PAPER

Attentional deficits affect activities of daily living in dementia-associated with Parkinson's disease

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Objective: To investigate the effects of attentional deficits on activities of daily living (ADL) in patients with dementia associated with Parkinson's disease (PDD).
Method: 461 patients were assessed neuropsychologically. Factor analyses were used to differentiate attention from other cognitive functions and to differentiate different aspects of ADL functions. The effects of the attentional measure on ADL were examined using sequential multiple regression, controlling for age, sex, education, severity of motor symptoms and other cognitive functions.
Results: Three cognitive factors were identified, with one factor emerging as a measure of vigilance and focused attention. This factor predicted different aspects of ADL status even after controlling for motor functions and other cognitive factors. The attention factor was the single strongest cognitive predictor of ADL status, matching the strength of the effects of motor functions on ADL status.
Conclusion: Impaired attention is an important determinant of ADL functions in patients with PDD.

Dementia among patients with Parkinson's disease (PDD) has an average prevalence of 31% in cross-sectional studies,[1] a cumulative prevalence approaching 80%,[2] and is associated with rapid motor[3] and functional decline.[4] Deficits in activities of daily living (ADL) develop in Parkinson's disease due to the motor symptoms, and also in PDD due to cognitive deficits. ADL deficits are associated with reduced quality of life for patients[5] and care givers,[6] and in general, with high nursing costs in nursing homes.[7] Thus, it is of vital importance to understand the causes of ADL deficits in patients with Parkinson's disease and to target treatment against these causes.

Attention deficit is increasingly acknowledged as an important cognitive symptom in Parkinson's disease.[8–13] The attention construct is heterogeneous, encompassing executive control functions, selective attention and sustained attention.[14] The executive control functions are complex, and include functions such as planning, sequencing, self-monitoring, response inhibition, set shifting, and in multi-tasking by coordinating cognitive resources between different simultaneous task demands. Selective attention refers to the selection of a limited aspect of environmental stimuli for full cognitive processing at the cost of the exclusion of other aspects. Listening to a conversation partner in a noisy environment is an example of selective attention. Sustained attention is often named ''vigilance''. It usually refers to the ability to detect and respond to stimuli over time.[15] Drowsiness and reduced arousal will usually be measurable as decreased vigilance.

The literature indicates that executive functions are often compromised even in early Parkinson's disease,[16 17] especially set shifting between task demands. Evidence also suggests a deficit in auditory[18] and visual selective attention.[13] The concept of ''fluctuating'' attention in patients with PDD and in those with dementia with Lewy bodies (DLB)[8] is probably closely related to vigilance deficits. Thus, there is evidence that a broad range of attentional phenomena is compromised in PDD.

Deficit in executive functions has been proposed as the most important cognitive predictor of ADL deficit in patients with Parkinson's disease.[19] However, not much work has been carried out on the effect of changes in vigilance and selective attention. Given the fundamental role of vigilance and selective attention for sustained goal-directed activity and the variable vigilance level of patients with PDD, we hypothesise that vigilance and selective attention, hereby just referred to as ''attention'', are major factors in explaining ADL deficits.

We are not aware of any previous published studies on the relationship between ADL and attention in patients with PDD, but the trail making B test[19] and a visuoconstruction task[20] has been proposed as a major predictor of ADL status in Parkinson's disease. Fluctuating attention among patients with DLB correlates with ADL deficits.[21] However, these studies have used small samples and limited cognitive testing.

To test the hypothesis that attentional deficit is related to ADL, we investigated the baseline data from a recent study[22] that investigated the effects of rivastigmine on patients with PDD, in which a large sample of patients with PDD was examined using several cognitive tests, some designed specifically to measure attention. The size of the sample made it possible to choose a factor-analytical approach to generate compound measures that represented the underlying attentional processes better than isolated neuropsychological tests, and to compare the effect of attention with that of other cognitive measures. Thus, our study aimed to investigate the effect of attention on level of ADL functions, and to compare this effect with other cognitive functions and with measures of motor function.

Abbreviations: ADAS-cog, Alzheimer's Disease Assessment Scale—cognitive; ADCS-ADL, Alzheimer's Disease Cooperative Study—Activities of Daily Living; ADL, activities of daily living; CDR, Cognitive Drug Research; DLB, dementia with Lewy bodies; MMSE, Mini-Mental State Examination; PCA, principal component analysis; PDD, dementia associated with Parkinson's disease; UPDRS, Unified Parkinson's Disease Rating Scale

METHODS

Patients

In all, 541 patients, at least 50 years old, were included in this retrospective analytical study. They were diagnosed with Parkinson's disease according to the clinical diagnostic criteria of the United Kingdom Parkinson's Disease Society Brain Bank[23] and with PDD according to the fourth edition of the *Diagnostic and statistical manual of mental disorders* (code 294.1).[24] Patients had mild to moderately severe dementia as defined by a Mini-Mental State Examination (MMSE) score of 10–24, with the onset of symptoms occurring at least 2 years after the diagnosis of Parkinson's disease.

The care givers and the mentally competent patients, or their legally authorised representative if mentally incompetent, gave informed written consent. Exclusion criteria included the presence of any primary neurodegenerative disorder other than Parkinson's disease or other causes of dementia, a history of a major depressive episode, the presence of an active, uncontrolled seizure disorder, the presence of any disability or unstable disease unrelated to Parkinson's disease, known hypersensitivity to drugs similar to rivastigmine and the use of a cholinesterase inhibitor or anticholinergic drugs during the 4 weeks before inclusion in the study.

Patients were recruited from centres in Austria, Belgium, Canada, France, Germany, Italy, The Netherlands, Norway, Portugal, Spain, Turkey and the UK. Before the study began, the protocol, informed consent form and other information provided to patients and care givers were reviewed by the institutional review board at each centre. All procedures were conducted in accordance with the ethical standards of the responsible committee on human experimentation and with the Declaration of Helsinki as revised in 1983.

MEASURES

Cognition

The MMSE[25] and the Alzheimer's Disease Assessment Scale—cognitive section (ADAS-cog)[26]—were administered, and each of the 11 items on the ADAS-cog and the ''Serial 7'' task in MMSE were included as separate variables. The first seven items on the ADAS-cog are word recall, commands, constructional praxis, naming objects or fingers, ideational praxis, orientation and word recognition. The last four of the ADAS-cog items are scored according to the judgement of the examiner, on the basis of the observations during the testing procedure, not by direct recording of patient responses. These four scales are remembering test instructions, spoken language ability, word-finding difficulty and comprehension.

The Delis–Kaplan Executive Function System verbal fluency test, which requires patients to produce as many words per minute as they can, starting with a particular letter, with higher scores indicating better performance,[27] was used for assessing executive functions. The number of correct words, set loss errors and repetition errors were included in the analyses.

The Cognitive Drug Research (CDR) computerised assessment system attention tests were used to assess attention. The three CDR attention tests—namely, simple reaction time, choice reaction time and digit vigilance—take around 7 min to complete. All tests use visual stimuli, and the patients respond using buttons on a response box that is independent of the keyboard and ensures millisecond accuracy of recording. Reaction times for all tasks were measured in milliseconds, with higher scores indicating poorer attention.[8 28 29] The digit vigilance test requires a response from the patient whenever a stimulus matches a continuously presented target stimulus. In addition to reaction times, the number of detected targets and false alarms from the digit vigilance task and the response accuracy on the choice reaction time task were included as variables.

All tests were administered during the ''ON'' phase.

Activities of daily living

A care giver of the patient filled out the Alzheimer's Disease Cooperative Study—Activities of Daily Living (ADCS-ADL) Scale, for which scores can range from 0 to 78 points, with higher scores indicating better functioning.[30] For the present study, the total score and each separate item score were included. The individual items were subjected to factor analysis. The ADCS-ADL includes measures of physical ADL skills such as bathing, walking and getting dressed, instrumental ADL skills such as using a telephone or household appliances, and activities such as reading, conversation and watching TV.

Motor symptoms

Parkinsonism was assessed by means of the motor examination section (part III) of the Unified Parkinson's Disease Rating Scale (UPDRS), for which scores can range from 0 to 108 points, with higher scores indicating more severe motor symptoms.[31] Before the study was started, investigators received 2 days of training on outcome measures to ensure that test administration was consistent across centres.

Statistical analyses

Data were analysed with SPSS V.12.02. A factor analysis using principal components factor extraction with varimax rotation[32] was carried out with the cognitive variables. All three reaction time variables were subjected to a logarithmic transform to correct a positive skew. The Kaiser–Meyer–Olkin measure of sampling adequacy was 0.88, and Bartlett's test of sphericity was highly significant at $p<0.001$, indicating that the data were appropriate for principal component analysis (PCA).[33] The resulting cognitive factors were interpreted by the authors regarding content and named accordingly, with emphasis on identifying the factor with items most clearly measuring attentional components.

The 22 items on the ADCS-ADL were also subjected to PCA with varimax rotation. Although several items were bimodally distributed, they were still included, as non-normality of data in PCA is a problem mainly when testing the significance of factors.[33] The measure of sampling adequacy was 0.92 and Bartlett's test of sphericity was highly significant at $p<0.001$, indicating that the ADL data were appropriate for PCA.[33]

For both factor analyses, to identify factors with simple structure, items were deleted from the analysis if the maximal factor loading was <0.5[32] on any of the factors. The number of factors was determined using the condition that the latent roots (eigenvalues) of each factor should be >1.[32] The final factor solution was used to generate new variables containing the factor scores for each factor for every patient. A regression-based approach was used for generating factor scores with maximal correlations with the factors,[32] resulting in uncorrelated variables with means of 0 and standard deviations (SDs) 1. Additionally, compound scales were generated for the ADCS-ADL by calculating the mean scores of the variables of each factor, thus retaining the clinical interpretability of the ADL scores.

Sequential multiple regression was used to assess the relative effect of cognitive factors on total ADL score and the ADL factors. To control for age, sex and years of completed education, these variables were entered in step 1 of the models. The motor part of UPDRS-III was entered in step 2 to control for the effect of motor function on the cognitive measures. In step 3, non-attentional cognitive measures were entered. In step 4, the measure of attention was entered to

determine whether attention independently contributed to ADL functions beyond motor functions and other cognitive functions.

The independent variables in the regression analyses did not show multicollinearity, as none of the condition indices exceeded a threshold of 15.[33] None of the standardised residuals was >3, indicating that the models were accurate reflections of the data.[33] None of the cases in the analysis exerted an undue influence on the final models, based on Mahalanobis' distances ($p<0.001$)[32] and Cook's distances ($D<1$).[33]

RESULTS

Sample properties

A complete cognitive examination was available for 461 of the patients. Table 1 summarises the baseline demographic and background characteristics.

Cognitive factors

The factor analyses showed a three-factor solution for the cognitive variables, and table 2 shows the included variables and factor loadings.

The attention measures from the CDR, with the exception of response accuracy on the choice reaction time task, loaded on the first factor, as well as constructional praxis from the ADAS-cog. The highest-loading single variable was the number of correct detections on the digit vigilance task. The factor was judged to be mostly a measure of the attentional function vigilance, given that most of the variables required sustained attention towards some target stimulus followed by a manual response. Selective attention was also important, given that the patients had to ignore some stimuli while responding to others. Thus, the factor was named ''attention''.

Four variables on the ADAS-cog, which were empirically judged by the test administrator on various aspects of cognitive performance, loaded on the second factor. The variables were judgements of word-finding difficulty, spoken language ability, comprehension and the ability to understand and remember test instructions. This factor was named ''verbal interaction'', factor, given that these variables were based on the examiner's subjective impressions of different aspects of verbal interaction with the patient.

The third factor was more heterogeneous, with its five variables sharing a language component. Verbal memory, confrontation naming, the serial 7 task from MMSE and verbal fluency loaded on this factor. The variables had lower loadings than those in the other factors, reflecting the larger heterogeneity of the third factor. This factor was named ''verbal cognition'', as all the included variables shared a language component; although attentional components, memory and basic naming ability were also associated, they contributed less. For all the cognitive factor scores, higher scores indicate worse performance.

Table 1 Descriptive statistics of patients (n = 461)

Age (SD) in years	72.5 (6.6)
Sex, n (%)	
Male	308 (66.8)
Female	153 (33.2)
Modified Hoehn and Yahr stage	2.7 (0.8)
UPDRS part III (motor score)	32.7 (13.7)
Time since diagnosis of dementia, years	2.3 (1.5)
Time since diagnosis of Parkinson's disease, years	9.8 (5.6)
MMSE score	19.8 (3.5)

MMSE, Mini-Mental State Examination; UPDRS, Unified Parkinson's Disease Rating Scale.
Values are mean (SD) unless specified.

Table 2 Principal component analysis with varimax rotation of the cognitive variables

	Component		
Rotated component matrix	Attention	Verbal interaction	Verbal cognitive
Digit vigilance—correct detections	**0.813**	0.169	0.131
Choice RT $\log_{10}$ corrected	**0.795**	0.211	0.175
Digit vigilance—speed of detections	**0.751**	—	0.222
Simple RT $\log_{10}$ corrected	**0.711**	—	0.226
Digit vigilance—false alarms	**0.564**	0.122	—
Constructional praxis	**0.509**	0.151	0.334
Word-finding difficulty	—	**0.865**	—
Spoken language ability	0.109	**0.862**	—
Comprehension	0.235	**0.805**	0.181
Remembering test instructions	0.397	**0.564**	0.280
Naming objects/fingers	—	—	**0.720**
Letter fluency: total correct responses	0.295	0.134	**0.638**
Serial 7's as a test of attention and calculation	0.131	—	**0.602**
Word recall	0.364	0.266	**0.562**
Word recognition	0.162	0.197	**0.546**

Extraction method: principal component analysis.
Rotation method: varimax with Kaiser normalisation.
Values in bold represent factor loadings >0.5.
—Indicate factor loadings <0.1.

ADL factors

Three factors were identified for the ADCS-ADL scale. Table 3 shows the included variables and factor scores.

The first factor was judged to be a basic physical ADL factor, with actions such as getting dressed, bathing and toileting loading highest. This factor was designated ''physical ADL''.

The tasks loading on the second factor were domestic chores, with the preparation of a meal and the use of household appliances loading highest. Thus, the factor was defined ''domestic chores'' or ''instrumental ADL''. However, the statistical distribution of scores on this factor was

Table 3 Principal component analysis with varimax rotation of the activities of daily living scale

	Component		
Rotated component matrix	Physical ADL	Instrumental ADL	Social orientation ADL
Getting dressed	**0.794**	0.232	0.138
Bathing	**0.763**	0.243	0.144
Toileting	**0.734**	0.220	—
Grooming	**0.686**	0.204	0.250
Walking	**0.647**	0.302	—
Selecting clothes	**0.604**	0.202	0.169
Eating	**0.602**	0.145	0.160
Travel	**0.538**	0.386	0.210
Meal or snack	0.230	**0.772**	0.154
Household appliance	0.238	**0.770**	0.242
Beverage	0.345	**0.737**	0.116
Clearing dishes	0.304	**0.673**	—
Disposing of garbage	0.280	**0.621**	0.254
Talking about current events	0.104	0.225	**0.759**
Watching television	0.150	0.121	**0.756**
Conversation	0.116	—	**0.698**
Reading	—	0.129	**0.634**
Keeping appointments	0.244	0.273	**0.541**

ADL, activities of daily living.
Extraction method: principal component analysis.
Rotation method: varimax with Kaiser normalisation.
Values in bold represent factor loadings >0.5.
—Indicate factor loadings <0.1.

extremely bimodal. This would have precluded the use of parametric statistics requiring normally distributed data. Given that some patients were living in nursing homes with limited options for independent use of household appliances or general use of kitchen facilities, we excluded this factor from further analysis.

Tasks associated with social interaction as well as reading and watching TV loaded on the third factor. This factor was called ''social orientation ADL''.

Interrelationship among ADL, cognitive and motor scores

Table 4 shows Pearson's correlation coefficients among the cognitive factor scores, total ADL score, basic ADL score, social ADL score and UPDRS-III motor score.

Most of the correlations, although statistically significant, were weak. However, the correlations between attention and total ADL score and attention and physical ADL score approached moderate strength. UPDRS-III motor score was moderately correlated with physical ADL and approached a moderate correlation with total ADL score.

Three separate sequential regression analyses were conducted, with total ADL score, physical ADL score, and social orientation ADL score as dependent variables. For each analysis, age, sex and years of completed education were entered first, followed by UPDRS-III motor score, the two non-attentional cognitive factor scores and finally the attention score.

Table 5 shows the results of the sequential regression at each of the four steps, where total ADL score is the dependent variable. The model was considerably improved at each step of the analysis, as shown by the highly significant R^2 changes. Adding attention as a predictor in step 4 increased the explained variance by 12%. The total explained variance was 38% at step 4, with all predictors included in the equation. At step 4, attention was the strongest predictor of total ADL score, and all the independent variables were major predictors.

Table 6 shows the results of a sequential regression analysis using physical ADL score as the dependent variable. At each step R^2 increased significantly, and at the final step 37% of the variance in physical ADL score was explained when all the independent variables were entered in the equation. Total UPDRS-III motor score was the strongest predictor, followed by attention.

Table 7 shows the results of a sequential regression analysis using social orientation ADL score as the dependent variable.

All the models were relevant, with a marked increase in R^2 at each step and with 20% of the variance in social orientation ADL score explained at the final step. However, at steps 3 and 4, UPDRS-III was no longer an important predictor of social orientation ADL score. Verbal interaction was most strongly related to social orientation ADL, followed by attention and verbal cognition.

DISCUSSION

Our findings support the main hypothesis of this study that attentional deficit is related to patients' performance in ADL. Attention contributed to the prediction of physical ADL skills such as bathing, eating and getting dressed, as well as social interaction skills such as participating in conversations, keeping appointments, watching TV and reading. The effects of attention were still present after controlling for sex, age, educational level, motor functions and other aspects of cognitive functions, indicating that the effects of attention were not simply a reflection of general cognitive or motor status. Thus, given the clinical importance of ADL, these results show the prognostic significance of attention deficits in patients with PDD.

The main strengths of the study are the large and well-described sample of patients with PDD from multiple clinics in different countries, the extensive measures of different aspects of cognition, including attention, and a validated measure of ADL.

Perhaps the most difficult aspect of the study is the precise content of the attention factor and its relationship with other cognitive variables. The variable with the highest factor loading on the attention factor was response accuracy on a digit vigilance test, measuring ability to correctly detect and respond to a stimulus matching a target stimulus, while ignoring non-matching stimuli. The second highest loading measure was choice reaction time. The factor solution closely replicates a similar factor analysis with patients with DLB,[8] where the same CDR measures were used. All variables contributing to the attention factor required a motor response and monitoring of external visual stimuli. Although we controlled for motor functions, it could be argued that the attention factor could still be influenced by motor speed. However, given that the highest loading variable on this factor is an accuracy score not dependent on simple motor reaction time and the very low correlation of 0.148 between the attention factor score and total motor score on the UPDRS-III, this seems unlikely. The attention factor seemed mostly to include functions related to sustained attention (vigilance) and attentional focus, while not being solely a strict measure of vigilance as defined by Parasuraman,[15] owing to the shorter duration of the CDR tests than typical vigilance tasks. Cognitive speed could explain some of the variability of the attention factor. However, it has been shown in patients with Parkinson's disease that prolonged simple reaction time may reflect deficits of focused attention,[34] and that even complex attentional control functions probably depend on cognitive speed.[35] Thus, we do not see a justification for correcting for simple reaction time.

The factor verbal cognition was more heterogeneous. Both letter fluency and the serial 7 task from MMSE, which loaded on this factor, are tests considered to require executive

Table 4 Correlations

	Correlation coefficient					
Measure	Total ADL score (DV)	Physical ADL	Social ADL	Attention	Verbal interaction	Verbal cognitive
Physical ADL	**0.874**					
Social ADL	**0.701**	**0.445**				
Attention	**−0.355**	**−0.359**	**−0.201**			
Verbal interaction	**−0.243**	**−0.208**	**−0.280**	0.000		
Verbal cognitive	**−0.286**	**−0.182**	**−0.239**	0.000	0.000	
UPDRS-III motor	**−0.374**	**−0.469**	**−0.133**	**0.148**	**0.158**	0.078

ADL, activities of daily living; DV, daily value; UPDRS, Unified Parkinson's Disease Rating Scale.
Values in bold are significant at $p<0.01$.

Table 5 Sequential regression with total activities of daily living score as the outcome

Step	Variable	R^2	R^2 change	F change**	β	p Value
1		0.06	0.06	8.76		
	Age				−0.19	<0.001
	Sex				0.10	0.032
	Education				0.14	0.003
2		0.18	0.12	68.75		
	Age				−0.15	<0.001
	Sex				0.10	0.021
	Education				0.13	0.002
	UPDRS-III motor				−0.35	<0.001
3		0.26	0.08	26.06		
	Age				−0.11	<0.001
	Sex				0.10	0.008
	Education				0.05	0.014
	UPDRS-III motor				−0.31	0.227
	Verbal interaction				−0.19	<0.001
	Verbal cognitive				−0.24	<0.001
4		0.38	0.12	80.90		
	Age				−0.09	0.018
	Sex				0.17	<0.001
	Education				0.11	0.008
	UPDRS-III motor				−0.26	<0.001
	Verbal interaction				−0.20	<0.001
	Verbal cognitive				−0.23	<0.001
	Attention				−0.35	<0.001

UPDRS, Unified Parkinson's Disease Rating Scale.
β is standardised.
**F change significant at $p<0.01$.

attentional control. These tests also loaded weakly on the attention factor. The most obvious differences between these tasks and the tasks contributing to the attention factor are the executive control demands, the verbal component, the lack of monitoring of external stimuli and the response modality being speech rather than a simple motor response using the dominant hand. The attentional demands of this factor are of a more executive nature, requiring internal control rather than monitoring of external events. The attentional components of this factor indicate that we should be careful not to treat the attention construct as a single entity. However, as the CDR tests are designed to assess attention independently of working memory, the attentional factor can be seen as a pure assessment of attention, whereas the attentional tests that involve working memory loaded separately, supporting this differentiation.

Table 6 Sequential regression with physical activities of daily living score as the outcome

Step	Variable	R^2	R^2 change	F change**	β	p Value
1		0.03	0.03	5.01		
	Age				−0.17	<0.001
	Sex				0.06	0.220
	Education				0.03	0.537
2		0.24	0.21	120.88		
	Age				−0.12	0.005
	Sex				0.06	0.168
	Education				0.02	0.607
	UPDRS-III motor				−0.46	<0.001
3		0.28	0.04	12.17		
	Age				−0.10	0.022
	Sex				0.06	0.152
	Education				−0.03	0.495
	UPDRS-III motor				−0.42	<0.001
	Verbal interaction				−0.14	<0.001
	Verbal cognitive				−0.15	<0.001
4		0.37	0.09	66.58		
	Age				−0.08	0.049
	Sex				0.12	0.003
	Education				0.02	0.592
	UPDRS-III motor				−0.38	0.001
	Verbal interaction				−0.15	0.001
	Verbal cognitive				−0.15	0.001
	Attention				−0.32	0.001

UPDRS, Unified Parkinson's Disease Rating Scale.
β is standardised.
**F change significant at $p<0.01$.

Table 7 Sequential regression with social orientation activities of daily living score as the outcome

Step	Variable	R^2	R^2 change	F change**	β	p Value
1		0.04	0.04	5.67		
	Age				−0.06	0.194
	Sex				0.03	0.577
	Education				0.19	<0.001
2		0.05	0.01	7.53		
	Age				−0.04	0.340
	Sex				0.03	0.574
	Education				0.19	<0.001
	UPDRS-III motor				−0.13	0.006
3		0.15	0.10	27.20		
	Age				−0.02	0.687
	Sex				0.03	0.548
	Education				0.12	0.012
	UPDRS-III motor				−0.07	0.095
	Verbal interaction				−0.27	<0.001
	Verbal cognitive				−0.20	<0.001
4		0.20	0.05	26.58		
	Age				−0.01	0.912
	Sex				0.07	0.121
	Education				0.16	0.001
	UPDRS-III motor				−0.04	0.331
	Verbal interaction				−0.27	<0.001
	Verbal cognitive				−0.19	<0.001
	Attention				−0.23	<0.001

UPDRS, Unified Parkinson's Disease Scale.
β is standardised.
**F change significant at $p<0.01$.

Our study shows that attentional dysfunction may be one of the primary cognitive factors associated with functional impairment in patients with PDD. Several implications can be drawn from this finding. More work should be carried out on the nature of attentional deficits in PDD, as several theoretical issues remain. Although earlier neuropsychological work on PDD focused on dopaminergic depletion and frontal, executive dysfunctions,[36 37] more interest has recently been directed towards impairment in cholinergic[38 39] and noradrenergic pathways.[40 41] The recent staging of Parkinson's disease proposed by Braak *et al*[42] indicate that noradrenergic and cholinergic networks related to control of arousal and vigilance are affected early in Parkinson's disease. Perhaps most important in this regard is the nucleus of Meynert in the basal forebrain. This nucleus has large cholinergic projections to the cortex and is part of an important afferent regulatory system of the cortex, affecting arousal and selective attention.[43] This nucleus has been proposed as central to the fluctuating level of consciousness seen in patients with DLB,[44] and may contribute to attentional deficits in those with PDD. Although the nucleus of Meynert is also affected in patients with Alzheimer disease, the cholinergic deficit seems to be more severe in those with PDD.[38 39]

Thus, a larger cholinergic deficit in PDD than Alzheimer's disease, may explain the improvement of attentional functions under treatment with rivastigmine in DLB[45] and PDD.[22 28] In a recent study, ADL, attention and other cognitive measures improved,[22] and patients with the most severe attention deficits responded best to rivastigmine.[46] We believe that our findings indicate that attention is of fundamental importance for ADL performance in PDD. A practical implication is that we could more often use a test of attention in diagnosing cognitive impairment and treatment efficacy in patients with PDD. A standard computer-based vigilance test with adequate norms could be used, as digit vigilance accuracy loaded most strongly on our attention factor.

The effect of impaired attention may be mediated by the known attentional requirements of complex motor tasks[10] and of a wide range of cognitive processes.[14] There may also be a direct effect of attentional deficits on ADL. Further studies are justified to explore whether positive effects on ADL and cognition under treatment with rivastigmine in patients with PDD[22] are mediated by an improvement in attention.

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