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Brain Gamma-Aminobutyric Acid Levels in Internet and Smartphone Addiction: A Comprehensive Review

Dr. Gagan Kumar Banodhe[1], Prof. Dr. Tribhuwan Kumar[2], Dr. MD Zabihullah[3], Dr. Devika Santhosh[4]

[1,3]Assistant Professor, [2]Professor, [4]Senior Resident
[1,2,3,4]Physiology, AIIMS, Patna

Abstract:
Internet and smartphone addiction have emerged as important behavioural disorders characterized by compulsive digital technology use, impaired self-control, withdrawal symptoms, and significant psychosocial dysfunction. Growing evidence suggests that these conditions share neurobiological mechanisms with substance use disorders, particularly involving dysfunction of the brain's inhibitory and reward pathways. Gamma-aminobutyric acid (GABA), the primary inhibitory neurotransmitter in the central nervous system, plays a critical role in regulating executive function, reward processing, emotional regulation, and inhibitory control. This review summarizes current evidence on GABAergic alterations in internet and smartphone addiction and their therapeutic implications. Studies consistently demonstrate significantly elevated GABA-to-creatine ratios within the anterior cingulate cortex of adolescents with internet and smartphone addiction compared with healthy controls. In contrast to several psychiatric disorders, including depression, anxiety, and attention-deficit/hyperactivity disorder, where reduced GABA levels are commonly reported, digital addiction exhibits a distinct neurochemical profile characterized by increased GABA concentrations. Elevated GABA levels are positively associated with addiction severity, anxiety, and depressive symptoms, suggesting disrupted inhibitory control and maladaptive reward processing. Although current evidence is limited by small sample sizes and methodological constraints, altered GABAergic neurotransmission appears to be a promising biomarker of digital addiction. Future longitudinal and multicentre studies incorporating advanced neuroimaging techniques are warranted to validate these findings, clarify the underlying pathophysiological mechanisms, and facilitate the development of targeted, evidence-based therapeutic interventions for internet and smartphone addiction.

Keywords: Gamma-aminobutyric acid, Internet and Smartphone Addiction, Behavioural disorders,

1. Introduction:

Modern life is now more connected and convenient than ever because to the widespread use of digital technologies, but it has also brought forth new types of behavioural addiction that present serious public health issues. The hallmarks of internet and smartphone addiction, a severe behavioural condition that affects millions of individuals worldwide, include compulsive usage patterns, tolerance, withdrawal

symptoms, and functional impairment (1,2). The pathophysiology of digital addictions is significantly influenced by gamma-aminobutyric acid (GABA), the primary inhibitory neurotransmitter in the brain. Magnetic resonance spectroscopy (MRS) and other recent advancements in neuroimaging techniques have allowed researchers to investigate the neurochemical foundations of these addictions.

2. Neurobiological Foundations of GABA in Addiction

GABA, the most common inhibitory neurotransmitter in the central nervous system, is present in around 25 to 50% of synapses and has concentrations of 0.8–1.8 mM in the healthy human cortex (3,4). The GABAergic system plays a crucial role in controlling the mesolimbic-dopaminergic reward neurocircuitry because it is closely related to the endogenous opioid and cannabinoid systems that support addictive behaviours (3,5). This intricate balance between excitatory and inhibitory neurotransmission is required to maintain proper inhibitory control, reward processing, motivation, stress responses, and memory formation (3,6,7).

The mesocorticolimbic system, which processes reward-related stimuli and salient networks, includes the anterior cingulate cortex (ACC), which has become a crucial brain region in addiction studies (1,8). Because of its advantageous location, this area is especially pertinent to the study of behavioural addictions since it combines cognitive and emotional processing and is crucial for motivation, decision-making, cognitive inhibition, and emotion regulation (9). The ACC's role in behavioural and substance addiction points to common neurobiological pathways that could account for the comparable treatment outcomes and clinical manifestations of various addictive diseases (8,10).

GABA Alterations in Internet and Smartphone Addiction

The first direct proof of GABA neurochemical changes in internet and smartphone addiction has been presented by groundbreaking study by Seo and colleagues utilizing the sophisticated MRS techniques (1,11). In their groundbreaking research, they used Meshcher-Garwood point-resolved spectroscopy (MEGA-PRESS) to compare the levels of GABA and glutamate-glutamine (Glx) in the anterior cingulate cortex of 19 teenagers who were addicted to smartphones and the internet to 19 healthy controls who were matched for age and sex. The results showed the first neurochemical evidence of GABAergic dysfunction in digital addictions, with significantly higher brain parenchymal and grey matter volume-adjusted GABA-to-creatine ratios in the addiction group, P values being 0.028 and 0.016, respectively (1,12,13). GABA levels are generally lower in other mental illnesses, such as depression, attention deficit/ hyperactivity disorder, panic disorder, and autism spectrum disorders, however these higher levels in internet and smartphone addiction stand in stark contrast to these findings (1,14). In contrast to classic substance addictions and other mental illnesses, this particular neurochemical signature raises the possibility that internet and smartphone addictions entail alternative pathophysiological pathways, possibly reflecting different adaptive responses to long-term behavioural stimulus (15,16).

Strong associations between GABA levels and markers of addiction severity were shown by correlation studies, highlighting the clinical importance of these GABA changes. Scores on the Internet Addiction Test, Smartphone Addiction Scale, and their combined measures showed a strong correlation with gray matter volume-adjusted GABA-to-creatine ratios (1,17). The mental comorbidities frequently seen in digital addictions may be exacerbated by GABAergic dysfunction, as seen by the positive relationships

found between GABA levels and depression scores, state anxiety levels, and overall anxiety measures (18–20).

Therapeutic Normalisation Through Cognitive Behavioural Therapy

The study's treatment component, which showed that cognitive behavioural therapy (CBT) could restore the increased GABA levels seen in internet and smartphone addiction, may have produced the most clinically significant results (1,21,22). The brain parenchymal and grey matter volume-adjusted GABA-to-creatine ratios of twelve teenagers who finished a nine week cognitive behavioural therapy program significantly decreased, P values being 0.034 and 0.026, respectively, indicating that the neurochemical changes reflect functional rather than structural changes in GABAergic neurotransmission (1).

In order to address addictions like internet and substance abuse, the CBT intervention was adapted from cognitive behavioural therapy protocols and included elements related to emotional identification and expression (23). The main areas addressed in the treatment program of internet addiction are , identifying problematic online behaviour, correcting cognitive distortions, finding suitable substitute activities, encouraging self-control, identifying one's own and others' emotions, effectively expressing emotions, and resolving interpersonal conflicts (24). These all-encompassing strategy led to notable improvements in markers of addiction severity, although less noticeable changes were seen in psychological and sleep-related symptoms (24,25).

Understanding how behavioural therapy works in the treatment of addiction is significantly impacted by CBT's capacity to restore GABA levels. In contrast to pharmaceutical treatments for depression, such as electroconvulsive therapy and selective serotonin reuptake inhibitors, which usually raise GABA levels, cognitive behavioural therapy seems to operate via distinct neurochemical pathways (26–28). In contrast to direct neurochemical modulation, psychotherapy therapies may address GABAergic dysfunction through top-down cognitive and emotional regulatory processes (29).

Pathophysiological Mechanisms and Glutamate-GABA Balance

High GABA levels in internet and smartphone addiction are probably caused by intricate processes including the development of tolerance and compensatory brain adaptation. There are two main theories that have been put out to explain this occurrence (1). First, different underlying reward and reinforcement systems may be reflected in the higher GABA, which may be a unique neurobiological characteristic of behavioural addictions as opposed to drug addictions (30,31). Second, a compensatory anti-reward mechanism that was created in reaction to long-term overstimulation of reward circuits may be represented by the enhanced GABAergic inhibition (30,32,33).

As an inhibitory neurotransmitter, GABA primarily works by hyperpolarizing neurons by activating GABA-A and GABA-B receptors, which lowers the production of action potentials and neurotransmission (33,34). The functional down regulation of ACC activity may be facilitated by the increased GABA levels linked to internet and smartphone addiction, which may have an impact on impulsive control when making decisions in high-risk situations (35,36). The typical lack of control and poor decision-making seen in people with digital addictions may be explained by this mechanism (36,37).

An important factor in the pathophysiology of addiction is the balance between GABA and glutamate, the primary excitatory neurotransmitter in the brain (38). Glutamate, the brain's primary excitatory neurotransmitter, and GABA, an inhibitory neurotransmitter, must be in balance for addiction pathophysiology to take place. Although internet and smartphone addiction was consistently associated with higher GABA levels, glutamate-related changes were more subtle, with Glx levels exhibiting negative relationships with sleep quality and insomnia severity rather than addiction severity assessments (39). This divergent pattern implies that GABAergic dysfunction, rather than glutamatergic dysfunction, may be the primary cause of the GABA-glutamate imbalance in addictions (40).

Neuroplasticity and Recovery Mechanisms

GABA levels returning to normal after cognitive behavioural therapy (CBT) is strong evidence of the brain's neuroplastic ability to heal from addiction-related neurochemical changes (41,42). This finding aligns with broader understanding of neuroplasticity in addiction, where chronic substance abuse induces persistent alterations in neurotransmitter systems that can be reversed through appropriate interventions (43). The brain's considerable capacity for adaptive change even after the emergence of addictive behaviours is suggested by Cognitive behavioural therapy's ability to restore normal GABAergic activity. Research in substance addictions has demonstrated that, neuroplasticity underlies the onset and recovery stages of addictive illnesses (44,45).

Chronic exposure to addictive substances or behaviours induces compensatory adaptations in glutamatergic and GABAergic systems, particularly within frontal cortices and their connections to midbrain and basal forebrain regions (3). Glutamatergic and GABAergic systems undergo compensatory modifications as a result of long-term exposure to addictive drugs or behaviors, especially in frontal cortices and their linkages to the midbrain and basal forebrain regions (45).

Beyond conventional psychotherapy techniques, neuroplasticity has therapeutic implications for digital addictions (46). By specifically addressing the altered brainwave patterns linked to addictive behaviours, emerging therapies like neurofeedback training have demonstrated potential in the treatment of addiction (47). Particularly, alpha-theta neurofeedback techniques have shown promise in lowering relapse rates and enhancing psychological results in This finding aligns with a broader understanding of neuroplasticity in addiction, which maintains that chronic substance use results in alterations to the neurotransmitter system that can be undone with appropriate therapy. drug abuse diseases, possibly via GABA system modulation methods (46,48).

Clinical Implications and Therapeutic Considerations

The finding that internet and smartphone addiction are associated with higher GABA levels has important ramifications for clinical evaluation and treatment strategies. First, these results raise the possibility that neurochemical biomarkers could be used as objective indicators of the severity of addiction and response to treatment, which could enhance the precision of diagnosis and treatment tracking (49). The potential clinical value of MRS-based measures is supported by the high correlations found between GABA levels and established addiction assessment instruments (50).

Second, CBT's ability to normalise GABA levels confirms the effectiveness of psychotherapy treatments for digital addictions and offers neurobiological support for their mechanisms of action (51,52). This research could assist dispel doubts regarding the biological basis of behavioural addictions and argue in favour of clinical practice standards that incorporate evidence-based psychological treatments (1).

Third, rather than merely modifying treatment procedures from substance use disorders, treatment approaches may need to be uniquely customised for digital addictions due to the distinct neurochemical profile of internet and smartphone addiction, which is characterised by high rather than lowered GABA levels. This distinctiveness could help to explain why some people with digital addictions don't react as well to conventional methods of addiction therapy (53,54).

In addition to behavioural therapies, the therapeutic potential of GABAergic system control in addiction therapy also includes pharmacological approaches. In a number of substances use disorders, Baclofen and other GABA-B receptor agonists have shown promise in reducing cravings and withdrawal symptoms (38,55). However, given the higher GABA levels seen in digital addictions, it's possible that GABA modulatory techniques are more appropriate for these circumstances rather than GABA augmentation techniques (56,57).

Methodological Considerations and Limitations

It must be accepted that, despite being novel, the present research on GABA levels in internet and smartphone addiction has a number of methodological flaws. The main drawback of GABA measurement with MRS is its technical difficulties, which include problems with repeatability, the effects of age and sex, and the influence of circadian rhythm (58–60). Furthermore, the specificity of glutamatergic measures is limited by the present MEGA-PRESS technique's inability to distinguish between glutamate and glutamine peaks (1). Another major issue with CBT intervention research is sample size limits, as only 12 patients finished the entire therapy program.(1). In order to validate these preliminary results and investigate potential moderating factors including the degree of addiction, comorbid conditions, and demographic characteristics, larger, more robust research will be required (61). The temporal dynamics of GABA alterations during the stages of addiction, development and recovery should also be explored in future research.

Although technically useful and theoretically acceptable for MRS studies, the emphasis on the anterior cingulate cortex restricts knowledge of GABAergic dysfunction in other brain regions related to addiction (62). Magnetic resonance spectroscopy (MRSI) multi-voxel techniques may offer more thorough mapping of neurochemical changes across addiction-related brain networks (63).

Future Research Directions

The current understanding of GABA changes in internet and smartphone addiction points to several significant research paths. Firstly, long-term research monitoring GABA levels from before addiction to recovery stages would offer vital information about the progression of neurochemical alterations over time and how they relate to clinical results (50). Potential biomarkers for addiction risk and treatment response prediction could be found through such studies. Second, it might be possible to determine if higher GABA is unique to digital technologies or a general characteristic of behavioural addictions by comparing research that look at GABA levels across various behavioural addictions

(gaming, social media or pornography etc.) and substance addictions higher GABA is unique to digital technologies or a general characteristic of behavioural addictions (57,64). These comparisons would guide efforts to create treatments and nosological considerations.

Third, in order to comprehend the underlying pathophysiology of digital addiction, mechanistic research examining the cellular and molecular underpinnings of high GABA levels is required. Such studies could use complementary methodologies such as neurochemical, electrophysiological, and molecular techniques to investigate GABA production, release, reuptake, and receptor activity.Fourth, research on the effects of various treatment modalities on GABA levels could improve treatment strategies for digital addictions. It would be beneficial to develop evidence-based treatment regimens if comparative effectiveness studies examining cognitive behavioural therapy, medication, neurofeedback, and combination therapies were conducted.

Fifth, developmental research looking at GABA variations in various age groups would help address teenagers' unique susceptibility to digital addictions and guide age-appropriate treatments. Understanding how digital addiction impacts GABAergic maturation may have significant ramifications for preventive and early intervention techniques, given the continuing brain growth that occurs during adolescence.

3. Conclusion

Understanding the neurological underpinnings of digital addictions has advanced significantly with the identification of increased GABA levels in the anterior cingulate cortex of those who are addicted to smartphones and the internet. These results show that such changes can be corrected with cognitive behavioural treatment and offer the first direct neurochemical evidence for GABAergic dysfunction in behavioural addictions. Digital addictions differ from other mental illnesses due to the unusual pattern of elevated rather than lowered GABA levels, which also points to different pathophysiological pathways.
The brain's neuroplastic potential to recover from addiction-related changes is strongly supported by CBT's ability to restore normal GABAergic function, which also confirms the effectiveness of psychotherapy therapies. Given that MRS-based GABA measures may be used as objective biomarkers for addiction severity and treatment response tracking, these findings have significant clinical practice implications.

Larger, long-term studies that look at GABA dynamics throughout the addiction cycle, comparisons between various addiction types, and mechanistic assessments of the underlying pathophysiology should be the main emphasis of future research in order to build on these findings. Furthermore, research on the neurochemical impacts of different treatment methods could improve therapeutic strategies for digital addictions.

Understanding and treating addiction problems in the twenty-first century requires a multidisciplinary approach, which is exemplified by this research's combination of neurochemical, psychological, and behavioural views. Knowing the neurobiological processes behind digital addictions is crucial for creating efficient prevention and treatment plans to deal with this expanding public health issue as the usage of digital technology continues to rise throughout the world.

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