Overview of Neurodegenerative Disorders

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Abstract Neurodegenerative disorders (NDDs) place a significant medical and public health burden on people all over the world. Three important NDDs are Alzheimer's disease (AD), Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS), spinocerebellar ataxia (SCA), epilepsy, Lewy body disease, Huntington's Disorder (HD), and cerebral aneurysm. The number of cases is anticipated to keep increasing in the near future as life expectancies in many nations rise, as the prevalence and incidence of many diseases dramatically increase with age. With a few notable exceptions, it is difficult to determine how genetic and environmental factors interact causally. While identifying high-risk genes for familial NDDs, classifying disease prognostic factors, determining common genetic variants that may predict susceptibility to non-familial forms of these diseases, and quantifying environmental exposures have all been accomplished using molecular epidemiology approaches. Brief overviews of the epidemiologic features of PD, AD, ALS, SCA, epilepsy, Lewy body disease, HD, and cerebral aneurysm, are provided in this chapter, can help in diagnosis of underlying disease and their associated risk factors, potentially improving medical care and, in the end, illness prevention.

Keywords Amyotrophic lateral sclerosis (ALS) · Neurodegenerative disorders · Parkinson's disease · Alzheimer's disease

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1 Introduction

Neurological disorders affect millions of people globally [1]. Progressive disorder of synapses, neuron, glial cells and their networks are the characteristics of neurodegenerative diseases (NDDs). The accumulation of physiochemically altered alternatives of physiological proteins in the nervous system is a critical element of NDDs. Significantly, neurons as well as glial cells collect these pathological proteins [2]. NDDs represent a serious health risk to humans. Certain age-related illnesses are becoming more widespread, in part due to the large increase in the population of the elderly [3].

Alzheimer's disease (AD), spinocerebellar ataxias (SCA), Huntington's disease (HD), amyotrophic lateral sclerosis (ALS), and Parkinson's disease (PD), epilepsy, cerebral aneurysm, and Lewy body disease are the examples of neurodegenerative diseases. The pathophysiology among these disorders differs, a few affecting memory and cerebral impairments and others factors that affect a person's ability to move, speak, and respire [4–7].

Despite the fact that age is the single most important risk factor for the development of all NDs, current studies have shown that a person's genetic make-up in addition to environmental factors might increase their risk for NDDs [8]. AD, PD, and ALS, among others, are incessantly progressive and evenly potentially lethal neurological diseases distinguished by irretrievable neuron loss and gliosis. Although dementia occurrence as a proportion of the aged has reduced in developed countries, the overall incidence of dementia is rising as the population ages [9]. External factors, nutrient deficiencies, genetic factors, infectious diseases, lifestyle-related causes, and physical injuries can all contribute to the above-mentioned disorders [10].

A physiological protein's structural conformation variations, results in impaired function or neurotoxic extra or intracellular formation. Mutations in the encoding genes have been related to inherited diseases. Molecular pathological, biochemical, and hereditary studies resulted in the reclassification of several dysfunction, along with the opening of totally different avenues for biomarker development or targeted therapies [11].

2 Neurodegenerative Disorders (NDDs)

2.1 Alzheimer's Disease

The most severe group of neurological disorders, AD accounts for over two-thirds of dementia cases in individuals with 65 years of age and older [10, 12, 13]. According to WHO, research estimates that 50 million individuals worldwide have some form of dementia, with AD responsible for 60–70% of those occurrences [14]. Around 5.8 million Americans already suffer with Alzheimer's disease, and by the middle of the next century, that figure is predicted to reach 13.8 million [15]. The development

of amyloid plaques formed of aggregated amyloid beta (Ab), neurofibrillary tangles, which are intracellular collections of hyperphosphorylated tau protein, and brain atrophy brought on by the loss of synapses and neurons are all made possible by a pathological explanation of AD [16]. Basically two neuropathological features of AD are (i) extracellular plaques made of the 40–42 residue Aβ peptide and (ii) neurofibrillary tangles, which are constituted of abnormally phosphorylated Tau protein [17, 18]. More and more data suggests that Aβ peptides build up inside neurons in addition to the parenchyma's well-known amyloid plaques accumulation [19]. To explain this complex condition, a number of ideas have been proposed, including the cholinergic theory, the inflammatory hypothesis, the tau hypothesis, and the Ab hypothesis [20]. According to the tau hypothesis, abnormally high levels of tau phosphorylation cause adult tau to transform into PHF-tau (paired helical filament) and neurofibrillary tangles [21]. In the pathological condition, tau is more frequently hyperphosphorylated, which causes protein denaturation and ultimately disrupts with cytoplasmic function and axonal transport, perhaps leading to apoptosis [10]. Therapeutic strategies for AD concentrate on lowering levels of Aβ oligomers and phosphorylated tau, minimizing OS, and maintaining epigenetic alterations [22, 23]. The majority of anti-AD medications use components with neuroprotective, anti-inflammatory, and antioxidant characteristics [24, 25].

2.2 Parkinson's Disease

PD is one of the diseases, which is related to brain. This disease is related to aging, which causes impairment in the various regions of the brain. This disease can cause seizures, balancing problems while standing, slow movements of limbs, tremors etc. This can be inherited or can be caused in humans due to unknown reasons [26]. This type of disease has no cure but there are different treatments available to control its effect on to the body. This disease affects basal ganglia of brain. As this specific area starts deteriorating, the person starts losing abilities to perform normal functions [27]. In normal conditions, our brain uses some chemical messengers known as neurotransmitters to send messages to brain cells and communicate with each other but person with Parkinson's lacks dopamine, which is one of the important neurotransmitters. So, when your brain sends signals to activate muscles to move or perform certain action via chemical messengers, it fails to do so because of dopamine insufficiency. Due to this body feels tremors and slow body movements known as Parkinson's disease [28].

2.2.1 Symptoms

- Bradykinesia means person shows typically slow movements.
- Tremors-continuous shaking of muscles even the body is at resting.
- Unstable posture.

- Less blinking than usual.
- Micrographia
- Dysphagia [26].

2.2.2 Stages of Parkinson's Disease

This disease occurs in different types of stages. At the initial stage, mild symptoms show up like slow movements and then the symptoms come in stages [27].

Stage I

This is the very first initial stage of Parkinson's disease. In this stage only mild symptoms appear which includes slow body part movements, difficulty while walking, changes in posture, changes in facial expressions etc. Also, one side of the body is affected in initial period [27].

Stage II

In this stage patient faces some serious disabilities related to walking, tremors, difficult speech, rigidity, or muscle spasms on both sides of the body unlike Stage I in which it affects one side of the body [27].

Stage III

It is considered mid-stage of Parkinson's disease. In this specific stage, person starts facing serious illness and most of the body shows tremors and body balancing issues. Drooling and dysphagia are other symptoms related to this stage. Falls commonly happens [27].

Stage IV

At this stage, symptoms move from mild to severity with serious consequences. Person is unable to walk without support or walker and is unable to perform daily activities [27].

Stage V

This is the most serious and end stage of this disease. Person is unable to stand and is bed ridden. To perform daily activities is impossible and assistance is required 24 h. Person can experience episodes of hallucinogens and delusions [27].

2.3 Huntington Disorder

Another type of inherited NDDs condition known as HD causes irrational behaviour, emotional problems, and cognitive decline [28, 29]. Less often occurring juvenile HD begins in infancy or adolescence. It also leads to changes in the thoughts and emotions as well as problems with movement. Some signs of the juvenile form include rigidity,

slurred speech, drooling, slow movements, and frequent falls. We may also state that these are the first symptoms to manifest [30]. Academic achievement declines as one's capacity for cognition and reasoning weakens. This disorder is also known as Huntington chorea because it is likely to be associated with basal ganglia and causes hyperkinetic movement disorder known as chorea. As this disorder reaches to the later stage, more prominent and specific symptoms come up of involuntary body movements. After the person is suffers from it than the physical activity of the patient gradually worsens making it difficult for person to speak [31].

2.4 Lewy Body Disease

The protein alpha-synuclein abnormally accumulates in the brain in this condition. The chemical structure of the brain is altered by these Lewy body deposits, and this alteration can result in issues with cognition, behaviour, movement, and mood. One of the most common forms of dementia is Lewy body dementia [32]. It is a kind of progressive disorder which get worsens over the time with symptoms gradually increased and confused with other brain disorders. In early stage of LWD, person can work normally but with the worsening of the disease person has decline thinking and movement abilities [33].

2.5 Cerebral Aneurysm

It is an abnormal localised dilatation of a cerebral artery caused by thinning of the inner muscular layer (the intima) of the blood vessel wall [34]. The vessel dilates in a way that feels like a "blister," which can thin out and suddenly explode. The resulting bleeding into the region around the brain is known medically as a subarachnoid haemorrhage (SAH) [35]. Such haemorrhage could cause a stroke, unconsciousness, or even death. However, several factors, are believed to contribute in the development of cerebral aneurysms like Hypertension (high blood pressure), smoking cigarettes, birth defect or genetic predisposition, blood vessel damage or trauma, a side effect of certain blood illnesses [36]. An extension of the blood artery wall that affects all of the wall's layers is considered a genuine aneurysm. Saccular and fusiform aneurysms are the two most well-known varieties, whereas mycotic, pseudo, and blister aneurysms are more uncommon. The majority of aneurysms are sporadic; however they can also be brought on by other illnesses such Ehlers-Danlos syndrome, fibromuscular dysplasia (FMD), polycystic kidney disease, and Marfan's syndrome [3, 37].

2.6 Epilepsy

It is a disorder when a person gets continuous or repeated seizures. According to standard definitions, a seizure is a transient interruption in the electrical activity of the brain that results in an abrupt change in behaviour [38]. Ordinarily, the brain generates tiny electrical impulses with a known sequence [39, 40]. Neurotransmitters are chemical messengers that transfer these messages along neurons, the network of nerve cells in the brain, and all over the whole body [41]. When these brain electrical signals become disrupted due to any reasons results in recurrent seizures and affects persons consciousness, movements, and muscle spasms [42, 43].

2.7 Spinocerebellar Ataxia (SCA)

This is another type of neurogenerative disorder in which ataxia is a symptom not a disease. Ataxia means poor coordination of the movements of different parts of the body. Person has an unsteady and uncoordinated walking. Also, ataxia affects movement of fingers, hands, spasm, and sometimes eye movements [44]. Most frequently, the cerebellum, that regulates motor coordination in the brain, is harmed, or shrinks (atrophy) as a result of ataxia [45]. The two important types of ataxia include congenital and acquired ataxia. Congenital ataxia is an ataxia, which passed from family. This is also known as inherited ataxia. The majority of hereditary ataxia types are inherited in an autosomal dominant form, while a small number (such as Friedreich ataxia) are inherited in an autosomal recessive style [44]. Acquired ataxia is a type which is caused due to some environmental factors like tumor, injury to the brain, stroke, swelling etc. Acquired ataxia is not passed on to offspring or children so there is no increased risk of ataxia in children [46, 47].

2.8 Amyotrophic Lateral Sclerosis (ALS)

Upper and lower motor neurons both degenerate in ALS, also known as motor neuron disease (MND), which results in muscle weakening and eventually paralysis [48]. Until recently, ALS was primarily categorized as belonging to the neuromuscular domain, however newer imaging and neuropathological studies have shown that the non-motor neuraxis is involved in disease pathology [49]. Although a small percentage of ALS patients have a family disease and carry gene abnormalities that affect many aspects of neuronal function, the processes underlying the disease's development in the majority of individuals are still poorly understood [50]. For ALS, there are two potential disease-modifying treatments that may decrease the disease's development, although most symptomatic treatments, such as speech therapy for dysarthria and the use of muscle relaxants for spasticity are used to manage patients [51].

3 Conclusion

Significant adverse effects can result from conventional pharmaceutical therapies for NDDs. Currently, improvements in the research of gene replacement and addition, as well as stem cell therapies, offer effective, promising therapies for a wide range of diseases. The recent translation of several of these medications into clinical trials and the growing importance of preclinical research have set the stage for continued improvement, even if there is still more work to be done. Future clinical approaches for treating NDD may heavily rely on the use of stem cells and gene therapy to replace damaged neurons and provide neuroprotective and neurorestorative effects. Additionally, recent technological developments utilising nanoparticles and hydrogels have increased the efficacy of drug delivery and regeneration therapy. Hence, it's expected that brain replacement and regenerative therapies will soon be successfully used in the therapeutic setting.

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Conflict of Interest None.

References

1. Cheong, K.H., Acharya, U.R.: Automated detection of schizophrenia using nonlinear signal processing methods. Artif. Intell. Med. (2019). https://doi.org/10.1016/j.artmed.2019.07.006
2. Kovacs, G.G.: Molecular pathology of neurodegenerative diseases: principles and practice. J. Clin. Pathol. **72**, 725–735 (2019). https://doi.org/10.1136/jclinpath-2019-205952
3. Gitler, A.D., Dhillon, P., Shorter, J.: Neurodegenerative disease: models, mechanisms, and a new hope. Dis. Model. Mech. **10**, 499–502 (2017). https://doi.org/10.1242/DMM.030205
4. Abeliovich, A., Gitler, A.D.: Defects in trafficking bridge Parkinson's disease pathology and genetics. Nature **539**, 207–216 (2016). https://doi.org/10.1038/nature20414
5. Canter, R.G., Penney, J., Tsai, L.H.: The road to restoring neural circuits for the treatment of Alzheimer's disease. Nature **539**, 187–196 (2016). https://doi.org/10.1038/nature20412
6. Taylor, J.P., Brown, R.H., Cleveland, D.W.: Decoding ALS: from genes to mechanism. Nature **539**, 197–206 (2016). https://doi.org/10.1038/nature20413
7. Wyss-Coray, T.: Ageing, neurodegeneration and brain rejuvenation. Nature **539**, 180–186 (2016). https://doi.org/10.1038/nature20411
8. Lamptey, R.N.L., Chaulagain, B., Trivedi, R., Gothwal, A., Layek, B., Singh, J.: A review of the common neurodegenerative disorders: current therapeutic approaches and the potential role of nanotherapeutics. Int. J. Mol. Sci. **23**, 1–18 (2022). https://doi.org/10.3390/ijms23031851
9. Langa, K.M., Larson, E.B., Crimmins, E.M., Faul, J.D., Levine, D.A., Kabeto, M.U., Weir, D.R.: A comparison of the prevalence of dementia in the United States in 2000 and 2012. JAMA Intern. Med. **177**, 51–58 (2017). https://doi.org/10.1001/JAMAINTERNMED.2016.6807
10. Sethi, M., Ahuja, S., Rani, S., Koundal, D., Zaguia, A., Enbeyle, W.: An exploration: Alzheimer's disease classification based on convolutional neural network. BioMed Res. Int. **2022** (2022)

11. Gerg, G.G.K.: Protein coding of neurodegenerative dementias: the neuropathological basis of biomarker diagnostics. Acta Neuropathologica, 389–408 (2010). https://doi.org/10.1007/s00401-010-0658-1
12. Oboudiyat, C., Glazer, H., Seifan, A., Greer, C., Isaacson, R.S.: Alzheimer's disease. Semin. Neurol. **33**, 313–329 (2013). https://doi.org/10.1055/s-0033-1359319
13. Brody, H., Grayson, M., Mandavilli, A., Scully, T., Haines, N.: Alzheimer's disease. Nature **475** (2011). https://doi.org/10.1038/475S1A
14. Vishnu, V.Y., Modi, M., Garg, V.K., Mohanty, M., Goyal, M.K., Lal, V., Mittal, B.R., Prabhakar, S.: Role of inflammatory and hemostatic biomarkers in Alzheimer's and vascular dementia—a pilot study from a tertiary center in Northern India. Asian J. Psychiatr. **29**, 59–62 (2017). https://doi.org/10.1016/j.ajp.2017.04.015
15. Kumar, A., Singh, A.: Ekavali: a review on Alzheimer's disease pathophysiology and its management: an update. Pharmacol. Rep. **67**, 195–203 (2015). https://doi.org/10.1016/j.pharep.2014.09.004
16. Pickett, E.K., Herrmann, A.G., McQueen, J., Abt, K., Dando, O., Tulloch, J., Jain, P., Dunnett, S., Sohrabi, S., Fjeldstad, M.P., Calkin, W., Murison, L., Jackson, R.J., Tzioras, M., Stevenson, A., d'Orange, M., Hooley, M., Davies, C., Colom-Cadena, M., Anton-Fernandez, A., King, D., Oren, I., Rose, J., McKenzie, C.A., Allison, E., Smith, C., Hardt, O., Henstridge, C.M., Hardingham, G.E., Spires-Jones, T.L.: Amyloid beta and tau cooperate to cause reversible behavioral and transcriptional deficits in a model of Alzheimer's disease. Cell Rep. **29**, 3592-3604.e5 (2019). https://doi.org/10.1016/J.CELREP.2019.11.044/ATTACHMENT/CD084EC7-2360-473E-B9C1-63ACE5ED64AC/MMC5.XLSX
17. Hardy, J., Allsop, D.: Amyloid deposition as the central event in the aetiology of Alzheimer's disease. Trends Pharmacol. Sci. **12**, 383–388 (1991). https://doi.org/10.1016/0165-6147(91)90609-V
18. Braak, H., Braak, E.: Neuropathological stageing of Alzheimer-related changes. Acta Neuropathol. **82**, 239–259 (1991). https://doi.org/10.1007/BF00308809
19. Bayer, T.A., Wirths, O.: Intracellular accumulation of amyloid-beta—a predictor for synaptic dysfunction and neuron loss in Alzheimer's disease. Front. Aging Neurosci. **2**, 8 (2010). https://doi.org/10.3389/FNAGI.2010.00008/BIBTEX
20. Kurz, A., Perneczky, R.: Novel insights for the treatment of Alzheimer's disease. Prog. Neuro-Psychopharmacol. Biol. Psychiatry **35**, 373–379 (2011). https://doi.org/10.1016/j.pnpbp.2010.07.018
21. Arnsten, A.F.T., Datta, D., Del Tredici, K., Braak, H.: Hypothesis: tau pathology is an initiating factor in sporadic Alzheimer's disease. Alzheimer's Dement **17**, 115–124 (2021). https://doi.org/10.1002/ALZ.12192
22. Dysken, M.W., Guarino, P.D., Vertrees, J.E., Asthana, S., Sano, M., Llorente, M., Pallaki, M., Love, S., Schellenberg, G.D., McCarten, J.R., Malphurs, J., Prieto, S., Chen, P., Loreck, D.J., Carney, S., Trapp, G., Bakshi, R.S., Mintzer, J.E., Heidebrink, J.L., Vidal-Cardona, A., Arroyo, L.M., Cruz, A.R., Kowall, N.W., Chopra, M.P., Craft, S., Thielke, S., Turvey, C.L., Woodman, C., Monnell, K.A., Gordon, K., Tomaska, J., Vatassery, G.: Vitamin E and memantine in Alzheimer's disease: clinical trial methods and baseline data. Alzheimer's Dement. **10**, 36–44 (2014). https://doi.org/10.1016/j.jalz.2013.01.014
23. Selkoe, D.J.: Alzheimer's disease: genes, proteins, and therapy. Physiol. Rev. **81**, 741–766 (2001). https://doi.org/10.1152/PHYSREV.2001.81.2.741/ASSET/IMAGES/LARGE/9J0210134004.JPEG
24. Dumont, M., Beal, M.F.: Neuroprotective strategies involving ROS in Alzheimer's disease. Free Radic. Biol. Med. **51**, 1014 (2011). https://doi.org/10.1016/J.FREERADBIOMED.2010.11.026
25. Atkinson, S.P.: Alzheimer's disease: a special collection. Stem Cells Transl. Med. **6**, 1951–1955 (2017). https://doi.org/10.1002/SCTM.12217
26. Balestrino, R., Schapira, A.H.V.: Parkinson disease. Eur. J. Neurol. **27**, 27–42 (2020). https://doi.org/10.1111/ene.14108

27. Antony, P.M.A., Diederich, N.J., Krüger, R., Balling, R.: The hallmarks of Parkinson's disease. FEBS J. **280**, 5981–5993 (2013). https://doi.org/10.1111/FEBS.12335
28. Dugger, B.N., Dickson, D.W.: Pathology of neurodegenerative diseases. Cold Spring Harb. Perspect. Biol. **9** (2017). https://doi.org/10.1101/CSHPERSPECT.A028035
29. Walker, F.O.: Huntington's disease. Lancet (London, England) **369**, 218–228 (2007). https://doi.org/10.1016/S0140-6736(07)60111-1
30. Wyant, K.J., Ridder, A.J., Dayalu, P.: Huntington's disease—update on treatments. Curr. Neurol. Neurosci. Rep. **17** (2017). https://doi.org/10.1007/S11910-017-0739-9
31. Ha, A.D., Fung, V.S.C.: Huntington's disease. Curr. Opin. Neurol. **25**, 491–498 (2012). https://doi.org/10.1097/WCO.0B013E3283550C97
32. Lin, Y.W., Truong, D.: Diffuse Lewy body disease. J. Neurol. Sci. **399**, 144–150 (2019). https://doi.org/10.1016/J.JNS.2019.02.021
33. Sanford, A.M.: Lewy body dementia. Clin. Geriatr. Med. **34**, 603–615 (2018). https://doi.org/10.1016/J.CGER.2018.06.007
34. Chalouhi, N., Hoh, B.L., Hasan, D.: Review of cerebral aneurysm formation, growth, and rupture. Stroke **44**, 3613–3622 (2013). https://doi.org/10.1161/STROKEAHA.113.002390
35. Jiang, B., Paff, M., Colby, G.P., Coon, A.L., Lin, L.M.: Cerebral aneurysm treatment: modern neurovascular techniques. Stroke Vasc. Neurol. **1**, 93–100 (2016). https://doi.org/10.1136/SVN-2016-000027
36. Samson, D.: Aneurysm perspective. Clin. Neurosurg. **40**, 124–136 (1993)
37. Contera, S., De La Serna, J.B., Tetley, T.D.: Biotechnology, nanotechnology and medicine. Emerg. Top. Life Sci. **4**, 551–554 (2020). https://doi.org/10.1042/ETLS20200350
38. Garg, V.K., Supriya, Shree, R., Prakash, A., Takkar, A., Khullar, M., Saikia, B., Medhi, B., Modi, M.: Genetic abnormality of cytochrome-P2C9*3 allele predisposes to epilepsy and phenytoin-induced adverse drug reactions: genotyping findings of cytochrome-alleles in the North Indian population. Futur. J. Pharm. Sci. **8**, 1–8 (2022). https://doi.org/10.1186/s43094-022-00432-6
39. Modi, M., Singh, R., Goyal, M.K., Gairolla, J., Singh, G., Rishi, V., Thakur, J.S., Sehgal, R.K., Garg, V.K., Khandelwal, N., Kharbanda, P.S., Prabhakar, S., Lal, V.: Prevalence of epilepsy and its association with exposure to *Toxocara canis*: a community based, case-control study from rural Northern India. Ann. Indian Acad. Neurol. **21**, 263–269 (2018). https://doi.org/10.4103/aian.AIAN_384_17
40. Modi, M., Singh, R., Goyal, M., Gairolla, J., Singh, G., Rishi, V., Thakur, J., Sehgal, R., Garg, V., Khandelwal, N., Kharbanda, P., Prabhakar, S., Lal, V.: Prevalence of epilepsy and its association with exposure to *Toxocara canis*: a community-based, case-control study from rural Northern India. https://pubmed.ncbi.nlm.nih.gov/31736600/ (2019). https://doi.org/10.4103/aian.AIAN_32_19
41. Rishi, V., Singh, R., Goyal, M.K., Modi, M., Garg, V., Thakur, J.S., Sehgal, R.K., Khandelwal, N., Jain, G., Kumar, A.S., Choudhary, A., Prabhakar, S., Lal, V.: Exposure to *Toxocara canis* is not associated with new-onset epilepsy. Neurol. India **70**, 2383–2387 (2022). https://doi.org/10.4103/0028-3886.364076
42. Garg, V., Goyal, M., Khullar, M., Saikia, B., Medhi, B., Prakash, A., Prabhat, N., Tandyala, N., Mahesh, K., Kharbanda, P., Prabhakar, S., Modi, M., Lal, V., Shree, R., Sachdeva, J.: Presence of allele CYP3A4*16 does not have any bearing on carbamazepine-induced adverse drug reactions in North Indian people with epilepsy. Indian J. Pharmacol. **52**, 378 (2020). https://doi.org/10.4103/ijp.ijp_549_20
43. Aggarwal, R., Sharma, M., Modi, M., Garg, V. kumar, Salaria, M.: HLA-B*1502 is associated with carbamazepine induced Stevens-Johnson syndrome in North Indian population. Hum. Immunol. **75**, 1120–1122 (2014). https://doi.org/10.1016/j.humimm.2014.09.022
44. Mondal, B., Paul, P., Paul, M., Kumar, H.: An update on Spino-cerebellar ataxias. Ann. Indian Acad. Neurol. **16**, 295–303 (2013). https://doi.org/10.4103/0972-2327.116896
45. Vatsala, A., Gupta, S., Koundal, D., Nayak, S.R., Nayak, J., Vimal, S.: Multi-class skin disease classification using transfer learning model. Int. J. Artif. Intell. Tools **31**(02), 2250029

46. Marcos-Rabal, P., González-Fuentes, J., Castro-Vázquez, L., Lozano, M.V., Rodríguez-Robledo, V., Santander-Ortega, M.J., Selva-Clemente, J., Villaseca-González, N., del Mar Arroyo-Jiménez, M.: Neurodegenerative diseases: a multidisciplinary approach. Curr. Pharm. Des. **27**, 3305–3336 (2021). https://doi.org/10.2174/1381612827666210608152745
47. Kovacs, G.G.: Concepts and classification of neurodegenerative diseases. In: Handbook of Clinical Neurology, pp. 301–307 (2018). https://doi.org/10.1016/B978-0-12-802395-2.00021-3
48. Siddique, T., Dellefave, L.: Amyotrophic lateral sclerosis. In: Longo, D.L. (ed.) Neurogenetics: Scientific and Clinical Advances, pp. 693–728 (2005). https://doi.org/10.2307/3423735
49. Salankar, N., Koundal, D., Chakraborty, C., Garg, L.: Automated attention deficit classification system from multimodal physiological signals. Multimed. Tools Appl., 1–16 (2022)
50. Hussain, M., Koundal, D., Manhas, J.: Deep learning-based diagnosis of disc degenerative diseases using MRI: a comprehensive review. Comput. Electr. Eng. **105**, 108524 (2023)
51. Wijesekera, L.C., Leigh, P.N.: Amyotrophic lateral sclerosis. Orphanet J. Rare Dis. **4** (2009). https://doi.org/10.1186/1750-1172-4-3