ORIGINAL ARTICLE

Fact-finding survey on diagnostic procedures and therapeutic interventions for parkinsonism accompanying dementia with Lewy bodies

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Abstract

Background: We performed a questionnaire survey of medical doctors engaged in the management of dementia to identify the actual status of treatment for dementia with Lewy bodies (DLB) in Japan.
Methods: Among participating medical doctors, we selected neurologists (Group N) and psychiatrists (Group P) because these physicians are usually involved in the management of DLB patients. The two groups were compared based on their diagnosis and treatment of DLB and in particular, parkinsonism.
Results: Neurological examinations and biomarker tests were less frequently performed by Group P than Group N. Antipsychotics and other psychotropics excluding anti-dementia drugs were significantly more frequently administered by Group P than Group N. The proportion of physicians who selected L-dopa as a first-line therapy for parkinsonism was significantly higher in Group N than in Group P. Despite these between-group differences, the following findings were common to the two groups: there was a discrepancy between the symptom that patients expressed the greatest desire to treat, and the awareness of physicians regarding the treatment of these symptoms; the initial agent was L-dopa; and physicians exercised caution against the occurrence of hallucinations, delusions, and other adverse drug reactions.
Conclusions: The results of the present survey offer valuable insight for the formulation of future DLB therapeutic strategies.

INTRODUCTION

The Diagnosis and Management of Dementia with Lewy bodies (DLB) were revised in 2017.[1] In the new DLB clinical diagnostic criteria, rapid eye movement (REM) sleep behaviour disorder (RBD) was upgraded to a core clinical feature, and suggestive findings were changed to indicative biomarkers; thus, diagnostic accuracy should improve. Regarding treatment, DLB disease modifiers remain absent, and currently symptomatic treatment is administered for each symptom. For motor symptom treatment, L-dopa is recommended.[1,2] However, adverse events such as visual hallucinations may be related to L-dopa. Functional impairments in activities of daily living (ADL) such as eating, brushing teeth, bathing, transferring, and walking correlate with the seriousness of parkinsonism, and reduce the quality of life (QOL) of DLB patients.[3] Thus, when treating patients with L-dopa, a balance between risks and benefits should be evaluated. If the demands of patients and caregivers and appropriate implementation of therapeutic interventions for motor symptoms contribute to improved QOL, then it is important to understand how DLB is treated in actual clinical settings.

Therefore, we performed an internet-aided questionnaire survey of physicians in departments of neurology and psychiatry, which are primary medical care units for treating DLB, who are engaged in the diagnosis and treatment of DLB, to determine the actual status of therapeutic interventions for parkinsonism.

METHODS

Among medical doctors registered at Medical Collective Intelligence Co., Ltd. engaged in the diagnosis and management of dementia, we selected 100 neurologists and 100 psychiatrists. The total number of all panel physicians registered with Medical Collective Intelligence Co., Ltd. was 50 675, and among the 3319 physicians included in the sample survey, the percentage of those who responded that they had examined and treated patients with dementia within the past 3 months was 35.2% (1169 physicians). Among all the panel physicians of Medical Collective Intelligence Co., Ltd., the percentage of physicians who had treated 20 or more dementia patients and at least one DLB patient, estimated based on the results of this survey and the past incidence survey conducted by Medical Collective Intelligence Co., Ltd., was 9.9%: 71.1% for the neurologists and 40.0% for the psychiatrists.

Eligibility criterion was the management of ≥ 20 dementia patients and at least one DLB patient per month. Of the selected medical doctors, 200 physicians primarily belonging to departments of neurology and psychiatry were included in our analyses. The response rate among all the panel physicians expected to meet these criteria (treating ≥ 20 dementia patients and at least one DLB patient) was 7%: 14% for the neurologists and 11.9% for the psychiatrists.

Neurologists and psychiatrists consisted of 50 specialists and 50 non-specialists, respectively. Specialists had obtained at least one of the following qualifications: qualified by the Japan Society for Dementia Research; or the Japanese Psychogeriatric Society; clinical specialist for dementia qualified by the Japan Psychiatric Medical Conference; neurological specialist; psychiatric specialist; and geriatric specialist.

A questionnaire was available to participants on an internet website between 12 July 2017 and 10 August 2017. Each participant accessed the website and responded anonymously to the questionnaire. Prior to initiation of the internet-aided survey, respondents received an explanation that survey results would be analyzed, disclosed, and provided to medical institutions and companies, and published at scientific conferences, in scientific papers, and on any other relevant occasions. The questionnaire was only available to those who gave informed consent. Based on the questionnaire, two groups consisting of neurologists (Group N) or psychiatrists (Group P) were compiled and compared. SPSS Version 24 (IBM Corp., Tokyo, Japan) was used for statistical analyses and population rates were tested.

The purpose of this study was to explore the actual status of diagnosis and treatment of parkinsonism accompanying DLB, and not to test a hypothesis. Accordingly, statistical analyses indicate exploratory results.

RESULTS

Background factors of survey participants (Table 1)

Evaluation of the age groups of physicians engaged primarily in the diagnosis and management of dementia revealed that physicians in their 40s accounted for 36% in Group N and 34% in Group P, and those in their 50s, for 37% and 32%, respectively, indicating no differences between groups. The proportion of physicians working at hospitals attached to national, prefectural, other public universities and private university hospitals was 25% for Group N, but 7% for Group P. Furthermore, 34% of physicians in Group N and 55% in Group P worked at private general hospitals. The proportion of

Table 1 Background factors of survey participants

	Group N	Group P
The age groups of physicians		
Physicians in their 40s	36%	34%
Physicians in their 50s	37%	32%
The proportion of physicians working at hospitals		
University hospitals	25%	7%
Private general hospitals	34%	55%
Medical care centres for dementia	18%	27%
The mean number of patients with dementia-related disorders who the respondents examined in the past month		
Total number of patients	59.4	54.7
Alzheimer type dementia	61.6%	60.0%
Cerebrovascular dementia	14.2%	18.7%
Dementia with Lewy bodies	17.0%	14.2%
Physicians alone diagnosed patients and decided the therapeutic strategies	99%	91%
Physicians asked specialists to make a diagnosis, formulate therapeutic strategies, and prescribe therapeutic drugs	0%	1%

[Correction added on 3 July 2019, after first online publication: the proportion of physicians working at university hospitals in Table 1 has been corrected to '7%'.]

physicians in medical care centres for dementia was 27% for Group P and 18% for Group N.

The mean number of patients with dementia-related disorders whom the respondents examined in the past month was 59.4 (median: 35.0; Group N) and 54.7 (median: 35.0; Group P) indicating no differences between groups. Regarding patient type, Alzheimer type disease (ATD) accounted for 61.6% in Group N and 60.0% in Group P, cerebrovascular dementia accounted for 14.2% in Group N and 18.7% in Group P, and DLB accounted for 17.0% in Group N and 14.2% in Group P. Additionally, 99% and 91% of physicians in Groups N and P, respectively, answered that they alone diagnosed patients and decided the therapeutic strategies. No physicians in Group N and 1% in Group P asked specialists to make a diagnosis, formulate therapeutic strategies, and prescribe therapeutic drugs.

Among drugs prescribed by respondents for dementia patients during the past 6 months, antipsychotics, Yokukansan and Yokukansankachimpihange of Japanese herbal medicine, trazodone, benzodiazepine anti-anxiety drugs, and mood stabilisers were significantly more frequently prescribed in Group P.

Diagnosis and treatment of DLB

The proportion of patients with parkinsonism was 75.6% for Group N and 59.3% for Group P. The proportion of physicians who conducted medical interviews, including history taking, when making a diagnosis was 97% and 94% for Groups N and P, respectively. However, 84% in Group N and 38% in Group P always performed neurological examinations such as computed tomography / magnetic resonance imaging (CT/MRI) of the head (89% for Group N and 62.0% for Group P), dopamine transporter – single-photon emission computed tomography (DAT-SPECT) (17% Group N; 2.0% Group P), cerebral blood flow SPECT (22% Group N; 13% Group P), and ^{123}I-metaiodobenzylguanidine (MIBG)-imaging (19% Group N; 7.0% Group P). Thus, CT/MRI of the head and DAT-SPECT were significantly more frequently performed by Group N than Group P. When 'always conducted' and 'conducted as appropriate' were combined, cerebral blood flow SPECT and MIBG-imaging were significantly more frequently performed in Group N. No differences were noted for implementation of RBD screening tests (Japanese version of REM Sleep Behaviour Disorder Screening Questionnaire (RBDSQ-J) and sleep talking test), olfactometry, and overnight polysomnography. [Correction added on 3 July 2019, after first online publication: the statement '…cerebral blood flow SPECT (17% Group N; 13% Group P.)…' has been corrected to '…cerebral blood flow SPECT (22% Group N; 13% Group P)…']

Time from suspected DLB to definite diagnosis was most frequently < 3 months (54% Group N; 49% Group P), then ≥ 3 to < 6 months (35% Group N; 40% Group P), then ≥ 6 months to < 1 year (8% Groups N, P).

Clinical diagnoses most frequently made prior to definite diagnosis of DLB were Parkinson's disease (PD) (47% Group N) and ATD (45% Group P), then ATD (33% Group N) and delirium (18% Group P), depression (7%) and delusional disorders (4%) in Group N, depression (12%), Parkinson's disease (15%), delusional disorders (6%), and vascular dementia, frontotemporal dementia, and schizophrenia (all 1%) in Group P. [Correction added on 3 July 2019, after first online publication: the statement '…depression (12%), Parkinson's disease (15%), delusional disorders (6%)…' has been corrected to '…depression (12%), Parkinson's disease (15%), delusional disorders (6%)…']

In both groups, the greatest proportion of respondents selected 'symptoms are not stable' as the most challenging issue when diagnosing DLB (53% and 62% in Groups N and P) followed by 'difficulty in obtaining neurological findings' (7% and 18% for Groups N and P).

Status of treatment of parkinsonism in DLB patients

Ninety-eight physicians in Group N and 90 in Group P answered they managed DLB patients presenting with parkinsonism. Symptoms of parkinsonism in DLB patients were (in descending order) bradykinesia/akinesia (71%), rigidity (69.3%), postural instability (49.1%), frozen gait (39.6%), and tremor including resting and postural tremor (36.6%) in Group N, and rigidity (40.1%), tremor including resting and postural tremor (39.4%), bradykinesia/akinesia (38.9%), postural instability (31.3%), and frozen gait (31.2%) in Group P, indicating different frequencies of parkinsonism symptoms between the groups (Fig. 1). Tremor was significantly less frequent than the other
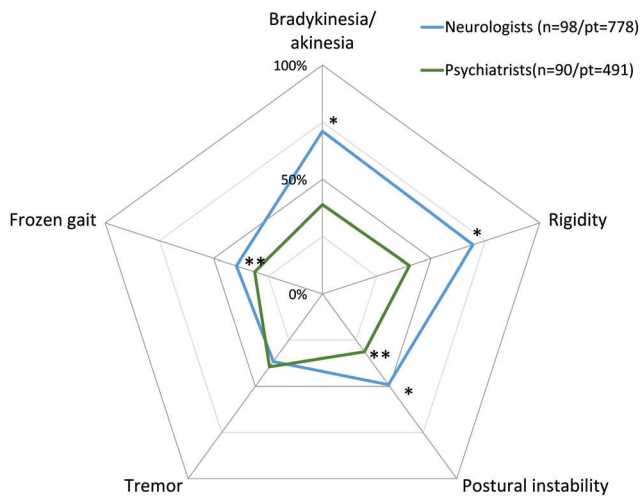
Figure 1 Types of parkinsonism noted in patients with dementia with Lewy bodies (DLB). Q4. Regarding parkinsonian symptoms in DLB patients, please indicate the proportion of patients presenting with each of the symptoms listed below, when the proportion of patients with parkinsonian symptoms is taken as 100. Differences in population rates were tested (unpaired). *P < 0.01 vs. tremor, neurology; **P < 0.01 vs. tremor, psychiatry. pt, patients

symptoms excluding frozen gait in Group N (P < 0.01), whereas tremor was significantly more frequent than postural instability and frozen gait in Group P (P < 0.01).

In both groups, 'going out' accounted for the greatest proportion of disturbed ADL in DLB patients

presenting with parkinsonism (Fig. 2) and the parkinsonism that DLB patients expressed the greatest desire to treat was gait disturbance. However, physicians' highest treatment priorities were bradykinesia/akinesia in Group N and tremor in Group P, indicating a discrepancy between patient need and medical care provider awareness of treatment (Fig. 3).

For the treatment of parkinsonism accompanying DLB, 39.0% and 33.0% of physicians in Groups N and P attached the greatest importance to lower incidences of hallucinations/delusions and other adverse drug reactions followed by: (Group N) highly effective (20.0%); continuous long-term administration is possible (7.0%); long-lasting effects (5.0%); sufficient and appropriate evidence obtained (5.0%); fast-acting (3.0%); good patient compliance (2.0%); few drug–drug interactions (2.0%); and (Group P) long-lasting effects (12.0%); highly effective (11.0%); continuous long-term administration (7.0%); fast-acting (7.0%); sufficient and appropriate evidence (4.0%); few drug–drug interactions (2.0%); easy dose modification (2.0%); drug has been used successfully (2.0%); and good patient compliance (1.0%) (Fig. 4). [Correction added on 3 July 2019, after first online publication: the statement 'For the treatment of parkinsonism accompanying DLB, 56.0% and 52.0% of physicians…" on the first sentence has been corrected to "For the treatment of parkinsonism accompanying DLB, 39.0% and 33.0% of physicians…']
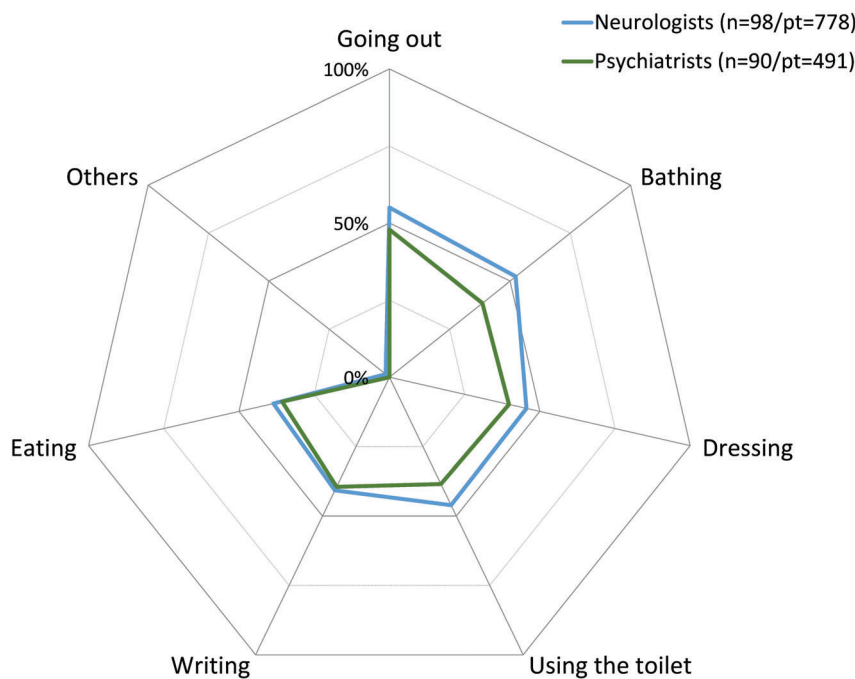

Figure 2 Disturbed activities of daily living areas in dementia with Lewy bodies (DLB) patients. Q6. When the proportion of DLB patients who present with parkinsonian symptoms is taken as 100, please indicate the proportion of patients in whom each of the activities of daily living listed below is disturbed by the parkinsonian symptoms. pt, patients.
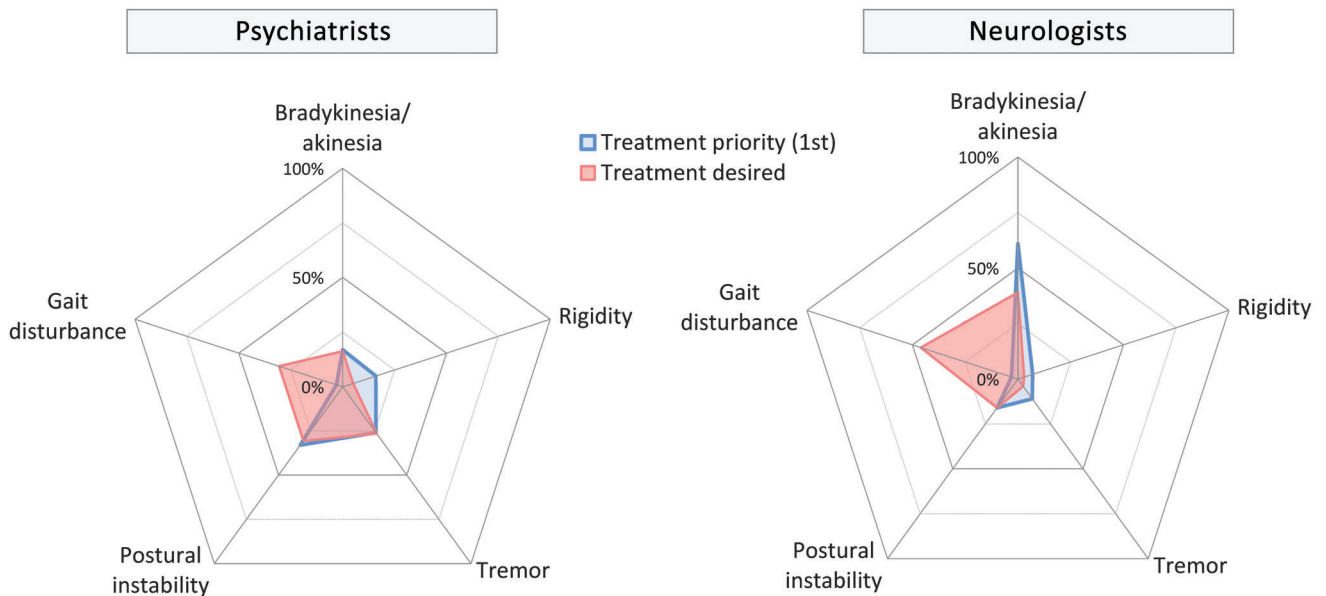
Psychiatrists

Neurologists

Figure 3 Discrepancy between parkinsonism symptoms which dementia with Lewy bodies (DLB) patients want to treat and symptoms to which physicians consider to give the highest treatment priority. Discrepancy between the prioritised parkinsonian symptoms in DLB patients to be treated and the parkinsonian symptoms DLB patients want to treat (Q5 vs. Q8SQ1). [Correction added on 3 July 2019, after first online publication: Titles of the left and right graphs have been corrected.]

The most frequently chosen first-line therapy for parkinsonism accompanying DLB was L-dopa in both groups (88.9% Group N vs. 38.6% Group P; $P < 0.01$) followed by dopamine agonists and anticholinergic agents (26.5% and 25.3%, Group P vs. 5.1% and 1.0%, Group N; $P < 0.01$). No significant differences were noted for other anti-Parkinson's medications (Fig. 5).

The mean doses of L-dopa were markedly different at < 200 mg/day (11.5% and 48.9% in Groups N and P) and ≥ 300 mg/day (38.6% and 12.8% in Groups N

and P) but not for ≥ 200 to < 300 mg/day (50% and 38% in Groups N and P).

Features of L-dopa which physicians were satisfied with were (descending order) highly effective (65.6% Group N, 48.9% Group P); fast-acting (39.6% Group N, 27.7% Group P), and continuous long-term administration (28.1% Group N, 27.7% Group P). Few were satisfied with long-lasting effectiveness (11.5% Group N, 10.6% Group P) and low incidences of hallucinations/delusions as adverse drug reactions (19.8% Group N, 8.5% Group P). Features of L-dopa

Figure 4 Matters given the greatest importance by physicians when they select medications for the treatment of parkinsonism accompanying dementia with Lewy bodies (DLB). Q19. Please indicate the matter you attach the greatest importance to when you select therapeutic drugs for parkinsonian symptoms associated with DLB. [Correction added on 3 July 2019, after first online publication: Image and caption of Figure 4 have been corrected.]
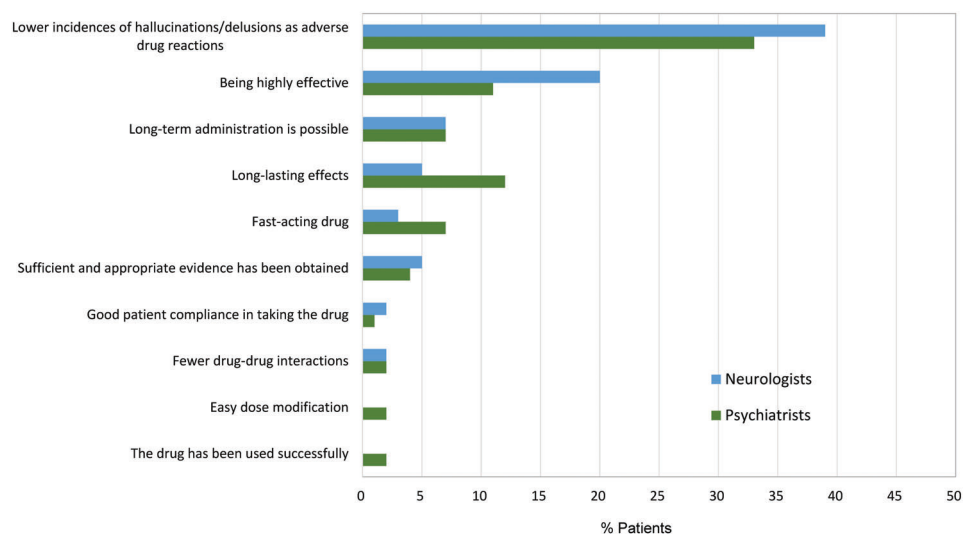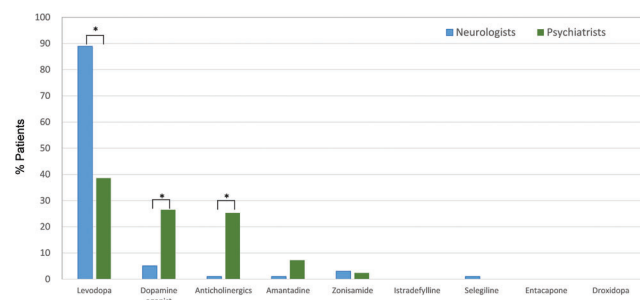
Figure 5 First-line therapies for parkinsonism accompanying dementia with Lewy bodies (DLB). Q10. First-line drugs prescribed for treatment of parkinsonian symptoms in DLB patients. Differences in population rates were tested (unpaired). Neurology vs. psychiatry, significant difference, *P < 0.01. [Correction added on 3 July 2019, after first online publication: Image and caption of Figure 5 have been corrected.]

which physicians were dissatisfied with were 'high frequencies of hallucinations/delusions as adverse drug reactions' (38.5% and 46.8% in Groups N and P), which were highest in both groups followed by 'short-lasting effects' (30.2% Group N, 10.6% Group P).

In Group N, time from prescription of L-dopa to attenuation of L-dopa effect was ≥ 1 year to < 3 years (36.5%), followed by ≥ 3 years to < 5 years (34.4%), and ≥ 3 months to < 1 year (16.7%). In contrast, Group P was ≥ 1 year to < 3 years (42.6%), ≥ 3 months to < 1 year (34.0%), and ≥ 3 years to < 5 years (12.8%). Proportions of patients who responded inadequately to L-dopa was 47.0% and 39.5% in Groups N and P. In 37.7% and 53.9% of these (Groups N and P) physicians wanted to increase doses of L-dopa but did not. The most frequently selected answer for not increasing the dose was possible aggravation of visual hallucinations by pharmacological effects of L-dopa (46.1% Group N, 54.5% Group P).

Eight physicians in Group N and 30 in Group P responded it was unnecessary to treat parkinsonism accompanying DLB because 'psychiatric symptoms worsen' (50% Group N, 26.7% Group P).

DISCUSSION

We performed an internet-aided survey of physicians routinely engaged in the diagnosis and management of dementia to identify the actual status of therapeutic interventions for parkinsonism accompanying DLB in Japan. Among participating medical doctors, we selected neurologists (Group N) and psychiatrists (Group P) because the departments of neurology and psychiatry are usually involved in the management of DLB patients. Furthermore, these departments are at opposite ends, one specialising in Parkinson's disease with a focus on treatment with D2 receptor agonists, and the other specialising in schizophrenia with a focus on treatment with D2 receptor blockers. We considered that first finding commonalities and differences in treatment of the same disease at departments having a relationship as above would lead to a powerful guide for future surveys and in setting the direction of research. We therefore limited the survey results to two departments, neurology and psychiatry, to include in this study. We compared the two groups by each questionnaire item to identify differences and trends.

The evaluation of demographic factors of physicians routinely engaged in the diagnosis and treatment of DLB revealed no differences between Groups N and P for the age of physicians, mean number of dementia patients per month (range 51–59 in both groups), and top three causative diseases (ATD, cerebrovascular dementia, and DLB). The proportion of physicians who made a diagnosis themselves and decided on their own therapeutic strategies was high in both groups, and almost none of the participating physicians answered that they entrusted to specialists all of the following actions: making a diagnosis, formulating therapeutic strategies, and prescribing therapeutic drugs. These results are not contradictory to the perception in Japan, that DLB is primarily managed in the departments of neurology and psychiatry. Differences between the groups were found for types of drugs prescribed for the past 6 months: Group P more frequently prescribed psychotropics such as antipsychotic drugs, Yokukansan and Yokukansankachimpihange, trazodone, benzodiazepine anti-anxiety drugs, and mood stabilisers. This difference may reflect the characteristic features of the psychiatric department. Psychotropics prescribed for the past 6 months in Group P are shown for reference (Fig. 6).

Surprisingly, results for the diagnosis and treatment of DLB revealed the proportion of physicians performing neurological examinations was lower in Group P compared with Group N. This may be related to another finding that the proportion of physicians who answered that the most challenging issue when diagnosing DLB was 'difficulty in
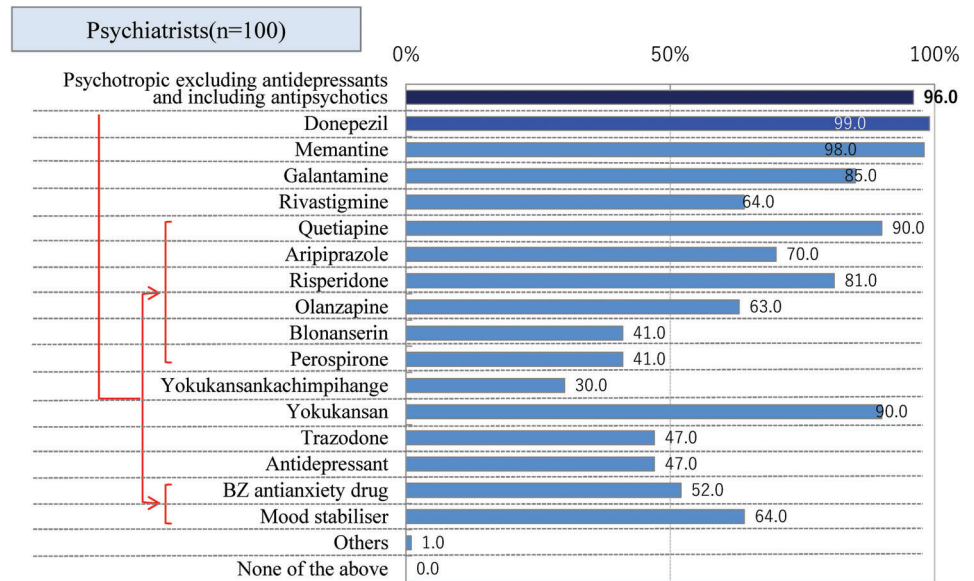
Figure 6 Types of psychotropics prescribed for the past 6 months in Group P.

Psychiatrists(n=100)

Drug	Value
Psychotropic excluding antidepressants and including antipsychotics	96.0
Donepezil	99.0
Memantine	98.0
Galantamine	85.0
Rivastigmine	64.0
Quetiapine	90.0
Aripiprazole	70.0
Risperidone	81.0
Olanzapine	63.0
Blonanserin	41.0
Perospirone	41.0
Yokukansankachimpihange	30.0
Yokukansan	90.0
Trazodone	47.0
Antidepressant	47.0
BZ antianxiety drug	52.0
Mood stabiliser	64.0
Others	1.0
None of the above	0.0

Difference in population rates was tested (unpaired).
Neurologists/Neurosurgeons vs. Psychiatrists, **p<0.01, *p<0.05, -: no significant difference .

obtaining neurological findings' was more than two times greater in Group P than in Group N. These findings together with the other relevant finding that imaging examinations are more frequently performed in Group N indicates the method of managing the disease is fundamentally different between the two departments. These differences may be partly explained by the process of making a diagnosis. In the department of psychiatry, relevant symptoms are identified through medical interview and based on these symptoms, a diagnosis is made according to the *Diagnostic and Statistical Manual of Mental Disorders* fifth edition in an operational manner. In the department of neurology, pathophysiological abnormalities based on organic factors constitute the foundation of diagnosis making, which is combined with diagnostic axes including general physical examinations, neurological examinations, and imaging examinations, leading to a diagnosis. The differences in how a medical care unit manages patients may determine whether the unit is more proactive in conducting neurological examinations. Although resting tremors occur less frequently in DLB than in PD,[4] the disease-specific tremor is a resting tremor with bilateral differences because the neuropathological continuity of each disease exists behind the manifestation of tremor. In Group P, the most frequently noted symptoms of parkinsonism in DLB patients was rigidity, followed by tremor, which substantially different

from Group N. This suggests that in Group P in which many physicians answered 'difficult to obtain neurological findings', resting tremor and action tremor may be mixed up. This possibility is inferred from the significantly higher frequency of prescribing antipsychotics in Group P where drug-related parkinsonism may have been included in the primary tremor (resting tremor). Resting tremor typically shows a unique pattern and rhythm called 'pill rolling': if a physician accumulates their experience of seeing actual resting tremor and understands its characteristics, then they can easily differentiate resting tremor from other types of tremor. Therefore, if learning tools such as video training materials that explain the characteristic features of neurological findings and how to interpret neurological examination results are prepared to standardise the skills of care providers, the results of this questionnaire item may change in the future.

Regarding enlightenment activities to improve diagnostic accuracy, we found that in both groups, screening for RBD was one of the issues that can be better utilised. RBD is listed as a core clinical symptom in the new DLB clinical diagnostic criteria,[1] indicating it is an extremely important clinical symptom. Identifying RBD by screening in a more proactive manner facilitates the subsequent implementation of overnight polysomnography, and ultimately contributes to the improvement of diagnostic accuracy. Screening tests such as RBDSQ-J,[5,6] and Sleep

Talking Test,[7] for which evidence has been accumulated for validity and utility are not complicated and do not require an excessively long period of time to perform. For future enlightenment activities, it is important to make the usefulness of these screening tests well known to those concerned. In addition, the new DLB clinical diagnostic criteria has set indicative biomarkers for the management of DLB, indicating more weight should be attached to the importance of objective indicators such as DAT-SPECT and MIBG-imaging. In particular, MIBG-imaging provides a highly accurate diagnosis even with early images alone and is less invasive to patients; consequently, it may be worthwhile to consider more proactively the implementation of MIBG-imaging.[8]

The two groups differed from each other in clinical diagnoses made prior to the definite diagnosis of DLB. The top three diagnoses were PD, ATD, and depression in Group N, and ATD, delirium, and depression in Group P. These differences may be explained by the phenomenon that depending on which symptoms patients and their family members attach importance to, the medical care unit they visit varies: DLB patients in whom motor symptoms attract more attention than the other symptoms inevitably select Group N, whereas DLB patients in whom cognitive impairment and behavioural and psychological symptoms of dementia attract more attention select Group P. One of the reasons why delirium was frequently used for diagnosis before a definite diagnosis of DLB in Group P is because generally speaking, the frequency of asking for the management of delirium in psychiatry departments is high in Japan. The clinical manifestations of delirium are extremely close to those of cognitive fluctuation, which is a core clinical symptom of DLB, and it is extremely difficult to differentiate between these. Even the Confusion Assessment Method (CAM), which identifies delirium with a sensitivity of 94% and a specificity of 89%,[9,10] overlaps with the clinical manifestations observed in cognitive fluctuation in DLB. Delirium was reported to occur significantly more frequently in DLB than in ATD.[11] Accordingly, Group P, in particular, should take care of patients while keeping delirium in mind because Group P has many opportunities to manage delirium. The third frequently used diagnosis prior to the definite diagnosis of DLB in both groups was depression. It is known that DLB is frequently complicated by depression, including

pre-dementia stages.[12,13] Therefore, in the elderly, physicians need to try and differentiate between depression and DLB.

Evaluation of the actual status of treatment of motor symptoms revealed that in both groups, motor symptoms were treated in parallel with cognitive impairment and behavioural and psychological symptoms of dementia, although individual treatments differed from each another. As described in the Results, the parkinsonism that DLB patients expressed the greatest desire to treat was 'gait disturbance' in both groups. In contrast, the symptom to which physicians give the highest treatment priority was bradykinesia/akinesia in Group N and tremor in Group P. These results indicate a discrepancy between the patients' needs and the physicians' awareness of treatment.

However, in the case of Group N, discrepancy is acknowledged as an item, but in reality, gait disturbance in patients with parkinsonism results from a combination of basic features, among which bradykinesia is often predominant. Thus, it may be that, at least among opinions of neurologists, there is no discrepancy between patients' expectations and medical priorities of treatment.

The area of ADL disturbed by parkinsonism was 'going out' in both groups. This finding is linked to the symptom that patients expressed the greatest desire to treat. These results are important because they suggest that when a patient's QOL is taken into account, physicians should carefully determine whether the treatment administered to a patient satisfies the patient's needs while managing the patient from a medical viewpoint.

The evaluation of drugs used for the treatment of motor symptoms revealed that physicians in both groups attached the greatest importance to lower incidences of hallucinations/delusions and other adverse drug reactions. In addition, physicians in Group N used drugs that are 'highly effective', 'can continuously be administered for a long period of time', 'exert long-lasting effects', and 'quickly exert the effects.' However, physicians in Group P attached more importance to 'long-lasting effects', 'continuous long-term administration is possible', 'fast-acting drug', and 'fewer drug–drug interactions' than to 'being highly effective.' The motivations to select drugs are similar between the two groups. Based on these motivations, L-dopa was selected as a first-line therapy, and this selection is considered

valid based on the evidence level. McKeith *et al.* described that levodopa can be used for the motor disorder of both DLB and Parkinson's disease with dementia, and thus recommended L-dopa for the treatment of parkinsonism accompanying DLB.[2] Molloy *et al.* compared the usefulness of L-dopa in PD, Parkinson's disease dementia, and DLB and reported L-dopa was useful.[14] Stinton *et al.* performed a meta-analysis and reported the efficacy of L-dopa in DLB.[15] However, the results of this survey revealed that in both groups, care providers wanted to increase doses of L-dopa but did not because they had concerns about the possible aggravation of visual hallucinations. Furthermore, some care providers, although small in number, considered it unnecessary to treat parkinsonism accompanying DLB because such treatments may worsen psychiatric symptoms. The concern expressed by these care providers cannot be totally denied because researchers reported that only a small number of patients treated with L-dopa (mean dose of 370 mg/day) for whom the motor symptoms were improved did not have aggravated psychiatric symptoms.[16] Thus, it is important to administer L-dopa carefully while evaluating the risks and benefits of the drug, and multi-centre joint research is necessary to evaluate the efficacy and safety of L-dopa, including the optimal dosage.

Regarding the selection of therapeutic drugs, an interesting result was that 26.5% and 25.3% of physicians in Group P answered that they selected dopamine agonists and anticholinergic agents as first-line therapies. These proportions were significantly different from the corresponding figures in Group N and differed from the mainstream treatment of parkinsonism accompanying DLB.

There is much evidence that L-dopa improves motor symptoms better than dopamine agonists. Many researchers have reported that the frequencies of hallucinations and daytime drowsiness are significantly higher with dopamine agonists than with L-dopa.[17–21] Based on these findings, neurologists share a common understanding that in the elderly and patients with dementia, dopamine agonists are not chosen as first-line therapies, and the same applies to DLB. Sharing this understanding among more medical professionals is a future issue we need to address.

Regarding anticholinergic drugs, Group P had many patients presenting with resting tremor, which the psychiatrists prioritised for treatment. Based on the characteristic features of psychiatric departments, psychiatrists commonly administer D2 receptor blockers, and anticholinergic drugs to treat drug-related parkinsonism caused by D2 receptor blockers. In addition, psychiatrists try to avoid the aggravation of psychiatric symptoms such as hallucinations and delusions. It is therefore presumed that these multiple factors are reflected by the survey results, indicating that the number of physicians who select anticholinergic agents as a first-line therapy was significantly greater in Group P (psychiatrists) than in Group N (neurologists). From the viewpoint of pharmacological mechanism of action, anticholinergic drugs are useful for tremor, although their efficacy is inferior to that of L-dopa.[22] Above all, anticholinergic drugs inhibit the acetylcholine system in the nucleus basalis of Meynert to induce cognitive impairment.[23] It was reported that an increase in anticholinergic serum activity that indicates anticholinergic activity was correlated with the occurrence of delirium and cognitive impairment.[24] Furthermore, Ehrt *et al.* reported a relationship between anticholinergic drugs and cognitive impairment in PD patients.[25] In DLB in which the degeneration and loss of cholinergic nerve cells in the nucleus basalis of Meynert are marked and the activity of choline acetyltransferase is reduced,[26] drugs that inhibit the acetylcholine system at the basal nucleus of Meynert should be avoided. Further multifaceted studies are necessary, and regarding the risks of anticholinergic drugs in particular, we need to make these risks more widely known among the physicians concerned. (Partly due to the characteristic features of the department as described above, it is difficult to provide reasons or motivations as to why anticholinergic drugs are prescribed by some psychiatrists. Either way, risks of anticholinergic drugs must be made more widely known.) Some Japanese psychiatrists prescribe anticholinergic drugs for patients with antipsychotic drug-induced parkinsonism. Therefore, when DLB patients taking antipsychotic drugs are associated with parkinsonism, anticholinergic drugs may be prescribed considering that parkinsonism was induced by antipsychotic drugs.

The present survey had some limitations. For example, it was performed on a small number of physicians who are registered at a survey company. However, to the best of our knowledge no previous studies have identified the actual status of the management of DLB and treatment of parkinsonism, and compared neurologists and psychiatrists who are primarily engaged in the management of DLB. This survey identified similarities and differences between the two medical care units and the results of this survey will have substantial implications for the development of future DLB therapeutic strategies. We plan to perform a larger-scale follow-up investigation.

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