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Contents

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Selected from Movement Disorders Vol.30 No.11 - No.12, 2015

Abstract

パーキンソン病に対する疾患修飾戦略

Disease-Modifying Strategies for Parkinson's Disease

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Movement Disorders, Vol. 30, No. 11, 2015, pp. 1442–1450

パーキンソン病（Parkinson's disease; PD）は，進行性の運動障害を伴う神経変性疾患であり，その有病率はますます上昇している。PD による患者やその家族への影響および保健医療制度の負担は，疾患修飾療法により，神経変性の進行を遅延させたり，疾患の過程を停止させたりすることで大幅に軽減する可能性がある。いくつもの薬剤について，PD に対する疾患修飾効果を評価するための臨床試験が実施されているが，いずれも失敗に終わっている。過去 3 年間には，2 型アデノ随伴ウイルス（adeno-associated virus serotype; AAV）ベクターによる neurturin の送達，コエンザイム Q10，クレアチン，プラミペキソール，ピオグリタゾンに関して検討されたが，陰性または無効であることを示す臨床試験結果が報告された。これらの残念な結果の一方で，研究は進展している。新たな治療標的の発見を可能とする PD の分子病態の理解は進み，前臨床試験のための新規動物モデルが開発されている。現在，少なくとも 8 件の臨床試験が進行中であり，isradipine，カフェイン，ニコチン，グルタチオン，2 型 AAV ベクターによるグリア細胞株由来神経栄養因子（glial cell-line derived neurotrophic factor; GDNF）の送達や，α シヌクレイン（α-synuclein; α-Syn）に対する能動免疫および受動免疫が検討されている。本総説では，2013 年以降に発表された PD の疾患修飾療法の臨床試験および現在進行中の臨床試験について要約する。PD における本研究分野で有望と考えられる治療戦略と現在の課題についても考察する。

（監訳：宇川　義一）

KEY WORD　オートファジー，遺伝子治療，LRRK2，ミトコンドリア，神経保護

Table 1　2013～2015 年における有効性が証明出来なかった PD の疾患修飾療法の臨床試験

Study	Drug	Mechanism of Action	Trial Design	Subjects	Follow-up Period	Primary Outcome Measure(s)	Results
Olanow et al., 2015[6]	AAV2-Neuturin (injection into bilateral SNpc and putamen)	Neurotrophic factor	Multi-center, randomized, double-blind, sham surgery-controlled, phase 2 trial	Advanced PD subjects (n = 51)	15-24 months	Change in UPDRS part 3 in practically defined "off"-state	No statistically significant difference between treated and control groups
PSG et al., 2014 (QE3)[8]	Coenzyme Q10 (1200 mg/d or 2400 mg/d) + vitamin E (1200 IU/d)	Bioenergetic; Antioxidant	Multi-center, randomized, double-blind, placebo-controlled, phase 3 trial	Early PD subjects not requiring dopaminergic therapy (n = 600)	16 months (or until requiring dopaminergic therapy if sooner)	Change in total UPDRS score	Prematurely terminated due to futility
NET-PD et al., 2015 (LS1)[9]	Creatine (10 g/d)	Bioenergetic	Multi-center, randomized, double-blind, placebo-controlled, phase 3 trial	Early PD subjects receiving dopaminergic therapy (n = 1741)	4 years (median)	Difference in decline of clinical status defined by 5 outcome measures	Prematurely terminated due to futility
Schapira et al., 2013 (PROUD)[13]	Pramipexole (1.5 mg/day)	D2/D3 dopamine receptor agonist	Multi-center, randomized, double-blind, placebo-controlled, delayed-start trial	Early PD subjects not requiring dopaminergic therapy (n = 535)	15 months	Change in total UPDRS score	No statistically significant difference between early-start and delayed-start groups
NET-PD, 2015 (FS-ZONE)[15]	Pioglitazone (15 mg/d or 45 mg/d)	PPAR-γ agonist	Multi-center, randomized, double-blind, placebo-controlled, futility trial	Early PD subjects on rasagiline or selegiline (n = 210)	44 weeks	Change in total UPDRS score	Futility

AAV2 = 2 型アデノ随伴ウイルス，LS1 = Long-term Study 1，PD = パーキンソン病，PPAR = ペルオキシソーム増殖因子活性化受容体（peroxisome proliferator-activated receptor），PROUD = Pramipexole On Underlying Disease，QE3 = Coenzyme Q10 in Early Parkinson Disease，SNpc = 黒質緻密部（substantia nigra pars compacta），UPDRS = Unified Parkinson's Disease Rating Scale

※日本語版注釈：Table 1 の参考文献は wileyonlinelibrary.com のオンライン版で閲覧可能です。

Table 2　2015 年において進行中の PD の疾患修飾療法の臨床試験

Study	Drug	Mechanism of Action	Trial Design	Estimated Enrollment	Follow-up Period	Primary Outcome Measure(s)	Status
NCT02216188	PD01A + adjuvant (subcutaneous injection; 15μg or 75μg booster x 1)	Active immunization against α-synuclein	Single-center (Austria), randomized, single-blind, follow-up, phase 1 trial	PD subjects who previously received PD01A and untreated controls (n = 32)	6 months	Safety and tolerability	Enrolling by invitation
NCT01885494	PD01A + adjuvant (subcutaneous injection; 15 μg or 75 μg × 4)	Active immunization against α-synuclein	Single-center (Austria), observational, follow-up, phase 1 extension trial	PD subjects who previously received PD01A and untreated controls (n = 32)	52 weeks	Safety and tolerability	Active but not recruiting
NCT02267434	PD03A + adjuvant (subcutaneous injection; 15 μg or 75 μg × 4)	Active immunization against α-synuclein	Dual-center (Austria), randomized, single-blind, placebo-controlled, phase 1 trial	Early PD subjects (n = 36)	52 weeks	Safety and tolerability	Recruiting
NCT02157714	PRX002 (intravenous infusion)	Passive immunization against α-synuclein	Multi-center (United States), randomized, double-blind, placebo-controlled, phase 1 trial	PD subjects (n = 60)	6 months	Safety and tolerability; several pharmacokinetic parameters	Recruiting
NCT01738178	Caffeine (400 mg/d)	Nonspecific adenosine receptor antagonist	Multi-center (Canada, Brazil), randomized, double-blind, placebo-controlled, phase 3 trial with delayed-start component	PD subjects (n = 250)	5 years	MDS-UPDRS score	Recruiting
NCT01621581	AAV2-GDNF (convection enhanced delivery to bilateral putamen)	Neurotrophic factor	Single-center (United States), open-label, phase 1 trial	Advanced PD subjects (n = 24)	5 years	Safety and tolerability; several clinical measures	Recruiting
NCT02168842 (STEADY-PD III)	Isradipine (immediate release; 10 mg/d)	Dihydropyridine calcium channel blocker	Multi-center trial (United States, Canada), randomized, double-blind, placebo-controlled, phase 3 trial	Early PD subjects not requiring dopaminergic therapy (n = 336)	36 months	Change in total UPDRS score	Recruiting
NCT01560754 (NIC-PD)	Nicotine (transdermal patch; 7-28 mg/d)	Nicotinic acetylcholine receptor agonist	Multi-center (Germany, United States), randomized, double-blind, placebo-controlled, phase 2 trial with washout period	Early PD subjects not requiring dopaminergic therapy (n = 160)	12 months followed by 2-month washout period	Change in total UPDRS score	Recruiting
NCT02424708	GSH (intranasal; 300 mg/d or 600 mg/d)	Antioxidant	Dual-center (United States), randomized, double-blind, placebo-controlled, phase 2 trial	PD subjects (n = 45)	12 weeks	Change in total UPDRS score	Recruiting
NCT01470027	N-acetylcysteine (1800 mg/d or 3600 mg/d)	GSH precursor	Single-center (United States), randomized, double-blind, placebo-controlled, phase 1/2 trial	PD subjects on no medications for PD (n = 60)	4 weeks	Change in cerebral GSH levels measured by proton magnetic resonance spectroscopy	Recruiting
NCT01882010	Sagramostim (subcutaneous injection; 6 μg/kg/d)	GM-CSF	Dual-center (United States), randomized, double-blind, placebo-controlled phase 1 trial	PD subjects and non-PD controls (n = 32)	52 weeks	Safety and tolerability	Recruiting
NCT01453803	Adipose-derived stromal stem cells (intraarterial and intravenous infusion)	Multiple	Single-center (Mexico), open-label, phase 1/2 trial	PD subjects with motor complications (n = 10)	6 months	Safety and tolerability; UPDRS scores	Recruiting

AAV2 = 2 型アデノ随伴ウイルス，GDNF = グリア細胞株由来神経栄養因子（glial cell-line derived neurotrophic factor），GM-CSF = 顆粒球 - マクロファージコロニー刺激因子（granulocyte-macrophage colonystimulating factor），GSH = グルタチオン（glutathione），MDS-UPDRS = Movement Disorder Society による Unified Parkinson's Disease Rating Scale 改訂版，PD = パーキンソン病，UPDRS = Unified Parkinson's Disease Rating Scale

Abstract

レボドパ誘発性運動合併症に対する新たな治療法

New Treatments for Levodopa-Induced Motor Complications

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Motor fluctuation やジスキネジアなどのレボドパ（L-ドパ）誘発性運動合併症は，パーキンソン病（Parkinson's disease; PD）の経過中，ほぼすべての患者にみられ，健康状態全般に影響を及ぼす。これらの合併症の管理には，種々のドパミン作動性薬剤および非ドパミン作動性薬剤の投与に加え，医療用具の使用や機能改善のための手術など，より侵襲的な方法も利用できるようになった。この数十年間に治療法が改善したことに疑問の余地はないが，なお多くの患者が重大な運動障害に悩まされており，L-ドパ誘発性運動合併症に対する完全に満足のいく管理法の確立は，PD の治療において今後の研究が必要とされる領域である。本稿では，2013 年～ 2015 年 4 月に発表された，運動合併症に対する薬物療法および非薬物療法に関する最近の臨床試験結果をレビューする。合併症が既に確立した患者を対象とする無作為化対照試験では，L-ドパ－カルビドパ空腸内注入および L-ドパ－カルビドパ二層性徐放性製剤（IPX066）など，新たな L-ドパ製剤により motor fluctuation が改善することが示されている。また，新規のモノアミンオキシダーゼ B（monoamine oxidase B; MAO-B）阻害薬（safinamide）およびカテコール -O- メチルトランスフェラーゼ（catechol-O-methyltransferase; COMT）阻害薬（opicapone）でも，肯定的な結果が得られている。さらに，予備的データではあるが，ドパミンアゴニストの新規製剤（アポモルヒネ吸入剤）も有望であることが示唆されている。一方で，新規の非ドパミン作動性アデノシン A_{2A} 受容体拮抗薬（istradefylline，preladenant および tozadenant）が motor fluctuation の治療を目的に開発されているが，第 II 相および第 III 相試験の結果には矛盾がある。ジスキネジアについては，新しいアマンタジン徐放性製剤の臨床試験を通じ，グルタミン酸作動性 *N*-メチル -D- アスパラギン酸（NMDA）型アンタゴニストによる治療への期待が高まっている。Eltoprazine などのセロトニン作動性薬剤や mavoglurant などのグルタミン酸受容体 mGluR5 修飾剤（modulator）についても，最近の予備的な試験において，肯定的な抗ジスキネジア作用が報告されている。しかし，その後，mavoglurant の抗ジスキネジア作用を確認するための第 II 相試験は失敗に終わっており，この適応における本化合物の開発は中断されている。したがって，このような革新的な開発コンセプトの実地臨床への応用については，依然として課題がある。

（監訳：梶　龍兒）

KEY WORD　パーキンソン病，motor fluctuation，ジスキネジア，ウェアリングオフ現象，レボドパ，薬物療法

Table 1 2013～2015年における運動合併症に対する新たな薬剤または製剤

Drug and formulation	New studies in the period 2013-2015	Main results	Safety	Development/ marketing status
New formulations of levodopa				
Continuous intrajejunal infusion of levodopa-carbidopa intestinal gel	1 R, DB, DD trial vs levodopa IR[12]	Reduced daily OFF-time, increased "good" ON-time	Related to the device or infusion	Commercialized in USA and Europe
IPX066	1 R, DB, DD vs levodopa IR[20] 1 R, DB, CO, DD trial vs entacapone[21]	Reduced daily OFF-time, increased "good" ON-time	Same as L-dopa IR	Commercialized in USA
XP21279	1 R, DB, DD, CO vs levodopa IR[25]	No effects on OFF-time, reduced percentage deviation from the mean L-dopa concentration	Same as L-dopa IR	In Phase II
Melevodopa	1 OL, CS, vs levodopa IR[26]	Shorter onset of motor benefit after an oral dose	Same as L-dopa IR	In Phase II
New COMT or MAO-B inhibitors				
Opicapone	2 R, DB vs placebo or entacapone[32,33]	Increased L-dopa exposure, reduced off-time	Dyskinesia, insomnia, dizziness, nausea	In Phase III
Safinamide	1 R, DB vs placebo[38]	Increased "good" ON-time	Dyskinesia, worsening of PD, cataract, back pain, depression, headache, and hypertension	Commercialized in Europe. NDA submitted to FDA
New formulation of apomorphine				
Inhaled apomorphine	3 R, DB, vs placebo[42-44]	Greater motor improvements after a single dose	Somnolence, yawning, flushing, dysgeusia, dizziness, orthostatic hypotension	In Phase III
New formulation of amantadine				
Extended-release amantadine	1 R, DB vs placebo[56]	Reduced dyskinesia frequency/severity	Constipation, hallucinations, dizziness, dry mouth	In Phase III
New A2A antagonists				
Istradefylline	1 R, DB vs placebo[47]	Reduced OFF-time	Dyskinesia	Marketed in Japan and USA
Tozadenant	1 R, DB vs placebo[64]	Reduced daily OFF-time	Dyskinesia, nausea, dizziness	In Phase III
Caffeine	1 Exploratory cohort study[63]	Less frequent dyskinesia in consumers of 12 oz/d	—	Worldwide available in supermarket
New glutamatergic antagonists				
Mavoglurant	1 R, DB vs placebo[57] 1 R, DB vs placebo[58]	Reduced dyskinesia frequency/severity, NS reduction in OFF-time	Dizziness, hallucination, fatigue, nasopharyngitis, diarrhea, insomnia	In Phase III
New serotoninergic drugs				
Eltoprazine	1 R, DB vs placebo[62]	Reduction of dyskinesia frequency/severity	Nausea, dizziness	In Phase III
Other drugs				
Tetrabenazine	1 OL, UC[65]	Reduced dyskinesia frequency/severity	—	Available worldwide for hyperkinetic disorders
Simvastatin	1 n-of-1 trial[66]	No effects on dyskinesia	—	Available worldwide for hypercholesterolemia
Topiramate	1 R, DB, CO vs placebo[67]	No effects on dyskinesia	Dry mouth, cognitive, breathing problems	Available worldwide for epilepsy

DB＝二重盲検，DD＝二重ダミー，CO＝クロスオーバー，CS＝横断的，IR＝速放性，NS＝非有意，OL＝非盲検，R＝無作為化，UC＝非対照

"Good" ON-time＝患者を悩ませるジスキネジアのないオン時間

STN-DBS＝視床下核の深部脳刺激療法

※日本語版注釈：Table 1 の参考文献は wileyonlinelibrary.com のオンライン版で閲覧可能です。

Abstract

多系統萎縮症と進行性核上性麻痺における治療の進歩

Therapeutic Advances in Multiple System Atrophy and Progressive Supranuclear Palsy

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多系統萎縮症（multiple system atrophy; MSA）および進行性核上性麻痺（progressive supranuclear palsy; PSP）は絶え間なく進行する神経変性疾患であり，患者は高度の身体機能障害に至り，最終的に 10 年以内に死亡する。基礎研究および臨床研究はますます盛んに行われているが，これらの非定型パーキンソン病症状に対する有効な治療法は存在しない。以前に実施された MSA および PSP に関する小規模の臨床試験では主に対症療法が検討されたが，その後，これらの疾患の分子レベルの基礎に関する理解やバイオマーカーの探索が進み，疾患修飾療法に関する十分にデザインされた大規模臨床試験が実施されている。これらの試験における介入の標的として，MSA ではαシヌクレイン封入体病変，PSP ではタウ関連の機序がある。2013 年以降，疾患修飾療法に関する 4 件の大規模無作為化プラセボ対照二重盲検試験が完了し，結果が発表された。これらの試験では rasagiline（MSA），リファンピシン（MSA），tideglusib（PSP），davunetide（PSP）が検討されたが，いずれでも主要評価項目に関する有効性は認められなかった。別の 2 件の無作為化プラセボ対照二重盲検試験では，MSA 患者も被験者となり，神経原性起立性低血圧の対症療法におけるドロキシドパの有効性が検討され，1 件の試験では肯定的な結果が得られている。本総説では，これらの臨床試験や 2013 年以降に発表された他の小規模試験のデザインと成績について要約し，今後の MSA および PSP の治療研究で優先すべき分野に注目する。

（監訳：服部　信孝）

KEY WORD　多系統萎縮症，進行性核上性麻痺，臨床試験，治療法

Table 1　MSA の臨床試験（2013～2015 年）

Study	Compound	Mechanism of Action	Trial Design (AAN Class of Evidence)	Patients (n) (MSA Patients)	Follow-up Period	Outcome Measure(s)	Results
Saccà et al., 2013[14]	Lithium	Stimulation of autophagy in an attempt to reduce alpha-synuclein deposits	Randomized placebo-controlled, double-blind trial (Class I)	Screened for eligibility: 10 Randomized: 9 Study completers: 1	48 weeks	**Primary:** Frequency of (serious) adverse events. **Secondary:** UMSARS total, magnetic resonance spectroscopy, EQ-5D, BDI-II	Study terminated due to safety concerns
Low et al., 2014[16]	Rifampicin	Inhibition of formation of alpha-synuclein fibrils and dis-aggregation of already formed fibrils; preclini-cal MSA model suggested neu-roprotective efficacy	Randomized placebo-controlled, double-blind trial (Class I)	Screened for eligibility: 285 Randomized: 100 Study completers: 91	52 weeks	**Primary:** UMSARS pt. I **Secondary:** UMSARS pt. II, UMSARS sum score (pt. I and II), COMPASS-select, disability milestones (speech, swallowing, falling)	Study terminated because futility criteria were met at a preplanned interim analysis
Poewe et al., 2014[25]	Rasagiline	Monoamine oxi-dase B inhibi-tion; preclinical MSA model suggested neu-roprotective efficacy	Randomized placebo-controlled, double-blind trial (Class I)	Screened for eligibility: 208 Randomized: 174 Study completers: 138	48 weeks	**Primary:** UMSARS sum score (pt. I and II) **Secondary:** CGI-I, change from base-line to week 24 in UMSARS total score, frequency of loss of independent ambula-tion, COMPASS-Select, MSA-QoL	No difference between treatment and placebo group

UMSARS = Unified Multiple System Atrophy Rating Scale，BDI-II = ベックうつ評価尺度（Beck Depression Inventory）II，EQ-5D = EuroQol 5 Dimensions Quality of Life Questionnaire，COMPASS = Composite Autonomic Symptom Scale，CGI = 臨床的全般印象度（Clinical Global Impression），MSA-QoL = Multiple-System Atrophy Quality of Life Questionnaire

※日本語版注釈：Table 1 の参考文献は wileyonlinelibrary.com のオンライン版で閲覧可能です。

Table 4 未発表および現在進行中の MSA の臨床試験

Study Identifier	Compound/ Intervention	Mechanism of Action	Trial Design	Patients (n)	Follow-up Period	Type of Study	Outcome Measure(s)	Status
NCT01146548	Fluoxetine	Selective inhibitor of serotonin reuptake	Randomized, double-blind, controlled trial	88	6 months	Disease-modification	Primary: UMSARS (baseline to three months), Secondary: UMSARS total (baseline to 6 months), UMSARS total (baseline to 6 weeks), rate of mortality, SCOPA-AUT, UMSARS part III, Beck's depression inventory, MSA-QoL	Unpublished
NCT02071459	Droxidopa	Norepinephrine precursor	Randomized, double-blind, controlled trial	108	12 weeks	Symptomatic	Primary: OHQ part I, Secondary: relative change in mean score of Item 1 of the Orthostatic Hypotension Symptom Assessment (OHSA), UMSARS total, COMPASS, Frequency adverse events	Recruiting
NCT02315027	Autologous mesenchymal stem cells	Cell replacement	Open-label study	24	14 months (safety endpoint), 12 months (efficacy endpoint)	Disease modification	Primary: Adverse event frequency. Secondary (compared with historical control cohort): UMSARS I, UMSARS II, UMSARS total score, COMPASS-select, CASS, thermoregulatory sweat test (%), MRI morphometric changes, CSF biomarkers	Active, not recruiting
NCT02008721	EGCG	Inhibition of toxic α-synuclein oligomers formation	Randomized, double-blind, controlled trial	86	12 months	Disease modification	Primary: UMSARS II, Secondary: UMSARS total score, clinical global impression, global and regional cerebral atrophy (3D MP-RAGE MRI volumetry, 3D FLAIR), global and regional cerebral iron deposition in pons and striatum (T2* MRI), adverse events	Recruiting
NCT02149901	Water/ pseudoephedrine	Alpha-1-adrenergic receptor agonist	Open-label, crossover	35	4 d	Symptomatic	Primary: Change in systolic blood pressure. Secondary: Change in diastolic blood pressure, change in heart rate, absolute systolic blood pressure, absolute diastolic blood pressure, peak plasma norepinephrine concentration	Recruiting
NCT02270489	AFFITOPE® PD01A or PD03A	Active immunization	Randomized, single-blind (subject), controlled trial	30	12 months	Disease modification	Primary: Adverse events, vital signs. Secondary: Immunological activity, UMSARS I, UMSARS II, UMSARS IV, CGI, GDS	Recruiting
NCT01044693	Nebivolol or metoprolol tartrate or Sildenafil	β-Blocker	Randomized, double-blind, crossover trial	18	1 d	Symptomatic	Primary: Fall in systolic blood pressure (from 8:00 p.m. to 8:00 a.m.). Secondary: Urinary volume, SBP and DBP 1 minute post standing the following morning, OHQ Item 1	Active, not recruiting
NCT01927055	Droxidopa	Norepinephrine precursor	Randomized, double-blind, controlled trial	450	17 weeks	Symptomatic	Primary: OHQ Item 1. Secondary: Falls, Standing blood pressure, OHQ, CGI, Boston University Activity Measure for Post-Acute Care Basic Mobility	Active, not recruiting
NCT02388295	AZD3241 MPO inhibitor	Microglial inhibition by myeloperoxidase inhibition	Randomized, double-blind, controlled trial	64	12 weeks	Disease modification	Primary: Adverse events, vital signs, Assessment of the effect on microglia activation via PET imaging. Secondary: Assessment of myeloperoxidase activity by activity assay	Not yet recruiting

UMSARS = Unified Multiple System Atrophy Rating Scale, BDI-II＝ベックうつ評価尺度（Beck Depression Inventory）II, EQ-5D = EuroQol 5 Dimensions Quality of Life Questionnaire, COMPASS = Composite Autonomic Symptom Scale, CGI＝臨床的全般印象度（Clinical Global Impression）, OHQ = Orthostatic Hypotension Questionnaire, OHSA = Orthostatic Hypotension Symptom Assessment, OHDAS = Orthostatic Hypotension Daily Activity Scale, MSA-QoL = Multiple-System Atrophy Quality of Life Questionnaire, BP＝血圧

Abstract

King's Parkinson's Disease Pain Scale（初のパーキンソン病の疼痛に関する評価尺度）：国際的な妥当性の検証

King's Parkinson's Disease Pain Scale, The First Scale for Pain in PD: An International Validation

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疼痛は，パーキンソン病（Parkinson's disease; PD）における主要な非運動症状の 1 つであり，今後の研究が必要とされる領域である。これまでのところ，PD 患者の様々なタイプの疼痛を同定し，その程度を評価することを目的とした，妥当性検証済みの特異的な尺度は存在しない。本稿では，PD に特異的な初の疼痛評価尺度として King's PD Pain Scale を検討し，国際的な多施設共同の横断的非盲検試験〔1 時点（one-point-in-time）の評価，再テスト法〕の結果を報告する。本尺度は 7 領域，14 項目で構成される。重症度（0～3）を項目ごとに評価し，これに頻度（0～4）を乗じることで，0～12 のサブスコアを算出する。総スコアの範囲は 0～168 である。他の原因では説明のつかない疼痛を伴う PD 患者 178 例〔年齢（平均値 ± SD）：64.38 ± 11.38 歳（範囲：29～85 歳），男性：62.92%，罹病期間：5.40 ± 4.93 年〕と，年齢（64.25 ± 11.10 歳）および性別（男性：61.45%）をマッチさせた非配偶者かつ非 PD の対照被験者 83 例を対象とした。欠測データはなかったが，すべての評価領域で床効果が認められた。King's PD Pain Scale の総スコアにおける平均値と中央値との差は，観察された最大値の 10% 未満であった。歪度はわずかに高かった（PD 患者で 1.48）。因子分析では，King's PD Pain Scale の 4 つの因子により，分散の 57% が説明可能であった（Kaiser-Mayer-Olkin：0.73，球面性検定）。Cronbach の α 係数は 0.78，項目－全体の相関の平均値は 0.40，項目の均質性に関する値は 0.22 であった。King's PD Pain Scale の各領域および総スコアと他の疼痛評価尺度との相関係数は高かった。Scale for Outcomes in PD-Motor の総スコア，Non-Motor Symptoms Scale の総スコア，生活の質に関する評価尺度との間に高い相関が認められた。King's PD Pain Scale は，PD 患者にみられる様々なタイプの疼痛を評価するための尺度として，信頼性が高く，有効であると考えられる。

（監訳：望月　秀樹）

KEY WORD　疼痛，パーキンソン病，評価尺度

Table 5b　本試験における King's Parkinson's Disease Pain Scale と他の変数との相関

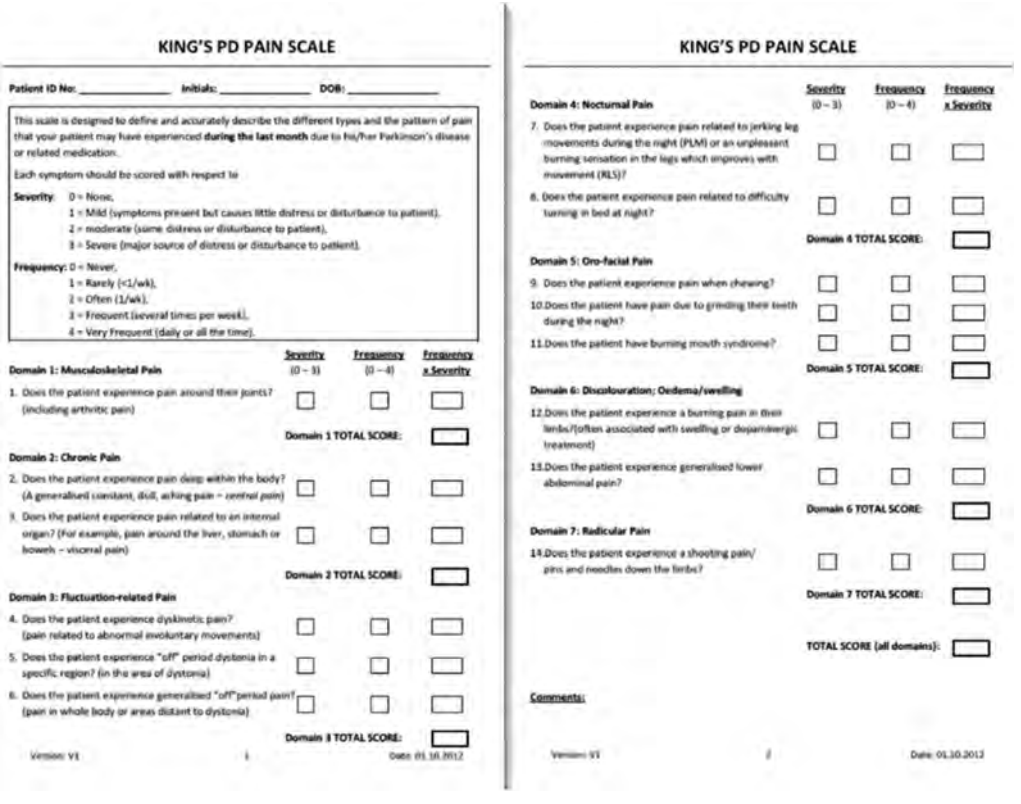
	Spearman *R*	*P*		Spearman *R*	*P*
Age	0.00	1.00	SCOPA-Motor Total score[a]	0.51	<0.0001
Years of education	−0.19	0.01	Non-Motors Symptoms Scale[a]	0.59	<0.0001
Age at onset of PD	−0.14	0.07	HADS-Anxiety	0.43	<0.0001
PD duration	0.36	<0.0001	HADS-Depression	0.48	<0.0001
Hoehn and Yahr staging	0.24	0.001	CISI-PD Total score[a]	0.53	<0.0001
SCOPA-Motor Examination	0.27	0.0003	LEDD	0.30	<0.0001
SCOPA-Motor ADL[a]	0.58	<0.0001	EQ-5D-3L Summary Index[a]	−0.56	<0.0001
SCOPA-Motor Complications	0.49	<0.0001	PDQ-8 Summary Index[a]	0.58	<0.0001

[a]King's Parkinson's Disease Pain Scale の総スコアとの間に高い相関が認められる。

PD ＝パーキンソン病，SCOPA ＝ Scale for Outcomes in PD，HADS ＝ Hospital Anxiety Depression Rating Scale，CISI-PD=Clinical Impression of Severity Index in PD，LEDD ＝レボドパ換算 1 日用量，EQ-5D-3L ＝ European Quality of Life-5 Dimensions-3 Levels，PDQ-8 ＝ Parkinson's Disease Questionnaire-8

Table 1 本試験で使用した評価尺度

Name of Scale	Scale Characteristics	Patients		
		Rater-Based	Patient-Based	Controls
Hoehn & Yahr staging	Motor staging of PD: Original staging: 1, 2, 3, 5, and 5.	X		
SCOPA-Motor scale	Assessment of motor disability and complications Item score: 0 (normal) to 3 (severe) Total score: sum of items (0-75)	X		
Non-Motor Symptoms Scale (NMSS)	Assessment of NMS over the last month: 30 items in 9 domains. Item score: severity (0-3) multiplied by frequency (1-4). Total score: sum of domains (0-360)	X		
Clinical Impression of Severity Index (CISI-PD)	Clinical estimate of current PD global severity Item score: 0 (normal) to 6 (very severe) Total score: sum of items (0-24).	X		
King's PD Pain Scale (KPP)	Assessing pain over the last month 14 items in 9 domains (see Fig. 1) Item score: severity (0-3) multiplied by frequency (0-4). Total score: sum of domains (0-168)	X		X
Hospital Anxiety and Depression Scale (HADS)	Assessing current description of feelings 14 items, 7 for anxiety and 7 for depression Item score: 0 (best case) to 3 (worst case) Total score: sum of items (0-42)		X	X
European Quality of Life-5 Dimensions-3 Levels (EQ-5D-3L)	5 items for assessment of health state today Item score: 1 (best case) to 3 (worst case) Total score: sum of items (5-15)		X	X
Parkinson's Disease Questionnaire - 8 items (PDQ-8)	Assessment of HRQoL over the last month 8 items, each scoring 0 to 4 Total score: sum of items (0-32). PDQ-8 Summary Index: % total score of maximum possible score		X	
Parkinson's Disease Sleep Scale 2 (PDSS-2)	15 items assessing sleep in the last week Item score: 0 (best case) to 4 (worst case) Total score: sum of items (0-60)		X	
Wearing-Off Questionnaire - 9 items (WOQ-9)	9 items assessing wearing off in the past month for presence and improvement of symptom (yes/no) Item score: 1 for "yes" or 0 for "no" Total score: sum of items (0-9)		X	
Visual analogue pain scales	Assessing pain over the last month Severity (0, not at all to 100, very severe) Frequency (0, not at all to 100, all the time) Total score: severity multiplied by frequency (0-10,000)		X	



KING'S PD PAIN SCALE

Patient ID No: _____ Initials: _____ DOB: _____

This scale is designed to define and accurately describe the different types and the pattern of pain that your patient may have experienced **during the last month** due to his/her Parkinson's disease or related medication.

Each symptom should be scored with respect to

Severity: 0 = None,
1 = Mild (symptoms present but causes little distress or disturbance to patient),
2 = moderate (some distress or disturbance to patient),
3 = Severe (major source of distress or disturbance to patient).

Frequency: 0 = Never,
1 = Rarely (<1/wk),
2 = Often (1/wk),
3 = Frequent (several times per week),
4 = Very Frequent (daily or all the time).

	Severity (0 – 3)	Frequency (0 – 4)	Frequency x Severity
Domain 1: Musculoskeletal Pain			
1. Does the patient experience pain around their joints? (including arthritic pain)	☐	☐	☐
Domain 1 TOTAL SCORE:			☐
Domain 2: Chronic Pain			
2. Does the patient experience pain deep within the body? (A generalised constant, dull, aching pain – *central pain*)	☐	☐	☐
3. Does the patient experience pain related to an internal organ? (For example, pain around the liver, stomach or bowels – visceral pain)	☐	☐	☐
Domain 2 TOTAL SCORE:			☐
Domain 3: Fluctuation-related Pain			
4. Does the patient experience dyskinetic pain? (pain related to abnormal involuntary movements)	☐	☐	☐
5. Does the patient experience "off" period dystonia in a specific region? (in the area of dystonia)	☐	☐	☐
6. Does the patient experience generalised "off"period pain? (pain in whole body or areas distant to dystonia)	☐	☐	☐
Domain 3 TOTAL SCORE:			☐

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KING'S PD PAIN SCALE

	Severity (0 – 3)	Frequency (0 – 4)	Frequency x Severity
Domain 4: Nocturnal Pain			
7. Does the patient experience pain related to jerking leg movements during the night (PLM) or an unpleasant burning sensation in the legs which improves with movement (RLS)?	☐	☐	☐
8. Does the patient experience pain related to difficulty turning in bed at night?	☐	☐	☐
Domain 4 TOTAL SCORE:			☐
Domain 5: Oro-facial Pain			
9. Does the patient experience pain when chewing?	☐	☐	☐
10. Does the patient have pain due to grinding their teeth during the night?	☐	☐	☐
11. Does the patient have burning mouth syndrome?	☐	☐	☐
Domain 5 TOTAL SCORE:			☐
Domain 6: Discolouration; Oedema/swelling			
12. Does the patient experience a burning pain in their limbs/(often associated with swelling or dysaesthesia treatment)	☐	☐	☐
13. Does the patient experience generalised lower abdominal pain?	☐	☐	☐
Domain 6 TOTAL SCORE:			☐
Domain 7: Radicular Pain			
14. Does the patient experience a shooting pain/ pins and needles down the limbs?	☐	☐	☐
Domain 7 TOTAL SCORE:			☐
TOTAL SCORE (all domains):			☐

Comments:

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Figure 1 King's Parkinson's Disease Pain Scale (KPPS)

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