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Treating autism by targeting the temporal lobes

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ABSTRACT

Compelling new findings suggest that an early core signature of autism is a deficient left anterior temporal lobe response to language and an atypical over-activation of the right anterior temporal lobe. Intriguingly, our recent results from an entirely different line of reasoning and experiments also show that applying cathodal stimulation (suppressing) at the left anterior temporal lobe together with anodal stimulation (facilitating) at the right anterior temporal lobe, by transcranial direct current stimulation (tDCS), can induce some autistic-like cognitive abilities in otherwise normal adults. If we could briefly induce autistic like cognitive abilities in healthy individuals, it follows that we might be able to mitigate some autistic traits by reversing the above stimulation protocol, in an attempt to restore the typical dominance of the left anterior temporal lobe. Accordingly, we hypothesize that at least some autistic traits can be mitigated, by applying anodal stimulation (facilitating) at the left anterior temporal lobe together with cathodal stimulation (suppressing) at the right anterior temporal lobe. Our hypothesis is supported by strong convergent evidence that autistic symptoms can emerge and later reverse due to the onset and subsequent recovery of various temporal lobe (predominantly the left) pathologies. It is also consistent with evidence that the temporal lobes (especially the left) are a conceptual hub, critical for extracting meaning from lower level sensory information to form a coherent representation, and that a deficit in the temporal lobes underlies autistic traits.

Introduction

Autism spectrum disorder is a complex neurodevelopmental condition that is estimated to affect 1 in 68 children in the United States [1]. It is theorized to have multiple etiologies, "an emergent property of developmental interactions between many brain regions and functions" [2]. However, based on convergent evidence that autistic symptoms can emerge and later reverse due to changes in temporal lobe physiology (e.g. caused by pathologies [3–10] or temporarily induced by brain stimulation [11]), here we hypothesize a possibility for an early intervention.

Compelling new findings in infants show that a core signature of autism is a deficient left anterior temporal cortex response to language and "a reversed or absent laterality patterns" [12]. This signature grows more pronounced with age in toddlers at risk for autism, whereas typically developing children show opposite developmental trajectories [12,13]. Indeed, there has been extensive evidence implicating the temporal lobes with autism. For example, in young children, autistic traits have been associated with deficit in the left temporal lobe [3,4,6,14–18], enlargement of the right temporal lobe [19,20] and atypical hemispheric lateralization [21,22], especially for language related areas in the temporal lobes [13,23–27].

Intriguingly, such evidence fits nicely with results from an entirely different line of reasoning and associated experiments. We have observed that some autistic-like cognitive abilities can be induced to a degree in otherwise healthy adults by suppressing the left anterior temporal lobe while simultaneously facilitating the contralateral right anterior temporal lobe [11] using transcranial direct current stimulation (tDCS). Specifically, Chi and colleagues [11] showed that applying cathodal stimulation (decreasing excitability) at the left anterior temporal lobe together with anodal stimulation (increasing excitability) at the right anterior temporal lobe enabled a superior visual memory, an advantage similar to those with high functioning autism on an identical memory task [28].

If autistic traits in children are associated with a deficit in the left temporal lobe as discussed above, and if we could temporarily induce autistic like cognitive abilities in healthy people by suppressing left temporal lobe dominance with tDCS [11], then it follows that there is a possibility we could mitigate autistic traits by using a reverse stimulation procedure, in an attempt to restore normal functioning and lateralization of the left temporal lobe.

This possibility is consistent with intriguing cases where autistic traits can emerge in previous healthy people as a result

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of temporal lobe pathologies (predominantly the left temporal lobe) [3–8] and spontaneously disappear upon temporal lobes recovery [5,6,9,10]. For example, DeLong and colleagues observed a 14 year old girl where autistic traits, emerged due to predominantly left temporal lobe pathology caused by acute encephalitis, later spontaneously reversed following temporal lobe recovery [5]. Similarly, Hoon and Reiss observed that a constellation of autistic features emerged in a 2 year old boy as a result of a left medial temporal lobe tumour, including the amygdala [6]. But after the tumour was removed, much of the autistic symptoms spontaneously disappeared. More directly, Deonna and colleagues found that anti-epileptic medication, carbamazepine, resulted in a complete reversal of autistic symptoms in a 2 year old child with predominantly left frontotemporal lobe pathology and epileptiform discharges [9]. While pathologies in such cases are not exclusively confined to the left anterior temporal lobe, they raise the possibility that there is a direct intervention targeting the temporal cortex that can reverse some autistic traits early in their developmental trajectories.

Importantly, while the majority of studies implicate the bilateral temporal lobe abnormalities with the emergence and manifestation of autistic traits [29–35], evidence suggests that, in children, autism is especially associated with deficit in the left temporal lobe [7,8,12–14,16–18,36–38], the hemisphere that is typically dominant for language. For example, Hauser and colleagues observed that 15 out of 18 autistic children in their study showed abnormality at the left temporal lobe and argued that temporal lobe dysfunction "may be a major factor in the pathogenesis of the syndrome of infantile autism" [14]. Similarly, White and Rosenbloom reported a case of a 2-year-old autistic boy who had a partial absence of the left temporal lobe. They suggested that "malfunction or malformation of temporal-lobe structures, especially when they occur in early development and in the dominant hemisphere, may be correlated with the development of autistic behaviours" [18]. From the above, there is extensive evidence that the emergence and manifestation of autistic traits are associated with atypical functioning and lateralization of the left temporal lobe, whether due to suppression of the left temporal lobe or due to bilateral temporal lobe pathologies. Our stimulation protocol aims to mitigate autistic traits by correcting such temporal lobe abnormalities.

Hypothesis

Accordingly, we hypothesize that at least some autistic traits can be mitigated by restoring normal functioning and lateralization of the left temporal lobe. Specifically, we propose to do this with transcranial direct current stimulation (tDCS) by applying anodal stimulation (facilitating) at the left anterior temporal lobe and cathodal stimulation (suppressing) at the right anterior temporal lobe.

Importantly and contrary to extensive evidence noted above that implicates different areas of the temporal lobes, our stimulation protocol specifically targets the anterior region of the temporal lobes. This is because we have had success in modulating autistic like cognitive ability in healthy people with tDCS by placing the electrodes (5 cm × 7 cm) at the anterior temporal lobes [11]. One reason [39] that the anterior temporal lobes are not more often implicated for autism is that, until 2011, functional magnetic resonance imaging (fMRI) was known to produce distortion and signal drop out at this area [40,41]. However a definitive recent study by Eyler and colleagues shows that deficit and atypical lateralization of the left anterior temporal lobe is a core early signature of autism, before such deficit disrupts developmental trajectories downstream [12]. This view is consistent with evidence that the anterior temporal lobes (especially the left), in particular, are theorized to be the conceptual hub. This region is critical for extracting meaning from lower level sensory information to form a coherent representation [42–44], a process that is impaired in those with autism [37,45] (see the Discussion).

Non-invasive stimulation technique

Transcranial direct current stimulation (tDCS) consists of applying weak electrical constant currents to the scalp, via two saline-soaked sponge electrodes, thereby polarizing the underlying brain tissue with electrical fields [46]. Physiologically, anodal tDCS is theorized to induce membrane depolarization (increasing excitability) whereas cathodal stimulation is thought to cause hyper-polarization (decreasing excitability) [47]. Our stimulation protocol is predicated upon evidence that tDCS can suppress or facilitate a brain region and modulate hemispheric rivalry (e.g. increasing a left hemisphere bias) to enable a beneficial cognitive [11,48–50] or clinical outcome [51–54].

Testing the hypothesis

A starting point in testing our hypothesis would be to employ the same tDCS setup as used in the study by Chi and colleagues. Specifically, the anodal sponge electrode (5 cm × 7 cm) should be placed approximately half way between T7 and FT7 on the International 10–20 System (the left anterior temporal area) and the cathodal sponge electrode (5 cm × 7 cm) approximately half way between T8 and FT8 on the same 10–20 System (the right anterior temporal area). Nevertheless, given that the electrodes we used are 5 cm × 7 cm, it is possible that the entire temporal lobes could be affected by our stimulation protocol.

Importantly, while our proposed stimulation could well be most effective for arresting autistic traits early in their development (e.g. in toddlers), there should be caution and qualified supervision in any attempt to apply brain stimulation on children. Because there are only very few studies that have applied brain stimulation on underage subjects to date, it is uncertain what effects tDCS have on the developing mind of children, who have smaller skulls (and thus different distribution of current density) and higher plasticity [55,56].

Accordingly, in testing our hypothesis, the first experiment might involve applying tDCS on young autistic adults (who are otherwise healthy) rather than in toddlers. For additional margin of safety, it would be sensible to increase the stimulation intensity and dosage progressively; beginning with low intensity (1 mA) for 10 min a session and increase, gradually, to up to 2 mA for 30 min.

Furthermore, we do not suggest that our proposed stimulation method is the optimal protocol for treating autism. While there is evidence that tDCS can modulate neuronal excitability and cerebral blood flow at the region under the electrodes [57,58], we cannot exclude the possibility that areas adjacent to the electrodes (5 cm × 7 cm) such as the inferior frontal gyri would be affected by our stimulation protocol. Moreover, bearing in mind that the effects of tDCS are known to be mental state dependent [59] and variable across individuals [60], future studies should explore the use of other neuromodulation methods to restore abnormal functioning and lateralization of the left temporal lobe.

Discussion

How does a left anterior temporal lobe deficit contribute to autistic traits?

Because autism is a highly complex developmental disorder, it is difficult to have a definitive explanation for how autistic traits can emerge as a result of abnormal physiology in the temporal