

Influential Factors Contributing to Stroke Recovery: A Review

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Abstract

Stroke is a major public health problem affecting disability to people after stroke. Deficits in motor function resulting from stroke can impact the mobility of patient, ability to perform tasks in everyday life, social interaction, and likelihood of resuming work. The recovery of stroke is important for the survivors to return to daily life. Several factors influence the stroke recovery and can predict the conditions of the patients to obtain the optimal rehabilitative therapeutics individually. The aim of the paper is to evaluate the influential factors contributing to stroke recovery. When the clinicians from rehabilitation teams have a better understanding of these individualized factors, the therapeutic goals can become holistic, effective and realistic for the patients to achieve the maximal motor function recovery after stroke.

Keywords: factors, recovery, stroke

Introduction

Stroke is the major consequence of cerebrovascular disease. It ranks among the second most frequent causes of death globally (Prasad et al., 2012). The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2017 data that was extracted shows that between 1990 and 2017, the prevalence increased only in upper-middle-income countries, where it increased at a mean growth rate of 11% (from 1.40 to 1.55%). In low- and high-income countries, it decreased by 3% (from 1.03 to 1.00%) and 8% (from 1.26 to 1.16%), respectively, and remained unchanged (1.08%) in lower-middle-income countries (Avan et al., 2019; Chantkran et al., 2021). Moreover, modifiable risk factors have been linked to nearly a 34% decrease in the stroke death rate (67.8, uncertainty CI 64.1 to 71.1 per 100,000 in 2017), with the decline being most pronounced in wealthy nations (Avan et al., 2019).

Consequently, there has been a rise in the prevalence of cardiovascular illnesses, such as stroke, and metabolic syndrome. History of hypertension, diabetes mellitus, dyslipidemia, and hypercholesterolemia, older age, male gender and occupational class (manual class and jobless) were also found to be related with a higher prevalence of stroke (Chantkran et al., 2021).

Influential factors contributing to stroke recovery

Following a stroke, motor recovery is a multifaceted, dynamic, and diverse process that is influenced by sociodemographic, genetic, pathophysiologic, and therapeutic factors. Rehabilitation therapies meant to enhance post-stroke recovery are impacted by these characteristics. These factors can be divided into three categories: socio-demographic, clinical, and genetic factors (Alawieh et al., 2018).

1. Socio-demographic factors

1) Age

Following ischemic and hemorrhagic stroke, older age is a significant predictive factor for poorer outcome and half of older patients with stroke have mild-to-severe disability (D'Amore et al., 2013). As a result, age is one of the independent predictors of early stroke outcomes (Kwah et al., 2013; Umeano et al., 2013). To test for the independent predictive variable as age alone, the influence of age on post-stroke recovery is different from age-associated factors such as co-morbidities and socioeconomic variables (Alawieh et al., 2018).

2) Race

Six months after a stroke, recovery in functional activity is worse in adults of Asian and Pacific descent. Asians, Pacific Islanders, and Maori performed higher than Europeans in quality of life factors relating to physical health. Pacific Islanders were more likely than Europeans to be dependent on others for assistance, but Asians had a lower death rate. Compared to Europeans, Pacific Islanders were higher in dependence or dead. Compared to Europeans, Asians and Pacific Islanders were higher in living at home (McNaughton et al., 2011).

3) Socioeconomic status

Socioeconomic factors such household income, education level, and insurance status have an impact on stroke recovery. Poor recovery outcomes may result from delays or barriers to accessing rehabilitation programs brought on by underinsurance or uninsurance. While income is correlated highly with rehabilitation therapy after being discharged from a rehabilitation institution, higher education is also correlated with the improved motor and functional improvement during inpatient rehabilitation centers. It is asserted that people with strokes are more likely to occur in low-, middle-, and high-income nations, and that their short- and long-term results are worse (Marshall et al., 2015). Due to socioeconomic disparities, not everyone may have equal access to general healthcare and rehabilitation services (Marshall et al., 2015).

4) Other factors

Other factors including disease awareness, mistrust, marital status, caregiver support, volition, quality of life, healthcare system access, self-efficacy, and activities of daily living are the influential factors in stroke recovery (Alawieh et al., 2018; Cheong et al., 2021).

2. Clinical factors

1) Stroke subtype

The hemorrhagic and ischemic stroke which are the two most common types of strokes, can change the acute and chronic therapeutic patterns. Hemorrhagic stroke patients have increased functional disability at the time of presentation. Patients who suffer intracranial hemorrhage, on the other hand, recover more clearly and quickly than those who have an ischemic stroke of the same intensity (Bhalla et al., 2013). Between ischemic and hemorrhagic strokes, there is no discernible difference in recovery (Lubis et al., 2017).

2) Location and side of stroke

The location of the anatomical damage limits the amount of function recovery in the upper extremities (Frenkel-Toledo et al., 2019). Upper extremity recovery is supposed to decrease progressively with lesion sites such as cortex—corona radiata—posterior limb of the internal capsule during the acute phase of stroke (Frenkel-Toledo et al., 2020). Damage to subcortical regions

has a stronger correlation with suboptimal upper extremity motor function throughout the subacute phase (Frenkel-Toledo et al., 2020).

When patients with right and left hemisphere damage were assembled, differences in the conditions of motor recovery (Wu et al., 2014) could be found based on the differences between the dominant left and the non-dominant right cerebral hemispheres in the functional neuroanatomy of motor control (Mani et al., 2013). Trauma to the putamen, insula, and white matter tracts primarily affects upper extremity motor abilities in the sub-acute period after left hemisphere trauma. But in the chronic phase, damage is limited to the white matter tracts (Frenkel-Toledo et al., 2020). However, injury to a wide range of cortical and subcortical regions, including the insula, white matter tracts, and basal ganglia, impacted upper extremity function after right hemisphere damage in both stages (Frenkel-Toledo et al., 2019). The brain region damaged by the stroke should be divided into smaller groups in order to categorize the uniformity of results and assess the recovery of upper extremity function.

After receiving bilateral upper extremity training, patients with right-hand dominant stroke who have a motor dominant stroke (left hemisphere lesion) exhibit a response advantage over those with a motor nondominant stroke (right hemisphere lesion). Depending on which side of the stroke occurred, treatment strategies for upper extremity hemiparesis may need to be more carefully chosen (Waller, Whitall, 2005).

3) Severity of stroke

Over the course of three months of follow-up, patients with severe and moderate ischemic stroke validate sustained enhancement with the use of three neurological and functional levels (Murie-Fernández, Marzo, 2020). As a general rule patients with milder deficits might recover faster than those with more severe deficits in stroke recovery (Grefkes, Fink, 2020). Particularly patients with more severe impairments state different from the general rule presenting with severe motor recovery (van der Vliet et al., 2020). Contrary to current recovery models with severe stages, some stroke patients with major deficits, such as hemiplegia, may recover within 10 days after stroke (Grefkes, Fink, 2014).

4) The initial injury

An essential component of long-term and functional healing is the initial injury's severity. Accordingly, more severely and acutely motor impairment is associated with more severely and chronically deficits, and so effective thrombolytic therapy can lessen chronic deficits while also preventing immediate injury (Grefkes, Fink, 2020). Within the different groups of stroke severity, the first thirty days show the greatest improvement. Furthermore, for an additional 90 days or more, patients with severe and moderate initial impairment continue to improve (Alawieh et al., 2018). At three months, most patients with less severe disabilities had recovered to a moderate or mild disability needing some assistance, unlike those who had severe dependency on basic daily activities upon admission.

5) Post-stroke depression

One-third of patients with stroke experience post-stroke depression, which is the most prevalent neuropsychiatric condition after stroke. According to Guiraud et al. (2016), there are several factors that contribute to post-stroke depression, including a history of depression, female gender, stressful life events prior to the stroke, and a significant physical disability. After a stroke, antidepressants should be taken as soon as feasible to aid in cognitive and physical recovery (Mead et al., 2013). Antidepressants can also alter serotonergic transmission, which prolongs the time of neural plasticity and influences activity in the primary motor cortex (Alawieh et al., 2018).

6) Co-morbidities

Following a stroke, patients with uncontrolled diabetes have a poorer prognosis (Desilles et al., 2013). Similarly, recovery after a stroke may be negatively impacted by notable peri-ventricular white matter damage. Discharge-related comorbidities have negative correlation with post-stroke global outcomes. Towfighi et al. (2017) state that in order to effectively estimate the predictive variable of other factors affecting stroke recovery, it is necessary to precisely classify the contribution of varied stroke co-

morbidities. Moreover, urinary tract infections can prolong hospital stays, impede recovery, and raise medical expenses during the acute phase of a stroke (Alawieh et al., 2018).

7) *Rehabilitation therapeutics*

The effect of various rehabilitation therapies, such as treatment kind, timing, and dosage, all play a part in chronic motor recovery (Claflin et al., 2015). It's tough to know how much rehabilitation therapy to give and what the optimum neurorehabilitation method is for increasing motor recovery after a stroke (Hattem et al., 2016). Constraint induced Movement Therapy (CIMT) is a neurobehavioral treatment that has been shown in a multi-center randomized clinical trial to improve upper extremity motor recovery in chronic stroke patients (Kwakkel et al., 2015).

There is minimal evidence that single or combined rehabilitation treatments are considerably superior to typical occupational and physical therapy in helping people restore their motor abilities after a stroke (Hattem et al., 2016). Combinatory approaches can assist stroke survivors in maximizing their window of brain plasticity, such as combining physical therapy and brain stimulation. Developing therapies that could alter the healing process include brain-computer interfaces (BCI), cell-based therapy, repetitive transcranial magnetic stimulation (rTMS), robotic-assisted devices (RAD), and transcranial direct current stimulation (tDCS) (Hattem et al., 2016).

3. *Genetic factors*

Multiple single nucleotide polymorphisms (SNPs) have been linked to an increased risk or severity of ischemic stroke (Zhong, et al., 2017). These genetic variations influence inter-individual heterogeneity in recovery of stroke, which could take consequences in personalized rehabilitation regimens. Polymorphisms in the genes for Brain Derived Neurotrophic Factor (BDNF), Apolipoprotein E (Apo-E), Neurotrophic Tyrosine Kinase Receptor, and mitochondrial DNA may affect all stroke recovery. BDNF is a neurotrophic factor that supports learning, synaptic plasticity, and memory in the brain (Balkaya, Cho, 2019).

Conclusion

This research aims to assess the factors influencing stroke recovery. Improved knowledge of the pathophysiology and recovery process following a stroke can complement existing therapeutic expertise and improve novel rehabilitation approaches. Thus, depending on the post-stroke neurophysiological and neuropathological characteristics, physical therapists and other medical experts can combine numerous therapy modalities and approaches to produce accessible and effective neuro-rehabilitative therapies. To improve the recovery of stroke patients, it is critical that the elements impacting post-stroke recovery can be coordinated and customized in the comprehensive rehabilitation plan.

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References

- Alawieh A, Zhao J, Feng W. Factors affecting post-stroke motor recovery: implications on neurotherapy after brain injury. *Behav Brain Res* 2018; 340: 94-101.
- Avan A, Digaleh H, Di Napoli M, Stranges S, Behrouz R, Shojaeianbabaei G, et al. Socioeconomic status and stroke incidence, prevalence, mortality, and worldwide burden: an ecological analysis from the Global Burden of Disease Study 2017. *BMC Med* 2019; 17(1): 1-30.
- Balkaya M, Cho S. Genetics of stroke recovery: BDNF val66met polymorphism in stroke recovery and its interaction with aging. *Neurobiol Dis* 2019; 126: 36-46.

- Bhalla A, Wang Y, Rudd A, Wolfe CD. Differences in outcome and predictors between ischemic and intracerebral hemorrhage: the South London Stroke Register. *Stroke* 2013; 44(8): 2174-81.
- Chantkran W, Chaisakul J, Rangsin R, Mungthin M, Sakboonyarat B. Prevalence of and factors associated with stroke in hypertensive patients in Thailand from 2014 to 2018: A nationwide cross-sectional study. *Sci Rep* 2021; 11(1): 1-2.
- Cheong MJ, Kang Y, Kang HW. Psychosocial Factors Related to Stroke Patients' Rehabilitation Motivation: A Scoping Review and Meta-Analysis Focused on South Korea. *Int J Healthc* 2021; 9(1211): 1-15.
- Claflin ES, Krishnan C, Khot SP. Emerging treatments for motor rehabilitation after stroke. *Neurohospitalist The* 2015; 5(2): 77-88.
- D'Amore C, Paciaroni M, Silvestrelli G, Agnelli G, Santucci P, Lanari A, et al. Severity of acute intracerebral haemorrhage, elderly age and atrial fibrillation: independent predictors of poor outcome at three months. *Eur J Intern Med* 2013; 24(4): 310-3.
- Desilles JP, Meseguer E, Labreuche J, Lapergue B, Sirimarco G, Gonzalez-Valcarcel J, et al. Diabetes mellitus, admission glucose, and outcomes after stroke thrombolysis: a registry and systematic review. *Stroke* 2013; 44(7): 1915-23.
- Frenkel-Toledo S, Fridberg G, Ofir S, Bartur G, Lowenthal-Raz J, Granot O, et al. Lesion location impact on functional recovery of the hemiparetic upper limb. *PLoS One* 2019; 14(7): 1-28.
- Frenkel-Toledo S, Ofir-Geva S, Soroker N. Lesion topography impact on shoulder abduction and finger extension following left and right hemispheric stroke. *Front Hum Neurosci* 2020; 14(282): 1-12.
- Grefkes C, Fink GR. Connectivity-based approaches in stroke and recovery of function. *Lancet Neurol* 2014; 13(2): 206-16.
- Grefkes C, Fink GR. Disruption of motor network connectivity post-stroke and its noninvasive neuromodulation. *Curr Opin Neurol* 2012; 25(6): 670-5.
- Grefkes C, Fink GR. Recovery from stroke: current concepts and future perspectives. *Neurol Res Pract* 2020; 2(1): 1-10.
- Guiraud V, Gallarda T, Calvet D, Turc G, Oppenheim C, Rouillon F, et al. Depression predictors within six months of ischemic stroke: The DEPRESS Study. *Int J Stroke* 2016; 11(5): 519-25.
- Hatem SM, Saussez G, Della Faille M, Prist V, Zhang X, Dispa D, et al. Rehabilitation of motor function after stroke: a multiple systematic review focused on techniques to stimulate upper extremity recovery. *Front Hum Neurosci* 2016; 10(442): 1-22.
- Kwah LK, Harvey LA, Diong J, Herbert RD. Models containing age and NIHSS predict recovery of ambulation and upper limb function six months after stroke: an observational study. *J Physiother* 2013; 59(3): 189-97.
- Kwakkel G, Veerbeek JM, van Wegen EE, Wolf SL. Constraint-induced movement therapy after stroke. *Lancet Neurol* 2015; 14(2): 224-34.
- Lubis SA, Novitri N, Rizal A. Comparison of post-stroke functional recovery between ischemic and hemorrhagic stroke patients: a prospective cohort study. *Althea Med J* 2017; 4(2): 267-70.
- Mani S, Mutha PK, Przybyla A, Haaland KY, Good DC, Sainburg RL. Contralesional motor deficits after unilateral stroke reflect hemisphere-specific control mechanisms. *Brain* 2013; 136(4): 1288-303.
- Marshall IJ, Wang Y, Crichton S, McKeivitt C, Rudd AG, Wolfe CD. The effects of socioeconomic status on stroke risk and outcomes. *Lancet Neurol* 2015; 14(12): 1206-18.
- McNaughton H, Feigin V, Kerse N, Barber PA, Weatherall M, Bennett D, et al. Ethnicity and functional outcome after stroke. *Stroke* 2011; 42(4): 960-4.
- Mead GE, Hsieh CF, Lee R, Kutlubayev M, Claxton A, Hankey GJ, et al. Selective serotonin reuptake inhibitors for stroke recovery: a systematic review and meta-analysis. *Stroke* 2013; 44(3): 844-50.
- Murie-Fernández M, Marzo MM. Predictors of Neurological and Functional Recovery in Patients with Moderate to Severe Ischemic Stroke: The EPICA Study. *Stroke Res Treat* 2020; 2020: 1-13.

- Prasad K, Vibha D, Meenakshi. Cerebrovascular disease in South Asia—Part I: A burning problem. *JRSM Cardiovasc Dis* 2012; 1(7): 1-7.
- Towfighi A, Ovbiagele B, El Hussein N, Hackett ML, Jorge RE, Kissela BM, et al. Poststroke depression: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2017; 48(2): 30-43.
- Umeano O, Phillips-Bute B, Hailey CE, Sun W, Gray MC, Roulhac-Wilson B, et al. Gender and age interact to affect early outcome after intracerebral hemorrhage. *PloS one* 2013; 8(11): 1-6.
- van der Vliet R, Selles RW, Andrinopoulou ER, Nijland R, Ribbers GM, Frens MA, et al. Predicting upper limb motor impairment recovery after stroke: a mixture model. *Ann Neurol* 2020; 87(3): 383-93.
- Waller SM, Whittall J. Hand dominance and side of stroke affect rehabilitation in chronic stroke. *Clin Rehabil* 2005; 19(5): 544-51.
- Wu F, Catano M, Echeverry R, Torre E, Haile WB, An J, et al. Urokinase-type plasminogen activator promotes dendritic spine recovery and improves neurological outcome following ischemic stroke. *J Neurosci* 2014; 34(43): 14219-32.
- Zhong LL, Ding LS, He W, Tian XY, Cao H, Song YQ, et al. Systolic hypertension related single nucleotide polymorphism is associated with susceptibility of ischemic stroke. *Eur Rev Med Pharmacol Sci* 2017; 21(12): 2901-6.