Review Article

Catatonia: Towards an Integrated Neuropsychiatric Approach

Jyoti Prakash, H RA Prabhu, Kalpana Srivastava, P S Bhat, R Shashikumar
Department of Psychiatry, Armed Forces Medical College, Pune

History

Catatonic state stands out as one of the most puzzling condition in psychiatric practice till date. While Karl Ludwig Kahlbaum[1] described it to be due to a specific disturbance in motor function in mania, depression and psychosis ending in dementia, Emil Kraeplin[2] incorporated catatonic features in dementia precox, an earlier name for schizophrenia and suggested it to be due to mental blocking. Bleuler[3] described catatonia to be a subtype of schizophrenia only till Morrison[4] reawakened association between catatonia and mood disorder in mid 1970s, a view which got support from the findings of Abrams and Taylor[5, 6] later. Gelenberg[7] worked on Catatonia and found it to be associated with several neurological and general medical conditions, which was substantiated by Fink and Taylor subsequently[8]. Gjessing[9] gave the concept of Periodic Catatonia. However regardless of these findings because of prominence of behavior as a problem, its management has been largely under the care of psychiatrists.

Definition

Catatonia in Greek means to stretch tightly. It has been defined as a state of apparent unresponsiveness to external stimuli in a person who is awake and is associated with changes in thought, mood and vigilance. It is difficult to differentiate from diffuse encephalopathy and non convulsive status epilepticus[10].

Nosology

Catatonia is a syndromic state and there is no separate classification for it in medical literature. In DSM IV, it is a specific subtype of schizophrenia requiring minimum of two criteria for diagnosis. It is also a specifier in mood disorder which again required minimum of two criteria. As a specifier for catatonia due to general medical condition it required only one criterion. In ICD 10 it features as a subtype of schizophrenia and as organic catatonic disorder.

Epidemiology

Most of the studies on catatonia have been done in psychiatric patients. Prevalence of catatonia varied anywhere from 7.6%-38% among psychiatric inpatients and constitutes 10% of acutely ill psychiatric patients. Gender distribution was found to be 1.3:1 (female versus male). It was found to be more common in India than in Europe and North America[11]. The frequency of catatonia in specific races is unknown. Although rare in children, catatonia has been reported in adolescents and adults. The prognosis in adolescents is poor. Adolescents with catatonia experience striking morbidity and mortality[10]. Frequency of catatonia is unknown in general population. Incidence of catatonia seems to be falling dramatically and literature reveals significant reduction in incidence of catatonia from 6% to 0.5% over last one century [12].

Symptomatology

Researchers have described more than 40 symptoms of Catatonia. Some of these are immobility, mutism, *gegenhalten* (opposition) automatic obedience, ambitendence, posturing, stupor, stereotypy, catalepsy, *mitgehen*, (extreme form of cooperation), *mitmachen*, (a form of cooperation), echophenomenon, echolalia, echopraxia etc.[10]. In this background there is a thinking of spectrum disorder- catatonic spectrum. Catatonic spectrum would include various other features like whisper/ robotic speech, unexplained

foreign accent, tiptoe walking/ hopping, rituals, mannerisms which are not usually identified as signs of catatonia. Robert and Morgan has described Grasp reflex as a secondary feature of catatonia[10]. Most common signs of catatonia are mutism, posturing, negativism, staring, rigidity and echophenomenon.[13].

Bone of contention

The present concept of the catatonia leaves room for many questions. There is too much of overlap of symptoms. Not all stupurose & mute patients are suffering from catatonia, manic patients may have purposeless movements and autistic features may overlap. Motor and movement abnormalities are seen in many medical, neurological and psychiatric disorders. Should catatonia be classified as separate syndrome as delirium has been? Do the criteria for catatonia need to be modified?[11]. As there are no duration specifiers (Several to 24 hours), should one be more precise in the duration criteria?

Proposed Diagnostic Criteria for Catatonic Syndrome

Researchers have proposed diagnostic criteria for the catatonic syndrome. It entails immobility, mutism or stupor of at least one hour duration associated with at least one of the following: catalepsy, automatic obedience or posturing observed or elicited on more than two occasions. In the absence of immobility, mutism or stupor, at least two of the following observed or elicited on more than 2 occasions: stereotypy, echopheno-menon, catalepsy, automatic obedience, posturing, negativism, gegnhalten,(opposition), ambitendency [11].

Catatonia: Forms and subtypes

Taylor & Fink[11] emphasized that catatonia should be classified as an independent syndrome with the following subtypes: non-malignant, delirious and malignant. The non-malignant type refers to the classic features first described by Kahlbaum, delirious type includes delirious mania, and the malignant type includes lethal catatonia, neuroleptic malignant syndrome and serotonin syndrome. Van Den Eede and Sabbe[14] have proposed an alternative classificatory system. They divided catatonia broadly into non-malignant and malignant types, with each further divided into retarded and excited subtypes. In their system, classic catatonia (Kahlbaum syndrome), delirious mania, neuroleptic malignant syndrome and lethal catatonia would respectively be examples of the non-malignant retarded, non-malignant excited, malignant retarded and malignant excited subtypes respectively. A further classification, used by the Wernicke– Kleist– Leonhard school of psychiatry identifies two main types of catatonia – systematic and periodic[15]. Periodic catatonia, according to Stober et al[16], is the first subtype of schizophrenia with confirmed genetic linkage, the susceptibility site being 15q15. Meyer[17] also reported an autosomal dominant pattern of familial catatonia. Leonhard[18] differentiated chronic catatonia, on the basis of the speech abnormalities present, into speech-prompt and speech-sluggish (speech inactive) types. A specific category of autistic catatonia has been suggested for catatonia occurring in people with developmental disorders[19]. Ictal catatonia, in which the seizure manifests itself as catatonia, is postulated to be due to involvement of the limbic system[18].

Course

Catatonia is an episodic event with periods of remission. Studies report recovery rates from 12% to more than 40% regardless of the treatment administered. A response to benzodiazepines has been reported in more than 70% of patients with catatonia who undergo treatment. Failure to institute treatment early in the course of the condition is associated with a poor prognosis[11]. In general, the prognosis for the acute catatonic phase seems to be good, but the long-term prognosis probably depends on the underlying cause of the catatonia[18].

Differential diagnosis

As compared to quantum of work done in psychiatric patients about catatonic symptoms, lack of research of such symptoms in general medical conditions is quite glaring. In psychiatry though traditionally linked to schizophrenia, catatonia has been seen more commonly associated with mood disorders[20].More than half of the catatonics have Bipolar affective disorder. In 50% of patients, catatonia begins with depressive episode, 25% of catatonia meets criteria for mania and 10% to 15%

catatonics meet criteria for schizophrenia. Other psychiatric disorders which can have catatonia are acute stress disorder, anorexia nervosa, autistic disorder, acute psychosis, dissociative disorder, somatoform disorder etc. General medical causes of catatonia may be many. Metabolic disorder (Carbon Monoxide and tetraethyl lead poisoning, hypercalcemia, hypothermia, hyponatremia, renal failure, uremia, acute intermittent porphyria, homocystinuria, Tay sachs disease, hepatic failure etc), endocrinopathies (hyperparathyroidism, hyperthyroidism, Addison's disease, SIADH, carcinoid syndrome, Sheehan syndrome, diabetic ketoacidosis etc), infections (post encephalitic state, herpes simplex encephalitis, TB meningitis, HIV infection, meningo-encephalitis, septicemia, neurosyphilis, Von economo encephalitis, post encephalitic parkinsonism etc), drugs (antipsychotic drugs, illicit recreational drugs, benzodiazepine withdrawal, dopaminergic withdrawal, opiate intoxication, neuroleptic malignant syndrome etc), neurological (non convulsive status epilepticus, Parkinsons disease, bilateral globus pallidus disease, thalamic & frontal lobe lesion, frontal lobe disease, head injury, Huntingtons disease, hydrocephalus, Wilson disease, corpus callosum or 3rd ventricle tumour, multiple sclerosis, cerebellar catalepsy, temporal lobe haemorrhagic lesion, frontal lobotomy etc) and cerebrovascular conditions (cerebral infarct, sub arachnoid haemorrhage, sub dural haemorrrhage, cortical venous thrombosis, basilar thrombosis and other cerebro vascular accidents)[11].

Pathophysiology

Etiology of catatonia symptoms is unclear. There are several hypothesis- some blaming neurodevelopmental defects, others blaming altered or abnormal reactivity of receptor functions[11, 21-23]. Imaging studies have suggested that there is a altered ventricular-brain ratio in CT scanning of brain.[22] cerebral blood flow (CBF) studies on SPECT have suggested decreased blood flow in right lower inferior prefrontal & right parietal cortex. PET studies have shown bitemporal hypometabolism, altered laterality during motor activation, problems in online processing & monitoring and deficits in right OFC activation & abnormal OFC- premotor/ motor connectivity during negative emotional stimulation[22, 24-26]. Neuropsychological tests have pointed to the possibility of specific deficits in visuospatial attention (involving right parietal cortex) and emotionally guided intuitive decisions (involving orbitofrontal cortex). In animal model it was seen that amantadine (NMDA antagonist) reverses bulbocapnine (D2 receptor antagonist) induced catatonia and GABA-A antagonist injection produced catatonia like picture.[22]. Autopsy findings have revealed lesions of sylvian fossa and 2 & 3 frontal gyri.[1]

Proposed dysfunction

Georg Northoff a neurologist, based on his intensive research and imaging studies proposed the catatonia to be due to dysfunction of Cortico-cortical modulation (circuit involving orbitofrontal,prefrontal and parietal cortex) and top down modulation (circuit involving orbitofrontal cortex and basal ganglia). Models were proposed for the various catatonic signs. Akinesia (deficit in execution of movement) was related to down regulation of motor loop caused by GABA. Effective connectivity from OFC to premotor/ motor cortex was significantly reduced during emotional motor stimulation[22]. Posturing was seen to be due to alteration in right parietal cortical function causing deficit in termination of movement and visuospatial ability[21,26]. Motor agnosognosia was found closely related to dysregulation of functional network activity in ventrolateral prefrontal cortex (VLPFC), DLPFC and post parietal cortex in right hemisphere. Mutism & stupor (deficits in verbal & nonverbal contact) are attributed to deficit in OFC activation during negative emotional processing and consequent disturbance in the cortico-cortical circuit. Mutism is proposed to be due to high activity in affective part with reciprocal suppression of motor part of anterior cingulate (Anterior cingulate has affective, cognitive & motor part), whereas secondary dysregulation of medial prefrontal cortex, leads to Stupor[22, 27]. Northoff [22] further brought out that the similarities and differences between Parkinson's disease and catatonia may be accounted for by distinct kinds of modulation between cortico-cortical and cortico-subcortical relations. Catatonia can be characterized by concurrent motor,

emotional, and behavioural symptoms. The different symptoms may be accounted for by dysfunction in orbitofrontal-prefrontal/parietal cortical connectivity. Where motor symptoms of catatonia have been attributed to top down modulation of basal ganglia by GABAergic mediated orbitofrontal circuits, motor symptoms of parkinson's disease may be attributed to bottom up modulation of cortical circuits due to basal ganglia dysfunction. Clinical differences with respect to emotional and behavioural symptoms may be related with involvement of different cortical areas, that is, orbitofrontal/parietal and premotor/motor cortex implying distinct kinds of modulation – "vertical" and "horizontal" modulation, respectively. (Figure 1) In the light of above discussion, it is prudent to look at catatonia as a phenotypical expression of corticostriato thalamocortical pathway defects seen in various psychiatric, neurological and general medical conditions. The nature of presentation of symptomatology is probably contingent on the specific site or pathway affected in a particular patient. Should one continue with the artificial divide between neurology-psychiatry when dealing

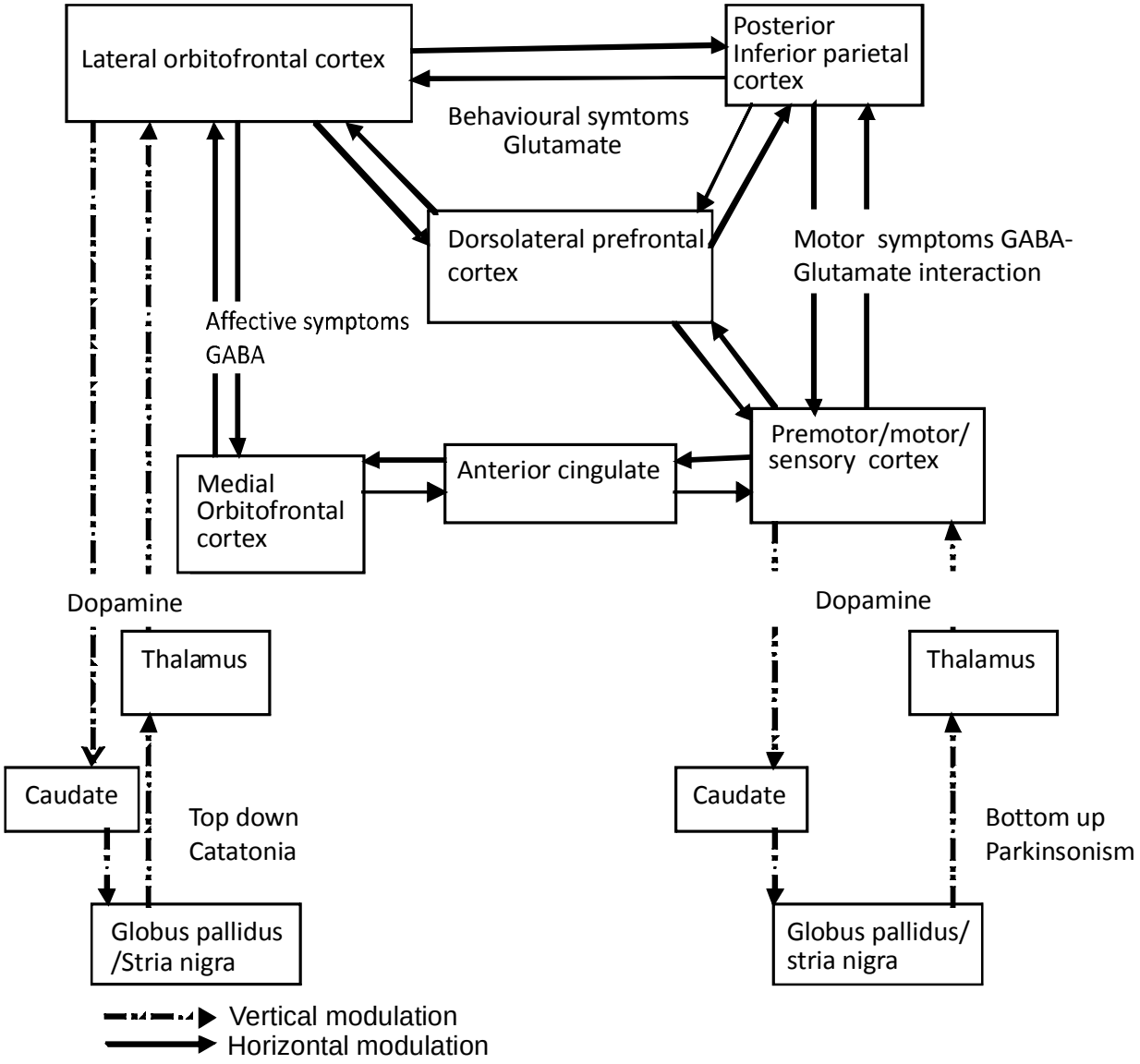

Fig 1: Proposed neurological dysfunction in Catatonia vis-a-vis Parkinsonism (top down and bottom up approach (Courtesy- Northoff G. What catatonia can tell us about "top down modulation": a neuropsycvhiatric hypothesis. Behavioural and brain sciences.2002; 25:555-604)

with catatonia in patients merely because of prominent involvement of volitional motor activity is a moot question. On the lines of delirium it appears prudent to consider catatonia as a separate syndromic entity where the different symptoms have come together in varying frequency. This helps in uniformity of approach in managing the patients of catatonia.

Management

The cornerstone of management of catatonia is identifying the primary cause. Investigations are done as per protocol which includes complete blood count, serum electrolytes, liver function tests, CPK, CT Scan or MR Brain, EEG, serum Iron (for Neuroleptic Malignant Syndrome), lumbar puncture and others based on suspected etiology[10]. Identifying emergencies like neuroleptic malignant syndrome, encephalitis, nonconvulsive status epilepticus, acute psychosis is important. Supportive interventions include fluid, nutrition and basic life support. Prevention of complications like hyperthermia, exhaustion, electrolyte disturbance, injury etc. is looked into.

Varous rating scales are available for assessment of catatonia. The Bush–Francis Catatonia Rating Scale appears to be the most widely used instrument. This scale has 23 items and a shorter, 14-item screening version[31] Modified Rogers Scale (MRS), has also been validated [32]. Peralta and Cuesta have postulated that the presence of three or more of the following 11 signs constitutes a diagnosis of catatonic syndrome:immobility/stupor, mutism, negativism, oppositionism, posturing, catalepsy, automatic obedience, echophenomena, rigidity, verbigeration and withdrawal.[33] Other scales in use are those by Braunig et al[34] and Northoff et al[35] with interrater reliability of 0.96-0.97, and 0.9 respectively.

Treatment of the primary etiology and judicious use of medication for catatonia are required. Non malignant (earstwhile Kahlbaum syndrome) responds well to lorazepam,[28] delirious catatonia responds to high dose lorazepam or ECT[11]. Malignant catatonia is a severe form with fever and dehydration which would require high dose lorazepam or ECT and life support measures. If persisting for more than 4 days it may lead to permanent disability and increased risk of death [13, 29, 30].

In catatonia the goal of treatment is to reduce morbidity and prevent complication. GABAergic bezodiazepine especially lorazepam is preferred because of early onset of action and relatively long half life. Dosage used ranges from 1-16 mg and can be given orally, intravenous and intramuscular (maximum 16mg/day)[36]. Majority of patients (70%) respond to benzodiazepine. Response may be as fast as in 5-10 minutes but may take up to 24 hours. Patients with strong & intense emotions respond well. In febrile catatonia, Risperidone, a serotonin dopamine antagonist antipsychotic with lower affinity for D2 than 5HT2, is preferred in dosage range of 2-6 mg/day[37]. Carbamazepine and Valproate has also been tried but take longer time to give response[10]. Dosage range from 600-1200 mg/day. Amantadine, a glutamate antagonist can be given in the dosage of 100 mg tds, however its dopamine agonist activity may worsen psychosis[38]. Memantine a non competitive antagonist of NMDA has been effective in the dosage of 10 mg BD[39]. ECT has also been found to be effective. Other medications like amobarbital, lithium carbonate, zolpidem, tricyclic antidepressants, atypical antipsychotics, muscle relaxants, dantrolene, reserpine, thyroid harmone have been found to give variable response. Cyclooxygenase (COX) inhibitors have been reported to be protective against catatonia in rats[10].

Conclusion

Catatonia, though less common that earlier times is still a problem to be reckoned with as an emergency. Catatonia as a syndrome or as a spectrum disorder has varied causes and identification of the primary cause is essential to plan treatment. There is a need to bring in clarity in the definition of the syndrome and deal with confusion in nosology. Symptomatic treatment of this condition is quite rewarding. However, further research into and understanding of its psychoneurobiological basis is required to clarify its nosological status. The present level of knowledge though appears to justify its independent status of a syndrome without any artificial segregation into neurological or psychological paradigms.

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