THE PREVALENCE AND ONE YEAR INCIDENCE OF FRONTOTEMPORAL DEMENTIA IN INDIVIDUALS WITH AMYOTROPHIC LATERAL SCLEROSIS BASED ON RACE

BY:

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ALS: Amyotrophic Lateral Sclerosis

ALSFRS: ALS Functional Rating Scale

BMI: Body Mass Index

CBS: Cognitive Behavioral Screen

EMG: Electromyography

FALS: Familial ALS

FTD: Frontotemporal Dementia

FTLD: Frontotemporal Lobar Degeneration

PEG: Percutaneous Endoscopic Gastrostomy

%FVC: Percent Forced Vital Capacity

MND: Motor Neuron Disease

MRI: Magnetic Resonance Imaging

NIV: Noninvasive Ventilation

UMN: Upper Motor Neuron

LMN: Lower Motor Neuron

PBA: Pseudobulbar affect

SAS: Statistical Analysis System

STD: Standard deviation

SE: Standard Error

TTD: Time to Diagnosis

ABSTRACT

Amyotrophic lateral sclerosis (ALS) is a motor neuron disease with progressive loss of upper and lower motor neurons, whereas frontotemporal dementia (FTD) is a progressive dementing condition characterized by selective degeneration of the frontal and anterior temporal lobes. A link between ALS and FTD is well-established, and case studies document a strong association between amyotrophic lateral sclerosis and the behavioral form of FTD. A retrospective cohort study was conducted from patients visits to the Wake Forest School of Medicine. Individuals with ALS were identified from Epic chart review from the past ten years. The charts were matched, Caucasian to African-American patients, regarding the following variables: race, age, and site of onset. Cognitive behavioral screen (CBS) scores were collected from all cases and compared between Caucasian and African American cohorts. In the Epic database there are 36 African-Americans patients and 102 Caucasian patients that received ALS-CBS testing. The CBS scores were reviewed and we performed logistic regression to compare their scores. No clear association was found between CBS scores and race in individuals with ALS, although after controlling for multiple variables some patterns arose suggesting lower CBS scores in African Americans. The evolving knowledge of the links between ALS and FTD has allowed for better understanding of how these conditions affect each other. Determining the prevalence of FTD in different races may provide insight

regarding who is at risk, and it may also impact how physicians recognize and treat dementia in those with ALS.

CHAPTER I

INTRODUCTION

ALS Overview

Amyotrophic lateral sclerosis (ALS), also referred to as Lou Gehrig's disease, is a progressive neurodegenerative disease. ALS was first discovered in 1869 by French neurologist Jean-Martin Charcot. ALS directly affects motor neurons in the brain and spinal cord, resulting in neurons that are not able to send impulses to the muscles for movement. In some cases, upper motor neurons and lower motor neurons can stop functioning at the same time. As a result, affected individuals experience limb weakness, difficulty speaking, difficulty eating or swallowing, and respiratory failure, and this progressive weakness eventually leads to death. In the U.S. about 5,000 people are diagnosed with ALS each year.[1] ALS is 20 percent more common in men than women, and it is most common in people who are between the ages of 58 to 70 years. However, cases can appear in people who are younger, and ALS can affect anyone regardless of racial, ethnic, or socioeconomic status. The life expectancy of a person with ALS is 2 to 5 years from the time of diagnosis; the average survival time is about 3 years. In some cases, a person diagnosed with ALS can live longer than 5 years, as some individuals have slower rates of progression. According to the ALS Patient Care Database, 93 % of ALS patients in the U.S. are Caucasian. Also, U.S military veterans, particularly those deployed during the Gulf War, are twice as likely to develop ALS, and it is not clear why

this occurs. According to the CDC, “In 2015, the estimated prevalence of ALS cases was 5.2 per 100,000 populations with a total of 16,583 cases identified.”

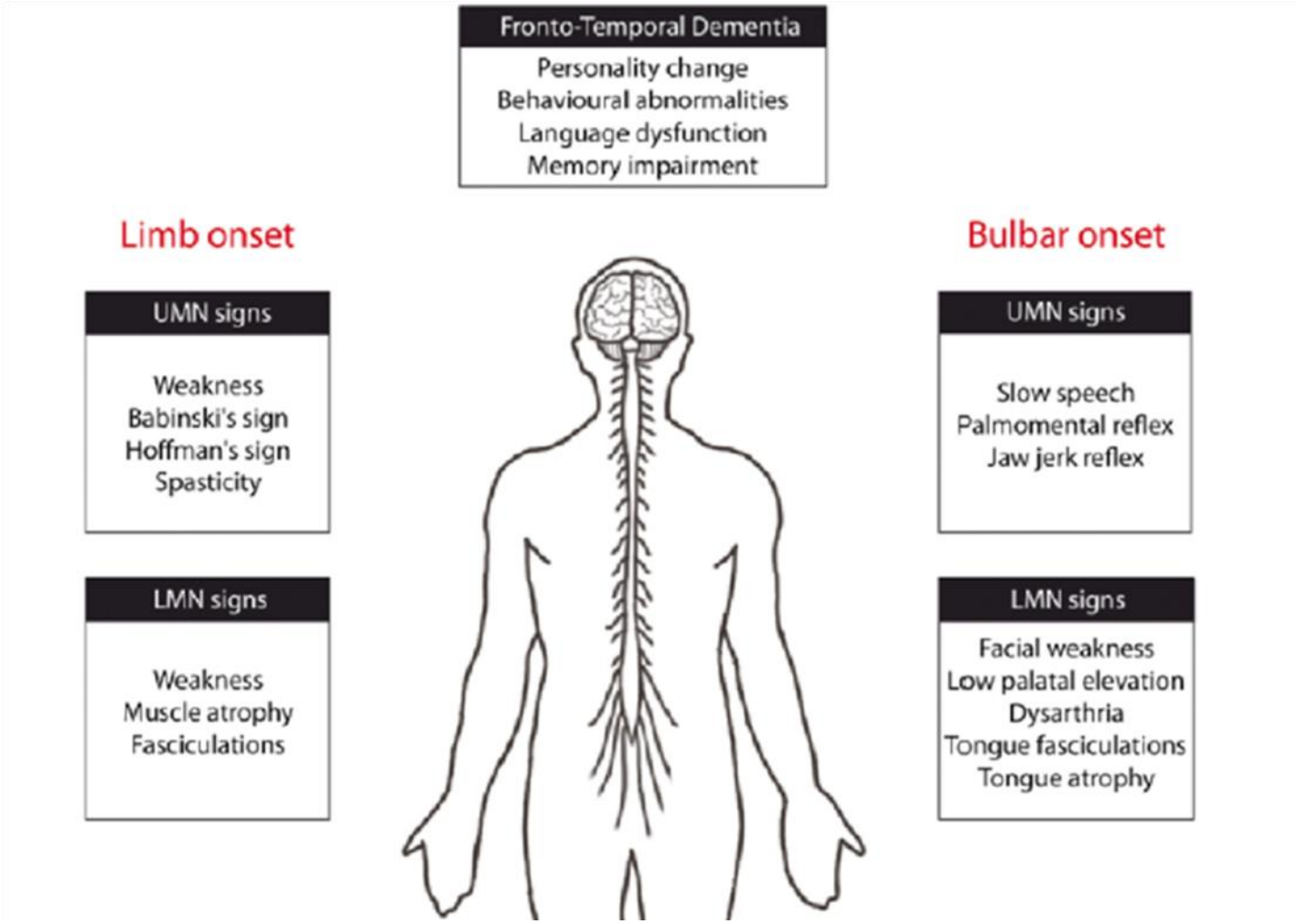

Figure 1.1 Signs Associated with Site of ALS Onset. Upper motor neuron (UMN) and lower motor neuron (LMN) signs based on site of onset. In some cases of cognitive decline, signs of frontotemporal dementia occur.[21]

The cause of ALS is unknown, however, there are several theories as to why neuronal degeneration occurs, such as genetic and environmental theories. One way to organize ALS is into sporadic and familial ALS (fALS). Sporadic ALS is the most common form of ALS and affects 85-90% of people with the disease. fALS is caused by a genetic mutation, and it accounts for 10 to 15% of cases, with most cases being autosomal dominant. Rarely, people with fALS develop symptoms in childhood or their teenage years. Generally, ALS occurs in greater percentages as both men and women grow older. There are many genes associated with ALS, including C9ORF72, SOD1, TARDB, UBQLN2, NEK1, KIF5A, TDP43P, FUS, ANG, OPTN, SETX, and SQSTM1 genes. C9ORF72 and SOD1 are the two most common mutations. Thirty to 40 percent of familial ALS cases are caused by mutations in the C9orf72 gene in the United States and Europe.[23] Worldwide, SOD1 gene mutations cause 15 to 20 percent of familial ALS cases, and TARDBP and FUS gene mutations each account for about 5 percent of cases.[3] The other genes account for a small proportion of cases in familial ALS. It is estimated that about 60 percent of individuals with familial ALS have an identified genetic mutation.[24] These genetic mutations can differ by ethnicities. For instance, the C9ORF72 gene associated ALS cases are more common in Europeans, while the SOD1 gene associated ALS cases are more common in Asians.[2] In 1993, it was discovered that some familial ALS cases are associated mutations in the SOD1 gene, making it the first ALS gene discovered. The SOD1 gene provides instructions for making an enzyme called superoxide dismutase, which is abundant in cells throughout the body. This enzyme attaches to molecules of copper and zinc to break down toxic, charged oxygen molecules called superoxide radicals.[3] Although it is still not clear how mutations in the SOD1 gene

lead to motor neuron degeneration, there is increasing evidence that the gene playing a role in producing mutant SOD1 protein can become toxic.[3] In 2011, it was discovered that a hexanucleotide repeat in C9ORF72 was found in a significant subset of individuals with ALS and in patients with FTD. The C9ORF72 gene is responsible for providing instructions to make a C9ORF72 protein, which is found abundantly in nerve cells in the outer layers of the brain and in motor neurons. C9ORF72 is in an area of the nerve cell that is involved in signaling, and repeats in this gene cause the most common form of fALS. There are many theories regarding ALS pathogenesis. The glutamate excitotoxicity theory states that in ALS toxic concentrations of glutamate accumulate at the synapse due to abnormal glutamate metabolism and the inability of astrocytes to uptake the excess glutamate. This glutamate excitotoxicity leads to neuronal death. Currently, several areas of research postulate a dysfunction of the immune system that may lead to ALS as well, and several other theories regarding ALS pathogenesis exist.

Table 1.1 Genes associated with ALS

Gene	Protein	Year of discovery
SOD1	Superoxide dismutase-1	1993
SETX	Senataxin	1994
ANG	Angiogenium	2004
TARDBP	TAR-DNA-binding protein 43 kDa	2006
TDP43	TAR DNA binding protein 43	2008
FUS	Fused in sarcoma	2009
OPTN	Optineurin	2010
UBQLN2	Ubiquilin-2	2011
SQSTMI	Sequestosome 1	2011
C9ORF72	Chromosome 9 open reading frame72	2011
NEK1	NIMA Related Kinase 1	2016
KIF5A	kinesin family member 5A	2018

In the last two decades, genome sequencing of ALS patients has identified mutations across a wide range of genes.

There is no one test that can diagnose ALS. Physicians observe the signs and symptoms outlined in the El Escorial criteria to diagnose ALS. The El Escorial criteria were established about 20 years ago, and they are mainly used for research purposes. The diagnosis of ALS has two main aspects. The first part requires the presence of upper motor and lower motor neuron degradation. In addition, there must be evidence of ALS spreading in the body. The second part of the diagnosis relies on the ability to exclude other diseases. The diagnosis of ALS requires the absence of signs of both upper and lower motor neurons degradation that were caused by another disease. ALS can be a challenging disease to diagnose, as it is mainly based on history and examination. It is through a clinical examination and series of diagnostic tests, often ruling out other diseases that mimic ALS, that a diagnosis can be made.

Physicians also use various test such as electromyography (EMG), magnetic resonance imaging (MRI), lumbar puncture and spinal fluid analyses, and blood and urine tests to diagnosis patients with ALS. EMG is used to determine the health of the muscle and the motor neurons that control the muscle. Muscle movement is controlled by electrical signals from the neurons and the EMG records the electrical activity from the muscle when contracting and at rest. During EMG, those with ALS may show abnormal spontaneous activity. MRI can also be used to produce imaging of the brain and spinal cord to help rule out other diseases. A spinal tap is the removal a sample of cerebrospinal fluid (CSF). The CSF can be analyzed for the presence of an infection or abnormal cells. It can be used by measuring the pressure of the fluid in the brain and spinal canal. Blood and urine tests are used to exclude disease mimics.

There is no cure for ALS, though the U.S. Food and Drug Administration (FDA) has approved the drugs riluzole (Rilutek) and edaravone (Radicava) to slow disease progression. Riluzole can increase life expectancy up to 6 months. Similarly, edaravone is used to decrease oxidative stress that can lead to the death of motor neurons, and slows the disease by months.

FTD Overview

FTD covers a wide range of different conditions in which cells in the frontal and temporal lobes of the brain are damaged. The changes in behavior caused by FTD can be challenging for the person with dementia and those around them. Patients with FTD typically experience extreme changes of behavior such as loss of empathy and other interpersonal skills. It is helpful to remember that such behavior is a result of the condition and the person with FTD may not realize the behavior is unusual or inappropriate. To counteract this, it is suggested that caregivers engage with meaningful activities to prevent these behaviors. Speech and language therapists may suggest other ways to communicate better with people who experience FTD, such as non-verbal ways to communicate or shorter sentences. FTD represents an estimated 10%-20% of all dementia cases. It is recognized as one of the most common presenile dementias (meaning it occurs in a younger population). The prevalence worldwide is uncertain, with estimates of FTD amongst people ages 45 to 64 between 15 - 22 per 100,000 people.[7]

It is now clear that ALS and some forms of FTD are related, and about 25% of individuals with ALS will show symptoms of FTD. The overlap between ALS and FTD occurs at clinical, genetic, and pathological levels. Cognitive dysfunction in FTD results in the loss of intellectual functions such as reasoning, memory, and other neurological

abilities that are severe enough to interfere with daily functioning. Cognitive dysfunction is seen in 20–50% of ALS cases. Approximately 3–5% of these cases develop dementia that is usually of frontotemporal type. Cognitive impairment in ALS can directly affect language (written and oral expression), as well as comprehension. Individuals demonstrate slowed word-finding, even in the absence of bulbar symptoms of dysphagia and dysarthria. Spelling can also be disturbed, although studies of spelling impairment in ALS have been confounded by the influence of educational quality and quantity.[8] Individuals will not be able to recognize words or use them in sentences. Cognitive and memory impairment has been observed in individuals with ALS. Studies show individuals who are older, less educated, and with bulbar symptoms of ALS are more likely to have cognitive and/or behavioral impairment.[8] These factors remain poorly understood, however, and are an important focus of ongoing research. Individuals with cognitive and/or behavioral impairment in ALS have been shown to have shorter survival times. It is unclear whether this relates to older age in the cognitively and/or behaviorally impaired, or a more diffuse disease process resulting in faster longitudinal progression of illness.[8]

A screening method for detecting cognitive and behavioral impairment in ALS is helpful in clinical settings. The ALS-Cognitive Behavioral Screen (CBS) is a brief assessment tool, which entails tasks and questions sensitive to frontal lobe dysfunction. The screen consists of a cognitive section with five domains specific to frontal lobe function, and a behavioral section composed of caregiver-directed questions intended to

detect changes since disease onset. The ALS-CBS takes approximately 5 minutes to complete. It consists of a 15 item ALS specific behavioral questionnaire filled out by the caregiver, and an 8-item cognitive assessment of the patient that includes verbal fluency. It has been validated in ALS. ALS-CBS screening is intended to identify patients in need of further assessment. The total score is calculated from 4 subtests in initiation and retrieval, concentration, attention, and tracking/monitoring. Using pre-specified normative cutoffs, patients can be divided into 3 categories based on their total score (maximum 20): normal, ALS-cognitive impairment or possible FTD-level impairment.[22] A diagnosis of FTD or other dementia should not be based solely on this screening, but Individuals with ALS-FTD typically score ≤10.

The ALS Functional Rating Scale (ALSFRS) is a validated, clinician-administered instrument for assessment in the domains of gross and fine motor function, bulbar symptoms and breathing ability in patients with ALS. The score reflects deterioration of function in the natural course of ALS but may have lower sensitivity in advanced disease stages.

ALS CBS
ALS Cognitive Behavioral Screen

Susan C. Woolley, Ph.D.

Patient Id: _____ **DOB/Age:** _____ **Gender:** _____
Onset Date: _____ **FVC:** _____ **Education:** _____
Onset Region: bulbar, arm, leg, trunk, respiratory (circle one)

☐ Mark if pt responses were written, attach sheet

HAND PAGE 2 TO CAREGIVER

Attention

a. Commands: *I am going to say some commands. Please listen carefully and then do what I say. (If patient is unable to indicate with finger, movement can be substituted with eyes, arm or other means).*
1. Point/indicate (with your finger) to the ceiling and then to your left.
2. Touch your shoulder, point to the floor, and then make a fist.

errors 0 1+
Score (circle) 1 0

b. Mental Addition/Language: *I am going to say some phrases. I want you to tell me the number of syllables in each phrase. For example, "the table" has 3 syllables. (Repetition of each phrase is allowed once).*
1. The weather is nice. (correct response: 5) answer _____
2. Tomorrow will be sunny. (correct response: 7) answer _____

errors 0 1+
Score (circle) 1 0
(score 0 if >20 seconds on either)

c. Eye Movements: *Saccades and Antisaccades.*
# of Correct Saccades out of 8: ____/8 Score: 8/8 =**1** points, ≤7/8 = **0** points
# of Correct Antisaccades out of 8: ____/8 Score: 8/8 =**2** points, 7/8 = **1** points, ≤ 6/8 = **0 points**

/5

Concentration

I am going to say some numbers. After I say them, I want you to say them to me backwards, or in reverse order. For example, if I say 3-6, you would say 6-3. (If written, do not allow pt to write forward span. Discontinue after failure on two consecutive trials).

		Correct	Incorrect			Correct	Incorrect
2-9	(9-2)	__	__	7-8-6-4	(4-6-8-7)	__	__
6-4	(4-6)	__	__	5-4-1-9	(9-1-4-5)	__	__
3-7-2	(2-7-3)	__	__	8-2-5-9-3	(3-9-5-2-8)	__	__
5-8-1	(1-8-5)	__	__	5-7-6-3-9	(9-3-6-7-5)	__	__

Maximum Span Correct: (Enter score)

/5

Tracking/Monitoring

a. Months: *Please say the months of the year backwards, starting with December. (circle omissions/mark repetitions & intrusions)*
Dec Nov Oct Sep Aug Jul Jun May Apr Mar Feb Jan

errors 0 1 2+
Score (circle) **2** **1** **0**

b. Alphabet: *Please say/write the alphabet for me. (mark uncorrected errors, omissions or intrusions)*
A B C D E F G H I J K L M N O P Q R S T U V W X Y Z

errors 0 1+
Score (circle) **1** **0**

c. Alternation Task: *I want you to alternate between numbers and letters, starting with 1-A, and then 2-B, 3-C, and so on. Please continue from there, alternating between number-letter, number- letter, in order, without skipping any until I tell you to stop. (Errors: Any mistake in sequencing, i.e., 7-H, or 8-9).*
4-D 5-E 6-F 7-G 8-H 9-I 10-J 11-K 12-L 13-M

errors 0 1 2
Score (circle) **2** **1** **0**

/5

Initiation and Retrieval

Say (write) as many words as you can starting with the letter F, as quickly as you can, in 1 minute. (Show pt Fluency Rules) You cannot say/write the names of people, places or numbers. Please do not say/write the same word with just a different ending, like truck, trucks. (S words can be substituted for F words). Errors: repetitions, rule violations.

1. _____	9. _____	17. _____
2. _____	10. _____	18. _____
3. _____	11. _____	19. _____
4. _____	12. _____	20. _____
5. _____	13. _____	
6. _____	14. _____	
7. _____	15. _____	
8. _____	16. _____	

correct words >12 12-8 <8 ≤4
Score (circle): **3** **2** **1** **0***

plus

errors 0 1 2+
Score (circle): **2** **1** **0**

*if ≤4 words, total verbal fluency score = **0** regardless of # of errors

/5

TOTAL SCORE

/20

ALS CBS
ALS Cognitive Behavioral Screen

Susan C. Woolley, Ph.D.

ALS Caregiver Behavioral Questionnaire

These questions pertain to possible changes that you have noticed since the onset of ALS symptoms. As best you can, consider changes that are unrelated to physical weakness. For example, question #1 asks about interest in activities. If the person can no longer play tennis but still seems interested in it (i.e. talks about it, watches it on television), then you would circle 3 for no change in level of interest.

If the person has always had the trait in question, please respond No Change, since there has been no change over time.

Compared to before ALS, does he/she:

	No Change	Small Change	Medium Change	Large Change
1. Have less interest in topics/events that used to be important to them?	3	2	1	0
2. Show little emotion, or seem less responsive emotionally?	3	2	1	0
3. Seem more agreeable or pleasant than in the past with fewer worries?	3	2	1	0
4. Fail to think things through before acting?	3	2	1	0
5. Seem more withdrawn from others but not sad?	3	2	1	0
6. Get confused or distracted more easily?	3	2	1	0
7. Have less ability to deal with frustration or stress?	3	2	1	0
8. Seem less concerned about the feelings or concerns of others than before?	3	2	1	0
9. Get angry or irritable more easily than before?	3	2	1	0
10. Seem more sarcastic or childlike than before?	3	2	1	0
11. Eat more or have a new preference for particular foods (i.e. sweets)?	3	2	1	0
12. Have more trouble changing opinions or adapting to new situations?	3	2	1	0
13. Show less judgment or more problems making good decisions (i.e. regarding safety, finances, etc)?	3	2	1	0
14. Have less awareness of obvious problems or changes, or deny them?	3	2	1	0
15. Have new problems with language, such as saying the wrong word more often, making up new words, or declines in spelling ability?	3	2	1	0

TOTAL SCORE: _____/45

The following questions relate to current symptoms, not changes over time:

Do you think your loved one:	**YES**	**NO**
• Seems depressed on most days?	[ ]	[ ]
• Seems anxious on most days?	[ ]	[ ]
• Seems extremely fatigued on most days?	[ ]	[ ]
• Suffers from unexpected crying or laughing spells?	[ ]	[ ]

Figure 1.2 The ALS-CBS™, yielding a total cognitive score ranging from 0 to 20 (ALS CBS-Cog), is generated from 4 subtests: initiation and retrieval, concentration, attention, and tracking-monitoring. [14]

The ALS Functional Rating Scale

1. Speech
4 Normal speech processes.
3 Detectable speech disturbance.
2 Intelligible with repeating.
1 Speech combined with nonvocal communication.
0 Loss of useful speech.

2. Salivation
4 Normal.
3 Slight but definite excess of saliva in mouth; may have nighttime drooling.
2 Moderately excessive saliva; may have minimal drooling.
1 Marked excess of saliva with some drooling.
0 Marked drooling; requires constant tissue or handkerchief.

3. Swallowing
4 Normal eating habits.
3 Early eating problems—occasional choking.
2 Dietary consistency changes.
1 Needs supplemental tube feeding.
0 NPO (exclusively parenteral or enteral feeding).

4. Handwriting
4 Normal.
3 Slow or sloppy: all words are legible.
2 Not all words are legible.
1 Able to grip pen but unable to write.
0 Unable to grip pen.

5a. Cutting food and handling utensils (no gastrostomy)
4 Normal.
3 Somewhat slow and clumsy, but no help needed.
2 Can cut most foods, although clumsy and slow; some help needed.
1 Food must be cut by someone, but can still feed slowly.
0 Needs to be fed.

5b. Cutting food and handling utensils (patients with gastrostomy)
4 Normal.
3 Clumsy but able to perform all manipulations independently.
2 Some help needed with closures and fasteners.
1 Provides minimal assistance to caregiver.
0 Unable to perform any aspect of task.

6. Dressing and hygiene.
4 Normal function.
3 Independent and complete self-care with effort or decreased efficiency.
2 Intermittent assistance or substitute methods.
1 Needs attendant for self-care.
0 Total dependence.

7. Turning in bed and adjusting bed clothes
4 Normal.
3 Somewhat slow and clumsy, but no help needed.
2 Can turn alone or adjust sheets, but with great difficulty.
1 Can initiate, but not turn or adjust sheets alone.
0 Helpless.

8. Walking
4 Normal.
3 Early ambulation difficulties.
2 Walks with assistance.
1 Nonambulatory functional movement only.
0 No purposeful leg movement.

9. Climbing stairs
4 Normal.
3 Slow.
2 Mild unsteadiness or fatigue.
1 Needs assistance.
0 Cannot do.

10. Breathing
4 Normal.
3 Shortness of breath with minimal exertion (e.g. walking, talking).
2 Shortness of breath at rest.
1 Intermittent (e.g. nocturnal) ventilatory assistance.
0 Ventilator dependent.

Figure 1.3 ALSFRS variables and associated grading scale.[13]

Health Disparities Overview

Health disparities are differences in the burden of disease, injury, violence, or opportunities to achieve optimal health that are experienced by socially disadvantaged populations. These populations can be defined by factors such as race or ethnicity, gender, education or income, disability, geographic location (e.g., rural or urban), or sexual orientation. Health disparities are directly related to the historical and current unequal distribution of social, political, economic, and environmental resources.[5] Disparities in "health" and "health care" are related. Health care disparities refers to differences between populations in health insurance coverage, access to and use of care, and quality of care. Health and health care disparities often refer to differences that cannot be explained by variations in health needs, patient preferences, or treatment recommendations.

Today, many populations in America face disparities in access to and utilization of health care. People of color generally face more barriers and utilize less care than Caucasians. Additionally, low-income individuals and households also experience more barriers to care and receive poorer quality care than high-income individuals. Disparities in access and utilization also occur across other dimensions.[9] For instance**,** people that live in rural areas have limited access to private coverage compared to those in urban areas, causing people to face significant barriers to accessing care. Additionally, some groups are at higher risk for health conditions and experience poorer health outcomes compared to other groups. Little is known about how ALS affects people of different racial and ethnic backgrounds in the United States. Studies show that ALS rates are higher among non-Hispanic Caucasians in Western countries compared with those of

African, Asian, and Hispanic descent (minorities).[10] Nonetheless, this is difficult to gauge due to the limited number of minority cases identified in the epidemiologic studies. It is likely that the influence of genetic risk factors for the disease may vary by ethnicity. "It is now widely accepted that the incidence of ALS is uniform across Caucasian populations, but whether racial variation across other ethnicities exists remains unknown. ALS occurs less frequently in those that are African-American, Asian, and Hispanic compared with Caucasians and non-Hispanics in the U.S. It is unclear if this finding is due to methodological issues or can be attributed to behavioral factors, socioeconomic status, environmental exposures or genetic factors.[12]" Based on previous studies, age at diagnosis was slightly lower among African-American cases than the other racial groups.[11] Differences between races may be due in part to Caucasians traditionally having better access to healthcare and receipt of health services, thereby increasing their likelihood of being diagnosed versus their non-Caucasian counterparts. Additionally, African Americans have been found to have more heterozygosity in single nucleotide polymorphisms and fewer damaging alleles compared with US Caucasians, due to the genetic bottleneck experienced among European ancestral populations around the time of migration out of Africa, which may be protective against ALS.[5]

ALS, FTD, and Race

With FTD occurring in ALS, it is not clear if it differs by race in the United States. However, ALS and FTD have been analyzed independently in other countries. The prevalence rates of ALS were highest in Uruguay, New Zealand, and the United States, and lowest in Serbia, China and Taiwan.[19] While this is the case, the most frequent finding is that African Americans and Hispanics have higher prevalence and incidence of dementia and Alzheimer (AD) than Caucasians.[20] There is limited information about ALS-FTD in African-Americans, which can be due to a multitude of reasons such as African Americans are underrepresented in academic studies, and Caucasians are more susceptible to the ALS. Understanding and learning more about ALS-FTD in African Americans is vital because knowledge could lead to a better treatment and/or diagnosis.[9]

Specific Aims

The primary goal of this study was to determine the prevalence of cognitive involvement in African-American patients with ALS and compare it to Caucasian patients with ALS. Differences in these groups may provide insight regarding who is at risk for ALS-FTD, and it may also impact how physicians recognize and treat behavioral issues in those with ALS. In order to address this, Specific Aim 1 will be to determine the prevalence of cognitive involvement in African American and Caucasian individuals with ALS, based on CBS score at time of diagnosis. Specific Aim 2 will be to determine the one-year incidence of FTD in ALS in these different ethnic groups.

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CHAPTER II

THE PREVALENCE AND ONE YEAR INCIDENCE OF FRONTOTEMPORAL DEMENTIA IN INDIVIDUALS WITH AMYOTROPHIC LATERAL SCLEROSIS BASED ON RACE

THE PREVALENCE AND ONE YEAR INCIDENCE OF FRONTOTEMPORAL DEMENTIA IN INDIVIDUALS WITH AMYOTROPHIC LATERAL SCLEROSIS BASED ON RACE

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Abstract

Introduction: Amyotrophic lateral sclerosis (ALS) is a progressive motor degenerative disease. 20% of individuals with ALS may develop frontotemporal dementia (FTD). However, the prevalence of FTD has not been specifically studied in African-American individuals with ALS. This study is designed to assess the prevalence and one-year incidence of cognitive involvement in African-American and Caucasian individuals with ALS.

Methods: Individuals with ALS were matched in a 3:1 ratio (3 Caucasian individuals for each African-American) based on gender, age at diagnosis, and site of onset (bulbar, upper limb, or lower limb). The following demographic variables were collected: age, BMI, site of onset, cognitive behavioral scores (CBS scores), time to diagnosis and duration of symptoms to time of cognition assessment. Baseline severity variables such as the amyotrophic lateral sclerosis functional rating scale (ALSFRS) and forced vital capacity (FVC) of percent-predicted at time of diagnosis were also collected.

Results: Patient demographics showed no significant differences between African-Americans and Caucasians. African-Americans and Caucasians did not show a difference in baseline CBS scores (p-value: 0.2183). However, African-Americans had a lower CBS score at one-year compared to Caucasians (p-value: 0.0083). In addition, African-Americans also had a greater change in CBS scores at one-year compared to Caucasians (p-value: 0.0473). After accounting for age, BMI and FVC, CBS scores at baseline were bordering significance (p-value: 0.0744) with African Americans scoring lower. After

accounting for gender, site of onset, and race, the differences in CBS scores at one-year were significant, with African Americans scoring lower (p-value: 0.0487).

Discussion: There was no significant differences in the patient characteristics between African-Americans and Caucasians. The baseline CBS scores did not differ between the two groups. African Americans had lower CBS scores after one-year, even after controlling for multiple variables. After accounting for gender, site of onset, and race, age, BMI and FVC, time to diagnosis (TTD) and duration of symptoms to time of cognition assessment, race may play a role in CBS scores.

Key Words: Amyotrophic lateral sclerosis, amyotrophic lateral sclerosis functional rating scale, cognitive behavior scores, cognitive decline, frontotemporal dementia, incidence, prevalence, time to diagnosis

Introduction

Amyotrophic lateral sclerosis (ALS) is a severe neurodegenerative disease that causes weakness and muscle atrophy. Over time, the physical effects, along with cognitive and behavior symptoms worsen. Twenty percent of ALS patients experience severe behavioral changes, including cognitive decline and emotional liability.[1] Monitoring cognitive decline can be performed by assessing CBS scores.

Health disparities refers to particular groups of people being at higher risk of being uninsured, having more limited access to care, experiencing poorer quality of care, and ultimately experiencing worse health than others.[3] Disparities can exist across many dimensions, such as gender, sexual orientation, age, disability status, socioeconomic status, and geographic location. Research shows that health disparities still exist in the United States and are increasing in severity. However, little is known about how ALS affects people of different racial and ethnic background.[2]

Understanding the racial and ethnic variations in ALS-FTD may help in the understanding of disease progression, possible treatments, and ways to limit health disparity. Most studies have focused on comparing rates of Alzheimer disease among African-Americans and Hispanics to rates among Caucasians. These studies found higher rates of cognitive impairment, dementia, and Alzheimer disease among ethnic minorities than among Caucasians.[11] Studies also found differences in cognitive scores between ALS-FTD and ALS patients without FTD (ALS-normal), with those withALS-FTD having lower scores than ALS patients without dementia.[7] We hypothesized that African-American individuals with ALS will show lower CBS scores at baseline and at one-year,

and they will show an overall decrease in CBS scores over one year. Research has shown that although Caucasians are more susceptible to the disease, African-Americans with ALS have more severe cases and possibly faster progression of the disease, which is why we hypothesize they will have lower CBS scores.[4] This study will help assess the relationship between race and cognitive decline in ALS patients.

Materials and Methods

IRB Approval and Ethics

This study was approved by the Institutional Review Board at Wake Forest University School of Medicine (#IRB00043923). The inclusion criteria were as follows: male and female patient charts from 2012-2017 with the clinical diagnosis of ALS according to EL Escorial criteria, African-American or Caucasian ethnic background, and over the age of 21. Exclusion criteria include patients under the age of 21. Patients with ALS variants with primary lateral sclerosis (PLS) and primary muscular atrophy (PMA) were also excluded. Additionally, patients of other racial ethnic backgrounds such as Asians and Hispanics were also excluded.

Patient Sample

Patients at the Wake Forest Baptist Medical ALS Center of Excellence are diagnosed with ALS according to the El Escorial Criteria by physicians. 36 African-American patients were matched in an almost 3:1 ratio with 102 Caucasian patients based on gender, age at diagnosis, and site of onset (bulbar, upper limb, or lower limb) for a balanced dataset. CBS scores were recorded at baseline and 1 year later. Time to diagnosis, duration of symptoms to time of cognition assessment, ALSFRS and FVC were also collected.

Statistical Analyses

Descriptive statistics were calculated for all variables using means and standard deviations (STD). Multiple linear regression was conducted to analyze CBS scores and the change in CBS scores by race. Additionally, we measured the association between race and cognitive decline. A Kaplan-Meier Curve was used to measure time to diagnosis. Calculation of ALS-FTD incidence and prevalence was also assessed, and 95% confidence intervals were calculated.

Results

Table 2.1 Patient Demographics

Characteristics	*Overall (n=138)*	*African-Americans (n=36)*	*Caucasians (n=102)*	*P-value**
Age	*63.13 ± 9.72 (62.00)*	*62.47 ± 10.47 (60.00)*	*63.37 ± 9.50 (62.00)*	*0.6992*
Gender % Female	*49.28*	*52.8*	*48.0*	*0.6279*
ALSFRS	*38.64 ± 5.8 (40.00)*	*38.47 ± 6.33 (41.00)*	*38.70 ± 5.66 (39.50)*	*0.8691*
FVC	*76.69 ± 22.7 (76.50)*	*77.92 ± 21.62 (77.00)*	*76.25 ± 23.09 (76.00)*	*0.6584*
Time to diagnosis (Days)	*392.1 ± 290.0 (278.00)*	*407.63 ± 341.77 (370.00)*	*386.60 ± 271.10 (330.00)*	***0.0190*
Duration of symptoms to time of cognition (Days)	*768.42 ± 734.32 (608.50)*	*811.94 ± 1122.28 (498.00)*	*753.06 ± 542.26 (649.50)*	***0.1626*
Site of onset % Bulbar	*7.25*	*5.55*	*7.84*	
Upper Extremity	*53.62*	*55.56*	*52.94*	*0.6895*
Lower Extremity	*39.13*	*38.89*	*39.22*	
Body mass index (BMI)	*28.36 ± 5.66 (27.46)*	*29.3 ± 5.9 (28.00)*	*28.03 ± 5.6 (27.29)*	*0.2509*

*P-value for comparing characteristics across race groups based on two-sample t test (continuous variables) and chi-squared test (dichotomous variables)

**P-value calculated by a nonparametric analysis (Wilcoxon test) due to the originally variables being skewed

As indicated in Table 2.1, there is no difference between time to diagnosis between Caucasians (386.60 days) and African-Americans (407.63 days). This was not statistically significant (p-value: 0.7097). There was no significant difference between duration of symptoms to time of cognition testing between Caucasians (753.06 days) and African-Americans (811.94 days) (p-value: 0.6807). In our study, the percentage of African American females represented was higher than Caucasian females (52.8% and 48.0%, respectfully). This finding was not shown to be statically significant (p-value: 0.6279).

Table 2.2 Cognitive Testing of African-Americans and Caucasians with ALS

Characteristics	Overall	African-Americans (n=36)	Caucasian (n=102)	P-value
Baseline CBS Score	15.99 ± 3.41 (17.00)	15.39 ± 2.77 (16.00)	16.15 ± 3.59 (17.00)	0.2183
CBS score at Year-1	15.63 ± 3.60 (16.00)	14.28 ± 3.11 (14.50)	16.22 ± 3.68 (17.00)	0.0083
Change in CBS score over 1 year	-0.36 ± 2.64 (-1.00)	-1.11 ± 2.41 (-1.50)	0.10 ± 2.66 (0.00)	0.0473

*P value for comparing characteristics across race groups based on two-sample t test (continuous variables) and chi-squared test (dichotomous variables)

Table 2.2, indicates the difference between CBS scores in African-American individuals (14.28 mean ± 3.11 STD) at one-year were slightly lower than Caucasians individuals (16.22 mean ± 3.68 STD) also measured at one-year. The p-value: shows statistical significance (p-value: 0.0083). We found that there was a significant difference in the change in CBS scores between African-Americans (-1.11 mean ± 2.41 STD) and Caucasians (0.10 mean ± 2.66 STD) over 1 year (p-value: 0.0473).

Table 2.3 Multiple Linear Regression Controlling Variables for CBS Scores

Variables	African-American (n=36)	Caucasian (n=102)	P-value*	P-value**	P-value***
CBS scores at baseline	15.39 ± 2.77 (16.00)	16.15 ± 3.59 (17.00)	0.5322	0.0744	0.1335
CBS scores at one-year	14.28 ± 3.11 (14.50)	16.22 ± 3.68 (17.00)	0.0487	0.0005	0.0022
Change in CBS scores	-1.11 ± 2.41 (1.50)	0.10 ± 2.66 (0.00)	0.1898	0.2831	0.0561

*P-value based on multilinear regression adjusting for gender, site of onset, and race.

**P-value based on multilinear regression adjusting for gender, site of onset, race, age, BMI and FVC.

***P-value based on multilinear regression adjusting for gender, site of onset, race, age, BMI, FVC, TTD and time to cognition assessment.

Overall, both African-Americans and Caucasians individuals had similar CBS scores at baseline. After adjusting for gender, site of onset and race had no statistical significance (p-value: 0.5322). After adjusting for gender, site of onset, race, age, BMI and FVC, CBS scores at baseline showed no significance (p-value: 0.0744). CBS scores remained non-significant (p-value: 0.1335) after adjusting for gender, site of onset, race, age, BMI, FVC, TTD and duration of symptoms to time of cognition assessment.

Different from CBS scores at baseline, CBS scores at one-year showed statistical significance after adjusting for gender, site of onset and race (p-value: 0.0487). These CBS scores remained significant (p-value: 0.0022) after adjusting for gender, site of onset, race, age, BMI, FVC, TTD and duration of symptoms to time of cognition. CBS scores at one-year incidence showed a slight difference in the means (14.28 mean ± 3.11 STD, 16.22 mean ± 3.68 STD, respectively) between African-American and Caucasian individuals. Although there was a difference in the change in CBS scores between African-American and Caucasian means, there was no statistical significance (p-value: 0.1898) after adjusting for gender, site of onset and race. Similarly, after adjusting for gender, site of onset, race, age, BMI and FVC we did not observe statistical significance (p-value: 0.2831). Finally, after controlling for gender, site of onset, race, age, BMI, FVC, TTD and duration of symptoms to time of cognition testing, the change in CBS scores had no statistical significance (p-value: 0.0561).

Discussion

The objective of this study was to analyze cognitive impairment at baseline and one-year incidence in African-Americans and Caucasians individuals with ALS. Although none of the patient characteristic variables were considered statistically significant, African-Americans may have a longer TTD and duration of symptoms to time of cognition assessment when compared to Caucasians. This trend is understandable when considering the slight decline in the CBS scores in African-Americans in comparison to Caucasians. Age, percent site of onset, ALSFRS and FVC are similar between African-Americans and Caucasians. Analyzing CBS scores at one-year showed results were congruent with findings in other studies, which found that African-Americans with ALS have a faster disease progression than Caucasians. CBS score was relatively the same for Caucasians at one-year, as it was at baseline. After adjusting for predictor variables there was a statistical significance for CBS at one-year (p-value: 0.0487).

Our hypothesis was African-Americans will have a lower CBS scores at baseline and at one year. Although not statically significant, African-Americans did have a lower CBS score at baseline. There was a greater difference between African-Americans and Caucasians groups in regards to cognitive impairment at one-year. African-Americans having a lower CBS score at baseline could be to the fact that African-Americans have a longer time to diagnosis than Caucasians. This suggest that the CBS scores are lower because the African-Americans are further in the disease at the time of diagnosis and have already experience cognitive impairment. African-Americans having a greater

change in CBS score suggest that this group will experience more cognitive decline throughout the disease compared to Caucasians. This can also suggest that African-Americans have more severe disease severity in comparison to Caucasians and a greater chance that African-Americans could be diagnosed with ALS-FTD. This is aligned with previous studies.

One limitation of this study is a small sample size of African Americans. Future studies may include a larger sample size of African Americans to determine if there are statistically significant differences exist in variables bordering significance. Also including more African Americans could also give more insight of the onset of the disease for African-Americans. Another limitation could be selection bias. Some African-Americans and Caucasian patients were excluded from this study because they did not fit the inclusion criteria. These patients could not be matched in the 3:1 ratio based on age, site of onset and gender.

Future studies also may include using the Amyotrophic Lateral Sclerosis-Frontotemporal Dementia Questionnaire (ALS-FTD-Q) instead of the ALS-CBS. ALS-FTD-Q is used for the detection of behavioral variant FTD and mild behavioral disturbances in ALS [5]. Conversely, ALS-FTD-Q has more questions that can better detect behavioral disturbances than the CBS could. This could possibly be a significant tool when looking at ALS-FTD specifically.

Abbreviations

ALS = Amyotrophic Lateral Sclerosis

ALS-FTD-Q = Amyotrophic Lateral Sclerosis- Frontotemporal Dementia Questionnaire

FTD = Frontotemporal Dementia

BMI = Body mass index

CBS = Cognitive behavior screen

FVC = Forced vital capacity

TTD = Time to diagnosis

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CHAPTER III

DISCUSSION

The goal of this study was to assess differences in cognitive impairment based on CBS scores at baseline and at one-year by race. Our hypotheses were: (1) African-Americans will have a lower CBS score at time of diagnosis when compared to Caucasians, and (2) African-Americans will have lower CBS scores a year later when compared to Caucasians. It is important to look at ALS-FTD to determine possible differences in disease severity and cognitive impairment between races. Since information about ALS-FTD is limited in regards to African-Americans, there becomes a need in understanding the knowledge of ALS and FTD. This information will shed light on the two disorders and will help more effective diagnostic and treatment options.

We decided to further investigate the medians of these variables knowing the median value truly represents the middle of the data set. The median is less affected by outliers and skewed data and therefore may be more of a fair representation of the data. Overall, there was no significant difference in patient demographics between African-American and Caucasian groups. The mean TTD for African-Americans (407.63 days) when compared to the Caucasian group (386.59 days) was not statistically different. The medians for TTD are 370.00 days and 330.00 days, respectively (African-Americans &

Caucasians). The mean and median were somewhat divergent, therefore, a Wilcoxon nonparametric analysis test was used to account for the original variable was skewed, which showed s significant difference. Multilinear regression analysis is sensitive to outliers. Therefore, a larger sample size of African-Americans could assist with the linear regression assumptions.

CBS at baseline scores

In regards to CBS scores, there was no significant difference in the CBS baseline score between African-Americans and Caucasians. The median was 17.00 for Caucasians and 16.00 for African-Americans. The mean between the two races are 16.15 and 15.39 respectively.

CBS scores at one-year

In regards to CBS scores, there is a significant difference in the CBS score at one-year. Caucasians CBS score at one year maintained. However African-Americans showed a decline in the CBS score. The median score for Caucasians and African-Americans are 17.00 and 14.50 respectfully. The means for CBS scores at one-year are 16.10 and 14.27. This suggests that African-Americans experience more of a cognitive impairment in comparison to Caucasians over 1 year. The reasoning for this is ultimately unknown.

Time to Diagnosis Analysis

Figure 3.1 Kaplan-Meier Curve detailing Time to Diagnosis between African-Americans and Caucasians with ALS.

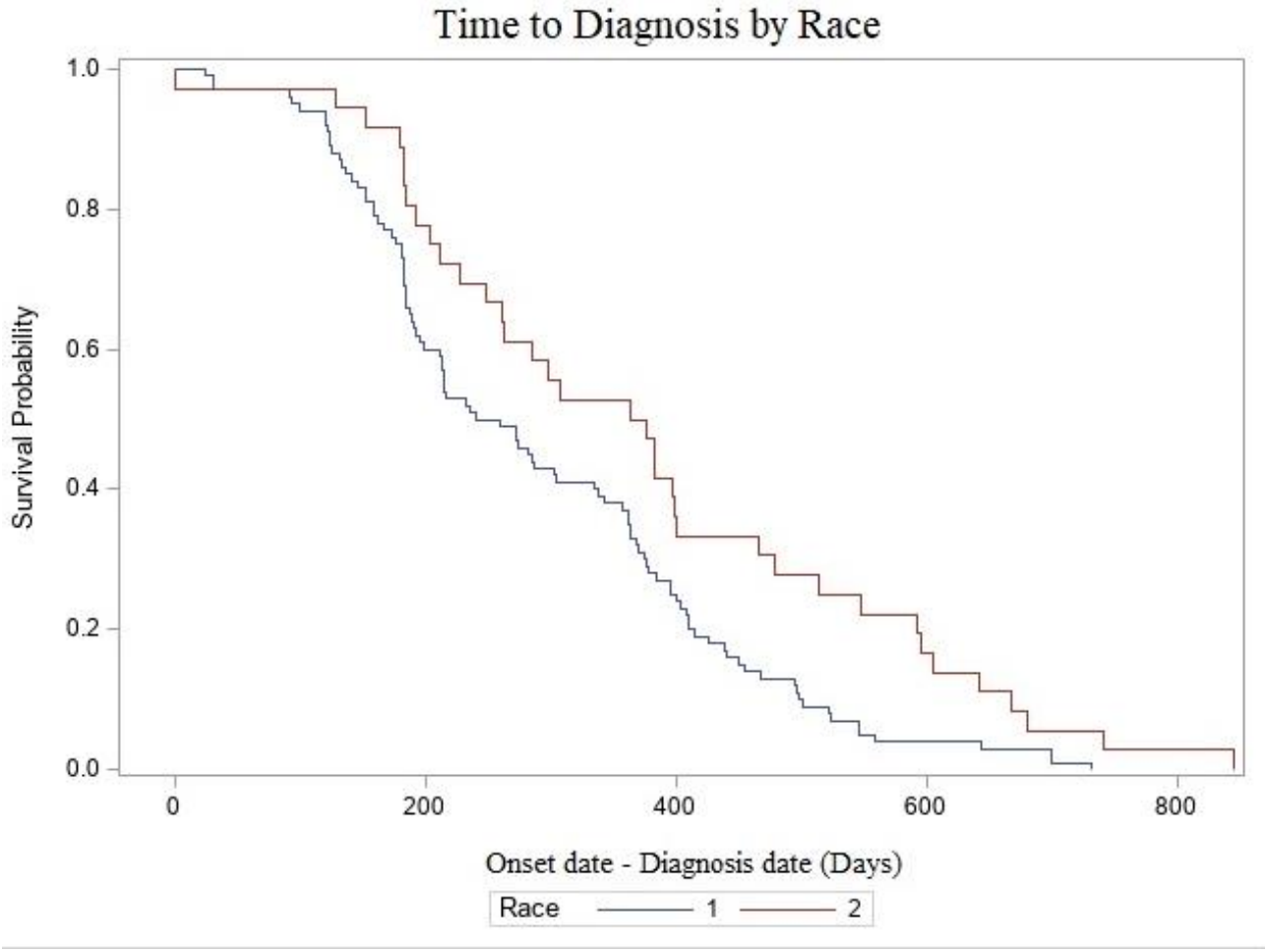

Figure 3.1 Displays the TTD from the first onset of symptoms to the diagnosis of ALS. Race 1 represents Caucasians and Race 2 represents African Americans. TTD between African-Americans and Caucasians are very similar and have no statistical significance.

Figure 3.1 Kaplan-Meier Curve Time to Diagnosis by Race

Figure 3.1 indicates African-Americans seem to have a longer TTD in comparison to Caucasians. The average TTD is 407.63 days for African-Americans and 386.60 days for Caucasians (log rank test p-value: 0.0100) (Wilcoxon test p-value: 0.0237). There were no censored patients that contributed information to the Kaplan-Meier Curve. Based on previous studies, the average TTD is about 9 to 12 months for someone to be diagnosed with ALS, from the time they first began to notice symptoms. However, this is not always the case. Some cases of ALS have slow progression and the symptoms are mild.

Prevalence & Incidence of ALS-FTD

ALS-CBS is validated to detect cognitive and behavioral change in patients with ALS. Screening tools such as ALS-CBS have been developed to detect such changes. According to previous studies, the ALS-CBS is scored out of 20 and a score of ≤10 is indicative of probable FTD. A score of ≤16 suggests cognitive impairment (ALSci).[12] ALS patients who are cognitively normal at baseline are more likely to remain cognitively unchanged over time.[13] This is important to analyze because ALS-FTD patients have shorter survival. Also, patients who present with any degree of executive dysfunction at the time of diagnosis are more likely to exhibit faster cognitive and motor progression.[4] Based on previous studies we wanted to know if African-Americans with possible ALS-FTD are more susceptible to this disease in comparison to Caucasians.

Table 3.1. Possible ALS-FTD based in CBS scores at baseline.

Demographic Groups	Number of cases of Possible ALS-FTD (CBS Score ≤ 10)	Total Number in the Population	Possible Prevalence of ALS-FTD (per 100)	95% Confidence Intervals (Lower, Upper)
African-Americans	3	36	8.33	[5.07, 11.60]
Caucasians	8	102	7.84	[5.59 , 8.41]

Table 3.1 indicates the possibility of FTD among the patients with ALS at baseline. A score of 10 and below is the cut off for FTD [12]. 3 African-Americans and 8 Caucasians had a CBS score of 10 and below. African-Americans had a prevalence of 8.33 cases per 100. Caucasians had a prevalence of 7.84 cases per 100.

Table 3.2 Number of new cases of possible ALS-FTD based on CBS scores at one-year.

Demographic Groups	Number of new cases of possible ALS-FTD (CBS Score ≤ 10)	Total Number in the Population	Possible Incidence of ALS-FTD (per 100)	95% Confidence Intervals (Lower, Upper)
African-Americans	1	33	3.03	[3.81, 16.2]
Caucasians	1	94	1.06	[1.82, 12.2]

Table 3.2 indicates the new cases of FTD among patients with ALS at one-year. (Not including the other cases used in table 2) A score of 10 and below is the cut off for FTD[12]. 1 African-American and 1 Caucasian scored below 10. Cumulative incidence of 3.03 cases per 100 African-Americans after one year. Cumulative incidence of 1.06 cases per 100 Caucasians after one year.

What this research could mean for the future of ALS in underrepresented populations?

Findings from this study could facilitate improvement for the future of ALS in underrepresented populations, specifically for African-Americans. Limiting health is important in reference to ALS to close the gap between races, age, sex, disability status, social economic status and education. Limiting disparities can lower the risk of ALS mortality and detect differences between races in cognitive decline between races.

Future Directions

Amyotrophic Lateral Sclerosis- Frontotemporal Dementia – Questionnaire (ALS-FTD-Q) is a new screening tool for behavioral disturbances in ALS. Although similar to CBS, ALS-FTD-Q has questions that can possibly better accommodate patients with ALS-FTD. Using a new questionnaire might better cater to African-Americans and Caucasians and help obtain an understanding of the difference in cognitive decline and detect any behavior differences between African-Americans and Caucasians or if there is truly a difference at all. This research can help determine if the treatments available are adequate between races. This research can help aid clinical diagnosis. Understanding the diagnosis for different races is important because the health of all American racial and ethnic groups has improved dramatically, particularly over the last few decades. ALS may affect different races differently. It's also important to study different races to understand the different genetic makeup and might experience different environmental factors culturally.

Conclusion

CBS scores at baseline did not differ between African-Americans and Caucasians. CBS scores differed at one year between African-Americans and Caucasians. African-Americans had a greater change in CBS scores at one-year compared to Caucasians. There are quite a few possibilities as to why the CBS scores differed at one year. First, African-Americans had a longer TTD, so they might be further along in the disease process. Second, based on recent studies, African-Americans have a higher prevalence and incidence rate of dementia and Alzheimer's disease than Caucasians. This suggests that African-Americans may be more susceptible to FTD in comparison to Caucasians. Third, it is possible the CBS culturally caters better to Caucasians than African-Americans, explaining the difference between the CBS scores at one year. Lastly, the type of ALS, caregivers, environmental factors and therapy (speech, physical) may have an impact on the difference between the CBS scores.

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Julia Yancey

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Education

Wake Forest University Graduate School of Arts & Sciences, Winston-Salem, NC, 2017-2019

Master of Science in Biomedical Sciences, Health Disparities in Neuroscience-Related Disorders

Thesis: The prevalence and one-year incidence of frontotemporal dementia in individuals with Amyotrophic Lateral Sclerosis based on race

Faculty Advisor: Michael S. Cartwright, MD, MS

GPA: 3.0

Bennett College, Greensboro, NC, 2013-2017

Bachelor of Science in Biology,

GPA: 3.273

Research Experience

Researcher, Department of Neurobiology and Anatomy, Wake Forest University, 2017 – Present

Research Advisor: Michael Cartwright, MS, MD

- Assisted in designing a research study that assessed the prevalence and incidence of frontotemporal dementia in individuals with ALS, based on race
- Analyzed and plotted the data collected after running human participants. Learned to how to write consent forms and protocols.

Research Assistant, Biology Department at Wake Forest University, Summer 2016

Research Advisor: Mathew Fuxjager, MS., PhD.

- Sexually dimorphic androgenic sensitivity in *Staurios parvus* muscles that underlie rapid gestural displays
- Overall male Saurios parvus frogs express more androgen receptor. Significant sex difference.
- Performed a phenol-chloroform extraction on muscles
- Used reverse transcriptase for cDNA synthesis

Research Assistant, Biology Department at Wake Forest University, Summer 2016

Research Advisor: Mathew Fuxjager, MS., PHD.

- Examined how androgenic sex hormones act through the skeletal muscular system to mediate elaborate courtship acrobatics in a tropical bird called the golden-collared manakin.
- Measured SH twitch speeds in response to 70-, 90-, and 110-Hz
- stimulation frequencies.
- Measured isometric contractile force and length change in response to electrical stimulation.

Volunteer Experience

Volunteer, Our Children's House, Greensboro NC, Spring 2014-Spring 2017

- Introduced children to STEM professions and jobs and getting them interested in these fields so they will consider taking science and math classes in high school and even go on to pursue a STEM career.

Volunteer, Cyprus Red Cross Society blood drive, Nicosia Cyprus, Fall 2015

- Assist with clerical duties including any operational support needed in the main administrative center.
- Monitor donors for post-donation reactions (such as paleness, sweating, nausea, and dizziness).
- Encourage donors to sign up for their next appointment.

Volunteer, Habitat for Humanity, Greensboro NC, Spring 2016

- Provided lunch for the construction volunteers on Saturdays. Brought the food to the job site and will often stay through lunch, helping to serve the meal and interacting with volunteers, staff, and homeowners.

Volunteer, The International Civil Rights Center & Museum Ignite for Change, Greensboro NC, Spring 2016

- Assisted with the assembly of the 2016 International Civil Rights Center & Museum Gala.

Volunteer, The Volunteer Center and United Way of Greater Greensboro, Greensboro NC Spring 2017

- Sorted food, packed food bags, sorted/inventory hygiene, sorted clothing and more that was distributed to local youth across Guilford County.

Volunteer, Alpha Kappa Alpha Community Day, Winston Salem NC Summer 2017

- Assisted with the assembly of the 2017 Alpha Kappa Alpha Community Day event
- Donated bookbags, school supplies and clothing for children.
- Assisted with face painting and haircuts for children

Volunteer, Triple P's Foundation, Inc, Greensboro NC Fall 2017 & Spring 2018

- Collected 1,000 prom dresses for the youth in the city of Greensboro
- Serve the youth by alleviating the financial burdens associated with prom
- Building self-confidence and exemplifying the importance of investing in the community.

Volunteer, Sisters of Service, Greensboro NC Fall 2018 & Spring 2019

- Interacting with children (ages 4-6), teaching them about math & science
- Reading to children in the community.

Volunteer, Martin Luther King, Jr. Service Project, Winston-Salem NC Spring 2019

- Lunch and clothing giveaway to the homeless

University Service

Honor's Hall Vice President, Resident Life, Aug 2013 – May 2014

- The duties of President include: calling and preside over regular and special meetings of the Residence Hall Association and RHA Executive Council.
- They oversee and supervise RHA Committees and their concurrent functions.

Tour Guide, Ambassadors in Admissions, Bennett College, 2014 – 2016

- Represented Bennett College by giving campus tours monthly and answering questions about academics, community service, and campus life

Resident Assistant, Hall Council, Aug 2014 – May 2015

- The Resident Assistant (RA) facilitates the social, academic, and personal adjustment of students to the residence hall and University.
- The RA develops a sense of community among residents as members of a floor, residents of a hall, and active participants in the residence life system.
- The RA serves as a positive role model to residents and peer staff members.
- The RA enforces the rules and policies of Residence Life, Housing and Dining Services and the University.
- The RA acts as a liaison between residents and the University administration.

Bennett College Peer Tutor, Aug 2015 – May 2016

- Peer tutors work with students in their content areas of expertise.
- Tutors are hired for the Academic Success and Career Center (ASCC) (formerly CACD) drop-in Tutoring Program.
- Tutors work with students on a one-on-one basis or in small group sessions to answer questions on course content, to aid in comprehension of course material, and to help with studying the course.
- They can also be available to tutor students privately.
- Private tutors are hired by students for help in understanding course content.

LSAMP Scholar, Greensboro, NC, Bennett College Aug 2016 – May 2017

- This program is aimed at increasing the quality and quantity of students successfully completing science, technology, engineering and mathematics (STEM) baccalaureate degree programs, and increasing the number of students interested in, academically qualified for and matriculated into programs of graduate study.

Selected Honors & Awards

Outstanding Biology of the Year Award 2013-2017 (Freshman, Sophomore, Junior & Senior years)

Bennett's Honor's and Dean's list 2013-2015

Resident Assistant "Best Educational Program of the Year Award" 2015

Resident Assistant "Full of Heart Award" 2015

Who's Among Students in American Universities and Colleges - Nominee 2016

LSAMP Scholar Aug 2016 – May 2017

Membership

Alpha Kappa Alpha Sorority Inc., 2017-Present

Beta Kappa Chi Honor society, 2017-Present

Work Experience

Swim Instructor & Lifeguard, City of Winston-Salem, Summer 2011, Summer 2012 & Summer 2013

- Noted swimming level of students, developed lesson plans, conducted swimming lessons, and performed weekly evaluations to determine progress.
- Responsible for the coordination, education, and safety of 10-20 children on a given day.
- Valid lifeguard certification. Certified in CPR, AED, and first aid.

Bennett College Peer Tutor, Aug 2015- May 2016

- Peer tutors work with students in their content areas of expertise.
- Tutors are hired for the Academic Success and Career Center (ASCC) (formerly CACD) drop-in Tutoring Program.
- Tutors work with students on a one-on-one basis or in small group sessions to answer questions on course content, to aid in comprehension of course material, and to help with studying the course.
- They can also be available to tutor students privately.
- Private tutors are hired by students for help in understanding course content.

Duke Tip, Instructor, June 2019-Aug 2019

- Summer Studies is a three-week residential program for high-achieving students in grades seven through ten.
- Taking place at thirteen college campuses across the country over two different summer sessions, the programs provide the social and intellectual stimulus that gifted students need.
- Instructors support the student experience and implement the academic life mission of Duke TIP.

- Instructors are responsible for preparing and teaching challenging and engaging courses and managing the learning environment.

Duke Tip, Instructor, Dec 2019

- Scholar Weekends are designed to emulate the college experience and offer academically talented high school students the challenge they don't always receive in a traditional classroom.
- The program provides a supportive environment in which students can gain enough confidence in their abilities to take academic risks and propose their own ideas.
- Scholar Weekends are hands-on learning experiences taught by content experts who emphasize projects and other interactive activities that require students to be creative.

Publications

Journal Articles:

Fuxjager, M. J., Miles, M. C., Goller, F., Petersen, J., & Yancey, J. (2017). Androgens Support Male Acrobatic Courtship Behavior by Enhancing Muscle Speed and Easing the Severity of Its Tradeoff With Force. Endocrinology, 158(11), 4038-4046. doi:10.1210/en.2017-00599