Stimulating the Aging Brain

Success in using noninvasive neural stimulation in humans has paved the way for several exciting additions to the ever-expanding toolkit used by cognitive neuroscientists to understand the relationship between brain and behavior (eg, transcranial magnetic stimulation and transcranial direct current stimulation [tDCS]). Although neuroimaging methods such as functional MRI and electroencephalography are not always strictly correlational,[1] the ability to modulate behavior via training and targeted brain stimulation provides critical causal data to inform psychological and neuroimaging findings (eg, Zanto et al[2]). Moreover, these approaches have the additional potential to serve as effective cognitive enhancers to augment abilities in healthy populations,[3–5] as well as therapeutic interventions to remediate deficits in individuals with neurological and psychiatric conditions.[6–8]

tDCS modulates neuronal excitability, putatively by increasing calcium levels at the site of anodal stimulation even at relatively weak currents of a few milliamperes[9], altering neuronal resting membrane potential,[10] and possibly increasing neuroplasticity by inducing long-term potentiation.[11] In humans, tDCS is usually applied at the scalp noninvasively at 1 to 2 mA for 10 to 30 minutes, during which time participants are asked to perform a behavioral task of interest.[12] The rapid adoption of tDCS by the neuroscientific community since 2000 is evident in the exponential increase in the number of tDCS-related papers indexed in PubMed over the years (Fig). It has been applied to basic cognitive neuroscience and cognitive enhancement in healthy adults, as well as for the potential treatment of diseases such as depression,[8] Parkinson disease,[13] and Alzheimer disease.[7]

In this issue of the *Annals of Neurology*, Zimerman and colleagues put tDCS to excellent use in their study, "Neuroenhancement of the Aging Brain: Restoring Skill Acquisition in Old Subjects."[14] As the authors note, the fastest growing segment of the labor market is persons older than 50 years. Despite high expectations of many older adults in terms of how they would like to perform, insidious impairments in cognitive abilities are a common phenomenon, with deficits spanning multiple cognitive domains, including attention, working memory, and perceptual abilities,[15,16] possibly due to widespread disruptions in neural communication.[17] Even a mild deficit in cognition can constrain an otherwise productive life and reduce independence. Such cognitive deficits are a cause of great distress to many older adults who feel that their ability to lead high-quality lives is negatively impacted, and these impairments are often considered the most debilitating aspect of aging.[18] Understanding the neurobiology of healthy cognitive aging is becoming increasingly important for public policy. Additionally, the potential to maintain cognitive abilities in this population would have far-reaching consequences.

Zimerman et al operationalized skill acquisition using a classic manual motor sequence learning task in which participants were asked to press a 5-element sequence on a 4-button keyboard. Corroborating previous work, the authors find that skill acquisition is reduced in older, compared to younger adults. The authors go on to find that 20 minutes of anodal tDCS (atDCS) over the contralateral motor cortex concurrent with training results in improved skill acquisition in older adults.

Motor skill acquisition is known to improve after a night of restful sleep. This process, known as sleep-dependent consolidation, has been shown to be disrupted with aging.[19] Zimerman and colleagues examined the effect of retention and consolidation by retesting their subjects after 90 minutes and 24 hours. They found that both younger and older adults had better retention after 24 hours than after 90 minutes, corroborating sleep-dependent consolidation results. Interestingly, they found that the atDCS-related improvements in skill acquisition remained pronounced relative to baseline levels even after 24 hours, which suggests that the neuroplastic changes induced by the 20 minutes of motor cortical stimulation actually resulted in better skill acquisition, rather than being due to a transitory improvement.

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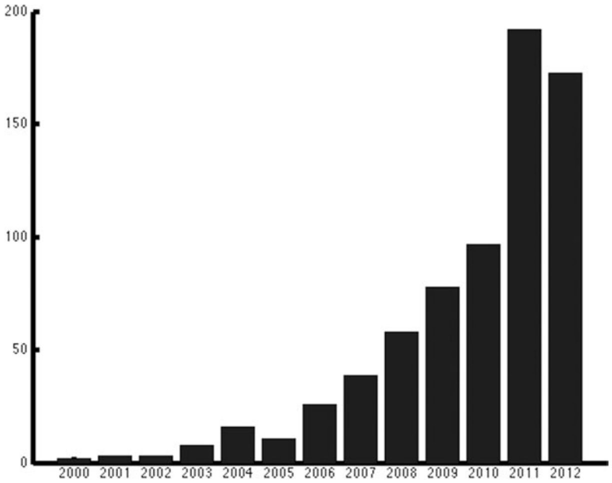

FIGURE : The number of papers published using transcranial direct current stimulation (as indexed by PubMed) has grown exponentially since 2000, with the number of papers published as of September 2012 almost matching the number published in all of 2011.

Understanding the underlying neurobiology of age-related cognitive changes will require the integration of decades of psychological and neuroscientific results collected using a variety of behavioral and technological methodologies. Although their findings do not necessarily address the underlying neurobiological mechanisms of skill acquisition or age-related cognitive decline, their results do provide experimental evidence that widens the path for future research. Zimerman and colleagues' elegant experiment adds important causal evidence of the short-lasting benefits of neocortical stimulation in skill acquisition among older adults. Importantly, it shows that plasticity can be enhanced in the older brain to result in learning gains that are on the order of those obtained by younger adults.

tDCS is rapidly becoming a common tool in the neuroscientific arsenal, and we will begin seeing a wide array of neuroscientific, medical, and psychological experiments that seek to use this technique in innovate ways. As Zimerman and coauthors note in their article, however, there are a number of caveats associated with both the tDCS technique and their results specifically. First, the spatial specificity of tDCS stimulation is very low given that the skull acts as a low-pass spatial filter for electrical activity. This makes it difficult to dissect the neural networks mediating the process of interest. Of note, the authors also failed to show any tDCS-specific enhancement of learning in younger adults. This adds another data point to a mixed literature, where tDCS enhancement effects are not guaranteed.[20]

Although the finding that skill acquisition in older adults can be improved by the application of short, low-current, noninvasive neural stimulation is exciting, tDCS is still in its experimental infancy, and the literature is mixed. There will also be emerging ethical challenges that present themselves if tDCS becomes used to boost cognition in healthy individuals.[21] Although neuroplasticity is retained throughout the lifespan, allowing for skill learning throughout adulthood, plasticity is reduced in older adults. These results hint at the possibility of using tDCS to increase plasticity to improve learning in older adults. As the research community more broadly adopts this technique, its applications and limitations will become better delineated. Nevertheless, the results of this study are tantalizing in their possibility, and mark another milestone on the path toward effective cognitive enhancement tools.

Potential Conflicts of Interest

A.G.: consultancy, stock/stock options, travel expenses, Akili Interactive Labs; patents, "Enhancing Cognition in the Presence of Distraction and/or Interruption."

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