Epilepsy & Behavior 57 (2016) 230–233

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Review

Epilepsy treatment and creativity

Sarah Zubkov, Daniel Friedman *

Comprehensive Epilepsy Center, New York University Langone Medical Center, 223 East 34th St, New York, NY 10016, USA

ARTICLE INFO

Article history:
Accepted 31 December 2015
Available online 29 January 2016

Keywords:
Epilepsy
Antiepileptic medications
Epilepsy surgery
Creativity

ABSTRACT

Creativity can be defined as the ability to understand, develop, and express, in a systematic fashion, novel orderly relationships. It is sometimes difficult to separate cognitive skills requisite for the creative process from the drive that generates unique new ideas and associations. Epilepsy itself may affect the creative process. The treatment of epilepsy and its comorbidities, by altering or disrupting the same neural networks through antiseizure drugs (ASDs), treatment of epilepsy comorbidities, ablative surgery, or neurostimulation may also affect creativity. In this review, we discuss the potential mechanisms by which treatment can influence the creative process and review the literature on the consequences of therapy on different aspects of creativity in people with epilepsy.

This article is part of a Special Issue entitled "Epilepsy, Art, and Creativity".

1. Introduction

The ability to generate ideas is uniquely human. Diversity of ideas in our society can be attributed, in part, to a wide range of genetic expressions and life experiences. It has also been well documented that diseases of the brain and/or mind can influence creativity. However, the impact of treatment of these disorders is less well studied and is the subject of this review.

2. Creativity in epilepsy

Creativity can be defined as the ability to understand, develop, and express, in a systematic fashion, novel orderly relationships [1]. In the scientific study of creativity, one must objectify creative expression to draw standardized comparisons. It is sometimes difficult to separate cognitive skills requisite for the creative process from the drive that generates unique new ideas and associations. A combination of both talent and motivation fuels creativity [1,2]. In considering the effects of treatment of neurological illness on creativity, more evidence exists for an impact on motivation, mediated by subcortical circuits, than for effects on talent, likely mediated by cortical networks. In addition, a certain degree of cognition is required for the creative process [3]. Creative artwork, for example, be it painting, sculpture, or music, requires an understanding of the individual components of the whole and how they fit together and builds on these principles in an original and/or unusual way. Dissociating the effects of the disorder or its treatment on creativity from effects on the expression of the creative process such as drawing, music perception, playing an instrument, or writing is challenging, making studies of creativity difficult to design and interpret.

Before considering the effects of epilepsy treatment on the creative process, it is worthwhile to note that epilepsy itself may affect creativity in multiple domains. For example, one study found that patients with epilepsy demonstrated poor control over drawing, making disorganized lines [4]. In addition, patients with temporal lobe epilepsy (TLE) and complex partial seizures produced drawings with highly detailed individual components that were not well related to one another. Children with epilepsy were found to draw less-developed human figures than normal for their chronological age, with impaired self-concept, distorted body image, low self-esteem, and a sense of vulnerability and lack of control [5].

Creativity depends, in part, on motivation, i.e., an inner drive to produce. Geschwind's description of an interictal behavioral syndrome in patients with temporal lobe epilepsy included hypergraphia, increased religiosity, and philosophical concerns (as well as hyposexuality and aggression) [6]. Though hypergraphia itself does not necessarily imply creative output, the increased productivity raises the chance that a percentage of the output will be deemed creative. Hypergraphia may be responsible for prolific writings of people with epilepsy (Fyodor Dostoevsky is a prominent example).

3. Anatomy of creativity

Creativity involves processing diffuse heteromodal, or higher-order, outputs, which is most understood to occur in the frontal and temporal lobes [2,7,8]. The frontal lobes have both facilitatory and inhibitory effects on creative processing. They are involved in motivation, planning, and interpretation of stimuli [7]. As mentioned above, the creative innovator must think in a different direction than what is accepted, a process

* Corresponding author. Tel.: +1 646 558 0868, fax: +1 646 385 7164.
E-mail addresses: sarah.zubkov@nyumc.org (S. Zubkov), daniel.friedman@nyumc.org (D. Friedman).

http://dx.doi.org/10.1016/j.yebeh.2015.12.048
1525-5050/

termed divergent thinking [1]. One measure of creativity is the "brick test", in which subjects must come up with as many uses of a brick as they can think of, both common and uncommon. Subjects who thought of more uses of a brick were found to have more activation of their frontal lobes [9]. Functional MRI studies have implicated the inferior prefrontal cortex in idea generation during creative tasks, as well as the default mode network, which is active during internal thought, mental imagery, and mind wandering, and which consists of the medial prefrontal cortex, posterior cingulate cortex, precuneus, and bilateral inferior parietal lobes [10]. The frontal lobe networks are also important for initiating actions; lesions to the frontal lobes result in apathy and depression. The frontal lobes, in turn, project broadly to areas of higher-order processing in the temporal and parietal lobes, perhaps inhibiting commonly used connections and favoring alternate pathways [1].

The temporal lobes process sensory output from association cortices adjacent to the primary cortex, assigning meaning [11] and emotion [8], the latter via limbic connections. The argument that TLE may be linked with creativity is based upon the observation in some cases and speculation in others that important writers, musicians, and visual artists have suffered from epilepsy [8,12–14]. While TLE best fits the description of strong emotion, déjà vu, hallucinations, delusions, and other symptoms of psychosis that many artists have described, little to no proof of diagnosis exists in most cases. However, there are fundamental properties of TLE that may foster creativity. Firstly, neurochemical lability in epilepsy may be the neural correlate of cognitive overinclusiveness (or increased associations between seemingly unrelated concepts), leading to original and unusual yet useful ideas [8]. Secondly, interictal limbic discharges may lead to emotionalization of internal and external stimuli via a process similar to kindling in animal models of epilepsy [8,15]. Thus, TLE may promote unusual relationships between concepts while simultaneously infusing emotion and meaningfulness into them.

It follows that disruption of neural activity in the temporal lobes may affect processing of sensory inputs. Snyder [16] reported on the effects of low-frequency repetitive transcranial magnetic stimulation (rTMS) on the dominant anterior temporal lobe. Low-frequency rTMS creates virtual lesions by transiently disrupting neural activity in the region to which it is applied [17]. When applied to the dominant anterior temporal lobe of healthy subjects, rTMS can induce savant skills such as realistic drawing. The implication is that disrupting activity in the left temporal lobe allows for the bottom-up processing that savants rely on to produce incredibly detailed drawings [16]. Temporal lobe rTMS has also led to improved error detection in proofreading and an increased ability to accurately estimate the size of a large number of objects.

The temporal lobes, in turn, project reciprocal inhibitory connections to the frontal lobes [2]. Thus, a temporal lobe lesion can result in frontal disinhibition, resulting in increased generation of ideas that may be suboptimally judged [2]. Such is the case in Wernicke's aphasia, where patients produce prolific, yet meaningless, speech.

4. Medical treatment of the epilepsies and creativity

Geschwind proposed that antiseizure drugs (ASDs) should not diminish the traits of the interictal syndrome he described [6], as the treatment does not restore the function of the disordered temporal lobe network involved in the seizure focus. However, his proposal is purely speculative. In fact, ASDs, by reducing the frequency and severity of seizures, may limit the degree of temporal lobe neuronal injury and volume loss, preserving limbic function.

Several authors have proposed that low arousal states are associated with creativity [1,18]. An experiment where subjects were given either ephedrine or propranolol, a centrally-acting beta-blocker, before solving anagrams revealed that those treated with the latter outperformed the former [18]. Sympathomimetic agents provoke a "fight-or-flight" response, attuning us to stimuli in the external world while dampening internal signals. Notably, the frontal lobes, in addition to promoting set-shifting responses, project to the locus coeruleus, inhibiting widespread norepinephrine release [19], another mechanism by which frontal activity may foster creativity. Although some ASDs, such as benzodiazepines and barbiturates, lower arousal, they can also lower motivation, making them counterproductive to the creative process. However, no studies examining the effects of individual ASDs on the creative process have been performed.

5. Medical treatment of epilepsy comorbidities and creativity

Psychiatric disorders are significant comorbidities of epilepsy. People with epilepsy have high rates of depression, anxiety, and postictal and interictal psychotic symptoms [20]. Psychiatric comorbidities themselves may influence creativity. Hermann [21] studied 50 patients, 84% of whom had temporal lobe epilepsy, and rated their writing to determine whether they displayed traits of hypergraphia. The degree of hypergraphia was significantly inversely correlated with age of onset and directly correlated with disease duration. Additionally, severity of depression was inversely correlated, and severity of hypomania was directly correlated with the rating of hypergraphia.

Treatment of psychiatric comorbidities may alter the creative process. Selective serotonin reuptake inhibitors (SSRIs) can foster creativity, as may be the case in patients with severe depression [2,22]. However, in some cases, SSRIs can also hinder goal-directed activity via inhibition of the dopaminergic system [20,23]. Therefore, treatment with SSRIs may also lead to apathy [24].

Antipsychotic medications, commonly used to treat interictal and postictal psychotic symptoms, can also influence creative behavior. Dopamine pathways play a central role in motivation behaviors. The dopaminergic system is involved in mania, compulsive gambling, and substance abuse; it drives action without judgmental thinking. An elevated dopaminergic state would be expected to cause generation of ideas without the screen of meaningfulness. Treatment with dopamine agonists can lead to increase in motivation; however, the work produced may differ from the patient's original interests [25,26]. For example, one man who developed Parkinson's disease changed his painting style from realistic to more impressionistic after starting a dopamine agonist [25]. Conversely, traditional neuroleptics may lead to a decrease in creativity. Atypical antipsychotics improve negative symptoms, allowing for creative work to flourish [25].

Other mood-stabilizing or antidepressant medications, such as lamotrigine, bupropion, or mirtazapine, may be better alternatives to preserve creativity in patients with psychiatric symptoms [2]. One case series [27] reported cognitive dulling, apathy, and loss of "spark" in seven patients on lithium, which improved after they were partially or fully switched to divalproex sodium.

6. Surgical treatment of the epilepsies and creativity

As the anatomical substrates of creativity, the temporal and frontal lobe are also the most common location of the epileptogenic zone, and it is reasonable to postulate that ablative epilepsy surgery may alter the creative process. Only a few case series examining the effects of epilepsy surgery on the creative process exist.

6.1. Corpus callosotomy

Because creative expression requires simultaneous use of the brain's specialized regions, epilepsy and its treatment, particularly through ablative surgery, may disrupt the creative process. In addition, as interactions between cortical regions are important for associations of seemingly unrelated concepts, the generation of novel ideas may rely to some extent on intact white matter tracts both within and between cerebral hemispheres. Early conceptual models of creativity postulated that the right hemisphere fostered creativity while the left worked to inhibit it