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Neuroenhancement and Vulnerability in Adolescence

SUMMARY

The very definition, scope, and practical implications of the concept of vulnerability are among the most debated questions in the field of vulnerability research. However, a consensus seems to exist regarding children and adolescents: they are generally considered vulnerable and in need of special protection due to their physical and psychological immaturity, lack of knowledge and life experience, and overall dependency on adults. The special status of this population is safeguarded in numerous legal and ethics documents. In this paper, we discuss the commercial use of transcranial direct current stimulation (tDCS), as a method that have potential to affect functioning of the brain tissue with electrical currents, but also a variety of digital methods used to influence the brain. tDCS is openly advertised, affordable and accessible, even to minors. However, changes that tDCS and similar methods could induce in developing brain tissue and consequently their interference with the normal neurodevelopmental processes could have far-reaching health ramifications and thus represent new sources of vulnerability that slip under the radar of formalized legal and ethics documents. This article discusses changes in the adolescent brain during development and address whether adolescents who would wish to use these neuroenhancement procedures should be considered vulnerable and on what grounds.

Keywords: vulnerability, neuroenhancement, tDCS, digital therapeutics, digiceuticals, digital drugs (i/dosing), wearables.

1. The concept of vulnerability

Vulnerability is generally understood as a complex concept that describes one's state of dependency, which is caused by a certain weakness and the one's

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subsequent susceptibility to being harmed or wronged. Challenge for the theories of vulnerability is to find the common denominator between numerous types and levels of vulnerability. Not surprisingly, there are several taxonomies presented in the literature.

Schroeder and Gefenas differ between external and internal elements of vulnerability, i.e. between being exposed to the possibility of harm and being unable to protect oneself.[1] There is a degree of consensus among scholars that vulnerability indeed consists of these two aspects. Moreover, they correspond with most people intuitive views on what constitutes one's vulnerability. On the other hand, the scope of the concept of vulnerability is still a subject of debate. The conflict arises on whether vulnerability should be understood as 'general', i.e. as an inherent characteristic of human embodiment, which, as such, cannot be entirely eradicated, or as 'special', i.e. situational and contextual.[2] The concept of 'general vulnerability' finds its place in the field of philosophy, where it is notably under-theorized. On the other hand, the field of medical ethics is saturated with the (uncritical) use of the descriptor 'vulnerable'.[3] The field of medical ethics emphasizes the context-dependency of 'vulnerable condition' and asks for an ethical response tailored by the demands of a particular setting. It introduces levels and types of vulnerability (different kinds of 'special vulnerability') with the goal of defining special guidelines for dealing with subjects who are detected as vulnerable. Proponents of this understanding focus on defining features that cause certain individuals or groups to be vulnerable – some examples of such features are very young or very old age, illness, poverty, inadequate education, etc. The background assumption is that once it is clear what causes vulnerability, the individuals and groups "affected" by certain feature would be entitled to a special protection.

Onora O'Neill used the distinction between 'persistent' (typical for the whole species) and 'variable' vulnerability which results from the actions of the particular other or a particular institution. O'Neill observed that the social network which protects and strengthens its members also creates further vulnerabilities by

1 Schroeder, Doris and Gefenas, Eugenijus (2009), Vulnerability: Too Vague and Too Broad?, *Cambridge Quarterly of Healthcare Ethics*, 18 (2), 116.

2 Zagorac, Ivana (2016), How Should We Treat the Vulnerable? Qualitative Study of Authoritative Ethics Documents, *Journal of Health Care for the Poor and Underserved*, 27, 1655–1671.

3 Hurst, Samia (2008), Vulnerability in Research and Health Care: Describing the Elephant in the Room?, *Bioethics*, 22 (4), 191–202; Levine, Carol; Faden, Ruth; Grady, Christine; Hammerschmidt, Dale; Eckenwiler, Lisa and Sugarman, Jeremy (2004), The Limitations of "Vulnerability" as a Protection for Human Research Participants, *American Journal of Bioethics*, 4 (3), 44–49; Luna, Florencia (2009), Elucidating the Concept of Vulnerability: Layers not Labels, *International Journal of Feminist Approaches to Bioethics*, 2 (1), 121–139; Macklin, Ruth (2003), Bioethics, Vulnerability, and Protection, *Bioethics*, 17 (5–6), 472–486; Schroeder and Gefenas (2009); cf. Zagorac, Ivana (2017), What Vulnerability? Whose Vulnerability? Conflict of Understandings in the Debate on Vulnerability, *Facta universitatis*, Series: Law and Politics, 15 (2), 157–169.

developing new dependencies.[4] Henk ten Have follows this distinction, but uses the terms 'philosophical' and 'political' perspectives on vulnerability.[5] The 'philosophical' perspective on vulnerability is most clearly outlined in the *Barcelona Declaration*. Vulnerability is here listed as one of the European ethical principles for bioethics and biolaw, next to the principles of autonomy, dignity, and integrity. Principle of vulnerability is grounded in rich philosophical heritage and calls for respect of vulnerability as it is "a universal expression of the human condition".[6]

Even though such understanding has its proponents, the 'philosophical' vulnerability account as presented in the *Barcelona Declaration* is often characterized as too broad. For example, Kottow describes vulnerability as "an essential attribute of mankind" and "a substantial feature of being human,"[7] but observes that such definition cannot be properly utilized when dealing with specific vulnerabilities. He proposes the term 'susceptibility' for describing instances of "specific and accidental condition to be diagnosed and treated".[8] Samia Hurst also refers to the European 'principle of vulnerability' and argues that such a broad definition cannot provide reason for *special* protection. On the other hand, she finds restrictive definitions (consent-based, harm-based) insufficiently comprehensive.[9] Luna[10] fears that too broad definition of vulnerability might make the entire concept of vulnerability irrelevant[11] and proposes a view on vulnerability that focuses on the relation between the person or a group and the circumstances or the context. Consent-based, harm-based, or even fairness-based[12] definitions of vulnerability are generally considered too narrow. Additionally, such theories have been criticized for their rigidness, but also for promoting discrimination and stereotyping.[13]

But taking sides and aligning with one or the other understanding of vulnerability is not the only way in which one can address the apparent conflict between the two perspectives. One possibility is to acknowledge them both, as suggested by Rogers

4 O'Neill, Onora (1996). *Towards Justice and Virtue*, Cambridge: Cambridge University Press, 192.

5 ten Have, Henk (2015), Respect for Human Vulnerability: The Emergence of a New Principle in Bioethics, *Journal of Bioethical Inquiry*, 12, 395–408.

6 Kemp, Peter and Rendtorff, Jacob Dahl (2008), The Barcelona Declaration. Towards an Integrated Approach to Basic Ethical Principles, *Synthesis Philosophica*, 46, (2), 240.

7 Kottow, Michael H. (2004), Vulnerability: What Kind of Principle Is It?, *Medicine, Health Care and Philosophy*, 7, 283–284.

8 Ibid, 283.

9 Hurst, S. (2008).

10 Luna, F. (2009), 128.

11 Levine, C. et al. (2004), 45.

12 Nickel, Philip J. (2006), Vulnerable Populations in Research: The Case of the Seriously Ill, *Theoretical Medicine and Bioethics*, 27, 245–264.

13 Zagorac, I. (2016); Zagorac, I. (2017).

et al. (2012). Authors propose taxonomy of three overlapping kinds of vulnerability: inherent – vulnerabilities that are inherent to a human condition; situational – i.e. context-specific; and pathogenic – responses to one's vulnerability that in effect may increase existing vulnerability or even generate a new one.[14] On the other side, Martin et al. (2014) believe that the conflict represents a philosophical pseudo problem: as authors argue, the two views on vulnerability refer to the same concept with different likelihoods of manifestation.[15] Another analysis of the conflict between the two perspectives suggested that the key issue that should be addressed in order to resolve the conflict is the perceived overall negativity of vulnerability.[16]

The very definition, scope, and perception of vulnerability are among the most debated questions in the field of vulnerability research, mostly because of their far-reaching effects in practice. However, these are not the only open questions related to our understanding of vulnerability. One example refers to the limited reach of special protection. Namely, an individual has firstly to be identified as vulnerable in order to qualify for special protection.[17] In effect, the instrument of special protection shields from *additional* harm only. Another open question is how moral norms and moral obligations relate to vulnerability. How is a demand for helping the vulnerable grounded? Does merely preventing additional harm suffice, or one should help the vulnerable to regain their self-sufficiency, or even help them flourish? The latter is advocated for in the *Barcelona Declaration*, but also in Goodin (1985). Goodin's "principle of protecting the vulnerable" claims that the responsibility of a stronger subject strictly depends upon the degree to which one can affect interests of a weaker subject.[18] The *Barcelona Declaration* clearly states that "the moral principle requiring care for the vulnerable […] also specifically requires not merely non-interference with the autonomy, dignity or integrity of beings, but also that they receive assistance to enable them to realise their potential".[19]

14 Rogers, Wendy; Mackenzie, Catriona; Dodds, Susan (2012), Why Bioethics Needs a Concept of Vulnerability, *International Journal of Feminist Approaches to Bioethics*, 5 (2), 11–38.

15 Martin, Angela K.; Tavaglione, Nicolas and Hurst, Samia (2014), Resolving the Conflict: Clarifying 'Vulnerability' in Health Care Ethics, *Kennedy Institute of Ethics Journal*, 24 (1), 51–72, cf.: Zagorac, I. (2017), 165.

16 Zagorac, I. (2017).

17 Kottow, M.H. (2003), Kottow, M.H. (2004), Zagorac, I. (2016), 1662.

18 Goodin, Robert E. (1985). *Protecting the Vulnerable. A Reanalysis of Our Social Responsibilities*, The University of Chicago Press, 118.

19 Kemp and Rendtorff (2008), 248.

2. Vulnerability of children and adolescents

In this paper, we shall focus on the children and adolescents – the group that is commonly regarded as vulnerable and whose members are generally entitled for special protection. Special status of this population is safeguarded in numerous legal and ethics documents, both national and international. Such status is granted regardless of the particular perspective or adopted criteria for defining vulnerability. When it comes to the extent of moral act, most people would be intrinsically motivated to help a child, even beyond the present emergency. In some cases, especially when parents and their children are concerned, it is generally assumed that the adult will do their best to enable the child to flourish. In sum, when it comes to finding reasons for both protecting and helping, the population of children and adolescents is the least controversial one.

The central thesis of this paper is emergence of the new sources of vulnerabilities. Following the taxonomies briefly discussed above, they would fit the description of 'pathogenic' vulnerabilities – the ones that emerge from the responses to initial vulnerability.[20] More specifically, we shall discuss the use of some popular neuroenhancement techniques that have been marketed as safe ways to improve cognition, mood, motor functioning, etc. In our focus are non-invasive brain stimulation methods (e.g. transcranial direct current stimulation, tDCS) when they are used outside of the diagnostics and medical treatment. Such methods and devices are openly advertised, affordable and accessible, even to children and adolescents. In their commercial use or amateur self-experimentation, they are used for improving certain capabilities of the brain (e.g. learning) and applied without the proper supervision.[21] What makes them a possible source of 'pathogenic' vulnerabilities in the hands of non-professionals is a risk of inflicting harm and inducing unforeseeable far-reaching negative consequences in individuals who use them.

Under-age individuals are generally considered vulnerable due to their physical and psychological immaturity, lack of knowledge, skills and experience: all what makes them an ideal target for products that promise an improved performance with little effort. Additionally, as we shall examine later in more detail, an impact of electrical stimulation on the developing brain is still undetermined, which calls for an extra caution in its employment, both in professional (research, medical treatment, clinical trials) and amateur context. The practice of using medications and medical treatments by the healthy to improve their performance is not new. For example, different stimulants that are prescribed for the treatment of attention deficit hyperactivity

20 Rogers et al. (2012).

21 Pustovrh, Toni (2014), The Neuroenhancement of Healthy Individuals using tDCS: Some Ethical, Legal and Societal Aspects, *Interdisciplinary Description of Complex Systems*, 12 (4), 270–279.

disorder (ADHD) or medications developed for the treatment of Alzheimer's disease are sometimes (illegally) used by the healthy for cognitive enhancement.[22] Enhancement technologies raise many ethical issues which even the enhancement-enthusiasts cannot deny. Moreover, some authors are concerned that biotechnology may alter our view of human nature and undermine the idea of human equality.[23] Regardless of their disparate views, most of the both enthusiasts and sceptics seem to recognize the need to protect children and minors against their parents' grandiose plans of enhancing certain features of their offspring. For example, Greely et al. (2008) advocate for regulation which would enable that mentally competent adults engage in cognitive enhancement using drugs. The authors are well aware that children represent a special case as they cannot make their own decisions, so in case of allowing the use of enhancement drugs among adults, the authors believe that such practice should be strictly prohibited among children.[24]

Special status of minors in medical research and treatment has been acknowledged either explicitly or implicitly in leading international ethics documents in the field of (bio)medicine.[25] Normative documents (e.g. laws, conventions, professional codices) strongly promote special measures of protecting children in such setting. Some types of medical research and treatment explicitly exclude children, while other deny them the decision-making capacity and turn to their parents or legal representatives for consent. In recent years, voices are being raised against the "blanket categorisation" of children as vulnerable research participants, with a suggestion that their vulnerability should instead be assessed within the specific context and as related to the specific study.[26] An effort is being made to include children in the decision-making process. One of the mechanisms is the institution of "assent" which in certain respect parallels "consent" of adults.[27] Next to the vulnerabilities that are part of the inherent nature of childhood, there are also situational vulnerabilities that in many cases of medical research can be minimalized by encouraging more active role of young research participants.[28] Active role of minors as research participants is promoted through the

22 Greely, Henry; Sahakian, Barbara; Harris, John; Kessler, Ronald C.; Gazzaniga, Michael; Campbell, Philip; Farah, Martha J. (2008), Towards responsible use of cognitive-enhancing drugs by the healthy, *Nature*, Vol. 456, 702–705 (11 December 2008).

23 Fukuyama, Francis (2003), *Our Posthuman Future: Consequences of the Biotechnology Revolution*, Picador.

24 Greely et al. (2008).

25 Zagorac, I. (2016).

26 Cheah, Phaik Yeong and Parker, Michael (2015), Are Children Always Vulnerable Research Participants?, *Asian Bioethics Review*, 7 (2), 151–163.

27 Ho, Calvin W.L.; Reis, Reas and Saxena, Abha (2015), Vulnerability in International Policy Discussion on Research Involving Children, *Asian Bioethics Review*, 7 (2), 230–249.

28 Wright, Katharine (2015), Are Children Vulnerable in Research?, *Asian Bioethics Review*, 7 (2), 201–213.

conceptual change, which refers to the "research *with* minors" and not "*on* minors".[29] Involving children in the decision-making process related to their health and medical treatment is a sensitive issue because of all the elements that make children vulnerable and dependable in the first place (immaturity, lack of knowledge and life experience, physical and psychological fragility, etc.). On the other hand, relying exclusively on the consent provided by the legal representatives of a minor might prove inadequate. Hurst (2015) notices that paternalism of the adult in charge over the child is grounded on at least two assumptions: adult caregivers can better understand the terms of informed consent, and they wish to protect the overall interests of a child. However, both of these aspects could be compromised. Regarding the first, the adult in charge of the child might himself be vulnerable due to lack of specific knowledge needed for fully informed consent. Secondly, adults might negotiate the best interest of a child with other interests. In both cases, the adults are becoming an additional source of vulnerability for children.[30]

The 'best interests' or 'welfare' of a child is a key issue in making decisions that influence the child's everyday life and future. It is possible that the concerned parent or guardian would use the enhancement technologies to improve their child's different traits. However, a recent survey[31] among the U.S. public found that the majority of respondents was unwilling to enhance their child with tDCS, even though they were asked to consider the hypothetical version of tDCS that was known to be safe and effective. Respondents were especially reluctant to enhance their child's motivation and empathy, traits considered fundamental to the self. But the study also showed that initial reluctance of a parent might change to acceptance if other parents were using tDCS for their children, and as a result their own child could be disadvantaged.[32] Implicit coercion and the reinterpretation of child's best interest might turn a concerned parent into a new source of vulnerability for a child. Such findings strongly suggest that the usage of tDCS has to be regulated to prevent misuse, especially in non-medical context. Unlike the hypothetical version of tDCS presented in the study,[33] current version of tDCS lacks reliable evidence on its safety for use among children and adolescents due to specificities of the developing brain and problematic transfer of findings on adults to younger population. The biggest changes in the brain take place in the pre- and post-natal periods and in

29 Ibid, 207–208.

30 Hurst, Samia (2015), Clarifying Vulnerability: The Case of Children, *Asian Bioethics Review*, 7 (2), 126–138.

31 Wagner, Katy; Maslen, Hannah; Oakley, Justin and Savulescu, Julian (2018), Would You Be Willing to Zap Your Child's Brain? Public Perspectives on Parental Responsibilities and the Ethics of Enhancing Children with Transcranial Direct Current Stimulation, *AJOB Empirical Bioethics*, 9 (1), 29–38.

32 Ibid.

33 Ibid.

early childhood. The adolescent years present a 'second window of opportunity' for brain development, during which children need to gain full independence and make a transition to adulthood.[34] This process takes place with increasing independence in decision-making and freedom of action about their own life. At the same time, due to specificities in the development of the brain adolescents are vulnerable to different self-inflicted harms, but also to external risks and dangers. The development of the adolescent brain that makes them so vulnerable is presented below.[35]

3. Adolescent brain development

Adolescence is the period that begins at the beginning of puberty and ends with the establishment of social independence.[36] However, there is no consensus about the exact start and end of the period of adolescence, and today it lasts longer than in previous generations. The beginning of adolescence usually coincides with the onset of puberty, while its end is being shifted because of societal changes, but also by neuroscientific findings about the development of the brain, which moved the end of adolescence from the teen years well into the twenties.[37] The commencement of puberty comes with a cascade of hormonal changes, which promote reproductive maturation, but also stimulate dynamic changes in the brain morphology, fiber architecture, biochemical alterations in neurotransmitter systems and neuroendocrine factors. All of these have great consequences on processing emotions, risks, rewards, and social relationships, behavior and also facilitate sexual differentiation of the brain.[38]

The brain has incredible computing capabilities that serve the purpose of integrating and harmonizing all intrinsic and environmental influences, and creating a meaningful output while maintaining homeostasis. This brain malleability, called neuroplasticity, is the property that allows structural and functional changes in response to injuries, or as a result of a new experience, sensory inputs, etc. To enable an increased opportunity for growth, balance needs to be achieved between neural stability and plasticity.[39]

34 UNICEF Office of Research (2017). The Adolescent Brain: A second window of opportunity, UNICEF Office of Research - Innocenti, Florence.

35 Ibid.

36 Curtis, Alexa (2015), Defining adolescence, *J Adolesc Family Health*, 7: 2, Article 2. Available at: https://scholar.utc.edu/jafh/vol7/iss2/2

37 Ledford, Heidi (2018), Who exactly counts as an adolescent, *Nature News feature*. Available at: https://www.nature.com/articles/d41586-018-02169-w. Accessed on 05. Jan 2019..

38 Herting, Megan M. and Sowell, Elisabeth R. (2017), Puberty and structural brain development in humans, *Front Neuroendocrinol*, Jan. 44, 122-137. doi:10.1016/j.yfrne.2016.12.003.

39 Takesian, Anne E. and Hensch, Takao K. (2013), Balancing Plasticity/Stability Across Brain Development, *Prog Brain Res*, 207. http://dx.doi.org/10.1016/B978-0-444-63327-9.00001-1

Neuroplasticity is enabled by genetic and cellular mechanisms that modulate changes on the synapse and therefore affect the plasticity of the neural circuitry by affecting neurogenesis, synaptogenesis and synaptic pruning. Neuroplasticity is especially fascinating during phases of increased changes and growth like the one that happens during maturation in childhood and adolescence.

The onset of pubertal brain maturation seems to be under the influence of sex steroids. Adolescent physical maturation (pubertal development according to the Tanner scale) is related to cortical and subcortical grey matter volumes.[40] In addition, sex steroids have also affected pre-myelination and myelination events affecting white matter volumes and microstructure. Testosterone is also important in various aspects of white matter maturation seen across adolescence. The pubertal development has also been shown to affect synapse number, dendritic branching, and outgrowth.[41]

Neurodevelopmental morphology studies indicate that while grey matter volume decreases from childhood to young adulthood, grey matter density actually increases in adolescence.[42]

Brain maturation processes follow the caudal-to-rostral direction. At the early stage of development the occipital regions, sensomotor cortices and striatum mature, while the maturation of the prefrontal cortex and association cortices extends to the late twenties. The structural and metabolic maturation of the prefrontal cortex is the latest event in brain development. The adolescent brain changes not only in volume and shape, but also in its microstructure. Structural magnetic resonance imaging (MRI) is used to quantify the size and shape of gray and white matter areas and make inferences about their microstructural properties.[43] During childhood and adolescence, both cortical and subcortical brain regions undergo significant changes.[44] Longitudinal studies have suggested maturation in white matter with

40 Bramen, Jennifer E., Hranilovich, Jennifer A., Dahl, Ronald E., Forbes, Erika E. , Chen, Jessica, Toga, Arthur W. et al. (2011), Puberty Influences Medial Temporal Lobe and Cortical Gray Matter Maturation Differently in Boys Than Girls Matched for Sexual Maturity, *Cerebral Cortex March*, 21. 636–646. doi: 10.1093/cercor/bhq137.

41 Ibid.

42 Gennatas, Efstathios D., Avants, Brian B., Wolf, Daniel H., Satterthwaite, Theodore D., Ruparel, Kosha, Ciric, Rastko et al. (2017), Age-related effects and sex differences in gray matter density, volume, mass, and cortical thickness from childhood to young adulthood, *J. Neurosci*, May 17; 37(20), 5065–5073. doi: 10.1523/JNEUROSCI.3550-16.2017.

43 Alexander, Andrew L., Lee, Jee Eun, Lazar, Mariana, Field, Aaron S. (2007), Diffusion Tensor Imaging of the Brain, *Neurotherapeutics*, July; 4 (3), 316–329.

44 Koolschijn, P. Cedric M. P., Peper, Jiska S., Crone, Eveline A. (2013), The Influence of Sex Steroids on Structural Brain Maturation in Adolescence, *PLoS ONE* 9(1): e83929. doi:10.1371/journal.pone.0083929; Spear, Linda Patia (2013), Adolescent Neurodevelopment, *J. Adolesc Health*, 2013 Feb; 52 (202): S7–13. doi:10.1016/j.jadohealth.2012.05.006.

a greater myelin and/or fiber organization and adult-like microstructural patterns being reached only after the completion of puberty.[45]

During development, from birth to adulthood, the brain passes through 'critical periods' in which appropriate stimulus must be encountered for normal development to occur. It further goes through several 'sensitive periods' in which the child and/or adolescent is able to acquire certain skills or knowledge very easily.[46] In these 'sensitive periods' or 'windows of opportunity', a cascade of intracellular and synaptic events is triggered, which renders the developing brain more susceptible to perturbation, and results in a brain that is primed to learn specific information. Research focused on sensitive periods mainly discuses early sensory, motor, and language development, but has recently suggested that adolescence presents a second 'window of opportunity' in brain development. It is considered a sensitive period of development characterized by changes in the brain structure and function, particularly in regions of the cortex that are involved in higher-level cognitive processes. The outcomes of the increased brain plasticity are not only development opportunities, but also increased vulnerabilities, as it can trigger not only positive, but also negative behavioral and developmental trajectories. During the maturation processes, the traits like risk taking, impulsivity and/or reward processing could end up being functional and positive for the future wellbeing of adolescent, but could also be dysfunctional and harmful.[47]

The beginning of puberty comes with a redirection of attention towards social and emotional information processing and the understanding of social hierarchies. Sexual and romantic behavior becomes a primary interest. Acceptance and belonging become very important with an increased sensitivity to feelings of rejection, disrespect, embarrassment, and humiliation. Adolescents also become highly driven by the promise of obtaining immediate rewards, which leads to sensation seeking and risk-taking.[48]

Intelligence seems to be related to dynamic properties of cortical maturation and to the pattern of cortical growth during childhood and adolescence. Higher intelligence is related to a particularly plastic cortex that demonstrates an accelerated and

45 Simmonds, Daniel J., Hallquist Michael N., Asato, Miya, Luna, Beatriz. (2014), Developmental stages and sex differences of white matter and behavioural development through adolescence: a longitudinal diffusion tensor imaging (DTI) study, *NeuroImage*, 92, 356–368.

46 Knudsen, Eric I. (2004), Sensitive Periods in the Development of the Brain and Behavior, *J. Cogn Neurosci*, 16 (8), 1412–1425; Fuhrmann, Delia., Knoll, Lisa J., Blackmore, Sarah-Jayne (2015), Adolescence as a Sensitive Period of Brain Development, *Trends in Cognitive Sciences*, Oct: 19 (10), 558-566.

47 van Duijvenvoorde, Anna C. K., Peters, Sabine, Braams, Barbara R., Crone, Eveline A. (2016), What motivates adolescents? Neural responses to rewards and their influence on adolescents' risk taking, learning, and cognitive control, *Neurosci Biobehav Rev*, 2016 Nov;70, 135-147. doi: 10.1016/j.neubiorev.2016.06.037.

48 Ibid.

prolonged initial phase of cortical increase and equally vigorous cortical thinning by early adolescence.[49]

Adolescence is also the time when psychopathologies are first developed, with disproportionate increases in rates of anxiety and depression seen in girls and an increased prevalence of substance abuse and externalizing disorders in boys.[50] The trajectories of brain development and puberty overlap, however, widespread individual differences in these patterns exist.

4. Neuroenhancement

Immersed in super-hero pop culture and driven by the advancement of science and technology, children and adolescents sometimes have expectations of themselves that exceed the human frame. Moreover, in a world driven by *citius, altius, forties* principles, the human body and mind are becoming subjects that need to be perfected. The use of technological means to alter human characteristics and capacities that lie beyond the existing "normal" is considered "human enhancement", with the mind being a very attractive enhancement target.

Modification of the brain processes of a person beyond the level necessary to restore and/or maintain health[51] is called neuroenhancement. For the purposes of therapy, certain side effects could be considered acceptable, however the methods used with the sole purpose of neuroenhancement should not have side effects greater than other comparable legally permitted substances and methods. The target could be the cognitive, the affective and/or the motor functioning capacities, and the desired change should be based on the knowledge of the underlying biology of these processes in the brain. The change could be introduced using pharmacological or non-pharmacological means, which both serve the purpose of affecting the transmission of the electrical signals between neurons. The message transferred between the neurons, or between the neuron and effector organ, could be induced, amplified, or suppressed. The transmission of these signals presents the basis of synaptic plasticity, which results in brain neuroplasticity. This enables the reorganization of the brain's structure and function, in response to new information, sensory inputs, experience,

49 Shaw, P., Greenstein, D., Lerch, J., Clasen, L., Lenroot, R., Gogtay, N., et al. (2006), Intellectual ability and cortical development in children and adolescents, *Nature lett.*, Vol 440, 30 March, doi:10.1038/nature04513.

50 Angold A., Costello E. J., (1998), Worthman C. M. Puberty and depression: the roles of age, pubertal status and pubertal timing, *Psychol Med*, 28 (1), 1–61.

51 Farah, Martha. J., Illes, Judy., Cook-Degen, Robert, Gardner, Howard, Kandel, Eric, King, Patricia, et al. (2004), Neurocognitive enhancement: what can we do and what should we do?, *Nat Rev Neurosci*, 5, 421–425. doi: https://doi.org/10.1038/nrn1390; Husain, Masud, Mehta, Mitul A. (2011), Cognitive enhancement by drugs in health and disease, *Trends Cogn Sci*, 15 (1), 28–34. doi: https://doi.org/10.1016/j.tics.2010.11.002.

or trauma. There has been an exponential growth in the number of methods that measure and evaluate brain functions, as well as those that can manipulate brain functions, or just guide a person to control their emotions and mind states.[52] Further, we will comment on the methods that are finding their way to the population of minors. Some of these methods treat the brain with electrical current and are usually described as non-invasive, as no part of the devices breaches the skin. However, they have the potential to induce changes in neuron firing and can therefore affect the brain neuroplasticity, which cannot be considered harmless. The use of devices that affect the neuroplasticity of a developing brain could lead to aberrant brain development with abnormal patterns of brain activity and potentially damaging consequences on future health.[53]

4.1. tDCS (and other electrical stimulation methods)

Transcranial direct current stimulation (tDCS) is among the most frequently studied and used methods that treat the brain with the electrical current. tDCS works by sending a constant, weak electrical current through electrodes placed on the scalp, which induce an intracerebral current. The current, which is applied constantly over a short period of time, passes the scalp and alters spontaneous neuronal activity.[54] The stimulations affect the brain functions by either depolarizing the neuron's resting membrane potential and therefore promoting the transition of signals, or by preventing or hindering signal transmission by the hyperpolarization of the post-synaptic neurons. tDCS is affordable, simple and attractively made and marketed. It shows promising results in treating certain illnesses, as demonstrated in numerous clinical research studies. In addition, studies in healthy individuals have shown the potential of tDCS to improve working memory, attention, language, mathematics and decision making, but also improve the functions of the frontal lobe related to impulse control, cognitive control and creativity.[55]

52 Fernandez, Alvaro (2015), 10 Neurotechnologies About to Transform Brain Enhancement and Brain Health. Available at: https://sharpbrains.com/blog/2015/11/10/10-neurotechnologies-about-to-transform-brain-enhancement-and-brain-health/ (accessed on 3 December 2018); Lynch, Zack (2018), Neurotechnology and Society. Available at: https://lifeboat.com/ex/neurotechnology.and.society (accessed on 11 December 2018).

53 Krishnam, Chandramouli, Santos, Luciana, Peterson, Mark D., Ehinger, Margaret (2015), Safety of Noninvasive Brain Stimulation in Children and Adolescents, *Brain Stimul*, Jan-Feb; 8 (1), 76–87. doi: 10.1016/j.brs.2014.10.012; Erhardt, Julija; Švob Štrac, Dubravka (2016), Non-Pharmacological Tools for Neuroenhancement. Neuroethical Issues, *Synthesis philosophica*, 31 (1), 181–194. Doi: https://doi.org/10.21464/sp31113.

54 Woods, A. J., Antal, A., Bikson, M., Boggio, P. S., Brunoni, A. R., Celnik, P., et al. (2015), A technical guide to tDCS, and related non-invasive brain stimulation tools, *Clin. Neurophysiol*, 8 (2/2015), 412. doi: https://doi.org/10.1016/j.clinph.2015.11.012.

55 Luedtke, Kerstin; Rushton, Alison; Wright, Christine; Geiss, Benjamin; Juergens, Tim P.; May, Arne (2012), Transcranial Direct Current Stimulation for the Reduction of Clinical and Experimentally Induced Pain. A Systematic

The size and shape of the electrodes, as well as their exact positioning on the head, significantly alters the distribution of the current delivered to the scalp, and consequently the intensity of the brain stimulation. For reliable results of tDCS treatments, proper positioning of the electrodes is crucial. However, the proper montage of electrodes is a challenging task, due to different shapes and sizes of heads and slightly different individual brain organization. Furthermore, anodal and cathodal stimulations cause opposite effects, therefore applying the polarity of the electrodes properly is crucial, but could be puzzling for nonprofessionals. Exceeding the optimal strength and duration of the stimulation may also be harmful. All of these factors contribute to the fact that the results of stimulation might not be as intended and can even be opposite to the expected ones.[56] The apparent absence of immediate and expressed side-effects is not sufficient evidence to make a conclusion about the harmlessness of the applied treatment. The mentioned side-effects that fall into the categories of 'prickling and burning sensations' or 'skin-burns' are potentially less serious than possible changes in the modulation of neural networking. Although the electrical field and the specificities of the treatment itself could be defined and reproducible, influence of factors such as individual tissue properties, anatomy, age, gender, neurotransmitter concentrations, genetics, and the dynamic state of the brain is hard to predict.[57]

However, several companies (Foc.us, Soterix Medical, Magstim, The Brain Stimulator, etc.) produce and sell affordable devices all over the world and advertise their use in gaming, sport, or work. As tDCS represents the simplest electrical stimulation technique, there is a growing community of "do it yourself" (DIY) tDCS users and internet bloggers and there are many instructions on the internet that explain how to make your own device.[58]

Review and Meta-analysis, *Clin J. Pain*, 28, 452–461, doi:https://doi.org/10.1097/ajp.0b013e31823853e3; Feng, Wuwei; Bowden; Mark G., Kautz, Steven (2013), Review of transcranial direct current stimulation in poststroke recovery, *Top Stroke Rehab*, 20 (1), 68–77. doi: https://doi.org/10.1310/tsr2001-68; Mondino, Marine; Bennabi, Djamila; Poulet, Emmanuel; Galvao, Filipe; Brunelin, Jerome; Haffen, Emmanuel (2014), Can transcranial direct current stimulation (tDCS) alleviate symptoms and improve cognition in psychiatric disorders?, *World J. Biol Psychia*, 15 (4), 261–275. doi: https://doi.org/10.3109/15622975.2013.876514.

56 Erhardt, J. (2016); Hurley, Roanne, Machado, Liana (2017), Using tDCS priming to improve brain function: Can metaplasticity provide the key to boosting outcomes?, *Neurosci Biobehav Rev.*, Dec; 83, 155–159. doi:10.1016/j.neubiorev.2017.09.029; Zhao, Haichao, Qiao, Lei, Fan, Dongquiong, Zhang, Shuyue, Turel, Ofir, Li, Yonghui et al. (2017), Modulation of Brain Activity with Noninvasive Transcranial Direct Current Stimulation (tDCS): Clinical Applications and Safety Concerns, *Front Psychol.*, 10 (8), 685. doi: 10.3389/fpsyg.2017.00685; Antal, A., Alekseichuk, I., Bikson, M., Brockmoller, J., Brunoni, A. R., Chen, R., Cohen, L. G. et al. (2017), Low intensity transcranial electric stimulation: Safety, ethical, legal regulatory and application guidelines, *Clin Neurophysiol.*, Sept; 128 (9), 1774–1809. doi: 10.1016/j.clinph.2017.06.001.

57 Antal, A. et al. (2017).

58 DIY tDCS, Keeping Tabs On Transcranial Direct Current Stimulation. Available at https://www.diytdcs.com/, accesssed 15 Dec 2018.

In order to make a mature decision on whether to use such a device and to properly understand its pros and cons, one must critically evaluate the facts about the gadgets and the underlining brain biology. Furthermore, a potential user should be capable of meaningful temporal self-projection about what they would like to achieve and a high level of auto-control to stick to guidelines and not exceed the maximally allowed device use time or intensity. Sticking to all of this seems unlikely for a potential adolescent, making the use of these devices detrimental.

Davis[59] (2014) has called for 'extreme caution' in the use of non-invasive brain stimulation (NIBS) methods to treat children, because of the unknown effects and mechanisms that produce these effects, unknown side-effects of the stimulation, both short- and long-term, lack of dosing guidelines and a lack of translational studies from adults to children. The neurobiology underlying cognition and motor function differs in young and older individuals, hence the stimulation of the same brain regions may have different effects in children/adolescents and in adults.[60] Brain regions do not exist in isolation and stimulating one region, and possibly enhancing its function, might be detrimental to some other cognitive trait, to the overall balance and/or to the overall cognitive performance.[61] Therefore, the cognitive cost of using this type of stimulation, especially in the developing brain, might be too high. Research done on tDCS is done in a laboratory setting and on adults, and can hardly be transferable to adolescents and/or an improper use.

There is no information about the response of a developing brain in its critical and/or sensitive periods of development on electrical stimulation. As Davies[62] (2014) has pointed out, there are no translational studies and we know nothing about the dosing and side-effects of the stimulation on minors. Electrical stimulation of brains in a state of increased plasticity (due to sensitive periods of development) has not yet been studied, and it is difficult to foresee possible outcomes of such treatments. However, the number of adolescents who have been using tDCS devices acquired either by purchase or DIY, is increasing.[63] A deeper understanding of these 'windows of opportunity' in the development of the adolescent brain might provide us with insights that could help treat illnesses and disorders.[64] Normal and

59 Davis, Nick, (2014), Transcranial stimulation of the developing brain: a plea for extreme caution', *Front Hum Neurosci*, 2014; 8, 600. doi: 10.3389/fnhum.2014.00600.

60 Gutchess, Angela (2014), Plasticity of the aging brain: New directions in cognitive neuroscience, *Science*, 346, 579–582. doi: 10.1126/science.1254604.

61 Luber, Bruce (2014), Neuroenhancement by non-invasive brain stimulation is not a net zero-sum proposition, *Front. Syst. Neurosci*, 8, 127. doi:10.3389/fnsys.2014.00127.

62 Davies, N. (2014).

63 Available at : https://www.reddit.com/r/tDCS/comments/8qli7n/list_of_best_selling_tdcs_devices_of_2018_as_well/ (accessed 10. Jan 2019).

64 Fuhrmann, D. (2015).

abnormal neuroplasticity and synaptic plasticity needs to be studied, all in the light of neuromodulation done by electrical stimulation. Abnormal synaptic plasticity is related to many disorders in childhood. The modulation of electrical activity of the developing brain could disturb developmental homeostasis, induce atypical neuroplasticity and contribute to an abnormal neurophysiology and behavior.[65] Over- and/or under-pruning of the synapses, is in the etiology of certain neurobehavioral disorders, and could be influenced by uncontrollable electrical treatments of the brain. The idea that disrupted pruning of neural connections during adolescence is a cause of schizophrenia was proposed a few decades ago, but has since been proved by imaging, genetic and molecular research.[66] Increased plasticity is not only a source of developmental opportunities, but could be a source of vulnerability and negative developmental trajectories with maladaptive outcomes. Whether neuromodulatory treatments could push an adolescent brain towards maladaptive outcomes depends on the specifics (strength, duration, etc.) of the treatment, the stage of neurodevelopment and the stability and integrity of the homeostatic regulatory mechanisms. Gaining this type of knowledge would be of outmost importance, however, this presents us with another ethically questionable issue of children as research subjects.

Although the field of brain activity modulation with electrical stimulation has shown promising technical, diagnostic and therapeutic advances in adult disorders of the brain, its application in children/adolescent disorders is still in its infancy. Finally, still a lot of research should be done before the safe use of these stimulators should be recommended, either as a treatment or for enhancement purposes.

4.2. Digital methods

Contemporary living is deeply immersed and interwoven with digital technologies/contents and children/adolescents have not known the world without them. They consider digital technologies and digital access as a 'natural and integral part of their day to day existence and their fundamental right'.[67] The widespread accessibility to information and social interactions that digital technologies have brought, has created a shift in societal expectations, which demand immediate responsiveness,

65 Maslen, Hannah., Earp, Brian D., Kadosh, Roi C., Savulescu, Julian (2014), Brain stimulation for treatment and enhancement in children: an ethical analysis, *Front Human Neurosci*, Dec 8, 953. doi: 10.3389/fnhum.2014.00953.

66 Boksa, Patricia (2012), Abnormal synaptic pruning in schizophrenia: Urban myth or reality?, *J. Psychiatry Neurosci*, 37 (2), 75-7. doi: 10.1503/jpn.120007; Feinberg, Irwin (1982), Schizophrenia: caused by a fault in programmes synaptic elimination during adolescence?, *J. Psychriat. Res.*, 17 (4), 319–334.

67 Rikkers, Wavne, Lawrence, David, Hafekost, Jennifer, Zubrick, Stephen R. (2016), BMC Public HealthBMC series; 16:399. https://doi.org/10.1186/s12889-016-3058-1.
Available at: https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-016-3058-1.

different productivity, as well as a 'fear of missing out', typical for the adolescent age. Further, the constant disruption of attention and its spread over several tasks at once is creating more stress and anxiety and has an influence on attention span, perception, memory, creativity, emotions, etc.

The development of tools and gadgets that can manipulate brain functions, or guide a user to control their emotions and mind states has undergone an exponential growth, as seen from the number of filed patents in the field of neurotechnology in the last several years.[68] If not combined with any other treatments, which could be harmful, these methods are non-invasive and can be helpful in different spheres of life.[69]

They are grouped under the name of *digital therapeutics* or *digiceuticals* and most of them use electroencephalography (EEG) to monitor the electrical activity of the brain, interpret the mental states of a person and respond in real-time with appropriate treatments or with suggestion of procedures that would help achieve the desired state of mind. Digital technologies can assist with many health issues and could complement traditional therapies or stand on their own. Many of these methods are known and historically used, but have now been brought to a new level with the increased sensitivity of detectors as well as new designs, applications or a combination of methods, etc.[70] They are increasingly included to already wide-spread general-fitness wearables.

Therefore, digital therapeutics could help ameliorate the symptoms that to a certain degree the overuse of digital technologies helped create, and are closing the loop with treatments and/or enhancements. Adolescents embrace gadgets and apps very easily and the adoption of these methods could help them build concentration and the self-regulation of skills.

These methods are all truly non-invasive and present only a minor safety risk if any at all. However, other types of ethical issues could arise, e.g. continuous recording of EEG data, which can reveal details about the functioning of the brain and the state of mind, leading to privacy issues, etc.

Both groups of methods, those that treat the brain with electrical currents and digital methods are increasingly being introduced and offered in an attractive way, as gadgets

68 Fernandez, Alvaro (2017), The Digital Revolution Meets the Human Brain. Available at: https://www.huffingtonpost.com/alvaro-fernandez/the-digital-revolution-me_b_7556038.html; Rucker, Michael. (2017), The Era of Pervasive Neurotechnology, *Verywell Health*. Available at: https://www.verywellhealth.com/the-era-of-pervasive-neurotechnology-1739113.

69 Sharp Brains, *Market report executive summary*. Available at: https://sharpbrains.com/pervasive-neurotechnology/.

70 Fernandez, A. (2015).

or apps, such that it is difficult for adults, and especially for children and adolescents, to anticipate the safety, privacy and future health consequences.

5. Conclusion

Growing technological power and the opportunities it provides has created new non-pharmacological methods of neuroenhancement. Adolescents do not have the critical thinking needed to assess these new devices and instruments and are therefore more accepting of new technologies, especially those that are attractively marketed. Synaptic and molecular mechanisms of neuronal excitability and plasticity are difficult to study. A certain amount of research has been done analyzing the effects of tDCS on the adult brain, however child and adolescent brains are not simply smaller adult brains. The excitation and inhibition of neuronal patterns changes as the brain develops, as well as long-term potentiation, long-term depression and plasticity. Therefore, the changes that these methods could induce in the tissue of a developing brain and consequently their interference with the normal neurodevelopmental processes could have far-reaching health ramifications. Methods like tDCS are advertised as a safe means of improving certain brain capabilities (e.g. learning) and might motivate parents or legal representatives of minors to approve their use without any medical justification and appropriate supervision. As the study by Wagner et al. (2018) suggests, adults might even feel pressured to embrace such methods if other parents are using them for their children, and as a result their own child could be disadvantaged.[71] In such cases, the use of the methods developed for therapeutic purposes for restoring or achieving the healthy functioning of a certain feature might themselves be a source of new vulnerabilities, i.e. under implicit coercion, the 'best interest of the child' might be uncritically reinterpreted by those who should protect it. The use of these new methods of neuroenhancement presents possible new causes of vulnerability that minors are exposed to. Neither the minors, nor their parents or guardians are likely to have sufficient knowledge to apprehend the scope of influences that these methods could have on their minds and bodies.

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71 Wagner et al. (2018).

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Neuropoboljšavanje i ranjivost u adolescenciji

SAŽETAK

Sama definicija, opseg i praktične implikacije koncepta ranjivosti su među najčešće raspravljanim pitanjima u području istraživanja ranjivosti. Zbog njihove fizičke i psihološke nezrelosti, nedostatka znanja i životnog iskustva te sveukupne ovisnosti o odraslima, postoji konsenzus da se djeca i adolescenti općenito smatraju ranjivima, te da ih je potrebno zaštititi. Poseban status ove populacije potvrđen je i u brojnim zakonskim i etičkim dokumentima. U radu raspravljamo o komercijalnoj upotrebi transkranijalne stimulacije istosmjernom strujom (tDCS) kao metode koja, djelujući s električnom strujom, može utjecati na funkcioniranje moždanog tkiva. Također govorimo i o ostalim digitalnim metodama koje se koriste za djelovanje na mozak. tDSC se otvoreno oglašava, pristupačan je cijenom i dostupan, čak i maloljetnicima. No, promjene koje bi tDCS i slične metode mogle potaknuti u razvoju moždanog tkiva i posljedično njihovu interferenciju s normalnim neurorazvojnim procesima mogle bi imati dalekosežne zdravstvene posljedice i tako predstavljati nove izvore ranjivosti koji nisu obuhvaćeni u formalnim pravnim i etičkim dokumentima. U ovom se članku raspravlja o promjenama u adolescentskom mozgu tijekom razvoja i pitanjem trebaju li se adolescenti koji žele koristiti ove postupke za neuropoboljšanje smatrati ranjivima i na temelju čega.

Ključne riječi: ranjivost, neuropoboljšavanje, tDCS, digitalna terapija, digiceutici, digitalni lijekovi (i/doziranje), „wearables“.