A Case-Control Study of ALS in Eastern North Carolina: Investigating the Role of Algae and Pesticides in a Region of High ALS Mortality

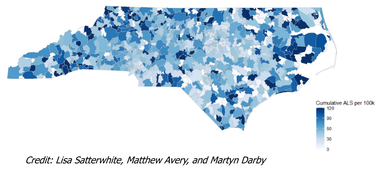
Danielle Levinson, BA, Michelle Ward, RN, Hailey Zampa, BS, Alexandra Linares, BS, Xiaoyan Li, MD, PhD, Kelly White, PA-C, Lisa Satterwhite, PhD, Richard Bedlack, MD, PhD

Duke University Hospital

Background

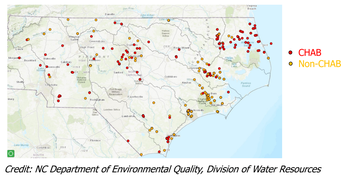
- Approximately 90% of amyotrophic lateral sclerosis cases are sporadic (no known family history) (1)
- Current theories suggest that ALS develops due to the cumulative effects of environmental exposures and genetic susceptibility (2)
- Cyanobacterial harmful algal blooms (CHABs) have been shown to produce the neurotoxin BMAA, which has been implicated in ALS development (3)
- There is evidence that pesticide exposure also increases ALS risk (4)
- A higher-than-expected number of ALS deaths have been found in Eastern North Carolina (Figure 1), where CHABs and agricultural activity are common (Figure 2)

Figure 1: ALS mortality/100,000 (1999-2023)



Credit: Lisa Satterwhite, Matthew Avery, and Martyn Darby

Figure 2: Confirmed algal blooms (2012-2019)



Credit: NC Department of Environmental Quality, Division of Water Resources

Hypotheses

1. Eastern NC residents are more likely than Central NC residents to have sporadic vs. familial ALS.
2. Eastern NC residents are more likely to have been exposed to cyanobacteria harmful algal blooms (CHABs) through residential proximity, activities, and diet.
3. Eastern NC residents are more likely to have been exposed to pesticides through work and/or hobbies.

Methods

- Eastern and Central NC regions were chosen based on ALS mortality and proximity to algal blooms (Figure 3)
- 24 ALS patients (8 Eastern, 16 Central) and 13 healthy controls (3 Eastern, 8 Central) were enrolled at the Duke ALS Clinic
- Subjects responded to a questionnaire developed by Stommel et al (5) to assess lifetime environmental exposures
- Statistical analysis was performed using Fisher's exact test, Mann-Whitney Test, and Kruskal-Wallis Test in JMP Pro 17.2.0

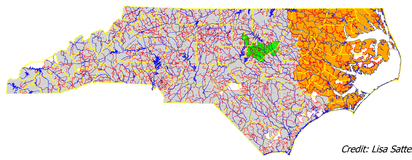


Figure 3: Study areas

Green: Central NC
Orange: Eastern NC

Credit: Lisa Satterwhite, Matthew Avery, and Martyn Darby

Results

	ALS EASTERN	ALS CENTRAL	p value
No	7 (88%)	14 (88%)	
Yes	1 (13%)	1 (6%)	
Unknown	0 (0%)	1 (6%)	
Total	8 (100%)	16 (100%)	1.00

Table 1: There was no difference in family history of ALS between the ALS Eastern and Central groups.

Table 2: ALS Eastern subjects were not more likely to report waterbody or algae exposure.

Prior to six months ago, had you ever lived in a home located on or near (within a two-mile distance) a lake, river, pond, estuary, ocean, or waterbody?

	ALS EASTERN	ALS CENTRAL	OR (95% CI)
No	2 (25%)	2 (13%)	1.0 (ref)
Yes, part-time residence	1 (13%)	1 (6%)	1.00 (0.03, 29.81)
Yes, full-time residence	5 (63%)	13 (81%)	0.38 (0.04, 3.52)
Total	8 (100%)	16 (100%)	

If yes to the previous question: Have there ever been blue green algae "blooms" or green surface scum on the water body's surface?

	ALS EASTERN	ALS CENTRAL	OR (95% CI)
No	3 (50%)	7 (50%)	1.0 (ref)
Yes	3 (50%)	7 (50%)	0.75 (0.12, 4.66)
Total	6 (75%)	14 (88%)	

Swimming in Lakes or Rivers

	ALS EASTERN	ALS CENTRAL	OR (95% CI)
No	4 (50)	15 (100)	1.0 (ref)
Yes	4 (50)	0 (0)	**31.00 (1.39, 691.30)***
Total	8 (100)	15 (94)	

Boating, sailing, or kayaking

	ALS EASTERN	ALS CENTRAL	OR (95% CI)
No	4 (50)	14 (93)	1.0 (ref)
Yes	4 (50)	1 (7)	**14.00 (1.20, 163.00)***
Total	8 (100)	15 (94)	

Table 3: ALS Eastern subjects were more likely to have regularly participated in water activities.

Table 4: Pesticide exposure was more common in ALS Eastern subjects.

	ALS EASTERN	ALS CENTRAL	OR (95% CI)
No	6 (75)	14 (88)	1.0 (ref)
Yes	2 (25)	2 (13)	2.33 (0.26, 20.66)
Total	8 (100)	16 (100)	

Conclusions

- The higher mortality in Eastern NC may not be due to familial cases
- Participation in water activities as well as direct pesticide exposure may play a role in higher ALS mortality in Eastern NC
- Active water exposure may be higher risk than passive exposure, as indicated in a similar study (5)
- Future studies should investigate the relationship between waterbody and pesticide exposure in the development of ALS
- More subjects should be recruited to increase the study's power
- Our study's design was limited by the potential for recall bias

Acknowledgments

I would like to thank Michelle Ward and Hailey Zampa for assisting me with data collection and documentation. I am grateful to the staff of the Duke ALS Clinic for helping me integrate into their busy and extraordinary clinic. I thank Dr. Michael Lutz for his support with data analysis and his helpful insights. I could not have asked for a better collaborator in Alexandra Linares, who was always supportive and provided excellent feedback. I thank my mentor, Dr. Bedlack, for answering my many questions, for supporting my growth as a researcher, for teaching me about ALS, and for reminding me of the importance of hope and passion for one's work. Lastly, I would like to express my gratitude to the patients and caregivers who generously donated their time to this study. This project became reality because of the passion and community advocacy of Ashley Stoop, Tommy Harrell and the Jim "Catfish" Hunter ALS Foundation.

References

1. Li TM, Alberman E, Swash M. Comparison of sporadic and familial disease amongst 580 cases of motor neuron disease. J Neurol Neurosurg Psychiatry. 1988;51(6):778-84.
2. Goutman SA, Savelieff MG, Jang DG, Hur J, Feldman EL. The amyotrophic lateral sclerosis exposome: recent advances and future directions. Nat Rev Neurol. 2023;19(10):617-34.
3. Cox PA, Banack SA, Murch SJ, Rasmussen U, Tien G, Bidigare RR, et al. Diverse taxa of cyanobacteria produce beta-N-methylamino-L-alanine, a neurotoxic amino acid. Proc Natl Acad Sci U S A. 2005;102(14):5074-8.
4. Kamel F, Umbach DM, Bedlack RS, Richards M, Watson M, Alavanja MC, et al. Pesticide exposure and amyotrophic lateral sclerosis. Neurotoxicology. 2012;33(3):457-62.
5. Andrew AS, Caller TA, Tandan R, Duell EJ, Henegan PL, Field NC, et al. Environmental and Occupational Exposures and Amyotrophic Lateral Sclerosis in New England. Neurodegener Dis. 2017;17(2-3):110-6.