Sophie Fitzsimmons
Word count: 2420

Transcranial direct current stimulation: A spark of hope for neurorehabilitation?

Introduction

Neurological diseases and accidents are some of the most traumatic and disabling found in modern medicine. Everyday activities may suddenly become impossible, and some patients are left impaired for the rest of their lives. Stroke, for example, is a major cause of neurological disability – in the UK, there are 111,000 new cases per year, and 62% of patients report persisting mobility problems even a year after their stroke (British Heart Foundation, 2009). A vital part of the management of these diseases is neurorehabilitation, which aims to help patients regain skills and abilities lost to their disease and to minimise or compensate for any functional disturbances. It is a complex, multidisciplinary process that must be tailored to the needs and abilities of the individual if it is to succeed in its aim. Neurorehabilitation takes many forms – just a few approaches that may be used include physiotherapy and occupational therapy for motor impairments; speech and language therapy; and cognitive rehabilitation to improve complex skills such as memory, attention and coordination. However, the efficacy of these approaches is limited. Fregni & Pascual-Leone (2007) point out that the success of physical and behavioural therapies depends heavily on the expertise of the therapist and the patient's cooperation – and indeed, one review found that only 44% of patients showed complete motor recovery after standard rehabilitation (Hendriks et al, 2002).

A recently revived technology could hold the key to improving the efficiency of existing neurorehabilitative approaches. Transcranial direct current stimulation (tDCS) is a safe, simple and non-invasive method of electrically stimulating the brain; and there is increasing evidence that it can not only potentiate the activity of healthy brains, but also enhance the recovery of damaged ones. In this essay, I will explain briefly how tDCS works, explore the known uses and efficacy of tDCS in the neurorehabililtation of three common neurological conditions (stroke, Parkinson's disease (PD), and traumatic brain injury (TBI)), and discuss whether electrical stimulation of the brain could be a feasible solution to the limits of current neurorehabilitative techniques.

Method and mechanism of tDCS

Electrical stimulation has been used to investigate the workings of the brain and as therapy for hundreds of years; this is by no means a new concept. The Italian physicist Giovanni Aldini

(1762-1834) reportedly gave electric shocks to the scalp as a method of curing depression and personality disorders (though he professed it to be a complete cure, it is unclear how rigorously this was tested) (Millar et al, 1989). tDCS as we know it today was first used on humans by Redfearn et al (1964) as an experimental (and effective) treatment for depression, but was largely ignored until Nitsche & Paulus resurrected the technique in a series of studies in the early 2000s, demonstrating that the technique of non-invasive electrical stimulation of the brain could increase motor excitability with an effect lasting for several minutes after the end of stimulation (Nitsche & Paulus, 2000). Since then, hundreds of tDCS studies on both healthy people and patients have been carried out, demonstrating that this technique can provide artificial lesions of or enhance brain functions such as motor, speech, vision, auditory and numerical functioning, as well as relief of cravings, depression, anxiety and pain (Nitsche & Paulus, 2011).

tDCS is performed by applying a low direct current of 1-2A to the scalp via two saline-soaked electrodes attached to a current stimulator (a small battery- or mains-powered device that provides a constant and adjustable current). One electrode (the stimulating electrode) is placed over the cortical area of interest (e.g. the motor cortex) and the other (the reference electrode) on a neutral area such as the forehead, neck or shoulder. The actual application of tDCS is a simple and painless procedure. The current is ramped up, which causes a tingling or warming sensation that quickly disappears when the current reaches a constant level (many devices have a sham mode which produces the same effect but switches off when the current reaches a plateau). The current is left on for 10-30 minutes, during which time activities, testing, therapy or infusions of drugs may be carried out. The effects of the stimulation may then last for several hours, allowing further testing or therapy (Schlaug & Renga, 2008).

Physiologcially, tDCS works by altering the excitability of neurons. The direction of alteration depends on the polarity of the electrodes: neurons at the positive, or anodal electrode (where current flows into the brain) have their excitability increased and their activity augmented while those at the negative, or cathodal electrode (where current flows out of the brain) have their excitability decreased and their activity suppressed – therefore, the correct placement of electrodes is vital depending on the desired effect on the brain, and potential effects of the reference electrode must be taken into account. The physiological mechanisms behind these changes in excitability are unknown, but recent research suggests that changes in neurotransmitter and neuronal ion levels may be responsible (indicating modulation of long-term potentiation and long-term depression) (Nitsche et al, 2003; Stagg et al, 2009).

Neurorehabilitative applications of tDCS

Stroke

The rationale behind the treatment of stroke with tDCS is as follows: Unilateral deficits (motor, speech and language impairments, visuospatial neglect etc.) post-stroke can be explained by a model of interhemispheric 'rivalry' – deficits are caused by reduced output from the lesioned hemisphere and/or increased inhibition from the contralesional hemisphere (Talelli & Rothwell, 2006) (though the precise role of the undamaged hemisphere in stroke recovery is controversial and considered by some to have a beneficial effect – see Hummel et al 2008). Either excitation of the lesioned hemisphere (using anodal tDCS) or inhibition of the contralesional hemisphere (using cathodal tDCS) could remove this obstacle to rehabilitation and allow improved plasticity and recovery of the damaged brain area. Indeed, studies involving a single session of either anodal or cathodal stimulation to the appropriate hemisphere in chronic stroke patients improves impairments such as loss of hand function (Fregni et al, 2005) and visuospatial neglect (Sparing et al, 2009) compared to sham treatment.

tDCS has also been shown to have a potentiating effect on existing neurorehabilitative approaches when delivered simultaneously – this is thought to be due to combined peripheral and central stimulation causing increased synaptic plasticity and improved task learning (Schlaug & Regna, 2008). Chronic stroke patients who received 30 minutes of cathodal tDCS with simultaneous occupational therapy were found to score much more highly in functional tests than those who received occupational therapy alone, with effects lasting for at least a week (Nair et al 2011). Speech and language therapy can also be combined with tDCS: Improvements in the outcome of anomia treatment (picture-word matching) and melodic intonation therapy (an aphasia treatment that teaches patients to sing or tap the melody and rhythm of common words and phrases) have both been observed when combined with anodal tDCS to the left and right frontal cortices as opposed to the therapy alone (Baker et al, 2010; Vines et al, 2011).

Some progress has been made in determining optimum tDCS treatment paradigms for stroke. In terms of which polarity of stimulation is most effective, experiments in healthy people looking at performance in a finger-tapping task suggest that bilateral tDCS (i.e. anodal of one hemisphere and cathodal of the other simultaneously) is more effective than either cathodal or anodal stimulation alone (Vines et al, 2008). While bilateral and unilateral stimulation have not been directly compared in stroke patients, bilateral tDCS seems to be particularly powerful. Lindenberg et al (2010) found that patients who received 5 consecutive sessions of bilateral tDCS combined with physical/occupational therapy had a 17.5% greater improvement on an assessment of motor impairment than those who received physical/occupational therapy with sham stimulation. In terms of frequency of treatment, daily as opposed to weekly application of either cathodal or anodal tDCS causes a cumulative improvement in motor function with an effect lasting for at least 2 weeks after treatment (Boggio et al, 2007). However, it is also becoming clear that the efficacy of tDCS is limited for the treatment of acute brain injury or for extremely severe lesions. Hesse et al (2011) found no difference in outcome between patients with severe arm and hand weakness who received robot arm therapy (a form of physiotherapy that uses a robotic arm to guide the patient's upper limb) with tDCS and patients who received robot arm therapy alone. This could be due to lack of structural integrity of the brain itself – patients with lesions that disrupt the integrity of their pyramidal tracts showed less improvement on treatment with tDCS and occupational therapy as those with intact pyramidal tracts (Schlaug & Renga, 2008). This limits the patient group to which tDCS can usefully be applied. For those to whom it can be applied, although much information has been gathered there are still questions to be answered – such as what the effect would be on patients who have multiple unilateral or bihemispheric lesions, or how long-lasting the positive effects really are and whether constant re-application is required for maintenance – before optimum treatment paradigms can be finalised.

Parkinson's Disease

tDCS has also been trialled with the neurorehabilitation of PD (though not as comprehensively as stroke). Very little is known about the mechanisms by which tDCS eases PD symptoms but it is thought that both excitation of cortical regions and increased dopamine release in subcortical regions are involved, the latter through indirect stimulation via corticostriatal circuits (Schulz et al, 2012). A randomised double-blind trial that tested the effect of 2 weeks of anodal tDCS to the motor and prefrontal cortices on various PD symptoms (bradykinesia, gait, reaction time, depression and others) found an improvement in gait and bradykinesia that lasted longer than 3 months (Benninger et al, 2010). tDCS also improves verbal fluency in PD (Pereira et al, 2012) and has even been shown to improve cognitive skills – a single application of anodal tDCS to the prefrontal cortex improved performance in a working memory task taken by PD patients (Boggio et al, 2006). However, due to the complex, multifactorial nature of this disease it will take a good deal more research before the optimal cortical stimulation locations and paradigms are discovered.

Traumatic Brain Injury

There has also been some very early research into the use of tDCS as a treatment for TBI, a condition that varies widely in character and severity but one whose treatment in the long term almost solely relies on neurorehabilitative techniques. It is thought that tDCS could help with recovery by suppressing damaging hyperexcitability in the early stages and enhancing excitability and plasticity in the later stages of TBI (Demirtas-Tatlidede et al, 2012). Only one tDCS pilot study has been performed on TBI patients thus far (Chew et al, 2009), but its results are promising, showing an enhancement in the effects of robot arm therapy. However, the complex nature of the pathophysiology of TBI and the large amount of variation between cases means that the effects of tDCS interventions are difficult to predict (especially as the effect on wider brain networks is unknown) and must be applied extremely cautiously, so it may be many years before sufficient evidence is gathered to allow tDCS to be used in the neurorehabilitation of this condition.

Discussion – could tDCS be used in a clinical setting?

It is clear that the addition of tDCS to current neurorehabilitative techniques could improve their efficacy greatly. However, there are many questions to be answered and obstacles to be overcome before tDCS can be used clinically. Some limitations specific to the conditions above have already been mentioned, but there are some more general problems that are yet to be solved. The greatest weakness of tDCS is the relative lack of research on the subject. Although it has been shown to be effective in broad terms, and that combination with other neurorehabilitative techniques renders it much more effective, it is still unknown what the optimal paradigm for stimulation is – how long to stimulate for, whether repeated sessions are required, what the ideal current strength is, and how these parameters need to be altered for different diseases, different severities and for different points in the time course of the disease. While some of these questions have begun to be answered for stroke, the same depth of research does not yet exist for other conditions that could potentially be treated with tDCS. The studies that do exist are extremely small – in the research quoted above, study sizes ranged from 6 (Vines et al 2011; Hummel et al 2005; Fregni et al 2005) to 25 participants (Benninger et al 2010), and many lack controls. Finally, although tDCS is widely considered to be very safe, with few side effects, its possible widespread and long term effects on the brain are unknown. It is clear that more detailed, larger-scale studies are needed.

Despite these limitations (most of which can be overcome by further research), there are many features of tDCS that make it very attractive as a possible neurorehabilitative technique. It is simple to apply, inexpensive and portable. Aside from rare mild itching and erythema at the electrode sites, neither physiological nor cognitive side effects have been reported (Schlaug & Regna 2008; Iyer et al, 2005). tDCS devices are equipped with a sham mode which has the same 'ramping up' sound and tingling that the real stimulation provides, making realistic randomised control trials possible. Finally, the greatest advantages of tDCS, as exemplified above, are its multi-applicability and its ability to combine with other therapies. The simple method of application means it can be applied to a large number of different diseases – only a few have been described here, but there have also been positive results for its use in chronic pain relief and for psychiatric conditions. The additive effect tDCS has been shown to have on physical, speech, robot arm and various other therapies, as well as pharmacological treatment (Kuo et al, 2008) means that tDCS has the potential to dramatically increase the potency of currently used neurorehabilitative techniques.

Conclusion

It is clear from these early stages of research that tDCS is capable of cheaply, safely and successfully treating a wide range of neurological conditions, improving the efficiency of current neurorehabilitative techniques and giving further relief of long term disabilities suffered by neurological patients. By far the greatest limitation of this therapy is the lack of research – with more comprehensive and larger-scale investigations into optimum treatment paradigms, long term outcomes and the long term safety of this newly emerging technology, further steps can be made in bringing this promising neurorehabilitative method to the bedside.

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