Brain Oscillations in Stroke Rehabilitation: What can they tell us about Impairment, Recovery and Response to Training?

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Abstract

Introduction: Stroke is the third leading cause of disability in the world with 80 percent of stroke survivors suffering from some degree of motor impairment. Yet the degree of motor impairment and subsequent recovery varies largely between individuals. Whilst neurorehabilitation programmes are available, not all individuals benefit from them equally. Hence this literature review aims to summarise the current literature around the use of EEG in predicting the degree of motor impairment, recovery and response to training in stroke patients.

Method: A non-systematic literature search of PubMed was conducted to identify articles reporting changes in brain oscillations in stroke patients.

Results: Here we discuss how changes in different parameters of brain oscillations, indices of different types of waves as well as EEG patterns are associated with different degrees of motor functions both in acute and chronic stages of stroke. The review demonstrates how recovery of motor function depends on re-establishment of symmetry between the two hemispheres and increased shift of activity from the unaffected to affected hemisphere and back to normal levels.

Conclusions: Recognition of such EEG patterns has furthered our understanding of causal relationship between pathophysiological processes and motor function, opening further opportunities to identify biomarkers which will allow us to predict the response of individual to training and tailor the therapeutic intervention in a personalised way to maximise motor recovery after stroke.

1 Introduction

Stroke is the second leading cause of death in the world (WHO, 2016). Despite increasing availability and effectiveness of acute treatment, 80 percent of stroke survivors are still left with some degree of motor impairment and disability (Langhorne, Coupar, & Pollock, ). According to the World Health Organisation (WHO), this makes stroke the third leading cause of disability worldwide (WHO, 2016). Neurorehabilitation programs aim to reduce the motor impairment and improve long-term functional outcome mainly through training (Kitago & Marshall, ). However, motor recovery appears to be a multifactorial process as reflected by the significant differences in motor improvement seen in patients with similar clinical profiles (Kitago & Marshall, ).

Whilst re-absorption of cerebral oedema and growth of collateral blood vessels leads to some recovery of motor function in short-term, complete recovery of motor function is highly variable between individuals due to the range of physiological repair processes which underlie restoration of function (Rossini, Calautti, Pauri, & Baron, ). These recovery processes encompasses a range of changes in neuronal circuit
such as: recruitment of functionally homologous pathways, activation of previously inhibited neurones, increased cortical representation, axonal sprouting around the injured tissues and the formation of new synapse and reorganisation of neuronal networks (Kitago & Marshall, ). These vast number of complex changes in neuronal circuits leading to recovery are collectively referred to as the process of ‘brain plasticity’ (Rossini et al., ).

One of the most important mechanism is the increase in strength of synapses and hence an improvement in synaptic efficacy in the remaining neurones by a process called long-term potentiation (Rossini et al., ). Most of the patients regain function partially or completely through these mechanisms in the first 3 months after stroke (Di Pino et al., ) because this time marks the “sensitive period” for neuronal plasticity (Kitago & Marshall, ). This is the period of hyperexcitability of cortical neurones characterised by increased glutamate-mediated excitation and decreased GABA mediated inhibition (due to downregulation of GABA-A receptors) creating the optimal environment for these neuronal reorganisation (Di Pino et al., ). It is therefore believed that it is essential to take advantage of this natural “sensitive period” in order to maximise the activity-dependent plasticity and functional recovery.

EEG waves record the sum of post-synaptic potentials of a number of neurones located at the surface of the cortex (J. E. Hall, ). The waves have a range of frequency (0.5-500 Hz) (Rabiller, He, Nishijima, Wong, & Liu, ) and intensities (0-200 mv) (J. E. Hall, ). The intensity or amplitude of the wave depends on the number of neurones firing synchronously. EEG oscillations have been divided into 5 main frequency groups which are observed in different parts of cortex during different activities: (1-4Hz), (4-8 Hz), (8-12 Hz), (12-30Hz) and (30-80 Hz) (Rabiller et al., ).

This review discusses some of the recent advances on the use of EEG to predict impairment, recovery and response of individuals to training. EEG allows us to monitor changes in the activity of brain overtime in a non-invasive way and allows us to follow these recovery processes more closely during rehabilitation.

2 Aims

The aim of this review was to synthesize the current literature regarding changes in brain oscillations observed following stroke as well as changes seen during recovery from motor impairment in stroke patients.

A non-systematic literature search of PubMed was conducted to identify articles reporting changes in brain oscillations in stroke patients.

3 Results

3.1 Interhemispheric Changes in Brain Oscillations

Following stroke, there is interhemispheric imbalance of activity. There is a reduction in the function of the affected hemisphere due to loss of neurones. There is also shift of activity from the primary motor cortex of affected hemisphere to contralesional primary and ipsilesional as well as contralesional secondary motor cortices (Rossini et al., ). These changes are thought to be acute recovery mechanisms to compensate for the loss of function (Rossini et al., ). Interhemispheric inhibition (IHI) is the inhibition of the activity of one hemisphere by the contralateral hemisphere (Di Pino et al., ). IHI measurements are taken through protocols involving TMS (Transmagnetic Stimulation) (Di Pino et al., ).

Additionally, there is greater interhemispheric inhibition (IHI) from unaffected hemisphere to affected hemisphere (Yang, Sau, Lai, Cichon, & Li, ). Normally, when healthy individuals try to move a hand, there is a reduction in the interhemispheric inhibition from ipsilateral to contralateral hemisphere during preparation, allowing activation of contralateral hemisphere neurones. However, in stroke patients, this decrease in interhemispheric inhibition from unaffected (ipsilateral) to affected (contralateral) hemisphere does not occur for movement of affected hand which makes initiation of movement in stroke patients difficult (Murase, Duque, Mazzocchio, & Cohen, ). This explains the negative correlation between the degree of IHI from unaffected to affected hemisphere and motor function (Murase et al., ).

Three models of recovery have been developed around this idea of interhemispheric inhibition: Vicariation model, Interhemispheric Competition Model and Bimodal balance-recovery model. Vicariation model suggests that recovery occurs through increased activity of the neurones in unaffected hemisphere (Di Pino et al., ). Interhemispheric Competition Model suggests that decreased activity of affected hemisphere leads to decreased inhibition of unaffected hemisphere which then causes increased inhibition of affected hemisphere and hence poor motor function. Since the evidence for these models are contradictory (Di Pino et al., ), bimodal balance model was proposed.

Bimodal balance-recovery model suggests that the dominance of the previous two models depends on the structural reserve which is defined as the amount of functionally remaining neurones. If there is increased damage, it could mean greater dependence on unaffected hemisphere for function as even removal of inhibition on affected hemisphere will not yield enough recovery. If there is increased functional reserve, interhemispheric model dominates as removal of inhibition on these neurones could be enough to regain functionality (Di Pino et al., ). This model is supported by by a meta-analysis (McDonell & Stinear, ) which suggests that in severe stroke, increased excitation of affected hemisphere using TMS is of little benefit as vicariation model dominates and reliance on unaffected hemisphere is greater.

However not many studies can be found which have used
EEG to test these models. Hence, using EEG to determine the level of interhemispheric imbalance could allow stratifying patients depending on the level of injury, and hence deciding which therapeutic intervention will provide maximum recovery in the individual.

Individuals with good recovery after rehabilitation show a shift of dominance of activity from unaffected to affected hemisphere (Hummel & Gerloff, ) (Tangwiriyasakul, Verhagen, Rutten, & van Putten, ). This interhemispheric symmetry predicts recovery. This observation is exemplified by studies comparing beta-waves in the two hemispheres. A study which compared beta-ERD of the two hemispheres using laterality index (Shiner, Tang, Johnson, & McNulty, ), showed that higher laterality index, which signifies increased contribution of affected hemisphere, were associated with better motor function. Studies which have compared activity of both hemisphere using indices such as BSI (Brain Symmetry Index) have shown that higher BSI scores, which means greater asymmetry of waves between hemispheres, is associated with worse motor function (Agius Anastasi, Falzon, Camilleri, Vella, & Muscat, ) (Van Putten & Tavy, ). Yet another study also suggested that recovery involves restoration of symmetry between hemispheres (Rossiter, Boudrias, & Ward, ).

3.2 Intrahemispheric Changes in Brain Oscillations

Following acute stroke, there is an increase in the amplitude of lower frequency waves (delta waves) (Iyer,2017) and a decrease in the amplitude of higher frequency waves (alpha and beta waves)(Iyer,2017) in ipsilesional sensorimotor cortex and contralesional parietal cortex (Wu et al., ). These increase and decrease in delta and beta waves respectively have been positively correlated with motor impairment (Wu et al., ). Furthermore, higher delta wave amplitude in ipsilesional hemisphere was associated with lower transferrin levels (Assenza et al., ). Since transferrin has been cited in the literature as a scavenger to counteract mediators of oxidative stress following reperfusion after stroke, lower levels (Assenza et al., ). Hence, the identification of these waves not only allows us to quantify the degree of impairment before rehabilitation but also allows us to understand the processes which lead to impairment.

Additionally, the relative power of these high and low frequency waves have been used to calculate Quantitative EEG Indices. These indices have also been shown to be significant predictors of outcomes after stroke. The most significant index reported by many studies is the ratio of amplitude of Delta:Alpha waves, known as Delta:Alpha Ratio (DAR) , where high DAR (S. P. Finnigan, Walsh, Rose, & Chalk, 2007; Leon-Carrion, Martin-Rodriguez, Damas-Lopez, Barroso y Martin, Dominguez-Morales, 2009; Trujillo et al., 2017) has been associated with lower recovery following training.

Use of other Indices such as Power Ratio Index (PRI), ratio of amplitude of Delta+Theta:Alpha+Beta waves, have shown contradictory conclusions. Some studies report negative correlation between PRI and recovery (Trujillo et al., ) whilst others find this correlation to be non-significant (S. P. Finnigan, Walsh, Rose, & Chalk, ). These inconsistencies between studies despite similar number of participants, 10 in (Trujillo et al., ) and 13 in (S. P. Finnigan et al., ), could be due to fact that the outcome measure of recovery were different in both studies. The study which demonstrated negative correlation used FMA (Fugl-Meyer Assessment) (Trujillo et al., ), which is more specific to stroke recovery, whereas the other study which did not find statistically significant different used the generic NIHSS (National Institute of Health Stroke Scale) score (S. P. Finnigan et al., ). However, considering the sample size of both studies were quite small, the use of these indices is yet debatable and studies with larger sample size are needed.

3.3 Event-Related Potentials in Beta Waves

Event-related potentials (ERP) are changes in the amplitude of cortical EEG waves during different stages of movement (Pfurtscheller & Lopes, ).

- Firstly, Event-Related Desynchronization (ERD) occurs which is characterised by a decrease in amplitude of beta waves during preparation and planning of movement. ERD occurs over the contralateral hemisphere due to an increase in desynchronised firing of neurones (Pfurtscheller & Neuper, ), hence suggestive of an activated cortex (Neuper, Wörtz, & Pfurtscheller, ).
- Secondly, ERD spreads to the ipsilateral hemisphere and therefore is present in both hemispheres during execution of movement (Neuper et al., ).
- Thirdly, Event-Related Synchronisation (ERS) occurs which is characterised by an increase in the amplitude of beta waves (Neuper et al., ). This increase in amplitude indicates reestablishment of synchronous neuronal firing, hence suggestive of deactivated cortex (Neuper et al., ).

Event Related Desynchronization (ERD) in Beta Waves is a very useful parameter to determine motor function because ERD is smaller in the affected hemisphere of stroke patients compared to control (Rossiter et al., ). This means that following stroke, there is decreased attenuation or modulation of beta wave activity (Rossiter et al., ). Furthermore, smaller ERD was associated with greater motor impairment within the stroke group (Rossiter et al., ).

Since oscillations arise due to feedback circuits between excitatory and inhibitory neurones (Rabiller et al., ), decreased ability to modulate these oscillations can be attributed to imbalances in these two processes. This idea is supported by the evidence that stroke patients with reduced ERD have decreased GABA-mediated inhibition (Muthukumaraswamy et al., ). Studies have not only shown reduced GABA levels in primary motor cortex of stroke patients compared to control (Blicher et al., ), but also shown that these decreased GABA levels are associated with decreased ERD. In particular, ERD seems to be mediated by GABA-A receptors since ERD is increased on administration of GABA-A receptor agonist, diazepam, to healthy individuals (S. D. Hall et al., ).
Even though low GABA levels is thought to decrease ERD detrimentally in acute phase, follow-up studies suggest that this low GABA levels may be beneficial in terms of rehabilitation. A study by Blicher et al. (2015) showed that changes in GABA levels over rehabilitation was negatively correlated with motor improvement, where greater improvement was seen in individuals with smallest increase in GABA levels after training (Blicher et al., ). Since long-term potentiation occurs in the presence of increased glutamergic excitation and removal of GABAergic inhibition (Rossini et al., ), the reduced GABA mediated inhibition in stroke could explain the increased plasticity (Rossini et al., ) seen in stroke patients in acute phase. This explains why individuals with reduced GABA levels over the course of rehabilitation had better recovery (Blicher et al., ). Additionally, lower GABA levels have been shown to increase use-dependent plasticity which leads to greater representation of the trained limb in the motor cortex (Paik & Yang, ).

Event-Related Synchronisation (ERS) in Beta Waves (Adam, Isabella, & Chan, ) is another parameter recorded in the first second following termination of movement (Ramos-Murguialday & Birbaumer, ). Studies have reported that lower -ERS is observed in unaffected hemisphere on tactile stimulation in stroke patients following acute stroke (Laaksonen et al., ). However, subsequent measurements at 1 and 3 months showed that -ERS increased overtime with recovery (Laaksonen et al., ). Based on evidence from previous studies, it has been proposed that this lower beta-ERS in the acute phase suggests increased cortical excitability of motor cortex which gradually decreases overtime with recovery (Laaksonen et al., ). These findings of tactile stimulation are of interest in terms of rehabilitation because studies have shown positive correlation between -ERS and motor function, where -ERS have been shown to be influenced by integrity of sensory proprioceptive afferents (Laaksonen et al., ). (Shiner et al., ). This highlights the role of afferent signals from hands in determining the functionality of motor cortex.

Putting all these observations together, it can be interpreted that during motor impairment following stroke, there is reduced sensory afferent signals to the brain which causes disinhibition of the motor cortex. This results in increased cortical excitability that can be observed as reduced beta-ERS. Increased excitability in acute phase leads to poor control of movement which leads to impaired motor function (Laaksonen et al., ). Furthermore, increase in -beta-ERS is correlated with improved motor function highlighting that role that sensory afferent signals plays in changing the cortical excitability is important for motor recovery following stroke (Laaksonen et al., ).

3.4 Limitations of EEG

EEG is a great tool in understanding the pathophysiology of stroke as it is widely available, relatively inexpensive and non-invasive (S. Finnigan & van Putten, ). However, as the potentials generated by individual neurones are very small and the current has to pass through layers of the scalp, it is more difficult to detect low energy waves. Furthermore, human factors which are difficult to control such as blinking, movement and muscle activity such as respiration can create artefacts even in otherwise still individuals (Rabiller et al., ). In addition, the wakefulness of the patient at the time of measurement could also affect the recordings as the delta wave measurements may be affected by sleep/drowsiness of the patient which may be due to medications (S. Finnigan & van Putten, ). Another limitation of EEG is the inability to detect the activity of deeper structures, which may be of great value in future research. Use of such technique is limited in human studies due to the invasive nature of the technique (Rabiller et al., ).

3.5 Clinical Implications and Future Development

EEG has a huge potential for developing predictive models of arm recovery which can then not only be used to determine the prognosis for an individual in acute phase, but also used to track the progress of recovery for the individual and tailor rehabilitation to maximise their recovery. Whilst some predictive models have been developed, these do not explain recovery in all patient groups (Kwah & Herbert, ). As suggested by the bimodal balance recovery model, the recovery depends on the structural reserve. Hence being able to stratify patient groups depending on pattern and degree of injury and then developing recovery models for individual groups could allow us to track recovery more realistically on individual basis, particularly for individuals with more severe impairment.

4 Conclusions

Distinct features and patterns of EEG waves have been seen in stroke patients with good and poor recovery in both acute and chronic stages. Recovery of function has been most in individuals with greatest restoration of symmetry and baseline activity. EEG can provide an avenue for development of biomarkers to determine efficacy of therapeutic interventions on individual basis and provide a personalised rehabilitation program.

Even though many studies have demonstrated the use of EEG to predict impairment and recovery after stroke, the evidence of using these oscillations to predict response after training is weak. Few studies have been reported where EEG markers of patients have been recorded before and after rehabilitation program. Hence this is an area which requires further research and would allow us to administer therapeutic interventions more effectively based on individual predicted outcomes, which could be our step towards bringing personalised medicine to the field of stroke rehabilitation.

Author statements

Conflicts of interest statement

No conflicts of interest have been declared by any authors.
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