

IN RE: NATIONAL FOOTBALL LEAGUE
PLAYERS' CONCUSSION INJURY
LITIGATION

MDL No. 2323

THIS DOCUMENT RELATES TO:
NFL PARTIES' APPEAL OF CLAIM
DETERMINATION FOR SETTLEMENT
CLASS MEMBER [REDACTED]

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The Settlement has particular boxes that must be checked and can create medical-legal processes which are not ordinary in the clinical setting.¹

I take those medical-legal processes as given. They require the appealing NFL Parties to show, by clear and convincing evidence, that the Claims Administrator erred in determining that Mr. [REDACTED]'s Qualifying Diagnosis satisfied the Amended Class Action Settlement's criteria for "Alzheimer's Disease." The Injury Definition for Alzheimer's Disease under the Amended Class Action Settlement, built on the scientific consensus of 2015, not only does not require, but counsels against dispositive use of biomarker correlates of clinical manifestations of Alzheimer's Disease. Thus, the absence of biomarkers of Alzheimer's cannot be clear and convincing evidence that the Claims Administrator's decision to grant Mr. [REDACTED] an Award was in error.

I deny the Appeal.

FACTUAL AND PROCEDURAL BACKGROUND

Mr. [REDACTED] submitted this Claim, his second, on June 29, 2022, originally for Level 2.0 Neurocognitive Impairment.² Doc. 266428. MAF neurologist Dr. [REDACTED] made the Diagnosis after considered two different neuropsychological testing batteries, one by Dr. [REDACTED] in 2022 and another by Dr. [REDACTED] in 2016.

Mr. [REDACTED] first saw Dr. [REDACTED] for cognitive testing on June 2, 2021. Doc. 266416. At that visit, Dr. [REDACTED] concluded, "[T]he most dominant area(s) of cognitive impairment were in visual-spatial perception, working memory, judgment, context free short term memory." *Id.* at 1. He referred Mr. [REDACTED] for an MRI and for CSF testing. *Id.* at 3, 6.

Mr. [REDACTED] completed an MRI on June 26, 2021. *Id.* at 23. The radiologist noted two impressions: "a few foci of subcortical T2 hyperintensity seen in the bifrontal lobes" and "[h]ippocampal volume is greater than 2 standard deviations above the mean." *Id.* at 24. Reviewing that MRI the following month, Dr. [REDACTED] interpreted it as indicating a "Slightly-Somewhat" likelihood of Alzheimer's Disease and a "Very-Extremely" likelihood of brain trauma. *Id.* at 6. As he summarized:

In conjunction with the history, cognitive testing, and other diagnostic tests, the present study's findings are most compatible with:

1. multifocal areas of atrophy consistent with Traumatic Brain Injury during football career
2. Lewy Body Disease > Alzheimer's disease based on atrophy patterns

¹ Special Master Ruling on Validity Testing, External Evidence, and Functional Impairment (Mar. 27, 2023), https://www.nflconcussionsettlement.com/Docs/validity_evidence_impairment_sm.pdf, at 24.

² Mr. Madison's first claim, submitted on May 9, 2017, for Level 2.0 Neurocognitive Impairment, was denied after the examining neuropsychologist, Dr. [REDACTED], was disqualified from participation in the Program. Docs. 67253; 151315.

3. Cerebral microhemorrhages that have largely resolved since 2015 qMRI
4. There is no significant cerebrovascular disease, no hemorrhage, no hydrocephalus, and no masses.
5. The cognitive and clinical symptoms are very consistent with the abnormal findings identified.
6. Progression of atrophy has occurred in frontal, parietal lobes.

Id.

Mr. [REDACTED] next completed CSF testing on August 17, 2021, and a diagnostic visit with Dr. [REDACTED] on October 14, 2021. *Id.* at 12. Mr. [REDACTED]'s initial CSF testing report stated that his tests were "Not consistent with Alzheimer Disease." *Id.* at 42. Dr. [REDACTED] concluded that Mr. [REDACTED]'s CSF tests were "normal except for an increase in the % of Neurofibrillary Tau relative to the total number of tau misfolded proteins. This is due to the prior Traumatic Brain Injury playing football." *Id.* at 13. At this visit, Dr. [REDACTED] identified the "Primary Cause of Identified Cognitive, Functional Difficulties, or Biomarker Pathology" using ICD Diagnostic Code F03.90, Unspecified Dementia, "due to tauopathy." *Id.* at 12.

Mr. [REDACTED] then saw Dr. [REDACTED] for neuropsychological testing on March 21 and 24, 2022. Doc. 266419. Per Dr. [REDACTED]'s evaluation, Mr. [REDACTED] met the Settlement Criteria for impairment across three cognitive domains: she assigned him scores of Level 1.5 Impairment in complex attention, Level 2.0 Impairment in learning & memory, and Level 2.0 Impairment in language. *Id.* Although Dr. [REDACTED] deferred diagnosis to Dr. [REDACTED], she concluded that his neuropsychological testing met the criteria for a Qualifying Diagnosis of Level 2.0 Neurocognitive Impairment. *Id.*

On May 12, 2022, after these appointments but before Mr. [REDACTED] submitted this Claim, Dr. [REDACTED] signed a Diagnosing Physician Certification Form that listed two Diagnoses: Level 2.0 Neurocognitive Impairment and Alzheimer's Disease, both dated May 12, 2022. Doc. 266425. On that Certification Form, he noted that Dr. [REDACTED] had assisted him in rendering a Diagnosis. *Id.*

Mr. [REDACTED] submitted his Claim Form on June 29, 2022, with a Diagnosis of Level 2.0 Neurocognitive Impairment. Doc. 266428. Mr. [REDACTED]'s counsel confirmed, in correspondence with the Claims Administrator on August 1, 2022, that the Claims Administrator should proceed with the Level 2.0 Neurocognitive Impairment Diagnosis rather than the Alzheimer's Diagnosis. Doc. 267675.

Over the next eight months, the Claims Administrator sought further clarification of predicate elements of the Claim. Mr. [REDACTED]'s counsel ultimately provided Administrator a 35-page brief and several exhibits highlighting descriptions of the severity of his functional impairment in sworn statements by Mr. [REDACTED]'s wife, [REDACTED], family friend, [REDACTED], and friend, [REDACTED]. Doc. 271648. Dr. [REDACTED] submitted the completed CDR Assessment Form on February 13, 2023. Docs. 274964; 277311. He assigned Mr. [REDACTED] CDR scores of 1 in Community Affairs and Home & Hobbies and 0 in Personal Care, writing that

Mr. [REDACTED] “can no longer drive due to cognitive impairment” and that he is “[u]nable to perform simple household chores without constant supervision. Hobbies abandoned.” Doc. 277311 at 4-6.

Alongside this CDR form, Dr. [REDACTED] submitted a new Diagnosing Physician Certification Form. Doc. 277304. This form only certified a Diagnosis of Alzheimer’s Disease. *Id.* Dr. [REDACTED] also recorded a different assisting neuropsychologist: Dr. [REDACTED], who had examined Mr. [REDACTED] six years earlier, in 2016. *Id.* Dr. [REDACTED]’s records, which are also included in Mr. [REDACTED]’s Claim, noted that Mr. [REDACTED] was experiencing “impaired memory, concentration that include forgetting directions and how to get home, forgets name and instructions,” and that his “wife takes care of shopping, cooking, driving, paying bills, his personal affairs, maintaining household.” Doc. 266420 at 10, 11.

Dr. [REDACTED] provided an addendum to Mr. [REDACTED]’s medical record with an extended diagnostic discussion highlighting specific symptoms:

He has had progressive memory loss for recalling recent events and conversations, first notable in 2012, while still playing in the NFL at 30-31 years old.

Progression of Symptoms.

Memory symptoms have progressed. Per wife, memory issues affect day to day function. As more responsibilities came, noticed more pronounced memory difficulties. Per wife, he needs constant reminders and will forget the same things she will tell him every day. He has become fully dependent on others for short-term memory and his working memory impairment has severely affected performance of well learned procedures.

EXAMPLES INCLUDE:

putting an appointment in google calendars, and requires regular reminders to make lunch for children at the same time every day, reminders for all household tasks.

IMPAIRED WELL LEARNED PROCEDURES.

He no longer drives because he can get lost and forgets where he is driving - even familiar routes (even with GPS), forgetting to put the car in park a few instances.

He can no longer manage finances, which have been taken over by his wife when she noticed he was forgetting car payments, checks not being cashed, etc..

Basic ADLs show psychomotor slowing -- Takes him a very long time to get dressed.

He is more indecisive in selecting the appropriate clothes to wear.

Takes longer to do well learned tasks, and cannot be relied upon to do household chores without constant supervision.

Visual spatial difficulties - walking closer to a person than someone would normally.

Doc. 277305. In the same addendum, Dr. [REDACTED] summarized Dr. [REDACTED]'s conclusions:

He also saw a psychologist in 2016, Dr. [REDACTED], who identified depression, impaired judgment, memory loss, executive dysfunction, anxiety. Dr. [REDACTED] also recorded the patient had periods of poor hygiene, who needed intermittent assistance with bathing. He had become dependent on shopping, driving, paying bills, personal affairs, and household chores.

Id.

On February 14, 2023, Mr. [REDACTED]'s counsel confirmed with the Claims Administrator that his Claim should now be processed with a Qualifying Diagnosis of Alzheimer's Disease. Doc. 277441.

The Claims Administrator granted Mr. [REDACTED] an Award for that Diagnosis on March 13, 2023. Doc. 278898. The NFL Parties timely appealed. Doc. 283612.

DISCUSSION

The issue this Appeal raises is what diagnostic material the Amended Class Action Settlement requires—or, what diagnostic material it treats as conclusive—for a Qualifying Diagnosis of Alzheimer's Disease.

The NFL Parties specifically highlight three biomarkers which they say “definitively disprove” a Qualifying Diagnosis of Alzheimer's: Mr. [REDACTED]'s hippocampal volume, which is “greater than 2 standard deviations above the mean compared to age matched controls,” his normal amyloid beta protein levels, and his normal tau protein levels. Doc. 266416 at 24, 42. I understand that these biomarkers are thought to be the physical, or pathological, signs of the disease, distinct from its clinical manifestations, as an exhibit to the NFL Parties' brief suggests. Docs. 283615. The NFL Parties acknowledge that biomarkers are not “explicitly required” for a diagnosis of Alzheimer's Disease under the Settlement, but nonetheless argue that medical science and clinical practice are sufficiently settled on their meaning that their absence gravely undermines Mr. [REDACTED]'s Claim. Doc. 283612 at 2.

The Amended Class Action Settlement defines Alzheimer's Disease by reference to either of two alternative sources: the World Health Organization's International Classification of Diseases 9th or 10th Edition (ICD-9 or ICD-10), *or* the definition of Neurocognitive Disorder due to

probable Alzheimer's Disease in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5).³

The ICD-10 defines "Dementia in Alzheimer's disease" as, in relevant part:

...a primary degenerative cerebral disease of unknown etiology, with characteristic neuropathological and neurochemical features. It is usually insidious in onset and develops slowly but steadily over a period of years. This period can be as short as 2 or 3 years, but can occasionally be considerably longer...

There are characteristic changes in the brain: a marked reduction in the population of neurons, particularly in the hippocampus, substantia innominate, locus ceruleus, and temporoparietal and frontal cortex; appearance of neurofibrillary tangles made of paired helical filaments, neuritic (Aβ-amyloid) plaques, which consist largely of amyloid and show a definite progression in their development (although plaques without amyloid are also known to exist); and granulovacuolar bodies. Neurochemical changes have also been found, including a marked reduction in the enzyme choline acetyltransferase, in acetylcholine itself, and in other neurotransmitters and neuromodulators.

As originally described, the clinical features are accompanied by the above brain changes. *However, it now appears that the two do not always progress in parallel: one may be indisputably present with only minimal evidence of the other. Nevertheless, the clinical features of Alzheimer's disease are such that it is often possible to make a presumptive diagnosis on clinical ground alone.*

The following features are essential for a definite diagnosis:

- (a) Presence of a dementia as described above.
- (b) Insidious onset with slow deterioration. While the onset usually seems difficult to pinpoint in time, realization by others that the defects exist may come suddenly. An apparent plateau may occur in the progression.
- (c) Absence of clinical evidence, or findings from special investigations, to suggest that the mental state may be due to other systemic or brain disease which can induce a dementia (e.g. hypothyroidism, hypercalcaemia, vitamin B₁₂ deficiency, niacin deficiency, neurosyphilis, normal pressure hydrocephalus, or subdural haematoma).
- (d) Absence of a sudden, apoplectic onset, or of neurological signs of focal damage such as hemiparesis, sensory loss, visual field defects, and incoordination

³ "For living Retired NFL Football Players, a diagnosis while living of the specific disease of Alzheimer's Disease as defined by the World Health Organization's International Classification of Diseases, 9th Edition (ICD-9), the World Health Organization's International Classification of Diseases, 10th Edition (ICD-10), or a diagnosis of Major Neurocognitive Disorder due to probable Alzheimer's Disease as defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), made by a Qualified MAF Physician or a board-certified or otherwise qualified neurologist, neurosurgeon, or other neuro-specialist physician, as set forth and provided in Sections 6.3(b)-(d) of the Settlement Agreement." Settlement Agreement, Exhibit A-1(3)(a).

occurring early in the illness (although these phenomena may be superimposed later.⁴

The DSM-5 diagnostic criteria for Major Neurocognitive Disorder due to probable Alzheimer's Disease are:

- A. The criteria are met for major or mild neurocognitive disorder.
- B. There is insidious onset and gradual progression of impairment in one or more cognitive domains (for major neurocognitive disorder, at least two domains must be impaired).
- C. Criteria are met for either probable or possible Alzheimer's disease as follows:
For major neurocognitive disorder:
Probable Alzheimer's disease is diagnosed if either of the following is present; otherwise, possible Alzheimer's disease should be diagnosed.
 - 1. Evidence of a causative Alzheimer's disease genetic mutation from family history or genetic testing.
 - 2. All three of the following are present:
 - a. Clear evidence of decline in memory and learning and at least one other cognitive domain (based on detailed history or serial neuropsychological testing).
 - b. Steadily progressive, gradual decline in cognition, without extended plateaus.
 - c. No evidence of mixed etiology (i.e., absence of other neurodegenerative or cerebrovascular disease, or another neurological, mental, or systemic disease or condition likely contributing to cognitive decline).⁵

Like the ICD-10, the DSM-5 considers diagnostic markers including biomarkers but emphasizes that, under its definition, they are not conclusive:

Cortical atrophy, amyloid-predominant neuritic plaques, and tau-predominant neurofibrillary tangles are hallmarks of the pathological diagnosis of Alzheimer's disease and may be confirmed via postmortem histopathological examination...

Since amyloid beta-42 deposition in the brain occurs early in the pathophysiological cascade, amyloid-based diagnostic tests such as amyloid imaging on brain positron emission tomography (PET) scans and reduced levels of amyloid beta-42 in the cerebrospinal fluid (CSF) may have diagnostic value. Signs of neuronal injury, such as hippocampal and temporoparietal cortical atrophy on a magnetic resonance image scan, temporoparietal hypometabolism on a fluorodeoxyglucose PET scan, and evidence for elevated total tau and phospho-tau levels in CSF, provide evidence

⁴ WORLD HEALTH ORGANIZATION, THE ICD-10 CLASSIFICATION OF MENTAL AND BEHAVIORAL DISORDERS: CLINICAL DESCRIPTIONS AND DIAGNOSTIC GUIDELINES 47 (1992) (emphasis added).

⁵ AMERICAN PSYCHIATRIC ASSOCIATION, DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS 611 (5th ed. 2013).

of neuronal damage but are less specific for Alzheimer's disease. *At present, these biomarkers are not fully validated, and many are available only in tertiary care settings.* However, some of them, along with novel bio-markers, will likely move into wider clinical practice in the coming years.⁶

Neither definition can bear the categorical weight the NFL Parties place on Mr. ██████'s Biomarker Testing. Instead, both primarily consider the clinical, and not the pathological, indicators of Alzheimer's. As such, they fit within the Settlement's broader framework. Emphasizing the identification of, and payment for, symptoms, rather than pathological markers of disease, has shaped the Program's development, approval, and administration.

The NFL Parties' own counsel, for example, said at the Fairness Hearing that the "purpose of the Settlement is not to compensate protein in the brain or not to compensate a particular structure, it's to compensate cognitive impairment."⁷ And as is therefore appropriate, the Program's FAQs deny the sufficiency of biomarkers: "[A] biomarker test, by itself, is not sufficient to establish a Qualifying Diagnosis of Alzheimer's Disease under the Settlement criteria... There must be an actual manifestation of cognitive impairment and/or actual neuromuscular impairment."⁸

Under the Injury Definitions, Mr. ██████'s Qualifying Diagnosis cannot turn on "protein in the brain," even if its absence flouts the 2023 consensus about the expected biological evidence of Alzheimer's Disease.⁹ Instead, the Claims Administrator should have, and did, consider whether Mr. ██████'s Qualifying Diagnosis satisfied either ICD-10's or the DSM-5's definitions of Alzheimer's Disease.¹⁰ It did. A Qualified MAF Physician, Dr. ██████, made the Qualifying Diagnosis in the final Diagnosing Physician Certification Form he submitted. Doc. 277304. His conclusion rests on an ample record of over 10 years of provider documentation and multiple third-party affidavits that meets the clinical (symptomatic) criteria for diagnosis under either the ICD-10 or the DSM-5. And the NFL Parties do not dispute that Mr. ██████ suffers from the symptoms that his records illustrate. Doc. 283612.

To assure myself that Mr. ██████'s Qualifying Diagnosis sufficiently met the DSM-5 and ICD-10 definitions, I conducted a call with two qualified AAP neurologists. On that call, they

⁶ *Id.* at 613 (emphasis added).

⁷ ECF No. 6463, Amended Transcript of Fairness Hearing at 193 (Dec. 11, 2014) (noting that some patients die with the pathology of Alzheimer's Disease but without experiencing any symptoms, and that those patients should not be compensated under the Settlement).

⁸ *Frequently Asked Questions: FAQ #116* (Is a biomarker test (such as an amyloid PET, spinal fluid test) enough to establish my Qualifying Diagnosis of Alzheimer's Disease?), NFL CONCUSSION SETTLEMENT, <https://www.nflconcussionsettlement.com>.

⁹ ECF No. 6463, *supra* note 8.

¹⁰ The NFL Parties cite to Judge Brody's recent decision stating "AAP review of the medical records underlying Claims Packages is integral to attaining the diagnostic accuracy administration of the Settlement requires, and is expressly provided for by the terms of the Settlement Agreement." Explanation and Order at 6, ECF No. 11931. But diagnostic accuracy relates to fidelity to the Settlement's Injury Definitions, not some abstract ideal. As the NFL Parties are well aware, for example, there is no diagnosis of Level 1.5 or Level 2 Neurocognitive Impairment as such in the clinical office.

explained that in today's clinical practice biomarkers are thought to be stigmatic of Alzheimer's Disease and are required for approval for treatment with Aducanumab. But they confirmed that under the Amended Settlement's definition and the ICD-10/DSM-5, such markers are not required for a diagnosis. Further, in their view, Dr. [REDACTED] adequately excluded other etiologies.¹¹ At the very least, the absence of biomarkers did not indicate any singular "mixed etiology" apart from degenerative processes attributable to head trauma itself. And, as the Parties jointly agreed in 2020, evidence of mixed etiology arising from head trauma (as identified by Dr. [REDACTED]) "should not foreclose a Qualifying Diagnosis of Alzheimer's Disease."¹²

The DSM-5 contemplates a future in which biomarkers would become diagnostic, and universally used, in clinical practice.¹³ The AAP informed me that while not all neurologists today use biomarkers as necessary for a presumptive Alzheimer's Diagnosis, an increasing number, including Dr. [REDACTED], usually do. And both the NFL Parties and the AAP pointed me to the National Institute on Aging and Alzheimer's Association (NIA-AA) 2011 diagnostic recommendations as indicating the centrality of biomarker testing to clinical practice.

Those diagnostic recommendations predate the establishment of the Settlement and could have been included in its Injury Definitions. Conspicuously, they were not. Although the NIA-AA published an update to its 2011 guidelines in 2018, it labelled that document a "research framework" and, in the same document the NFL cites, states that "it is premature and inappropriate to use this research framework in general medical practice."¹⁴ Thus, as the AAP informed me, some neurologists in practice continue to diagnose Alzheimer's Disease under the ICD-10/DSM-5 relying on its clinical manifestations alone.

If the science of Alzheimer's progresses to *require* the use of biomarkers for sound medical practice and identification of the disease, as opposed to pathologies of another type, the Settlement offers a path for that development's integration into its Injury Definitions. That would be a joint proposal by Class Counsel and the NFL Parties to modify the Settlement "in light of generally accepted advances in medical science."¹⁵ That joint proposal would follow good faith discussions, not the Appeals process, and would require Court approval.

My job is more mundane. As I interpret the Injury Definitions, neither the presence nor the absence of biomarkers can be dispositive of the Qualifying Diagnosis of Alzheimer's Disease. The AAP members I consulted advised that Mr. [REDACTED] has offered sufficient evidence for that

¹¹ The AAP informed me that measurement of hippocampal volume was particularly unreliable as a signal because it postdates the beginning of Alzheimer's progressions, sometimes by decades. I note that although the records indicate that Mr. [REDACTED]'s volume was normed by age, it does not exclude adjustment on impermissible demographic grounds. That said, Neuroquant, a common normative system for measuring volume of brain structures, apparently uses only age and gender in its adjustment formula.

¹² See NFL Concussion Program: Open Issue 11 (as of 1/31/2020) (Parties' joint statement on "Mixed Causation of Alzheimer's Disease and Parkinson's Disease").

¹³ AMERICAN PSYCHIATRIC ASSOCIATION, *supra* note 4, at 613.

¹⁴ Clifford R. Jack, Jr. et al., *NIA-AA Research Framework: Toward a Biological Definition of Alzheimer's Disease*, 14 *Alzheimer's & Dementia* 535, 536 (2018).

¹⁵ Settlement Agreement, Section 6.6(a).

Diagnosis as defined by the DSM-5 and ICD-10 (though they likely would not make the same Diagnosis in their practices today). Thus, the NFL Parties have not met their heavy burden on Appeal to demonstrate clear and convincing evidence of error in the Claims Administrator's decision.

CONCLUSION

Because the NFL Parties have not offered clear and convincing evidence that the Claims Administrator erred, I deny their Appeal.

Date: September 8, 2023



David A. Hoffman, Special Master