cations that have been approved by the FDA for treating ALS. These include Riluzole, which can improve life expectancy by 3 to 6 months but can cause functional changes in the liver (*Amyotrophic lateral sclerosis* (*ALS*) 2022). Edaravone is an intravenous medication or can be taken orally to help reduce the progression of symptoms, but it can also come with side effects such as headaches and shortness of breath (*Amyotrophic lateral sclerosis* (*ALS*) 2022). The third medication is Sodium phenylbutyrate and taurursodiol, which can slow the rate of decline, specifically when performing daily tasks (*Amyotrophic lateral sclerosis* (*ALS*) 2022).

What is known about ALS
Neuroinflammation, glia, and motor neurons

ALS has been heavily researched over the past several decades in an attempt to learn more about the mechanisms underpinning the disease. Many biological processes implicated in ALS are related to neuroinflammation, or inflammation of the brain and nervous system (Ransohoff, 2016). This is linked to neurodegeneration, which is a gradual loss of neurons and the impairment of their normal functioning (Ransohoff,

ALS eventually causes loss of muscle control in those who have it. It usually starts with twitching or noticeable weakness in limbs. It may also impair the individual's ability to speak, eat, and breathe (*Amyotrophic lateral sclerosis* (*ALS*) 2022). Symptoms that accompany ALS include difficulty walking, falling, weakness in legs or hands, slurred speech, trouble swallowing, as well as various cognitive and behavioral changes (*Amyotrophic lateral sclerosis* (*ALS*) 2022). In the early stages of the disease, symptoms tend to start in the hands, feet, or limbs and eventually progress to other parts of the body. This is because when the disease progresses, it increasingly deteriorates the motor neurons, leading to more muscles getting weaker. However, the beginning stages are not typically ass1 0 0 2age6oEMC t6/Lang (en-S)/PC 1 -0 5 Tf8 usuaanor ain,ages are -0 7 (to s ainm[also (.ing a fr

er medical conditions. Lifestyle choices include smoking, physical health, and dietary factors. Smoking has been identified as a potential risk factor, but results are a bit conflicting regarding how influential this may be on the progression or onset of ALS. Some research has identified a causal link (Peters et al., 2019), while others have found no evidence for a causal relationship (Opie-Martin et al., 2020). Dietary factors can also play a protective role; a correlational link has been found between increased antioxidant intake and reduced risk of ALS (Caplliure-Llopis et al., 2019). Other genome-wide association studies have identified a link between ALS and having a higher body mass index, higher body fat percentage, and type 2 diabetes (Li et al., 2021). Environmental risk factors affect those who are exposed to higher levels of different chemicals and pesticides, such as military workers, carpenters, and construction workers, which may be linked with an increased risk of developing ALS (Beard & Kamel, 2014; Fang et al., 2009; Roos, 2017). Other medical conditions, such as enteroviral viruses, head trauma, cancer, and neuroinflammation, have been linked to ALS (Farace et al., 2020; Gu et al., 2021; Xue et al., 2018).

There is currently not a single method for definitively diagnosing ALS but instead requires a healthcare provider to conduct a physical and neurological exam to determine a diagnosis (*Amyotrophic lateral sclerosis* (*ALS*)). Some forms of imaging include electromyography, a nerve conduction study, magnetic resonance imaging, blood and urine tests, or muscle biopsies (*Amyotrophic lateral sclerosis* (*ALS*)). While there currently is no cure for ALS either, there are some treatments to help slow the progression of symptoms. There are currently three medi-

Protein Aggregation

Related, abnormal protein aggregation is seen across many neurodegenerative diseases (Tanikawa et al., 2018). ALS is characterized by ubiquitinated proteins that aggregate in motor neurons, including FUS, TDP-43, OPTN, and UBQLN2, and are related to the C9orf72 gene (Chisholm et al., 2021). Recent research has also found the novel role of PAD-4-mediated citrullination in protein aggregation in ALS. Tanikawa et al. found that many of the PAD4 substrates were highly expressed in the brain tissue and that they inhibited the aggregation of FET proteins, which are commonly found in neurodegenerative diseases. They also looked at FUS protein levels and saw that these increased in a PAD4 knockout mouse model, highlighting that PAD4-mediated citrullination plays a role in ALS pathogenesis (Tanikawa et al., 2018).

Overall, research has come a long way since the start of ALS research. There have been many technological advancements that bettered our understanding of the disease and the mechanisms underpinning it. Researchers have been able to identify the genetic roots of the disease and learned about the roles that mitochondrial dysfunction, oxidative stress, and neuroinflammation play, as well as the effects of RNA misprocessing and protein aggregation. Despite these findings, however, there is still a lot we do not understand about the cellular mechanisms of these processes.

Current treatments for ALS
Functional Analysis

Functional analysis refers to the analysis of a behavior to identify what sustains that behavior related to a disease (Apa Dictionary of Psychology). In the current context, ALS functional analysis broadly looks at the function of muscles and motor neurons. There are several different areas that are looked at in connection to ALS, including electromyography, muscle strength testing, pulmonary function, and cognitive and speech tests.

Electromyography is a test that looks at the electrical activity of muscles, and because motor neurons and muscles are affected by the degeneration of motor neurons in ALS, it is used to monitor symptoms (Bashford et al., 2020). Bashford et al. conducted a systematic review of the use of EMG in ALS. It was originally and continually used because of its non-invasive and practical manner (Bashford et al., 2020). Practi-

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