Cognitive Impairment in Parkinson Disease Clinical, Neuropsychological and Proton Magnetic Resonance Spectroscopy Study

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ABSTRACT

Objective: *This study aimed at assessing the cognitive impairment in PD patients on formal neuropsychological testing and its correlates with the neurochemical markers detected by using the proton Magnetic Resonance Spectroscopy (^{1}H-MRS).* ***Methods:*** *Twelve patients with Parkinson Disease Dementia (PDD), twelve patients with PD and ten normal control subjects were included in this study. Dementia was evaluated by M.M.S.E., Blessed dementia rating scale, DSMIV. Parkinsonian patients were clinically evaluated by Hoehn and Yahr staging, UPDRS and Schwab and England Score. Neuropsychological assessment was performed by using the CAMCOG scale, Mood evaluation using Hamilton depression scale. Brain metabolites ratios were measured in the left temporo-parietal area, occipital area and basal ganglia using ^{1}H-MRS.* ***Results:*** *Patients with PDD had significantly more disease severity, higher grading of dementia and more impairment of daily activities than patients with PD and control subjects. PDD patients differ significantly than other groups in all neuropsychological measures studied, however, PD patients differ significantly than control subjects in measures for language, memory and perception only. Moreover, the disease duration and severity significantly correlated with the grading of dementia and daily activities, and measures for language and calculation only. Significant reduction of NAA/Cr and NAA/MI ratios in left temporo-parietal area and occipital area of PDD patients was found compared with other groups. Moreover, there was a significant correlation between reduced NAA/Cr ratio and impairment in measures of language, memory and attention.* ***Conclusion:*** *Clinical evaluation of cognitive functions using formal neuropsychological testing and the reduction of NAA in cortical areas of the brain by the use of ^{1}H-MRS and their correlates are helpful tools in evaluating PD patients developing dementia.*

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INTRODUCTION

The prevalence of dementia in Parkinson diseases is estimated to be 20 to 40% and the frequency increases with age[1-3]. Moreover, patients with idiopathic Parkinson disease (PD) are 6 times more likely than healthy elderly people to develop dementia[4].

Cognitive impairment is relatively frequent in Parkinson disease (PD) especially at an advanced stage, in its severe form, it may be global and meet the Diagnostic and Statistical Manual of Mental Disorders (4th ed. DSM-IV) criteria for dementia[5] even in absence of overt dementia, mild cognitive slowing is common feature of PD[6] with specific impairments in executive function, visual memory and visuo-spatial abilities[6-10].

Proton Magnetic Resonance Spectroscopy (^{1}H-MRS) allows the non invasive, in vivo measurement of brain metabolism and has been widely applied to study disease mechanisms in the CNS[11,12]. Four major hydrogen containing metabolites may be identified and measured by means of ^{1}H-MRS. One of these is N-acetyl aspartate (NAA)[13] which is present in functioning neurons and their processes but absent in mature glial cell cultures[14,15] and has been taken as a putative neuronal markers. Other metabolites that can be identified are Creatine (Cre) related to general metabolism, Choline-containing compounds (Cho) which may be altered in processes with increased membrane turnover, and

Myoinositol (MI) which is mainly contained in glial cells[15,16].

In Parkinson disease, ^{1}H-MRS showed a reduction in the NAA/Cre ratio in the putamen[17] and in the temporo-parietal region[16,18]. In another study on patients with Parkinson disease with dementia (PDD), there was increased levels of lactate/NAA in the occipital lobe in patients with PDD and PD relative to controls[19].

Based on these initial findings, the aim of this study was to assess the cognitive impairment in PD patients on formal neuro-psychological testing, and its correlation with the neurochemical markers detected by ^{1}H-MRS.

SUBJECTS AND METHODS

Subjects:

Thirty-four subjects aged between 60 and 79 years were included in this study and were divided into 3 groups. The Parkinson Disease Dementia group (PDD) consisted of 12 patients (7 males and 5 females) with an initial diagnosis of idiopathic PD, who years later developed cognitive decline and fulfilled dementia criteria. Their ages ranged between 61 and 79 years (with a mean 71.3±7.92 SD). The Parkinson Disease group (PD) included 12 patients (8 males and 4 females) with idiopathic PD who did not meet dementia criteria. Their ages ranged between 60-79 years (with a mean 72.5±6.97 SD).

The control group, consisted of 10 individuals with no history of neurologic disease (6 males and 4 females). None of these control subjects meet dementia criteria or had Parkinsonism. Their ages ranged between 60 and 78 years (with a mean 71.1±7.21 SD).

Methods:

All subjects in this work were subjected to the following: Thorough history taking with complete general and neurological examination.

I. Diagnosis of PD was done by means of proposed diagnostic criteria for Parkinson Disease[20]. Excluded from the study patients who might have atypical PD syndromes as progressive supranuclear palsy or multiple-system atrophy.

II. Diagnosis of Dementia was done by means of:
- Mini-Mental State Examination (MMSE)[21].
- Blessed dementia rating scale[22].
- The Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV)[23].

Subjects who meet dementia criteria, exhibited MMSE score of less than 23, blessed dementia rating of 1, and fulfilled items in the DSM-IV.

Excluded from the study: Patients having history of stroke, cerebral tumor, traumatic brain injury, epilepsy or psychiatric illness other than depression. Also patients with pacemakers or prosthetic implants were excluded.

III. Clinical evaluation of the PD patients with or without dementia participating in this study was through the following:
1. The Hoehn and Yahr staging[24].
2. Unified Parkinson Disease Rating Scale[25].
3. Schwab and England score[26] for daily activities.

IV. Neuropsychological assessment: through the following:
1. CAMCOG scale[27,28], which is the cognitive part of the Cambridge Examination for Mental Disorders of the Elderly (CAMDEX), a standardized instrument for the diagnosis and grading of dementia. The CAMCOG consists of 67 items and it can be divided in several subscales: orientation, expressive and comprehensive language, memory (remote, recent, and learning), attention, praxis, calculation, abstraction, and perception.
2. Hamilton depression scale[29].

V. Magnetic Resonance Spectroscopy (MRS): had been done for all patients and control subjects. All subjects underwent scanning with a 1.5-T magnetic resonance machine with a head coil. T_1-weighted images in sagittal and coronal planes were obtained for localizing the ^{1}H-MRS voxel. ^{1}H-MRS studies were performed with Lx system automated SV MRS package (proton brain examination/SV) (PROBE/SV). Point

resolved spectroscopy (PRESS) pulse sequence with repetition time (TR) = 2000 Msec, 2048 data points, and 128 excitations were used for the examinations. The single-voxel ^{1}H-MRS scan time is about 5 minutes.

The metabolite intensity ratios were analyzed and automatically calculated at the end of each PROBE / SV acquisition, using the physiologically stable metabolite ratios NAA/Cr, NAA/MI, Cho/Cr, and MI/Cr.

Three different regions (volumes) of interest (VOI) were studied in all patients and subjects: An 8 cm^3 (2X2X2 cm) occipital VOI, prescribed on a midsagittal T_1 weighted image, and was placed below the parieto-occipital sulci and covered both of the medial occipital lobes. A left temporo-parietal (predominantly superior temporal) VOI was prescribed on a coronal T_1-weighted image using a smaller voxel size of 7.2 cm^3 (2X2X1.8 cm). A basal ganglionic VOI in a voxel size 12 cm^3 (3X2X2 cm) was localized on a T_1-weighted image covering as much as possible of the lentiform and caudate nuclei.

RESULTS

Clinical Results:

Various demographic data and clinical variables of all patients and control subjects were shown in Table (1) and revealed that the 3 groups studied (PDD, PD, and control group) did not differ significantly in age, years of education, Hamilton depression inventory score. Similarly patients with Parkinson disease with dementia (PDD) and those with Parkinson disease (PD) did not differ significantly on the mean of disease duration and mean of levo-dopa per day. However, they differed significantly on the mean of Hoehn and Yahr staging, scores of the Unified Parkinson's Disease Rating Scale, means of MMSE score, Blessed dementia rating scale and Schwab and England scale. As those with PDD had significantly more disease severity, and they were worse in mental examination, severity of dementia, and disturbances in activity of daily living.

Neuropsychological Results:

Results of performance on various neuropsychological tests of CAMCOG scale applied in this study were shown in Table (2) and revealed a statistically significant difference among the 3 groups (PDD, PD, and control) in all tests used, as PDD patients were significantly impaired relative to both patients with PD and control subjects in all tests. Moreover, those with PD differ significantly relative to control subjects in tests for language, memory and perception only.

Magnetic Resonance Spectroscopy Results:

Comparing the means and SDs of the ratios of different metabolites (NAA/Cr, NAA/MI, Cho/Cr, and MI/Cr) as determined with 1H-MRS in left temporo-parietal area, occipital area, and basal ganglia of all patient groups and control subjects were recorded and analysis of variance (ANOVA) revealed statistically significant difference between the 3 groups regarding the NAA/Cr and NAA/MI ratios in the left temporo-parietal area and occipital area, being more severely reduced in those with PDD. Again, a statistically significant difference was observed between PDD and PD groups of patients regarding the ratios of NAA/Cr and NAA/MI in the temporo-parietal and occipital areas. Similarly, PD patients differ significantly compared with normal control subjects regarding the NAA/Cr and NAA/MI ratio in the temporo-parietal area.

On the other hand, a non-significant difference was observed among the 3 groups for the ratios of other metabolites (Cho/Cr and MI/Cr). Finally, in the basal ganglia analysis of variance showed no significant difference in the ratios of different metabolites among the 3 groups studied. These results are shown in table (3) and figure (1).

Correlative Results:

Correlation between the clinical variables of the disease (duration, Hoehn and Yahr staging and UPDRS scores) and neuro-psychological results in PDD group was illustrated in Table (4), and revealed a significant correlation between the disease severity and duration and the results of MMSE, Blessed dementia rating scale, Schwab and England scale, tests for memory, and attention/ concentration. Disease severity also

significantly correlated with the measures of language, and calculation.

Correlation between NAA/Cr ratio in the left temporo-parietal area and occipital area and various clinical and neuropsychological variables in patients with PDD was illustrated in Table (5) and revealed a significant correlation between left temporo-parietal and occipital NAA/Cr ratios and language tests scores (motor, verbal, naming, definition, repetition, and verbal fluency), memory tests (recent information, remote information, recognition of pictures, recall of pictures, recognition of words and address and registration), and concentration/attention tests. However, a non significant correlation was observed between NAA/Cr ratio and other clinical and neuro-psychological variables (either for the PD or PDD or both combined). Again, there was no significant correlation observed between any of the clinical and neuropsychological variables in patients with PD and PDD in relation to the basal ganglia NAA/Cr ratio or other ratios recorded (NAA/MI, Cho/Cr, MI/Cr).

Table 1. Demographic data of all subjects and clinical variables of the patient's groups

Demographics and clinical variables	Parkinson's disease with Dementia N.=12	Parkinson's disease N. = 12	Control subjects N. = 10	P-value
Age in years	71.3±7.92	72.5±6.97	71.1±7.21	>0.05
Years of education	9.62±3.91	9.85±5.23	10.25±4.38	>0.05
Hamilton depression inventory score	3.71±3.91	2.1±2.81	0.81±1.23	>0.05
Blessed dementia fating scale	13.6±19	5.9±2.28	2.2±1.31	<0.01**
Disease duration	10.73±5.67	7.64±4.53	NA	>0.05
MMSE score	16.9±5.32	26.31±0.95	NA	<0.01**
Hoehn and Yahr stage	3.51±0.87	2.63±0.69	NA	<0.05*
UPDRS Part I score	6.13±4.31	2.1±1.45	NA	<0.05*
UPDRS Part II score	23.32±11.95	10.64±6.1	NA	<0.01**
UPDRS Part III score	37.47±13.71	25.72±11.92	NA	<0.05*
Levodopa dose mg/day	631±209	645±235	NA	>0.05

Data are mean±SD. * Significant P<0.05.
MMSE = Mini-Mental State Examination. ** Highly Significant P<0.01.
UPDRS: Unified Parkinson's Disease Rating Scale. NA: Not applicable.

Table 2. Neuropsychological tests results in patient's groups and control subjects using the CAMCOG scale.

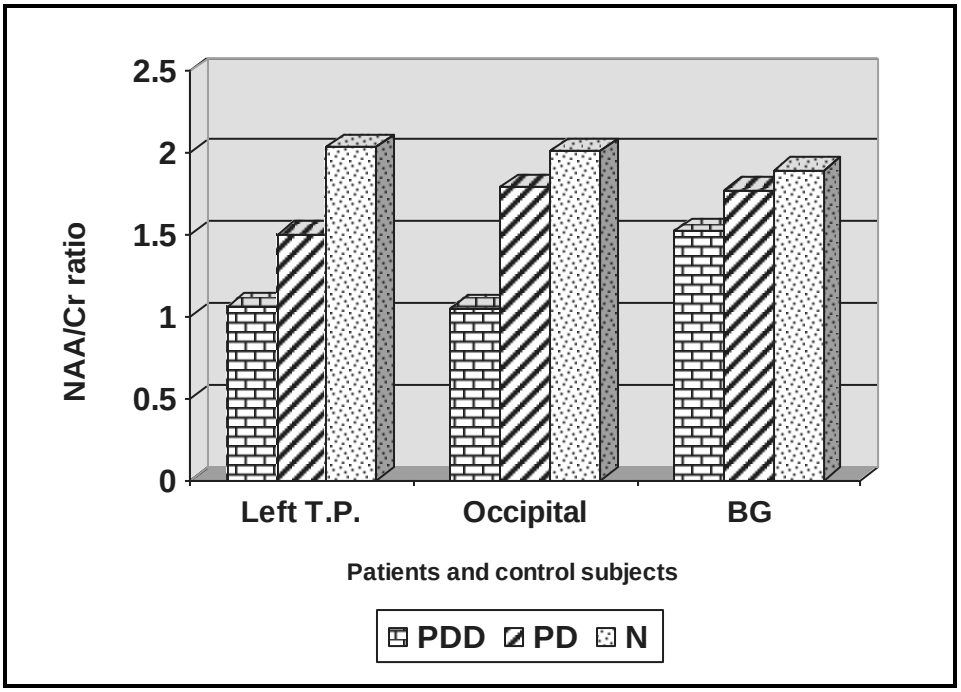
Neuro-Psychological tests	PDD N = 12	PD N = 12	Control subjects N = 10	ANOVA P-value	PD vs PDD P-value	Control vs PDD P-value	Control vs PD P-value
Orientation	4.7±1.3	7.3±0.95	8.5±0.65	<0.01**	<0.01**	<0.01**	>0.05
Language	12.6±1.97	19.4±0.85	24.5±0.92	<0.01**	<0.01**	<0.01**	<0.05*
Memory	14.2±2.2	21.1±2.6	27.3±2.9	<0.01**	<0.01**	<0.01**	<0.05*
Attention/conc	2.7±1.08	4.1±0.31	5.3±0.42	<0.01**	<0.05*	<0.01**	>0.05
Praxis	4.5±0.99	9.5±0.85	9.8±0.92	<0.01**	<0.01**	<0.01**	>0.05
Calculation	0.3±0.48	1.3±0.32	1.7±0.27	<0.01**	<0.01**	<0.01**	>0.05
Abstract think	1.2±0.92	3.6±0.82	3.7±0.79	<0.01**	<0.01**	<0.01**	>0.05
Perception	1.3±0.72	2.9±0.91	5.3±0.82	<0.01**	<0.05*	<0.01**	<0.05*
Recognition	2.8±0.57	5.7±0.92	5.9±0.42	<0.01**	<0.01**	<0.01**	>0.05

*P<0.05 Significant. **P<0.01 Highly significant.

Table 3. Ratios of different brain metabolites on 1H-MRS of the patients groups and control subjects.

Ratios of brain metabolites	PDD (N=12)	PD (N=12)	Control subjects (N=10)
NAA/Cr:			
Lt. temporo-parietal area	1.06±0.24**	1.5±0.17**	2.03±0.34
Occipital area	1.05±0.36**	1.79±0.21	2.01±0.27
Basal ganglia	1.52±0.27	1.77±0.31	1.89±0.37
NAA/MI:			
Lt. temporo-parietal area	2.01±0.39**	2.93±0.41*	3.81±0.43
Occipital area	2.07±0.37**	3.82±0.42	3.92±0.43
Basal ganglia	2.13±0.29	2.24±0.39	2.57±0.42
Cho/CR:			
Lt. temporo-parietal area	1.71±0.31	1.62±0.42	1.67±0.39
Occipital area	1.55±0.37	1.73±0.29	1.7±0.31
Basal ganglia	1.4±0.23	1.53±0.39	1.59±0.42
MI/Cr:			
Lt. temporo-parietal area	1.23±0.09	1.07±0.12	1.2±0.13
Occipital area	1.04±0.11	1.05±0.15	1.2±0.12
Basal ganglia	0.87±0.13	0.89±0.11	0.97±0.09

NAA: N-acetyl-aspartate. MI: Myoinositol. Cr.: Creatine.
Cho: Choline containing compound. *P<0.05 = significant **P<0.01 = highly significant



Left T.P.: left temporo-parietal B.G.: basal ganglia P<0.01 = highly significant

Fig. (1): NAA/Cr ratio in Parkinsonian patients and control subjects.

Table 4. Correlation between the clinical variables of the disease and the neuropsychological variables in patients with PDD

Neuropsychological variables	Clinical Variables					
	Disease duration		Hoehn and Yahr		UPDRS	
	Correl. Coeff.	Sig.	Correl. Coeff.	Sig.	Correl. Coeff.	Sig.
MMSE	-0.612	<0.05*	-0.721	<0.05*	0.695	<0.05*
Blessed Dementia Scale	0.592	<0.05*	0.631	<0.05*	0.671	<0.05*
Schwab and England	-0.597	<0.05*	-0.593	<0.05*	-0.623	<0.05*
Orientation	-0.411	>0.05	-0.321	>0.05	-0.312	>0.05
Language	-0.321	>0.05	-0.613	<0.05*	-0.592	<0.05*
Memory	-0.719	<0.05*	-0.695	<0.05*	-0.613	<0.05*
Attention/Concentration	-0.615	<0.05*	-0.593	<0.05*	-0.609	<0.05*
Praxis	-0.317	>0.05	-0.411	>0.05	-0.329	>0.05
Calculation	-0.179	>0.05	-0.315	>0.05	-0.513	<0.05*
Recognition	-0.295	>0.05	-0.372	>0.05	-0.392	>0.05
Abstract-Thinking	-0.193	>0.05	-0.297	>0.05	-0.325	>0.05
Perception	-0.431	>0.05	-0.401	>0.05	-0.431	>0.05

* P <0.05 = Significant.

Table 5. Correlation between the NAA/Cr ratio in Lt. temporo-parietal and occipital areas and various clinical and neuropsychological variables in patients with PDD.

Clinical and neuropsychological variables	Temporo-parietal area		Occipital area	
	Correlation Coeff.	Sig.	Correlation Coeff.	Sig.
Duration of the disease	-0.021	>0.05	-0.032	>0.05
Hoehn and Yahr stage	-0.024	>0.05	-0.015	>0.05
UPDRS	-0.272	>0.05	-0.305	>0.05
MMSE	0.215	>0.05	0.204	>0.05
Blessed Dementia rating scale	-0.273	>0.05	0.193	>0.05
Schwab and England	0.214	>0.05	0.235	>0.05
Orientation	0.237	>0.05	0.247	>0.05
Language	0.751	<0.05*	0.665	<0.05*
Memory	0.592	<0.05*	0.573	<0.05*
Attention and Conc.	0.613	<0.05*	0.642	<0.05*
Praxis	0.127	>0.05	0.112	>0.05
Calculation	0.411	>0.05	0.421	>0.05
Recognition	0.487	>0.05	0.484	>0.05
Abstract-thinking	0.271	>0.05	0.267	>0.05
Perception	0.493	>0.05	0.321	>0.05

* P<0.05 Significant.

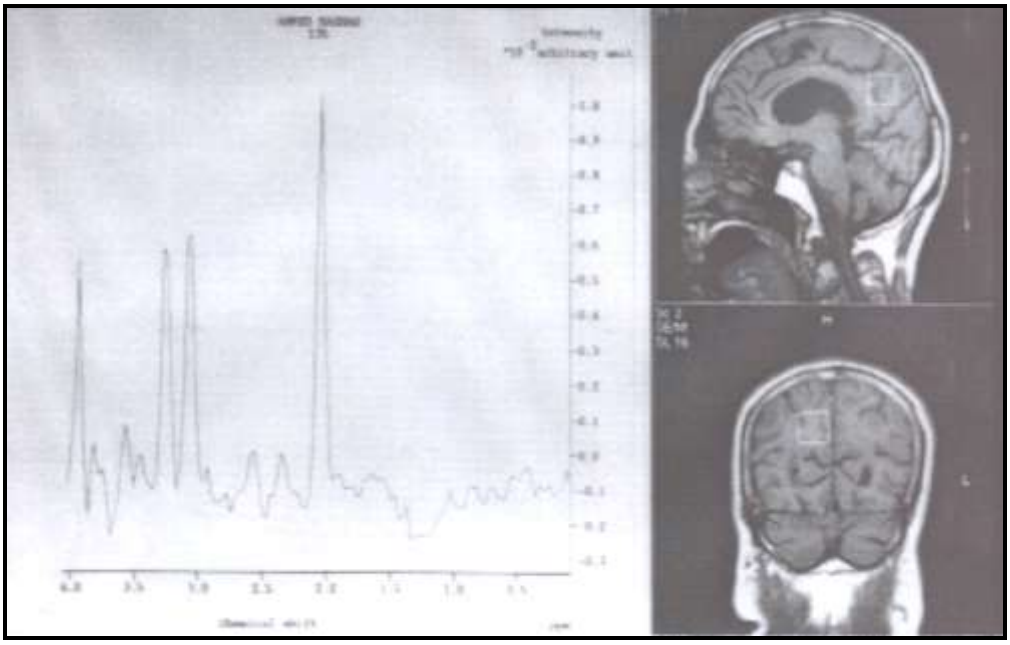


Fig. (2): MRS of the left temporo-parietal area.

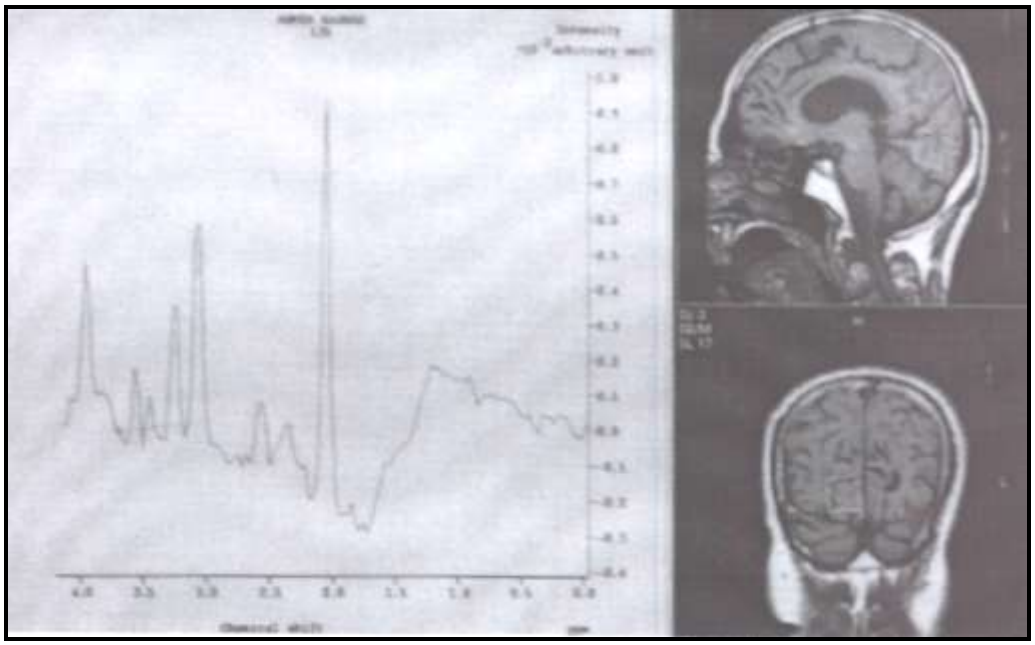


Fig. (3): MRS of the occipital area

MRS of 2 patients with PDD showing reduced NAA/Cr ratio in the

left temporo-parietal area (Fig. 2) and occipital area Fig. (3).

DISCUSSION

The results of this study revealed that patients with Parkinson's disease with dementia (PDD) had significantly an impaired performance in all aspects of neuropsychological testing used than those with Parkinson's disease (PD) without dementia and control subjects, with marked deficits in attention, executive, visuo-spatial and constructional abilities. A finding which was supported by others[4,15]. Moreover those with PD differ significantly than control subjects in the measures of language, memory and perception.

Pathological processes contributing to these cognitive impairments in PD may include striatal and extra-striatal dopamine deficiency, ascending nor-adrenergic, cholinergic and serotonergic cortical deficits and the presence of co-existent Alzheimer's pathology or cortical Lewy bodies[6,7,10]. Moreover, Summerfield et al.[15] reported that both cortical and subcortical pathologies occur in PDD with potential implications in cognitive function, but the brain structures contributing to the cognitive impairment are still not clearly identified.

There was no significant difference in medication dosage, age in years, disease duration, Hamilton depression score between the PDD patients and non-demented PD. However, the disease duration of PDD patients tend to be longer than in those with PD patients, which is consistent with a previous observation that longer disease duration is a risk factor for dementia in PD[1,5,8].

Increased severity of neurologic symptoms is a risk factor for dementia in PD[30,31]. As expected, it is found that patients with PDD exhibited greater severity of extrapyramidal symptoms than did patients with PD, reflected by Hoehn and Yahr staging and scores of the Unified Parkinson's Disease Rating Scale.

Moreover, a significant correlation was observed between disease duration and severity and the grading of dementia, daily activity scores and tests for memory, attention, language and calculations.

This finding about the relation between cognitive impairment and severity of motor symptoms in PD can be explained partially by the influence of some cortical areas (primary implicated in cognitive impairment) and severity of motor symptoms in PD. This was supported by the data given from experimental studies showed cortico-striatal connections between the parietal and temporal cortex and the ipsilateral caudate nucleus and putamen in monkeys[16]. Moreover, connections from rostral superior parietal lobule to dorsal putamen and the dorsolateral caudate nucleus may have a role in reaching as well as the preparation and kinematic coding of movements[16]. It is therefore possible that some of the motor symptoms of PD may be due to temporo-parietal cortical pathology and disruption of the cortico-striatal connections, rather than being purely mediated through the basal ganglia[16].

Another suggested contributing factors for the relation between cognitive deficit and severity of motor symptoms were the longer disease duration in patients with PDD and the bad performance of PDD patients in various scales evaluating the disease severity.

On the other hand, Nagano-Saito et al.[5] and Gronin-Golomb & Brown[32] reported that cognitive impairment on neuro-psychological performance did not correlate significantly with the increase in PD motor symptoms or disease severity.

This controversy about correlations between disease severity and cognitive impairment was explained by other authors[5,33,34] regarding the effectiveness of dopamine deficiency related to disease severity and the effect of its replacement on cognitive impairment in PD. As in PD patients, the combined presence of impairment of the basal ganglia-thalamo-cortical circuit due to dopamine deficiency and prefrontal cortex and parahippocampal gyrus due to grey matter atrophy may account for cognitive decline in the PD patients and the lack of effect of dopamine repletion on cognition.

These data confirms that reported by Bruck et al.[35], who mentioned that PD patients have known impairments in cognitive performance and these impairments can be detected especially in tests measuring frontal lobe functions and memory but as the disease proceeds, they can lead to an overall cognitive decline and dementia. Also, they found atrophy in the hippocampus and the prefrontal cortex, left hippocampal atrophy is related to

impaired memory, and prefrontal cortical atrophy is associated with the prolonged reaction time.

Metabolic concentrations were acquired by ^{1}H-MRS in three areas of interest in this study, named occipital area, temporo-parietal area and basal ganglionic area. It has been mentioned that the occipital region is more sensitive to increase in MI than other brain areas and it has been suggested that in the pathologic progression of Alzheimer's dementia (AD), increases in MI preceed decrease in NAA[36,37], a good differentiating point between dementia of AD and other types of dementia. Moreover, Bowen et al.[19], in their study on PD patients revealed increased levels of lactate/NAA in the occipital lobe in patients with PDD and PD relative to controls. Additionally, Summerfield et al.[15] reported that all patients with PDD either exhibited visual hallucination or were taking neuroleptic medications to control hallucinatory symptoms, an observation which suggest early occipital involvement in PDD patients.

Hu et al.[16] obtained significant NAA/Cr reduction in 17 non-demented patients with PD in a voxel localized to the temporo-parietal region. The basal ganglia was selected because it is known that striato-nigral degeneration is the principle neurochemical correlate of PD[15].

Comparing patients with PDD to those with PD and control subjects revealed that in the occipital and left temporo-parietal areas, patients with PDD showed significantly lower NAA/Cr and NAA/MI ratios than patients with PD or control subjects. No further significant differences were found in any of the other metabolites in the occipital region, left temporo-parietal area or in the basal ganglia among the three groups. These results suggested predominantly a cortical involvement in PDD patients and are in agreement with the studies demonstrating cerebral hypometabolism in the visual cortex of patients with PDD, in contrast to those patients with AD or healthy control subjects[38,39].

On the other hand, Other authors[40,41] reported that patients with PD and overt clinical dementia showed more extensive reductions in glucose metabolism throughout frontal, temporal, parietal, and occipital cortices in a pattern similar to that seen in AD.

This study revealed that PD patients differ significantly compared with control subjects regarding the NAA/Cr and NAA/MI ratios in left temporo-parietal area. This was supported by Hu et al.[16] who obtained significant NAA/Cr reduction in non-demented patients with PD localized to the temporo-parietal region. This finding was also supported by other two different studies[40,42] which showed absolute reductions in regional glucose metabolism and oxidative metabolism in the parietal cortex in PD in PET studies.

The failure to record a difference in metabolites ratios concentrations between PD and control subjects in other brain areas is in agreement with previous studies examining the occipital lobe or the basal ganglia regions[19,43,44,45].

The reduction in NAA/Cr values in the occipital and left temporo-parietal regions of patients with PDD suggest neuronal dysfunction or neuronal loss[46]. This suggestion was supported by Hu et al.[16] who reported that this reduction in NAA may be attributed to either reductions of neuronal density or in the mitochondrial synthesis of NAA-reflecting neuronal viability.

It might be argued that reduction in NAA/Cr ratios seen in the temporo-parietal cortex of PD patients was occurring secondary to cerebral atrophy. However, only 3 out of 14 patients who underwent volumetric MRI showed atrophic changes, and these were mild making it unlikely that the reduction seen was due to neuronal loss[16].

Others[41,47] reported that the mechanism of cortical NAA/Cr reduction is unclear but may be secondary to Alzheimer's or cortical Lewy body pathology or due to deficiency in ascending dopaminergic, cholinergic or serotonergic projections that occur in PD and PDD.

Increased MI/Cr and decreased NAA/Cr ratios are consistent findings in the temporo-parietal or occipital cortex of patients with PDD[36]. In this study, there was a decrease in NAA in the temporo-parietal and occipital cortices of patients with PDD, but no differences in MI values. This goes hand in hand with the report of Shonk et al.[48], who found that in occipital and temporo-parietal cortex of patients with AD, absolute NAA concentrations are reduced and MI levels are increased, whereas patients with non-Alzheimer's dementia syndromes including (PDD) showed reduced NAA levels but

relatively stable concentration of MI. So it is proposed that MRS may be a useful marker of distinguishing AD and non-AD.

Moreover, the results of our study agreed with other studies[16,17,19], which showed that Cho/Cr ratios were unchanged in patients with PD and this provides circumstantial evidence that the NAA/Cr reduction found reflects reduction in the NAA peak itself rather than an increase in Cr concentration.

Motor impairment, staging of the disease, and severity of extrapyramidal symptoms (Hoehn and Yahr, UPDRS) did not significantly correlate with the reduction in NAA/Cr levels in PD or PDD. So, it is likely that motor impairment and disease extrapyramidal severity in PD is related to the degeneration of the nigrostriatal pathway. However, in PDD group we found significant correlation between NAA values and neuropsychological performance (language tests scores, memory tests and concentration/attention tests). So we suggest that the level of NAA in the occipital cortex and temporo-parietal regions may serve as a biological marker for the severity of cognitive decline in patients with PDD. These previous findings were supported with that of other authors[16,49] who reported a significant correlation between reduction in NAA/Cr ratios and neuro-psychological measures of global cognitive decline and individual neuropsychological tests assessing language, executive and visuo-spatial functions and was present independently of the effects of motor impairments.

In Conclusion: Patients with PDD have metabolic changes in the occipital and temporo-parietal regions indicating predominant neuronal cell dysfunction or loss with little or no glial involvement. These results support the view that PDD is not just the result of AD developing in patients with long standing PD. Moreover, there is a correlation observed between the reduction in NAA level in the occipital and temporo-parietal cortex and cognitive status of patients with PDD. ^{1}H-MRS may be potentially useful in improving the diagnosis of patients with PD who developed dementia.

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الملخـص العربـــى

الاضطراب المعرفي في مرضى الشلل الرعاش (باركنسون)
دراسـة إكلينيكية، سيكولوجية، وباستخدام أشعة الرنين المغناطيسي الطيفي على المخ

تمت هذه الدراسة على 34 شخص، منهم 12 مريض يعانون من عته الشلل الرعاش، 12 يعانون من مرض الشلل الرعاش و10 أشخاص أصحاء كمجموعة مقارنة.

وتم تقييم نسبة العته في المرضى باستخدام اختبار الحالة الذهية لفولشتين، مقياس بلسيد للعته وكتاب اليد لتشخيص وإحصاء الاضطرابات الذهنية (الطبعة الرابعة). وتم تقييم مرضى الشلل الرعاش باستخدام مقياس هون ويار ومقياس مرض باركنسون الموحد ومقياس شواب وانجلاند. تم التقييم السيكولوجي الإكلينيكي باستخدام الجزء المعرفي من اختبار كمبردج لكبار السن ومقياس هاملتون للاكتئاب. تم قياس التغييرات الكيميائية باستخدام أشعة الرنين المغناطيسي الطيفي للمخ في ثلاث مناطق: المنطقة الصدغية الجدارية اليسرى، المنطقة القفوية والخلايا القاعدية.

وقد أظهرت النتائج أن مرضى عته الشلل الرعاش يعانون من درجة متقدمة من المرض ودرجة متقدمة ملحوظة من العته واختلال الأنشطة اليومية وكذلك الاضطراب في كل القياسات السيكولوجية، وإن كان مرضى داء باركنسون بدون عته يعانون من اضطراب في اختبارات اللغة والذاكرة والاستقبال فقط. كما أن مدة ودرجة المرض ترتبط ارتباطا ملحوظا بدرجة العته وتدهور والأنشطة اليومية والاضطراب المعرفي.

وجد أن نقص النسبة بين إن اسيتيل اسبارتات إلى الكرياتنين ونسبة إن اسيتيل اسبارتات إلى الميوانيزيتول في المنطقة الصدغية الجدارية اليسرى والقفوية يحدث بشكل ملحوظ في مرضى عته الشلل الرعاش عن الآخرين. كما وجدت علاقة بين نقص نسبة إن اسيتيل اسبارتات/كرياتنين والاضطرابات في قياس اللغة والذاكرة والانتباه في القياسات السيكولوجية المعرفية.

ومن هنا توضح هذه الدراسة أهمية التقييم الإكلينيكي للحالة المعرفية باستخدام القياسات السيكولوجية ونقص إن اسيتيل اسبارتات في القشرة المخية باستخدام أشعة الرنين المغناطيسي الطيفي في تقييم مرضى الشلل الرعاش (باركنسون) الذين يعانون العته الذهني المصاحب لهذا المرض.