Introduction

It is well established that depression is more common among those with chronic physical health problems and that these patients are often challenging to diagnose and treat.\(^1,2\) Rates of depression among those with chronic kidney disease (CKD) and, in particular, those on dialysis, have been estimated to be even greater than those reported for patients with other chronic disease, with prevalence rates of approximately 20%.\(^3,4\) Depression in CKD has been shown to be associated with multiple poor outcomes, including more frequent and longer hospitalizations, decreased treatment compliance, poorer quality of life, and higher mortality rates.\(^5,6,7\) Unfortunately, despite these associations, rates of detection and treatment of depression in patients with CKD remain very low.\(^8\)

Treating depression with antidepressant medications in patients with hemodialysis poses particular challenges.\(^8\) Although the relative activity and mode of excretion of antidepressants in this population group are well described, the choice of medication is somewhat limited. Considerations when using antidepressant medications in those on hemodialysis include increased risk of drug interactions,\(^8,9\) anticholinergic effects, including urinary retention (tricyclics),\(^8,9\) QTc prolongation (tricyclics),\(^8,9\) accumulation of toxic metabolites (venlafaxine and bupropion),\(^9\) and increased risk of bleeding (serotonin selective reuptake inhibitors).\(^10\) These problems suggest that effective nonpharmacological treatments may be of particular use in this patient population. Although there are other promising nonpharmacological treatments for depression, including psychotherapy, the focus of this case report is on the use of brain stimulation, and in particular, transcranial direct current stimulation (tDCS).

TDCS is a noninvasive form of brain stimulation in which a low-amplitude direct current is passed into the cerebral cortex through scalp electrodes. The currents used are relatively weak (1–3 mA, compared with 800–900 mA in electroconvulsive therapy (ECT)), and the patient can remain awake and alert during treatment sessions, with no anesthetic being required. Rather than inducing action potentials such as in ECT and transcranial magnetic stimulation (TMS), tDCS primarily works by modulating the spontaneous neuronal network activity.\(^11,12\) These neuromodulatory effects have made tDCS of interest in the treatment of neurologic and psychiatric disease. The fact that tDCS does not induce action potentials is an important difference, particularly for those with CKD, in whom electrolyte disturbance, polypharmacy, metabolic derangements, and frequent comorbidities can make the use of ECT problematic.

TDCS has been explored as a potential treatment for depression for several decades. However, there has been a surge in interest in tDCS since 2000, possibly as a result of advances in understanding the underlying mechanisms of action and the development of more effective stimulation protocols.
result of commercial tDCS machines becoming more readily available. Although the methodology, study design, and stimulus parameters differ among studies, most recent studies, including this case report, have focused on excitatory (anodal) stimulation of the left dorsolateral prefrontal cortex. tDCS has been shown to be a promising treatment for depression, with a recent meta-analysis finding an effective size within the same range found for antidepressant medication. Given the challenges of treating depression in those with CKD, particularly those requiring hemodialysis, tDCS has the potential to be a safe and efficacious treatment.

In this case report, we describe the successful administration of tDCS to a patient with chronic renal failure treated with hemodialysis. This patient was treated as part of an open-labeled pilot study (HREC approval ref: 12/267 (HREC/13/POWH/132) which aimed to demonstrate the feasibility and acceptability of using brain stimulation in the unique setting of a hemodialysis unit. In all, 45 patients with hemodialysis at St George Hospital, a large teaching hospital in Sydney, Australia, were screened for depression by a clinician. Of these 45 patients, 6 were diagnosed with depression on clinical interview using DSM IV criteria and standardized measures; 2 patients subsequently agreed to a trial of tDCS treatment, although 1 decided not to proceed following the first treatment because of a change in social circumstances that were unrelated to the tDCS treatment. The following case report describes the remaining patient who received tDCS as a treatment for depression for a 6-week period. This case is reported because of the novelty of using brain stimulation in this patient population, as well as the potential for tDCS to be a major treatment advance for those with depression in the setting of chronic comorbid physical health problems.

Case Report

Mr. A, a 77-year-old man with end-stage kidney disease secondary to glomerulonephritis, had been treated with hemodialysis for 7 years. He described several months history of depressive symptoms, including sleep disturbance, low energy, low mood, decreased motivation, and ruminating thoughts regarding past events and regrets. He also described negative views of the future and had fleeting suicidal thoughts, although he denied wanting to harm himself. He had no previous psychiatric history, specifically he denied any history of depression or psychotropic medication use. There was no known family history of any psychiatric illness. He had multiple comorbidities including hypertension, dyslipidemia, gout, and a previous stroke that had resulted in a left homonymous hemianopia and disequilibrium. The stroke had occurred over 2 years before the tDCS study and was not thought to be related to the onset of depression. Mr. A was taking multiple medications, including gabapentin, pantoprazole, pravastatin, allopurinol, clopidogrel, latanoprost eye drops, metoprolol, and fish oil. He continued to live with his wife, who was also his caregiver. Mr. A received hemodialysis 3 times per week.

An assessment battery was completed before any treatment (baseline) and at completion of treatment (6 weeks). This battery involved standardized measures of (1) mood—self-rated Beck Depression Inventory (BDI) and the clinician-rated Montgomery and Asberg Depression Rating Scale (MADRS), (2) cognitive function—Montreal Cognitive Assessment (MOCA), and (3) quality of life—SF-36. The SF-36 provides separate normative scores for the effect of both physical and mental health symptoms on functioning. During the tDCS treatment course, subsequent mood assessments using the BDI and the MADRS were then completed on a weekly and fortnightly basis, respectively.

tDCS was administered at 2.5 mA for 30 minutes with each session for a period of 6 weeks (18 sessions total), with each session taking place during Mr. A’s hemodialysis sessions. tDCS was stopped following the completion of the 18 treatment sessions with no taper period. tDCS was delivered using an Eldith DC-stimulator (NeuroConn, Germany) with the anode placed over the left dorsolateral prefrontal cortex (F3 on the EEG 10/20 system) and the cathode positioned over F8. Mr. A completed an adverse event assessment at the end of each tDCS session. Mood outcome measures were then repeated at 1 month following completion of tDCS treatment.

Results

Both clinician-rated (MADRS) and patient-rated (BDI) measures of mood improved throughout the study as shown in the Figure. Actual scores for BDI were 22 (baseline) and 11 (completion), and for MADRS 20 (baseline) and 7 (completion). These
measures were also reflected in clinician interview, with the patient meeting criteria for remission of the major depressive episode both at the end of the treatment course and at 1-month follow-up. Both physical (SF-36 physical health component score; baseline: 35.6, completion: 32.4) and mental health functioning (SF-36 mental health component score; baseline: 37.8, completion: 29.3) aspects of quality of life also improved. Assessment of cognition at the completion of treatment revealed no significant changes (MOCA baseline 21/25 and MOCA completion 22/25).

The tDCS treatments were well tolerated, with the only side effect reported being a mild skin tingling or burning sensation at the beginning of each treatment session, consistent with previous reports of tDCS. Additionally, the tDCS did not appear to have any negative effect on hemodialysis adequacy, as measured by Kt/V, urea reduction ratios, fluid gain between dialysis sessions, and biochemical and hematological testing.

At the completion of the study, consideration was given to further treatment, including antidepressant medication or psychotherapy or both. However, given the improvement in the patient's depressive symptoms, such treatments were declined at this time. The patient was referred back to his renal physician and family doctor with the knowledge that these treatments could be considered in the future should the need arise.

Discussion

This case report demonstrates that tDCS can be successfully administered to a patient with multiple medical comorbidities in a hemodialysis unit. Although there are obvious limitations in the conclusions that can be drawn regarding efficacy, given that there were no major changes in the patient that would explain the improvement in their previously persistent depressive symptoms, it appears that tDCS was beneficial in the treatment of depression in this case. Importantly, administering tDCS in this unique setting was shown to be both feasible and well tolerated.

Although there are case reports of excellent response to ECT in patients with CKD and severe depression refractory to antidepressant medication, special precautions are required in such patients. These include the need to control abrupt increases in blood pressure, adequate muscle relaxation to prevent strong contractions and the subsequent risk of fractures in an osteopenic patient, careful management of potassium levels that are further increased by succinyl choline, a muscle relaxant commonly administered during ECT, and attention to ECT dose levels, ideally established by individual seizure threshold titration, as the latter may be altered by acidosis and hypocalcaemia. tDCS does not require such precautions and is a safe and easily administered treatment. Furthermore, the fact that tDCS is portable, low in cost, well tolerated, and has a favorable side effect profile makes it very suitable for the general hospital or dialysis unit setting. However, using tDCS in the hemodialysis setting poses some challenges. Having patients so close together and in need of regular nursing review created difficult, but not unsolvable, problems relating to privacy and confidentiality. Patients are often prone during hemodialysis, which also made the positioning of the electrodes somewhat difficult. The logistics of working within the dialysis treatment setting also had to be carefully planned through frequent consultation.
with nursing staff. To this end, tDCS was administered in the middle 1–2 hours of the hemodialysis session, so as to minimize any complications during the connecting and disconnecting to the dialysis machine. However, the fact that tDCS could be administered during hemodialysis sessions, without any need for extra appointments or time spent at the hospital, was a major benefit.

Although the evidence base for the use of tDCS in the treatment of depression is growing, to date, most studies have excluded participants with major physical health problems. To our knowledge, there is only one study looking at the use of tDCS for the treatment of depression in those with chronic physical illness. This was a pilot study in 10 HIV-infected persons, 20 with results suggesting that tDCS was a well-tolerated and seemingly efficacious treatment among this group. Before our report, there have been no studies describing the use of tDCS for the treatment of depression in renal patients. Although the results from this case report need further study and evaluation in larger randomized trials, based on our report tDCS can be considered to be a promising alternative treatment for depression among those with CKD or, potentially, other chronic physical illness. Among selected patients it appears to be feasible and generally well tolerated.

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**References**