Investigating the Relationship Between *Fusobacterium nucleatum and Neurodegenerative Disease*

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INTRODUCTION

Fusobacterium nucleatum(Fn): opportunistic gram-negative anaerobic bacteria

- Commensal to the human oral cavity
- Prevalence increases with disease presence and severity
- Has novel adhesin and invasin protein known as FadA

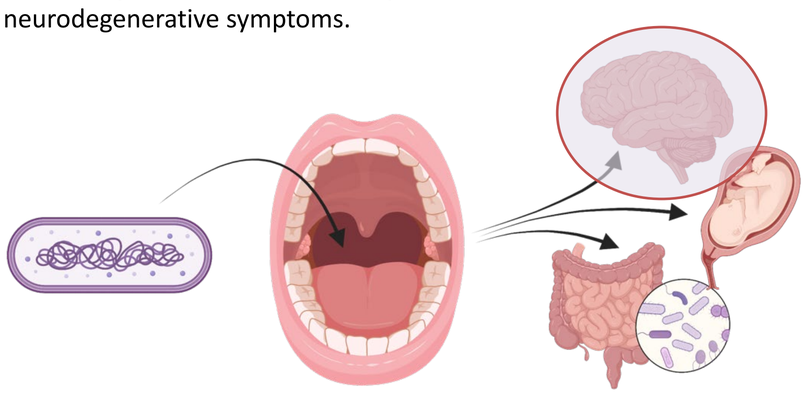
FadA: responsible for the bacterial attachment and invasion of host cells, allowing *Fn* to translocate hematogenously from its primary site of colonization into extra-oral sites

- Extra-oral colonization → systemic disease
- May also be associated with the bacteria's ability to cross the blood brain barrier and polymerize into an amyloid-like protein

Amyloid-like proteins are a hallmark of neurodegenerative diseases suggesting that *Fn* colonization may contribute to the development of such diseases.

OBJECTIVES

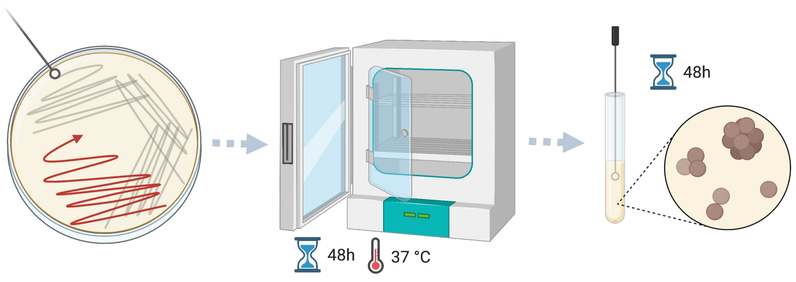
The purpose of this study was to elucidate the potential link between the extra-oral presence of F. nucleatum and neurodegenerative symptoms.



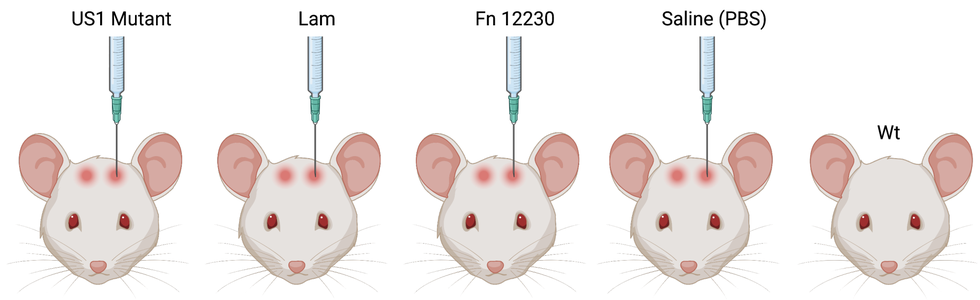
METHODS & MATERIALS

A total of 46 mice (23 males, 23 females) were evaluated using two different behavioral tests that assess learning, memory and sensorimotor skills.

1. Bacterial Culturing: 3 different strains of Fn were cultured.



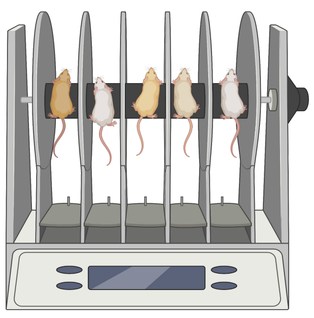
2. Cranial Cavity Injections: 22 mice, 8-12 weeks old, were cranially injected with three different strains F. nucleatum strains - Fn 12230 (wild-type), US1 (fadA-deletion mutant) and Lam (secretion mutant). An additional 14 mice received saline injections and the rest received no injections.



3. Behavioral Testing: After a 3-week surgical recovery, behavioral testing began with the Barnes Maze and Rotarod. Rotarod testing was conducted for 10 consecutive weeks, and Barnes Maze testing was conducted for 3 weeks with 2 rest weeks in between.

Rotarod

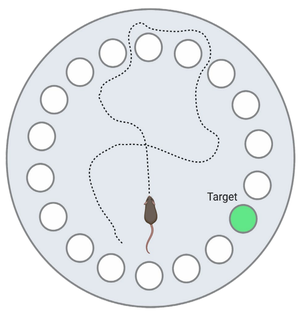
- 2 days per week
- 3 trials/day
- Acceleration: 4-40rpm over 5min
- Time spent on rod recorded



Barnes Maze

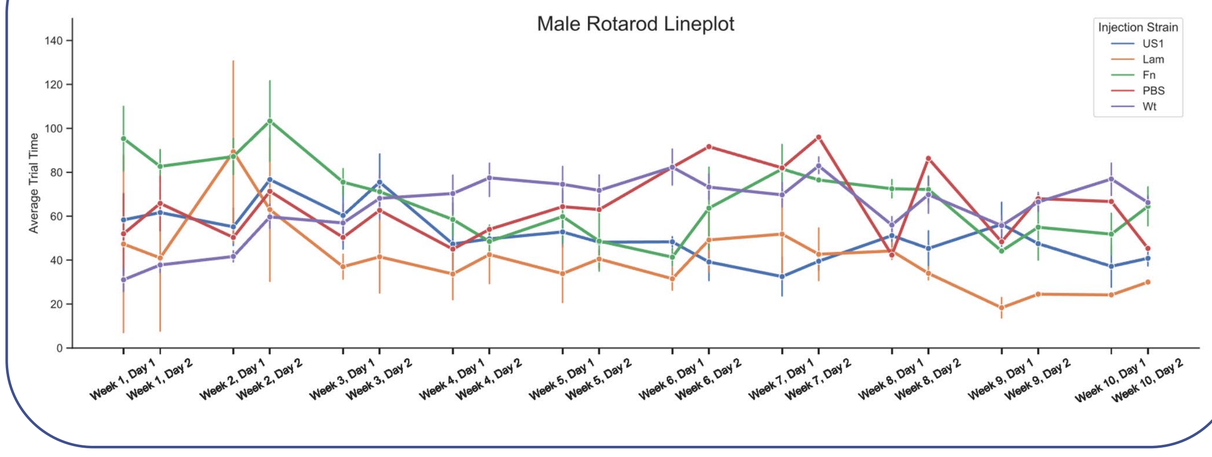
5 day protocol:

- Day 1: training day
- 4 trial days/week
- 4 trials/day
- Time to reach target hole recorded (Maximum: 3min)



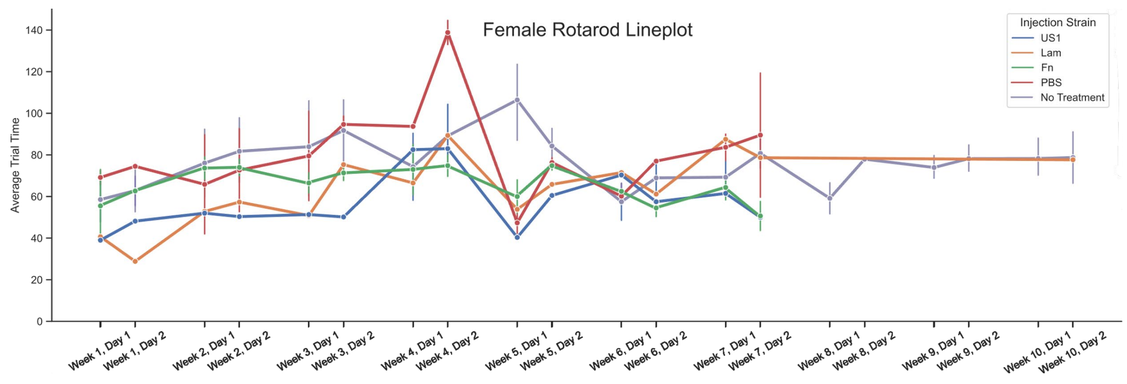
RESULTS

Rotarod Data:

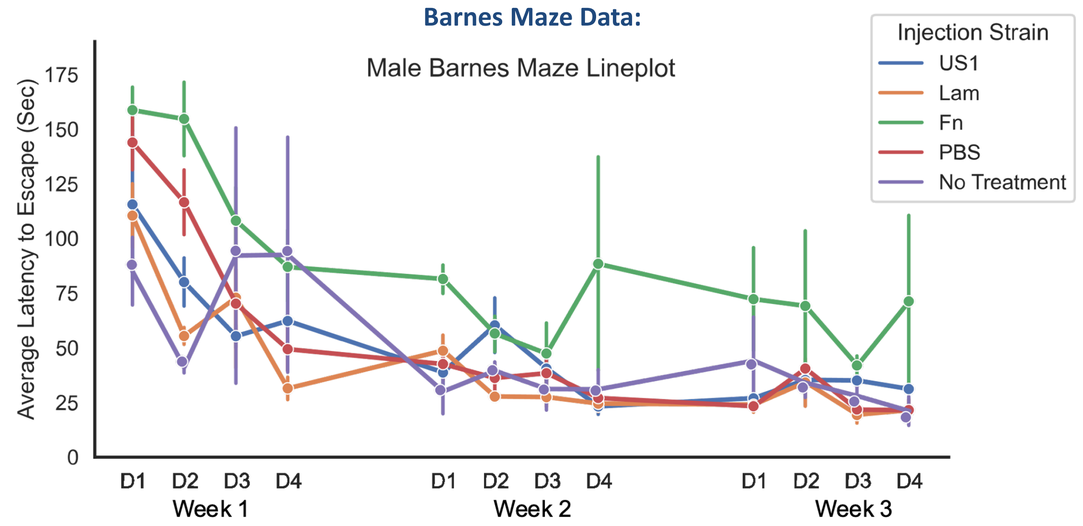


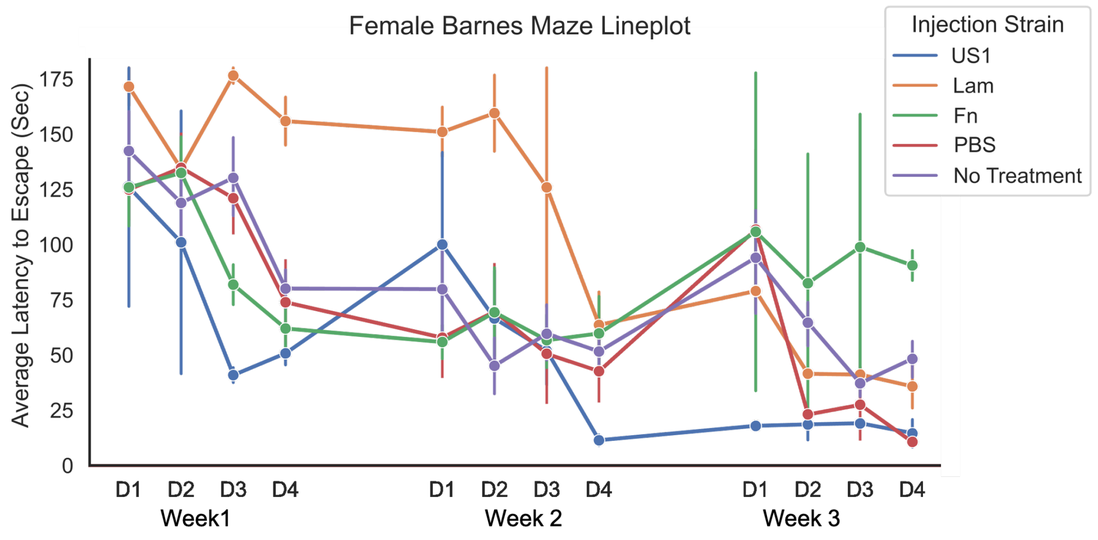
RESULTS

Rotarod Data (cont'd):



Barnes Maze Data:





DISCUSSION

Rotarod:

- Inconclusive data – did not see an overall upward trend in times spent on Rotarod
- Sensorimotor abilities of mice may require more time to improve than was allotted for experiments

Barnes Maze:

- Downward trend in the time to locate the "escape hole" seen across all treatment groups during the first week of trials
- Female *Fn*-injected mice latency times to escape remained relatively high despite training → suggests that *Fn*-injected mice may have diminished long-term memory
- Male *Fn*-injected mice latency times to escape decreased at a slower pace than other treatment groups

CONCLUSION

Neurodegenerative diseases are typically adult-onset conditions that are gradually progressive. Our data shows that Fn has the potential to elucidate neurodegenerative symptoms in mice, however more data collected at older ages is needed to make a definitive conclusion.

Limitations:

- Small sample size and data collection times
- Fn may not exacerbate symptoms de novo, but rather worsen existing symptoms

Future direction:

- Brain imaging to verify injections of bacteria
- Further testing – more mice for longer periods of time

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REFERENCES

- Han Y. W. (2015). Fusobacterium nucleatum: a commensal-turned pathogen. Current opinion in microbiology, 23, 141–147. https://doi.org/10.1016/j.mib.2014.11.013

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