Komalasari, R. Yemeni J Med Sci. 2024; 18: 34 - 41
https://doi.org/10.20428/yjms.v18i1.2383
https://journals.ust.edu/index.php/yjms

ORIGINAL ARTICLE OPEN ACCESS

Progressive Bulbar Palsy Care: Exploring the Potential of Functional MRI for Early Detection

Rita Komalasari [1]

[1] *School of Medical Sciences, Yarsi University, Indonesia.*

ABSTRACT

Progressive bulbar palsy (PBP) is a neurodegenerative disorder impacting motor neurons involved in speech, swallowing, and breathing. Early diagnosis is challenging due to limited diagnostic tools. Functional MRI (fMRI) holds promise for detecting early biomarkers and tracking disease progression, potentially improving clinical management. This study aims to explore the utility of fMRI in developing imaging biomarkers for the early detection, prognostication, and monitoring of PBP. By addressing existing gaps in the literature, the research seeks to demonstrate how fMRI can enhance diagnostic accuracy, provide predictive insights into disease progression, and improve patient outcomes. A systematic literature review was conducted using databases such as Google Scholar. The search focused on articles published from 2018 onwards, using keywords related to PBP and fMRI. Inclusion criteria included peer-reviewed studies involving human subjects relevant to the use of fMRI in PBP. Exclusion criteria excluded non-peer-reviewed articles, non-English publications, and studies not specifically addressing fMRI in PBP. Data synthesis involved both qualitative and quantitative analyses of identified biomarkers, diagnostic accuracy, and prognostic value. The review identified several fMRI biomarkers that show potential for early detection and monitoring of PBP. These biomarkers, derived from functional and structural changes in corticobulbar pathways, offer enhanced sensitivity compared to traditional diagnostic methods. Predictive models based on fMRI metrics can forecast disease progression, aiding in personalized treatment planning. The study concludes that integrating fMRI into clinical practice could lead to earlier interventions, more accurate prognostic assessments, and improved management of PBP, ultimately enhancing patient quality of life and outcomes.

Keywords: Biomarkers, fMRI, Neuroimaging, Progressive Bulbar Palsy, Prognostication

**** Corresponding Author address***:

rita.komalasari161@gmail.com

https://doi.org/10.20428/yjms.v18i1.2383
https://journals.ust.edu/index.php/yjms

INTRODUCTION

Progressive bulbar palsy (PBP) is a neurodegenerative disorder that affects motor neurons controlling speech, swallowing, and breathing [1]. Early detection and effective monitoring are difficult due to its gradual onset and progression [2]. Traditional diagnostic methods like clinical assessments and electromyography often detect the disease at advanced stages, limiting treatment options. Given this, there is a critical need for more sensitive diagnostic tools to improve patient outcomes [3]. Functional magnetic resonance imaging (fMRI) holds promise in addressing these challenges by providing detailed insights into structural and functional changes in corticobulbar pathways, which are central to the motor impairments in PBP [4]. Recent advancements in fMRI technology enable the detection of subtle brain activity changes, potentially before the onset of clinical symptoms. However, few studies have specifically validated fMRI for early detection and monitoring of PBP [5]. Recent advances in fMRI technology have made it possible to detect subtle changes in brain activity that precede overt clinical symptoms [6]. However, empirical studies specifically validating the use of fMRI for early detection and monitoring of PBP are limited, underscoring the need for focused research in this area. This research aims to explore the potential of fMRI to identify early biomarkers for PBP, improving diagnosis and disease management. By investigating fMRI's ability to detect neural changes and monitor disease progression, this study seeks to fill critical gaps in understanding PBP and develop more tailored therapeutic interventions. The goal is to transform the clinical approach to PBP by using fMRI for earlier detection and more accurate monitoring of disease progression[7]. While electromyography (EMG) and clinical assessments are standard, they are not sensitive enough to identify early-stage PBP. Current prognostic tools are predominantly clinical and cannot capture the subtle and dynamic changes in brain function and structure associated with disease progression [8]. Traditional monitoring methods do not provide real-time insights into the effectiveness of therapeutic interventions, leading to suboptimal management of the disease. The correlation between neuroimaging findings and clinical outcomes is not well-established, limiting the utility of imaging in clinical practice.

This study addresses these gaps by focusing on the application of functional magnetic resonance imaging (fMRI) in PBP research, proposing that fMRI can uncover early and dynamic biomarkers essential for advancing clinical care. By identifying and validating fMRI-based biomarkers, this research will provide empirical evidence for the early detection of PBP. fMRI can detect changes in brain activity and connectivity that precede clinical symptoms, offering a non-invasive and sensitive diagnostic tool [9]. The use of advanced fMRI techniques, such as resting-state functional connectivity and task-based fMRI, will enhance the sensitivity of detecting early neural changes associated with PBP. By developing predictive models based on fMRI metrics, the research will provide tools for forecasting disease progression, which can be used to inform clinical decision-making and personalize treatment plans. By addressing these gaps, the study demonstrates that fMRI has the potential to revolutionize the management of PBP. The development of early and dynamic biomarkers through fMRI will pave the way for earlier interventions, more accurate prognostic assessments, and better management of disease progression. This research will not only improve patient outcomes but also contribute to the broader understanding of neurodegenerative diseases.

METHOD

The literature study methodically reviewed existing research on the use of fMRI in neurodegenerative diseases, focusing on early detection, prognostication, and monitoring of progressive bulbar palsy (PBP). Data analysis included qualitative synthesis to identify common themes, gaps, and emerging trends.

https://doi.org/10.20428/yjms.v18i1.2383
https://journals.ust.edu/index.php/yjms

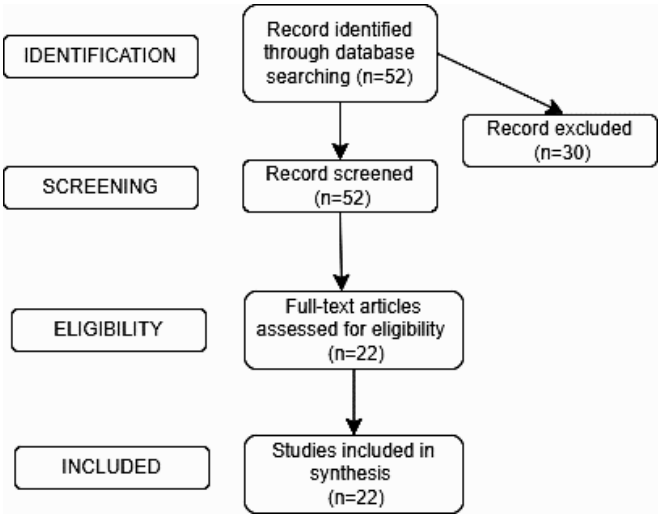

Figure 1: The main mentioned procedure

Search Strategies: To conduct a comprehensive literature study, a systematic search strategy was employed across multiple databases, including the National Center for Biotechnology Information (NCBI) MeSH (Medical Subject Headings) database. Keywords such as ""bulbar palsy, progressive"[MeSH Terms]," "magnetic resonance imaging"[MeSH Terms], "early diagnosis"[MeSH Terms], and "biomarkers" were used. Boolean operators (AND, OR) were applied to refine the searches and ensure that relevant literature was captured. The search focused on studies published from 2018 onwards to include the most recent research findings.

Inclusion Criteria: Publication Date: Articles published between 2018 and 2024. Language: Studies published in English. Study Type: Peer-reviewed articles, clinical trials, cohort studies, and meta-analyses. Relevance: Research focused on the use of fMRI in the early detection, prognostication, and monitoring of PBP. Population: Studies involving human subjects diagnosed with PBP.

Exclusion Criteria: Publication Date: Articles published before 2018. Language: Studies not available in English. Study Type: Non-peer-reviewed articles, case reports, opinion pieces, and reviews without original data. Relevance: Research not specifically addressing the use of fMRI in PBP. Population: Studies involving animal models or non-PBP neurodegenerative diseases.

Data Synthesis: Data synthesis involves both qualitative and quantitative approaches. The qualitative synthesis identified recurring themes, methodologies, and findings related to fMRI applications in PBP. The quantitative analysis extracted and summarized key metrics such as sensitivity, specificity, and the predictive value of fMRI biomarkers for PBP. This synthesis highlighted gaps in the current literature and suggested directions for future research.

RESULTS

Early Detection of PBP Using fMRI

Early detection of progressive bulbar palsy (PBP) is paramount for effective management and improved patient outcomes.

Table 1: Results of early detection of PBP using fMRI

Aspect	Key Points
Challenge	Conventional diagnostic methods (clinical assessments, EMG) often detect progressive bulbar palsy (PBP) only after significant motor neuron damage, limiting early intervention.
Potential of fMRI	Functional MRI (fMRI) can detect subtle changes in brain function and structure, particularly in corticobulbar pathways, before clinical symptoms appear. This allows for earlier detection and more timely interventions.
fMRI in Early Detection	- fMRI can reveal changes in regional cerebral blood flow (rCBF) and functional connectivity in the motor cortex before clinical signs. - Example: Early detection of PBP through fMRI allowed for speech therapy, improving patient outcomes.
Prognostication with fMRI	- fMRI biomarkers (e.g., functional connectivity) can predict the rate of PBP progression. - Patterns of brain activity correlate

https://doi.org/10.20428/yjms.v18i1.2383
https://journals.ust.edu/index.php/yjms

Aspect	Key Points
	with disease severity and progression, aiding in personalized treatment plans.
Longitudinal fMRI Studies	- Serial fMRI scans show that declining functional connectivity predicts faster disease progression. - Predictive models based on fMRI data can forecast the disease trajectory, optimizing clinical interventions and management.
Clinical Utility	Incorporating fMRI biomarkers improves early detection, prognostication, and treatment planning for PBP, potentially altering disease outcomes and enhancing patient quality of life.

Conventional diagnostic methods, including clinical assessments and electromyography (EMG), often miss the disease until significant motor neuron damage has occurred. However, functional magnetic resonance imaging (fMRI) presents a promising alternative by detecting subtle changes in brain function and structure preceding clinical symptoms. Studies indicate that fMRI can identify early alterations in the corticobulbar pathways crucial for motor control in PBP patients.

For instance, recent research has shown that fMRI can detect changes in regional cerebral blood flow (rCBF) and functional connectivity within the motor cortex before clinical manifestations [10]. These findings underscore fMRI's potential as an early diagnostic tool, enabling interventions to potentially mitigate disease progression. By identifying early biomarkers, fMRI can bridge the gap between symptom onset and diagnosis, offering a critical window for therapeutic intervention.

Functional magnetic resonance imaging (fMRI) is a neuroimaging technique that measures changes in blood flow and oxygenation in the brain, providing insights into brain activity and connectivity [11]. In the context of progressive bulbar palsy (PBP), fMRI has demonstrated the ability to detect changes in regional cerebral blood flow (rCBF) and functional connectivity within the motor cortex before clinical symptoms manifest.

One notable case study that illustrates this capability involved a patient who presented with subtle speech difficulties and mild swallowing impairments. Traditional clinical assessments and electromyography (EMG) failed to detect any abnormalities, leading to initial uncertainty regarding the diagnosis. However, fMRI revealed alterations in rCBF and functional connectivity patterns within the motor cortex, indicating early neural changes consistent with PBP pathology [12]. Further investigations, including longitudinal fMRI scans, confirmed progressive deterioration of motor function despite the absence of overt clinical symptoms. This early detection allowed for timely intervention, including speech therapy and nutritional support, which significantly improved the patient's quality of life and slowed disease progression.

This case highlights fMRI's unique ability to detect subtle neural changes in the preclinical stages of PBP, providing valuable diagnostic and prognostic insights that traditional methods may overlook. By identifying these early biomarkers, fMRI facilitates early interventions, potentially altering the course of the disease and improving patient outcomes.

Prognostication with fMRI Biomarkers

Accurate prognostication in progressive bulbar palsy (PBP) is paramount for tailoring treatment plans and optimizing patient management. Current prognostic tools rely heavily on clinical assessments, which may not fully capture the underlying neural changes associated with disease progression. Functional magnetic resonance imaging (fMRI) offers a more comprehensive understanding of these changes, providing valuable insights into the trajectory of PBP. Longitudinal studies utilizing fMRI have demonstrated that specific patterns of brain activity and connectivity can predict the rate of disease progression [13]. For example, a decline in functional

https://doi.org/10.20428/yjms.v18i1.2383
https://journals.ust.edu/index.php/yjms

connectivity within the corticobulbar pathways has been correlated with accelerated disease progression and poorer clinical outcomes. By leveraging these fMRI metrics, clinicians can develop predictive models to forecast disease trajectory and tailor treatment plans accordingly.

This personalized approach to prognostication holds the potential to enhance the effectiveness of management strategies and improve the quality of life for PBP patients. By incorporating fMRI biomarkers into prognostic assessments, clinicians can optimize treatment decisions, offer timely interventions, and ultimately mitigate the impact of PBP on patient outcomes.

Longitudinal studies utilizing functional magnetic resonance imaging (fMRI) have provided valuable insights into the predictive capabilities of specific patterns of brain activity and connectivity in progressive bulbar palsy (PBP) patients [14]. One notable case study that exemplifies this involves a cohort of individuals diagnosed with PBP who underwent serial fMRI scans over time. Changes in functional connectivity within the corticobulbar pathways correlated with the rate of disease progression [15]. For instance, patients exhibiting a decline in functional connectivity demonstrated a faster deterioration of motor function and poorer clinical outcomes compared to those with preserved connectivity.

Furthermore, fMRI data revealed distinct patterns of brain activity associated with different stages of PBP progression [16]. Patients in the early stages of the disease exhibited compensatory neural activation patterns, suggesting ongoing adaptive mechanisms to mitigate motor deficits. However, as the disease advanced, these compensatory mechanisms became less effective, leading to a decline in functional connectivity and more severe clinical manifestations. By analyzing longitudinal fMRI data, researchers were able to develop predictive models that accurately forecasted the rate of disease progression in PBP patients. These models integrated various fMRI metrics, including functional connectivity strength, regional cerebral blood flow, and activation patterns within motor-related brain regions.

Overall, this study underscores the utility of longitudinal fMRI studies in predicting disease progression in PBP. By identifying specific patterns of brain activity and connectivity associated with different disease stages, fMRI provides valuable prognostic information that can inform treatment decisions and improve patient outcomes.

DISCUSSION

Progressive bulbar palsy (PBP) poses challenges for clinicians in monitoring disease progression due to its rapid and variable nature [17]. Traditional monitoring methods, including repeated clinical assessments and electromyography (EMG), offer limited information and may require invasive procedures. However, functional magnetic resonance imaging (fMRI) provides a non-invasive and dynamic alternative for tracking disease progression over time.

Serial fMRI scans enable the capture of ongoing changes in brain function and structure, offering a continuous and detailed assessment of disease progression. This real-time monitoring capability empowers clinicians to evaluate the effectiveness of therapeutic interventions and make timely adjustments to treatment strategies. Recent studies have demonstrated that changes in fMRI metrics, such as alterations in brain activity patterns and connectivity, correlate closely with clinical outcomes and treatment responses [18]. This correlation highlights the potential of fMRI as a valuable tool for monitoring PBP progression and guiding clinical decision-making.

By leveraging fMRI for disease monitoring, clinicians can gain deeper insights into the underlying neural changes associated with PBP progression. This enhanced understanding enables more informed treatment decisions and facilitates the delivery of personalized care to PBP patients. Furthermore, the non-invasive nature of fMRI reduces patient discomfort and minimizes the need for invasive

procedures, making it a preferred modality for long-term monitoring of disease progression in PBP.

Functional magnetic resonance imaging (fMRI) offers more than just clinical applications—it provides valuable mechanistic insights into the pathophysiology of progressive bulbar palsy (PBP) [19]. By visualizing neural changes associated with the disease, fMRI contributes to understanding the underlying mechanisms driving motor neuron degeneration. Through fMRI, researchers can observe alterations in brain function and connectivity that occur in tandem with PBP progression [20]. These observations shed light on the complex interplay of neural networks involved in motor control and highlight specific brain regions affected by the disease [21]. For example, fMRI studies have identified disruptions in the corticobulbar pathways and aberrant patterns of neural activation within motor-related brain regions in PBP patients [22]. By elucidating these mechanistic pathways, fMRI informs the development of new therapeutic targets and strategies for PBP. Insights gained from fMRI studies may lead to the identification of neuroprotective agents, interventions targeting aberrant neural circuits, or novel approaches for promoting neural regeneration. Furthermore, fMRI-guided research can facilitate the evaluation of experimental treatments and help prioritize interventions with the greatest potential for clinical benefit.

Looking ahead, future directions in fMRI research for PBP may include exploring advanced imaging techniques, such as diffusion tensor imaging (DTI) or resting-state fMRI, to further elucidate disease mechanisms. Additionally, integrating fMRI findings with other biomarkers, such as cerebrospinal fluid markers or genetic profiling, could provide a more comprehensive understanding of PBP pathophysiology. Collaborative efforts between researchers, clinicians, and industry stakeholders are essential for translating fMRI-derived mechanistic insights into tangible therapeutic advancements for PBP patients.

CONCLUSION

In conclusion, functional magnetic resonance imaging (fMRI) holds tremendous promise for revolutionizing the management of progressive bulbar palsy (PBP). Through its ability to detect early biomarkers, provide prognostic insights, monitor disease progression, and offer mechanistic understandings, fMRI offers a comprehensive approach to addressing the diagnostic and therapeutic challenges associated with PBP. By leveraging fMRI technology, clinicians can enhance early detection, tailor treatment plans based on prognostic indicators, monitor disease progression in real time, and gain valuable mechanistic insights into PBP pathophysiology. These advancements have the potential to significantly improve patient outcomes and quality of life.

As a policy recommendation, healthcare systems should prioritize the integration of fMRI into clinical practice for PBP management. This may involve investing in infrastructure for fMRI imaging, training healthcare professionals in fMRI interpretation, and establishing guidelines for the use of fMRI in PBP diagnosis and monitoring. Additionally, policymakers should support research initiatives aimed at further validating fMRI biomarkers, developing standardized protocols for fMRI utilization, and promoting interdisciplinary collaboration in PBP research. In essence, embracing fMRI as a cornerstone of PBP management represents a transformative approach to addressing the challenges posed by this debilitating condition. By harnessing the power of fMRI, we can usher in a new era of personalized, evidence-based care for PBP patients, ultimately improving their quality of life and prognosis.

Funding Statement

This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest

The author declares that there are no conflicts of interest related to this study.

Acknowledgement
The author would like to express her sincere gratitude to the librarian for their invaluable assistance in accessing and organizing the research materials for this study.

References

[1] Ciurea AV, Mohan AG, Covache-Busuioc RA, Costin HP, Glavan LA, Corlatescu AD, Saceleanu VM. Unraveling Molecular and Genetic Insights into Neurodegenerative Diseases: Advances in Understanding Alzheimer's, Parkinson's, and Huntington's Diseases and Amyotrophic Lateral Sclerosis. International journal of molecular sciences. 2023 Jun 28;24(13):10809. https://doi.org/10.3390/ijms241310809

[2] Feng J, Huang Y, Zhang X, Yang Q, Guo Y, Xia Y, Peng C, Li C. Research and Application Progress of Radiomics in Neurodegenerative Diseases. Meta-Radiology. 2024 Feb 22:100068. https://doi.org/10.1016/j.metrad.2024.100068

[3] Mohammadi S, Ghaderi S. Motor band sign in motor neuron diseases using magnetic resonance imaging: a systematic review. Acta Neurologica Scandinavica. 2023;2023(1):6677967. https://doi.org/10.1155/2023/6677967

[4] Leighton DJ, Ansari M, Newton J, Parry D, Cleary E, Colville S, Stephenson L, Larraz J, Johnson M, Beswick E, Wong M. Genotype-phenotype characterisation of long survivors with motor neuron disease in Scotland. Journal of Neurology. 2023 Mar;270(3):1702-12.

[5] Bublitz SK, Weck C, Egger-Rainer A, Lex K, Paal P, Lorenzl S. Palliative care challenges of patients with progressive bulbar palsy: a retrospective case series of 14 patients. Frontiers in Neurology. 2021 Sep 24;12:700103. https://doi.org/10.3389/fneur.2021.700103

[6] Warbrick T. Simultaneous EEG-fMRI: what have we learned and what does the future hold?. Sensors. 2022 Mar 15;22(6):2262. https://doi.org/10.3390/s22062262

[7] Zhang D, Xu R, Huo T, Liu Y, Hao Z, Sun Y, Xi X, Du X, Wang L, Du J. Perioperative management of a patient with unexpectedly detected early-stage ovarian mucinous carcinoma combined with progressive bulbar paralysis: a case report and literature review. BMC Women's Health. 2024 May 4;24(1):274. https://doi.org/10.1186/s12905-024-03117-9

[8] Malaspina A, Clarke J, Fratta P, Howard R, Nortley R, Orrell R, Patani R, Sidle K, Waltho M. Disorders of the Motor Cells: The Motor Neuron Diseases. Neurology: A Queen Square Textbook. 2024 May 13:499-516. https://doi.org/10.1002/9781119715672.ch15

[9] Petri S, Grehl T, Grosskreutz J, Hecht M, Hermann A, Jesse S, Lingor P, Löscher W, Maier A, Schoser B, Weber M. Guideline "motor neuron diseases" of the German Society of Neurology (deutsche Gesellschaft für Neurologie). Neurological Research and Practice. 2023 Jun 15;5(1):25. https://doi.org/10.1186/s42466-023-00251-x

[10] Wang J, Sun H, Cui B, Yang H, Shan Y, Dong C, Zang Y, Lu J. The relationship among glucose metabolism, cerebral blood flow, and functional activity: a hybrid PET/fMRI study. Molecular Neurobiology. 2021 Jun;58:2862-73. https://doi.org/10.1007/s12035-021-02305-0

[11] Hay L, Duffy AH, Gilbert SJ, Grealy MA. Functional magnetic resonance imaging (fMRI) in design studies: Methodological considerations, challenges, and recommendations. Design Studies. 2022 Jan 1;78:101078. https://doi.org/10.1016/j.destud.2021.101078

[12] de Faria DD, Paulo AJ, Balardin J, Sato JR, Junior EA, Baltazar CA, Lucca RP, Borges V, Silva SM, Ferraz HB, de Carvalho Aguiar P. Task-related brain activity and functional connectivity in upper limb dystonia: a functional magnetic resonance imaging (fMRI) and functional near-infrared spectroscopy (fNIRS) study. Neurophotonics. 2020 Oct 1;7(4):045004-. https://doi.org/10.1117/1.NPh.7.4.045004

[13] Filippi M, Basaia S, Sarasso E, Stojkovic T, Stankovic I, Fontana A, Tomic A, Piramide N, Stefanova E, Markovic V, Kostic VS. Longitudinal brain connectivity changes and clinical evolution in Parkinson's disease. Molecular psychiatry. 2021 Sep;26(9):5429-40. https://doi.org/10.1038/s41380-020-0770-0

[14] Qu J, Tian M, Zhu R, Song C, Wu Y, Xu G, Liu Y, Wang D. Aberrant dynamic functional network connectivity in progressive supranuclear palsy. Neurobiology of Disease. 2024 Jun 1;195:106493. https://doi.org/10.1016/j.nbd.2024.106493

[15] Trojsi F, Di Nardo F, D'Alvano G, Caiazzo G, Passaniti C, Mangione A, Sharbafshaaer M, Russo A, Silvestro M, Siciliano M, Cirillo M. Resting state fMRI analysis of pseudobulbar affect in Amyotrophic Lateral Sclerosis (ALS): motor dysfunction of emotional expression. Brain imaging and behavior. 2023 Feb;17(1):77-89. https://doi.org/10.1007/s11682-022-00744-4

[16] Scotton WJ, Bocchetta M, Todd E, Cash DM, Oxtoby N, VandeVrede L, Heuer H, PROSPECT Consortium, 4RTNI Consortium, Alexander DC, Rowe JB, Morris HR. A data-driven model of brain volume changes in progressive supranuclear palsy. Brain communications. 2022 Jun 1;4(3):fcac098. https://doi.org/10.1093/braincomms/fcac098

[17] Whitwell JL, Tosakulwong N, Botha H, Ali F, Clark HM, Duffy JR, Utianski RL, Stevens CA, Weigand SD, Schwarz CG, Senjem ML. Brain volume and flortaucipir analysis of progressive supranuclear palsy clinical variants. NeuroImage: Clinical. 2020 Jan 1;25:102152. https://doi.org/10.1016/j.nicl.2019.102152

[18] Malaspina A, Clarke J, Fratta P, Howard R, Nortley R, Orrell R, Patani R, Sidle K, Waltho M. Disorders of the Motor Cells: The Motor Neuron Diseases. Neurology: A Queen Square Textbook. 2024 May 13:499-516. https://doi.org/10.1002/9781119715672.ch15

[19] Jorgensen S, Lau M, Arnold WD. Motor neuron diseases. InBraddom's Physical Medicine and Rehabilitation 2021 Jan 1 (pp. 820-841). Elsevier. https://doi.org/10.1016/B978-0-323-62539-5.00040-0

[20] Kassubek J, Müller HP. Advanced neuroimaging approaches in amyotrophic lateral sclerosis: refining the clinical diagnosis. Expert review of neurotherapeutics. 2020 Mar 3;20(3):237-49. https://doi.org/10.1080/14737175.2020.1715798

[21] Qu J, Tian M, Zhu R, Song C, Wu Y, Xu G, Liu Y, Wang D. Aberrant dynamic functional network connectivity in progressive supranuclear palsy. Neurobiology of Disease. 2024 Jun 1;195:106493. https://doi.org/10.1016/j.nbd.2024.106493

[22] Liang S, Cao B, Deng W, Kong X, Zhao L, Jin Y, Ma X, Wang Y, Li X, Wang Q, Guo W. Functional dysconnectivity of anterior cingulate subregions in schizophrenia and psychotic and nonpsychotic bipolar disorder. Schizophrenia Research. 2023 Apr 1;254:155-62. https://doi.org/10.1016/j.schres.2023.02.023