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Non-invasive Brain Stimulation as a Set of Research Tools in NeuroIS: Opportunities and Methodological Considerations

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Abstract:

NeuroIS is a growing field that builds on neuroscience to improve the understanding of human interaction with information technologies and information systems. One can investigate causal relationships between brain activity patterns, cognitive processes, and behavior in a non-invasive way via using non-invasive brain stimulation (NIBS) tools, but researchers in the neuroIS community have yet to do so. We introduce NIBS, show how it can address caveats found in current research, describe the implementation of a NIBS protocol, and assess what these tools can bring to the neuroIS field.

Keywords: NeuroIS, Non-invasive Brain Stimulation, TMS, tDCS, Causality.

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1 Introduction

In the past several years, information systems (IS) researchers have conducted an increasing number of studies using neuroscience tools and theories (Quazilbash & Asif, 2017; Riedl, Davis, Banker, & Kenning, 2017; Riedl & Léger, 2015). Using eye-tracking, skin conductance, electroencephalography (EEG), functional magnetic resonance imaging (fMRI), functional near-infrared spectroscopy (fNIRS), and hormone measurement, scholars in a research field called neuroIS bridge the gap between neuroscience and IS research by investigating automatic and unconscious phenomena that one cannot easily capture with traditional research approaches (e.g., self-report measures). Most contemporary neuroIS research focuses on refining the understanding of the cognitive and affective processes that occur while a user interacts with an IT artifact. Detailed literature reviews of the field have recently been published to celebrate its 10-year anniversary (Quazilbash & Asif, 2017; Riedl et al., 2017).

As for brain imaging research, finding activity in discrete brain structures that correlates with IS constructs and that specific experimental tasks induce provides possibilities to advance our understanding of human interaction with IT. One could so by 1) drawing on cognitive neuroscience research that has highlighted the functional role of those brain areas or 2) identifying the neural correlates of IS constructs (that have not been studied previously in other fields such as cognitive neuroscience). Example studies of the first category include fMRI examinations in the context of online trust (Dimoka, 2010; Riedl, Hubert, & Kenning, 2010a; Riedl, Mohr, Kenning, Davis, & Heekeren, 2014b); these examinations extensively discuss related work published in cognitive neuroscience and neuroeconomics among papers from other fields. Thus, if scholars in other scientific fields have previously studied the neural correlates of an IS construct such as trust, IS researchers can base their hypotheses on the known relationships between a construct and brain function.

Up until now, the neuroIS field has relied on neuroscience methodologies that are primarily correlational given that they do not directly manipulate the object of study (i.e., the brain). By using correlational analysis with technologies such as fMRI, EEG, MEG, and fNIRS, one can draw only primarily associative conclusions about the relationship between IS constructs, brain regions, and brain function, and such conclusions do not provide direct evidence about whether a brain area, or its associated function, is necessary or sufficient to give rise to a given construct (Kable, 2011). Thus, to take a step towards experimental and causal relationships in neuroIS, we need to explore other neuroscience tools.

In this paper, we explore what neuromodulation methods, a set of tools used in neuroscience to directly interfere with brain function, can bring to neuroIS and methodologically discuss previous research. First, we present and discuss the most widely used neuroIS tools. Second, we present non-invasive brain stimulation (NIBS) tools and describe the key points that one needs to know about to adequately develop corresponding experimental protocols. Third, we discuss the tools' safety and ethical considerations. Finally, we explore possible contributions of NIBS to the neuroIS field.

2 Correlational Approaches

2.1 Conditions for Causality

John Stuart Mill (1843) and Karl Popper (1959) define causality as the assertion that any event can be causally explained and, as a result, that an effect can be deductively predicted. Causality has three main conditions.

First, cause must precede effect. In experimental protocols, researchers believe the variables that they manipulate to cause a phenomenon of interest. Because researchers manipulate an independent variable first, the independent variable's impact on the dependent variable has more chances of being causal. Most published neuroIS research fulfills this condition. When researchers have manipulated an experimental (most often in the version of a website or IT artifact), they have first made efforts to establish a relationship in which the experimental manipulation of a variable of interest causes changes in brain activity and other outcomes (self-reported attitudes, perceptions, etc.). Yet, these manipulations are not sufficient to infer causality between brain activity and self-reported measures.

Second, the cause has to relate to—or correlate with— the effect. A correlation describes how two variables vary with each other. Since the correlation only involves observation and the researcher does not manipulate any variable, the influence A and B have on each other has no directionality. A could cause B in the observed phenomenon, but the opposite may also hold true. When one has fulfilled both

the second and first conditions for causality, the direction of the impact is clearer and points to a causal link.

Third, no explanation should be able to explain the effect other than its presumed cause. Other variables could also influence A and B in a related or unrelated fashion and, thus, lead to a faulty impression of causality. Confounding variables, moderation, and mediation (among other factors) can cause one to mistake correlation for causation (Schlesselman, 1978).

Research based on self-reported measures has discussed the conditions under which it is reasonable to presume causality (Freedman, 2010) and has partially resolved this issue with analytical methods such as structural equation models (SEM) (Kline, 2015) or Granger causality analyses (Kostelecki, 2013). However, the neuroIS field's young age means we need to bring forward statistical and design methods that will allow researchers to achieve stronger conclusions.

Even if one fulfills all three conditions for causality, a causal relationship still may not exist. In situations where behavior follows brain activity (e.g., motor commands come from brain activity), it seems logical to infer causality. However, one needs to determine what is specific to a particular behavior and rule out unrelated activity that may occur simultaneously in the brain.

While statistical and experimental design can improve the plausibility of a causal link, NIBS-induced changes in neuronal excitability or oscillatory activity allow experimental manipulations from which one can draw stronger conclusions on the links between brain activity and interactions with information systems. This type of manipulation also strengthens the plausibility of a causal link and helps validate associations between brain and behavior.

2.2 Tools

Functional magnetic resonance imaging (fMRI) uses a metric called blood oxygen level dependent (BOLD) signal that contrasts the magnetic properties of oxygenated and deoxygenated blood circulating in the brain (Li, Guo, Nie, Li, & Liu, 2009). This metric allows one to localize brain activity that induces an increase in blood flow to a specific brain area. Analyzing the BOLD signal usually requires a contrast between conditions to determine whether a given task significantly involves a brain area given that different regions of the brain have different baseline BOLD levels (Li et al., 2009). While fMRI offers good spatial resolution, it has limited temporal resolution (a little under a second) (Uğurbil et al., 2013). Using different imaging sequences, MRI can also inform researchers about white and grey matter anatomy (Oishi, Faria, Yoshida, Chang, & Mori, 2013), connections between regions using tractography (Reveley et al., 2015) and resting state fMRI (van den Heuvel & Hulshoff Pol, 2010), and levels of various neurochemicals using spectroscopy (Al-Iedani, Lechner-Scott, Ribbons, & Ramadan, 2017).

Electroencephalography (EEG) indirectly measures changes in neuronal membrane conductivity via voltage fluctuations on the scalp (Müller-Putz, Riedl, & Wriessnegger, 2015). Electrodes capture the post-synaptic potentials of a large number of neurons in a given area. EEG offers great temporal resolution that is closely related to the frequency of acquisition of the signal (usually around 500-1000 Hz). As for its spatial resolution, EEG-based methodologies experience the inverse problem: different neural activities in the brain can generate identical surface potentials (Luck & Kappenman, 2011). Thus, EEG analysis requires a priori knowledge about sources and parameters of volume conduction to infer the involvement of a brain structure related to the studied phenomenon.

Magnetoencephalography (MEG) measures changes in magnetic fields induced by electrical activity in the brain (Darvas, Pantazis, Kucukaltun-Yildirim, & Leahy, 2004). Thus, MEG has many similarities with EEG, but it relies on magnetic properties of the brain, which has the advantage of allowing it to resolve activity in deeper brain structures (Attal & Schwartz, 2013). Still, the inverse problem associated with EEG also applies to MEG.

Near-infrared spectroscopy (NIRS) tracks the absorption level of different wavelengths of light by oxygenated and deoxygenated blood in the brain (Ferrari & Quaresima, 2012). Using this signal, one can infer neural activity given knowledge of hemodynamical changes that such activity provokes (Gefen, Ayaz, & Onaral, 2014).

2.3 Critics

In reviewing the neuroIS literature, Riedl and Léger (2015) found that all brain imaging papers published in peer-reviewed journals have used statistical analysis and methods that do not fully allow causal

inferences. Note that one can use causal statistical analysis such as Granger causality (Roebroeck, Formisano, & Goebel, 2005) with fMRI experimental designs, but none of the neuroIS studies we found used this type of analysis. Given that researchers did not use such methods, they simply measured brain activity while subjects performed a specific task (e.g., perception of or interaction with user interfaces in fMRI or EEG studies). However, correlation is necessary but not sufficient for causality. Hence, by applying correlational analysis methods, one can observe brain activity but cannot make any causal inferences of the type "activity in brain region x → construct y" (note that "→" denotes "leads to" or "results in").

For example, neuroIS research (Dimoka, Pavlou, & Davis, 2011) first investigated which brain structures are involved in each dimension of the technology acceptance model (TAM) (Davis, 1985; Venkatesh, Davis, & Wallton, 2000). One can divide TAM into two main constructs—perceived ease of use (PEOU) and perceived usefulness (PU)—which one can measure using psychometric scales adapted from Pavlou (2003). Alternative methods of measuring TAM in websites include WebQual (Loiacono, Watson, & Goodhue, 2007) in the context of electronic commerce websites. In their fMRI study, Dimoka et al. (2011) concluded that PEOU "is mapped on the DLPFC [dorsolateral prefrontal cortex], a brain area linked to cognitive effort and working memory" and that PU "is associated with brain areas associated with utility (caudate nucleus and anterior cingulate cortex) and potential for loss (insular cortex)" (p. 696). While plausible, these statements imply that observed activity in a brain region shows that an IS construct is akin to the associated cognitive function. However, this type of inference has a potential problem: researchers have attributed a wide variety of cognitive functions to each of these structures, which makes the choice of one or two comparative functions possibly arbitrary. For example, consider the insula: Kurth, Zilles, Fox, Laird, and Eickhoff (2010) conducted a meta-analysis of 1,768 functional neuroimaging experiments and concluded that it comprises four different functional regions that underlie different constructs: socio-emotional, sensori-motor, olfacto-gustatory and cognitive. As a result, one could arbitrarily associate any of the known insular functions with the IS construct of interest.

Indeed, because specific areas in the human brain are linked to cognitive functions in a "many-to-many" as opposed to a "one-to-one" fashion, inference from a brain activity pattern to a specific mental process is necessarily speculative. This kind of inference, known as "reverse inference" (Hutzler, 2014; Poldrack, 2006), is inherent to the design of many fMRI studies regardless of the field. Yet, it offers significant potential for theorizing on the nature of a construct largely because it allows one to develop insights into the dimensions of a construct. Once one has made this speculation on underlying functions, one should seek confirmation of this link in one of two ways.

First, one can specifically measure the indicators of the cognitive function that the reverse inference implies (Hutzler, 2014). Take for example the long-standing claim that meditation requires attention since it involves similar brain structures and processes (Cahn & Polich, 2006). If one does not directly measure both attentional capacities and meditative states and link them to brain activity, this claim remains speculative at best. Second, one can seek out confirmation and validation using the experimental manipulation of other variables in the causal chain; namely, the brain itself. If one can directly influence brain activity instead of manipulating a stimulus to influence brain activity and behavior, one has a stronger probability of correctly inferring a causal link. Seeking confirming evidence in either of these ways could increase the possibility of correctly inferring a causal relationship between an IS construct, a brain structure, and a specific cognitive function.

Building on Dimoka et al.'s (2011) study, one could investigate many of the reported associations between brain activity and behavior in a causal way. If we take perceived usefulness (PU), which Dimoka et al. state to be linked to the insula, caudate nucleus, and anterior cingulate cortex, one could conduct a similar experiment with patients presenting lesions in one of these areas and determine experimentally the extent to which the lesions affect PU. If PU is indeed linked to one of these structures, one should see changes in PU or in different dimensions of PU depending on brain damage extent and localization. A much simpler way to investigate the reported associations, however, is to non-invasively modulate activity in the brain structures identified with fMRI, such as DLPFC (which Dimoka et al. (2011) linked to PEoU).

3 Neuromodulation

As we discuss in Section 2.3, when using an experimental manipulation that has a direct impact on brain activity, one can better establish causal relationships between brain activity and behavior (Bestmann et al., 2008). In essence, NIBS rests on the following logic: 1) that one experimentally manipulates brain

activity (independent variable) and 2) that one determines whether this manipulation leads to changes in behavior (dependent variable). Thus, in contrast to traditional neuroIS fMRI and EEG studies in which researchers manipulate some aspect of the IT artifact to observe subsequent brain activity along with changes in perception (self-reports) or behavior (observation), NIBS introduces complementary information regarding directionality. While the traditional approach is correlational in nature, and, hence, one infers the causal nature of the link between brain activity due to a time difference between the stimulus and subsequent reactions (t1: stimulus, t2: brain activity, t3: perception or behavior), neuromodulation directly manipulates brain activity during an interaction with a stimulus and creates possible changes in perception or behavior. Methodologically, the neuromodulation approach better suits establishing direct causality between neuronal activity and behavior compared to traditional correlational approaches. In that sense, NIBS can provide complementary and compelling evidence for an association between brain activity, cognitive processes, and behavior.

3.1 History

Neuromodulation dates back to Ancient Egypt, where medical practitioners used electric fish living in the Nile to generate electricity on a patient's scalp to reduce pain (Knotkova & Rasche, 2015). During the 18th century, when society developed batteries and machines that could generate electrostatic charges, electrotherapy emerged for psychiatric disorders and other medical conditions such as paralysis and pain. Guillaume Duchesne (1806-1875), a French neurologist known as the father of electrotherapy, popularized using interrupted and alternating currents to treat psychiatric disorders (Parent, 2004). In the 19th century, major discoveries in neurophysiology coincided with advances in physics, mainly in the use of electricity for medical applications. The merging of these fields would eventually lead to contemporary neuromodulation (Keller & Krames, 2009). The 18th century also marked the advent of transcranial electrical stimulation (TES)—stimulation that used high current intensities—to treat major psychiatric illnesses. Doctors still use TES to treat chronic major depression and epilepsy (Berényi, Belluscio, Mao, & Buzsáki, 2012; Guleyupoglu, Schestatsky, Edwards, Fregni, & Bikson, 2013).

Penfield and Jasper (1954) developed another seminal approach: directly stimulating the brain of epileptic patients with electricity to determine which behavior or subjective state is associated with specific brain regions. One can implant modern versions of these electrodes in deep brain structures with a technique called deep brain stimulation (DBS) to treat neurological diseases such as Parkinson's disease (Bronstein, Tagliati, & Alterman, 2011), obsessive compulsive disorder (De Koning, Figee, Van Den Munckhof, Schuurman, & Denys, 2011), and depression (Morishita, Fayad, Higuchi, Nestor, & Foote, 2014).

Less-invasive techniques have also emerged, including transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS). Barker, Jalinous, and Freeston (1985) developed the modern transcranial magnetic stimulation device to painlessly stimulate the cortex and peripheral nerves via electromagnetic induction to induce electric currents in the brain from the magnetic field emitted by an insulated coil of wire. Researchers first tested tDCS, as it is known today, in humans by observing changes in excitability of the motor cortex after applying a weak electric current (0.5 mA) on the scalp (Priori, Berardelli, Rona, Accornero, & Manfredi, 1998b).

Researchers have also conducted numerous animal studies (Creutzfeldt, Fromm, & Kapp, 1962; Jackson et al., 2017; Rosen & Stamm, 1972) involving cats, rats, and monkeys to explore neurostimulation effects and determine safety levels and harm thresholds. More recently, researchers have conducted modelization studies (Wagner et al., 2007, 2014) to determine the spatial distribution of current density in the brain during neurostimulation to better understand the underlying neurophysiological phenomena occurring during neuromodulation.

3.2 Description of NIBS Tools

Many tools that we describe in Section 3.1, such as DBS and ECT, are invasive, and, as such, one should not use them, although some remain in use marginally in the neuroIS community. However, a wide variety of non-invasive brain stimulation tools that one can use in neuroIS exist. These tools are safe when compliant with current safety guidelines (Bikson et al., 2016; Woods et al., 2016) and relatively easy to use. Riedl, Randolph, von Brocke, Léger, and Dimoka (2010b) have already suggested potential uses for these techniques in neuroIS, but we focus on guiding researchers interested in implementing projects in the field. While no IS research has used NIBS yet, the reader might find interesting examples of applied NIBS research in the gaming domain (Jeong, Oh, Choi, Song, & Chung, 2017; Looi et al., 2016).

3.2.1 TMS

Transcranial magnetic stimulation (TMS) is a technique that uses strong electromagnets made of insulated coils that generate magnetic fields around them of up to several teslas for short periods of time (< 1ms). These magnetic fields are transduced to electrical current once they reach biological tissue, which can provoke the depolarization of neurons near the point of focus of the magnet (Hallett, 2007; Iorio & Rossini, 2017; Rossi et al., 2009; Sparing & Mottaghy, 2008).

The spatial properties of magnetic fields, where strength decreases with the square root of the distance, limits areas of stimulation to surface cortical areas, but stimulation can still affect deeper structures due to propagating neuronal discharges (Chouinard, van der Werf, & Leonard, 2005) and specific coil configurations (Zangen, Roth, Voller, & Hallett, 2005). Researchers believe specific TMS waveforms or pulse combinations to affect different populations of neurons mainly through facilitatory networks in excitatory effects and through neuronal refractory periods and GABAa (gamma-aminobutyric acid is a neurotransmitter that has type-a and type-b receptors) networks in inhibitory effects (see Rossini et al., 2015, for a detailed description of these effects).

3.2.2 tDCS

The most easily available tool of the NIBS family is transcranial direct current stimulation (tDCS), which works on the premise that a weak constant current can modulate the potential of the neuronal membrane, the distribution of positive and negative ions, on which one applies it (Kuo, Polanía, & Nitsche, 2016). One applies a low amperage, usually below 2 milliamps (mA), on the skin, and the tDCS device continuously monitors it to insure constant and safe stimulation (Woods et al., 2016).

Contrary to TMS, tDCS cannot provoke neuronal discharges. Rather, the current finds the most efficient route from the positive electrode, the anode, to the negative electrode, the cathode, and affects the polarity of the neurons that are in the flow of current (Kuo et al., 2016). The tool mainly achieves this process via a certain type of neurons called cortical pyramidal neurons. When these neurons are perpendicular to the surface of the skull and/or are aligned with the flow of the current between the two electrodes (Kuo et al., 2016), it allows a clear effect. Neurons that are well aligned with the current under the anode show a pattern of hyperpolarization and depolarization, which results in increased excitability of the stimulated neurons. One can observe the opposite polarity shift for cells aligned the other way around, under and perpendicular to the cathode.

However, neurons subjected to a tangential electrical field or that are not well aligned with the current flow show a pattern of changed polarity that does not have any clear effect on neuronal excitability (Rahman et al., 2013). Researchers have also proposed an alternative mechanism of action involving glial cells instead of neurons but continue to investigate it (Gellner, Reis, & Fritsch, 2016; Ruohonen & Karhu, 2012).

3.2.3 tACS and tRNS

Instead of using a direct current source, one can apply a sinusoidal alternating current source to the brain. Depending on the frequency of this current, one can call it either transcranial alternating current stimulation (tACS) when the current waveform comprises one or a few specific frequencies or transcranial random noise stimulation (tRNS) when the current alternates randomly between a normal distribution of frequencies from 0 to 640 Hz (or half the sampling rate of the stimulation device) (Kuo et al., 2016).

Either form of stimulation affects the brain and cellular mechanisms in a completely different way than tDCS. tACS increases the probability of triggering the type of brainwave that it stimulates through either entrainment of neuronal firing (Helfrich et al., 2014b) or neuronal resonance (Ali, Sellers, & Frohlich, 2013). On the other hand, tRNS seems to have a general excitatory effect mostly through higher stimulation frequencies (over 100Hz) that would affect the opening of the sodium channels of neurons and activation of glutamatergic synapses (Terney, Chaieb, Moliadze, Antal, & Paulus, 2008).

4 NIBS Protocol Development

In this section, we focus on how one can develop and implement an experimental protocol using NIBS techniques (tDCS, tACS, tRNS and TMS). One needs to keep many factors in mind when designing a NIBS experimental protocol, all of which have a complex relationship with each other.

First, we note that, contrary to TMS, no “gold standard” protocol exists in electrical stimulation paradigms (Parkin, Ekhtiari, & Walsh, 2015). As a result, the published literature contains important variations in stimulation parameters to the extent that meta-analyses that investigate the behavioral and neurophysiological effects of tDCS must pool different stimulation protocols and often rely on arbitrary parameter determination (Nitsche, Bikson, & Bestmann, 2015). Because an insufficient number of past studies have systematically evaluated the effects of protocol variations, researchers do not have strong evidence to guide the parameters they choose except in replication studies. Thus, they usually select parameters based on arbitrary choices made in previous studies instead of robustly determining the optimal parameters for a specific application. In this section, we review the known effects of parameter variation in the neuroscience literature. Since the effects of stimulation protocols on primary motor cortex (M1) excitability are easy to probe using single-pulse TMS, which provides a quantifiable measure of excitability known as the motor evoked potential (MEP), most studies rely on data obtained following stimulation of this one area. Researchers have yet to conduct similar studies for cognitive stimulation protocols where the aftereffects are harder to measure objectively. We need more research that assesses parameter space in NIBS before drawing parallels between what researchers have found in M1 and potential effects in other structures.

We first describe the material and present how one should select it in an experiment. Then, we review the variables that impact stimulation effects to guide protocol development. Finally, we explore sham stimulation and control conditions along with considerations about variability of response to stimulation protocols. Readers should note that many technical papers (Bikson et al., 2016; Rossi et al., 2009; Woods et al., 2016) provide clear technical guides and lists of best practices to use in laboratories using TMS and electrical NIBS. While the technical manipulations required for a NIBS protocol do not require certification, researchers should strive to achieve high replicability standards by abiding to best practices.

4.1 Material

4.1.1 TMS Coil and Stimulator

From thoroughly reviewing the stimulation depth and focality of 50 different coil designs, Deng, Lisanby, and Peterchev (2013) provide valuable information for selecting the adequate instrument for one’s intended use. The most popular TMS coil, the figure of eight, which researchers first tested in 1990 (Maccabee, Eberle, Amassian, Cracco, & Rudell, 1990), provides a focal stimulation at the intersection of the magnetic field that both circles of the coil generate. Recent developments in coil design have led to the H-coil, which Zangen et al. (2005) first used to target deeper structures of the brain. To deliver stimulation, one places the coil on the scalp over the targeted cortical area in a position coherent with the neuronal architecture of the targeted neural circuit (Sparing & Mottaghy, 2008). Figure 1 presents an example of a TMS device.

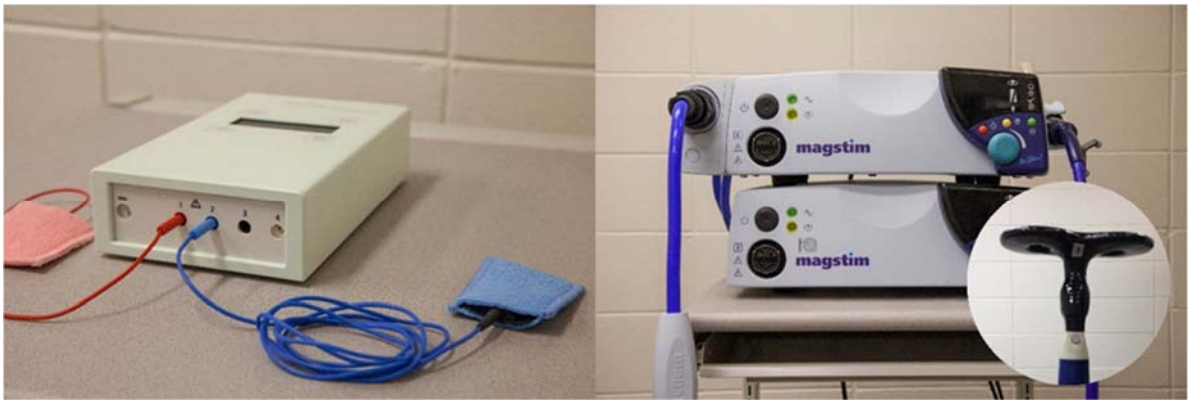

Figure 1. tDCS and TMS Devices

4.1.2 Electrical Stimulation Apparatus

To perform tDCS, tACS, or tRNS experiments with a human participant, one equips a secure and controlled eight-volt current source with two wires and electrodes (see Figure 1). One fits the electrodes on the scalp to minimize resistance (with conductive gel, paste, or saline water). Research-grade tools

usually cost around US$10,000 and respect state-of-the-art standards. More and more stimulation devices, which do not necessarily require the Food and Drug Administration's (FDA) approval, have recently appeared on the market as consumer-grade products. Also, one can easily access the parts and skills necessary to build a tDCS device. As a result, one can easily build a functioning device with minimum knowledge. Thus, a large do-it-yourself (DIY) tDCS community that often lacks the necessary scientific and clinical knowledge needed to perform brain stimulation has emerged (Jwa, 2015). Currently, no body regulates the commercial use of NIBS devices or subjects them to clinical trials before sale to the public. As a result, many in the NIBS community have requested a better legal framework (Bikson, Bestmann, & Edwards, 2013; Carter & Forte, 2016). One should consider the variables that Table 1 shows when choosing a NIBS device for research and clinical use.

Table 1. Different Features to Consider in the Choice of a NIBS Device

Features of the device
Adequate trials and certification of the device
Previous use in literature
Safety features
Compatibility with different software
Quality and durability of the material
Cost and supply of consumables (electrodes, conductive medium, etc.)
Possibility to conduct double blind studies
Transparency of the impedance check
Control over protocol parameters: • Ramp-up and ramp-down of current • Stimulation duration • Quantity of current delivered • Current waveform

4.2 Stimulation Parameters

4.2.1 Stimulation Site

One can determine the stimulation site in at least three different ways. First, one can place the stimulation device following the 10-20 EEG electrode system, which ensures replicability and standardization across laboratories. Second, when anatomical or functional scans are available for every participant, one can use frameless stereotaxy, which allows precise and constant 3D positioning of the stimulation apparatus relative to the participant's skull, to guide the electrode placement (Paus, 1998). Third, in areas where TMS can elicit an overt response, such as visual and motor areas, one can determine stimulation location functionally with single-pulse TMS, which induces phosphenes (Antal, Kincses, Nitsche, & Paulus, 2003) and muscle twitches (Wassermann, 2002), respectively.

4.2.2 TMS Stimulation Parameters

TMS stimulation protocols have several features such as intensity, pulse organization (or inter stimuli interval), train duration, and inter-train intervals.

Stimulation intensity: researchers usually calculate stimulation intensities as percentages of two different thresholds or standard response rates, which they assess separately for every individual. The resting motor threshold (RMT) refers to the intensity at which one has to deliver a single TMS pulse to induce a 50μV electromyographic response five times out of 10 consecutive trials, whereas one calculates the active motor threshold (AMT) in a similar way but with the target muscle contracted (see Section 6.1 in Rossi et al., 2009). One can also stimulate the cortical structure at the intensity that will reliably induce a MEP of a pre-determined amplitude (usually 1 mV peak-to-peak on electromyography) in a target muscle. One can also assess the threshold in the visual cortex, where stimulation to the back of the head can induce the perception of light (phosphenes) in stimulated participants. Similar to the motor threshold, the phosphene threshold refers to the minimum intensity required to induced phosphenes (Marg & Rudiak, 1994).

Pulse organization: **i**n single-pulse TMS, one applies a TMS pulse to generate neuronal discharges. Researchers often use single-pulse TMS to perform cortical mapping, to assess conduction time in the central nervous system, or to interfere with time-dependent activity in a given cognitive process. One applies paired-pulse TMS using two pulses with different inter-pulse intervals delivered with one coil at a given location or two coils at different locations. Researchers mostly use it to assess inhibitory and facilitatory networks or interactions between two targeted locations. One cannot characterize these two types of pulse organizations in terms of train duration or inter-train interval (see Section 2.1 in Rossi et al., 2009).

Pulses can also be arranged in sequences with stimulation frequencies that can be slow (≤ 1 Hz; usually inhibitory) or fast (> 1 Hz; usually excitatory), which is called repeated TMS (rTMS) (Fitzgerald, Fountain, & Daskalakis, 2006). Patterned rTMS comprises short trains of high frequency bursts followed by pauses, the most popular being 50 Hz theta burst stimulation (TBS). Continuous TBS usually produces inhibitory effects, whereas intermittent TBS is usually associated with excitatory effects (Huang, Edwards, Rounis, Bhatia, & Rothwell, 2005).

4.2.3 Electrical Stimulation Parameters

Electrode size: standard-sized saline-soaked sponges range between 3.5 and 100 cm^2. One can also use smaller gel-based electrodes of approximately 1 cm^2 (Villamar et al., 2013). Researchers also believe electrode size to underlie sensations induced by electrical stimulation (Fertonani, Ferrari, & Miniussi, 2015; Turi et al., 2014). Bastani and Jaberzadeh (2013) compared the magnitude of cortical excitability changes in M1 following stimulation using three electrode sizes at a constant current density (current amplitude divided by electrode size). Data showed that smaller electrodes (12 cm^2) yielded the largest increase in corticospinal excitability despite the fact that current density diminishes more rapidly as it penetrates the brain with small electrodes (Faria, Hallett, & Miranda, 2012), which suggests non-linear relationships between electrode size and stimulation efficacy. To this effect, Ho et al. (2016) found that larger electrodes (35 cm^2) were associated with greater cortical excitability changes compared to smaller electrodes (16 cm^2) without regard to current intensity.

In the cognitive domain, researchers have yet to conduct similar studies that have directly compared the efficacy of different electrode size. We would need such studies to make similar claims about the superiority of specific electrode sizes in inducing behavioral changes.

Electrode montage: when one uses two stimulation electrodes in tDCS, one can position them over the same structure of the left and right hemisphere, which is called bilateral stimulation. In certain cases, bilateral stimulation takes advantage of interhemispheric inhibition to enhance stimulation effects (Vines, Nair, & Schlaug, 2006). One can also position electrodes in different locations, which is called unilateral stimulation. One places the first electrode over the area of interest and the second over an unrelated area, usually the supraorbital area of the forehead or an extracephalic site such as the shoulder (Bikson et al., 2016). Note that, in this so-called “unilateral” stimulation, both electrodes are still active and stimulation occurs beneath and between both electrodes. Finally, new stimulation protocols such as high-definition tDCS (HD-tDCS) use an electrode of a given polarity circled by a number of “return” electrodes of the opposite polarity, which provides a more focused area of stimulation (Helfrich et al., 2014a; Villamar et al., 2013).

Current intensity and current density: most research-grade electrical stimulation systems allow a current intensity range of 0 to 2mA. Current densities (calculated by dividing the current intensity by the surface of the electrode) used in most tDCS studies do not to induce tissue damage in animal models when below 142.9 A/m^2 (Liebetanz et al., 2009), which is well above what a 1 cm^2 electrode delivers at 2 mA (20 A/m^2). Importantly, more current does not necessarily mean more effect. While initial studies in M1 excitability suggested larger effects with increased current density (Nitsche & Paulus, 2000), newer studies show a non-linear dose-effect relationship in tDCS (Antal et al., 2008; Carvalho et al., 2015).

Frequency and phase: two main ways to select stimulation frequency in tACS protocols exist. One can used a fixed frequency for all participants—usually based on previous literature or on the standard frequencies of interest (Antal & Paulus, 2013). Or one can also use a personalized frequency for each participant by recording EEG data and determining the peak frequency in each band. Given the crucial role of phase synchronization on performance, which recent developments in phase amplitude coupling (PAC) highlight (Tort, Komorowski, Eichenbaum, & Kopell, 2010), the timing between stimulation phase and stimulus presentation is crucial. Data suggest that stimulation protocols that increase PAC lead to

performance improvement while the opposite effect is seen with protocols that decrease PAC (Helfrich et al., 2014a; Polanía, Nitsche, Korman, Batsikadze, & Paulus, 2012).

Duration of stimulation: one can induce tDCS effects following very short stimulation protocols (Nitsche & Paulus, 2000). However, researchers have suggested that sensory stimulation rather than delivery of current to the brain may explain these effects (Furubayashi et al., 2008). Studies have reported after-effects with stimulation durations above three minutes (Nitsche & Paulus, 2000) and up to 40 minutes or more (Bikson et al., 2016). Similarly to stimulation intensity, stimulation duration effects do not appear to be linear: one can reverse the direction of neurophysiological effects by increasing stimulation duration (Monte-Silva, Kuo, Liebetanz, Paulus, & Nitsche, 2010).

4.3 Moment of Effect Evaluation

One can either apply NIBS protocols during (online stimulation) or before (offline stimulation) a task of interest. In the case of TMS, one can use online stimulation to disrupt cognitive processes that occur at specific moments in time, which can provide chronometric information where, in addition to probing the causal relationship between brain structure and behavior, stimulation provides data on when task-dependent activity occurs. Researchers generally use offline TMS, on the other hand, to create "virtual lesions"—transient dysfunctions of a targeted structure induced by trains of TMS pulses that outlast the stimulation period (Pascual-Leone, Walsh, & Rothwell, 2000; Ziemann, 2010). Researchers that have studied rTMS effects of EEG signal have provided important data relating to the duration of rTMS aftereffects. In reviewing 11 studies, Rossi et al. (2009) reported aftereffects that lasted between 20 and 70 minutes using various protocols. Yet, they could not consistently determine which protocol yielded longer-lasting effects given variability and confounding variables. Treatment protocols where repeated sessions of rTMS can reduce depression (Berlim, van den Eynde, Tovar-Perdomo, & Daskalakis, 2013; Chau, Fogelman, Nordanskog, Drevets, & Hamilton, 2017) and stroke (Simonetta-Moreau, 2014) symptoms for months perhaps best exemplify the lasting effects of rTMS. Researchers that have systematically reviewed the duration of rTMS's cognitive effects (Guse, Falkai, & Wobrock, 2010; Thut & Pascual-Leone, 2010) have found similar durations (generally 70 minutes or less) of the effect of a single stimulation session (depending on stimulation duration), but protocols that include more than one stimulation session can yield longer-lasting effects as therapeutic protocols show.

The duration of electrical stimulation effects varies as a function of stimulation technique and parameter selection, and research has not clearly established these relationships. Initial studies that evaluated the lasting effects of nine to 13 minutes of 1 mA tDCS targeting M1 could have lasting effects for around one hour on cortical excitability (Nitsche et al., 2005), but some resaerchers have reported even longer-lasting effects—up to 24 hours after a series of two nine-minute 1 mA stimulation sessions separated by periods of up to 30 minutes (Monte-Silva et al., 2013, 2010). tRNS effect seems to be present between five and 60 minutes after stimulation (Terney et al., 2008). As for tACS, the duration and importance of changes lasting after the stimulation seem less robust and varies between stimulation frequencies (Antal & Paulus, 2013). For tDCS, lasting offline effects seem to have different mechanisms of action than online effects, where long-term effects would be due to modulation of plasticity mechanisms rather than hyper- or de-polarization of the membrane (Kronberg, Bridi, Abel, Bikson, & Parra, 2017; Ridding & Ziemann, 2010). Once again, we still do not know how one should translate these parameters to structures other than M1, which would benefit from further investigation.

4.4 Control Conditions

In NIBS, control conditions focus on controlling for sensory and placebo effects. TMS can induce sensory discomfort induced by direct muscle and nerve stimulation and produces large clicking noises, whereas electrical stimulation is associated with tingling under the electrodes. As such, one needs to rule out the possibility that stimulation-induced sensations or discomfort underlie parts of the expected physiological or behavioral effects. A proper control site condition will target a brain area that does not contribute to the behavior of interest but produces similar sensory effects. Alternatively, a control task condition will evaluate participant performance using a task that does not depend on the stimulated structure (sensory effects being identical to the task of interest). Control conditions can also inform on the specifity of stimulation by ensuring that the observed effects are specific to both the task and the stimulated area. Researchers have recently suggested that one should perform proper control stimulation not only in "random" areas not involved in the task of interest but also in an area that belongs to the wider network

that underlies a behavior. In doing so, one can test for the specificity of the targeted structure rather than the whole network (Parkin et al., 2015).

Placebo effects refer to individuals' self-generated effects on their behavior and attitude that occur when perceiving the effect brain stimulation will have on them. Sham stimulation, which mimics the sensory effects of stimulation and induces participant expectations, can partly control for placebo effects. One can assess the success of blinding procedures simply by asking participants to guess the experimental condition they underwent, and one should do so for any NIBS experiment. Fertonani et al. (2015) present a detailed and validated questionnaire to assess sensory aftereffects and the success of blinding procedures.

4.4.1 Sham Stimulation

Various manufacturers have produced sham TMS coils—"fake" TMS coils used exclusively for placebo conditions. They usually comprise a regular coil equipped with a magnetic shield that mimics the sound of the active device without stimulating the cortex, and one can pair them with surface electrodes to stimulate the skin, which replicates the sensory effects of stimulation. If one does not have access to sham coils, one can tilt the active coil 45 to 90 degrees from its optimal position to direct the electromagnetic field away from the scalp such that only one or two wings of the coil touch the scalp (when using a figure of eight coil). Studies have shown that coil tilting can reduce currents that reach the brain by up to 73 percent (Lisanby, Gutman, Luber, Schroeder, & Sackeim, 2001). Few studies have systematically assessed the efficacy of TMS blinding procedures in healthy individuals (Jelić, Stevanović, Milanović, Ljubisavljević, & Filipović, 2013), but recent reviews of clinical studies suggest that patients usually cannot distinguish between active and sham TMS (Berlim et al., 2013; Broadbent et al., 2011). However, given that less than 15 percent of sham-controlled TMS studies report the efficacy of the blinding procedure, these reviews might overevaluate the effectiveness of the blinding procedure (Duecker & Sack, 2015).

Specific sensory effects of electrical NIBS techniques include a weak tickling and itching sensation on the scalp that individuals might also feel as a burning sensation (Fertonani et al., 2015). This sensation usually lasts for less than a minute at the start of the stimulation. tACS can also induce retinal or cortical phosphenes at certain stimulation locations and intensities. At frequencies between 8 and 20 Hz and over 1 mA, phosphenes can significantly impede a participant's visual abilities (Schutter & Hortensius, 2010).

Researchers usually achieve sham stimulation by ramping up the current to its "active" value for the first 15 or 30 seconds of stimulation and then ramping it down immediately to zero or turning off the device altogether after the ramp-up. Researchers use this method because the tingling sensation associated with stimulation usually disappears after the first few seconds of active stimulation. Researchers believe this method to not have any lasting effect on brain function. While initial assessments of this blinding procedure indicated that participants felt no difference in sensation compared to active stimulation (Gandiga, Hummel, & Cohen, 2006), Kessler, Turkeltaub, Benson, and Hamilton (2012) reported significantly more sensory effects in active conditions. Further, when Russo, Wallace, Fitzgerald, and Cooper (2013) asked participants directly to guess the stimulation condition after the experiment, participants could not do so despite reporting more sensory aftereffects. However, O'Connell et al. (2012) found that participants could in fact distinguish conditions, which suggests that sensations at 2 mA may be more easily distinguishable than those at lower intensities. Horvath (2015) discusses this controversy in detail and argues that blinding on the side of the experimenter lacks adequate support and that researchers have yet to demonstrate proper participant blinding.

4.4.2 Blinding Procedure Efficacy

The efficacy of the blinding procedure varies according to the stimulation protocol given that the sensory effects differ to begin with. Terney et al. (2008) found that it took three times the amount of current in tRNS for half of their participants to detect physiological sensations related to the stimulation compared to tDCS when they set this threshold to 400 mA, which suggests that the blinding procedure is easier to detect in tDCS than tRNS. As for tACS, intensities as low as 250 mA induce retinal phosphenes (depolarization of the retina provoking flashes of light), which makes it easier for participants to detect active stimulation. Also, sham tDCS may be easily detectable in stimulation protocols with an intensity of 2 mA given longer-lasting cutaneous sensations (Kessler et al., 2012; O'Connell et al., 2012).

4.5 Variability in Response

One of the most important issues that the NIBS field faces concerns high inter-subject variability in the response to stimulation protocols. As we mention above, initial studies in tDCS (Nitsche & Paulus, 2000; Priori et al., 1998) suggested strict polarity effects: anodal stimulation increased corticospinal excitability and cathodal stimulation decreased it. However, recent studies have shown that the so-called "polarity effect" and the effect of tDCS as a whole on corticospinal excitability is not as robust as previously thought (Horvath, Forte, & Carter, 2015). For example, Fricke et al. (2011) report that two different groups that underwent an identical tDCS stimulation protocol showed an 84 percent difference in the magnitude of stimulation-induced changes in corticospinal excitability. Inter- and intra-individual variation in the response to tDCS is sufficiently important (Li, Uehara, & Hanakawa, 2015; López-Alonso, Cheeran, Río-Rodríguez, & Fernández-Del-Olmo, 2014; López-Alonso, Fernández-del-Olmo, Costantini, Gonzalez-Henriquez, & Cheeran, 2015; Wiethoff, Hamada, & Rothwell, 2014) that recent efforts have tried to identify what characteristics can predict response to tDCS. Ridding and Ziemann (2010) propose a list of possible individual variables that impact the effect of NIBS (in order of significance): gender, aerobic exercise, time of day, age, attention synaptic history, pharmacology, and genetics.

This issue exists not only in tDCS because recent studies have also shown important inter-subject variability in rTMS. They have found that between 50 and 73 percent of participants may not respond in the expected manner (Hamada, Murase, Hasan, Balaratnam, & Rothwell, 2013; Hinder et al., 2014; López-Alonso et al., 2014).

5 Methodological Considerations

Riedl, Davis, and Hevner (2014a) suggest six methodological considerations that researchers need to address when making the transition between theory and method. We present and discuss these concerns in the context of NIBS.

5.1 Reliability

Recent neuromodulation studies have raised many questions regarding reliability. Horvath et al. (2015) conducted a systematic review to evaluate the reliability of tDCS in various methodological frameworks. They did not find support for a reliable neurophysiological effect in the prefrontal cortex but did find some support for such an effect in the motor cortex. We can partially explain these results based on the fact that different studies use different stimulation parameters and in different ways, which limits comparison. Standardized protocols and replication studies are needed to determine the level of variability associated with parameter variations. Also, as we mention above, the NIBS field suffers from considerable inter-group, inter-subject, and intra-subject variability, which further limits reliability studies. Researchers should estimate and report the proportion of responding participants, as Simeoni et al. (2016) show, when adequate baseline measures exist for a behavior of interest.

5.2 Validity

Since tDCS modulates excitability through an electric current that courses through brain tissue, one needs detailed knowledge of the path that the current takes through the cortex to draw accurate conclusions that consider stimulation, anatomy, and behavioral effects. Many studies have examined such pathways through modeling techniques (Edwards et al., 2013; Wagner et al., 2014). One determines current magnitude and direction through calculations that consider electrode position. Both electrode montage and cranial anatomy can modulate the quantity of current delivered to the brain and its targeting accuracy and, thus, generate inter-subject variability and impact tDCS validity. Researchers can modelize current distributions using simple online software and should always report the exact position of the electrodes.

5.3 Sensitivity

As we discuss above, many studies have investigated the extent to which and how precisely tDCS current intensity can modulate activity in a specific brain area. Initial research in the field first expected a linear relationship between induced current density and effect: the stronger the current, the stronger the facilitation or inhibition. Yet, studies on the prefrontal and motor cortex have shown that this relationship is non-linear, which one should consider when developing protocols. Hence, one should not assume that longer durations or stronger currents necessarily provide larger effects.

5.4 Diagnosticity

When using tDCS to experimentally demonstrate that a specific brain area is responsible for a given cognitive function, one cannot assume that the administrated current flow passes only through the targeted area. Traditional tDCS montages use large electrodes that lead to widespread current distribution that generates diffuse modulation (Datta et al., 2009). In response to this lack of accuracy, researchers have suggested HD-tDCS (Villamar et al., 2013). This type of montage uses small electrodes placed in a concentric pattern to pinpoint specific areas. Modeling studies have shown that currents usually stay in the vicinity of the outer ring of electrodes, and, depending on the polarity of the center electrode, the current can either flow towards the center or towards its edges (Edwards et al., 2013). Therefore, whether one uses HD-tDCS or a classical two-electrode montage, modulation of brain activity under only one electrode cannot explain observed effects. As such, one cannot characterize a stimulation protocol as solely *anodal* or *cathodal*.

5.5 Objectivity

Since neurostimulation can generate a placebo effect (Horvath, 2015), one needs to integrate a sham and/or control stimulation session in any protocol. Doing so allows one to make intra-individual comparisons and can help one determine whether an observed effect was due to NIBS or to a placebo effect. A double-blind protocol in which the test administrator is blind to the stimulation parameters (which includes the sham and/or control condition as we explain in Section 4.4) should help prevent administrator bias.

5.6 Intrusiveness

The level of intrusiveness indicates how much a measurement instrument interferes with an ongoing task and, thereby, how much it distorts the observed effect (Riedl et al., 2014a). To assess how ecologically an individual can perform an IT task while using a neuroscience tool, one has to consider three dimensions: its degree of movement freedom, degree of natural position, and degree of invasiveness (Riedl et al., 2014a). During a NIBS session, one should limit participants from moving to prevent coil or electrode displacement and wire disconnection. Given the sensitivity of TMS coil placement, participants should remain as still as possible during stimulation. With electrical stimulation methods, one typically asks participants to move as little as possible, but they do not necessarily need to stay still. Also, researchers typically comfortably seat subjects who undergo NIBS, which allows the subjects to conduct a multitude of tasks and tests in a natural or close to natural position. Finally, the technique has a higher invasiveness than EEG or fMRI but does not physically penetrate the skin and does not leave any visible mark once the stimulation protocol is over other than transient skin irritation in a minority of cases.

6 Safety Considerations

Researchers need to address ethical issues in NIBS given the perception of the general public towards neuromodulation (Bikson et al., 2013) and reported health hazards (Brunoni et al., 2011). Researchers have to make sure that the ethics board that evaluates the project has the required expertise because most business schools do not.

Contraindications to NIBS exist, which one should consider without exception. TMS, in exceptional circumstances, can induce vaso-vagal or syncopal responses at normal settings (Hadar, Makris, & Yarrow, 2012). For this reason, one should exclude any individual that has a history of fainting or that is not in optimal shape (tiredness or hunger) at the moment of the experimentation from NIBS protocols (Bikson et al., 2016). Further, researchers who conduct neurostimulation studies of normal cognitive processes should not include participants who have a history of drug abuse, who currently take neuroactive medication, or who have any other neurological diagnostic. Rossi, Hallett, Rossini, and Pascual-Leone (2011) have developed a complete questionnaire to screen participants prior a neurostimulation that researchers should use in their NIBS studies.

Despite safety procedures, cases have occurred in which rTMS and single-pulse TMS have triggered epileptic seizures (see Section 4.3 of Rossi et al., 2009, for a systematic review of the cases and risk assessment of each type of protocol). These seizures have occurred in participants who took small doses of psychoactive medication or presented with a hereditary predisposition to epileptic disorders (Tharayil, Gangadhar, Thirthalli, & Anand, 2005). Researchers have also reported seizures in otherwise healthy

participants (Hadar et al., 2012; Kratz et al., 2011). TMS and rTMS are never totally free of risk. However, cases of seizures are extremely rare and have been mostly associated with pre-existing conditions or the use of medication. As for electrical stimulation, Brunoni et al. (2011) systematically reviewed reported adverse effects and identified mostly mild symptoms such as itching and tingling. Researchers should thoroughly document any adverse effect or dropout from a study due to intolerability of the stimulation, report it to the ethics committee, and share it with the scientific community when possible.

7 Fulfilling Opportunities for IS Research with Neuromodulation

Dimoka et al. (2011) have proposed "a set of seven opportunities that IS researchers can use to inform IS phenomena" (p. 687). In this section, we explore how NIBS could contribute to some of these research opportunities.

NeuroIS focuses on finding neural correlates of IS constructs (i.e., to localize brain structures that are associated with IS constructs). That process enriches theoretical views based on what we know about the brain. NIBS allows one to investigate the role of a specific brain area—mostly at the level of lower order and localized cognitive or affective functions. NIBS gives complementary evidence to help move the neuroIS literature from studying the neural correlates of IS constructs to the neural causes of IS constructs.

NIBS can also go one step further by helping to determine how different constructs interact with each other. Different aspects of an IT task may involve overlapping brain structures. If we take, for example, the fact that PEOU is linked to the DLPFC, it is unlikely that no other neuroIS study will find this structure to be correlated with other constructs from other theories. The use of NIBS might inform IS theories since clear conceptual bridges between these constructs might not previously have existed. By using cognitive processes and brain structures involved in IS constructs to enrich data collection, researchers can not only make bridges between the brain and IS but also draw conceptual links between IS and neuropsychology.

In terms of identifying antecedents of IS constructs, evidence suggests that no one area of the brain exclusively handles interactions with IT stimuli; hence, one needs to take particular care to rule out specific cognitive functions that may underlie an observed effect that may not be related to the IS construct of interest. Yet, some antecedents of IS constructs might be cognitive functions that NIBS can affect, which could help build the causal chain that leads to behavior in an IT context.

As we discuss in Section 2.3, brain structures and functions have a many-to-many relationship. Modulating the excitability of one of these structures, or a larger network in some cases, can help explain the role of these structures in the larger scheme of behaviors that interest IT researchers—information that participants themselves cannot report. In that regard, NIBS can help capture hidden mental processes and support causal conclusions.

Also, to our knowledge, researchers have developed all IS theories with subjects who had unimpaired brain functions. Studies that alter specific brain functions with NIBS might challenge some assumptions that long-standing theories make. This type of design may give rise to new patterns of behavior that our theoretical assumptions should account for. NIBS allows researchers to observe behavior while a brain structure's normal functioning is impaired, which provides a complementary source of data that can help explain the role of brain structures in interactions with IS artifacts. As such, one can tease apart each brain structure's unique contribution to better understand its contribution to the behavior of interest. Virtual lesions such as those that one can provoke with NIBS enable less-intrusive ways to generate behavior in which only a specific part of the brain's contribution is altered.

8 Conclusion

NIBS has the potential to help researchers draw causal links between activity in precise brain structures or networks and IS constructs. Using these techniques can help researchers validate neuroIS theories and develop new hypotheses. To experimentally manipulate membrane polarization, neuroplasticity, and brain oscillations through NIBS, one needs to fundamentally understand many methodological factors, and fundamental research has yet to assess the parameter space, which would benefit from more systematic investigation. Nevertheless, NIBS in neuroIS has the potential to contribute to many research opportunities as Dimoka et al. (2011) suggest.

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