Introduction

Mild cognitive impairment (MCI), a transitional condition between normal aging and dementia, is characterized by the presence of cognitive dysfunctions in the absence of significant functional loss ***(Petersen et al., 2001).***

Its estimated prevalence in the general population is 19% among individuals age >65 and 29% in those age >85 ***(Lopez, et al., 2003).***

MCI is not a stable condition; subjects may progress to dementia, may continue to have MCI or may improve. Studies indicated that, on average 10% of subjects with MCI develop dementia at each year of follow up and half of patients progress to dementia in a span of five years or fewer ***(Bruscoli and lovestone et al., 2004).***

Findings suggest that although the classification of MCI is based on the presence of cognitive impairment, individuals with MCI show a much broader range of symptoms, including motor and psycho-behavioral disturbances ***(Louis et al., 2005).***

The co-occurrence of cognitive and non-cognitive symptoms may indicate a shared pathogenesis, the presence of one increases the odds of having the other ***(Rozzini et al 2007).*** ***Louis et al. (2005)*** have examined the association between mild Parkinsonian signs and MCI, confirming their presence in the clinical phase of the disease preceding dementia, and

reporting that mild Parkinsonian signs are associated in particular with MCI of the amnestic type (aMCI).

Mild Parkinsonian signs including rigidity, changes in axial function and resting tremors occur in 15 to 40% of community-dwelling elderly and are associated with functional impairment ***(Louis et al., 2005).***

Recent data, ***Boyle et al., (2005); Chilovi et al., (2006)*** further confirmed that MCI may be accompanied by extra-pyramidal signs (EPS), both of them could be related to vascular risk factors ***(Tervo et al., 2004).***

Furthermore, some authors have demonstrated that patients with Parkinsonism and MCI have a higher risk of developing dementia than cognitively intact Parkinsonian subjects ***(Janvin et al., 2006).*** And the presence of Parkinsonian features is associated with the severity of MCI ***(Louis et al., 2005).***

Aim of the Work

The primary objective: is to examine the association between Parkinsonian features and MCI.

The secondary objective: is to find out the relation between Parkinsonian features and the severity of MCI.

Parkinsonian Features in the Elderly and their Relation to Cognitive Function

Mild Parkinsonian signs (MPS)(extrapyramidal signs or Parkinsonian Features) including rigidity, changes in axial function, and resting tremor occur in 15 to 40% of community-dwelling older people, and are associated with functional impairment ***(Louis et al., 2005)***.

In longitudinal studies, MPS increase in severity over time ***(Wilson et al., 2002)*** and they are associated with incident dementia ***(Louis et al., 2004)***.

It is unclear whether the emergence of MPS reflects an age-associated decline in nigrostriatal dopaminergic activity or whether these motor signs are due to the presence of emerging dementia or sub cortical cerebrovascular disease ***(Yamanouchi et al., 1997)***.

- ***Causes of Parkinsonian Features:***

The most common cause of parkinsonism is Parkinson's disease (PD). But not everyone who has parkinsonism has Parkinson's disease.

Other causes of parkinsonism include:

- Stroke
- Encephalitis, inflammation of the brain usually caused by infection

- Meningitis, inflammation of the membranes covering the brain and spinal cord.
- Certain medications, such as some antipsychotics and metoclopramide.
- Head trauma, isolated or repeated, such as injuries sustained in boxing.

Parkinson Plus Syndrome:

A) Progressive supranuclear palsy, a rare degenerative brain disorder

B) Multiple systems atrophy, a degenerative disorder that destroys nerve tissue

C) Corticobasal degeneration, a rare neurological disease.

These are group of disorders having parkinsinian features but differ from PD in:

- Lack of response to levodopa/carbidopa (Sinemet) or dopamine agonists in the early stages of the disease.
- Early onset of dementia.
- Early onset of postural instability.
- Early onset of hallucinations or psychosis with low doses of levodopa/carbidopa or dopamine agonists.
- Ocular signs, such as impaired vertical gaze, blinking on saccade, square-wave jerks, nystagmus, blepharospasm, and apraxia of eyelid opening or closure.

- Pyramidal tract signs not explained by previous stroke or spinal cord lesions.
- Autonomic symptoms such as postural hypotension and incontinence early in the course of the disease.
- Prominent motor apraxia
- Marked symmetry of signs in early stages of the disease
- Truncal symptoms prominent
- Absence of structural etiology such as a normal-pressure hydrocephalus (NPH)

(Weiner et al., 2005).

Pathophysiology of Parkinsonian Features:

Pathological studies have demonstrated a rising prevalence of Lewy bodies in the substantia nigra with increasing age in subjects without clinical evidence of PD, and a correlation between this and a reduction in numbers of pigmented neurons ***(Wakabayashi et al., 1993)***.

More direct evidence of functional change in the extrapyramidal system comes from the finding of an age-related decline in the concentration of tyrosine hydroxylase, one of the enzymes involved in dopamine synthesis, in the caudate nucleus, putamen and nucleus accumbens. Bradykinetic abnormalities are most strongly correlated with reduced nigrostriatal F-6-fluorodopa uptake in a positron emission tomography ***(Vingerhoets et al., 1997)***.

- ***Differential diagnosis of Parkinsonian Features:***

- Multiple system atrophy: initially appears as parkinsonism but has more rapid pulse and is characterised by an inability to look down voluntarily.

- Benign essential tremor: far more common, tremor is worse on movement and rare while at rest. No rigidity or bradykinesia.

- Huntington's disease: can present earlier with rigidity instead of chorea when parkinsonism not expected.

- Wilson's disease: earlier onset with characteristic Kayser–Fleischer rings and hepatitis.

- Progressive supranuclear palsy: characterised by paresis of conjugate gaze with initially problems looking up and down on request, advancing to difficulty in following objects up and down.

- Corticobasal degeneration: manifest by obvious signs of cortical dysfunction, e. g. apraxia, dementia and aphasia.

- Creutzfeldt-Jakob dementia: usually apparent with myoclonic jerking, ataxia and pyramidal signs common.

- Multi–infarct dementia – this is characterised by cognitive impairment, spasticity, and extra–pyramidal signs.

- Pick Disease – affects the frontal and/or temporal lobes. Level of consciousness is not affected, unlike Alzheimer's, Parkinsonism is usually mild.

- Drug or toxin induced – numerous drugs or toxins may cause tremor, notably selective serotonin reuptake inhibitors, caffeine, amphetamins, beta–adrenergic blockers, tricyclics, carbon monoxide, carbon disulfide, manganese, and lithium.

- Cerebellar tremor – this presents as a unilateral or bilateral, low–frequency intention tremor. It may be caused by stroke, brainstem tumor, or multiple sclerosis.

- Pyschogenic tremor: the tremor is variable, increases under direct observation, decreases with distraction, and changes with voluntary movement of contralateral limb.

- Acquired immunodeficiency syndrome AIDS can sometimes lead to the symptoms of Parkinson's disease, due to commonly causing dopaminergic dysfunction

- Paraneoplastic syndrome: Neurological symptoms caused by antibodies associated with various cancers.

(Aminoff et al., 2004)

Different Parkinsonian features are:

I. Bradykinesia

It is one of the principal features of parkinsonism, and it is probably, for the patient, one of the most distressing tiring and disabling features of their disease ***(Nutt et al., 2005)***.

Bradykinesia is literally slowness of movement but also includes a paucity of spontaneous movements and decreased amplitude of movement. Bradykinesia is also expressed as

micrographia (small handwriting), hypomimia (decreased facial expression), decreased blink rate, and hypophonia (soft speech) ***(Langston et al., 2006)***.

Small muscle movement is affected first, and often unilaterally. Bradykinesia is most easily demonstrated by asking patient to tap their forefinger on their thumb. Normally an individual will be able to tap at ٤ or ٥ Hz; the bradykinesic individual may only be able to manage ١ Hz or less ***(Nutt et al., 2005)***.

Pathophysiology:

Weakness, tremor and rigidity may contribute to but do not fully explain bradykinesia. It is argued that bradykinesia results from a failure of basal ganglia output to reinforce the cortical mechanisms that prepare and execute the commands to move or due to reduced dopaminergic function. The cortical deficit is most apparent in midline motor areas. This leads to particular difficulty with self-paced movements, prolonged reaction times and abnormal pre-movement electro-encephalogram (EEG) activity ***(Berardelli et al., 2001)***.

Movements are often performed with normally timed electromyelogram (EMG) bursts but the amount of EMG activity is underscaled relative to the desired movement parameters. There are also abnormalities in sensory scaling and sensorimotor integration ***(Berardelli et al., 2001)***.

The brain appears to be able to compensate to some degree for the basal ganglia deficit. There is overactivity in the

lateral premotor areas during task performance and movements can be speeded by giving sensory cues. Attention to movement is also beneficial. However, it is proposed that the engagement of compensatory processes may also lead to reduced performance in other tasks. For example, patients' problems in performing more than one task at the same time could result from lack of sufficient resources both to compensate for their basal ganglia deficit and to run two tasks simultaneously ***(Rothwell et al., 2001)***.

Treatment of bradykinesia:

Off-treatment: it means 12 hours without the effect of the drug

(1) Anticholinergics and Dopamine agonists:

(2) Pallidotomy (producing lesion in globus pallidus):

In terms of bradykinesia, pallidotomy produces an improvement of ~30% in Off-period symptoms on the side contralateral to the lesion that is sustained for 2 years or more after the operation. There is less effect on measures of postural stability or on the best On-therapy scores **(Bronstein et al., 1999)**.

(3) Deep brain stimulation:

Pallidal stimulation has similar effects, but is considered to be potentially safer in terms of adverse cognitive side-effects if bilateral procedures are performed ***(Brown et al., 1999).***

Chronic stimulation of the subthalamic nucleus may be more effective than pallidotomy or pallidal stimulation in

improving Off-treatment bradykinesia scores. Improvements in balance and posture are also more evident. It is usually possible to reduce the dose of L-dopa, and this ameliorates problems with dyskinesias ***(Limousin et al., 1998)***.

II. Tremors:

Parkinsonian tremor is 4–6 Hz tremor of variable amplitude, maximal when the limb is at rest, and decreased with voluntary movement. It is typically unilateral at onset. This is the most apparent and well-known symptom, though an estimated 30% of patients have little perceptible tremor; these are classified as akinetic-rigid. It may precede the rigidity of the condition by a time course of months to years **(*Jankovic et al., 2008).***

Pathogenesis:

In Parkinson's disease, it is known that the death of nigrostriatal neurons leads to abnormal intermittent oscillations in the neurons of the motor cortex, basal ganglia, and thalamus and that these abnormal oscillations can produce tremor ***(Elble et al., 1996)***.

The exact cause of the oscillations is unclear; however, the cerebellum is involved in control of the Parkinsonian rest tremor ***(Deushl et al., 1999)***.

Primary features include:

- May be unilateral
- Aggravation by resting, walking, and the use of other limbs.
- The tremor disappears when the patient is asleep.

- A degree of voluntary control over the tremors (the patient may attempt to control it by tightly gripping a rolled up newspaper or another object).
- Typically, the tremor could be either of; a flexion–extension elbow movement, a pronation–supination of the forearm, or a pill–rolling finger movement.

(Jankovic et al., 2008).

Distribution of tremors:

Rest tremor in patients with PD can involve the lips, chin, jaw and legs but, unlike essential tremor, rarely involves the neck/head or voice. Thus a patient who presents with head tremor most likely has essential tremor, cervical dystonia, or both, rather than PD. Some patients also report an "internal" shaking that is not associated with a visible tremor ***(Shulman et al., 1996)***.

Tremors of PD is differentiated from that of essential tremor:

Feature	Parkinson's disease	Essential tremor
Age at onset (y)	5٥-75	١٠-80
Family history	–/+	++
Tremor frequency (Hz)	4-6	٥-10
Tremor characteristics	Supination–pronation	Flexion–extension
Influencing factors		
Rest	Increases	Decreases
Action	Decreases	Increases
Mental concentration	Decreases	Increases
Writing	Decreases(micrograp-hia)	Increases (tremulous)
Walking	Increases	Decreases
Alcohol	—	Decreases
Kinetic tremor	–/+	Yes
Limb tremor	Asymmetric	Symmetric
Distribution other than limbs	Face, jaw, lips, chin	Head, voice
Neuroimaging—dopamine-rgic system	Marked dopaminergic deficit	Mild dopaminergic deficit
Mid-brain sonography	Marked hyper-echogenicity	Mild hyper-echogenicity
Neuropathology	Nigrostriatal degeneration, Lewy bodies	Mild cerebellar degeneration, Lewy bodies in the substantia nigra, brainstem and cerebellum in some cases
Treatment	Anticholinergics, amantadine, dopaminergic drugs, deep brain stimulation	Alcohol, beta-blockers, primidone, topiramate, gabapentin, botulinum toxin, deep brain stimulation

(Shulman et al., 1996)

Treatment of Parkinsonian tremors:

In patients with early Parkinson's disease in whom tremor is the only manifestation with no functional limitation. The use of medication is thus essential only when other symptoms are present, and all anti-Parkinsonian drugs must be started at a small dose and gradually increased in strength and frequency ***(Miller et al., 1986).***

1.Anticholinergic agents:

Anti-cholinergics constitute a reasonable first line of treatment in Parkinson's disease. Potential adverse effects include urinary retention, confusion, and hallucinations; they also can worsen glaucoma in older patients.

2.Amantadine: When anticholinergic agents are inadequate, amantadine can be added.

3.levodopa-carbidopa: If maximum tolerable dosages of both drugs are unsuccessful in treating the patient, they are discontinued and levodopa-carbidopa is begun.

One of the problems of using levodopa-carbidopa is the fluctuation_between high and low blood levels of the drugs, leading to on-off phenomenon and dyskinesia. To avoid this, smaller doses can be given at regular intervals.

4.Dopamine agonists:

-Bromocriptine can help in the management of on-off phenomenon and decrease the dose of levodopa.

5.Others: Recent studies have found apomorphine and clozapine useful in the treatment of Parkinsonian tremor.

(Friedman et al., 1997).

III. Parkinsonian gait:

Gait disorders are common in elderly populations and their prevalence increases with age. At the age of 60 years, 85% of people have a normal gait, but at the age of 85 years or older this proportion has dropped to 18% ***(Sudarsky et al., 2001)***.

Normal gait requires a delicate balance between various interacting neuronal systems and consists of three primary components: locomotion (including initiation and maintenance of rhythmic stepping), balance; and ability to adapt to the environment. Dysfunction in any of these systems can disturb gait, but virtually all levels of the nervous system are needed for normal gait ***(Morton et al., 2004).***

Parkinsonism gait is the manner of walking that is seen in patients with parkinsonism. Characteristics of this gait are: hesitation in starting, akinesia, small, shuffling, hurried steps, festination (combination of stooped posture, imbalance, and short steps). It leads to a gait that gets progressively faster and faster, often ending in a fall, lack of normal arm swing, kinesia paradoxical. With the aid of a walking frame, the Parkinsonian patient is often able to initiate a normal walking cycle ***(Nutt et al., 2005).***