-in-syndrome, amongst others.

### Terminology and General Considerations

Terms such as apathy, abulia, and akinetic mutism (AM) are used to designate behavioural abnormalities relating to reduced activity and slowness. It is believed that these clinical disorders exist along a continuum of severity of reduced behaviour, and AM may be an extreme form.<sup>1</sup> The term abulia was initially used by Auerbach<sup>2</sup> and later called akinesia. Fischer<sup>3</sup> used the term abulia to embrace the full spectrum of abnormalities, characterized by a reduction in speech, spontaneous activity, prolonged latency in

responding to questions, and lack of persistence with tasks.

In 1865, Broca<sup>4</sup> used the term aphemia to describe eight patients with loss of speech, which Trousseau later referred to as aphasia.<sup>5</sup> Aphemia is now recognized as an articulatory disorder with normal propositional language. Aphemia has often been misdiagnosed as aphasia; this is partly due to confusion resulting from the numerous terms that have been used to describe this syndrome.<sup>6</sup> In mutism, unlike in aphemia, the patient makes no attempt to communicate verbally or by gesture.<sup>7</sup> Aphemia more often than not follows mutism.

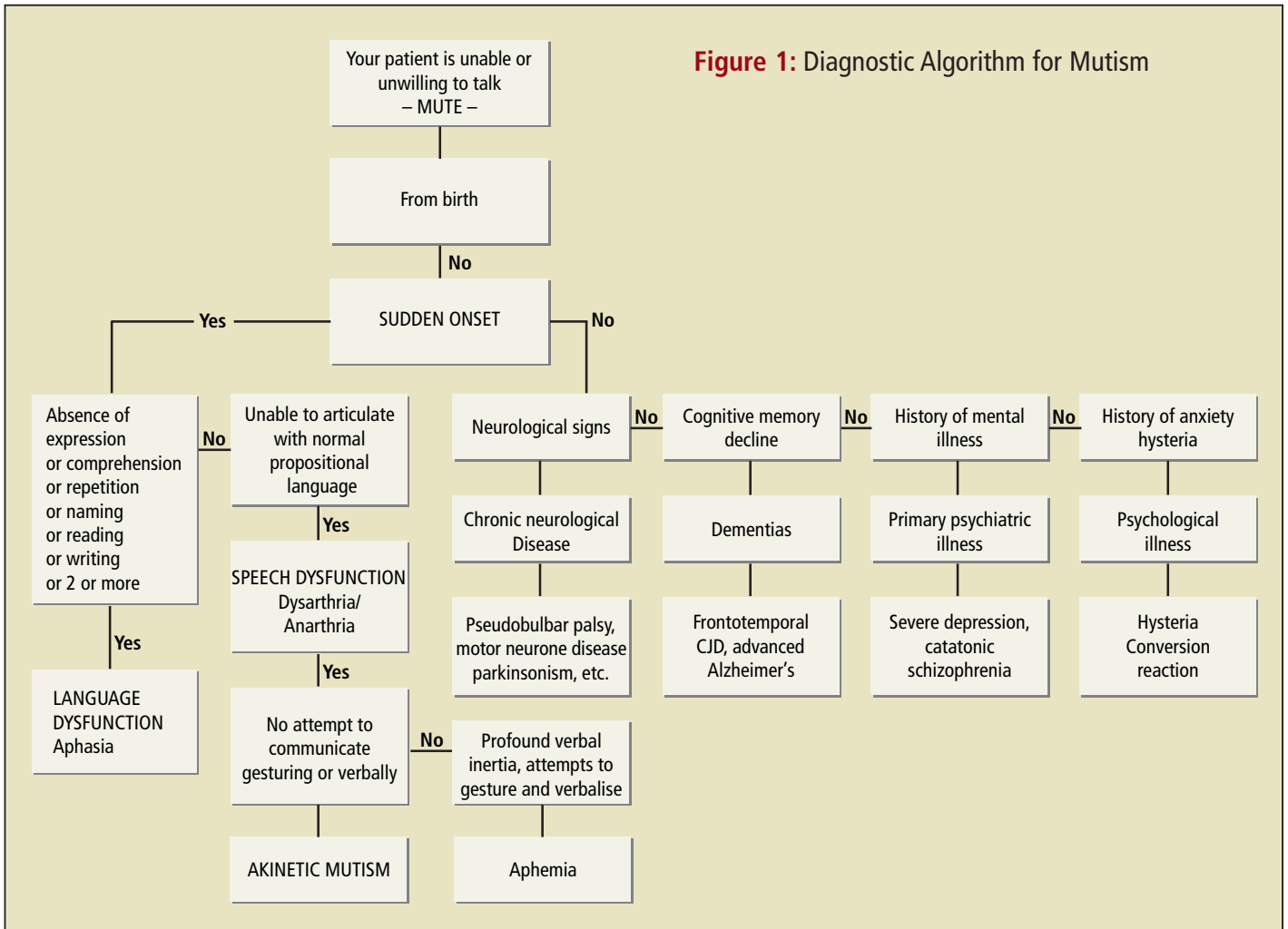
### Clinical Considerations

There is marked heterogeneity among patients with mutism, which raises the possibility of such varied conditions as advanced Alzheimer's disease, Pick's disease, and Creutzfeldt-Jakob Disease. It may also complicate certain psychiatric disorders including catatonic schizophrenia, severe depression, and conversion reaction. Mutism can be both a syndrome and a symptom, and is often associated with akinesia.

### Akinetic Mutism

Following the landmark case report of Cairns *et al.*,<sup>8</sup> the term akinetic mutism (AM) has been used to describe a syndrome characterized by marked reduction of nearly all motor functions, including facial expression, gestures, and speech output, but with some degree of alertness. Following this report, the term AM has been used in situations with similar clinical pictures associated with different etiologies and pathologies.

Figure 1: Diagnostic Algorithm for Mutism



Depending on the clinical picture, AM had been subdivided into two pathology types based on the anatomic location of the lesion. One is related to the mesencephalic region and is described as apathetic akinetic mutism or somnolent mutism. The other is known as hyperpathic akinetic mutism and is associated with bilateral frontal damage (Figure 2).<sup>9</sup>

The critical areas involved are the frontal lobe (cingulate gyrus, supplementary motor area [SMA], and the dorso-lateral border zones), basal ganglia (caudate and putamen), and the mesencephalus and thalamus.<sup>10</sup> The vascular syndromes giving rise to AM are the most striking, particularly those related to the anterior cerebral artery (ACA) which could be either unilateral or bilateral, transient or prolonged. Neuroimaging is an important diagnostic test (Figure 3). Apart from cerebral infarction or hemorrhage,<sup>11</sup> a

variety of focal pathologies can produce AM.<sup>8,12-15</sup> CJD is a rapidly progressive disease, characterized by dementia and myoclonus, and is highly protean in its manifestations. AM has been described as a symptom of CJD and included as a classification criterion for its diagnosis.<sup>14</sup> AM commences within an average of 7.5 weeks in CJD.<sup>16</sup>

Lim *et al.*<sup>15</sup> described AM with findings of white matter intensities. There are two types of white matter changes: periventricular and deep white matter lesions. The deep matter lesions are separate from the ventricles; they have a different pathogenesis.<sup>17</sup> There are several causes for these lesions apart from normal aging, but the more severe types can be associated with atherosclerotic disease.<sup>18,19</sup> According to some investigators, these changes detected by computed tomography or solely by magnetic resonance imag-

ing have different meanings, and when these changes are seen on the CT they may indicate associated dementia.<sup>20</sup>

Somnolent AM of the mesencephalic type can vary in intensity.<sup>9,21</sup> AM has been reported after thalamic lesions<sup>22,23</sup> and thalamocapsular lesions.<sup>13</sup> Brown<sup>24</sup> identified two broad classes of disturbances with unilateral left thalamic lesions: one showing AM, often with a stuporose state, and the other with a fluent type of speech disorder.

AM is often erroneously diagnosed as locked-in syndrome or persistent vegetative state. Distinguishing between them is important because management differs. The distinguishing characteristics are shown in Table 1. The blunted emotional expression and apathy in patients with severe depression, together with psychomotor retardation such as slurred speech and body movements, may mimic AM.

### Chronic Neurological Disorders

There are a number of chronic neurological disorders that exhibit pseudobulbar or bulbar palsy (dysarthria and dysphagia) and in which mutism supervenes. In pseudobulbar palsy there are bilateral lesions following cerebrovascular incidents resulting in involvement of the corticobulbar pathways; this causes dysarthria, dysphagia, and slow tongue movements together with corticospinal tract signs. Progressive supranuclear palsy (PSP) is a nonfamilial progressive disorder of gait and balance with supranuclear gaze palsy, bradykinesia, and pseudobulbar palsy. Motor neurone disease (progressive bulbar palsy and amyotrophic lateral sclerosis) is characterized by progressive degeneration of the corticospinal tracts, anterior horn cells, and/or bulbar motor nuclei. In Parkinson's disease the speech is characterised by hypophonia, dysarthria, reduced variability of rhythm and pitch, and, finally, unintelligible speech.

### Dementias

In frontotemporal dementia (FTD), emphasis on one or other of the lobes has led to two main types: frontal variant<sup>26</sup> and temporal variant.<sup>27</sup> Prominent manifestations of the temporal subtype are language disturbance (primary progressive aphasia) and behavioural disorders. According to Kertesz and Munoz,<sup>28</sup> mutism is a mid-stage characteristic heedless of how this group of illnesses begin. It tends to be the end stage characteristic of all forms of FTDs (now referred to as the Pick's complex) irrespective of whether they present with disturbance of behaviour or language. There are few initial neurological signs but with progression, striatal signs of akinesia and rigidity emerge.<sup>29,30</sup>

Aphasia is one of the essential requirements for the diagnosis of Alzheimer's disease, along with agnosia and apraxia. The aphasia of Alzheimer's disease often fits with an extrasylvian pattern.<sup>31</sup> Initially, the patients have an anomic aphasia, followed by a transcortical sensory aphasia or Wernicke's aphasia.<sup>32</sup> As the dementia progresses there is

decreased fluency together with perseveration, echolalia, and nonspeech utterances such as grunting to complete dissolution of speech. These features are rarely seen in patients with global aphasia following stroke.<sup>33</sup>

Binswanger's disease (BD), or subacute arteriosclerotic encephalopathy, is characterized by diffuse demyelination of the white matter with lacunar lesions in the basal ganglia and brain stem. Depending on the location and severity of the lesion, a variety of symptom-clusters may emerge. Clinically, it is characterized by disorders of memory, cognition, and mood changes together with pyramidal and extrapyramidal abnormalities. Pseudobulbar palsy (dysarthria and dysphagia) is frequent.

### Primary Psychiatric Disorders

#### Catatonia

Stupor and excitement are outstanding catatonic symptoms. A patient in stupor is unresponsive and, although fully conscious, is immobile and mute. The stupor may suddenly change to excitement and

increased motor activity.<sup>34</sup> These patients are usually adolescents and young adults; however, onset in late life is not uncommon.

#### Psychological

In hysterical mutism there is an obstinate and voluntary silence that is not accompanied by any abnormality in the muscles of articulation. The patient is able to cough normally. There is a psychological component in conversion disorders and the patient mimics a pathophysiological disorder such as paralysis or amongst others, loss of vision. Any symptom may become a conversion symptom.

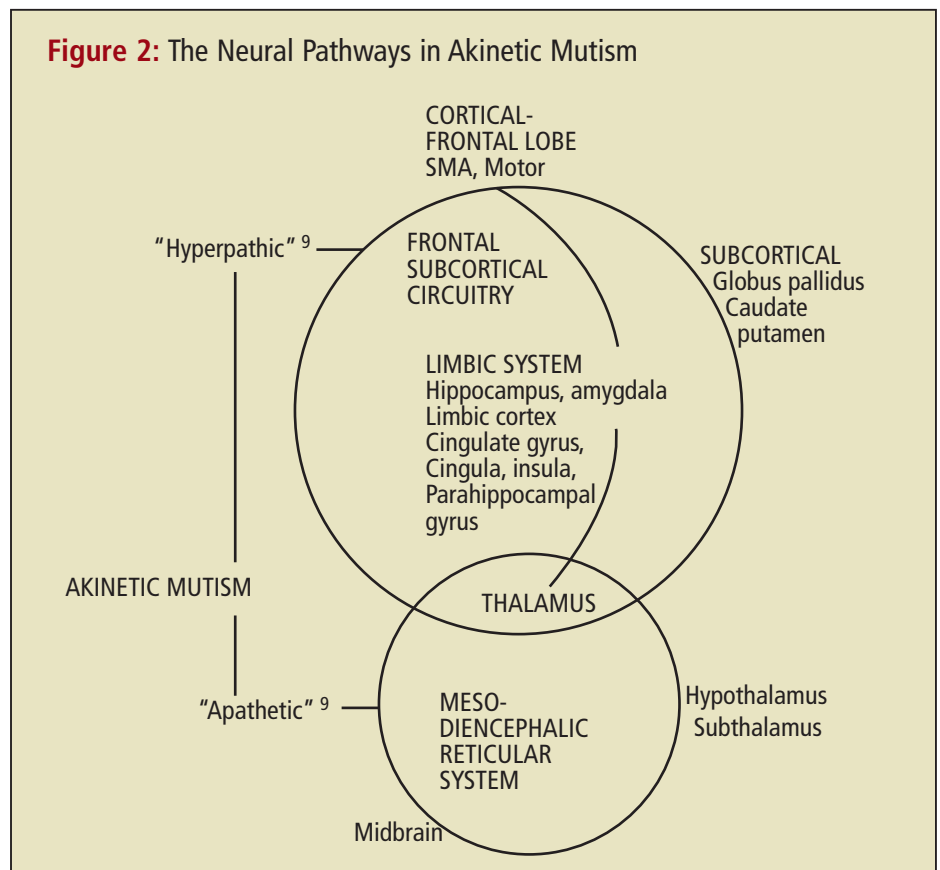
#### Neuroanatomic Correlates

The frontal lobe plays an important role in behaviour and speech.

#### Supplementary Motor Areas

The supplementary motor areas (SMAs) have extensive afferent and efferent connections with the motor and premotor cortex.<sup>35</sup> The SMAs are concerned with programming motor subroutines before voluntary

Figure 2: The Neural Pathways in Akinetic Mutism



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movements can be executed. The right SMA is concerned with activation of the motor output<sup>36</sup> and the left SMA is less involved with motor activation but is more concerned with sequencing of primary motor routines. Impaired functioning of the SMA could give rise to abnormalities of Parkinsonian motor programme, and the SMA acts as the “energizer unit.”<sup>37</sup> Tremor, rigidity, and akinesia have been described following a low grade glioma involving the left SMA.<sup>38</sup> Petrovic<sup>39</sup> described eight patients with tumours of the SMA who could be categorized into two types: one with speech block, aphemia (mutism), and reiteration, and the other group with dysphasic manifestations occurring with lesions of the speech dominant hemisphere.

### Cingulate Gyrus

The anterior cingulate gyrus is very similar to the SMA which has connections with the cingulate gyrus.<sup>37</sup> The anterior cingulate gyrus has short connections with the dorso-lateral prefrontal cortex. Lesions of the cingulate gyrus, SMA, or both give rise to akinesia and mutism with restriction of spontaneous activity.<sup>36</sup> The anterior cingulate influences goal-directed behaviour through the cortical

gateway for limbic motivation.<sup>40</sup> AM is typically associated with bilateral anterior cingulate lesions.<sup>41,42</sup>

### Basal Ganglia

AM has been reported following bilateral globus pallidal lesions.<sup>43,44</sup> De Long and Georgeopolous<sup>45</sup> proposed a relationship between basal ganglia and the frontal cortical areas through a concept of motor and complex loops (Figure 4A). Lesions of the loop may therefore cause SMA dysfunction, and SMA dysfunction may lead to akinesia.<sup>46</sup>

### Paramedian Diencephalic and Midbrain

AM also results from bilateral subcortical paramedian diencephalic and midbrain lesions.<sup>8,23</sup> The mesencephalic-diencephalic reticular activating system—which includes the midbrain, reticular formation, thalamus, and hypothalamus—has projections to the frontal lobe.<sup>9,13</sup>

Alexander *et al.*<sup>48</sup> described five frontal-subcortical circuits according to their function or cortical site. The motor and oculomotor circuits are associated with sensorimotor functions; the dorso-lateral prefrontal and the orbitofrontal

circuits are associated with cognitive functions, and the anterior cingulate circuit (medial frontal) with limbic mechanisms,<sup>45</sup> featuring reduced motivation, interest activity, maintenance, and apathy. Each circuit includes the frontal lobe, striatum, globus pallidus/substantia nigra thalamus, and connecting links between these structures.<sup>50</sup> The dorsal-lateral prefrontal circuit originates from the lateral convexity of the frontal lobe anterior to the premotor area and the circuit structures include the caudate nucleus, globus pallidus, substantia nigra, and ventral anterior dorsal medial nuclei of the thalamus. The medial frontal circuit begins in the anterior cingulate cortex and the circuit includes the nucleus accumbens (also known as the limbic striatum), globus pallidus, substantia nigra, and the medial dorsal nucleus of the thalamus. Damage to these areas or interruption of the circuit either by focal lesions or by diffuse brain damage could give rise to mutism and akinesia.

## Treatment

### A Trial with Dopaminergic Therapy

There are three dopaminergic pathways, namely the striatonigral pathway

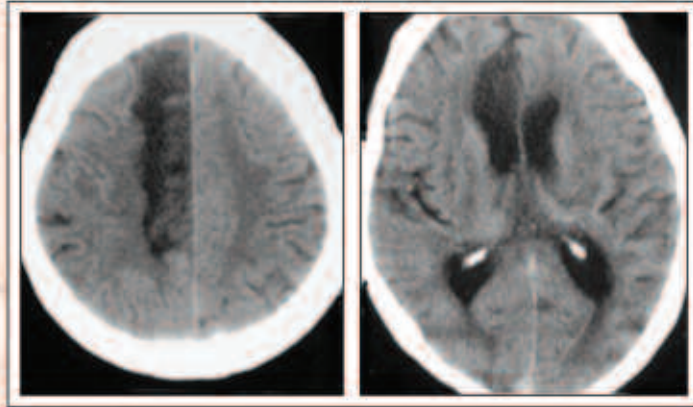
**Table 1:** Differential Diagnosis of Akinetic Mutism

Symptoms and Signs	Akinetic Mutism	Locked-In Syndrome	Persistent Vegetative State
wakefulness	present	present	cycles of eye opening and closure
alertness	present	present	none
awareness	present	present	none
attentiveness	present	present	none
<b>Communication</b>			
speech output	reduced (occasionally in monosyllables)	nil (able to with eye and head movements)	nil
motor responses	reduced	as above	none purposeful
cognition	not for higher cognitive responses	near normal	none
localization of lesion	cingulate gyrus SMA, mesencephalo-thalamic	ventral pons	diffuse cortical damage
prognosis	transient or prolonged (usually days to few months)	persistent	poor

Source: Adapted from TBI and limited overt responsiveness: Nebraska’s Brain Injury Resource Network.<sup>25</sup>



Figure 3: Demonstration of a Cerebral Infarction



Cerebral infarction in the territory of the anterior cerebral artery at two levels:

- A. involving the supplementary motor cortex and motor cortex
- B. predominantly the cingulate gyrus

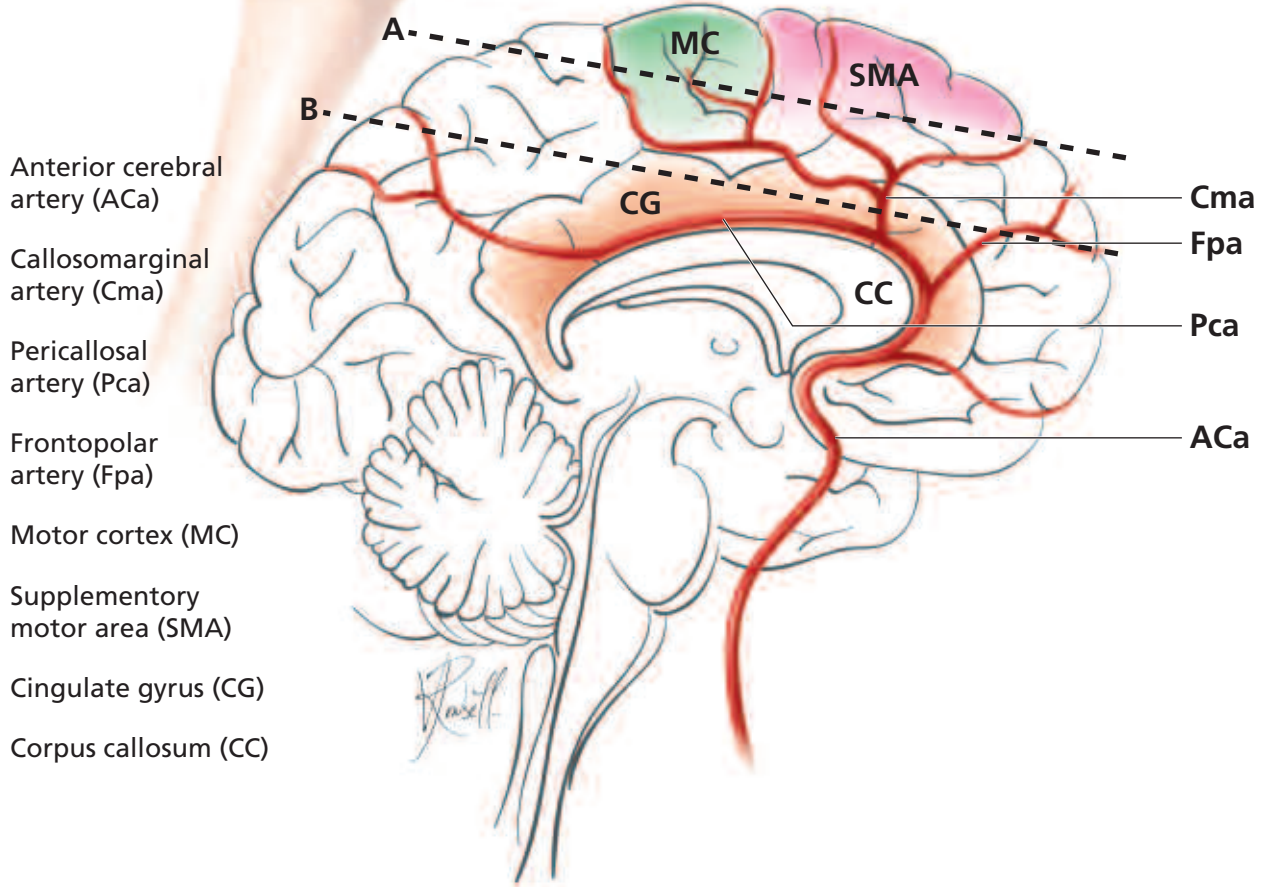
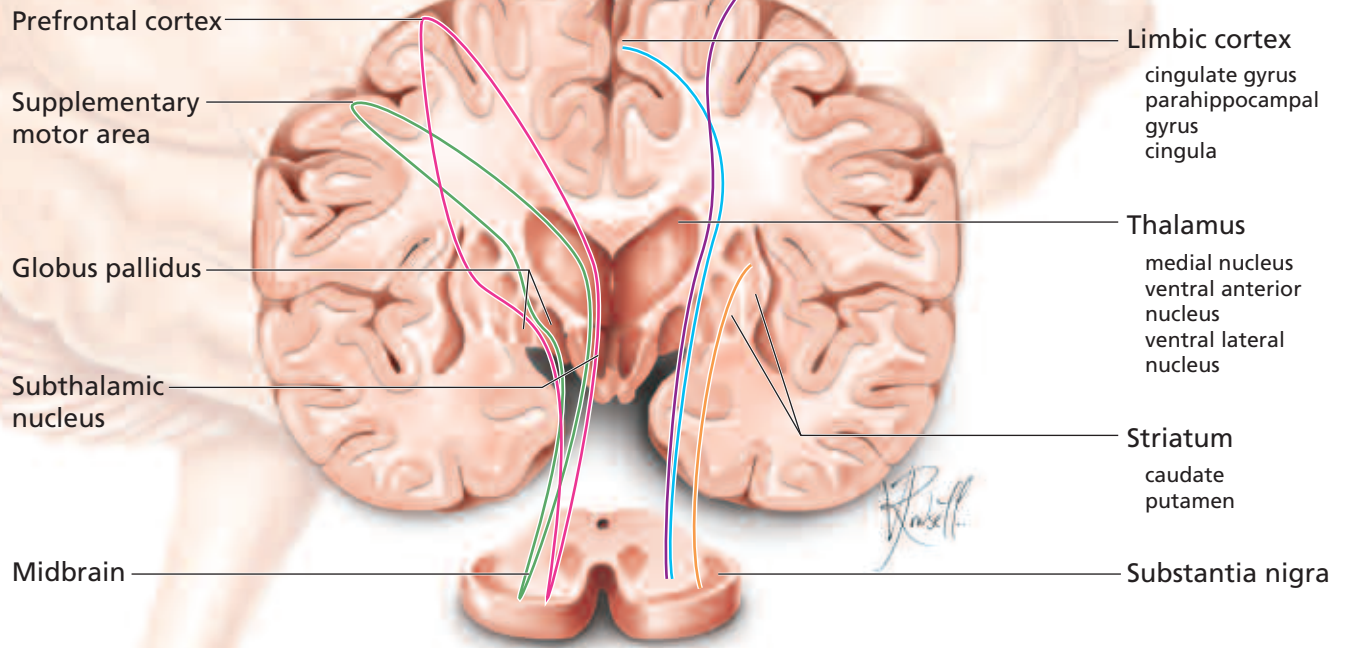


Figure 4

a: Basic Neural Pathways

b: Major Dopaminergic tracts



<b>Green line</b>				
supplementary motor area	globus pallidus	substantia nigra	thalamus	supplementary motor area
<b>Pink line</b>				
prefrontal cortex	caudate nucleus	globus pallidus/ substantia nigra	thalamus	prefrontal cortex

<b>The nigrostriatal (orange line)</b>	
substantia nigra	caudate & putamen
<b>The mesolimbic (blue line)</b>	
ventral tegmental area	limbic system (many components)
<b>The mesocortical (purple line)</b>	
ventral tegmental area	neocortex (prefrontal area)

(substantia nigra to caudate and putamen), the mesolimbic pathway (ventral tegmental area of midbrain to limbic areas of basal forebrain), and the mesocortical pathway (ventral tegmental area of midbrain to frontal and cingulate cortices) (Figure 4B). Destruction of the ascending dopaminergic pathway, blocking of dopamine receptors by drugs, inhibition of dopamine synthesis, or prevention of dopamine storage has been shown to induce akinesia on animals in experimental studies. Drugs that release dopamine or act as dopamine agonists have been shown to increase the motor activity in experimental animals.<sup>50</sup> In Parkinson's disease (PD), the striatonigral outflow does not function normally because of the degeneration of the dopaminergic cells in the substantia nigra. The SMA appears to be the major target of a disordered nigrostriatal-thalamic outflow in PD. The striatum receiving inadequate dopaminergic stimulation results in functional deafferentation of the SMA and thereby gives rise to a defect in motor programming.

Results for the use of dopaminergic agonists in AM have been varied, which may be due to the site of the lesion giving rise to the AM. In one study of four patients who had global akinesia followed by hypokinesia, bradykinesia, and hypometria due to anterior cerebral artery infarction with damage to the SMA, there was poor response to dopamine agonists.<sup>51</sup> A patient with AM following bilateral damage to the anterior hypothalamus responded to treatment with bromocriptine, a direct dopaminergic receptor agonist.<sup>52</sup> The reason for this response, according to the investigators, was that the lesion was anterior to the site at which the nigrostriatal fibres diverge from the median forebrain bundle.

AM is a clinical syndrome, and the lesions implicated are in the mesencephalic-frontal activating system, which is a dopaminergic pathway. However, it has different etiologies and pathologies that are liable to be induced by diverse localized lesions, and as such, there is no one treatment, pharmacological or non-pharmacological, for AM.

### Use of Communicator Devices

One major source of disability in chronic neurological disorders in patients with pseudobulbar palsy is impaired communication. For the replacement of the voice in anarthritic and severely dysarthritic patients there are communication devices to augment other forms of communication therapy. The Canon communicator is like a mini-typewriter with typed messages on strips of paper. Patients unable to use their hands can use an eye communicator.

### Conclusion

Mutism is a neuropsychological disorder and is not uncommon in older adults. It is often mistaken for locked-in syndrome, severe depression, or persistent vegetative state. Mutism is both a symptom and a syndrome. It is often associated with such diverse conditions as advanced Alzheimer's disease, frontotemporal dementias, and certain other psychiatric and psychological disorders. When akinesia occurs concomitantly, the term akinetic mutism is used. Akinetic mutism has a number of causal factors with varied pathology. All of its manifestations can be explained by focal or diffuse brain lesions causing damage to the frontal lobe and/or interruption of the complex frontal subcortical circuits and frontal diencephalic brain stem system. A trial with dopaminergic therapy is justifiable in patients with AM associated with vascular lesions. Communicator devices are available to augment communication in patients with anarthria or severe dysarthria. ◆

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