Clinical, radiologic, and pathologic features of the globular glial tauopathy subtype of frontotemporal lobar degeneration in right temporal variant frontotemporal dementia with salient features of Geschwind syndrome

Sylvia Josephy-Hernandez, Michael Brickhouse, Samantha Champion, David Dongkyung Kim, Alexandra Touroutoglou, Matthew Frosch and Bradford C. Dickerson

Frontotemporal Disorders Unit, Department of Neurology, Massachusetts General Hospital & Harvard Medical School, Boston, MA, USA; Forensic Pathology, Miami-Dade County Medical Examiner Office, Miami, FL, USA; Department of Psychiatry, Centre of Addiction and Mental Health & University of Toronto, Toronto, ON, Canada; Neuropathology Service, Department of Pathology, Massachusetts General Hospital & Harvard Medical School, Boston, MA, USA.

ABSTRACT
Globular Glial Tauopathy (GGT) is a rare form of Frontotemporal Lobar Degeneration (FTLD) consisting of 4-repeat tau globular inclusions in astrocytes and oligodendrocytes. We present the pathological findings of GGT in a previously published case of a 73-year-old woman with behavioral symptoms concerning for right temporal variant frontotemporal dementia with initial and salient features of Geschwind syndrome. Clinically, she lacked motor abnormalities otherwise common in previously published GGT cases. Brain MRI showed focal right anterior temporal atrophy (indistinguishable from five FTLD-TDP cases) and subtle ipsilateral white matter signal abnormalities. Brain autopsy showed GGT type III and Alzheimer’s neuropathologic changes.

Introduction
Frontotemporal Lobar Degeneration (FTLD) is a family of neurodegenerative diseases that tend to affect frontal and anterior temporal brain systems and lead to a variety of Frontotemporal Dementia (FTD) clinical syndromes. The two major types of FTLD are FTLD-TDP and FTLD-tau. Subtypes of FTLD-tau include Pick’s disease, progressive supranuclear palsy (PSP), corticobasal degeneration, and rarer primary tauopathies, such as globular glial tauopathy (GGT), a 4-repeat tauopathy with tau globular inclusions in astrocytes and oligodendrocytes.

Three GGT subtypes have been defined according to their neuroanatomical distribution. In type I, the distribution of pathology is predominantly in prefrontal and temporal cortices. In type II, the pathology is mostly in the primary motor cortex with corticospinal tract degeneration. In type III, pathologic changes are found in frontal, temporal, and motor cortices, as well as in the corticospinal tract (Ahmed et al., 2013). Cases with type I and III are typically present with cognitive-behavioral syndromes, including behavioral variant frontotemporal dementia (bvFTD), while type II is most commonly present as a progressive motor neuron syndrome (Ahmed et al., 2013). Several authors have raised questions about this classification system, given that there are no definite clinical or radiologic features that would suggest GGT before autopsy examination (Burrell et al., 2016; Forrest et al., 2021). One recent case report of a patient with PSP (Richardson’s syndrome) suggested that if signs of corticospinal tract dysfunction were also present, GGT should be considered (Liu et al., 2020). Both Liu et al. (2020) and Ohno et al. (2021) have shown that white matter signal abnormalities not typical of vascular brain injury should also raise the possibility of GGT.

In this article, we present the autopsy findings of GGT Type III, from a case of right temporal variant of frontotemporal dementia (rtvFTD) with initial and salient features of Geschwind syndrome (Veronelli et al., 2017). Geschwind syndrome is an interictal behavioral syndrome, most frequently described in patients with temporal lobe epilepsy, comprising hyper-religiosity, hypergraphia, alterations in sexual behavior, and irritability (Bear & Fedio, 1977; Waxman & Geschwind, 1975). The clinical and radiographic features from this patient have been previously published (Veronelli et al., 2017). Here, we discuss this case’s characteristics in the context of previously published cases of GGT, their syndromic presentation, frequency of motor features, imaging findings, and coexistent histopathologies. We also perform a comparison of our patient’s imaging with that of pathology-proven FTLD-TDP. We believe that detailed case reports characterizing patients with clinical dementia syndromes arising from rare forms of FTLD, contextualized by the literature, may enable them to be better identified during life, which would facilitate their appropriate participation in biomarker studies and clinical therapeutic trials.

Case presentation
Clinical features for this patient, including detailed neuropsychological testing, have been previously published as a form of sporadic rtvFTD, with initial and predominant symptoms as
seen in Geschwind syndrome (Veronelli et al., 2017). Briefly, the patient presented at age 73 with 3 years of personality and behavioral symptoms including disinhibition, loss of empathy, and compulsive behavior with the development of hyper-religiosity, hypergraphia, and poor emotional regulation. A framework for the clinical-radiological features of the rtvFTD includes episodic memory problems, prosopagnosia, behavioral disinhibition, apathy or inertia, loss of empathy, egocentrism, and compulsive behavior, as symptoms present in 40% to 60% of patients, and language problems in 30% of patients (Ulugut Erkoyun et al., 2020). The patient presented here indeed had several of such features, including behavioral disinhibition, loss of empathy, difficulty recognizing familiar faces, egocentrism, and compulsive behavior. She presented language difficulties later in her disease course. Interestingly, her initial and salient features reminisced those described in Geschwind syndrome, with specific compulsive behavior including hypergraphia, hyper-religiosity, in addition to poor emotional regulation. Overall, her clinical presentation was considered to be that of rtvFTD with initial and salient features of Geschwind syndrome.

Subsequent to the history described in the prior report, she continued to gradually deteriorate with increasing need for assistance with basic activities of daily living. She expired at age 84 from complications of aspiration pneumonia. Throughout the 14-year course of her illness, she did not exhibit motor symptoms or signs on exam. Her MAPT gene was sequenced, and no pathogenic variants were identified.

### Neuroimaging

Structural and metabolic abnormalities in the patient’s MRI and FDG-PET scans were focally present in the right anterior temporal lobe (Figure 1, and as previously published (Veronelli et al., 2017)). Atrophy progressed in the right temporal lobe and subsequently in homologous regions of the left temporal lobe as previously described. Mild white matter signal abnormalities were observed, predominantly ipsilateral to areas of atrophy, though not specifically matching the areas of highest atrophy. There were very mild peri-ventricular white matter T2 hyperintensities, which are suggestive of cerebral small vessel disease, Fazekas scale of 1 (Fazekas et al., 1987).

We performed a quantitative analysis of cortical thickness from high-resolution T1-weighted 3D structural MR images collected on a 3T Siemens Magnetom Tim Trio system (Siemens Medical Solutions, Erlangen, Germany), using a 12-channel phased-array head coil. Cortical reconstructions and volumetric segmentation of the T1-weighted images were performed using the FreeSurfer analysis suite version 6.1 according to a procedure that has been previously described in detail (Dale, Fischl, & Sereno, 1999; Fischl & Dale, 2000; Fischl, Sereno, & Dale, 1999; Rosas et al., 2002; Salat et al., 2004). Cortical atrophy was assessed using a two class general linear model (GLM) as implemented in FreeSurfer, comparing cortical thickness in this patient to a group of 75 age-matched healthy controls (age: $M = 72.65$ yrs, $SD = 4.80$). Results were converted to W scores as previously described. We selected four cases from our database with focal anterior temporal presentations of frontotemporal dementia (FTD) who were followed to autopsy and found to have FTLD-TDP Type C neuropathologic changes for comparison. The results did not show any distinguishing features with regard to the spatial pattern of atrophy (a representative comparison case is shown in Figure 1).

### Neuropathological evaluation

The patient underwent a brain autopsy. The brain weighed 860 g. On gross inspection, there was marked atrophy of the frontal and temporal lobes, lesser atrophy of the occipital lobes, and sparing of the parietal lobes. Microscopically, the frontal and temporal cortices were moderately thin and gliotic. Immunohistochemistry for hyperphosphorylated tau revealed

---

![Figure 1. Imaging findings in GGT case and comparison to TDP. A. Patient’s T2 FLAIR MRI scan, with right greater than left anterior and medial temporal lobe, as well as bilateral frontal lobe atrophy. Mildly hyperintense signal in the gray and white matter can be observed in the anterior temporal lobes bilaterally and scattered hyperintensities predominantly in the right frontal and temporal lobes. B. Patient’s cortical atrophy maps. C. Representative case from our comparison group of autopsy-confirmed FTLD-TDP Type C. The spatial pattern of atrophy in the case with confirmed GGT pathology was indistinguishable from five cases with FTLD-TDP.](image-url)
many globular glial inclusions in the subcortical white matter of the frontal and temporal lobes, and the white matter of the brainstem including the cerebral peduncles, basal pontis, and medullary pyramids (Figure 2). No such inclusions were found in the primary motor cortex. The regional distribution of neuropathological findings with semi-quantitative measures can be observed in Table 1. White matter globular glial inclusions were not only observed in the frontal and temporal cortices but also in the descending corticospinal tracts (especially cerebral peduncles, pons, and pyramids). As observed in Figure 2, the tau deposits sit within the descending corticospinal tracts. Given the presence of globular glial inclusions with a frontotemporal distribution in addition to their presence in the descending corticospinal tracts, these changes are consistent with globular glial tauopathy, type III (Ahmed et al., 2013).

In addition to the findings detailed above, there was amyloid-β plaque deposition in the cortex, basal ganglia, periaqueductal gray midbrain, and cerebellum consistent with Thal stage 5 (Thal et al., 2002). Neurofibrillary tangles were present in the cortex (including primary visual cortex) and hippocampus. The frequency and distribution of neurofibrillary tangles are consistent with Braak tangle stage VI/VI (Braak & Braak, 1991), and neocortical neuritic plaques were consistent with an age-related CERAD score of moderate (C2) (Mirra et al., 1991). By the 2012 NIA-Alzheimer Association guidelines for the neuropathologic diagnosis of Alzheimer’s Disease, this case received a score of A3B3C2, suggesting high probability of findings diagnostic for Alzheimer’s Disease (Hyman et al., 2012; Montine et al., 2012; Nelson et al., 2012). Additional neuropathologic changes included that of hypertensive related changes and diffuse, cortical and leptomeningeal Cerebral Amyloid Angiopathy (Vonsattel grade 2 of 4 (Greenberg & Vonsattel, 1997)). Alpha-synuclein stains were performed and negative in the hippocampal formation, entorhinal cortex, cingulate gyrus, superior and inferior parietal lobules, temporal pole, superior frontal gyrus, primary motor/sensory cortex, amygdala, and pons. TDP-43 staining was performed and absent in the hippocampal formation and amygdala.

Discussion

Clinical presentation of GGT

We discuss this case in the context of a new literature review of published cases of GGT, aiming to determine whether clinical characteristics or imaging features could be used to predict FTLD-GGT neuropathologic changes.

First, we summarized the presenting clinical syndromes in patients determined at autopsy to have GGT (Table 2). From 87 published cases with GGT on autopsy (Supplementary table S1), age of onset was reported in 86 cases and was 67.13 on average (range 43 to 86); 51.7% female and 48.3% male. Regarding the clinical syndrome, 26 cases (29.9%) had a clinical presentation compatible with behavioral variant FTD (bvFTD), followed in frequency by corticobasal syndrome (16.1%), and primary progressive aphasia (13.8%).

In the past, there have been conflicting reports on whether motor neuron involvement could be a supportive clinical feature to suggest underlying GGT. Among these 87 cases, 77% of

![Figure 2. Tau staining of brain regions. A. White matter underlying BA8; B. Cortex from inferior temporal gyrus; C. White matter underlying inferior temporal gyrus; D. Basis pontis highlighting that the tau deposits sit within the descending corticospinal tracts; E. Medullary pyramids.](image-url)
them had motor system dysfunction of various types, including upper motor neuron signs, extrapyramidal signs, weakness, and changes in gait. In the recent review by Forrest et al. (2021), motor features were quantified only when present as isolated upper motor neuron signs, which were present in 12.5% of cases. The patient we reported here exhibited the unusual initial and salient features of Geschwind syndrome in the context of rTVFTD. However, she did not have motor neuron or extrapyramidal signs that could clinically suggest GGT.

Our patient did have a later age of onset and death than that typical of FTD, but this is not clearly characteristic of GGT. From our literature review, of the participants who presented with bvFTD or PPA (n = 37), the average age of symptom onset was 65.43 years (range 50 to 79), comparable to typical FTD (Onyike & Diehl-Schmid, 2013). Disease duration was reported for 34 of these patients and was 7.38 years (range 2 to 17), which is also similar to typical FTD (Onyike & Diehl-Schmid, 2013). A summary by syndrome of the age of onset or diagnosis, age at the time of death, and disease duration can be found in Table 2 of the supplementary material.

### Radiographic features

From the 87 published cases, 5 had a reported CT and 57 had a reported MRI. Of these, the predominant atrophy pattern was frontotemporal, described in 21 cases. White matter signal abnormalities (WMSA) were reported in 30 cases. Of these, WMSA in five cases were explicitly attributed to chronic small vessel disease (Bigio et al., 2001; Clark et al., 2015; Obara et al., 2002; Powers et al., 2003; Rusina et al., 2019). Six cases reported WMSA that seemed to preferentially affect the corresponding areas of atrophy (Ferrer et al., 2003; Hasegawa et al., 2018; Hirano et al., 2020; Liu et al., 2020; Tan et al., 2005). Josephs et al. (2006) reported 12 cases of atypical PSP, which all showed an increase in T2 signal in the subcortical white matter. Among the cases with reported subcortical WMSA, there was a disproportional clinical presentation of PSP or corticobasal syndrome. An interesting radiologic finding was reported by Tanaka et al. (2019) with a case of motor neuron disease-FTD, which had marked anterior temporal atrophy, and bilateral symmetrical T2-weighted high-intensity signal in the cerebral peduncles.

Changes in white matter have been described in the past as a distinguishing feature between tauopathies and TDP-43 pathology (McMillan et al., 2013). Tractography was not performed on the patient presented here. Mild WMSA were present and ipsilateral to regions of atrophy. The pattern of atrophy per se was indistinguishable from that of semantic variant PPA cases with FTLD-TDP neuropathologic changes (Collins et al., 2017; Mesulam et al., 2017; Rohrer et al., 2010; Whitwell et al., 2010). These findings highlight the lack of specificity of atrophy patterns to distinguish within underlying pathologies in FTLD.

### Concomitant pathologies

In the 87 cases summarized in this publication, concomitant pathology was noted in 26 cases. Alzheimer’s disease (AD) pathology was the most frequent co-pathology, described alone in 14 cases, with yet other co-pathologies in an additional 5 cases. α-synuclein was found in five cases (of which three had concomitant AD pathology and one concomitant neurofibrillary tangles without neuritic plaques). Interestingly, vascular pathology was only described in five cases, two of which also had AD pathology and one TDP-43 (References in table S3 supplementary material). This last finding is interesting given it raises the possibility that not all the subcortical WMSA observed in imaging pre-mortem can be attributed to vascular disease.

When comparing the age of death, cases with any other concomitant pathology had an average age of death of 77.92 years (n = 26), compared to 71.37 years in those without co-pathologies. Average age of death of patients with only AD as a co-pathology was 77.93 years. These findings raise the question of whether co-pathologies are present predominantly as a function of older age.

---

**Table 1. Regional distribution of neuropathological findings.**

| Area                      | Neuropathology |
|---------------------------|----------------|
|                           | NFT | NP | DP | GGI | LB/LN |
| Hippocampal formation     | +++ | ++ | ++ | NA  | -     |
| Entorhinal cortex         | +++ | +++| +++| +++ | -     |
| Temporal pole             |    | NA | NA | NA  | -     |
| Temporal white matter     | NA  | NA | NA | +++ | NA    |
| Superior frontal gyrus    | ++  | +  | +++| +++ | -     |
| Inferior frontal gyrus    |    | NA | NA | NA  | NA    |
| Cingulate gyrus           | ++  | ++ | +++| +++ | -     |
| Superior and inferior parietal lobules | ++ | + | +++ | + | - |
| Primary motor/ sensory cortex |   | + | +++ | NA | NA |
| Primary and association visual cortex |   | + | +++ | NA | NA |
| Amygdala                  | +   | NA | NA | +++| -     |
| Basal ganglia             | +   | NA | +++| NA  | NA    |
| Thalamus                  |    | -  | -  | NA  | NA    |
| Cerebellum                | -   | NA | +  | +   | NA    |
| Midbrain                  | +   | NA | +  | +++aNA |
| Pons                      | +   | NA | NA | +   | -     |
| Medulla                   | +   | NA | NA | +b | NA    |

DP = amyloid beta diffuse plaques; GGI = white matter globular glial inclusions; LB/LN = Lewy bodies or Lewy body neurites; NFT = neurofibrillary tangles; NP = amyloid beta neuritic plaques; TDP-43 = TDP-43 positive inclusions; +++ = numerous; ++ = scattered/moderate; + = sparse/rare; - = absent; NA = not evaluated.

*Especially in the cerebral peduncle.

*Predominantly located in the pyramids.
In our case, neuropathologic examination revealed a combination of GGT Type III, and AD neuropathologic changes. Both neuropathologic processes demonstrated a skewing of the burden of lesions toward the frontal and temporal lobes, mapping well onto the clinical symptomatology. Our patient died at the age of 84, which raises the possibility that AD pathology is present, at least in part, in relation to her older age. Increased frequency of neuropathologic changes with advancing age has been shown in prior studies of GGT (Kovacs et al., 2008), but it is unclear whether that is simply a function of age or whether there may be pathophysiologic synergies between the processes that lead to GGT and AD.

In conclusion, we present a case of rtvFTD with the unusual initial and salient features of Geschwind syndrome, who was found to have GGT at autopsy. Of the family of frontotemporal lobar degeneration tauopathies, GGT is rare. Clinically, it should be considered on the differential diagnosis in atypical cases of FTD, especially when motor features are present. Radiologically, white matter hyperintensities subjacent to areas of atrophy could be suggestive, though not specific, of GGT. The pattern of atrophy on neuroimaging in the case presented here was indistinguishable from that of autopsy-confirmed cases of TDP-43. Finally, concomitant pathological changes such as AD pathology can be present but likely as a function of age. This implies that the presence of AD biomarkers does not necessarily rule out co-pathology with GGT and should be considered in cases with presentations that include mixed features suggestive of FTLD and AD.

### Data availability statement

An SPSS file summarizing the characteristics of patients within the cited literature is available from the corresponding author, BCD, upon reasonable request. Otherwise, participants, whose imaging was analyzed in this study, did not agree for their data to be shared publicly, so supporting imaging data is not available.

### Disclosure statement

No potential conflict of interest was reported by the author(s).

### Funding

The work was supported by the National Institutes of Health [P30 AG062421, R01 DC014296]; Tommy Rickles Chair in Primary Progressive Aphasia Research, and the Sidney R. Baer, Jr. Foundation [Sidney R. Baer Jr. Foundation Fellowship].

### ORCID

Sylvia Josephy-Hernandez [http://orcid.org/0000-0002-5447-1073](http://orcid.org/0000-0002-5447-1073)

### References

Ahmed, Z., Bigio, E. H., Budka, H., Dickson, D. W., Ferrer, I., Ghezzi, B., Giaccone, G., Hatanpaa, K. J., Holton, J. L., & Josephs, K. A. (2013). Globular glial tauopathies (GGTs): Consensus recommendations. *Acta Neuropathologica*, 126(4), 537–544.

Bear, D. M., & Fedio, P. (1977). Quantitative analysis of interictal behavior in temporal lobe epilepsy. *Archives of Neurology*, 34(8), 454–467.

Bigio, E. H., Lipton, A. M., Yen, S.-H., Hutton, M. L., Baker, M., Nacharaju, P., White, C. L., III, Davies, P., Lin, W., & Dickson, D. W. (2001). Frontal lobe dementia with novel tauopathy: Sporadic multiple system tauopathy with dementia. *Journal of Neuropathology & Experimental Neurology*, 60(4), 328–341.

Braak, H., & Braak, E. (1991). Neuropathological staging of Alzheimer-related changes. *Acta Neuropathologica*, 82(4), 239–259.
Burrell, J. R., Forrest, S., Bak, T. H., Hodges, J. R., Halliday, G. M., & Kirl, J. J. (2016). Expanding the phenotypic associations of globular glial tau subtypes. Alzheimer’s & Dementia: Diagnosis, Assessment & Disease Monitoring, 4, 6–13.

Clark, C. N., Lashley, T., Mahoney, C. J., Warren, J. D., Revesz, T., & Rohrer, J. D. (2015). Temporal variant frontotemporal dementia is associated with globular glial tauopathy. Cognitive and Behavioral Neurology, 28(2), 92.

Collins, J. A., Montal, V., Hochberg, D., Quimby, M., Mandell, M. L., Makris, N., Seeley, W. W., Gorno-Tempini, M. L., & Dickerson, B. C. (2017). Focal temporal pole atrophy and network degeneration in semantic variant primary progressive aphasia. Brain, 140(2), 457–471.

Dale A M, Fischl B and Sereno M I. (1999). Cortical Surface-Based Analysis. Neuroimage, 9(2), 179–194. 10.1016/s1053-8119(98)00035-9

Fazekas, F., Chawluk, J. B., Alavi, A., Hurtig, H. I., & Zimmerman, R. A. (1987). MR signal abnormalities at 1.5 T in Alzheimer's dementia and normal aging. American Journal of Neuroradiology, 8(3), 421–426.

Ferrer, I., Hernandez, I., Boada, M., Llorente, A., Rey, M., Cardozo, A., Ezquerro, M., & Puig, B. (2003). Primary progressive aphasia as the initial manifestation of corticobasal degeneration and unusual tauopathies. Acta Neuropathologica, 106(5), 419–435.

Fischl, B., & Dale, A. M. (2000). Measuring the thickness of the human cerebral cortex from magnetic resonance images. Proceedings of the National Academy of Sciences of the United States of America, 97, 11050–11055. https://doi.org/10.1073/pnas.200033797

Fischl, B., Sereno, M. I., & Dale, A. M. (1999). Cortical Surface-Based Analysis. Neuroimage, 9, 195–207. https://doi.org/10.1016/s1053-8119(99)00036-7

Forrest, S. L., Kri, J. J., & Kovacs, G. G. (2021). Association between globular glial tauopathies and frontotemporal dementia—expanding the spectrum of gliocentric disorders: A review. JAMA Neurology, 78, 1004. https://doi.org/10.1001/jamaneurol.2021.1813

Greenberg, S. M., & Vonsattel, J.-P.-G. (1997). Diagnosis of cerebral amyloid angiopathy: Sensitivity and specificity of cortical biopsy. Stroke, 28(7), 1418–1422.

Hasegawa, I., Takeda, A., Hatsuta, H., Kudo, Y., Ohsawa, M., Nakano, Y., Ikeuchi, T., Hasegawa, M., Murayama, S., & Itoh, Y. (2018). An autopsy case of globular glial tauopathy presenting with clinical features of motor neuron disease with dementia and iron deposition in the motor cortex. Neuropsychology, 38(4), 372–379.

Hirano, M., Iritani, S., Fujishiro, H., Torii, Y., Kawashima, K., Sekiguchi, H., Habuchi, C., Yamada, K., Ikeda, T., Hasegawa, M., Ikeuchi, T., Yoshida, M., & Ozaki, N. (2020). Globular glial tauopathy type I presenting with behavioral variant frontotemporal dementia. Neurology, 51, 515–525. https://doi.org/10.1212/wnl.0000000000007668

Hyman, B. T., Phelps, C. H., Beach, T. G., Bigio, E. H., Cairns, N. J., Carrillo, M. C., Dickson, D. W., Dykaerts, C., Frosch, M. P., Masliah, E., Mirra, S. S., Nelson, P. T., Schneider, J. A., Thal, D. R., Thies, B., Trojanowski, J. Q., Vinters, H. V., & Montine, T. J. (2012). National institute on aging–Alzheimer’s association guidelines for the neuropathologic assessment of Alzheimer’s disease: A practical approach. Acta Neuropathologica, 123, 1–11. https://doi.org/10.1007/s00401-011-1910-3

Nelson, P. T., Alafuzoff, I., Bigio, E. H., Bouras, C., Braak, H., Cairns, N. J., Castellani, R. J., Crain, B. J., Davies, P., Tredici, K. D., Dykaerts, C., Frosch, M. P., Haroutunian, V., Hof, P. R., Hulette, C. M., Hyman, B. T., Iwatsubo, T., Jellinger, K. A., Jicha, G. A., … Beach, T. G. (2012). Correlation of Alzheimer disease neuropathologic changes with cognitive status: A review of the literature. Journal of Neuropathology & Experimental Neurology, 71, 362–381. https://doi.org/10.1097/NEN.0b013e3182501887

Ohara, S., Tsuyuzaki, J., Oide, T., Arai, H., Higuchi, S., Hasegawa, M., & Iwatsubo, T. (2002). A clinical and neuropathological study of an unusual case of sporadic tauopathy. A variant of corticobasal degeneration? Neuroscience Letters, 330(1), 84–88.

Ohsno, Y., Ikeda, T., Sakurai, K., Yamada, K., Tomonari, T., Iwasaki, Y., Yoshida, M., & Matsukawa, N. (2021). Rapid progression of white matter signal changes and frontotemporal atrophy in globular glial tauopathy. Journal of Neuropathology & Experimental Neurology, 80(5), 480–483.

Oniyike, C. U., & Diehl-Schmid, J. (2013). The epidemiology of frontotemporal dementia. International Review of Psychiatry, 25(2), 130–137.

Powers, J., Byrne, N., Ito, M., Takao, M., Yankoupoloulou, D., Spillantini, M., & Ghetti, B. (2003). A novel leukoencephalopathy associated with tau deposition primarily in white matter glia. Acta Neuropathologica, 106(2), 181–187.

Rohrer, J., Geser, F., Zhou, J., Gennatas, E., Sidhu, M., Trojanowski, J., Dearmond, S., Miller, B., & Seeley, W. (2010). TDP-43 subtypes are associated with distinct atrophy patterns in frontotemporal dementia. Neurology, 75(24), 2204–2211.

Rosas, H. D., Liu, A. K., Hersch, S., Glessner, M., Ferrante, R. J., Salat, D. H., van der Kouwe, A., Jenkins, B. G., Dale, A. M., & Fischl, B. (2002). Regional and progressive thinning of the cortical ribbon in Huntington’s disease. Neurology, 58, 695–701. https://doi.org/10.1212/wnl.58.5.695

Rusina, R., Csefalvy, Z., Kovacs, G. G., Keller, J., Javurková, A., & Matej, R. (2019). Globular glial tauopathy type I presenting as atypical progressive aphasia, with comorbid limbic-predominant age-related TDP-43 encephalopathy. Frontiers in Aging Neuroscience, 11, 336.

Salat, D. H., Buckner, R. L., Snyder, A. Z., Greve, D. N., Desikan, R. S., Busa, M., Morris, J. C., Dale, A. M., & Fischl, B. (2004). Thinning of the cerebral cortex in aging. Cerebral Cortex (New York, NY: 1991), 14, 721–30. https://doi.org/10.1093/cercor/bhh032

Tanaka, H., Kawakatsu, S., Toyoshima, Y., Miura, T., Mezaki, N., Mano, A., Sanpei, K., Kobayashi, R., Hayashi, H., Otani, K., Ikeuchi, T., Onodera, O., Kakita, A., & Takahashi, H. (2019). Globular glial tauopathy type II: Clinicopathological study of two autopsy cases. Neurology, 39, 111–119. https://doi.org/10.1212/wnl.12532
astrocytes, and severe degeneration of the cerebral white matter: A variant of corticobasal degeneration? *Acta Neuropathologica*, 109(3), 329–338.

Thal, D. R., Rüb, U., Orantes, M., & Braak, H. (2002). Phases of Aβ-deposition in the human brain and its relevance for the development of AD. *Neurology*, 58(12), 1791–1800.

Ulugut Erkoyun, H., Groot, C., Heilbron, R., Nelissen, A., van Rossum, J., Jutten, R., Koene, T., van der Flier, W. M., Wattjes, M. P., Scheltens, P., Ossenkoppele, R., Barkhof, F., & Pijnenburg, Y. (2020). A clinical-radiological framework of the right temporal variant of frontotemporal dementia. *Brain*, 143, 2831–2843. https://doi.org/10.1093/brain/awaa225

Veronelli, L., Makaretz, S. J., Quimby, M., Dickerson, B. C., & Collins, J. A. (2017). Geschwind Syndrome in frontotemporal lobar degeneration: Neuroanatomical and neuropsychological features over 9 years. *Cortex*, 94, 27–38.

Waxman, S. G., & Geschwind, N. (1975). The interictal behavior syndrome of temporal lobe epilepsy. *Archives of General Psychiatry*, 32 (12), 1580–1586.

Whitwell, J., Jack, C., Parisi, J., Senjem, M., Knopman, D., Boeve, B., Rademakers, R., Baker, M., Petersen, R., & Dickson, D. (2010). Does TDP-43 type confer a distinct pattern of atrophy in frontotemporal lobar degeneration? *Neurology*, 75(24), 2212–2220.