Trial registration: ACTRN12618000038291p

CASE STUDIES DOCUMENTING THE INTERACTION OF ANTIBIOTICS, PHOTOBIOMODULATION AND PARKINSON'S DISEASE

Brian Bicknell, PhD. University of Western Sydney
Ann Liebert, PhD. Sydney Adventist Hospital; Sydney University
Anita Saltmarche, BScN, MHSc. Saltmarche Health & Associates, Toronto, Canada

Orla Hares, BSc Physiotherapy. Gaitway Neurophysio, Hamilton, Canada
Hosen Kiat, MBBS, FRACP, FACP, FACC, FCCP, FCSANZ, DDU, DMSc.
Macquarie University, Macquarie Park, Australia

learn more about PBM and the microbiome

Background

PHOTOBIOMODULATION is the use of non-thermal light of particular wavelengths to bring about changes to the metabolism of cells and mitochondria

- Used for over 50 years clinically and in research
- Good pre-clinical evidence for a positive effect on the signs associated with PD[1]
- There are limited clinical trials[2,3], with one assessing microbiome changes[4]

Parkinson's disease has a well-established microbiome-gut-brain-axis (MGBA)[5,6]

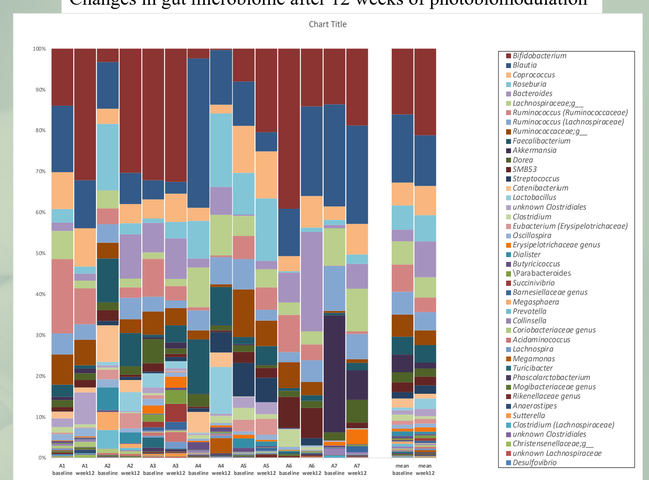
- Gut dysbiosis is associated with the disease (>70%) and gastrointestinal symptoms may be present many years before neurological symptoms
- Antibiotic use has been shown in epidemiological studies to increase the risk of Parkinson's disease[7]
- There is some evidence that *Desulfovibrio* species may be involved with PD[8]


International Journal of Molecular Sciences
MDPI
Review
Neurodegenerative and Neurodevelopmental Diseases and the Gut-Brain Axis: The Potential of Therapeutic Targeting of the Microbiome
Brian Bicknell [1,*], Ann Liebert [1,2,3], Thomas Borody [4], Geoffrey Herkes [3], Craig McLachlan [5] and Hosen Kiat [1,5,6,7]

frontiers | Frontiers in Aging Neuroscience
TYPE Review
PUBLISHED 30 May 2023
DOI 10.3389/fnagi.2023.1151850
Check for updates
OPEN ACCESS
EDITED BY
Mali Jiang,
Johns Hopkins University, United States
REVIEWED BY
Sharad Purohit,
Augusta University, United States
Michal Lubomski,
Royal North Shore Hospital, Australia
Therapies for Parkinson's disease and the gut microbiome: evidence for bidirectional connection
Grace Hey[1], Navya Nair[1], Emily Klann[2], Anjela Gurrala[1], Delaram Safarpour[3], Volker Mai[2], Adolfo Ramirez-Zamora[1] and Vinata Vedam-Mai[3]*

frontiers | Frontiers in Cellular and Infection Microbiology
TYPE Original Research
PUBLISHED 01 May 2023
DOI 10.3389/fcimb.2023.1181315
Check for updates
OPEN ACCESS
EDITED BY
Fernando Navarro-Garcia,
National Polytechnic Institute of Mexico (CINVESTAV), Mexico
REVIEWED BY
Claudia Perez-Cruz,
National Polytechnic Institute of Mexico (CINVESTAV), Mexico
Eng Guan Chua,
University of Western Australia, Australia
Desulfovibrio bacteria enhance alpha-synuclein aggregation in a *Caenorhabditis elegans* model of Parkinson's disease
Vy A. Huynh[1], Timo M. Takala[1], Kari E. Murros[2], Bidhi Diwedi[1,3] and Per E. J. Saris[1]*

Changes in gut microbiome after 12 weeks of photobiomodulation



- *Desulfovibrio* at very low levels (<0.001%); non-detect in 3 participants; minor decrease with PBM in 3 of 4 participants
- Non-significant increases in *Bifidobacterium, Faecalibacterium, Parabacteroides, Sutterella*
- Non-significant decreases in *Ruminococcus, Clostridium* (sensu stricto), *Turicibacter*, *Peptinophilus*, *Lactococcus, Enterococcus*

Case Study 1 (Australian Parkinson's clinical trial participant)

- Diagnosed 2 years, steadily getting worse
- Onset of PD coincided with broad-spectrum antibiotics for prostatitis
- No PD medication (sensitive)
- Presented with left foot drag, mask of PD (no expression), low speech, micrographia
- Gastrointestinal symptoms (constipation and diarrhea)

Improvement at 3 weeks:

- Steady <u>subjective improvement</u>, expression returned, foot drag disappeared

Antibiotics at 3 weeks for respiratory infection

- Immediate return of foot drag;

4-week assessment (as part of study cohort)

- <u>Decline</u> in outcome measures (median for study cohort was improvement in outcome measures[3])
- Self-reported worsening symptoms
- Reduced MoCA 30 → 28

Continued treatment to 12 weeks

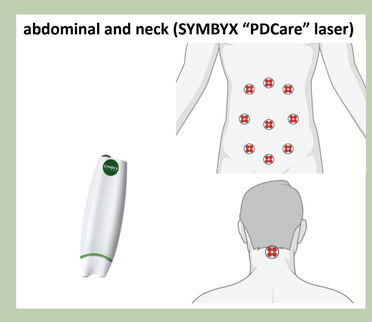
- Gradual improvement in outcomes; loss of foot drag
- Remission of gastro symptoms

MICROBIOME

- Sharp change pre and post antibiotics
  - decline in *Bifidobacterium*, *Streptococcus*, *Ruminococcus*, *Dorea*, *Klebsiella*
  - increases in *Blautia*, *Faecalibacterium*, *Bacteroides*, *Coprococcus*
  - no evidence of *Desulfovibrio* present (below detection limit?)
- Gradual change to week 12
- Increase in some healthy bacteria

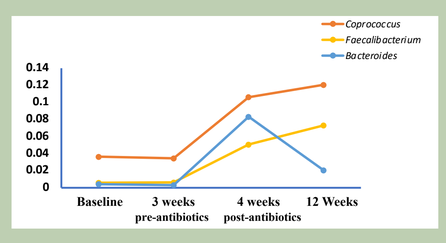
Treatment regimen

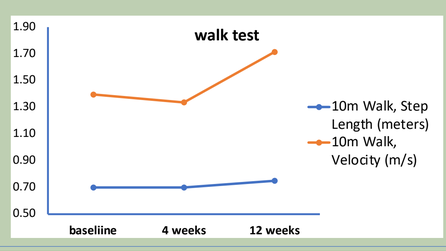
- Treatment with a low power laser (904nm; 30mW) over the abdomen and neck
- 20 minute treatment; 3 times per week; 12 weeks

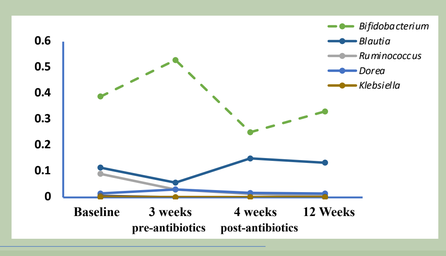


Assessment

- Movement assessment as previously described[2,3], performed before treatment and after 4 weeks and 12 weeks of PBM treatment
- Microbiome assessment as previously descibed[4], performed before treatment and after 3 weeks, 4 weeks and 12 weeks







Case Study 2 (Canadian Gaitway Neurophysio client)

- March 2021 - UPDRS score 24/199 (PD Stage 1.5)
- June 2022 Score of 29/199 (PD Stage 2)

PBM therapy July 2022

- **Began**December 2022 improved UPDRS score 10/199 (Stage 1)
- Improved fine motor control and hand coordination increased allowing her to crochet again
- Increased energy
- Improved walking in off periods (no longer shuffling in the morning)
- Reduced medications (no extra doses and extended times between meds)

Dental procedure with double dose of antibiotics for infection June – August 2022

- PBM improvements diminished
- meds were no longer effective (extra doses needed)
- shuffling gait returned overnight and first thing in the morning
- unable to crochet

After antibiotic therapy continued PBM therapy

- Sept-Dec 2022 returned to feeling well
- Quickly regained improvements
- Began crochet again; has now restarted cross stitching (not done for over 1 year)
- less shuffling
- improving sense of smell (can smell mint)
- Less fatigue
- UPDRS improved to Stage 1 again.
- Reduced medication frequency and work better

March 2023

- Increased dyskinesia with corresponding medication increase (Amantadine)

Conclusions

- There is a strong gut-brain axis in Parkinson's disease
- Antibiotics affects the microbiome and are implicated as a risk factor for PD
- Many symptoms of PD can be improved with PBM
- Antibiotic therapy can reverse the improvements seen with PBM therapy
- Improvements can return after antibiotic cessation with continued PBM treatment
- In this study, PBM to the abdomen has proven to be a novel and effective mechanism to treat Parkinson's disease symptoms potentially by targeting the microbiome
- The complicating effect of antibiotics, and potentially other factors that can influence the microbiome, need to be considered

References

1. Salehpour, F., Hamblin, M.R. *Biomolecules* **2020**, 10, 610
2. Liebert, A.; Bicknell, B.; Laakso, E.L.; et al. *BMC Neurology* **2021**, 21, 256,
3. Liebert, A.; Bicknell, B.; Laakso, E.L.; et al. *Photobiomodulation, Photomedicine & Laser Surgery* **2022** *40, 112-122*
4. Bicknell, B.; Liebert, A.; McLachlan, C.S.; et al. *Journal of Personalized medicine* **2022**, 12, 49.
5. Bicknell B, Liebert A, Borody T, Herkes G, et al *International Journal of Molecular Sciences* **2023** 24, 9577
6. Hey G, Nair N, Klann E, et al. Frontiers in Aging Neuroscience **2023** 15, 1151850.
7. Huynh VA, Takala TM, Murros KE, et al. *Frontiers in Cellular and Infection Microbiology* **2023** 13, 502
8. Mertsalmi TH, Pekkonen E, Scheperjans F. *Movement Disorders* **2020** 35, 431-442

We would like to a**cknowledge SYMBYX Pty Ltd** for supply of devices and the financial and research support of Olivia Nassaris of **Hospital Research Foundation Group**, and **San Foundation**.