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A systematic review investigating the relationship of electroencephalography and magnetoencephalography measurements with sensorimotor upper limb impairments after stroke

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Highlights
- Presence of SSEPs in acute can predict better outcome of upper limb motor recovery
- Interhemispheric imbalance of oscillatory signals is associated with impairment
- Neurophysiological and clinical measures could enhance upper limb motor prognosis
- Future research should explore oscillatory signals in acute stroke

Abstract

**Background:** Predicting sensorimotor upper limb outcome receives continued attention. Measures by electroencephalography (EEG) and magnetoencephalography (MEG) could be neurophysiological predictors for sensorimotor upper limb recovery.

**New Method:** The aim of this systematic review was to summarize the current evidence for EEG/MEG-based measures to index neural activity after stroke and the relationship between abnormal neural activity and sensorimotor upper limb impairment. Relevant papers from databases EMBASE, CINHAL, MEDLINE and pubMED were identified. Methodological quality of selected studies was assessed with the Modified Downs and Black form. Data collected was reported descriptively.

**Results:** Seventeen papers were included; 13 used EEG and 4 used MEG applications. Findings showed that: (a) the presence of somatosensory evoked potentials in the acute stage are related to better outcome of upper limb motor impairment from 10 weeks to 6 months post-stroke; (b) an interhemispheric imbalance of cortical oscillatory signals which associated with upper limb impairment; and (c) predictive models including beta oscillatory cortical signal factors with corticospinal integrity and clinical measures could enhance upper limb motor prognosis.

**Comparing with existing method:** The combination of neurological biomarkers with clinical measures results in higher statistical power than using neurological biomarkers alone when predicting motor recovery in stroke.

**Conclusions:** Alterations in neural activity by means of EEG and MEG are demonstrated from the early post-stroke stage onwards, and related to sensorimotor upper limb impairment.

Future work exploring cortical oscillatory signals in the acute stage could provide further insight about prediction of upper limb recovery.
Systematic Review Registration Number: PROSPERO ID: CRD42016038903

Keywords: Cerebrovascular accident; assessment; sensorimotor recovery; event related potentials; cortical oscillations
1. Introduction

Stroke is the third leading cause of adult disability worldwide (Hankey, 2013). One of the contributors to disability is upper limb impairment. Sensorimotor impairments can be defined as motor impairments such as muscle weakness and deficits in motor control in addition to somatosensory impairments. The latter are defined as deficiencies in the sensation arising from skin, muscles, or joints consisting of discriminative abilities, proprioception, or detection of sensation such as light touch, pressure, or pain (Squire et al. 2012). Within 72 hours after stroke, upper limb function deficits range from 48 to 77% (Persson et al. 2012) and at the chronic stage, 33 to 66% experience motor impairments and 21-54% of survivors experience somatosensory impairments (Meyer et al., 2016a; Kwakkel et al., 2003; Sunderland et al., 1994; Wade et al., 1983). Therefore, only 41% of people with moderate to severe stroke and 71% with mild stroke regain dexterity (Houwink et al., 2013). This results in limitations when using the upper limb during activities of daily living (Faria-Fortini et al., 2011).

Motor and sensory outcome prediction is useful in setting goals and planning treatment programs for improving upper limb impairments of people with stroke (Ward et al., 2017). Clinical examination has been the most common method to predicting upper limb motor recovery in stroke. Fugl Meyer Assessment (FMA), an outcome measure of motor impairment predicts upper limb motor function outcome. Patients will either recover about 70% of the maximum possible improvement or show little to no improvement (Winters et al., 2015). Motor problems resulting from additional sensory deficits after stroke are mainly due to impaired detection of sensory information and disturbed motor tasks performance requiring somatosensory information (Hunter, 2002). Somatosensory clinical outcomes of light touch, proprioception and stereognosis measured in acute stroke have also been associated with upper limb motor impairments at six months post-stroke (Meyer et al., 2016a). However, supplementary sensitive and specific outcome measures that identify crucial information about the underlying neural mechanisms are needed to distinguish between proportional versus poor sensorimotor recoverees in stroke rehabilitation (Guggisberg et al., 2017).
A stroke recovery biomarker has been defined as “an indicator of disease state that can be used as a measure of underlying molecular/cellular processes that may be difficult to measure directly in humans, or predict recovery or treatment response” (Bernhardt et al., 2016). Biomarkers should be easy to use, reliable and provide a predictive value to individual patients. They are typically measured in the acute stage, week after onset and subacute stage—between 1 week and 3 months after stroke onset (Kim and Winstein, 2017). The integrity of the corticospinal tract and premotor-motor pathways measured by transcranial magnetic stimulation (TMS) and functional magnetic resonance imaging (fMRI) have been identified as neurophysiological and neuroanatomical biomarkers for upper limb motor recovery (Schulz et al., 2017; Byblow et al., 2015). The presence or absence of a motor evoked potential in the first three days post-stroke has been suggested to predict between a good or limited/poor motor recovery respectively (Stinear et al., 2017). Motor network activity measured by fMRI could individualize prediction of 86% of motor outcome (Rehme et al., 2015). Recently, it has been identified that the integrity of the corticospinal tract and corticocortical connections between the ventral premotor cortex and primary motor cortex have a significant role in the residual motor output of people with sub-acute stroke (Schulz et al., 2017). Additionally, an intact sensory afferent signal is important for driving cortical remapping which is key for motor recovery (Murphy and Corbett, 2009). Thus, the somatosensory modalities may play an important role in modulating motor control processes as well (Bodmer and Beste, 2017). After stroke, voxel-based lesion-symptom methodology showed a lack of integrity of brain structures such as the superior thalamocortical radiation and the parietal operculum cortical regions, and associated with behavioral somatosensory deficits (Meyer et al., 2016b). Therefore, the assessment of both motor and somatosensory factors could increase the percentage of accurate prediction of upper limb outcome. However, apart from TMS and MRI methodologies, electrophysiological measures to guide sub-group stratification has been identified as a developmental priority at a Stroke Recovery and Rehabilitation Roundtable (Boyd et al., 2017).
Electroencephalography (EEG) records brain electrical fields using surface electrodes on the scalp while magnetoencephalography (MEG) records brain magnetic fields using sensitive magnetometers (Berger et al., 1929; Cohen et al., 1972). Both applications are close in methodologies since they have the same source of signals from ionic currents generated by biochemical processes at the cellular level (Lopes da Silva, 2013) and also have superior temporal resolution (Shiner et al., 2015). MEG has higher spatial resolution in separating cortical sources than EEG (Hari, 2011). However, MEG is more expensive and highly sensitive to external disturbances of the tiny magnetic fields measured.

Both EEG and MEG signals are described as frequency bands from infraslow, theta, alpha, beta, gamma and high-frequency oscillations. Alterations in frequency patterns have been associated with pathology including stroke (Tecchio et al., 2007a). Event-Related Synchronization/Desynchronization (ERS/ERD) of frequency band-limited power are usually indicative of patterns of cortical activation and deactivation underlying behavior (Stepien et al., 2011). Additionally, disruption of neural activity can be measured by time-locked-evoked or event-related potentials (ERP) measured by EEG or magnetic fields (ERF) measured by MEG. ERPs are the summated dipole fields of extracellular currents generated by cortical pyramidal cell populations that have become synchronously active in response to an external sensory event or an internal motor event (Okada et al., 1997; Bressler & Ding, 2006; Murakami & Okada, 2006). Specifically, somatosensory evoked potential (SSEPs) or somatosensory evoked fields (SEFs) can provide an index of somatosensory central nervous system pathways by stimulation of somatic receptors or electrical stimulation of peripheral nerve such as the median nerve (Allison et al., 1991). Additionally, EEG coherence has the ability to assess functional connectivity (FC) which is a measure of similarity between spontaneous brain activity signals measured at different locations at rest (Srinivasan et al., 2007). Alternations in cortical oscillatory signals, evoked potentials or functional connectivity could potentially be identified as biomarkers of upper limb recovery in stroke.
Recently a systematic review exploring the evidence and determining which neurological biomarker(s) meet the high evidence quality criteria for use in predicting motor recovery was has been conducted. However, only biomarkers using diffusion tensor imaging, TMS, functional MRI (fMRI), conventional structural MRI (sMRI), and a combination of these biomarkers were included (Kim and Winston, 2017). However, EEG and MEG has superior temporal compared to the aforementioned techniques (George et al., 1995). Therefore, allowing the examination of responses on a short time scales (milliseconds) and longer time scales (minutes) which is important for analyzing sensorimotor recovery. High temporal resolution also reduces the aliasing of higher frequencies and provided more data points per unit time resulting in more accurate correlation values (Magnuson et al. 2015). Therefore, we conducted a systematic review to: (1) evaluate high-quality evidence for high temporal resolution EEG/MEG-based measures to index neural activity after stroke and their relationships with abnormal neural activity with sensorimotor upper limb impairment in the acute, sub-acute and chronic stages and (2) determine if such measures could predict sensorimotor upper limb recovery. The results of this review could result in a better understanding of the longer-term outcome referring to recovery of upper limb impairments and use the information to identify promising biomarkers for future research and clinical consideration (Berhardt et al., 2017).

2. Methods

The systematic review was registered on PROSPERO (ID: CRD42016038903).

2.1 Study inclusion criteria

Types of study design: The studies included were: (i) Experimental studies (intervention and effectiveness studies with a prospective longitudinal design) and (ii) non-experimental studies (observational and cross-sectional studies) written in English. Sample size needed to be more than one participant.
Types of participants: Participants included in the studies needed to: (i) have a confirmed clinical diagnosis of a hemorrhagic or ischemic stroke by a neurologist or stroke consultant; (ii) have either somatosensory and/or motor upper limb impairments; and (iii) be at any time since stroke onset.

Outcome measures: EEG and MEG measurements including: event-related potentials, ERS/ERD of spectral bands power and functional connectivity.

2.2 Search strategy and study selection

A search of the databases MEDLINE, EMBASE (Excerpta Medica Database), CINAHL (Cumulated Index of Nursing and Allied Health Literature) and PubMed was conducted from database inception to February 2018 by LTT. A hand search of the reference lists of each included article and the identified literature reviews were also screened for relevant publications. Key words of "stroke", "cerebrovascular accident", "upper limb", "arm", "hand", "encephalography", "EEG", "magnetoencephalography", "MEG", "cortical activity", "neural activity", "somatosensory evoked potential", "motor recovery", "sensory recovery" and synonyms for the search on the electronic databases were used (Table 1). The reference lists of each search from the different databases containing the articles and narrative reviews were also scanned separately for relevant publications. This was followed by the selection process based on title, abstract and then full text independently by two reviewers (LTT and SM). Any conference abstracts and duplicates were excluded. Any disagreement about the selection at each stage between reviewers was resolved through discussion between the two review authors. Where resolution was not achieved, a third reviewer (GV) considered the paper(s) in question. At the end of this process, there was 100% agreement between all raters for the different items of the modified Downs and Black.

2.3 Risk of potential bias appraisal
Two review authors (LTT and SM) assessed the risk of bias independently using a standardized valid and reliable form called the modified Downs and Black tool (Downs and Black 1998; Eng et al. 2007). This tool assesses the methodological quality of non-randomized studies of health care interventions. The form contains 27 ‘yes’-or- ‘no’ questions across five sections. Items relating to intervention and randomization from the tool were deleted (Meyer et al. 2014). As a result, the tool contained questions about: 1) overall study quality (reporting) (8 items); 2) external validity (3 items) – the ability to generalize findings of the study; 3) internal validity (4 items) – to assess bias in the intervention and outcome measure(s) and 4) confounding and selection bias (4 items) – to determine bias from sampling or group assignment. As used in a similar review, papers achieving at least 65% of the maximum possible score as having substantial quality were included in this review (Meyer et al., 2014).

2.4 Data Extraction and analysis

Two reviewers (LTT, SM) carried out data extraction independently. The extracted data included: the design of the study, setting, inclusion and exclusion criteria, information about participants including: (i) number of participants, (ii) gender, (iii) side of stroke, (iv) type and (v) location of stroke and (vi) time since stroke, (vii) time-point of assessment, (viii) type of EEG or MEG methodology, (ix) outcome measures, (x) data analysis and (xi) results. Due to the heterogeneity of the data, meta-analyses could not be performed for this review. Therefore, data were grouped according to different EEG/MEG analyses of evoked potential, cortical oscillatory signals and functional connectivity analysis linked with clinical outcome and are reported descriptively in the results section.

3. Results

3.1. The evidence base

From 2616 related titles, 646 abstracts were screened and 96 full-text papers were assessed for eligibility in which 49 were then excluded. Using Modified Down’s and Black tool, risk of bias was
then assessed for the remaining 47 articles. Low quality papers (<65% score) (n=30) were removed and 17 papers were included in the review with 13 used EEG and four used MEG methodologies (Figure 1). Nine studies had a cross-sectional design (Pichiorri et al., 2018; Chen et al., 2017; Kawano et al., 2017; Thibaut et al., 2017; Campfens et al., 2015a; Rossiter et al., 2014; Kaiser et al., 2012; Oliviero et al., 2004; Platz et al., 2000), seven studies had a longitudinal design (Anastasi et al., 2017; Guggisberg et al., 2017; Parkkonen et al., 2017; Feys et al., 2000; Tzvetanov and Rousseff, 2005; Westlake et al., 2012; Keren et al., 1993) and one was an intervention study but only the baseline data was used for this review (Wu et al., 2015). The earliest study included in the review was in 1993. An increase in research exploring the relationship of EEG measures and upper limb clinical outcome in stroke from 2017 onwards was identified. A full summary of all the papers are presented in Tables 2,3 and 4.

3.2 Summary of Participant Characteristics

In total 581 people with stroke were included in the review. All papers excluding one (Pichiorri et al., 2017) reported the gender of the participants, consisting of 194 females (33.4%) and 357 males (61.4%). From the total sample, 189 (32.5%) were in the acute stage of stroke (≤2 weeks post-stroke), 280 (48.2%) were in the sub-acute stage of stroke (>2 weeks - ≤6 months post-stroke) and 112 (19.3%) were in the chronic stage of stroke (>6 months post-stroke). Fourteen papers reported that 213 (36.6%) had a right-sided stroke, 191 (32.9%) had a left-sided stroke and one participant had right-and left-sided stroke. Eleven papers reported that 354 (60.9%) had ischemic stroke and 70 (12.0%) had hemorrhagic stroke and the location of the stroke; out of these 120 (20.7%) had cortical; 154 (26.5%) sub-cortical and 44 (7.6%) had cortico-subcortical stroke.

3.3 Somatosensory evoked potential/field analysis and upper limb motor outcome

Presence, amplitude and latency of SSEPs or SEFs were explored in four studies. It was identified that participants with acute stroke with an absent median nerve SEP had lower muscle strength scores
(p < 0.01) (Tzvetanov and Rousseff, 2005; Feys et al., 2000; Keren et al., 1993). Present SSEP latency of the NI (negative component) complex and amplitude (P15/NI) measured by EEG at 3 weeks post-stroke correlated with motor ability measured at 10 weeks later (r=0.66 and r=0.62 respectively) (Keren et al., 1993). However, the correlation between N20-P25 amplitudes of SSEPs and muscle strength was weak in acute stroke (Tzvetanov and Rousseff, 2005). The correlations of amplitude parameters of SSEPs with motor impairments at 6 months were also weak (p < 0.05) (Tzvetanov and Rousseff, 2005). Participants with acute stoke with an absent median SSEP had lower MRC scores cross-sectionally (p < 0.01) (Tzvetanov and Rousseff, 2005; Feys et al., 2000; Keren et al., 1993).

Equivalent current dipole strength of SEFs measured by MEG in the affected hemisphere showed a direct relationship with motor scores in acute stroke (r=0.52; p=0.002 for M20 and r=0.37 p=0.037 for M30) (Oliviero et al., 2004).
3.4 Cortical oscillatory signal analysis and upper limb sensorimotor outcome

Participants with hemiparesis in the sub-acute and chronic stage had pronounced alpha ERD at frontal, temporal and centroparietal regions when carrying out a motor task with their affected UL compared to healthy controls (Platz et al. 2000). A significant positive correlation was found between low beta and upper limb motor impairments when measured at rest of people with sub-acute and chronic stroke ($Rs = 0.56, p=0.002$) (Pichiorri et al., 2018). In participants with somatosensory deficits in the sub-acute stage, a reduction in alpha activity was found at central and centroparietal regions where movement-related alpha-ERD is usually expected (Platz et al., 2000).

Asymmetry between hemispheres was reported in three studies exploring cortical oscillatory signals in combination with motor active tasks (Kaiser et al., 2013, Rossiter et al., 2014, Anastasi et al., 2017). Movement-related beta desynchronization was significantly smaller in the contralateral but not in the ipsilateral M1 ($p=0.005$) during movement of the affected UL in people in the sub-acute and chronic stages of stroke (Rossiter et al., 2014). Additionally, movement-related beta desynchronization (smaller reduction in beta power) in the contralateral hemisphere correlated negatively with motor impairment (standardized regression coefficient ($\beta$) = -0.52, $p=0.008$, $r^2=0.26$) (Rossiter et al., 2014). A significant higher brain symmetry index, especially in cortical stroke ($p=0.028$) was found in people with acute and sub-acute stroke (Anastasi et al., 2017). Severe upper limb motor impairments were also associated with imbalance oscillatory activity between the ipsilesional and contralesional hemispheres (Kaiser et al., 2013). During movement of the affected hand of people with sub-acute stroke, people with increased upper limb motor impairment showed higher ipsilateral alpha ERS whilst those with mild upper limb motor impairments showed significant higher contralateral ERS (Kaiser et al., 2013).

In two studies, brain symmetry index and interhemispheric phase synchrony index of alpha and beta bands did not significantly correlate with upper limb motor impairments of participants with sub-
acute stroke during active motor task and at rest respectively \((r=-0.543, p=0.266 \text{ [Anastasi et al., 2017], } p=0.49 \text{ and } p=0.22 \text{ alpha and beta band respectively [Kawano et al., 2017]})\). 

A specific oscillatory signal analysis after passive movement of the index finger showed that the amplitude of 20Hz rebound at the affected but not at the unaffected hemisphere significantly positively correlated with upper limb functional upper limb measures in the acute, sub-acute and chronic stages of stroke \((r= 0.6, p < 0.01 \text{ [acute], } r=0.7, p< 0.001 \text{ [sub-acute] and } r=0.6, p < 0.01 \text{ [chronic]} \text{ (Parkkonen et al., 2017)})\).

3.5 Functional connectivity analysis and upper limb motor outcome

Functional connectivity between ipsilesional and contralesional M1 was not significantly related to upper limb motor impairments in people with chronic stroke at rest \((p=0.87) \text{ (Wu et al., 2015).}\) Higher ipsilesional connectivity between M1 and premotor cortex were associated with milder upper limb impairments \(\text{ (Wu et al., 2015).}\) Greater reduction in resting state alpha-band functional under connected voxels at 8-12 weeks apart led to better composite clinical recovery score with participants in the acute, sub-acute and chronic stages of stroke \((r=0.81; p=0.003) \text{ (Westlake et al, 2012).}\) In the latter study, time of stroke was factored in the correlation analyses and a significant positive association was found between recovery and functional connectivity in the primary motor and somatosensory cortices \((r=0.64; P=0.01).\) A negative association was then found between functional connectivity in the contralesional sensorimotor cortex \((r=0.75, p=<0.0001)\) and the posterior parietal cortex \((r=0.75, p=0.0028).\)
3.6 Prediction regression models for upper limb motor impairments

Prediction models have been explored in relation to SSEP and frequency band analysis. Amplitude of SSEP in the lesioned hemisphere resulted in a predicted variance of $r^2 = 0.34$ for motor ability (Keren et al., 1993). Presence of a SSEP and motor performance measured at the early stage of sub-acute stroke resulted in 60% and 58% of the variance of prediction of motor recovery at 6 and 12 months post-stroke (Feys et al., 2000). Combined motor strength score and N20-P25 ratio of SSEPs resulted in a predictive value of 70% and 45% for ADLs and disability scores in ischemic and hemorrhagic stroke respectively (Tzvetanov and Rousseff, 2005).

Beta plus gamma or theta network features were identified as EEG-based motor network biomarkers yielding highest accuracies of 92% to the predictive model for stratifying people with stroke for upper limb rehabilitation in the sub-acute and chronic stages (Chen et al., 2017). EEG measures in addition with corticospinal tract integrity measured by structural imaging or TMS and FMA were added to predictive models. Corticospinal tract asymmetry, initial FMA and beta-band coherence measured in the sub-acute stage was found to have sensitivity of 0.89 and positive predictive values of 0.86 and 0.88 respectively in predicting upper limb motor recovery (Guggisberg et al., 2017). When factors of high beta in the affected and unaffected hemisphere measured at rest in addition with motor threshold measured by TMS, and clinical FMA score were added to separate predictive model, this resulted in the highest prediction level for upper limb motor impairments at the chronic stage (Adj $R^2 = 0.366$) (Thibaut et al., 2017).

4. Discussion

To our knowledge, this is the first review to have systematically evaluated the relationship between EEG or MEG measures with upper limb sensorimotor impairments post stroke. In summary, the main EEG or MEG measures were based on the study of evoked potentials or evoked fields, cortical oscillatory signals and functional connectivity. Median nerve SSEP latency measurement in the acute
stage are associated with upper limb motor recovery in the sub-acute and chronic stages. Study of cortical oscillatory signals reported interhemispheric imbalance between the contralesional and ipsilesional hemisphere, and associated with severity of upper limb motor impairments. Additionally, increased functional connectivity in the ipsilesional hemisphere has potential of predicting upper limb motor recovery. Finally, EEG measures of cortical oscillatory signals in combination with measurement of corticospinal integrity could be of relevance in predicting upper limb recovery but further work is warranted to collect oscillatory measures in the acute stage of stroke.

4.1 The relationship between somatosensory evoked potentials and upper limb motor recovery

Unilateral stimulation of the median nerve activates the contralateral primary somatosensory cortex representing the lowest level of cortical processing (Sutherland & Tang, 2006). Our results showed that presence or absence of median SSEPs in the acute and sub-acute stage of stroke could predict upper limb motor recovery. Additionally certain components such as the negative latency and amplitude measured at 3 weeks post-stroke associated with motor ability measured clinically measured at 10 weeks later (Keren et al., 1993). However, evidence provided for SSEPs comes from a majority of studies published over 10 years ago. Thus, due to lack of recent studies using this methodology, the conclusions drawn regarding the potential clinical utility should be considered with caution. Additionally, one must note that only two electrodes were used in the included studies and this does not depict a topographical image of the activity in the different areas of the brain. More channels were included for the measurement of somatosensory evoked fields by MEG which also provided information about upper limb motor recovery. The study of Oliviero et al. (2004) showed that such measurements had moderate to high association with motor function measures in acute stroke. MEG is dependent on the interaction between excitation and inhibition in cortical microcircuits which could be more responsive in the acute and sub-acute stages of stroke (Yamawaki et al., 2008). However, MEG is expensive and complex to employ (Boyd et al., 2017) and, therefore, using EEG with 32 electrodes or above when measuring SSEPs should be explored in future research.
4.2 Study of cortical oscillations in people with motor impairments after stroke

The role of intrahemispheric connectivity remains controversial in stroke. In animal studies, it has been reported that a reduction of alpha and beta waves in the ipsilesional hemisphere was identified (Moyanova & Dijkhuizen 2014) while other studies reported an increase in rhythmic alpha waves in the contralesional hemisphere during the first seven days after total middle cerebral artery occlusion (Lu et al, 2001). In humans, different results have also been presented about observations of contralesional changes in relation to motor recovery (Buetefisch 2015; Dodd et al. 2017; Rehme et al. 2010). In this review, cortical oscillatory asymmetry between hemispheres were reported in four studies with moderate/good quality. Movement-related beta desynchronization was significantly smaller in the contralesional M1 during movement of the affected upper limb in people in the sub-acute and chronic stages and correlated negatively with motor impairment (Rossiter et al., 2014). On the contrary, brain symmetry index and interhemispheric phase synchrony index of alpha and beta bands did not significantly correlate with upper limb motor impairments of participants with sub-acute stroke (Anastasi et al., 2017; Kawano et al., 2017). The different results could be due to measurements taken at different stages of stroke. Neural activity and network adaptations change over time (Koch & Hummel, 2017). Additionally, one included study reported that a significant higher brain symmetry index was found in people with cortical stroke (Anastasi et al., 2017). Stroke location and severity of upper limb impairments have been linked with the inhibitory role of the contralesional hemisphere (Huynh et al., 2016). The included studies in this review did not explore cortical oscillations in the acute stage. Predictive models of upper limb motor recovery include the initial TMS measurement within 72 hours post-stroke to predict upper limb motor recovery at three months (Stinear et al., 2017). Due to the critical time window for recovery is in the first 30 days post-stroke (Murphy and Corbett, 2009) and the feasibility of using EEG in the acute stroke, future research should explore cortical oscillatory signals within 72 hours post-stroke to three months post-stroke (Stinear, 2017).
4.3 Prediction of upper limb motor recovery

Different methodologies are able to investigate the wide field of underpinning motor recovery after stroke, such as TMS, fMRI and DTI. A recent systematic review identified that a combination of clinical and neurophysiological biomarkers measured by fMRI, DTI and TMS is more common and likely preferable than using neurophysiological biomarkers alone to accurately predicting motor recovery in stroke (Kim and Weinstein, 2017). Currently, a useful and promising tool for predicting upper limb motor recovery at three months post-stroke is the PREP algorithm which combines clinical and neuroimaging markers or the PREP2 algorithm which combines clinical and TMS markers (Stinear et al., 2017; Byblow et al., 2015). However, the algorithm makes correct predictions for 75% of patients. Apart from exploring the integrity of the corticospinal tract, it has been suggested to also study the damage in multiple cortical and sub-cortical brain regions when predicting upper limb motor recovery (Boyd et al., 2017; Rondina et al., 2017). Functional connectivity in high beta band measured between the ipsilesional primary motor cortex and premotor regions by EEG which has a superior temporal resolution to MRI or TMS, demonstrated a specific marker for motor status. An increase in connectivity was a good predictor for motor improvement after 28 days of training (Wu et al., 2015). Additionally, our review showed that EEG measures such beta oscillatory activity at the affected and unaffected hemisphere and beta coherence also provided good prediction for upper limb motor recovery. This shows that adding EEG measures to predictive models could provide additional prognostic value for upper limb motor recovery. In this light, the benefit of measuring both corticospinal tract integrity and beta oscillatory activity in addition with clinical measures needs to be further explored.

4.4 Strengths and limitations of the review

This is the first review to explore the current evidence of EEG and MEG measures of upper limb sensorimotor recovery. In order to present sound quality of evidence, a detailed thorough methodology for selection of papers was employed. However, there are some limitations in this
review. It was essential to include evidence from high-quality studies and therefore, only 17 from 47 full-text papers were included. This resulted in prohibiting subgroup analyses of different types and locations of stroke, highlighting the need for additional high-quality studies to evaluate the potential clinical utility of these imaging approaches to inform stroke rehabilitation. Additionally, an unusual number of only 25% of the sample were women included in this review which is usually around 50% (Di Carlo et al., 2003). Therefore, gender bias could have influenced the results.

4.5 Future work

As soon as a substantial amount of high-quality spatio-temporal electrophysiological and hemodynamic data is available, a meta-analyses using odds ratio should be conducted to explore the value of the EEG and MEG in addition with fMRI, DTI, TMS and near-infrared spectroscopy measures in predicting upper limb sensorimotor recovery. From the meta-analyses, new scientific hypothesis could be generated about exploring the effect of different interventions of upper limb recovery using EEG or MEG in addition with fMRI, DTI, TMS or near-infrared spectroscopy measures as primary or secondary outcome measures. For example, brain computer interfacing uses EEG to generate motor output, future reviews should explore its important role in the recovery sensorimotor upper limb impairments after stroke (Frolov et al., 2017; Ang et al., 2015). This will provide valuable information about the causal connection between brain signals and rehabilitation intervention. The majority of the included studies in this review mainly explored motor upper limb impairments. To date, there are also limited neuroimaging studies identifying biomarkers for somatosensory impairments in stroke (Goodin et al., 2018, Meyer et al., 2016b, Bannister et al., 2015, Schaechter et al., 2006). Therefore, a large sample of people after stroke with somatosensory in addition to motor upper limb impairments should be included when exploring including somatosensory evoked potentials and movement-related frequency measures in prediction models for upper limb recovery. Although acute stroke research has its challenges, future research should explore movement-related cortical oscillatory
signals in the very early stage post-stroke. This could have the potential to accurately predict motor recovery at three and six months post-stroke and plan treatment programs accordingly.

5. Conclusion

This is the first review to explore different types of EEG and MEG measures in relation to sensorimotor upper limb impairments after stroke. Seventeen studies were included in the review. Presence of SSEPs are related to better outcome of upper limb motor impairment post stroke in the sub-acute and chronic stages. An imbalance of cortical oscillatory signals between the ipsilateral and contralateral hemispheres with movement of the affected upper limb was identified. An increase in beta activity in contralateral hemisphere correlated with poorer upper limb motor outcome in chronic but not sub-acute stroke. Additionally, predictive models with beta oscillatory cortical signal factors with corticospinal integrity and motor clinical measures could predict upper limb motor recovery. Future research should explore EEG or MEG measurements in the acute stage of stroke with a larger sample of stroke participants with stratification for location of stroke and upper limb motor and somatosensory severity. This could provide accurate biomarkers of recovery leading to better stratification of patients for clinical trials and inform evidence-based practice.

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### Tables

Table 1: An example of a search strategy used to screen for relevant papers included in this review

| Search | Key words |
|--------|-----------|
| 1      | Electroencephalography |
| 2      | Magnetoencephalography |
| 3      | EEG |
| 4      | MEG |
| 5      | Cerebrovascular accident.mp.or exp "stroke/" |
| 6      | 1 or 3 |
| 7      | 2 or 4 |
| 8      | 6 or 7 |
| 9      | ‘upper limb' OR 'arm' OR 'hand'- title, abstract, keyword |
| 10     | 5 and 8 and 9 |
Table 2: Summary of all included papers exploring evoked potentials

| Reference | Modified Downs and Black Score | Technique | Design of study | Aim of study | Stroke Participant Characteristics | Brain Activity Measure/s (time-point) | Clinical Outcome Measure (time-point) | Results |
|-----------|---------------------------------|-----------|-----------------|--------------|-----------------------------------|--------------------------------------|--------------------------------------|---------|
| Keren et al., 1993 | 68% | EEG | Longitudinal study | Determination of the predictive capacity of upper limb short latency SSEP for clinical evaluation | N=19  
G=8F, 11M  
Mean Age=57.8 years (range 36-71 years)  
Mean Time post-stroke=20.5±8.8 days (sub-acute)  
Baseline UL motor impairment=Not specified  
Stroke Type=19 I  
Stroke location=Not specified | Median nerve SSEP amplitude and latency measured at C3 and C4 channels | Impairments measured by:  
- Motricity Index | - Non-detectable SSEP had worse outcomes at baseline  
- NI latency over dominant hemisphere correlated with motor ability and ADLs (r=0.66;0.69)  
- P15/NI amplitude over dominant hemisphere correlated with motor ability (r=0.62)  
-Multiple regression showed that only amplitude of
| Feys et al., 2000 | 74% | EEG | Longitudinal study | Assessment of the value of SSEPs in the prediction of motor recovery of the upper limb in people with stroke and to evaluate the combined predictive value of these measures and set of clinical variables | N=64  
G=27F, 37M  
Mean age=63.69 (SD=11.34) years  
Mean Time post-stroke=22.08 (SD=6.49) days (sub-acute)  
Baseline UL motor impairment (FMA)= 12.94 (SD=10.16) | Median nerve SSEP measured at C3 and C4 channels | Impairments measured by:  
- FMA  
- Modified Ashworth scale  
(Two time-point assessments at 2-5 weeks, 6 weeks, 6 months) | -Motor performance and SSEPs measured at baseline accounted for 60% and 58% of the variance at 6 and 12 months | damaged hemisphere significantly correlated with motor ability ($R^2=0.34$) |
| Olivier et al., 2004 | 75% | MEG | Cross-sectional correlation study | Assessment of relationship between MEG results, clinical status and neuroradiological findings | N=32 | G=15F, 17M | Mean age=68 ±12 years | Mean Time Post-stroke=5.2±2.6 days post-stroke (acute) | Baseline UL impairment=Not specified | Median nerve SEF measured at 28-channels | Impairments measured by: | - Canadian neurological scale | - Arbitrary four-degree scale for sensory impairment; | - NIH stroke scale | - Excessive interhemispheric latency asymmetry of M30 statistically correlated with a worse clinical picture (motor p=0.007; sensory=0.031; ADL=0.001) | - Significant correlation between lesion size and strength of M20 in the unaffected hemisphere (rho=0.43; p=0.019) |
|---------------------|-----|-----|-----------------------------------|---------------------------------------------------------------------------------|------|--------|---------------------|-----------------------------------------------|-----------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|
| Tzvetanov and Roussouff, 2005 | 68% | EEG | Longitudinal study | Assessment of the predictive value of SSEP changes in early phase of stroke | N=130 | G=43F, 87M | Mean age=62.5 (SD=11.4) years | Median nerve SSEP measured at C3 and C4 channels | Impairments measured by: | - Muscle strength | (One time-point assessment at a mean time 5.2 days post-stroke) | - Absent median SSEP was linked with lower muscle strength scores (p<0.01) |
| Campfens et al., 2015a | 69% | EEG | Cross-sectional correlation study | Exploring StrEPs in a group of sub-acute stroke and to evaluate whether the StrEPs and StrEP components can be measured in the acute phase | N= 8; G= 1F; 7M | Mean Age= 57 years | Range= 35-77 | Range Time post-stroke= 13-135 days post-stroke (1 acute; (5 sub-acute; 2 chronic) | Baseline UL motor impairment= Range FMA score=6-65 | Flexion and extension wrist manipulation StrEP measured at 64 channels | Impairments measured by: - FMA | - No significant differences in StrEPs waveforms between good and poor function (p=0.19 at contralateral motor cortex; p=0.14 at vertex) | Mean Time post-stroke= Not Specified | Baseline UL motor impairment= Not specified | Stroke Type= 89 I; 41 H | Stroke location= I: 48C; 33SC; 8CSC H: Lobar 7; Putamenal 24; Thalamic 10 | 0-7 days ischemic; 0-21days hemorrhagic | (One time-point assessment at 0-7 days ischemic stroke; and 0-21days Hemorrhagic stroke) | (One time-point assessment at 6 months post-stroke) | - Combined assessment of muscle strength and N20-P25 ratio in ischemic stroke leads to predictive power of 70% of ADLs and Disability |
| Stroke Type   | Stroke Location | Time Point Assessment | 135 weeks post-stroke |
|---------------|-----------------|-----------------------|-----------------------|
| Both I and H  | 3C; 5SC         | (One time-point assessment between 13-135 weeks post-stroke) | 135 weeks post-stroke |

* C=Cortical; CSC= cortico-subcortical; F=Female; FMA=Fugl-Meyer Assessment; G=Gender; H=Hemorrhagic; I=Ischemic; M=Male; N=Sample number; NIH=National Institute of Health; SC=Sub-cortical; SSEP=Somatosensory evoked potential; UL=Upper Limb
Table 3: Summary of all included papers exploring cortical oscillatory signals

| Reference          | Modified Downs and Black Score | Technique  | Design of study                  | Aim of study                                                                 | Stroke Participant Characteristics                                                                 | Brain Activity Measure/s (time-point)         | Clinical Outcome measure (time-point) | Results                                                                 |
|--------------------|--------------------------------|------------|----------------------------------|-------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|---------------------------------------------|----------------------------------|--------------------------------------------------------------------------------|
| Platz et al., 2000 | 75%                            | EEG        | Cross-sectional correlation study| Assessment of different subgroups of stroke patients with clinically distinct impairments and EEG analysis of movement-related brain activity | N=13, G= 3 F; 10M, Mean age (SD)= 54.9 (6.5), Mean Time post-stroke= 8.8 weeks (SD 7.3) (sub-acute), Baseline UL motor impairment= Mild to moderate paresis, Stroke Type= 13 I, Stroke location= 9C; 4SC | Active Movement-related frequency analysis measured at 27 channels | Impairments measured by no defined outcome measures - UL paresis - UL somatosensory deficit - Ideomotor apraxia | Pronounced alpha ERD at frontal, temporal and centroparietal regions in participants with hemiparesis |
| Study                                      | Percent | Method | Design                          | N | Gender | Mean Age | Mean Time Post-stroke | Baseline Motor Impairment | Active Movement-related Frequency Analysis | Impairments Measured by | Impairments Correlation |
|--------------------------------------------|---------|--------|---------------------------------|---|--------|----------|------------------------|---------------------------|---------------------------------|------------------------|------------------------|
| Kaiser et al., 2012                        | 81%     | EEG    | Cross-sectional correlation study | 29 | 14F; 15M | 58 ± 15 years | 4 ± 4 months (chronic) | Muscle Strength Score=57±13 |                                | - Significant negative correlation between muscle strength and LC for ERS of affected side (R=−0.51, P=0.037) |
| Rossiter et al. (2014)                     | 69%     | MEG    | Cross-sectional study           | 23 | 5F; 18M | 50 ± 13 years | 32 ± 50 months (chronic) | Grip Strength Score=38±22lb |                                | - Movemt-related Beta Desynchronization in contralateral M1 correlated negatively with motor impairment [standardized regression coefficient (β=−0.52, |
Anastasi et al., 2017 | 68% | EEG | Longitudinal study | *Investigation of the role of quantitative EEG parameters, particularly BSI, in the assessment and prognostication of motor function in the subacute phase poststroke* | N=10  
G= 0F; 10M  
Mean Age= 59.4 years  
Mean (SD) Time post-stroke at baseline= 25.7 (17.8) days  
Baseline UL motor impairment= FMA Score=40.3 (SD=25.6)  
Stroke Type= Not defined  
Stroke location= 4C; 6SC | *Active Movement-related frequency analysis measured at 32 channels* | *Impairments measured by:*  
- FMA  
- MRC  
- MI  
(Four time-point assessments:  
Session 1 Range 5-60 days post-stroke;  
Session 2 Range 31-91 days post-stroke,  
Session 3 Range 63-112 days post-stroke,  
Session 4 Range 113-174 days post-stroke) | *- A significant difference in BSI between stroke and healthy (p=0.023)*  
- Significant differences in BSI in cortical stroke versus healthy subjects (p = 0.028).  
- The correlation between FMA and BSIc1 at follow-up statistical
| Chen et al., (2017) | 81% | EEG | Cross-sectional study | Study the inter-areal communication and both frequency-specific parameters (using EEG) and network connectivity are of a prognostic value | N=37  
G= 10F; 27M  
Mean (SD) Age= 57.0 (12.6)  
Mean (SD) Time post-stroke= 6.5 (5.2) months  
Baseline UL motor impairment= FMA =30.9 (SD) 13.9  
Stroke Type= 20I/17H  
Stroke location= 14C;23SC | Active Movement-related frequency analysis measured at 32 channels | Impact measured by:  
- FMA  
- WMFT  
- Upper extremity performance evaluation test for the elderly | - Beta plus gamma or theta network features were identified as EEG-based motor network biomarkers yielding highest accuracies of 92% to the predictive model |  
Range 63-112 days post-stroke, Session 4 Range 92-146 days post-stroke |  
Session 4 Range 92-146 days post-stroke) | significance (r = −0.543, p = 0.266)  
- No statistical significant differences in BSI over time (p=0.077)  
Mean (SD) Age= 57.0 (12.6)  
Mean (SD) Time post-stroke= 6.5 (5.2) months  
Baseline UL motor impairment= FMA =30.9 (SD) 13.9  
Stroke Type= 20I/17H  
Stroke location= 14C;23SC  
Mean (SD) Time post-stroke= 6.5 (5.2) months  
Baseline UL motor impairment= FMA =30.9 (SD) 13.9  
Stroke Type= 20I/17H  
Stroke location= 14C;23SC  
Mean (SD) Time post-stroke= 6.5 (5.2) months  
Baseline UL motor impairment= FMA =30.9 (SD) 13.9  
Stroke Type= 20I/17H  
Stroke location= 14C;23SC  
Mean (SD) Time post-stroke= 6.5 (5.2) months  
Baseline UL motor impairment= FMA =30.9 (SD) 13.9  
Stroke Type= 20I/17H  
Stroke location= 14C;23SC  
Mean (SD) Time post-stroke= 6.5 (5.2) months  
Baseline UL motor impairment= FMA =30.9 (SD) 13.9  
Stroke Type= 20I/17H  
Stroke location= 14C;23SC  
Mean (SD) Time post-stroke= 6.5 (5.2) months  
Baseline UL motor impairment= FMA =30.9 (SD) 13.9  
Stroke Type= 20I/17H  
Stroke location= 14C;23SC  
Mean (SD) Time post-stroke= 6.5 (5.2) months  
Baseline UL motor impairment= FMA =30.9 (SD) 13.9  
Stroke Type= 20I/17H  
Stroke location= 14C;23SC  
Mean (SD) Time post-stroke= 6.5 (5.2) months  
Baseline UL motor impairment= FMA =30.9 (SD) 13.9  
Stroke Type= 20I/17H  
Stroke location= 14C;23SC  
Mean (SD) Time post-stroke= 6.5 (5.2) months  
Baseline UL motor impairment= FMA =30.9 (SD) 13.9  
Stroke Type= 20I/17H  
Stroke location= 14C;23SC  
Mean (SD) Time post-stroke= 6.5 (5.2) months  
Baseline UL motor impairment= FMA =30.9 (SD) 13.9  
Stroke Type= 20I/17H  
Stroke location= 14C;23SC  
Mean (SD) Time post-stroke= 6.5 (5.2) months  
Baseline UL motor impairment= FMA =30.9 (SD) 13.9  
Stroke Type= 20I/17H  
Stroke location= 14C;23SC  
Mean (SD) Time post-stroke= 6.5 (5.2) months  
Baseline UL motor impairment= FMA =30.9 (SD) 13.9  
Stroke Type= 20I/17H  
Stroke location= 14C;23SC  
Mean (SD) Time post-stroke= 6.5 (5.2) months  
Baseline UL motor impairment= FMA =30.9 (SD) 13.9  
Stroke Type= 20I/17H  
Stroke location= 14C;23SC  
Mean (SD) Time post-stroke= 6.5 (5.2) months  
Baseline UL motor impairment= FMA =30.9 (SD) 13.9  
Stroke Type= 20I/17H  
Stroke location= 14C;23SC  
Mean (SD) Time post-stroke= 6.5 (5.2) months  
Baseline UL motor impairment= FMA =30.9 (SD) 13.9  
Stroke Type= 20I/17H  
Stroke location= 14C;23SC  |  
Range 92-146 days post-stroke) |  
Session 4 Range 92-146 days post-stroke) |
| Authors          | Year | Study Type | Investigative Aim                                                                 | Sample Characteristics | Frequency Analysis | Impairments Measured by | Activities Measured by | Implications |
|------------------|------|------------|----------------------------------------------------------------------------------|------------------------|-------------------|--------------------------|------------------------|--------------|
| Kawan et al., (2017) | 94%  | EEG        | Cross-sectional study Investigating the clinical relevance of hemispheric phase synchrony in stroke patients by calculating its correlation with clinical status | N=19, G= 5F; 14M, Mean Age= 67.5 ± 10.1 years, Mean (SD) Time post-stroke= 52.5 (38.3) days, Baseline UL and LL motor impairment= FMA Score=63.5±26.0 | Frequency analysis at rest of 19 channels | Impairments measured by: - FMA | Activities measured by: - FIM | No significant correlations between interhemispheric phase synchrony in alpha and beta bands with FMA scores (p=0.49; 0.22) |
|                  |      |            |                                                                                  |                        |                   |                          |                        |              |
|                  |      |            |                                                                                  |                        |                   |                          |                        |              |
|                  |      |            |                                                                                  |                        |                   |                          |                        |              |

(One time-point assessment at 52.5 (38.3) days post-stroke)

(One time-point assessment at 52.5 (38.3) days post-stroke)

One time-point assessment at 52.5 (38.3) days post-stroke

No significant correlations between interhemispheric phase synchrony in alpha and beta bands with FMA scores (p=0.49; 0.22)

- Interhemispheric phase synchrony index in both alpha and beta bands positively correlated with FIM Motor scores (alpha band: p =0.799, p=0.0033, beta band: p =0.616, p=0.04)
| Study                                                                 | N | Gender | Task/Measurements                                                                 | Impairments measured by | Other measurements                                                                 |
|----------------------------------------------------------------------|---|--------|----------------------------------------------------------------------------------|--------------------------|-------------------------------------------------------------------------------------|
| Parkkonen et al., 2017                                               | 23| 10F; 13M | Mean Age= 65 ±2years, Time post-stroke= 1-7 days, Baseline UL motor impairment= Mean Dynamometer score=16±4kg, Stroke Type= Not defined, Stroke location= 2C; 65C; 15CSC | Passive index finger movement-related frequency analysis measured by 306-channel whole-scalp system |                      |
| Thibaut et al. 2017                                                  | 55| 17F; 38M | Mean Age= 62 ±14years, Time post-stroke= 32±42 months, Baseline UL motor impairment= Mean | Frequency analysis at rest of 128 channels | Impairments measured by: FMA - WMFT                                      |
| Cross-correlation study                                             | 55| 17F; 38M | Mean Age= 62 ±14years, Time post-stroke= 32±42 months, Baseline UL motor impairment= Mean | Frequency analysis at rest of 128 channels | Impairments measured by: FMA - WMFT                                      |

**Note:**
- **Passive index finger movement-related frequency analysis measured by 306-channel whole-scalp system**
- **Frequency analysis at rest of 128 channels**
- **Impairments measured by:** FMA - WMFT
- **Other measurements:**
  - Rebound amplitude of 20Hz frequency was stronger with higher scores of the Box and Block test at all time-points and Nine-Hole Peg test at baseline and 12-month follow-up
| Study                | Sample Size | Data Source | Definition of an index of interhemispheric connectivity derived from EEG | N=30 | Frequency analysis at rest of 61 channels | Impairments measured by: | Significant positive correlation identified between lower beta and FMA and ESS (FMA: Rs=0.56, p=0.002 and ESS: Rs=0.45, p=0.01) |
|---------------------|-------------|-------------|------------------------------------------------------------------------|------|------------------------------------------|--------------------------|----------------------------------------------------------------------------------------------------------------------------------|
| Pichiorri et al. 2018 | 81% EEG     | Cross-correlation study | FMA one center: 51.6±7.9; second centre: 35.6±22.9 | Stroke Type= 49I;6H | (One time-point assessment at 32±42 months post-stroke) | (One time-point assessment at 32±42 months post-stroke) | - FMA - ESS |
Table 4: Summary of all included papers exploring functional connectivity

| Reference       | Modified Downs and Black Score | Technique | Design of study | Aim of study                                                                 | Stroke Participant Characteristics | Brain Activity Measure/s (time-point) | Clinical Outcome Measure (time-point) | Results                                                                 |
|-----------------|---------------------------------|-----------|-----------------|------------------------------------------------------------------------------|------------------------------------|--------------------------------------|---------------------------------------|------------------------------------------------------------------------|
| Westlake et al., 2012 | 79%                             | MEG       | Longitudinal study | Determination of the relationship between sensorimotor recovery and changes in resting-state functional connectivity in perilesional region; | N=14; G=3F; 11M; Mean Age=61 (SD=11) years; Mean Time Post-Stroke = 15 (SD=13) weeks (2 acute; 10 sub-acute; 2 chronic) Baseline UL motor impairment (FMA)=27 (SD=14) Stroke Type= 14I Stroke location=4C; 2SC;8 CSC | Functional connectivity measured at rest using a whole-head 275-axial magnetometer system | Impairments measured by: - FMA - Grip strength measured by Dynamometer | -Reduction in underconnectivity from visit 1 to 2 was linked with better clinical recovery score (p<0.05) |
| Wu et al., 2015   | 69%                             | EEG       | Baseline Cross-sectional | Examination of resting-state EEG | N=12; G=6F; 6M | Functional connectivity | Impairments measured by: - | -Functional connectivity between | |


|    |    |    | correlational data taken from an intervention study | measure of functional connectivity, coherence with ipsilesional primary motor cortex in the beta band, as a biomarker of change in motor status | measured at rest using 256 channels | FMA (upper limb) | ipsilesional and contralesional M1 was not significantly related to upper limb motor impairments ($p=0.87$) |
|---|---|---|---|---|---|---|---|
| Guggisberg et al., 2017 | 74% | EEG | Longitudinal Study | Examining the multivariate relationship between structural and functional correlates of proportional recovery patterns | N=63 G= 27F; 36M | Mean Age= 64 years (range 28-85 years) | Time post-stroke= 2-4 weeks (sub-acute) | Baseline UL motor impairment= Mean 17.5 (SD=17.9) | Stroke Type= Not defined | Stroke location= Not defined | Functional connectivity measured at rest using 128 channels | Impairments measured by: | FMA (upper limb) | Impairments measured by: |
|    |    |    |    |    |    |    |    |    |    |    | (Two time-point assessment measured) |    |    |
|    |    |    |    | Mean Age=54.0 ±16.6 years | Mean Time Post-stroke= 7.3 ± 4.0 months (chronic) | Baseline UL motor impairment (FMA)=39 ± 12 | Stroke Type= 12I | Stroke location=9C; 2SC; 1 CSC | (One time-point assessment at 3 months post-stroke) | (One time-point assessment at 3 months post-stroke) |    |    |    | Participants with low scores on FMA at first time-point had disrupted beta-band weighted node degree at the affected hemisphere | Participants with higher FMA Scores had high beta-band weighted node degree |
| assessment measured at 2-4 weeks and 3 months | at 2-4 weeks and 3 months | in the frontal brain region including ventral premotor cortex |
|---------------------------------------------|---------------------------|-------------------------------------------------------------|
| - No longitudinal changes were observed between the two time-points |

* C=Cortical; CSC= cortico-subcortical; F=Female; FMA=Fugl-Meyer Assessment; G=Gender; H=Hemorrhagic; I=Ischemic; M=Male; N=Sample number; SC=Sub-cortical; UL= Upper Limb; WMFT=Wolf Motor Function Test
Figures and legends

Records identified through database searching (n = 2653)

Additional records identified through other sources (n = 5)

Records after duplicates removed (n = 2616)

Records screened (n = 646)

Studies included in qualitative synthesis (n = 47)

Full-text articles assessed for eligibility (n = 96)

Records excluded (n = 1970)

Full-text articles excluded, with reasons (n = 49)
  - Conference paper (n = 3)
  - Not Stroke (n = 17)
  - No clinical upper limb measurement (n = 19)
    - Non related methodology (n = 6)
    - Intervention evaluation without a control group
Figure 1: Prisma flow diagram showing the selection process for included studies in the review

**Studies included in data synthesis**
(Modified Downs and Black >65%)
(n = 17)

**Articles excluded**
(n = 30)
Kusoffsky et al., 1982, La et al., 1982, Labar et al., 1991, Giaquinto et al., 1994, Henricks et al., 1994, Keren et al., 1995, Timmerhuis et al., 1996, Chen et al., 1998, Rossini et al., 1998, Forss et al., 1999, Rossini et al., 1999, Rossini et al., 2001, Peurala et al., 2002, Cuspineda et al., 2003, Tzvetanov and Rousseff, 2003, Tzvetanov et al., 2005, Tecchio et al., 2007b, Altamura et al., 2007, Yoshida et al., 2008, Al Rawi et al., 2009, Yao et al., 2009, Stepien et al., 2011, Laaksonen et al., 2013, Bolton and Staines, 2014, Shiner et al., 2015, Campfens et al., 2015b, Haupt et al., 2015, Nicolo et al.