Cutaneous adverse drug reaction after continuous subcutaneous apomorphine infusion.

Related Articles

Cutaneous adverse drug reaction after continuous subcutaneous apomorphine infusion.

J Eur Acad Dermatol Venereol. 2020 Jan 28;:

Authors: Calvão J, Cardoso JC, Moreira F, Januário C, Gonçalo M

Abstract

A 48-year-old woman with a 12-year history of juvenile onset Parkinson’s Disease (PD) with severe motor complications (fluctuations and dyskinesia) and severe impact on her daily activity (baseline Hoehn & Yahr stage 2; Schwab & England of 30%; MDS-UPDRS part III of 61 in off motor condition) despite levodopa equivalent daily dose of 1200mg, started continuous subcutaneous (s.c.) apomorphine (APO) infusion (APO-go® gradually increased in one week to 3mg/h during daytime), with no immediate complications and a very good motor response within a week.

PMID: 31991500 [PubMed — as supplied by publisher]


Related Articles


Dement Geriatr Cogn Disord. 2020 Jan 28;1–16


Abstract

BACKGROUND: Changes in cerebrospinal fluid, neuroimaging, and cognitive functions have been used as diagnostic biomarkers of Alzheimer’s disease (AD). This study aimed to investigate the temporal trajectories of plasma biomarkers in subjects with mild cognitive impairment (MCI) and patients with AD relative to healthy controls (HCs).

METHODS: In this longitudinal study, 82 participants (31 HCs, 33 MCI patients, and 18 AD patients) were enrolled. After 3 years, 7 HCs had transitioned to MCI and 10 subjects with MCI had converted to AD. We analyzed plasma amyloid beta (Aβ) and tau proteins at baseline and annually to correlate with biochemical data and neuropsychological scores.

RESULTS: Longitudinal data analysis showed an evolution of Aβ-related biomarkers over time within patients, whereas tau-related biomarkers differed primarily across diagnostic classifications. An initial steady increase in Aβ42 in the MCI stage was followed by a decrease just prior to clinical AD onset. Hyperphosphorylated tau protein levels correlated with cognitive decline in the MCI stage, but not in the AD stage.

CONCLUSION: Plasma Aβ and tau levels change in a dynamic, nonlinear, nonparallel manner over the AD continuum. Changes in plasma Aβ concentration are time-dependent, whereas changes in hyperphosphorylated tau protein levels paralleled the clinical progression of MCI. It remains to be clarified whether diagnostic efficiency can be improved by combining multiple plasma markers or combining plasma markers with other diagnostic biomarkers.

PMID: 31991443 [PubMed — as supplied by publisher]

Frontal theta and beta oscillations during lower-limb movement in Parkinson’s disease.

Related Articles

Frontal theta and beta oscillations during lower-limb movement in Parkinson’s disease.


Authors: Singh A, Cole RC, Espinoza AI, Brown D, Cavanagh JF, Narayanan NS

Abstract

OBJECTIVES: Patients with Parkinson’s disease (PD) have deficits in lower-limb functions such as gait, which involves both cognitive and motor dysfunction. In PD, theta and beta brain rhythms are associated with cognitive and motor functions, respectively. We tested the hypothesis that PD patients with lower-limb abnormalities would exhibit abnormal theta and beta rhythms in the mid-frontal cortical region during lower-limb action.

METHODS: This study included thirty-nine participants; 13 PD patients with FOG (PDFOG+), 13 without FOG (PDFOG-), and 13...
demographically-matched controls. We recorded scalp electroencephalograms (EEG) during a lower-limb pedaling motor task, which required intentional initiation and stopping of a motor movement.

RESULTS: FOG scores were correlated with disease severity and cognition. PDFOG+ patients pedaled with reduced speed and decreased acceleration compared to PDFOG− patients and controls. PDFOG+ patients exhibited attenuated theta-band (4–8 Hz) power and increased beta-band (13–30 Hz) power at mid-frontal electrode Cz during pedaling. Frontal theta- and beta-band oscillations also correlated with motor and cognitive deficits.

CONCLUSION: Frontal theta and beta oscillations are predictors of lower-limb motor symptoms in PD and could be used to design neuromodulation for PD-related lower-limb abnormalities.

SIGNIFICANCE: These data provide insight into mechanisms of lower-limb dysfunction in PD with FOG.

PMID: 31991312 [PubMed — as supplied by publisher]

N-terminal acetylation mutants affect alpha-synuclein stability, protein levels and neuronal toxicity.

Abstract

Alpha-synuclein (aSyn) protein levels are sufficient to drive Parkinson’s disease (PD) and other synucleinopathies. Despite the biomedical/therapeutic potential of aSyn protein regulation, little is known about mechanisms that limit/control aSyn levels. Here, we investigate the role of a post-translational modification, N-terminal acetylation, in aSyn neurotoxicity. N-terminal acetylation occurs in all aSyn molecules and has been proposed to determine its lipid binding and aggregation capacities; however, its effect in aSyn stability/neurotoxicity has not been evaluated.

We generated N-terminal mutants that alter or block physiological aSyn N-terminal acetylation in wild-type or pathological mutant E46K aSyn versions and confirmed N-terminal acetylation status by mass spectrometry. By optical pulse-labeling in living primary neurons we documented a reduced half-life and accumulation of aSyn N-terminal mutants. To analyze the effect of N-terminal acetylation mutants in neuronal toxicity we took advantage of a neuronal model where aSyn toxicity was scored by longitudinal survival analysis. Salient features of aSyn neurotoxicity were previously investigated with this approach. aSyn-dependent neuronal death was recapitulated either by higher aSyn protein levels in the case of WT aSyn, or by the combined effect of protein levels and enhanced neurotoxicity conveyed by the E46K mutation.

PMID: 31991247 [PubMed — as supplied by publisher]
Local field potential dynamics in the primate cortex in relation to parkinsonism revealed by machine learning: A comparison between the primary motor cortex and the supplementary area.

Related Articles

Local field potential dynamics in the primate cortex in relation to parkinsonism revealed by machine learning: A comparison between the primary motor cortex and the supplementary area.

Neurosci Res. 2020 Jan 25;:
Authors: Darbin O, Hatanaka N, Takara S, Kaneko M, Chiken S, Naritoku D, Martino A, Nambu A
Abstract
The present study compares the cortical local field potentials (LFPs) in the primary motor cortex (M1) and the supplementary motor area (SMA) of non-human primates rendered Parkinsonian with administration of dopaminergic neurotoxin, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine. The dynamic of the LFPs was investigated under several mathematical frameworks and machine learning was used to discriminate the recordings based on these features between healthy, parkinsonian with off-medication and parkinsonian with on-medication states. The importance of each feature in the discrimination process was further investigated. The dynamic of the LFPs in M1 and SMA was affected regarding its variability (time domain analysis), oscillatory activities (frequency domain analysis) and complex patterns (non-linear domain analysis). Machine learning algorithms achieved accuracy near 0.90 for comparisons between conditions. The TreeBagger algorithm provided best accuracy. The relative importance of these features differed with the cortical location, condition and treatment. Overall, the most important features included beta oscillation, fractal dimension, gamma oscillation, entropy and asymmetry of amplitude fluctuation. The importance of features in discriminating between normal and pathological states, and on–or off-medication states depends on the pair-comparison and it is region-specific. These findings are discussed regarding the refinement of current models for movement disorders and the development of on-demand therapies.

PMID: 31991205 [PubMed — as supplied by publisher]

Exercise effects on brain and behavior in healthy mice, Alzheimer’s disease and Parkinson’s disease model — a systematic review and meta-analysis.

Related Articles

Exercise effects on brain and behavior in healthy mice, Alzheimer’s disease and Parkinson’s disease model — a systematic review and meta-analysis.

Behav Brain Res. 2020 Jan 25;112488
Authors: da Costa Daniele TM, de Bruin PFC, de Matos RS, de Bruin GS, Maia Chaves Junior C, de Bruin VMS
Abstract
This systematic review and meta-analysis examines how exercise modifies brain and behavior in healthy mice, dementia (D) and Parkinson disease (PD) models. A search was performed on the Medline and Scopus electronic databases (2008 to 2019). Search terms were "mice", "brain", "treadmill", "exercise", "physical exercise". In the total, 430 were found but only 103 were included. Animals (n = 1,172; 96 articles) exercised 4–8 weeks (Range 24 h to 32 weeks), 60 min/day (Range 8 to 120 min per day), and 10/12 m/min (Range 0.2 m/min to 36 m/min). Hippocampus, cerebral cortex, striatum and whole brain were more frequently investigated. Exercise improved learning and memory. Meta-analysis showed that exercise increased: cerebral BDNF in health (n = 150; z = 5.8, CI 3.43−12.05; p
PMID: 31991178 [PubMed — as supplied by publisher]

The contribution of Parkin, PINK1 and DJ-1 genes to selective neuronal degeneration in Parkinson’s disease.

Related Articles

The contribution of Parkin, PINK1 and DJ-1 genes to selective neuronal degeneration in Parkinson’s disease.

Eur J Neurosci. 2020 Jan 28;:
Authors: van der Vlag M, Havekes R, Heckman PRA
Abstract
Parkinson’s disease is characterised by selective and severe degeneration of the substantia nigra pars compacta and the locus coeruleus, which underlies the most prominent symptoms. Although α-synuclein accumulation has long been established to play a causal role in the disease, it alone cannot explain the selective degenerative pattern. Recent evidence shows that the selective vulnerability could arise due to the large presence of
cytosolic catecholamines and Ca2+ ions in the substantia nigra pars compacta and locus coeruleus specifically, that can be aberrantly affected by α-synuclein accumulation. Moreover, each has its own toxic potential, and disturbance of one can exacerbate the toxic effects of the others. This presents a mechanism unique to these areas that can lead to a vicious degenerative cycle. Interestingly, in familial variants of Parkinson’s disease, the exact same brain areas are affected, implying the underlying process is likely the same. However, the exact disease mechanisms of many of these genetic variants remain unclear. Here we review the effects of the Parkinson’s disease-related genes Parkin, PINK1 and DJ-1. We establish that these mutant varieties can set in motion the same degenerative process involving α-synuclein, cytosolic catecholamines and Ca2+ . Additionally, we show indications that model organisms might not accurately represent all components of this central mechanism, explaining why Parkin, PINK1 and DJ-1 model organisms often lack a convincing Parkinson’s disease-like phenotype.

PMID: 31991026 [PubMed — as supplied by publisher]

 Plasma tau protein and Aβ42 level as markers of cognitive impairment in patients with Parkinson’s disease.

Related Articles

Plasma tau protein and Aβ42 level as markers of cognitive impairment in patients with Parkinson’s disease.

Authors: Chojdak-Łukasiewicz J, Malodobra-Mazur M, Zimny A, Noga L, Paradowski B

Abstract

BACKGROUND: Parkinson’s disease (PD) is a progressive neurodegenerative disorder with a characteristic clinical picture. Apart from classical movement disorders, a significant role is also played by non-motor symptoms, in particular cognitive impairments, which have a significant impact on the quality of life of the patients. Tau protein and amyloid beta are well-known non-specific biomarkers in Alzheimer’s disease (AD).

OBJECTIVES: The study assessed the practical value of determining tau protein and amyloid beta (Aβ42) in the blood serum of patients with PD and their relationship with cognitive impairments, radiographic image and the used dose of L-DOPA.

MATERIAL AND METHODS: The neuropsychological assessment was carried for 64 patients with PD. The levels of amyloid beta 1-42 (Aβ42) and tau proteins in serum were also measured.

RESULTS: The Aβ42 level in the serum was statistically higher in patients with longer duration of the disease (p CONCLUSIONS: Serum levels of Aβ42 and tau protein in PD may be a useful marker for the assessment of cognitive impairments. The role of L-DOPA in the process of dementia in PD remains unclear.

PMID: 31990459 [PubMed — as supplied by publisher]

 T-495, a novel low cooperative M1 receptor positive allosteric modulator, improves memory deficits associated with cholinergic dysfunction and is characterized by low gastrointestinal side effect risk.

Related Articles

T-495, a novel low cooperative M1 receptor positive allosteric modulator, improves memory deficits associated with cholinergic dysfunction and is characterized by low gastrointestinal side effect risk.

Authors: Mandai T, Sako Y, Kurimoto E, Shimizu Y, Nakamura M, Fushimi M, Maeda R, Miyamoto M, Kimura H

Abstract

M1 muscarinic acetylcholine receptor (M1 R) activation can be a new therapeutic approach for the treatment of cognitive deficits associated with cholinergic hypofunction. However, M1 R activation causes gastrointestinal (GI) side effects in animals. We previously found that an M1 R positive allosteric modulator (PAM) with lower cooperativity (α-value) has a limited impact on ileum contraction and can produce a wider margin between cognitive improvement and GI side effects. In fact, TAK-071, a novel M1 R PAM with low cooperativity (α-value of 199), improved scopolamine-induced cognitive deficits with a wider margin against GI side effects than a high cooperative M1 R PAM, T-662 (α-value of 1786), in rats. Here, we describe the pharmacological characteristics of a novel low cooperative M1 R PAM T-495 (α-value of 170), using the clinically tested higher cooperative M1 R PAM MK-7622 (α-value of 511) as a control. In rats, T-495 caused diarrhea at a 100-fold higher dose than that required for the improvement of scopolamine-induced memory deficits. Contrastingly, MK-7622 showed memory improvement and induction of diarrhea at an equal dose. Combination of T-495, but not of MK-7622, and donepezil at each sub-effective dose improved scopolamine-induced memory deficits. Additionally, in mice with reduced acetylcholine levels in the forebrain via overexpression of A53T α-synuclein (ie, a mouse model of dementia with Lewy bodies and Parkinson’s disease with dementia), T-495, like donepezil, reversed the memory deficits in the contextual fear conditioning test and Y-maze task. Thus, low cooperative M1 R PAMs are promising agents for the treatment of memory deficits associated with cholinergic dysfunction.

PMID: 31990455 [PubMed — in process]
Alzheimer’s Disorder: Epigenetic connection and associated risk factors.

Related Articles

Alzheimer’s Disorder: Epigenetic connection and associated risk factors.

Curr Neuropharmacol. 2020 Jan 28;:
Authors: Sharma VK, Mehta V, Singh TG

Abstract
The gene based therapeutics and drug targets have shown incredible and appreciable advances in alleviating human sufferings and complexities. Epigenetics simply means above genetics or which controls the organism beyond genetics. At present it is very clear that all characteristics of an individual are not determined by DNA alone, rather the environment, stress, lifestyle and nutrition play a vital part in determining the response of an organism. Thus nature (genetic makeup) and nurture (exposure) play equally important roles in the responses observed, both at the cellular and organism levels. Epigenetics influence plethora of complications at cellular and molecular levels that includes cancer, metabolic and cardiovascular complications including neurological (psychosis) and neurodegenerative disorders (Alzheimer’s disease, Parkinson disease etc.). The epigenetic mechanisms include DNA methylation, histone modification and non coding RNA which have substantial impact on progression and pathways linked to Alzheimer’s disease. The epigenetic mechanism get deregulated in Alzheimer’s disease and is characterized by DNA hyper methylation, deacetylation of histones and general repressed chromatin state which alter gene expression at transcription level by upregulation, downregulation or silencing of genes. Thus the processes or modulators of these epigenetic processes have shown vast potential as therapeutic target in Alzheimer’s disease.

PMID: 31989902 [PubMed — as supplied by publisher]

Activation of CB2R with AM1241 ameliorates neurodegeneration via the Xist/miR-133b-3p/Pitx3 axis.

Related Articles

Activation of CB2R with AM1241 ameliorates neurodegeneration via the Xist/miR-133b-3p/Pitx3 axis.

J Cell Physiol. 2020 Jan 28;:

Abstract
Activation of cannabinoid receptor type II (CB2R) by AM1241 has been demonstrated to protect dopaminergic neurons in Parkinson’s disease (PD) animals. However, the specific mechanisms of the action of the CB2R agonist AM1241 for PD treatment have not been characterized. Wild-type (WT), CB1R knockout (CB1-KO), and CB2R knockout (CB2-KO) mice were exposed to 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) for 1 week to obtain a PD mouse model. The therapeutic effects of AM1241 were evaluated in each group. Behavioral tests, analysis of neurotransmitters, and immunofluorescence results demonstrated that AM1241 ameliorated PD in WT animals and CB1-KO animals. However, AM1241 did not ameliorate PD symptoms in CB2-KO mice. RNA-seq analysis identified the lncRNA Xist as an important regulator of the protective actions of AM1241. Specifically, AM1241 allowed WT and CB1-KO animals treated with MPTP to maintain normal expression of Xist, which affected the expression of miR-133b-3p and Pitx3. In vitro, overexpression of Xist or AM1241 protected neuronal cells from death induced by 6-hydroxydopamine and increased Pitx3 expression. The CB2 receptor agonist AM1241 alleviated PD via regulation of the Xist/miR-133b-3p/Pitx3 axis, and revealed a new approach for PD treatment.

PMID: 31989652 [PubMed — as supplied by publisher]

Parkinson’s disease and the non-motor symptoms: hyposmia, weight loss, osteosarcopenia.

Related Articles

Parkinson’s disease and the non-motor symptoms: hyposmia, weight loss, osteosarcopenia.

Aging Clin Exp Res. 2020 Jan 27;:
Authors: De Rui M, Inelmen EM, Trevisan C, Pigozzo S, Manzato E, Sergi G

Abstract
Non-motor symptoms (NMSs) are common in Parkinson’s disease (PD) and can precede, sometimes for several years. NMSs include, other than gastrointestinal symptoms like constipation and dysphagia, also hyposmia, weight loss and osteosarcopenia. These three NMSs seem to be inter-related and affect patients’ health and quality of life. Unfortunately, patients with these symptoms usually are not initially seen by a neurologist, and by the time they are consulted, nearly ~80% of the dopaminergic neurons in the substantia nigra have died. To date, no guidelines exist for screening, assessment and management of NMSs in general. A better understanding of these specific NMSs, likely in the context of others, will make it possible to approach and optimise the treatment of the motor symptoms thereby enhancing the welfare of PD patients. Identifying the NMSs could be very helpful, and among them, hyposmia, weight loss and osteosarcopenia may play an important role in solving the limitations in the diagnosis of PD. A strict collaboration between general practitioners, clinicians, geriatricians and neurologists can be one approach towards the diagnosis of pre-PD. Waiting until the motor symptoms develop and the patient is finally visited by the neurologist could be too late, considering the catastrophic prognosis of the disease.

PMID: 31989535 [PubMed — as supplied by publisher]
Patterns of intrinsic brain activity in essential tremor with resting tremor and tremor-dominant Parkinson’s disease.

Related Articles
Patterns of intrinsic brain activity in essential tremor with resting tremor and tremor-dominant Parkinson’s disease.

Brain Imaging Behav. 2020 Jan 27;:
Authors: Li JY, Lu ZJ, Suo XL, Li NN, Lei D, Wang L, Peng JX, Duan LR, Xi J, Jiang Y, Gong QY, Peng R

Abstract
The clinical pictures of essential tremor (ET) with resting tremor (rET) and tremor-dominant Parkinson’s disease (tPD) are often quite mimic at the early stage, current approaches to the diagnosis and treatment therefore remain challenging. The regional homogeneity (ReHo) method under resting-state functional magnetic resonance imaging (rs-fMRI) would help exhibit the patterns in neural activity, which further contribute to differentiate these disorders and explore the relationship between symptoms and regional functional abnormalities. Sixty-eight Chinese participants were recruited, including 19 rET patients, 24 tPD patients and 25 age- and gender-matched healthy controls (HCs). All participants underwent clinical assessment and rs-fMRI with a ReHo method to investigate the alterations of neural activity, and the correlation between them. Differences were compared by two-sample t-test (corrected with AlphaSim, p
PMID: 31989422 [PubMed — as supplied by publisher]

Gastrointestinal dysfunction in Parkinson’s disease.

Related Articles
Gastrointestinal dysfunction in Parkinson’s disease.

J Neurol. 2020 Jan 27;:
Authors: Lubomski M, Davis RL, Sue CM

Abstract
BACKGROUND: Gastrointestinal (GI) dysfunction is prevalent in Parkinson’s disease (PD). Symptoms are evident throughout the disease course, affect the length of the GI tract and impact on patient quality of life and management. We clarify real-life differences in the frequency and severity of GI symptoms in a cohort of PD and healthy control (HC) subjects.

METHODS: 103 PD patients were compared to 81 HC subjects. Outcome measures collected from validated questionnaires included constipation severity, upper and lower GI symptoms and physical activity.

RESULTS: PD patients were three-times more likely to experience constipation than HC subjects, (78.6% vs 28.4%), exhibited a fourfold increase in constipation severity and formed harder stools. PD patients also reported increased symptoms of indigestion, nausea, excessive fullness and bloating, compared to the HCs. A higher mean Leeds Dyspepsia Questionnaire score for PD patients (8.3 (standard deviation (SD) 7.7) vs 4.6 (SD 6.1), p = 0.001)) indicated increased symptom severity. Chronic pain was more frequently reported and correlated with constipation and upper GI dysfunction, being more prevalent and severe in women. Physical activity was notably decreased in the PD cohort (1823.6 (± 1693.6) vs 2942.4 (± 2620.9) metabolic equivalent-minutes/week, p = 0.001) and correlated with constipation severity. PD therapies were associated with increased fullness and bloating and harder stools.

CONCLUSIONS: PD patients report more prevalent and severe GI dysfunction, although our cohort comprised of many later-stage participants. Earlier recognition of GI dysfunction in PD provides the opportunity to direct treatment for chronic pain and constipation, promote physical activity and rationalise PD

Biglycan protects human neuroblastoma cells from nitric oxide-induced death by inhibiting AMPK-mTOR mediated autophagy and intracellular ROS level.

Related Articles
Biglycan protects human neuroblastoma cells from nitric oxide-induced death by inhibiting AMPK-mTOR mediated autophagy and intracellular ROS level.

Biotechnol Lett. 2020 Jan 27;:
Authors: Chen S, Guo D, Lei B, Bi J, Yang H

Abstract
The ubiquitous proteoglycan, biglycan (BGN) acts as an important modulator, regulating key molecular pathways of metabolism and brain function. Autophagy is documented as a defining feature of neurodegeneration in Alzheimer’s disease (AD), Parkinson’s disease (PD), and Huntington’s disease (HD). In the present study, we found that BGN protected neuronal cells from nitric oxide (NO)-induced cell apoptosis. However, it is still unclear that whether the neuroprotective effect of BGN relates to autophagy. Here, we discovered that an NO donor, sodium nitroprusside (SNP) induced autophagy in human SH-SY5Y neuroblastoma cells, including activating LC3B and inhibiting p62. Inhibiting autophagy by 3MA aggravated NO-induced cell death, otherwise promoting autophagy by Rapamycin rescued NO-triggered cell death. Notably, BGN downregulated by NO, significantly protected SH-SY5Y cells against NO-induced neurotoxicity by inhibiting the activation of autophagy-dependent AMPK signaling pathway. Moreover, BGN overexpression also diminished NO-induced the elevation of intracellular reactive oxygen species (ROS) level, but not NO content. These findings suggest that BGN protects neuroblastoma cells from NO-induced death by suppressing autophagy-dependent AMPK-mTOR signaling and intracellular ROS level.

PMID: 31989342 [PubMed — as supplied by publisher]
Corrections to: Hypothesis: neural mechanism of psychotherapy for the treatment of Parkinson’s disease: cognitive behavioral therapy (CBT), acceptance and commitment therapy (ACT), and Morita therapy?

Correction to: Hypothesis: neural mechanism of psychotherapy for the treatment of Parkinson’s disease: cognitive behavioral therapy (CBT), acceptance and commitment therapy (ACT), and Morita therapy?

J Neural Transm (Vienna). 2020 Jan 28;:
Authors: Nagatsu T

Abstract
The original version of this article unfortunately contained a mistake. The year in the Acknowledgements section should be “1963” not “1993”.

PMID: 31989267 [PubMed — as supplied by publisher]

Corrections to: Neural and dopaminergic correlates of fatigue in Parkinson’s disease.

Correction to: Neural and dopaminergic correlates of fatigue in Parkinson’s disease.

J Neural Transm (Vienna). 2020 Jan 28;:
Authors: Kang SY, Bang M, Hong JY, Oh J, Kim JS, Han YM, Chang SK, Lee SA, Yoon U, Shin NY

Abstract
The original version of this article unfortunately contained a mistake.

PMID: 31989266 [PubMed — as supplied by publisher]

Effect of the micro-environment on α-synuclein conversion and implication in seeded conversion assays.

Effect of the micro-environment on α-synuclein conversion and implication in seeded conversion assays.

Transl Neurodegener. 2020;9:5

Abstract
Background: α-Synuclein is a small soluble protein, whose physiological function in the healthy brain is poorly understood. Intracellular inclusions of α-synuclein, referred to as Lewy bodies...
(LBs), are pathological hallmarks of α-synucleinopathies, such as Parkinson’s disease (PD) or dementia with Lewy bodies (DLB). Main body: Understanding of the molecular basis as well as the factors or conditions promoting α-synuclein misfolding and aggregation is an important step towards the comprehension of pathological mechanism of α-synucleinopathies and for the development of efficient therapeutic strategies. Based on the conversion and aggregation mechanism of α-synuclein, novel diagnostic tests, such as protein misfolding seeded conversion assays, e.g. the real-time quaking-induced conversion (RT-QuIC), had been developed. In diagnostics, α-synuclein RT-QuIC exhibits a specificity between 82 and 100% while the sensitivity varies between 70 and 100% among different laboratories. In addition, the α-synuclein RT-QuIC can be used to study the α-synuclein-seeding-characteristics of different α-synucleinopathies and to differentiate between DLB and PD. Conclusion: The variable diagnostic accuracy of current α-synuclein RT-QuIC occurs due to different protocols, cohorts and material etc.. An impact of micro-environmental factors on the α-synuclein aggregation and conversion process and the occurrence and detection of differential misfolded α-synuclein types or strains might underpin the clinical heterogeneity of α-synucleinopathies.

PMID: 31988747 [PubMed]

iPSC modeling of young-onset Parkinson’s disease reveals a molecular signature of disease and novel therapeutic candidates.

Related Articles

iPSC modeling of young-onset Parkinson’s disease reveals a molecular signature of disease and novel therapeutic candidates.

Nat Med. 2020 Jan 27;:


Abstract
Young-onset Parkinson’s disease (YOPD), defined by onset at