The Virtual Assessment in Lewy Body Dementia: Pandemic and Beyond

Impact of COVID-19 in those with Lewy Body Dementia

An LBDA Research Centers of Excellence Webinar

May 27, 2021

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Housekeeping Notes

- The activity is being recorded.
- All attendee mics are automatically muted.
- If you have questions during the presentations, please submit them via the Q&A function

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Welcome

Today's event was organized by the Clinical Care and Professional Education Working Group for LBDA's Research Centers of Excellence (RCOE) Program

Co-Chairs/Course Directors

- Katherine Amodeo, MD, Westchester Medical Center, Poughkeepsie, NY
- Jennifer Goldman, MD, MS, Shirley Ryan AbilityLab and Northwestern University Feinberg School of Medicine, Chicago, IL

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Support Acknowledgement

This activity was supported by an educational grant from Acadia Pharmaceuticals Inc.

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Accreditation Statement

In support of improving patient care, this activity has been planned and implemented by the Postgraduate Institute for Medicine and Lewy Body Dementia Association. Postgraduate Institute for Medicine is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

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Designation Statement

Physicians

Postgraduate Institute for Medicine designates this internet live activity for a maximum of 1.0 *AMA PRA Category 1 credit*™. Physicians should claim only the credits commensurate with the extent of their participation in the activity.

Allied healthcare professionals

Participants will receive a Certificate of Attendance stating this program is designated for 1.0 *AMA PRA Category 1 Credit*™. This credit is accepted by the AANP and the AAPA.

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- ABPN Approval for Neurologists and Psychiatrists The American Board of Psychiatry and Neurology has reviewed the webinar "Understanding Current Research on Virtual Assessment" and has approved this program as part of a comprehensive CME program, which is mandated by the ABMS as a necessary component of Maintenance of Certification.

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Presenter/Panelist Disclosures

Katherine Amodeo, MD *Contracted research*: Genentech Roche Ltd., EIP Pharma Inc, Michael J. Fox Foundation, NINDS, Acadia Pharmaceuticals Inc, and Biogene through July 2020.

John-Paul Taylor, PhD *Contracted research*: Sosei Heptares *Consulting Fees:* Sosei Heptares, Kyowa Kirin. *Royalities:* Oxford University Press, GE Healthcare

Jennifer Goldman, MD, MS *Contracted research:* Acadia Pharmaceuticals Inc., Michael J. Fox Foundation, Parkinson's Foundation. *Honoraria:* International Parkinson and Movement Disorders Society, Medscape, Parkinson's Foundation

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Agenda

- Presentation by John-Paul Taylor, MBBS(hons) PhD MRC Psych
- Followed by Panel Discussion with Questions and Answers

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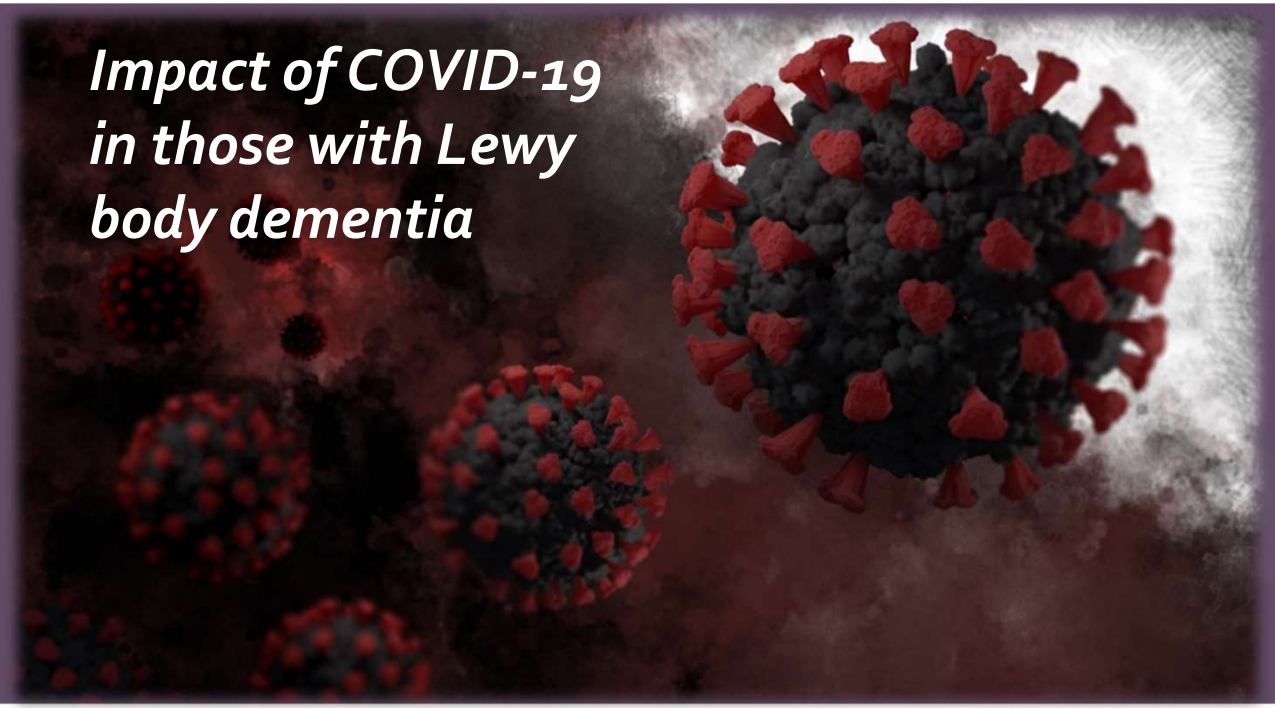
Educational Objectives

At the conclusion of the activity, learners should be able to:

- Analyze data on recent survey regarding the impact of COVID on LBD population.
- Review LBD and its clinical features, “what you should know” and what to be aware of.
- Discuss why this population is particularly at risk for complications of COVID-19.

Impact of COVID-19 in those with Lewy body dementia



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Newcastle University

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Outline

- DLB: A reminder of the diagnostic and clinical features
- COVID-19 and dementia
- COVID-19 and Parkinson's disease
- COVID-19 and DLB

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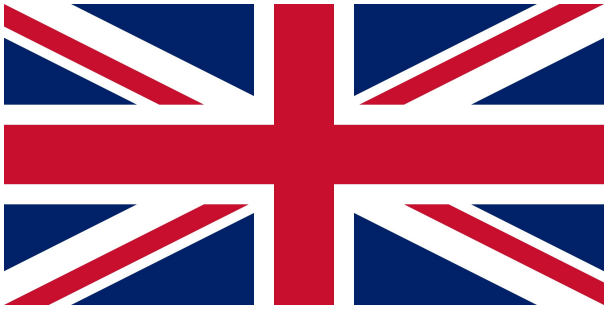
Disclaimer on this presentation:

- UK perspective
- Information remains marginal on LBD and COVID-19 – therefore maybe adding 2 and 2 and coming up with 5



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Published Ahead of Print on June 7, 2017 as 10.1212/WNL.0000000000004058

VIEWS & REVIEWS

Diagnosis and management of dementia with Lewy bodies

Fourth consensus report of the DLB Consortium

OPEN

Ian G. McKeith, MD, F Med Sci
Bradley F. Boeve, MD
Dennis W. Dickson, MD
Glenda Halliday, PhD
John-Paul Taylor, PhD, MRC Psych
Daniel Weintraub, MD
Dag Aarsland, MD
James Galvin, MD, MPH
Johannes Attems, MD
Clive G. Ballard, MRC Psych, MD
Ashley Bayston, BA, LLB
Thomas G. Beach, MD, PhD
Frédéric Blanc, MD, PhD
Nicolaas Bohnen, MD, PhD
Laura Bonanni, MD, PhD

ABSTRACT

The Dementia with Lewy Bodies (DLB) Consortium has refined its recommendations about the clinical and pathologic diagnosis of DLB, updating the previous report, which has been in widespread use for the last decade. The revised DLB consensus criteria now distinguish clearly between clinical features and diagnostic biomarkers, and give guidance about optimal methods to establish and interpret these. Substantial new information has been incorporated about previously reported aspects of DLB, with increased diagnostic weighting given to REM sleep behavior disorder and ^{123}iodine-metaiodobenzylguanidine (MIBG) myocardial scintigraphy. The diagnostic role of other neuroimaging, electrophysiologic, and laboratory investigations is also described. Minor modifications to pathologic methods and criteria are recommended to take account of Alzheimer disease neuropathologic change, to add previously omitted Lewy-related pathology categories, and to include assessments for substantia nigra neuronal loss. Recommendations about clinical management are largely based upon expert opinion since randomized controlled trials in DLB are few. Substantial progress has been made since the previous report in the detection and recognition of DLB as a common and important clinical disorder. During that period it has been incorporated into DSM-5, as major neurocognitive disorder with Lewy bodies. There remains a pressing need to understand the underlying neurobiology and pathophysiology of DLB, to develop and deliver clinical trials with both symptomatic and disease-modifying agents, and to help patients and carers worldwide to inform themselves about the disease, its prognosis, best available treatments, ongoing research, and how to get adequate support. *Neurology*® 2017;89:1–13

McKeith et al, *Neurology* 2017

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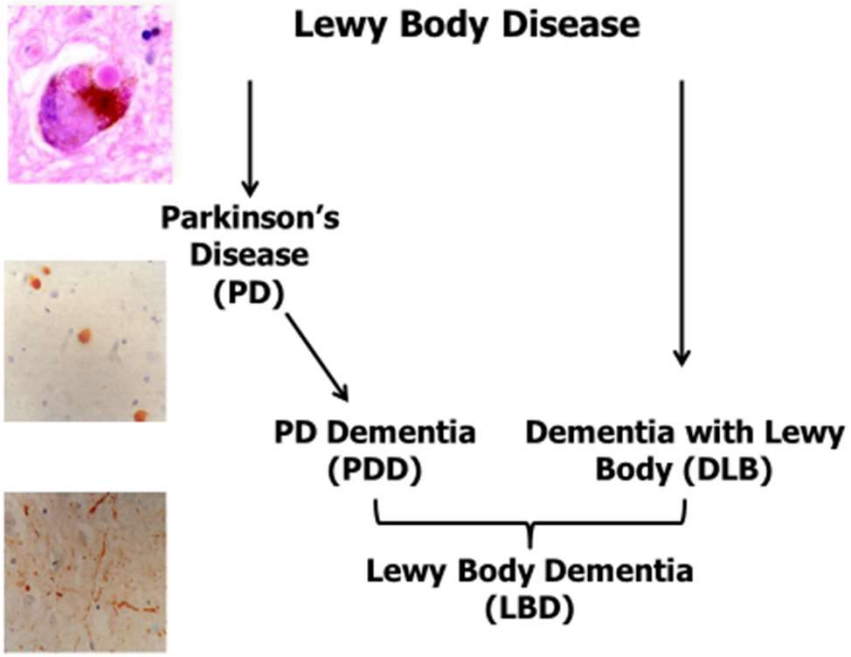
A brief word on diagnostic nomenclature



Lewy body dementia includes both:

Parkinson's disease dementia (PDD) dementia starting 1 year or more **after** well established Parkinson's disease

Dementia with Lewy bodies (DLB) dementia that occurs before or concurrently with parkinsonism or within 1 year of onset of motor symptoms

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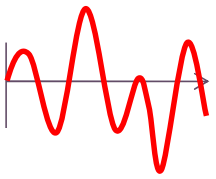
Clinical Diagnostic Criteria

Motor parkinsonism

Visual Hallucinations

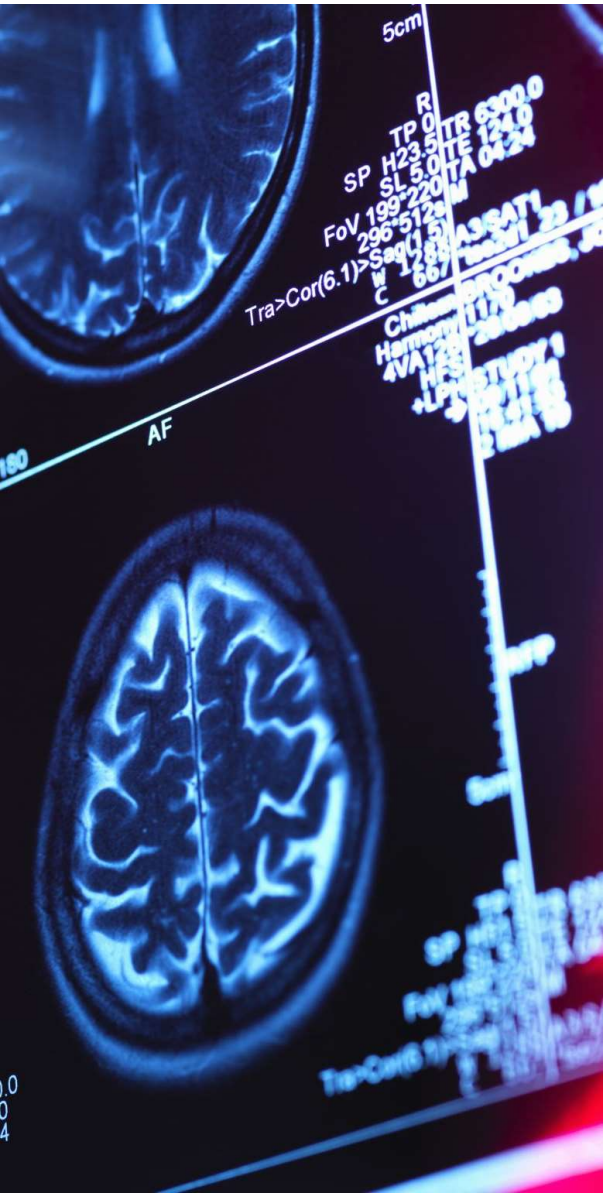
REM sleep behaviour disorder

Cognitive Fluctuation



- Probable DLB → 2 or more core clinical features
- Possible DLB → 1 core clinical feature

McKeith et al, 2017



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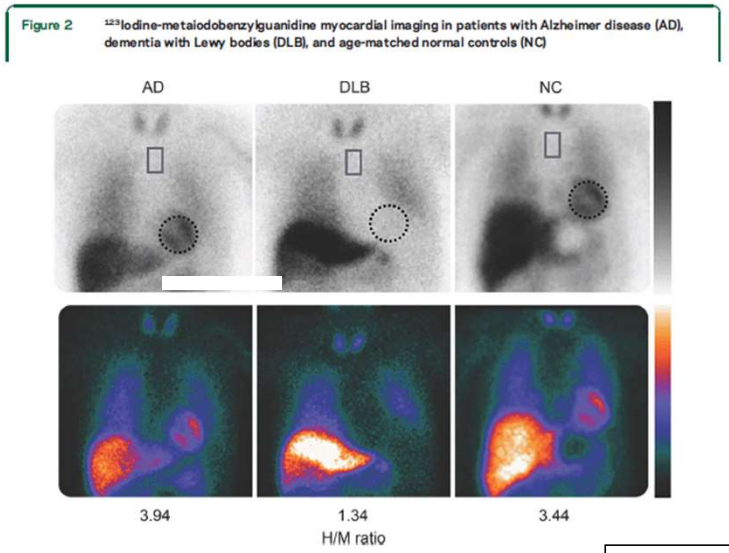
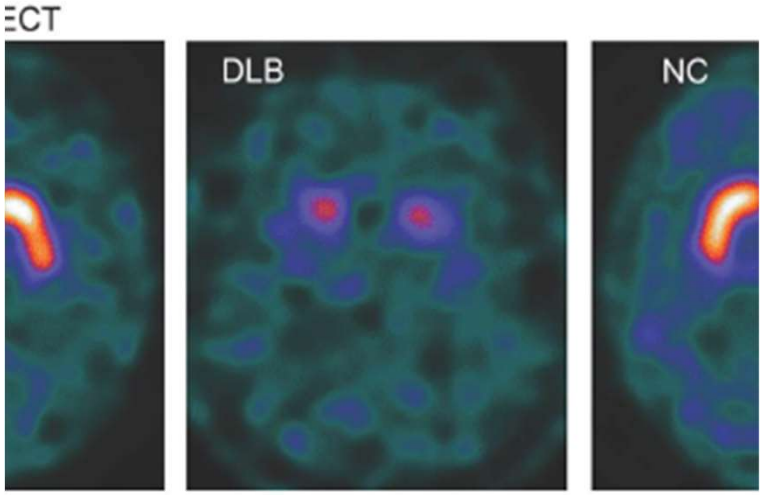
Clinical Diagnostic Criteria

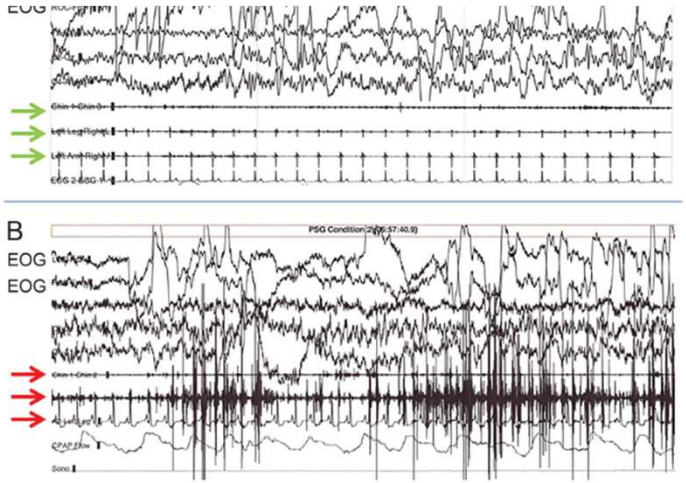
- **Supportive Clinical Features**
  - Severe antipsychotic sensitivity
  - Postural instability, repeated falls
  - Syncope or other transient episodes of unresponsiveness
  - Severe autonomic dysfunction
  - Hypersomnia
  - Hyposmia
  - Hallucinations in other modalities
  - Systematized delusions
  - Depression, Anxiety, Apathy

McKeith et al, *Neurology* 2017





Indicative biomarkers



McKeith et al, *Neurology* 2017

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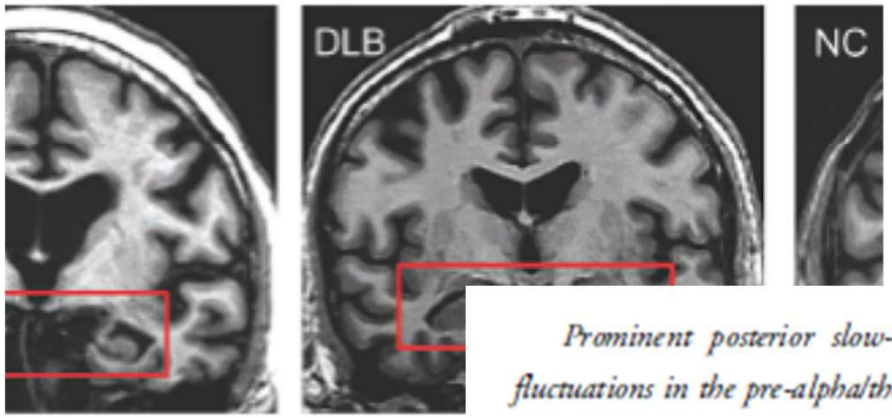
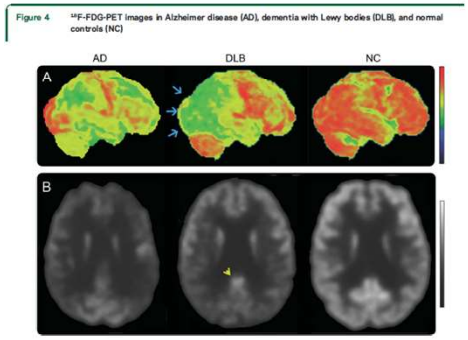
ıal T1-weighted MRI and ^{123}iodine FP-CIT SPECT images in Al
.ewy bodies (DLB), and normal controls (NC)





Supportive biomarkers

Prominent posterior slow-wave EEG activity with periodic fluctuations in the pre-alpha/theta range. Evidence is building to support quantitative EEG as a DLB biomarker, characterized by specific abnormalities in posterior derivations. These include a pre-alpha-dominant frequency, either stable or intermixed with alpha/theta/delta activities in pseudoperiodic patterns,[39] which together have a predictive value >90% for the diagnosis of DLB compared with AD.[e18] These specific EEG patterns also correlate positively with the severity of clinically observed cognitive fluctuations[e6] and may be seen at the MCI stage.[e19]

McKeith et al, *Neurology* 2017

DLB symptom management

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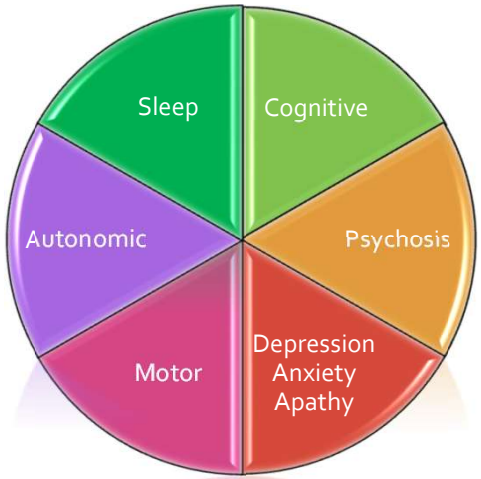
Complex multisystem disease

Treatment of one symptom leading to worsening of another



Heterogeneity in range of symptoms expressed between patients

Range in severity of symptoms between patients

Symptom severity fluctuation within individual patients and variations in manifestation of symptoms

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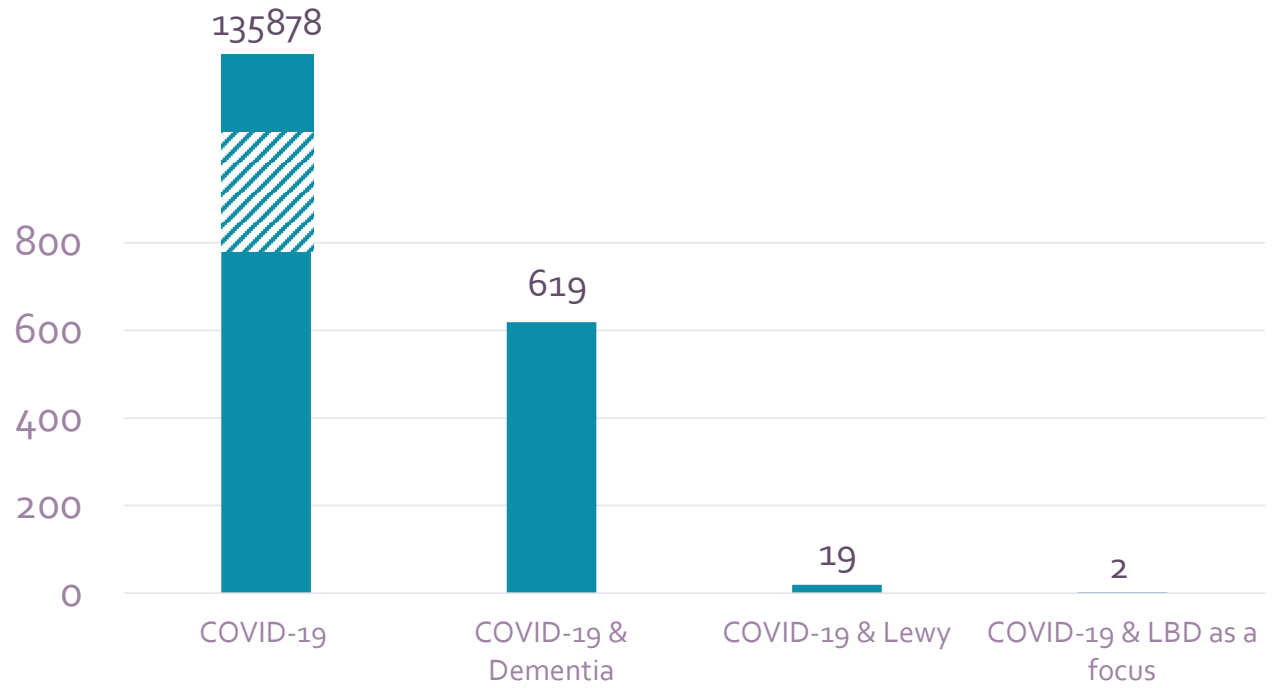
Pubmed publications COVID-19 (20th May 2021)



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Curr Psychol. 2021 May 8;1-10. doi: 10.1007/s12144-021-01811-7. Online ahead of print.

Subjective experience of time in dementia with Lewy bodies during COVID-19 lockdown

Dylan Torboli [1], Giovanna Mioni [1], Cinzia Bussé [2], Annachiara Cagnin [3], Antonino Vallesi [4 3]

Int J Geriatr Psychiatry. 2020 Dec;35(12):1431-1436. doi: 10.1002/gps.5393. Epub 2020 Aug 18.

The challenges of COVID-19 for people with dementia with Lewy bodies and family caregivers

Alison Killen [1], Kirsty Olsen [1], Ian G McKeith [1], Alan J Thomas [1], John T O'Brien [2], Paul Donaghy [1], John-Paul Taylor [1]

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COVID-19 and dementia

Received: 23 August 2020 | Revised: 6 November 2020 | Accepted: 18 December 2020
DOI: 10.1002/alz.12296

RESEARCH ARTICLE

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

COVID-19 and dementia: Analyses of risk, disparity, and outcomes from electronic health records in the US

QuanQiu Wang[1] | Pamela B. Davis[2] | Mark E. Gurney[3] | Rong Xu[1]

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Retrospective case-control analysis of EHRs

61.9 million adult and senior patients (age ≥ 18 years) in the United States up to August 21, 2020

Blacks with dementia had higher risk of COVID-19 than Whites (AOR: 2.86 [95% CI, 2.67–3.06], P < .001)

Dementia and COVID-19 6-month risk:
- Mortality 21%
- Hospitalization 59%

Odds of COVID–19 in patients with dementia (adjusted for demographics and known COVID–19 risk factors)

Exposure	Outcome	AOR (95% CI)	p
Dementia	COVID–19	2.00 (1.94–2.06)	<.001
Alzheimer's disease	COVID–19	1.86 (1.77–1.96)	<.001
Post–traumatic dementia	COVID–19	1.67 (1.51–1.86)	<.001
Presenile dementia	COVID–19	2.62 (2.28–3.00)	<.001
Senile dementia	COVID–19	1.99 (1.86–2.13)	<.001
Vascular dementia	COVID–19	3.17 (2.97–3.37)	<.001

Odds of COVID–19 infection in patients with dementia (adjusted for demographics only)

Exposure	Outcome	AOR (95% CI)	p
Dementia	COVID–19	3.17 (3.04–3.30)	<.001
Alzheimer's disease	COVID–19	2.98 (2.77–3.20)	<.001
Post–traumatic dementia	COVID–19	2.03 (1.76–2.33)	<.001
Presenile dementia	COVID–19	4.46 (3.70–5.38)	<.001
Senile dementia	COVID–19	3.13 (2.84–3.45)	<.001
Vascular dementia	COVID–19	5.26 (4.80–5.76)	<.001

Received: 23 August 2020 | Revised: 6 November 2020 | Accepted: 18 December 2020
DOI: 10.1002/alz.12296

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RESEARCH ARTICLE

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COVID-19 and dementia: Analyses of risk, disparity, and outcomes from electronic health records in the US

QuanQiu Wang[1] | Pamela B. Davis[2] | Mark E. Gurney[3] | Rong Xu[1]

Retrospective case-control analysis of EHRs

61.9 million adult and senior patients (age ≥ 18 years) in the United States up to August 21, 2020

- Controlled for nursing home stay
- Other latent factors?
- Cognitive impairment – limiting compliance with social distancing, mask wearing, or hand washing
- Dementia as state with increased susceptibility to SARS-CoV2 infection

Unable to examine DLB due to their insufficient sample sizes

CarePort
An Allscripts Company

COVID-19 REPORT

April 2020 data from the CarePort Transitions of Care Hub

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Trends in COVID-19 Infection and Deaths Observed Across 63,000 Nursing Home Residents

Dementia x1.7 risk of death even after adjusting for age

Residents with dementia accounted for 52% of COVID-19 cases

Constituted 72% of all COVID-19 deaths in the nursing home

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COVID-19 and Parkinson's disease

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COVID-19 and Parkinson's disease

- Risk of COVID-19 associated with:
  - Increasing age & frailty
  - Comorbidities including obesity, cardiovascular disease and diabetes
  - Pre-existing pulmonary disease
  - Male
  - Nursing home resident
  - Notably Vitamin D supplementation was associated with lower cases of COVID-19 in PD (data amalgamated, however, from non-randomised studies)

Chambergo-Michilot et al. *Eur J Neurol* 2021

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COVID-19 and Parkinson's disease

- Outcomes from COVID-19
  - Median infection prevalence ranged from 0.6% to 8.5% with median age of 74
  - 28.6% required hospital admission
  - 37.1% required L-dopa dose increase
  - 18.9% died

Artusi et al. *J Parkinsons Dis* 2021

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COVID-19 and Parkinson's disease

- Outcomes from COVID-19 pneumonia
  - Parkinson's Disease is associated with poor in-hospital outcomes [OR 2.64 (95% CI 1.75-3.99)]
    - Severe COVID-19 [OR 2.61 (95% CI 1.98-3.43)]
    - Mortality from COVID-19 [RR 2.63 (95% CI 1.50-4.60)]
  - Outcomes influenced by age but not gender or dementia

Putri et al. *Parkinsonism Relat Disord* 2021

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COVID-19 and Parkinson's disease

- Worsening of motor symptoms in 30-41% of PD patients
- Worsening of non-motor symptoms
  - Anxiety (25-31%)
  - Sleep (22-41%)
  - Emotional status (25-30%)
- Explanations include social isolation, lack of exercise, reduced face to face contact with clinical team

Chambergo-Michilot et al. *Eur J Neurol* 2021

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COVID-19 and Parkinson's disease

- **From a vaccination perspective:**
  - Incidence of side effects in Parkinson's disease seem to be no different than general population
  - Doesn't appear to affect therapies in Parkinson's disease
  - Data from frail elderly persons living in long-term care facilities suggests that extra caution is needed for this specific subgroup
  - Therefore prudent to be careful with administering the vaccine to very frail and terminally ill elderly persons with PD (and DLB?)

Torjesen et al. *BMJ* 2021
Bloem et al. *Journal of Parkinson's disease* 2021

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COVID-19 and DLB

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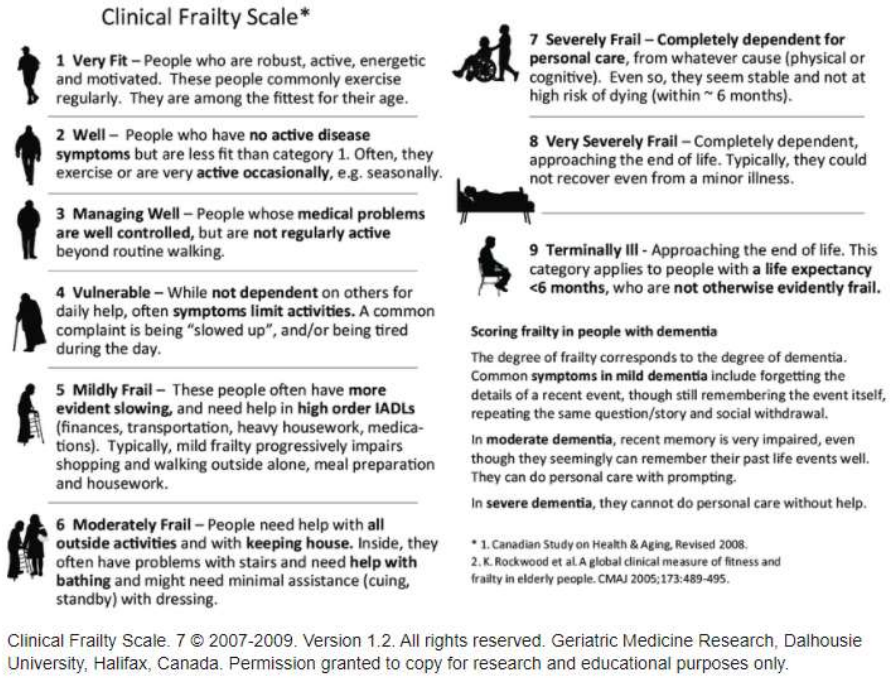
DLB and COVID-19

People with DLB will be biased against in treatment decision algorithms that consider multimorbidity for critical care



Clinical Frailty Scale*

1 **Very Fit** – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 **Well** – People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.

3 **Managing Well** – People whose **medical problems are well controlled,** but are **not regularly active** beyond routine walking.

4 **Vulnerable** – While **not dependent** on others for daily help, often **symptoms limit activities.** A common complaint is being "slowed up", and/or being tired during the day.

5 **Mildly Frail** – These people often have **more evident slowing,** and need help in **high order IADLs** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 **Moderately Frail** – People need help with **all outside activities** and with **keeping house.** Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.

7 **Severely Frail – Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 **Very Severely Frail** – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9 **Terminally Ill** - Approaching the end of life. This category applies to people with **a life expectancy <6 months**, who are **not otherwise evidently frail.**

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia**, they cannot do personal care without help.

* 1. Canadian Study on Health & Aging, Revised 2008.
2. K. Rockwood et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-495.

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DLB and COVID-19

- **Over-representation of people with DLB in nursing homes**
  - Swedish study[1] (n=650) found that 16% of residents have 2 or more core symptoms of DLB
  - Rising to 20% if parkinsonism included
- **Nursing home residents**
  - Population highly vulnerable to the spread of COVID-19
  - Represent 30-60%[2] of COVID-19 deaths
- **Intimation** is that people with DLB are likely to be at high risk of getting COVID-19 with likely significant morbidity / mortality

1. Zahirovic et al. *J Am Med Dir Assoc.* 2016
2. ECDC Public Health Emergency Team *Euro Surveill*. 2020

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DLB and COVID-19

- **Physical challenges – some examples:**
  - People with DLB are at increased risk of bronchopneumonia[1]
  - Failure to notice/report symptoms due to cognitive impairment
  - Failure to adhere to social distancing, mask-wearing rules due to cognitive impairment
  - Lack of face-to-face contact (professionals/family) due to isolation might lead to progression of symptoms
  - Increased risk of developing delirium compared to other dementias[2]

1. Hanyu et al. *Eur J Neurol.* 2009
2. McKeith et al. *Neurology* 2020

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DLB and COVID-19

- **Physical challenges – some examples:**
  - Social isolation with cognitive impairment leading to
    - Variability in adherence to medications
    - Poor hydration
  - Lack of exercise – increasing the risks of sarcopenia and falls

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DLB and COVID-19

- **Cognitive and Neuropsychiatric challenges – some examples:**
  - Lack of meaningful social contact
    - Exacerbation of hallucinations and worsening of cognitive fluctuations and apathy
    - Isolation exacerbating delusional ideas
    - Incomplete understanding of the situation leading to depression, anxiety and agitation
  - Virtual communication issues due to executive impairment and visuo-perceptual dysfunction and sometimes incorporation of what is on the “screen” into delusions/hallucinations
    - With healthcare teams
    - With family and friends

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DLB and COVID-19

- **Family and care-giver challenges – some examples:**
  - Higher baseline care-giver burden and depression with DLB compared to AD[1]
  - Likely to be exacerbated during COVID era
    - Closure of day care centres
    - Lack of overnight respite
    - Loss of formal/professional care-givers e.g. for personal care
    - COVID-19 risk issues for care-givers themselves esp. with comorbidities

1. Svendsboe et al. *Int J Geriatr Psychiatry* 2016

COVID and LBD survey

- Conducted via the Lewy body Society UK and led by Alison Killen, Newcastle University, UK
- Promoted by them in their newsletter, on social media and contact with Admiral nurse
- Ran for 5 weeks in Jan-Feb 2021
- Respondents 87 in total; carers responding were asked to do so on behalf of the care-recipient if they needed assistance rather than giving their own perspective
- Essentially sample of community dwelling people with DLB and their families/care-givers

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What has been the biggest change?

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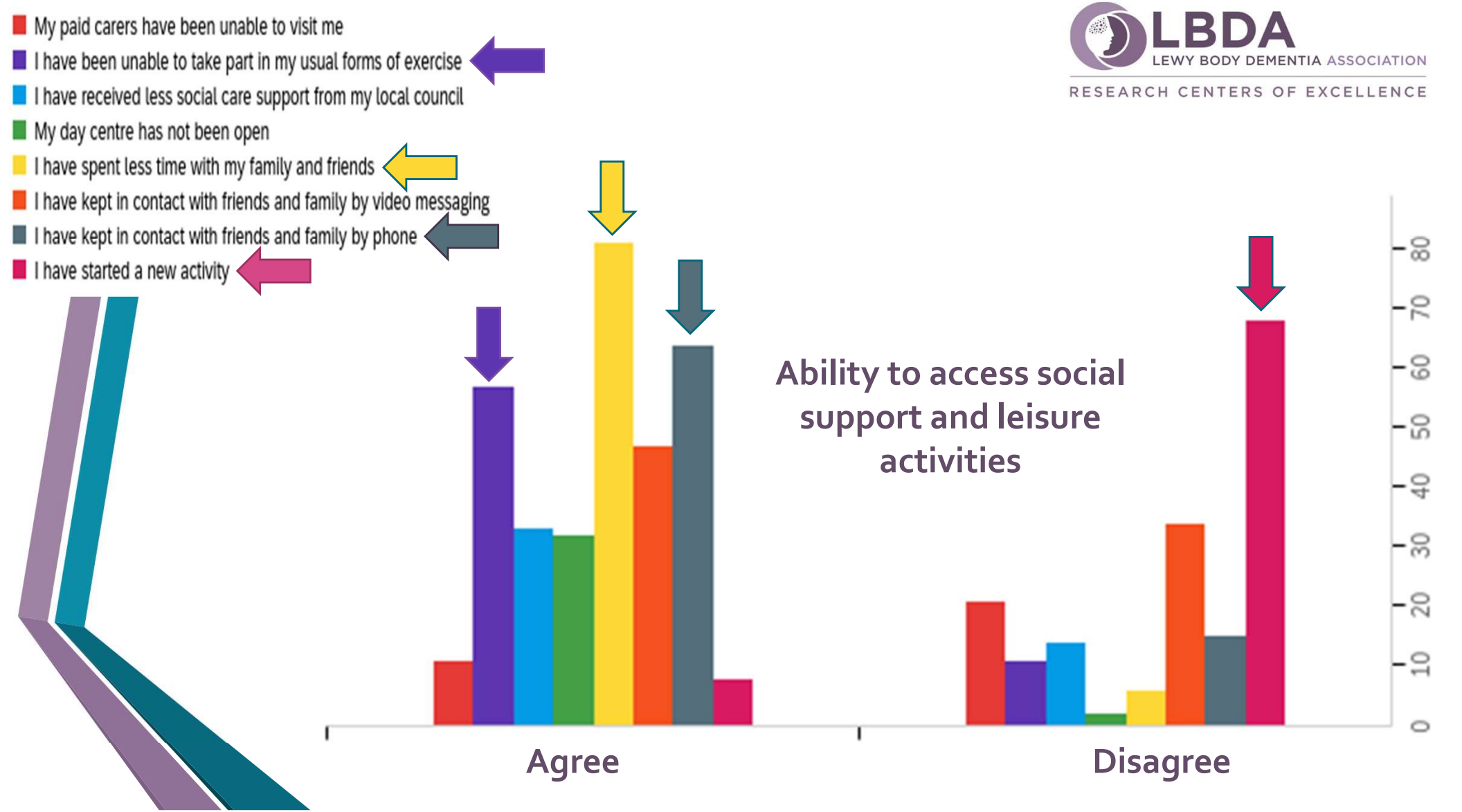

Access to health services

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Situation	Once		On 2 or more occasions		Not experienced		Total
Hospital appointment cancelled	13.8%	**12**	29.9%	**26**	56.3%	**49**	87
Hospital appointment by phone	18.4%	**16**	44.8%	**39**	36.8%	**32**	87
Hospital appointment by video call	18.4%	**16**	10.3%	**9**	71.3%	**62**	87
Primary care appointment by phone	20.7%	**18**	60.9%	**53**	18.4%	**16**	87
Primary care appointment by video call	3.5%	**3**	10.3%	**9**	86.2%	**75**	87
Offered a healthcare appointment by video call but unable to use this method	8.1%	**7**	6.9%	**6**	85.1%	**74**	87
Support from specialist nurse reduced or cancelled	19.5%	**17**	27.6%	**24**	52.8%	**46**	87
Support from an allied health professional reduced or cancelled	18.4%	**16**	24.1%	**21**	57.5%	**50**	87

Take home messages – about 50% experienced disruption

- Many cancelled appointments
- Greater use of telephone and video calls
- Reduced support from clinical teams

Impact of the COVID related restrictions and changes

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My mood has been low to an extent that is unusual for me	Agree strongly		Agree slightly		Neither agree or disagree		Not applicable		Total
	54.3%	44	32.1%	26	9.9%	8	3.7%	3	81

My husband's mood has deteriorated to the extent that he had suicidal thoughts and made a feeble attempt by throwing himself down a small flight of stairs

Feeling depressed at not being able to go out as much as usual. I also find it difficult to wear a mask and keep wanting to take it off. It's also difficult to understand what others are saying when they are wearing a mask.

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My memory and concentration have become worse	Agree strongly		Agree slightly		Neither agree or disagree		Total
	63.5%	54	32.9%	28	3.5%	3	85

Memory problems are worse, mobility is worse, so bored need to get back to normal routine

Being unable to spend quality time with family is so important and has ongoing effects. Seeing them on Zoom is ok but causes more confusion. It's hard to understand the rules of lockdown, more confusion!

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My hallucinations have become more frequent or severe	Agree strongly		Agree slightly		Neither agree or disagree		Not applicable		Total
	52.56%	41	26.92%	21	12.82%	10	7.69%	6	78

Fear triggered start of hallucinations beginning with hallucination of government COVID meeting taking place in living room and obliged to attend.

Increased hallucinations and loneliness. Worsened my condition and deterioration. Had to go into hospital and no-one could visit me. I had to be reminded every day about COVID. Wearing of masks put a barrier between me and others.

Any positives?

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- *Doing a lot of daily walks with our puppy*
- *Using supermarket delivery has been a bonus*
- *We have discovered how caring our next door neighbors are*
- *Reduced noise from planes & traffic*
- *I have had the company of my immediate family as they have been home from work a great deal and are able to work from my house for a couple of hours every now and again so that my wife has a break*
- *Social occasions with groups of people are no longer enjoyable for me so happy to be in one to one company. Happy to potter around and go for walks. I am in less stressful situations*

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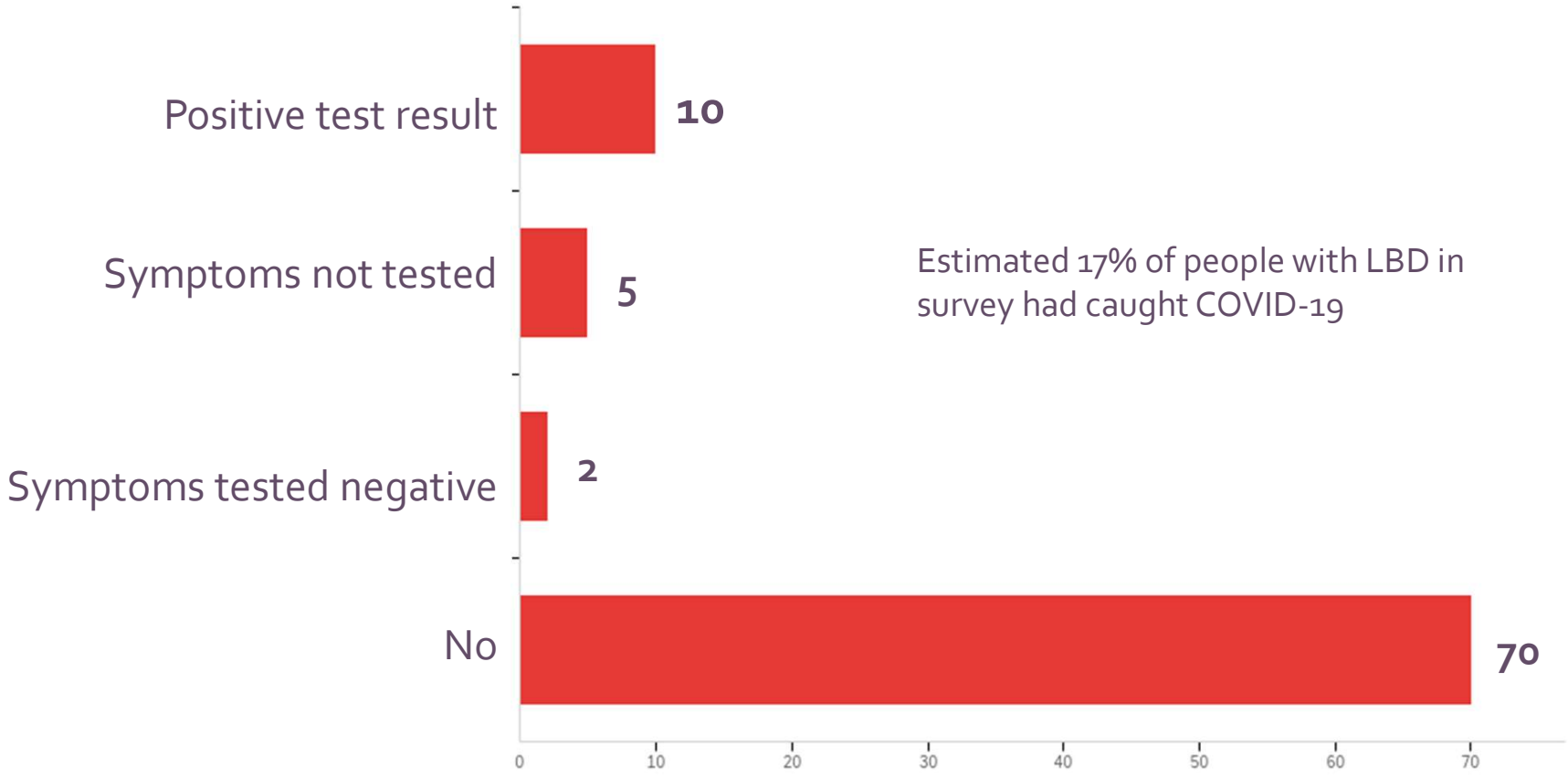
COVID status



Estimated 17% of people with LBD in survey had caught COVID-19

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Duration of COVID symptoms

Response	%	Count
up to 2 weeks	33.3%	5
2-4 weeks	40.0%	6
1-3 months	26.7%	4
over 3 months	0.00%	0
Total	100%	15

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Changes in symptoms since having COVID

Response	Improved		About the same		Slightly worse		Much worse		Symptom not experienced		Total
Physical symptoms i.e. movement difficulties	0.00%	0	31.3%	5	25.0%	4	43.8%	7	0.0%	0	16
Thinking and concentration	0.00%	0	37.5%	6	12.5%	2	50.0%	8	0.0%	0	16
Sleep disturbances	6.3%	1	25.0%	4	25.0%	4	37.5%	6	6.3%	1	16
Hallucinations	18.8%	3	37.5%	6	12.5%	2	31.3%	5	0.0%	0	16
Beliefs which others say are false	12.5%	2	25.0%	4	18.8%	3	25.0%	4	18.8%	3	16
Taste and or smell	0.0%	0	50.0%	8	0.0%	0	25.0%	4	25.0%	4	16

Take home messages

- In one third to half of people with DLB there was a worsening across majority of symptom domains (e.g. motor, cognitive, sleep and psychosis) with COVID-19 infection

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Limitations

- UK context
- Many of the surveys likely to be completed / supported by care-giver / family member
- Biased to those less severely affected
- Unrepresentative sample
- No definitive diagnosis
- Limit on information that could be collected online

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COVID-19 and direct brain effects

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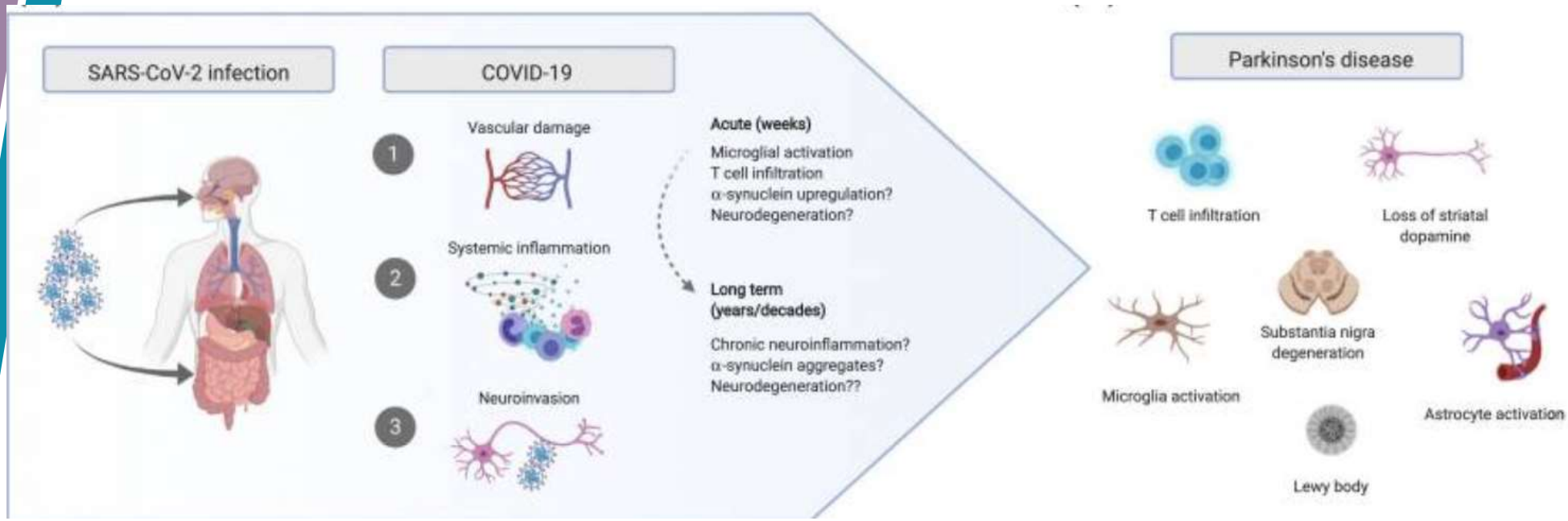

Brundin et al. 2020 Trends in Neurosci

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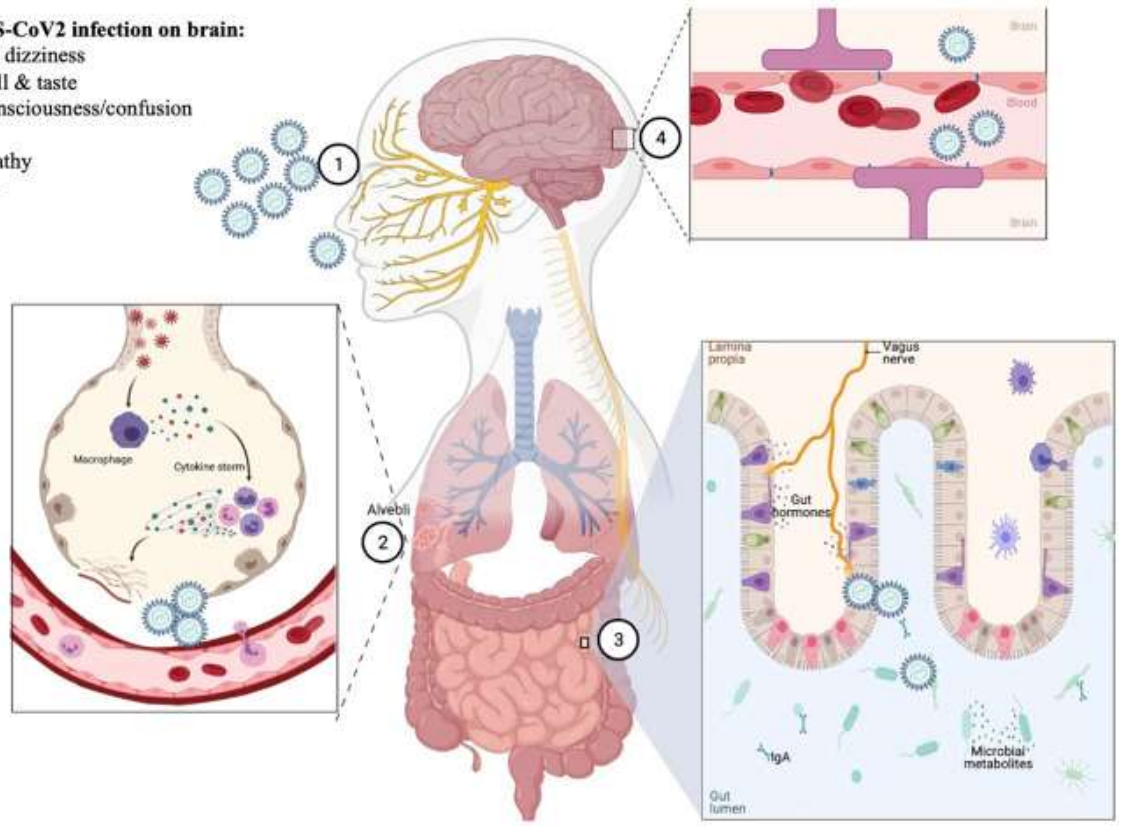
Effects of SARS-CoV2 infection on brain:

- Headache & dizziness
- Loss of smell & taste
- Impaired consciousness/confusion
- Seizures
- Encephalopathy
- Encephalitis
- Meningitis



Potential routes of entry of SARS-CoV2 and effects on brain function

Taken from : Dowd and McKernan *Neuronal Signal*, 2021

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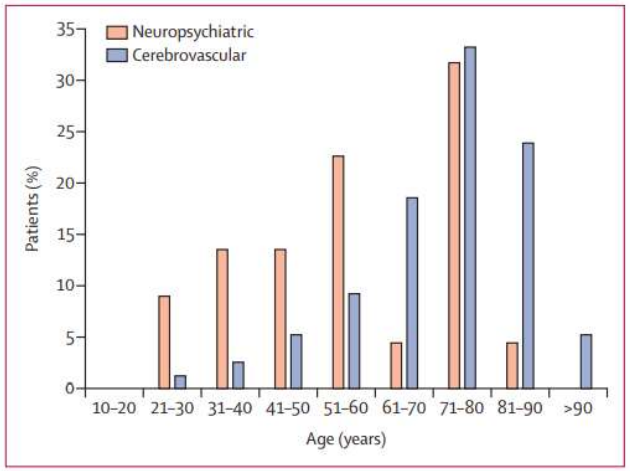
Neurological and neuropsychiatric complications of COVID-19 in 153 patients: a UK-wide surveillance study

Aravinthan Varatharaj, Naomi Thomas, Mark A Ellul, Nicholas W S Davies, Thomas A Pollak, Elizabeth L Tenorio, Mustafa Sultan, Ava Easton, Gerome Breen, Michael Zandi, Jonathan P Coles, Hadi Manji, Rustam Al-Shahi Salman, David K Menon, Timothy R Nicholson, Laura A Benjamin, Alan Carson, Craig Smith, Martin R Turner, Tom Solomon, Rachel Kneen, Sarah L Pett, Ian Galea, Rhys H Thomas*, Benedict D Michael*, on behalf of the CoroNerve Study Group†*



62% cerebrovascular event (ischaemic stroke, intracerebral haemorrhage, vasculitis)

31% altered mental state (encephalopathy and encephalitis, psychosis, dementia-like syndrome, affective)

20-30% of hospitalised COVID-19 patients have neurological/neuropsychiatric complications

Median age 71

Neuropsychiatric more common in younger

Cerebrovascular more common in older

CoroNerve Studies Group

Varatharaj et al. *Lancet Psychiatry* 2020

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Long term impact of COVID

- Concerns with regard to long COVID
  - Wide variety of symptoms e.g.
    - shortness of breath, palpitations, joint pain, tinnitus, anosmia
    - sleep disturbances, severe fatigue, depression, anxiety, cognitive dysfunction “brain fog”
  - In more severe disease possible long term neurological and neuropsychiatric sequelae

COVID-CNS
THE COVID-CLINICAL NEUROSCIENCE STUDY

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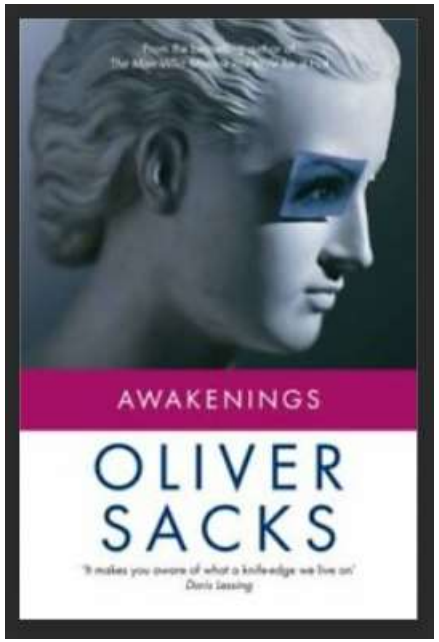
Theoretical concerns

- Sleeping sickness / encephalitis lethargica epidemic followed Influenza A H1N1 pandemic
- Fever, catatonia, coma and parkinsonism

- Presence of antibodies against coronavirus in CSF patients with Parkinson's disease, suggesting a certain relationship between both entities (Fazzini et al. *Movement Disorders* 1992)



New Results

PRE-PRINT

SARS-CoV-2 causes brain inflammation and induces Lewy body formation in macaques

Ingrid H.C.H.M. Philippens, Kinga P. Böszörményi, Jacqueline A.Wubben, Zahra C. Fagrouch, Nikki van Driel, Amber Q. Mayenburg, Diana Lozovagia, Eva Roos, Bernadette Schurink, Marianna Bugiani, Ronald E. Bontrop, Jinte Middeldorp, Willy M. Bogers, Lioe-Fee de Geus-Oei, Jan A.M. Langermans, Marieke A. Stammes, Babs E.Verstrepen, Ernst J.Verschoor

doi: https://doi.org/10.1101/2021.02.23.432474

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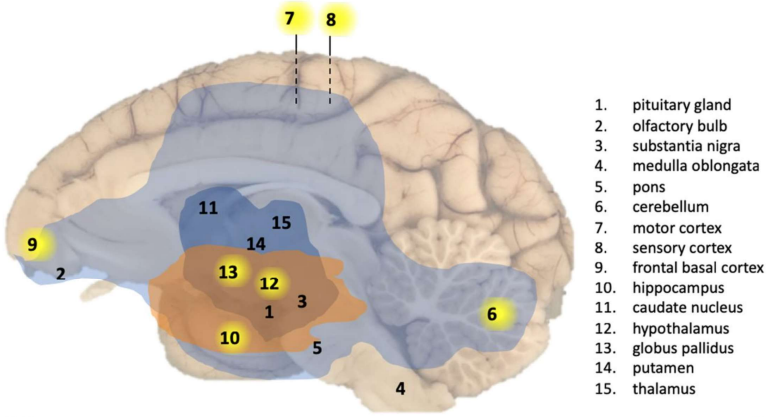
Potential for neurotropic viruses e.g. MERS and SARS coronaviruses to trigger formation of Lewy bodies and cause Parkinsonism

Infiltration of T-cells was found perivascular and in the brain parenchyma – altered blood brain barrier integrity?

Viral access to the brain via neuronal pathways e.g. through infected motor or sensory neurons or pituitary (ACE-2 receptors)



Viral RNA-positive regions in yellow
Activated microglia in blue
Lewy bodies (α-synuclein+) in orange

COVID-19 neuropathology at Columbia University Irving Medical Center/New York Presbyterian Hospital

Thakur et al. *Brain* 2021

- 41 consecutive patients with SARS-CoV-2 infections underwent autopsy
- Mean age 74
- 59% admitted to ICU
- Neuropathological examination of 20-30 areas from each brain
- 44% had evidence of neuropathology

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COVID-19 neuropathology at Columbia University Irving Medical Center/New York Presbyterian Hospital

Thakur et al. *Brain* 2021

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- Hypoxic/ischemic changes in all brains, both global and focal; large and small infarcts, many of which appeared haemorrhagic
- Microglial activation most prominently in the brainstem

But:

- Sparse T lymphocyte accumulation in either perivascular regions or in the brain parenchyma
- Very low viral RNA and protein and no correlation with histopathology

Findings suggest changes not result direct viral infection of brain but rather likely from systemic inflammation with synergistic contribution from hypoxia/ischemia

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Drugs used in LBD in relation to acute COVID-19 treatment

- Tocilizumab – might be potentiated by L-dopa
- Dexamethasone might decrease effectiveness of zonisamide, aripiprazole, clozapine, domperidone
- Be aware of potential effects of some other tremor related drugs (e.g. primidone, topiramate) affecting either tremor related drug or COVID-19 treatment although latter are rarely prescribed in DLB
- Cold/flue remedies may interact with MAO-B inhibitors

UPDATE: Treating COVID-19 in PD and other Movement Disorders: A Review of Drug Interactions

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Conclusions/Discussion Points

- Likely increased risk to exposure to COVID-19 and increased disease severity in DLB
- Unclear direct effects of COVID-19 on DLB

- Pandemic has had profound indirect impacts on day-to-day function and mood in people living with DLB
- Reduced healthcare contact likely to bring significant risks

Impact of COVID-19 on dementia research

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95% of researchers have had projects and trials delayed because of COVID-19

1 in 5 had research projects cancelled completely

Only 15% of research group leaders have resumed activity at their labs at more than 50% capacity

13% have not yet returned to their workplaces

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Panel Discussion and Q&A

Moderator:
Katherine Amodeo, MD

Panelists:
John-Paul Taylor, PhD
Jennifer Goldman, MD, MS

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Thank you!

- A follow up email will be sent to you at the end of this activity.
- Please complete the evaluation using the instructions in that email.
- After you complete the evaluation, you may download and print the CME credit/Certificate of Participation or save it to your computer in your files.

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CME Activities

- Medscape and LBDA collaboration
  - On demand: An Introduction to Lewy body dementia
  - More Medscape partnerships in development

Watch your inbox for more information about these activities!

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LBDA's Research of Excellence Program

A program consisting of 26 of the nation's leading LBD clinicians to which LBD patients and their families can turn for advanced LBD diagnosis and treatment.

Through our combined efforts we are connecting many experienced physicians and respected institutions that are committed to conducting LBD research, providing advanced LBD care, community outreach, and support.

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LBDA's Mission

Through outreach, education and research, we support those affected by Lewy body dementias, their families and caregivers.

We are dedicated to raising awareness and promoting scientific advances.

www.lbda.org