Chapter 13
Home-Based Patient-Delivered Remotely Supervised Transcranial Direct Current Stimulation

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Introduction

The attractive idea of tDCS application in home settings has been propelled by encouraging findings on tDCS neurophysiological and behavioral effects, as well as by a notion that tDCS effects are cumulative and a single application is not enough to elicit longer lasting effects.

The trend toward tDCS applications at home resonates with different groups of users, addressing variety of unmet needs (Knotkova et al. 2013, 2015; Rosedale et al. 2012; Woods et al. 2016). In research, tDCS application at home may improve retention of study subjects, decrease costs for subject's travel to the research facility and costs associated with the personnel time needed for the applications. It also opens new possibilities for participation in tDCS studies to seriously ill patients, and patients with specific disabilities that make travel to research facility excessively burdensome or impossible. The idea of tDCS applied at home

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may also be attractive from the scope of clinical/therapeutic settings, yielded by the vision of a medical professional sending selected patients home with a tDCS stimulator instead of a bottle of pills. And, of course, the at-home tDCS concept has been attractive to specific segments of the general healthy public, especially in recent years, as the evidence on tDCS effects is growing and medical and public attention to possibilities of functional enhancement in healthy subjects intensifies.

As with any other innovative idea, the use of tDCS in home settings has enormous potential - to enhance the tDCS practice-at-large, and to facilitate the overall development of the neurostimulation field - if used responsibly; on the other hand, careless/reckless tDCS use without provisions for safety, proper training, or access to assistance or resources can be counterproductive and lead to undesired outcomes for involved individuals or the field.

Therefore, it is of interest of all involved to facilitate the environment for tDCS applications in home settings in a safe and effective way.

Potential Benefits of At-Home tDCS

While there is warranted opposition against using "do-it-yourself" (DIY) devices of unknown origin or devices that do not have safety certifications, there are many potential benefits to conducting tDCS at-home as opposed to in a clinic setting. tDCS is a convenient and low cost method of treatment. The size and weight of the device is minimal and it is usually battery-powered making the ability for administration extremely user-friendly. Because of the device configuration and portability, tDCS has the most potential for use outside of a clinic setting (Alonzo and Charvet 2016; Knotkova et al. 2017a).

Another aspect in favor of an at-home approach is that the burden on the patient as well as the institution or clinic is reduced. tDCS sessions often take place at least one time daily, 5 days a week. Daily travel to a treatment facility is often not feasible for most individuals. Work and family schedules and often limited transportation capabilities contribute to the impracticality of daily in-clinic sessions (Kasschau et al. 2016). For those patients living in remote areas without the means of traveling to large cities where academic institutions are located, and are often the ones offering such services, the ability to conduct sessions at home is a tremendous benefit.

Further, remote tDCS is cost effective. The cost associated with trips to the clinic is lessened considerably when sessions are conducted in the home setting. For institutions, at-home tDCS is also financially beneficial. By minimizing the number of in-clinic visits, the cost of dedicated space and allotted staff time at the treatment facility is reduced.

Research has shown that cumulative sessions of tDCS may be more beneficial than a single treatment session (Monte-Silva et al. 2013). The availability of a tDCS

treatment option that does not consist of a need for recurring, in-person visits, may lead to a higher retention rate in research protocols.

At-home tDCS is also more accessible than other similar non-invasive brain stimulation techniques such as transcranial magnetic stimulation or TMS. Unlike tDCS, TMS involves strong magnetic field induction and cannot be performed outside of the clinic setting.

Still, another benefit to at-home tDCS use stems from the physical limitations often seen in patients with a number of various medical conditions. Many neurologic conditions, for example, can result in an inability to ambulate easily from place to place, making trips to clinic both challenging and frustrating for the patient. For example, multiple sclerosis, or MS, patients may benefit from tDCS in regards to a number of related symptoms, but these patients often have ongoing problems with ambulation. Recent survey results indicate that the majority of the MS population face mobility challenges on a daily basis (Larocca 2011). Such limitation can prevent patients from independently attending clinic visits, thus, requiring the need for caregiver assistance, and further increasing the existing patient burden. By limiting the need for such in-clinic visits, a potential larger number of subjects are able to complete protocols through to the final session.

Approaches to At-Home tDCS

There is still an underlying concern of safety and clinical guidance regarding at-home use and tDCS in general. Non-invasive brain stimulation, especially the use of tDCS, will eventually be available on a much greater scale. Therefore, it's important to look at the current approaches in at-home use, along with the pros and cons of these methods, in order to carefully inform those looking towards expanding this implementation.

The variety of approaches to at-home tDCS arises from differences in several elements:

- Specificity in selection of good candidates for at-home application
- Quality/intensity of training of the prospective user (and assurance of competence to perform tDCS safely and in accordance with good practices)
- Degree of adjustment of the tDCS procedure with regards to efficacious and safe use (e.g. adjustments allowing for precise electrode positioning at home)
- Quality and technological advancement of the device (e.g. including or not including functionalities allowing for dose control)
- Degree of rigor pertaining to monitoring for safety (adverse events) and compliance with the protocol
- Degree of rigor pertaining to outcome assessment and data collection
- Degree of support and remote assistance provided to the tDCS user

On the continuum of variability in these elements, the top tier is represented by approaches implementing the highest level of control/rigor, aiming for replicability

and thus, suitable for conditions with high rigor requirement, such as clinical controlled trials, and we discuss them in detail below (Charvet et al. 2015; Knotkova et al. 2017a, b; Riggs et al. 2017a, b).

The low end of the continuum includes DIY tDCS application by untrained individuals on their own, using devices that often do not meet the good manufacturing practices (CGMP) for quality assurance and internationally accepted standards, such as those codified by ISO 13485. Currently, there are several DIY websites and blogs that are making it as convenient as possible for the average lay person to obtain and/or construct their own DIY tDCS device. Many of these sites promote simply purchasing a 9-volt battery, wires, and sponges in order to meet the "requirements" of at-home brain stimulation. There are also devices currently being marketed for online purchase such as foc.us and The Brain Stimulator (Alonzo and Charvet 2016). While the cost of these products varies, they are still readily available to the average consumer. Purchase of devices such as these or creation of DIY tDCS kits should not be encouraged. There is no prescription needed to purchase these devices. With that, comes no supervision, safety standards, or the ability to control dosing over repeated sessions.

The ability to control dose administration incorporates correct electrode preparation, montage, and waveform. Although it can be argued that no formal oversight is required for a private use of publicly available tDCS devices (even those of questionable quality), it is important to understand that the potential adverse effects due to careless/uninformed tDCS application can negatively impact the entire tDCS field.

Besides the two approaches defining the top and lowest tier, there are other approaches of tDCS applications in home settings, utilizing various degree of compliance control, support or training. One approach in research involving tDCS in home settings has been to provide patient participants with devices and instruction for self-administration (Andre et al. 2016; Hagenacker et al. 2014; Hyvarinen et al. 2016). Another approach has been to combine tDCS with an extension of in-clinic treatments such as TMS (Cha et al. 2016). The advantage of this approach is that it most closely approximates real-world use, simulating a potential model of prescription use. However, in addition to any potential safety concerns, there are limitations to these studies in terms of understanding the exact doses administered and, especially, reproducibility of the findings. Further, participants may have some difficulty with self-administration if they have cognitive or motor disabilities, and may require ongoing guidance for use. Some clinicians are utilizing tDCS home-use to sustain clinical benefit (Andrade 2013; Narayanaswamy et al. 2014). This tailored individual approach can be helpful to the patient, but does not serve to answer overall research questions and is completed without parameters or guidance.

Home-Based Patient-Delivered Remotely-Supervised tDCS

The idea of remotely-supervised versus non-supervised at-home tDCS is one of the largest distinctions between the current approaches. The implementation of a remotely-supervised method is overall favored, as it adheres to the necessary safety

and standardized procedures previously mentioned. Further, in terms of the most important aspect of an at-home approach to tDCS is safety. A currently used remotely supervised (RS) tDCS protocol implements a number of safety features to minimize risk, maximize benefit that other at-home devices disregard. Sessions are conducted under direct supervision of a tDCS trained technician. The training the technician receives goes beyond the real-time supervision during sessions. Prior to any interaction with patients, technicians are trained on the proper technique of tDCS, how to correctly place the headset, the ability to identify unexpected adverse events, and how to overall screen for potential eligible subjects. With safety being one of the primary concerns surrounding remote tDCS sessions, a structured protocol inclusive of real-time monitoring helps to alleviate such unease (Charvet et al. 2015; Knotkova et al. 2017a, b).

In summary, the increased interest surrounding tDCS has been overall well-received in the scientific and medical communities. While it is clear that tDCS will ultimately be used at home, either directly by the consumer or through a prescription, research is needed to answer critical questions of safety and tolerability of extended treatments and dosing optimization. If an individual self-administers tDCS for treatment, there are currently no known parameters for how many sessions, and of what duration and strength, are safe and effective. In addition, they would not have objective measurements at baseline in which to measure any progress or response to treatment. Therefore, directed and monitored home use in a research context is essential for the guidance of the future of tDCS as a therapy.

Protocols, Technologies and Consumers

It has been recognized that even within the most rigorous remotely-supervised tDCS application in home settings, the treatment protocol and technology (functionality of the tDCS device) must reflect specific needs and limitations of the user. Below, we discuss three examples of specific patient-tailored adjustments of the remotely-supervised tDCS application in home settings to various patient populations – those with the Attention-Deficit/Hyperactivity Disorder (ADHD), Multiple Sclerosis (MS) and seriously ill polymorbid, polysymptomatic patients who are candidates for- or receiving specialist-level community-based palliative care.

Attention-Deficit/Hyperactivity Disorder

ADHD is a behaviorally-defined disorder affecting 5–7% of children and adolescents (Barkley et al. 2002; Kessler et al. 2006). DSM 5-defined ADHD (American Psychiatric Association 2013) is marked by excessive impulsivity/hyperactivity and inattention as well as frequent and diverse cognitive impairments (Frazier et al. 2004; Willcutt et al. 2012) that cause significant, academic, employment, legal or

psychosocial problems (Barkley et al. 2006; Breslau et al. 2009, 2011; Hinshaw 1992a, b; Polderman et al. 2010; Raggi and Chronis 2006) despite the best-supported treatments (Jensen et al. 2007; Molina et al. 2009; The MTA Cooperative Group 1999), and is linked to increased risk for other psychopathology and substance disorder (Breslau et al. 2011; Levin et al. 1998; Wilens 2004). These symptoms and the problems that are associated with ADHD represent a substantial burden to patients and typically require treatment to improve functioning. First- and second-line recommended treatment for ADHD is pharmacotherapy with psychostimulants that increase extracellular levels of dopamine or with atomoxetine that blocks reuptake of norepinephrine (Kooij et al. 2010; Pliszka and Issues AWGoQ 2007). Although the majority of ADHD patients show some degree of clinical improvement when using these medications, the parents of a surprisingly high number of ADHD-diagnosed children and adolescents seek alternative treatments to manage the behavioral and cognitive problems associated with the disorder. The reasons why medications are so unpopular with many parents are varied (Dosreis et al. 2003; McLeod et al. 2004), but often involve parent attitudes towards medications, such as misunderstanding of safety or concerns about the long-term effects of medication use (DosReis et al. 2009), as well as perceived social stigma or other concerns. Moreover, ADHD medications have meager effects on academic performance (Langberg and Becker 2012; Prasad et al. 2013), inconsistent effects on adult psychosocial outcome (Advokat 2009; Barkley and Cunningham 1978; Carlson and Bunner 1993; Cunningham and Barkley 1978; Gadow 1983; Loe and Feldman 2007; Swanson et al. 1991), and carry a high substance abuse potential (Bright 2008; Faraone and Upadhyaya 2007; Harpur et al. 2008; Johnston et al. 2008).

Among numerous non-pharmacological treatments that have been examined in ADHD (typically behavioral interventions or cognitive training) (Evans et al. 2014; Hodgson et al. 2014; Rabipour and Raz 2012; Rutledge et al. 2012; Sonuga-Barke et al. 2013; Toplak et al. 2008) tDCS has recently garnered interest based on theoretical arguments that it could have a potential clinical benefit (Demirtas-Tatlidede, et al. 2013; Rubio et al. 2016). Despite the interest, the available empirical evidence that tDCS has a meaningful positive effect on ADHD still remains limited at present. Laboratory studies conducted so far have typically examined whether single-session tDCS has an immediate facilitative effect on cognitive abilities found to be abnormal in ADHD. Most published evidence is supportive. For instance, anodal tDCS over the left dorsolateral prefrontal cortex improves attention and behavioral inhibition (Bandeira et al. 2016) or response accuracy (Soltaninejad et al. 2015). However, contrary evidence also exists; e.g., a similar study in ADHD adults found no improvement in inhibitory control after 1 mA anodal stimulation (Cosmo et al. 2015a, b). However, it remains unclear whether the differences compared to other studies are due to the age of the patients or other experimental factors. In addition, other applications of tDCS have been shown to influence ADHD-related cognitive deficits and suggest alternative uses for tDCS to treat ADHD that might engage different mechanisms of action. In one study,

ADHD-diagnosed children exposed to 0.75 Hz oscillating tDCS increased EEG-recorded slow wave oscillation during sleep, and improved subsequent memory recall the next day (Prehn-Kristensen et al. 2014), while in another study ADHD-diagnosed boys undergoing a similar treatment had less variable motor performance and generally slower reaction time during Go/NoGo task the next day (Munz et al. 2015). Also, cathodal tDCS was found to improve ADHD behavioral inhibition in one study (Soltaninejad et al. 2015). The basis of these potentially beneficial tDCS effects on neural function is not yet well understood, but so far appears consistent with known models of ADHD pathophysiology. A study using a spontaneously hyperactive rat model of ADHD not only found repeated tDCS administration over 8 days improved animal analogues of ADHD-related behavioral abnormalities, but also that dopamine levels in the striatum – a brain region linked to ADHD pathophysiology by several lines of research (Del Campo et al. 2011) – were higher after tDCS treatment (Leffa et al. 2016). In another study, anodal tDCS applied over the left prefrontal cortex altered ADHD brain dysfunction not only under the target area, but also in brain regions known to be interconnected within neural networks (Cosmo et al. 2015a, b). This indicates tDCS effects can propagate among brain regions within extended neural systems that numerous studies have implicated as dysfunctional in ADHD (Cao et al. 2014; Cortese et al. 2012; Rubia et al. 2014; Weyandt et al. 2013).

This emerging evidence that tDCS acutely improves neurocognitive task performance known to often be abnormal in ADHD along with the well-documented safety, general tolerability, and established long-term effects of tDCS on both cognitive performance (Ditye et al. 2012) and brain function (Miniussi and Ruzzoli 2013; Sale et al. 2015) suggest tDCS might be an option for an unmet ADHD treatment need that arises from patient and parent concerns about medication use, tolerability, or inadequate response. However, before tDCS can be used clinically, it must be validated by properly-designed clinical trials to test its clinical efficacy. To date, no study has looked at the effects of repeated tDCS administration in ADHD to determine if it has cumulative benefits on cognitive function. More importantly, there has not yet been a study to determine whether tDCS might reduce ADHD symptoms or associated social, academic, related functional impairments. The practical difficulties of such studies are considerable. For instance, a prototypical treatment protocol would require ADHD patients and their families to attend near-daily clinic visits over 2–4 weeks. This duration and frequency are needed not only to ensure adequate "dose" of neurostimulation, but also because such a timeframe is needed to evaluate meaningful change in clinical function. Typical families contend with the schedules of two working parents, school demands and extra-curricular activities, and often have to manage more than one child's needs. Therefore, any clinic-based tDCS trial for ADHD not only would miss potential recruitment opportunities because of family refusal, but would also likely be plagued by poor compliance and high dropout. Probably only the most motivated of families and subjects would complete treatment, complicating generalizability and efficacy inferences. Remotely-supervised tDCS represents a means to accelerate the pace and feasibility

of such clinical trials by opening interventions to a wider potential ADHD participant pool than would otherwise be possible.

There are two primary considerations for population-specific recommendations for tDCS performed at home for ADHD. The first is the patient or research participant age. Unlike many other clinical groups for which tDCS is being considered as a potential treatment, ADHD is a disorder usually diagnosed in childhood when problem behavior becomes severe enough to bring the patient to clinical attention. Administering tDCS at home for ADHD children and adolescents should require a family member to participate to help ensure proper protocol adherence. While some adolescents might have the maturity to set up and administer tDCS without direct parental assistance using remote supervision, it is an impractical idea for most children. Furthermore, most institutional review boards are unlikely to approve research trial protocols where youth are asked to set up and administer tDCS themselves. This suggests effective clinical trial design must overcome additional issues arising from parent training, parent-child interactions, and joint tDCS procedure troubleshooting in order to ensure that tDCS is administered properly each and every treatment session. Second, unlike other clinical populations who benefit from tDCS (e.g., stroke or multiple sclerosis) whose patients often require assistance in tDCS set up due to fine motor impairment, ADHD does not have frank motor disabilities to overcome. ADHD cognitive deficits not only are varied and not found in all ADHD patients (Willcutt et al. 2005), they also typically are not particularly severe – most often merely relative weaknesses. Thus, there are no specific disabilities in ADHD that require careful planning for the population as a whole to overcome. However, the problems with distractibility, inattention to detail, and persistence are hallmark problem behaviors in ADHD. ADHD neurobiological theory also implicates motivational brain systems in the disorder (Sonuga-Barke 2005), which could represent a similar hindrance to remaining engaged throughout a clinical trial of tDCS without proper oversight. Therefore, ADHD-specific recommendations for remotely-supervised tDCS fall primarily into the category of efforts tailored to the population to help ensure treatment protocol adherence, patient motivation, and continuity of optimal tDCS administration by capitalizing on parental engagement. As such, most recommendations would apply equally to either research-based clinical trials or to clinical services that eventually might be offered to ADHD patients if research evidence for tDCS efficacy ultimately is found.

Fortunately, considerable effort already has been made to understand what specific factors influence ADHD patients' compliance with treatment. This body of published research focuses on ADHD medication adherence, for which non-compliance or discontinuation rates vary from 13 to 81% across studies (Adler and Nierenberg 2010; Ferrin et al. 2012). Medication adherence can be operationalized in different ways. Typically, it is taken to mean the patient's and family's engagement in and consistency using a medication regimen that both the medical provider and family believe could be beneficial (Gearing et al. 2011). Although some reasons why ADHD patients choose to discontinue pharmacological

treatment are highly specific to medication use (e.g., drug side-effect intolerance), many of its lessons can be directly translated to non-pharmacological interventions. As might be expected, there are age-specific predictors of ADHD treatment adherence that track the developmental maturity of patients. For instance, younger children are more likely to adhere to treatment recommendations if they have more troublesome ADHD symptoms or associated problems (Charach and Gajaria 2008; Coletti et al. 2012), except for when those problems cause such severe levels of family discord they interfere with treatment (Coletti et al. 2012; Gau et al. 2006). ADHD-diagnosed adolescents often take increasing responsibility for managing their treatment as they develop insight into the functional aspect of medication in their lives (Brinkman et al. 2012). Adolescent treatment adherence is higher when academic benefits are perceived, side-effects are low, and any social stigma is controlled (Bussing et al. 2012). Adult ADHD medication non-compliance rates are similar to that found in youth, e.g., between 11–64% (Christensen et al. 2010; Olfson et al. 2007). For adults with ADHD, treatment adherence is lower when patients have more severe symptoms or engage in illicit substance use (Semerci et al. 2016). Factors that predict medication adherence for all ages of ADHD patients include beliefs that ADHD is a biological disorder (Charach and Gajaria 2008; Coletti et al. 2012), understanding the treatment safety profile (Bussing et al. 2012), and efforts to reduce the practical burden of treatment (Gau et al. 2006). It is also clear that familial and medical support are highly important. Not only does higher socioeconomic status and two-parent households predict treatment compliance (Charach and Gajaria 2008), studies that find patients and their families have active, supportive relationships with treatment providers are more likely to adhere to treatment as well (Coletti et al. 2012).

Taken together, these factors suggest several practical suggestions for ADHD tDCS treatment protocols performed at home. These suggestions emphasize establishing an effective treatment relationship between the clinicians or researchers overseeing the treatment and the ADHD patients and their families, educating parents and children about what to expect with tDCS treatment, and devising ways to plan, structure and otherwise facilitate interactions between parents and their children. All recommendations should be tailored to the developmental age of the patient. Nearly all should be considered for protocols involving ADHD-diagnosed adults.

Establish an Effective Treatment/Research Relationship Because research shows that ADHD treatment compliance is supported by a well-established relationship between patients and caregivers, tDCS protocol adherence likely will be facilitated if effort is made to explain the ways in which patients or their families can seek support during the treatment protocol. Although the protocols of clinical trials will differ from study to study, it is recommended that all protocols include a) a clinic visit for consent, clinical assessment, and training with particular attention paid to educating families that treatment must be a "whole family" cooperative effort, b) a home visit prior to treatment so that research staff can assess and advise tDCS

equipment set up and other technical issues, and c) a schedule of contacts for when the medical/research team will contact the family to check in about the protocol. Contact information for ways to reach a member of the treatment team should be provided not only for emergencies or reporting any adverse events believed to be related to the treatment, but also for routine questions. Having a direct and responsive avenue of contact is useful to avoid frustration that can lead to treatment non-compliance.

Provide tDCS Psychoeducation Because ADHD treatment adherence is greater when patients and the their parents understand ADHD is a neurobiological disorder, tDCS clinical trials or clinical treatment performed at home should include a standardized discussion that educates both the patient and family member who will be assisting the trial about (a) how tDCS is believed to work neurobiologically and its purported therapeutic effect on specific aspects of ADHD neural dysfunction, (b) tDCS risk profile, in particular age-specific caveats to existing safety/tolerability research for children where less information is known than for tDCS in adults (Brunoni et al. 2011a, b), (c) expectations for therapeutic effects that emphasize that treatment in clinical trials might not show an effect at all, or that effects might be small and not emerge until the end of treatment or long after. The latter should also include that current models of ADHD believe it likely is caused by multiple different etiologies (Sonuga-Barke, 2005), which may or may not be responsive to tDCS.

Describe Outcome Evaluation Process Perceived lack of benefit is a key reason for ADHD treatment discontinuation. For ADHD tDCS treatment protocols, it is recommended to explain that tests of attention, response inhibition, or other cognitive abilities are surrogate outcome measures that may or may not predict actual behavioral change. Evaluation of ADHD symptoms and associated problems is best done over a longer timeframe. For research protocols, this means explaining the use of standardized ADHD behavioral outcome measures (e.g., parent- or teacher-report ADHD symptom severity checklists) so parents can understand how the study plans to gauge the impact of the treatment over time. For clinical treatment, this might include goals for outcome evaluation that are patient-specific (e.g., sibling arguments, homework compliance, etc.) and devising ways to for parents and patients to measure gains towards those goals.

Parent Preparedness/Training When the patient is a child or adolescent, parental involvement should be required or at least strongly recommended. However, the interpersonal nature of the parent-child relationship should be discussed as a factor that can facilitate or hinder treatment adherence. A potentially effective approach is for each to articulate their hopes and goals for the treatment, i.e., to make clear what is motivating them. The role of the parent as a "coach" instead of "drill sergeant" should be emphasized. Youth with greater developmental maturity

can take more responsibility for the practical issues, relegating parental involvement to oversight and documentation. Because interpersonal factors that might influence both tDCS protocol adherence and outcome in ADHD are unknown, it is advised that formal assessments of parent-child dyadic interactions or familial relationship styles be conducted at treatment baseline of research studies. Such metrics can be examined as potential outcome moderators in the statistical analysis of outcome data. Finally, it should be emphasized that the trial should be a "whole family" effort. A pre-treatment training session should discuss family schedules such as extra-curricular activities for both the patient and other children in the family to identify in advance potential hurdles. Practical issues such as establishing a regular tDCS time, ensuring lack of interruption by siblings, etc. should be emphasized.

tDCS Equipment Training A trial using remotely-supervised tDCS is unlikely to succeed if patients or their families are unable to access the technology required. As described elsewhere in this chapter, training should cover both proper use of the tDCS equipment, but also the communication medium used for the study. Ideally, a videoconferencing system will be employed so that staff can confirm the proper positioning of tDCS electrodes. If concurrent cognitive stimulation (e.g., a "cognitive training" framework) is included as part of a tDCS experimental protocol, training on how to start those exercises must be provided. As intimated above, the roles of parents versus ADHD-diagnosed children or adolescents might optimally fall into one of two categories: a) one in which parents perform all set up, communication with caregiver staff, and documentation, or b) one in which parents supervise, but older youth might take responsibility for much of the practical set up.

Contingency Management The goal of tDCS treatment adherence ultimately is to complete a prescribed number and duration of stimulation sessions within a particular timeframe. As such, some ADHD patients might benefit from contingency management approaches (Kaiser et al. 2008). A system of small incentives might be established that rewards increasing levels of compliance throughout any lengthy treatment protocol. For example, a small reward can be provided after each daily tDCS session is successfully completed, followed by a choice of a larger reward on the weekend if all sessions that week were done. The benefit of such a system likely will depend on the age of the patients and developmental appropriateness of the rewards, but likely should be considered standard for the youngest patients. Moreover, if a contingency management approach is included in any treatment protocol, parents should be trained how to properly present contingencies in order to avoid a punitive or coercive approach. Protocol-specific guidelines on how and when to provide positive reinforcements should be made explicit, and their use should be quantified by trial staff weekly.

Multiple Sclerosis

For individuals living with multiple sclerosis (MS), tDCS has shown early promise in ameliorating many frequent and often disabling symptoms including cognitive impairment, fatigue, pain, and motor problems (Ayache et al. 2016; Cuypers et al. 2013; Ferrucci et al. 2014; Mattioli et al. 2016; Meesen et al. 2014; Palm et al. 2014). However, at-home use is critical for providing adequate access for patients for both treatment and participation in clinical study. Many of those living with MS are not able to travel to a clinic to receive treatment, especially if sessions span weeks or even months of daily stimulation. As MS often occurs in younger adults, typically with both work and family responsibilities, time for treatment, especially involving in-clinic appointments, is a major obstacle. In addition, for those that are more advanced in disability, traveling to a clinic appointment can be a tremendous burden, in terms of time and the need to make specific transportation arrangements, for both the patient and caregiver as well. To provide remote treatment for both clinical and research purposes in MS, there are several considerations for optimal use.

First, there is consideration for cognitive capacity to understand and participate in the tDCS procedures. While cognitive impairment is frequent (occurring in up to 70% of all individuals), deficits are typically marked by cognitive slowing and difficulty with new learning, but are not at the severity seen in dementias. A brief cognitive screening procedure can ensure that the potential tDCS candidate will be successful in executing the procedures. This can include checking for understanding during the screening process and completion of brief measures such as reading recognition (as a proxy for premorbid intellectual functioning) and information processing speed (e.g., Symbol Digit Modalities Test [SDMT]).

A second concern is sufficient fine motor functioning for headset placement. MS is frequently associated with fine motor impairment and slowed motor functioning. Therefore, devices must be designed as simplistically as possible. This includes easily-held devices with large buttons and press points for operation. In addition, headsets must be designed for simple placement (Fig. 13.1).

Headsets in a current MS protocol have been re-configured to include an adjustable headpiece so electrode placement is optimal for varying head sizes (Kasschau et al. 2015). The wires attached to the headset are color coded black and red for simple connection to the device. The anode and cathode are labeled red and black, respectively to also assist in proper, simplistic placement. In general, a cap-like design that can be easily grasped, lifted, and placed is important. Electrodes and sponges must also be easy to manipulate and place. This latter concern has been especially challenging, but pre-moistened sponges (that do not require the use of a saline syringe), provided in perforated single use packaging, have been most helpful. In addition, a snap connection placement for sponges to join the headset is preferred over a button connection.

In some cases, the individual with MS may meet screening requirements for cognitive ability, but might have too severe motor involvement to adequately place the headset and operate the device. In these cases, a caregiver proxy may be enlisted

Fig. 13.1 4 × 4 tDCS headgear. Custom-made headgear has been modified with the goal of simplifying placement and minimizing dependence on manual dexterity. Electrodes will be securely attached to specific markings on the headset with the use of pre-moistened sponges. The sponges are provided in single-use packets, and once opened, can be readily attached in the correct placement to the headgear. A marker guides accurate user placement of the headgear. (The figure is courtesy of L. Charvet)

depending on institution requirements. In these cases, the proxy must be screened and trained during the baseline visit in all procedures.

During the training period, tolerability can be tested as well as capacity. Once cleared, the MS participant (with or without a caregiver proxy) can be required to demonstrate successful headset placement and device operation. In addition, while in-clinic, the targeted dose should be tested on the participant, for at least 1 min, in order to ensure that the individual can tolerate the treatment. If the subject does not pass the initial tolerability test, they are terminated from further protocol participation. If the tolerability test is successful, it is then recommended to complete the first full session under the supervision of a study technician to stimulate the individual's

daily experience from home, and provide an extra measure of clearance. Only once cleared, they can be provided an "at-home" tDCS kit for remote sessions. Once again, the tDCS technician reviews with the subject and/or proxy each part of the tDCS kit (headset, device, laptop, and sponges) prior to departure so that at-home sessions are confidently and safely administered.

At-home devices must be designed for safety, reliability of stimulation delivery, and optimal remotely supervised operation. For instance, one device that has been studied, the Soterix Mini-CT, is dependent on a code to "unlock" delivery of only one "dose" for stimulation (or sham) to be administered. Once connected, the technician can coach the participant and/or proxy on correct placement and ensure all safety criteria are met. An impedance meter is included in the device which prevents access until the placement is adequate. The previously mentioned code is not provided until the device displays a "good" connection. Through the videoconferencing platform, visual confirmation of correct placement can also be made. Then, the session is monitored in real-time to ensure consistent stimulation and no unexpected adverse events including poor tolerance.

In addition, parameters to assess such adverse events and participant experiences must minimize user burden. For example, the study technician should adhere to brief, visual analog scales to assess pain and fatigue, with a standardized, verbal interview of any side effects experienced.

The currently used MS protocol includes extensive training procedures as well as highly detailed "stop" criteria that provide the technician with specific steps and guidelines to initiate and oversee each session. In cases of violations, including failure to observe safety features or report of any pain over a moderate level, the use code is not provided and/or the remote use is discontinued.

This protocol was initially demonstrated to be feasible in a sample of adults with MS (Kasschau et al. 2016). Twenty participants (n = 26), ages 30–69 years with a range of neurologic disability form mild to severe (using a proxy) and subtype including both relapsing remitting and progressive forms, were enrolled to test the feasibility of the methods. Protocol adherence exceeded what has been observed in studies with clinic-based treatment delivery, with all but one participant (95%) completing at least eight of the ten sessions. Across a total of 192 supervised treatment sessions, no session required discontinuation and no adverse events were reported. The most common side effects were itching/tingling at the electrode site with no side effect exceeding an intensity of moderate. The study was met with strong patient interest and highly positive feedback.

In a second and ongoing study, n = 32 MS participants have been randomized to either active or sham 2.0 mA tDCS for 20 sessions. Those in the sham condition are offered an additional 10 open-label active sessions at study end. A third trial has expanded this protocol to patients with Parkinson's disease (n = 12) for an initial 10 open-label sessions for feasibility. We continue to see very high protocol adherence with both the expanded session number (20 sessions) and sham conditions, as well as when applying the procedures to those with Parkinson's disease. In over 800 remotely-supervised sessions to date, only one session has been discontinued during stimulation (due to headache). There have been no serious adverse events, and

tolerability remains consistent with what is published in the extensive literature of in-clinic application (Bikson et al. 2016). In sum, remote supervision offers a platform to provide in-home treatment to those living with MS and potentially many other neurologic conditions.

Chronically Ill Patients with Multiple Symptoms

With aging of the worldwide population, the prevalence of chronic illness is rising (Centers for Medicare and Medicaid Services 2012; Hasselman 2013; Ortman et al. 2014). In the U.S., approximately 50% of adults have one or more chronic illness. Symptom management is challenging in those with multiple chronic conditions, particularly when age-related risk from drug therapy compounds the risks associated with disease-related organ dysfunction. Distress associated with poorly controlled symptoms such as pain, fatigue, depressed mood or cognitive difficulties, is highly prevalent in the chronically ill, and it can substantially affect patient's functional independence, as well as drive health-care costs (Dhingra et al. 2017; Hasselman 2013; Ortman et al. 2014).

Most chronically ill patients live at home and seek care that aims to mitigate illness burden and maintain a good quality of life. Therefore, adjunct non-pharmacological strategies for symptom control in home settings are highly relevant for this patient population. Although tDCS has shown promising potential for symptom control, the burden of repeated visits to receive tDCS in medical- or research facilities has been among the major obstacles that made an access to tDCS difficult for many chronically ill patients. Therefore, the development of tDCS protocols suitable for the patient's use in home settings represents a great opportunity specifically for those with multiple illnesses, complex symptoms and lower functional status. However, designing an at-home tDCS protocol for this potentially vulnerable patient population requires specific considerations, such as the following:

Involvement of Family Caregiver Seriously ill patients frequently rely on assistance of family caregivers. Therefore, it is likely that home-based tDCS applications in some patients may need to be assisted by an informal caregiver rather than self-applied by the patient. However, patients with higher functional status may find it important to be directly involved in tDCS application. Thus, both options should be included in the tDCS protocol and offered to the patient and the family.

Minimal Burden Both the patient and the informal caregiver bear the enormous burden of the illness and the level of their overall distress may be high. Therefore, study procedures pertaining to the tDCS administration and data collection must be user friendly, easy and not time-demanding. While data collection in healthy populations or patients with higher performance status may include extensive questionnaire sets and testing, data collection in frail, seriously ill patients must be carefully selected and include only a brief set of assessment tools.

Time Flexibility It is difficult for the patient and their informal caregiver to accommodate multiple day-to-day chores in daily life affected by the illness. Adding another element, such as participation in an at-home tDCS study only adds to an already full schedule. Therefore, time planning of tDCS procedures should leave reasonable margins acceptable for both the patient-caregiver dyad and the study personnel, for example when scheduling the real-time video monitoring of the procedure.

Maintaining the Medication Regimen Medical care and symptom management in seriously ill patients relies largely on pharmacological treatments, often including multiple medications. Due to ethic as well as regulatory reasons (seriously ill patients are considered potentially vulnerable subjects), medication wash-out prior to participation in a tDCS study is not feasible. This may represent a substantial methodological hurdle, because certain agents (such as NMDA antagonists) may alter tDCS effects. It requires careful consideration when planning the tDCS protocol and the study inclusion and exclusion criteria.

Other Considerations It has to be taken into account that the tDCS stimulation session usually takes 20–30 min during which the patient should remain seated or in a bed, without walking around. Therefore, subjects who are restless or are not comfortably able to comply with that requirement are not good candidates for the tDCS procedure.

Overall, the feasibility of home-delivered remotely-monitored tDCS in seriously ill patients is multifaceted, including (but not limited to) the following elements: (a) Patient's and family caregiver's understanding of the procedure, their willingness and ability to participate in tDCS applications; (b) Patient's or caregiver's ability to perform tDCS specific procedures after training; (c) Patient's acceptability and tolerability of the procedure, including being able to remain seated or in bed for the 20-min stimulation; (d) Patient's ability to provide a brief feedback or numerical rating when asked; (e) Home environment, including sufficient arrangements to accommodate tDCS administration; and tDCS acceptability in the frame of spiritual/religious beliefs and overall settings of the household (Riggs et al. 2017b).

A schema of a tDCS patient-tailored protocol suitable for polysymptomatic seriously ill patients aiming for symptom control in home settings (Knotkova et al. 2017a) is depicted in Fig. 13.2.

The protocol allows for an optional inclusion of assisting informal caregiver. There is 1 home visit for consenting, screening and familiarization with the tDCS device, followed by in-person initiation of training that will then continue in remote.

To facilitate familiarization with tDCS at the home visit, the tDCS technician demonstrates the equipment and function of the device, and the patient has an opportunity to experience the sensory sensation associated with tDCS procedure: the patient undergoes 1 min of tDCS first on their arm and then on their head, at the default intensity of 1.5 mA. As the protocol is tailored to the patient's needs,

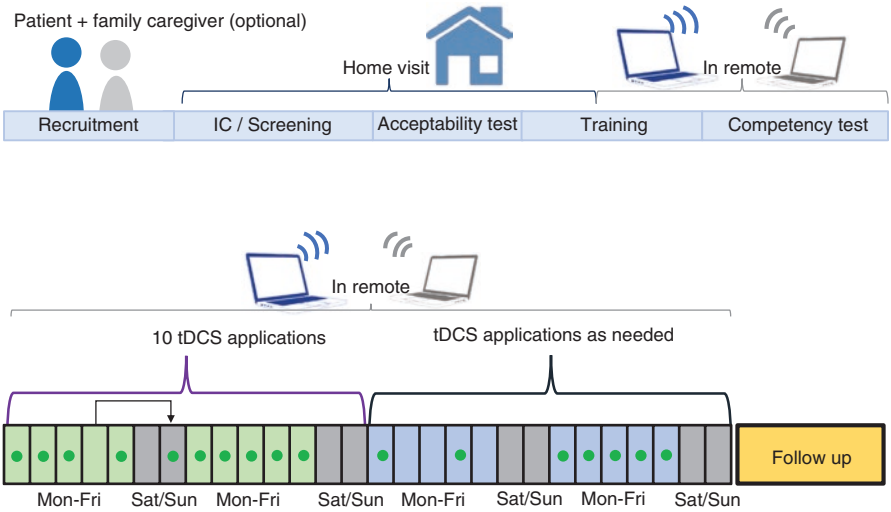

Fig. 13.2 Schema of tDCS protocol suitable for home-bound seriously ill patients with multiple symptoms. The protocol includes 1 at-home visit and has specific patient-tailored elements, such as an optional inclusion of an assisting informal caregiver, as well as elements that enhance compliance and safety, including remote visual contact with the patient via telehealth tablet. (The figure is courtesy of H. Knotkova and A. Riggs)

those who find the sensation not acceptable, may repeat the acceptability test at lower intensity of 1.0 mA, which - if accepted - then become the patient-specific stimulation intensity through the protocol. Patients who do not find the lower intensity acceptable are not suitable candidates for tDCS. Although tDCS is in general well accepted even at higher intensities, such as 2 mA, some patients may have increased skin sensitivity due to clinical condition, medications or other factors. After familiarization with the device and sensory sensation, the tDCS technician initiates patient's or informal caregiver's training in tDCS application. The training continues in remote for about 1 week with an assistance from the tDCS technician via videoconference as needed. tDCS skill-building is extremely important for tDCS applications in home settings and for that reason the training is concluded with a competency test, to assure that the designated individual (the patient or the caregiver) is able to perform tDCS in accordance with good practice.

After conclusion of the competency test, patients are encouraged to apply one tDCS session per day on multiple consecutive days. In the second phase, patients are allowed to apply tDCS as needed, ranging from none to two applications per day, and the applications are remotely supervised. The level of remote supervision is patient-tailored and varies upon the patient's/caregiver's tDCS skills and compliance with good practices for tDCS applications.

The initial feasibility and face validity of this protocol has been determined in an IRB-approved study (Riggs et al. 2017b).

Regulatory and Ethical Aspects Pertaining to At-Home tDCS

The regulatory framework that applies to tDCS in general, including at-home applications, is substantially different for tDCS in clinical/medical use vs research. Thus, regulations that apply to use of off-label devices in medical practice vs research differ, and the distinction between the two is guided by the respective definitions: The goal of medical practice is to "provide diagnosis, preventative treatment or therapy", while research is "designed to test a hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge." (Riley and Basilius 2007; Wittich et al. 2012). The FDA (and comparable organizations that regulate device manufacturers) does not regulate the practice of medicine, which instead is subject to the direction of state and federal professional and licensing boards. Thus, the federal Food, Drug, and Cosmetic Act of 1938 does not play a role in creating physician liability for off-label device use. When not classified as tools involved in research, medical devices can be used in an off-label manner in medical practice without FDA regulatory oversight. Currently, the general legality and value of off-label use is integral for medical practice, and under the U.S. law, physicians may prescribe drugs and devices for off-label use (Wittich et al. 2012). A limitation to this rule is that physicians may only prescribe off-label devices if the physicians are not employed by the medical or pharmaceutical companies in question. (Wilkes and Johns 2008).

Entirely different regulatory framework, however, applies to tDCS medical devices in clinical research outside of or contrary to FDA approval, and the following requirements must be met: (i) Approval by an institutional review board (IRB); and additionally, if the study involves a significant risk device (defined as one that presents a potential for serious risk to the health, safety, or welfare of a subject), approval of an investigational device exemption (IDE) by FDA; (ii) Informed consent from research participants; (iii) Labeling of the device for investigational use only; (iv) Monitoring of the study; and (v) Compliance with required records and reports.

In summary, there is duality in the regulatory framework that applies to tDCS use in research settings vs off-label clinical use, and this duality applies not only to a general tDCS use, but encompasses also at-home applications.

Challenges, Open Questions and Future Trends in At-Home tDCS

Any new approach faces hurdles to its widespread use and acceptance. The ability to conduct tDCS treatment or research outside of a clinic setting does not simply require technological advances to make it possible, but also must be able to surmount valid concerns about feasibility, safety, and proper oversight. As described above, many of the safety concerns can be addressed using technical design features

that prevent harm through uncontrolled stimulation. Oversight concerns are largely addressed both through focused training and by the ability to provide videoconferencing-based interaction to ensure proper tDCS use – either as periodic check-in assessments or at every tDCS treatment session if deemed necessary or useful. At this stage of remotely-supervised tDCS, feasibility issues are largely addressed. It currently is possible to conduct tDCS clinical trials in a wide range of clinical populations in home settings. However, a concise, thoughtful, and effective series of guidelines and recommendations is needed to navigate the development of protocols for these trials. We have endeavored to provide a generalized set of expectations for such protocols in this chapter and in our previous reports (Charvet et al. 2015).

- Although some remotely-supervised tDCS studies are underway (Kasschau et al. 2015, 2016; Knotkova et al. 2016), additional clinical trials conducted in a variety of patient populations are needed to ultimately demonstrate the feasibility of generalized use. Not only will more trials identify other possible practical barriers that might need to be overcome, continued demonstration that patients can effectively and reliably administer tDCS at home with remote supervision will promote general acceptance of the method as viable and informative. It is hoped that with increasing empirical support for tDCS as an effective treatment, there will be increased demand to streamline equipment for remotely-supervised use. One can envision that as technology progresses, so will construction of new devices that more seamlessly integrate tDCS delivery, videoconferencing-based telecommunications using built-in cellular capability, optional cognitive stimulation, and features to automatically upload clinical trial-relevant data via internet to a central monitoring site into a single unit such as a handheld PDA or tablet device. Such integrated systems would go even further to offer remotely-supervised tDCS to a greater number of households, including households without computers. However, smartphones are commonplace now, suggesting that families without extensive computer experience are likely to be able to use such devices with less familiarization and training.
- Perhaps the most significant near-term challenge for remotely-supervised tDCS is to facilitate the process of empirical research needed to validate the treatment approach in various disorders. Currently, tDCS shows the strongest empirical support for potential efficacy in Major Depressive Disorder, stroke and selected chronic pain conditions. However, complexity arises as there are a variety of ways to deliver tDCS in potentially therapeutic ways. The combination of these different tDCS approaches and different patient groups offers numerous options for exploratory treatment trial agendas. As with any new set of options to explore, potential delays and risks to scientific progress arise from the difficulty comparing the results across several small trials when they use disparate methodology. So in addition to a set of recommendations for optimal remotely-supervised tDCS protocol construction, a likely next step to facilitate tDCS research might be the construction of a tDCS-specific clinical trials informatics platform for researchers. Two things might specifically help. First, reporting standards should be developed

that detail the minimal information that should be collected about remotely-supervised tDCS in all future clinical trials. Such a system should not only follow, but expand upon CONSORT 2010 guidelines (Schulz et al. 2010) for clinical trial reporting with tDCS-specific information about tDCS equipment configuration, ratings of the quality of each session set up, the number and duration of tDCS treatment sessions, which tDCS equipment was used, and what methods were employed to remotely-supervise patients, etc. Second, a repository should be established so that patient-based data across different studies could be integrated. Such resources typically are feasible only when they are voluntary, but that clear expectations are made by the researchers who lead the field that investigator reporting compliance is in the field's best scientific interest. Moreover, there is an increasing trend for federally-funded research to require researchers to contribute data to such repositories. Therefore, it is possible that if such a system is made available, the reporting of tDCS-specific administration information might eventually be mandated for any tDCS research funded by the National Institutes of Health. However, the potential payoff for this effort is considerable. By fostering large-scale remotely-supervised tDCS clinical trial reporting, such standards would not merely facilitate accurate and rigorous reporting of tDCS trial results, they would guide the aggregation of a database that can be continually mined to assess the quality of remotely-supervised tDCS methodology as more research is done. If participant demographic data, basic clinical characteristics, and outcome data were included in this repository, it also could facilitate future meta-analytic studies. Such information could be integrated at the meta-analytic level to characterize factors that moderate tDCS protocol adherence or even outcome, determine whether those factors are disorder- or population-specific or generalized, etc. The availability of such a standardized reporting framework/repository likely would prompt other useful additions. For instance, researchers might develop a brief, standardized questionnaire to assess patient attitudes about tDCS and reasons for seeking tDCS treatment or participating in tDCS research trials.

- This sort of recommendation is feasible because the number of tDCS researchers currently is limited, and is unlikely to grow to unmanageable proportions unless tDCS becomes fully validated as a treatment for specific disorders and people begin arguments about whether tDCS should be offered to specific patient groups as standard care options. Looking forward, it is possible to envision future challenges involving how remotely-supervised tDCS is best delivered clinically. Although the technical demands are not prohibitive, it is unlikely that at home tDCS will ever become "over the counter" or practically fit into the scope of general medical practice. More reasonably it will be used by specialty medical clinics, whose staff are fully trained to manage the technical, education, and oversight responsibilities necessary for at-home tDCS to be administered validly. This raises questions about how those staff members should best be trained. The guidelines we offer here are geared to the state of the field today, which is far more dominated by research-related concerns than issues of clinical delivery. However, they provide a blueprint of many issues that will also be relevant when considering the development of clinical care protocols. For instance, at

minimum, future training standards for tDCS clinical services should be developed that are specific to remotely-supervised procedures. This includes training and possible accreditation of technical staff. Here, the remotely-supervised tDCS can learn from standards applied in telehealth centers where medical staff remotely monitors biomedical information from at-home patients. In fact, the remotely supervised tDCS would fit well into the scope of practice of specialized telehealth centers or units, and the adoption would not require excessive additional resources.

- It is possible that the availability of at-home tDCS with remote supervision may trigger interest in physicians prescribing tDCS application at home for therapeutic purposes. In the U.S., different regulations apply to research vs medical practice.

Conclusions

In conclusion, tDCS applied in home settings can have multiple benefits to all involved. However, existing approaches in at-home tDCS vary in many elements, such as degree of rigor pertaining to patients' training, data collection, compliance with stimulation protocol, and level of supervision or necessary assistance in administration. The top tier is represented by approaches implementing highest level of control/rigor, aiming for replicability and enhanced safety. An approach utilizing remote supervision and enhanced compliance monitoring and safety monitoring, with high requirement for replicability, is suitable for tDCS clinical trials in various populations; population-specific adjustments of protocol and technology, as illustrated on examples in this chapter, document wide usefulness of this approach. The future trends in the field of tDCS applied in home settings include further development of the tDCS technology paired with technical solutions for remote monitoring/supervision; broad data sharing via data repositories; and rigorous results-reporting that may facilitate replication studies.

References

Adler, L. D., & Nierenberg, A. A. (2010). Review of medication adherence in children and adults with ADHD. *Postgraduate Medicine, 122*(1), 184–191.

Advokat, C. (2009). What exactly are the benefits of stimulants for ADHD? *Journal of Attention Disorders, 12*(6), 495–498.

Alonzo, A., & Charvet, L. (2016). Home-based tDCS: Design, feasibility, and safety considerations. In *Transcranial direct current stimulation in neuropsychiatric disorders* (pp. 351–361). Springer.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders (DSM-5®)* (5th ed.). Arlington, TX: American Psychiatric Pub.

Andrade, C. (2013). Once- to twice-daily, 3-year domiciliary maintenance transcranial direct current stimulation for severe, disabling, clozapine-refractory continuous auditory hallucinations in schizophrenia. *The Journal of ECT, 29*(3), 239–242.

Andre, S., Heinrich, S., Kayser, F., Menzler, K., Kesselring, J., Khader, P. H., … Mylius, V. (2016). At-home tDCS of the left dorsolateral prefrontal cortex improves visual short-term memory in mild vascular dementia. *Journal of the Neurological Sciences, 369*, 185–190.

Ayache, S. S., Palm, U., Chalah, M. A., Al-Ani, T., Brignol, A., Abdellaoui, M., … Lefaucheur, J. P. (2016). Prefrontal tDCS decreases pain in patients with multiple sclerosis. *Frontiers in Neuroscience, 10*, 147.

Bandeira, I. D., Guimaraes, R. S., Jagersbacher, J. G., Barretto, T. L., de Jesus-Silva, J. R., Santos, S. N., … Lucena, R. (2016). Transcranial direct current stimulation in children and adolescents with attention-deficit/hyperactivity disorder (ADHD) a pilot study. *Journal of Child Neurology, 31*(7), 918–924.

Barkley, R. A., & Cunningham, C. E. (1978). Do stimulant drugs improve the academic performance of hyperkinetic children? A review of outcome studies. *La Clinica Pediatrica, 17*(1), 85–92.

Barkley, R. A., Fischer, M., Smallish, L., & Fletcher, K. (2002). The persistence of attention-deficit/hyperactivity disorder into young adulthood as a function of reporting source and definition of disorder. *Journal of Abnormal Psychology, 111*(2), 279–289.

Barkley, R. A., Fischer, M., Smallish, L., & Fletcher, K. (2006). Young adult outcome of hyperactive children: Adaptive functioning in major life activities. *Journal of the American Academy of Child and Adolescent Psychiatry, 45*(2), 192–202.

Bikson, M., Grossman, P., Thomas, C., Zannou, A. L., Jiang, J., Adnan, T., … Woods, A. J. (2016). Safety of transcranial direct current stimulation: Evidence based update 2016. *Brain Stimulation, 9*(5), 641–661.

Breslau, J., Miller, E., Breslau, N., Bohnert, K., Lucia, V., & Schweitzer, J. (2009). The impact of early behavior disturbances on academic achievement in high school. *Pediatrics, 123*(6), 1472–1476.

Breslau, J., Miller, E., Joanie Chung, W. J., & Schweitzer, J. B. (2011). Childhood and adolescent onset psychiatric disorders, substance use, and failure to graduate high school on time. *Journal of Psychiatric Research, 45*(3), 295–301.

Bright, G. M. (2008). Abuse of medications employed for the treatment of ADHD: Results from a large-scale community survey. *Medscape Journal of Medicine, 10*(5), 111.

Brinkman, W. B., Sherman, S. N., Zmitrovich, A. R., Visscher, M. O., Crosby, L. E., Phelan, K. J., & Donovan, E. F. (2012). In their own words: Adolescent views on ADHD and their evolving role managing medication. *Academic Pediatrics, 12*(1), 53–61.

Brunoni, A. R., Amadera, J., Berbel, B., Volz, M. S., Rizzerio, B. G., & Fregni, F. (2011a). A systematic review on reporting and assessment of adverse effects associated with transcranial direct current stimulation. *The International Journal of Neuropsychopharmacology, 14*(8), 1133–1145.

Brunoni, A. R., Fregni, F., & Pagano, R. L. (2011b). Translational research in transcranial direct current stimulation (tDCS): A systematic review of studies in animals. *Reviews in the Neurosciences, 22*(4), 471–481.

Bussing, R., Koro-Ljungberg, M., Noguchi, K., Mason, D., Mayerson, G., & Garvan, C. W. (2012). Willingness to use ADHD treatments: A mixed methods study of perceptions by adolescents, parents, health professionals and teachers. *Social Science & Medicine, 74*(1), 92–100.

Cao, M., Shu, N., Cao, Q., Wang, Y., & He, Y. (2014). Imaging functional and structural brain connectomics in attention-deficit/hyperactivity disorder. *Molecular Neurobiology, 50*(3), 1111–1123.

Carlson, C. L., & Bunner, M. R. (1993). Effects of methylphenidate on the academicperformance of children with attention deficit hyperactive disorder and learning disabilities. *School Psychology Review, 22*, 184–198.

Centers for Medicare and Medicaid Services. (2012). *Chronic conditions among medicare beneficiaries*. Baltimore, MD: Chartbook.

Cha, Y. H., Urbano, D., & Pariseau, N. (2016). Randomized single blind sham controlled trial of adjunctive home-based tDCS after rTMS for mal de debarquement syndrome: Safety, efficacy, and participant satisfaction assessment. *Brain Stimulation, 9*(4), 537–544.

Charach, A., & Gajaria, A. (2008). Improving psychostimulant adherence in children with ADHD. *Expert Review of Neurotherapeutics, 8*(10), 1563–1571.

Charvet, L. E., Kasschau, M., Datta, A., Knotkova, H., Stevens, M. C., Alonzo, A., … Bikson, M. (2015). Remotely-supervised transcranial direct current stimulation (tDCS) for clinical trials: Guidelines for technology and protocols. *Frontiers in Systems Neuroscience, 9*, 26.

Christensen, L., Sasane, R., Hodgkins, P., Harley, C., & Tetali, S. (2010). Pharmacological treatment patterns among patients with attention-deficit/hyperactivity disorder: Retrospective claims-based analysis of a managed care population. *Current Medical Research and Opinion, 26*(4), 977–989.

Coletti, D. J., Pappadopulos, E., Katsiotas, N. J., Berest, A., Jensen, P. S., & Kafantaris, V. (2012). Parent perspectives on the decision to initiate medication treatment of attention-deficit/hyperactivity disorder. *Journal of Child and Adolescent Psychopharmacology, 22*(3), 226–237.

Cortese, S., Kelly, C., Chabernaud, C., Proal, E., Di Martino, A., Milham, M. P., & Castellanos, F. X. (2012). Toward systems neuroscience of ADHD: A meta-analysis of 55 fMRI studies. *The American Journal of Psychiatry, 169*(10), 1038–1055.

Cosmo, C., Baptista, A. F., de Araujo, A. N., do Rosario, R. S., Miranda, J. G., Montoya, P., & de Sena, E. P. (2015a). A randomized, double-blind, sham-controlled trial of transcranial direct current stimulation in attention-deficit/hyperactivity disorder. *PLoS One, 10*(8), e0135371.

Cosmo, C., Ferreira, C., Miranda, J. G., do Rosario, R. S., Baptista, A. F., Montoya, P., & de Sena, E. P. (2015b). Spreading effect of tDCS in individuals with attention-deficit/hyperactivity disorder as shown by functional cortical networks: A randomized, double-blind, sham-controlled trial. *Frontiers in Psychiatry*.

Cunningham, C. E., & Barkley, R. A. (1978). The role of academic failure in hyperactive behavior. *Journal of Learning Disabilities, 11*(5), 274–280.

Cuypers, K., Leenus, D. J., Van Wijmeersch, B., Thijs, H., Levin, O., Swinnen, S. P., & Meesen, R. L. (2013). Anodal tDCS increases corticospinal output and projection strength in multiple sclerosis. *Neuroscience Letters, 554*, 151–155.

Del Campo, N., Chamberlain, S. R., Sahakian, B. J., & Robbins, T. W. (2011). The roles of dopamine and noradrenaline in the pathophysiology and treatment of attention-deficit/hyperactivity disorder. *Biological Psychiatry, 69*(12), 145–157.

Demirtas-Tatlidede, A., Vahabzadeh-Hagh, A. M., & Pascual-Leone, A. (2013). Can noninvasive brain stimulation enhance cognition in neuropsychiatric disorders? *Neuropharmacology, 64*, 566–578.

Dhingra, L., Barrett, M., Knotkova, H., Chen, J., Riggs, A., Lee, B., … Portenoy, R. (2017). Symptom sistress among diverse patients referred for community-based palliative care: Sociodemographic and medical correlates. *Journal of Pain and Symptom Management, 55*, 290–296.

Ditye, T., Jacobson, L., Walsh, V., & Lavidor, M. (2012). Modulating behavioral inhibition by tDCS combined with cognitive training. *Experimental Brain Research, 219*(3), 363–368.

DosReis, S., Mychailyszyn, M. P., Evans-Lacko, S. E., Beltran, A., Riley, A. W., & Myers, M. A. (2009). The meaning of attention-deficit/hyperactivity disorder medication and parents' initiation and continuity of treatment for their child. *Journal of Child and Adolescent Psychopharmacology, 19*(4), 377–383.

Dosreis, S., Zito, J. M., Safer, D. J., Soeken, K. L., Mitchell, J. W., Jr., & Ellwood, L. C. (2003). Parental perceptions and satisfaction with stimulant medication for attention-deficit hyperactivity disorder. *Journal of Developmental and Behavioral Pediatrics, 24*, 155–162.

Evans, S. W., Owens, J. S., & Bunford, N. (2014). Evidence-based psychosocial treatments for children and adolescents with attention-deficit/hyperactivity disorder. *Journal of Child & Adolescent Psychopharmacology, 43*(4), 527–551.

Faraone, S. V., & Upadhyaya, H. P. (2007). The effect of stimulant treatment for ADHD on later substance abuse and the potential for medication misuse, abuse, and diversion. *The Journal of Clinical Psychiatry, 68*(11), 15–22.

Ferrin, M., Ruiz-Veguilla, M., Blanc-Betes, M., Abd, S. E., Lax-Pericall, T., Sinclair, M., & Taylor, E. (2012). Evaluation of attitudes towards treatment in adolescents with attention

deficit hyperactivity disorder (ADHD). *European Child & Adolescent Psychiatry, 21*(7), 387–401.

Ferrucci, R., Vergari, M., Cogiamanian, F., Bocci, T., Ciocca, M., Tomasini, E., … Priori, A. (2014). Transcranial direct current stimulation (tDCS) for fatigue in multiple sclerosis. *NeuroRehabilitation, 34*(1), 121–127.

Frazier, T. W., Demaree, H. A., & Youngstrom, E. A. (2004). Meta-analysis of intellectual and neuropsychological test performance in attention-deficit/hyperactivity disorder. *Neuropsychology, 18*(3), 543–555.

Gadow, K. D. (1983). Effects of stimulant drugs on academic performance in hyperactive and learning disabled children. *Journal of Learning Disabilities, 16*(5), 290–299.

Gau, S. S., Shen, H. Y., Chou, M. C., Tang, C. S., Chiu, Y. N., & Gau, C. S. (2006). Determinants of adherence to methylphenidate and the impact of poor adherence on maternal and family measures. *Journal of Child & Adolescent Psychopharmacology, 16*(3), 286–297.

Gearing, R. E., Townsend, L., MacKenzie, M., & Charach, A. (2011). Reconceptualizing medication adherence: Six phases of dynamic adherence. *Harvard Review of Psychiatry, 19*(4), 177–189.

Hagenacker, T., Bude, V., Naegel, S., Holle, D., Katsarava, Z., Diener, H. C., & Obermann, M. (2014). Patient-conducted anodal transcranial direct current stimulation of the motor cortex alleviates pain in trigeminal neuralgia. *The Journal of Headache and Pain*.

Harpur, R. A., Thompson, M., Daley, D., Abikoff, H., & Sonuga-Barke, E. J. (2008). The attention-deficit/hyperactivity disorder medication-related attitudes of patients and their parents. *Journal of Child and Adolescent Psychopharmacology, 18*(5), 461–473.

Hasselman, D. (2013). *Super-utilizer summit: Common themes from innovation complex care management programs* (pp. 1–32). Center for Health Care Strategies Available via https://www.chcs.org/resource/super-utilizer-summit-common-themes-from-innovative-complex-care-management-programs/ Accessed 10 Oct 2017

Hinshaw, S. P. (1992a). Academic underachievement, attention deficits, and aggression: Comorbidity and implications for intervention. *Journal of Consulting and Clinical Psychology, 60*(6), 893–903.

Hinshaw, S. P. (1992b). Externalizing behavior problems and academic underachievement in childhood and adolescence: Causal relationships and underlying mechanisms. *Psychological Bulletin, 111*(1), 127–155.

Hodgson, K., Hutchinson, A. D., & Denson, L. (2014). Nonpharmacological treatments for ADHD: A meta-analytic review. *Journal of Attention Disorders, 18*(4), 275–282.

Hyvarinen, P., Makitie, A., & Aarnisalo, A. A. (2016). Self-administered domiciliary tDCS treatment for tinnitus: A double-blind sham-controlled study. *PLoS One, 11*(4), e0154286.

Jensen, P. S., Arnold, L. E., Swanson, J. M., Vitiello, B., Abikoff, H. B., Greenhill, L. L., … Hur, K. (2007). 3-year follow-up of the NIMH MTA study. *Journal of the American Academy of Child and Adolescent Psychiatry, 46*(8), 989–1002.

Johnston, C., Hommersen, P., & Seipp, C. (2008). Acceptability of behavioral and pharmacological treatments for attention-deficit/hyperactivity disorder: Relations to child and parent characteristics. *Behavior Therapy, 39*(1), 22–32.

Kaiser, N. M., Hoza, B., & Hurt, E. A. (2008). Multimodal treatment for childhood attention-deficit/hyperactivity disorder. *Expert Review of Neurotherapeutics, 8*(10), 1573–1583.

Kasschau, M., Reisner, J., Sherman, K., Bikson, M., Datta, A., & Charvet, L. E. (2016). Transcranial direct current stimulation is feasible for remotely supervised home delivery in multiple sclerosis. *Neuromodulation, 19*(8), 824–831.

Kasschau, M., Sherman, K., Haider, L., Frontario, A., Shaw, M., Datta, A., … Charvet, L. (2015). A protocol for the use of remotely-supervised transcranial direct current stimulation (tDCS) in multiple sclerosis (MS). *Journal of Visualized Experiments, 106*, e53542.

Kessler, R. C., Adler, L., Barkley, R., Biederman, J., Conners, C. K., Demler, O., … Zaslavsky, A. M. (2006). The prevalence and correlates of adult ADHD in the United States: Results from

the National Comorbidity Survey Replication. *The American Journal of Psychiatry, 163*(4), 716–723.

Knotkova, H., Greenberg, A., Leuschner, Z., Soto, E., & Cruciani, R. A. (2013). Evaluation of outcomes from transcranial direct current stimulation (tDCS) for the treatment of chronic pain. *Clinical Neurophysiology, 124*(10), 125–126.

Knotkova, H., Riggs, A., Patel, V., Harounian, J., Heshmati, P., Arce, D., … Bikson, M. (2016). Advances in transcranial direct current stimulation (tDCS): Adjustment of technology, protocol and training for home-based, self-delivered remotely supervised tDCS for community-dwelling patients with advanced chronic illness. *Neuromodulation, 19*, e10.

Knotkova, H., Riggs, A., Patel, V., Truong, D., Arce, D., Bernstein, H., … Bikson, M. (2017a). A novel approach to determining M1 tDCS montage without neuronavigational measurements, suitable for patients in home settings. *Brain Stimulation, 10*(4), 78–80.

Knotkova, H., Riggs, A., & Portenoy, R. K. (2017b). A patient-tailored protocol of tDCS stimulation paired with telehealth support for at-home symptom management in seriously ill patients with multiple chronic symptoms. *Brain Stimulation, 10*(4), 77–78.

Knotkova, H., Woods, A., & Bikson, M. (2015). Transcranial direct current stimulation (tDCS): What pain practitioners need to know. *Practical Pain Management, 15*(3), 58–65.

Kooij, S. J., Bejerot, S., Blackwell, A., Caci, H., Casas-Brugue, M., Carpentier, P. J., … Asherson, P. (2010). European consensus statement on diagnosis and treatment of adult ADHD: The European network adult ADHD. *BMC Psychiatry, 10*, 67.

Langberg, J. M., & Becker, S. P. (2012). Does long-term medication use improve the academic outcomes of youth with attention-deficit/hyperactivity disorder? *Clinical Child and Family Psychology Review, 15*(3), 215–233.

Larocca, N. G. (2011). Impact of walking impairment in multiple sclerosis: Perspectives of patients and care partners. *Patient, 4*(3), 189–201.

Leffa, D. T., de Souza, A., Scarabelot, V. L., Medeiros, L. F., de Oliveira, C., Grevet, E. H., … ILS, T. (2016). Transcranial direct current stimulation improves short-term memory in an animal model of attention-deficit/hyperactivity disorder. *European Neuropsychopharmacology, 26*(2), 368–377.

Levin, F. R., Evans, S. M., & Kleber, H. D. (1998). Prevalence of adult attention-deficit hyperactivity disorder among cocaine abusers seeking treatment. *Drug and Alcohol Dependence, 52*(1), 15–25.

Loe, I. M., & Feldman, H. M. (2007). Academic and educational outcomes of children with ADHD. *Ambulatory Pediatrics, 7*(1), 82–90.

Mattioli, F., Bellomi, F., Stampatori, C., Capra, R., & Miniussi, C. (2016). Neuroenhancement through cognitive training and anodal tDCS in multiple sclerosis. *Multiple Sclerosis, 22*(2), 222–230.

McLeod, J. D., Pescosolido, B. A., Takeuchi, D. T., & White, T. F. (2004). Public attitudes toward the use of psychiatric medications for children. *Journal of Health and Social Behavior, 45*(1), 53–67.

Meesen, R. L., Thijs, H., Leenus, D. J., & Cuypers, K. (2014). A single session of 1 mA anodal tDCS-supported motor training does not improve motor performance in patients with multiple sclerosis. *Restorative Neurology and Neuroscience, 32*(2), 293–300.

Miniussi, C., & Ruzzoli, M. (2013). Transcranial stimulation and cognition. *Handbook of Clinical Neurology, 116*, 739–750.

Molina, B. S., Hinshaw, S. P., Swanson, J. M., Arnold, L. E., Vitiello, B., Jensen, P. S., … MTA Cooperative Group. (2009). The MTA at 8 years: Prospective follow-up of children treated for combined-type ADHD in a multisite study. *Journal of the American Academy of Child and Adolescent Psychiatry, 48*(5), 484–500.

Monte-Silva, K., Kuo, M. F., Hessenthaler, S., Fresnoza, S., Liebetanz, D., Paulus, W., & Nitsche, M. A. (2013). Induction of late LTP-like plasticity in the human motor cortex by repeated non-invasive brain stimulation. *Brain Stimulation, 6*(3), 424–432.

Munz, M. T., Prehn-Kristensen, A., Thielking, F., Molle, M., Goder, R., & Baving, L. (2015). Slow oscillating transcranial direct current stimulation during non-rapid eye movement sleep improves behavioral inhibition in attention-deficit/hyperactivity disorder. *Frontiers in cellular neuroscience, 9*, 307:1–8.

Narayanaswamy, J. C., Shivakumar, V., Bose, A., Agarwal, S. M., Venkatasubramanian, G., & Gangadhar, B. N. (2014). Sustained improvement of negative symptoms in schizophrenia with add-on tDCS: A case report. *Clinical Schizophrenia & Related Psychoses, 8*(3), 135–136.

Olfson, M., Marcus, S. C., Zhang, H. F., & Wan, G. J. (2007). Continuity in methylphenidate treatment of adults with attention-deficit/hyperactivity disorder. *Journal of Managed Care Pharmacy, 13*(7), 570–577.

Ortman, J. M., Velkoff, V. A., & Hogan, H. (2014). *An aging nation: The older population in the United States, current population reports*. Washington, DC: U.S. Census Bureau.

Palm, U., Ayache, S. S., Padberg, F., & Lefaucheur, J. P. (2014). Non-invasive brain stimulation therapy in multiple sclerosis: A review of tDCS, rTMS and ECT results. *Brain Stimulation, 7*(6), 849–854.

Pliszka, S., & Issues AWGoQ. (2007). Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. *Journal of the American Academy of Child and Adolescent Psychiatry, 46*(7), 894–921.

Polderman, T. J., Boomsma, D. I., Bartels, M., Verhulst, F. C., & Huizink, A. C. (2010). A systematic review of prospective studies on attention problems and academic achievement. *Acta Psychiatrica Scandinavica, 122*(4), 271–284.

Prasad, V., Brogan, E., Mulvaney, C., Grainge, M., Stanton, W., & Sayal, K. (2013). How effective are drug treatments for children with ADHD at improving on-task behaviour and academic achievement in the school classroom? A systematic review and meta-analysis. *European Child & Adolescent Psychiatry, 22*(4), 203–216.

Prehn-Kristensen, A., Munz, M., Goder, R., Wilhelm, I., Korr, K., Vahl, W., … Baving, L. (2014). Transcranial oscillatory direct current stimulation during sleep improves declarative memory consolidation in children with attention-deficit/hyperactivity disorder to a level comparable to healthy controls. *Brain Stimulation, 7*(6), 793–799.

Rabipour, S., & Raz, A. (2012). Training the brain: Fact and fad in cognitive and behavioral remediation. *Brain and Cognition, 79*(2), 159–179.

Raggi, V. L., & Chronis, A. M. (2006). Interventions to address the academic impairment of children and adolescents with ADHD. *Clinical Child and Family Psychology Review, 9*(2), 85–111.

Riggs, A., Patel, V., Charvet, L., Kassachau, M., Harounian, J., & Knotkova, H. (2017a). Developing patient and caregiver instructional materials and training for at-home, remotely-supervised, transcranial direct current stimulation (tDCS) in seriously ill patients with multiple symptoms. *Brain Stimulation, 10*(4), 44.

Riggs, A., Patel, V., Harounian, J., Bikson, M., Paneri, B., et al. (2017b). A novel telehealth-neurostimulation intervention for at-home symptom management in chronically ill patients with multiple symptoms. *Neuromodulation, 20*(7), 232.

Riley, J. B., & Basilius, J. P. A. (2007). Physicians' liability for off-label prescriptions. *Hematology & Oncology News & Issues, 6*(5), 24–37.

Rosedale, M., Malaspina, D., Malamud, D., Strauss, S. M., Horne, J. D., Abouzied, S., … Knotkova, H. (2012). Developing patient-centered treatment protocols in brain stimulation: A rationale for combining quantitative and qualitative approaches in persons with HIV. *Journal of the American Psychiatric Nurses Association, 18*(3), 166–174.

Rubia, K., Alegria, A., & Brinson, H. (2014). Imaging the ADHD brain: Disorder-specificity, medication effects and clinical translation. *Expert Review of Neurotherapeutics, 14*(5), 519–538.

Rubio, B., Boes, A. D., Laganiere, S., Rotenberg, A., Jeurissen, D., & Pascual-Leone, A. (2016). Noninvasive brain stimulation in pediatric attention-deficit hyperactivity disorder (ADHD): A review. *Journal of Child Neurology, 31*(6), 784–796.

Rutledge, K. J., van den Bos, W., McClure, S. M., & Schweitzer, J. B. (2012). Training cognition in ADHD: Current findings, borrowed concepts, and future directions. *Neurotherapeutics, 9*(3), 542–558.

Sale, M. V., Mattingley, J. B., Zalesky, A., & Cocchi, L. (2015). Imaging human brain networks to improve the clinical efficacy of non-invasive brain stimulation. *Neuroscience and Biobehavioral Reviews, 57*, 187–198.

Schulz, K. F., Altman, D. G., Moher, D., & Group C. (2010). CONSORT 2010 statement: Updated guidelines for reporting parallel group randomised trials. *BMJ, 340*, c332.

Semerci, B., Taskiran, S., Tufan, E., & Sanli, I. (2016). Factors predicting treatment adherence in patients with adult attention-deficit/hyperactivity disorder: A preliminary study. *ADHD Attention Deficit and Hyperactivity Disorders, 8*(3), 139–147.

Soltaninejad, Z., Nejati, V., & Ekhtiari, H. (2015). Effect of anodal and cathodal transcranial direct current stimulation on DLPFC on modulation of inhibitory control in ADHD. *Journal of Attention Disorders*.

Sonuga-Barke, E. J. (2005). Causal models of attention-deficit/hyperactivity disorder: From common simple deficits to multiple developmental pathways. *Biological Psychiatry, 57*(11), 1231–1238.

Sonuga-Barke, E. J., Brandeis, D., Cortese, S., Daley, D., Ferrin, M., Holtmann, M., … European ADHD Guidelines Group. (2013). Nonpharmacological interventions for ADHD: Systematic review and meta-analyses of randomized controlled trials of dietary and psychological treatments. *The American Journal of Psychiatry, 170*(3), 275–289.

Swanson, J. M., Cantwell, D., Lerner, M., McBurnett, K., & Hanna, G. (1991). Effects of stimulant medication on learning in children with ADHD. *Journal of Learning Disabilities, 24*(4), 219–230.

The MTA Cooperative Group. (1999). A14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. Multimodal treatment study of children with ADHD. *Archives of General Psychiatry, 56*(12), 1073–1086.

Toplak, M. E., Connors, L., Shuster, J., Knezevic, B., & Parks, S. (2008). Review of cognitive, cognitive-behavioral, and neural-based interventions for attention-deficit/hyperactivity disorder ADHD. *Clinical Psychology Review, 28*(5), 801–823.

Weyandt, L., Swentosky, A., & Gudmundsdottir, B. G. (2013). Neuroimaging and ADHD: fMRI, PET, DTI findings, and methodological limitations. *Developmental Neuropsychology, 38*(4), 211–225.

Wilens, T. E. (2004). Attention-deficit/hyperactivity disorder and the substance use disorders: The nature of the relationship, subtypes at risk, and treatment issues. *The Psychiatric Clinics of North America, 27*(2), 283–301.

Wilkes, M., & Johns, M. (2008). Informed consent and shared decision-making: A requirement to disclose to patients off-label prescription. *PLoS Medicine, 5*(11), 1553–1556.

Willcutt, E. G., Doyle, A. E., Nigg, J. T., Faraone, S. V., & Pennington, B. F. (2005). Validity of the executive function theory of attention-deficit/hyperactivity disorder: A meta-analytic review. *Biological Psychiatry, 57*(11), 1336–1346.

Willcutt, E. G., Nigg, J. T., Pennington, B. F., Solanto, M. V., Rohde, L. A., Tannock, R., … Lahey, B. B. (2012). Validity of DSM-IV attention deficit/hyperactivity disorder symptom dimensions and subtypes. *Journal of Abnormal Psychology, 121*(4), 991–1010.

Wittich, C. M., Burkle, C. M., & Lanier, W. L. (2012). Ten common questions (and their answers) about off-label drug use. *Mayo Clinic Proceedings, 87*(10), 982–990.

Woods, A. J., Antal, A., Bikson, M., Boggio, P. S., Brunoni, A. R., Celnik, P., … Nitsche, M. A. (2016). A technical guide to tDCS, and related non-invasive brain stimulation tools. *Clinical Neurophysiology, 127*(2), 1031–1048.