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Clinical Pathways Illustrating the Dangers of Drug Abuse-Induced Cognitive Behaviour Impairment

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ABSTRACT

Pharmacology has risen to a new horizon with its many branches of clinical research and practices. One among these is the field of neuro-psycho-pharmacology. Neuroscience is the study incorporating the brain, nerves and vessels within. The brain is truly an amazing organ with many complex features and interesting feeds, which focus on many areas of expertise such as learning & cognitive developments, motor movements and many other various capabilities, which are yet to be understood. Combining the knowledge acquired through neuroscience, enabled scientists and researchers alike to understand behavioural and molecular aspect studies into one category known as psychology. This then helped scientists and pharmaceutical companies alike to research and develop drugs that could assist in conditions such as chronic depression, anxiety and various other psychotic disorders incapacitating the core cognitive developments of the brain and its associated nerves and blood vessels. This review thereby focuses on the adverse effects caused by excess consumption of certain drugs due to addictive tendencies and how this leads to impairment of cognitive behaviour.

Keywords
Drug addiction, Learning and cognitive development, Drug abuse-induced behaviour impairment, Drug usage-induced stress.

Introduction

The brain is a complex organ, and it is capable of capacitating roles in dealing with human behaviours. However, by doing so, it has to take a detailed approach to understand the actions and shape the action [1-3]. Motor cognition and or cortical motor areas subjectively control many features such as force, amplitude and direction [1]. It is also reported that motor cognition, referring to the cortical motor system plays a significant role in understanding and managing human behaviour [1,2]. These roles focus on the functionality of cortical motor areas, which capacitate action or intervention and in the establishment of automatized or compulsive behaviours, which may aid in the most severe phase of drug addiction [1].

Drug addiction is very much the leading concern for behaviour abnormalities due to excessive drug consumption despite the adverse consequences [1,3,4]. These abnormalities are believed to gradually progress during a course of repeated exposure to certain drug abuse and could persist for a long duration of months or years even after discontinuation of drug usage [4].

Many children from adolescence have an increased interest towards drugs, which could quite possibly affect their normal cognitive behaviour. Over the years, cocaine and cannabis have been of great interest not just to adolescents but also to religious fanatics. Drugs of this sort tend to affect in ways such as empathy-related deficits, especially in perspective taking, emotional decoding and emotional empathy [5-7]. Excess usage of cannabis can result in acute cannabinoid intoxication, a dysfunctional or distorted perceptive behaviour, recognized by the presence of euphoria and dis-inhalation; anxiety or agitation; mistrust or paranoid delusions; altered sense of time; limited power of judgment; attention

disorder; impaired reaction time; acoustic, optic or tactile illusions; hallucinations without lack of orientation; depersonalization; de-realization and impaired personal performance.

Moreover, one of the following is also present: tachycardia, conjunctival injections, appetite loss and dry mouth [8]. Therefore, it is imperative to understand the clinical physiological and psychological pathways of drug abuse-induced behaviour changes and therapeutic interventions to aid this leading concern.

Drug Addiction and Drug Abuse-Induced Clinical Pathways

Nestler [7] explains that repeated exposure to a drug may alternate gene expression in the brain. This may include changed rates of transcription of genes, causing a change in processing primary ribonucleic acid (RNA) transcripts into mature RNA (mRNA). Altered translation of these mRNAs, changes the process of proteins, which changes the maturation of proteins at the intracellular sites of action. A drug such as cannabis when smoked, tetrahydrocannabinol (THC), a main constituent of cannabis passes from the lungs into the bloodstream, reaching the internal organs and brain within minutes [5,8,9]. THC tends to exert its effect via the CB-1 cannabinoid receptors, located mainly in the regions of the cerebrum associated with locomotion, learning, memory and the reward systems [8]. While smoking cannabis may lead to acute intoxication depending on the preparation and composition of cannabis. The dose, frequency, mode of intake and circumstance of consumption, as well as the individual's experience of consumption is believed to lead to a hypnotic state involving hallucinations for a period, sometimes lasting more than 2-6 weeks [8]. When the pharmacological effects are worn off, hallucinations and other symptoms disappear but the cannabis metabolite THC-COOH can be seen in the urine for 2-6 weeks after the use [8,10,11].

Studies indicate that substance addiction plays a crucial role in triggering antisocial and or violent behaviours. However, there is no direct link that illustrates the relationship between addiction and violent behaviour but can result in the likely outcome due to drug usage [3,11]. Cocaine has been found to portray some positive relationship between its usage and violent behaviour [11]. This can be elicited either directly because of cocaine usage or indirectly due to cognitive deficits caused by exposure to this particular type of drug [1,10,11]. It is reported that men indulge in active violence more than women while consuming cocaine. This may also be due to the wild combination of alcohol and cocaine consumed at the same time [11]. It is also believed that the euphoria- inducing effects of cocaine usage increase in duration and intensity, which increases the risk of violent reactions [10-12].

More and more neuroendocrine and neurobiological systems are being recruited when opposed to stressful conditions [3,10]. Hormones found beneficial in a homeostatic environment are found to be the reasons for pathophysiological cascades, as they are persistently elevated due to the breakdown of negative feedback or failure of feedback regulations of corticotrophin-releasing factor (CRF) and adrenocorticotrophic hormone (ACTH) secretion. By doing so, peripheral and central pathological effects are hypothesized, where an imbalance occurs in noradrenergic systems, which may enhance anxiety, neural atrophy in the hippocampal CA3 region with cognitive consequences and other endocrine disorders such as elevated insulin levels, blood pressure and endothelial dysfunction [3,13]. An acute effect of drug intake and consequent glucocorticoid activation facilitates and triggers the counter- adaptive mechanisms such as neuro-adaptation within the dopamine and opioid peptide systems [14]. As a result, opposing systems are activated by brain stress systems such as corticotrophin-releasing factor and norepinephrine [3,15,16]. These counter-adaptive mechanisms are known as the driving force of multiple hormonal mechanisms combine to produce the allostatic state that underlies the severe pathology of substance addiction [3,17-21].

Salling and Martinez [9] mention that addiction can be measured through four main procedures to stimulate specific brain regions, and these include transcranial electrical stimulation (TES); transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS) and deep brain stimulation (DBS). TES delivers an electrical current to the brain via electrodes and contributes much of the neurophysiological effects of stimulating cortical regions and the central nervous system [9]. TES can be replaced by TMS consisting of conducting coil, which produces the current causing induction of a magnetic field orthogonal to the plane of the coil [9]. This then generates an electrical current in the brain. TMS is restricted to superficial cortical targets, and as a result, most studies of psychiatric disorders including addiction have stimulated the dorsolateral prefrontal cortex [9].

It is reported that TMS stimulating the motor cortex gives data concerning the neurophysiology of cortico-spinal connection as the changes in activation can be determined by measuring alterations in the motor evoked potential (MEP) [9]. The use of TMS is largely reported to investigate acute effects such as craving. Given the data, craving can be considered as the primary behaviour measure. tDCS was used to investigate as means to find treatment for addictive behaviour. Several studies focus on the effects of tDCS on nicotine dependence on cravings. Though nicotine reduced craving, it is not completely consistent because tDCS generates a very low-intensity electrical current of 1-2 mA, which cannot stimulate action potentials in the neuron but may alternate the firing rates by changing the membrane potentials of neurons [9]. DBS is currently in use in humans for the diagnosis of neurologic and psychiatric disorders [9]. Though no extensive use of DBS has been reported concerning addiction, it is found to stimulate the ventral striatum and or nucleus of patients suffering from anxiety or mood disorders to reduce active consumption of substance abuse such as alcohol, nicotine and heroin [9].

Deficits in dopaminergic systems are identified features of substance usage. Positron Emission Tomography (PET) imaging shows that low levels of D2/D3 are associated with drug use and associated behaviours. Though these receptors are a great

target for effective therapeutics, dopamine agonist therapy has shown very limited success in improving treatment outcomes for stimulant dependence [22]. Classic Psychedelics exert primary activity as agonists at the 5-HT2A receptors [7]. Psychedelic medicines that contain DMT contribute towards the benefits of treating drug addiction [7]. Moreover, pharmacological treatments with non-selective D2/D3 receptor agonists have untoward effects by augmenting D3 vs. D2 signalling pathway [22]. Cannabinoid medications such as Δ^9-THC exert pharmacological effects by activation of the two known cannabinoid receptors CB-1 and CB-2 [23]. Rimonabant – a CB-selective-receptor-antagonist, blocks drug addiction through positive subjectivity and reinforcing effects of the drug [23]. It is also found that cannabinoid agonists, work by reducing cannabis use by activating the same key binding sites as cannabis, reducing withdrawal and cravings [23,24].

Caffino et al. [10] re-iterate drug addiction as a devastating disorder due to its economic and social burden on modern society. The author and associates also agree that adolescents are at huge risk but only a few studies have focused on the elucidating underlay of cellular and molecular pathways for behaviour impairment. Though Tupper et al. [7], Robertson et al. [22], Copeland and Pokorski [23] and Ghitza [24] underline the beneficial use of psychedelic substances for treating illnesses such as addiction, depression, anxiety and post-traumatic stress disorder (PTSD), Caffino et al. [10] counter-argue that psychostimulant interactions among adolescents promote brain dysfunction. The progression to addiction is believed to be of maladaptive changes in the neural circuitry of reward learning and inhibition of response [3,9]. Such maladaptive changes have only been reported in animal studies and only occur from repeated exposure to substances in the context of drug administration [25-29]. Kalivas et al. [27] report that the cortical circulatory regulates behaviour flexibility and the inhibition of drug-seeking behaviour can certainly undergo adaptations. The root cause of motivation of drugs following exposure is believed to be a shift from positive to negative reinforcement [9,26], and as a result, drug abuse-induced behaviours become increasingly salient, thus driving drug-seeking behaviours despite negative consequences [3,26,30-33].

Caffino et al. [10] re-iterate the emphasis on understanding the molecular and cellular pathways to drug abuse-induced by conducting studies on rodents such as rats and mice, which intriguingly share features with adolescent humans. This then may aid in acquiring knowledge on the transition between adolescence and adulthood concerning drug abuse [10,34,35]. There are several debates surrounding the possibility of exposure to drugs of abuse, focussing on the fine-tuning of brain circuits that normally occurs during brain development, which may influence how the brain copes with external challenging events that may happen later in life [10,35]. For instance, this notion could be applied to individuals seeking a remedy for stimulant dependence who can often show depressive symptoms. Moustafa et al. [34] explain depressive disorders as the persistent feeling of sadness, emptiness, irritability, and most importantly by significant disturbances in an individual's functioning. In addition, individuals may experience helplessness and guilt, which can further lead to insomnia, weight loss, fatigue, poor concentration and suicidal thoughts [34]. Constant re-uptake of certain drugs affects monoamine release through various mechanisms, causing euphoria, alertness and loss of appetite [10,35]. It can also deplete dopamine, and act as a neurotoxin inducing apoptosis and oxidative stress [3,14,15,20,35].

Caffino et al. [10] state that even a single exposure to cocaine is enough to change the homeostasis in the adolescent brain. This then increases the extracellular levels of dopamine more in adolescents than adults [36], and may contribute to behavioural and dopaminergic responses in adolescence [10]. Studies indicate that repeated drug abuse contributes to the aberrant expression of trophic factors. Neurotrophic factors (NF) are essential for brain development including proliferation, migration, differentiation and survival [10]. NF also aid in synaptogenesis, myelination, neuroprotection and neuroplasticity [10]. Among these NFs, fibroblast growth factor (FGF-2) is expressed in the developing brain and is highly sensitive to manipulations or neurotoxins.

It is reported by Caffino et al. [10] that injection of cocaine causes regional differences in the FGF-2 expression, as it upregulates in the medial prefrontal cortex (mPFC) and is observed to have nucleus accumbens (NAc) and reduction in the hippocampus. It is also hypothesised that the diminution of hippocampal FGF-2 expression may cater to emotional response following a single dose of cocaine leading to anxiety-like symptoms [10,37,38].

Brain-derived neurotrophic factor (BDNF), is also notably crucial in modulating central and peripheral levels observed to oppose modulation due to a single injection of cocaine is led to trigger a depression-like state in rodents [39,40]. A single dose of cocaine during adolescence is also observed to change the actin dynamics, which causes morphological changes in dendritic spines [41,42]. These observations led Caffino et al. [10] to mark the changes as the initial step towards an effect that may sustain addictive behaviours. The author and associates also indicate that repeated exposure to cocaine revealed different adaptations to brain regions. This could indicate that the effects of the first injection of cocaine in the mPFC reached a maximum threshold whereas the subsequent injections normalised the increased actin ratios, suggesting the cytoskeleton has the potential to mount adaptive responses to psychostimulant [10]. It could also indicate that the corticoid cytoskeleton is more vulnerable when re-exposed to cocaine perhaps due to variance from the NAc, which matures earlier, and that the mPFC is still developing during adolescence and even more sensitive to psychostimulant interference [10].

Research studies report that exposure to cocaine during adolescence reduces the density of dendritic spines in the mPFC and increases filopodia, an immature protrusion [42]. Rearrangement of dendritic spines also re-modulates the organisation of glutamate synapse, which is caused by reduced expression of N-methyl-D-aspartate (NMDA) and the α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors subunits, and glutamatergic protein PSD-95 and cytoskeleton protein Arc/Arg3.1

[10]. Subsequent exposures to cocaine increased expressions of FGF-2 and BDNF in the mPFC indicating that exposure to psychostimulants affects brain homeostasis suggesting that these expressions might contribute to the incubation of craving [10]. Arc/Arg3.2 was observed to significantly increase in rats at adulthood in the mPFC through altered mechanisms regulating ubiquitin-protein ligase E3A and the metabotrophic glutamate mGlu5 receptor [10,43]. Prolonged exposure to drugs alters emotional behaviours as it is reportedly observed to trigger anxiety symptoms. This could indicate that anxiety is intermittently linked to drug addiction [44,45]. It is also reported that in adult humans' alterations of cognitive functions such as long-term memory processes or attention are widely affected [3,46-48].

However, not many studies have demonstrated the long-term after-effects of cocaine in adolescents. Caffino et al. [10] emphasise that structural re-modifications are likely to impact cognitive tasks. The Orbitofrontal cortex (oPFC) plays a crucial role in the cognitive process of decision-making, however, after substance abuse, oPFC is observed to be dysfunctional in addicts [14,27]. The Arg kinase is critical in regulating cytoskeletal regulatory proteins that maintain the structure of the dendritic spines at a molecular level, and thereby in its absence shows reversal learning task deficits, a readout of reduced cognitive flexibility [44,49-53]. DePoy et al. [49] reported that inhibition of Rho-kinase in the oPFC leads to neuro-behavioural defects, and suggests it may be a potential mechanism of drug-abuse-induced behavioural impairments.

Conclusion

Drug addiction is a life-threatening condition or disorder that through stimulation of psychostimulant drugs such as cocaine, adjusts the morphological changes of various structures of the brain causing behaviour impairment. Though there are stimulant drugs available to counter the adaptability of drug addiction, research has identified that these drugs can cause brain dysfunction. Addiction is driven by craving, primary behaviourism due to repeated drug abuse. Substance usage repeatedly can induce many dysfunctional behaviour patterns. Perhaps understanding the molecular and cellular pathway of Rho-kinase in oPFC may elevate some of these behaviour issues caused by drug abuse present in modern society.

References

1. Casartelli L, Chiamulera C. The motor way: Clinical implications of understanding and shaping actions with the motor system in autism and drug addiction. Cogn Affect Behav Neurosci. 2016; 16: 191-206.
2. Conrod PJ, Nikolaou K. Annual Research Review: On the developmental neuropsychology of substance use disorders. J Child Psychol Psychiatry. 2016; 57: 371-394.
3. Koob GF, Moal ML. Drug Addiction, Dysregulation of Reward, and Allostasis. Neuropsychopharmacology. 2001; 24: 97-129.
4. Nestler EJ. Molecular mechanisms of drug addiction. Neuropharmacology. 2004; 47: 24-32.
5. Cadet JL, Bisagno V. Neuropsychological Consequences of Chronic Drug Use: Relevance to Treatment Approaches. Front Psychiatry. 2015; 6: 189.
6. Ersche KD, Williams GB, Robbins TW, et al. Meta-analysis of structural brain abnormalities associated with stimulant drug dependence and neuroimaging of addiction vulnerability and resilience. Curr Opin Neurobiol. 2013; 23: 615-624.
7. Tupper KW, Wood E, Yensen R, et al. Psychedelic medicine: a re-emerging therapeutic paradigm. CMAJ. 2015; 187: 1054-1059.
8. Hoch E, Bonnet U, Thomasius R, et al. Risks associated with the non-medicinal use of cannabis. Dtsch Arztebl Int. 2015; 112: 271-278.
9. Salling MC, Martinez D. Brain Stimulation in Addiction. Neuropsychopharmacology. 2016; 41: 2798-2809.
10. Caffino L, Mottarlini F, Zita G, et al. The effects of cocaine exposure in adolescence: Behavioural effects and neuroplastic mechanisms in experimental models. Br J Pharmacol. 2022; 179: 4233-4253.
11. Romero-Martínez A, Moya-Albiol L. Neuropsychological impairments associated with the relation between cocaine abuse and violence: neurological facilitation mechanisms. DICCIONES. 2015; 27: 64-74.
12. Muller CP. Drug instrumentalization. Behav Brain Res. 2020; 390: 112672.
13. Tacey A, Qaradakhi T, Smith C, et al. The Effect of an Atherogenic Diet and Acute Hyperglycaemia on Endothelial Function in Rabbits Is Artery Specific. Nutrients. 2020; 12.
14. Volkow ND, Morales M. The Brain on Drugs: From Reward to Addiction. Cell. 2015; 162: 712-725.
15. Hill AS, Sahay A, Hen R. Increasing Adult Hippocampal Neurogenesis is Sufficient to Reduce Anxiety and Depression-Like Behaviors. Neuropsychopharmacology. 2015; 40: 2368-2378.
16. Otte C, Wingenfeld K, Kuehl LK, et al. Mineralocorticoid receptor stimulation improves cognitive function and decreases cortisol secretion in depressed patients and healthy individuals. Neuropsychopharmacology. 2015; 40: 386-393.
17. Chen Y, Baram TZ. Toward Understanding How Early-Life Stress Reprograms Cognitive and Emotional Brain Networks. Neuropsychopharmacology. 2016; 41: 197-206.
18. Mantsch JR, Baker DA, Funk D, et al. Stress-Induced Reinstatement of Drug Seeking: 20 Years of Progress. Neuropsychopharmacology. 2016; 41: 335-356.
19. McEwen BS, Nasca C, Gray JD. Stress Effects on Neuronal Structure: Hippocampus, Amygdala, and Prefrontal Cortex. Neuropsychopharmacology. 2016; 41: 3-23.
20. Morena M, Patel S, Bains JS, et al. Neurobiological Interactions between Stress and the Endocannabinoid System. Neuropsychopharmacology. 2016; 41: 80-102.
21. Yucel M, Lorenzetti V, Suo C, et al. Hippocampal harms, protection and recovery following regular cannabis use. Transl Psychiatry. 2016; 6: e710.
22. Robertson CL, Ishibashi K, Chudzynski J, et al. Effect of Exercise Training on Striatal Dopamine D2/D3 Receptors in Methamphetamine Users during Behavioral Treatment. Neuropsychopharmacology. 2016; 41: 1629-1636.
23. Copeland J, Pokorski I. Progress toward pharmacotherapies

for cannabis-use disorder: an evidence-based review. Subst Abuse Rehabil. 2016; 7: 41-53.
24. Ghitza UE. Needed Relapse-Prevention Research on Novel Framework (ASPIRE Model) for Substance Use Disorders Treatment. Front Psychiatry. 2015; 6: 37.
25. Conrad KL, Tseng KY, Uejima JL, et al. Formation of accumbens GluR2-lacking AMPA receptors mediates incubation of cocaine craving. Nature. 2008; 454: 118-121.
26. Everitt BJ. Neural and psychological mechanisms underlying compulsive drug seeking habits and drug memories--indications for novel treatments of addiction. Eur J Neurosci. 2014; 40: 2163-2182.
27. Kalivas PW, Volkow N, Seamans J. Unmanageable Motivation in Addiction: A Pathology in Prefrontal-Accumbens Glutamate Transmission. Neuron. 2005; 45: 647-650.
28. Luscher C. Drug-evoked synaptic plasticity causing addictive behavior. J Neurosci. 2013; 33: 17641-17646.
29. Luscher C, Pascoli V, Creed M. Optogenetic dissection of neural circuitry: from synaptic causalities to blue prints for novel treatments of behavioral diseases. Curr Opin Neurobiol. 2015; 35: 95-100.
30. Kauer JA, Malenka RC. Synaptic plasticity and addiction. Nature Reviews Neuroscience. 2007; 8: 844-858.
31. Kourrich S, Calu DJ, Bonci A. Intrinsic plasticity: an emerging player in addiction. Nature Reviews Neuroscience. 2015; 16: 173-184.
32. Schultz W. Potential vulnerabilities of neuronal reward, risk, and decision mechanisms to addictive drugs. Neuron. 2011; 69: 603-617.
33. Stuber GD, Hopf FW, Tye KM, et al. Neuroplastic Alterations in the Limbic System Following Cocaine or Alcohol Exposure. In D. Self & S. G. J. (Eds.), Behavioral Neuroscience of Drug Addiction. Heidelburg: Springer, Berlin. 2009; 3.
34. Moustafa AA, Tindle R, Cashel S, et al. Bidirectional relationship between heroin addiction and depression: Behavioural and neural studies. Current Psychology. 2020; 41: 5195-5211.
35. Swanepoel T, Moller M, Harvey BH. N-acetyl cysteine reverses bio-behavioural changes induced by prenatal inflammation, adolescent methamphetamine exposure and combined challenges. Psychopharmacology (Berl). 2018; 235: 351-368.
36. Walker QD, Kuhn CM. Cocaine increases stimulated dopamine release more in periadolescent than adult rats. Neurotoxicol Teratol. 2008; 30: 412-418.
37. Eren-Kocak E, Turner CA, Watson SJ, et al. Short-hairpin RNA silencing of endogenous fibroblast growth factor 2 in rat hippocampus increases anxiety behavior. Biol Psychiatry. 2011; 69: 534-540.
38. Turner CA, Clinton SM, Thompson RC, et al. Fibroblast growth factor-2 (FGF2) augmentation early in life alters hippocampal development and rescues the anxiety phenotype in vulnerable animals. Proc Natl Acad Sci U S A. 2011; 108: 8021-8025.
39. Caffino L, Mottarlini F, Fumagalli F. Born to Protect: Leveraging BDNF Against Cognitive Deficit in Alzheimer's Disease. CNS Drugs. 2020; 34: 281-297.
40. Caffino L, Mottarlini F, Mingardi J, et al. Anhedonic-like behavior and BDNF dysregulation following a single injection of cocaine during adolescence. Neuropharmacology. 2020; 175: 108161.
41. Caffino L, Giannotti G, Racagni G, et al. A single cocaine exposure disrupts actin dynamics in the cortico-accumbal pathway of adolescent rats: modulation by a second cocaine injection. Psychopharmacology (Berl). 2017; 234: 1217-1222.
42. Caffino L, Messa G, Fumagalli F. A single cocaine administration alters dendritic spine morphology and impairs glutamate receptor synaptic retention in the medial prefrontal cortex of adolescent rats. Neuropharmacology. 2018; 140: 209-216.
43. Caffino L, Giannotti G, Malpighi C, et al. Long-term abstinence from developmental cocaine exposure alters Arc/Arg3.1 modulation in the rat medial prefrontal cortex. Neurotox Res. 2014; 26: 299-306.
44. Buffalari DM, Baldwin CK, See RE. Treatment of cocaine withdrawal anxiety with guanfacine: relationships to cocaine intake and reinstatement of cocaine seeking in rats. Psychopharmacology (Berl). 2012; 223: 179-190.
45. Burton AC, Bissonette GB, Vazquez D, et al. Previous cocaine self-administration disrupts reward expectancy encoding in ventral striatum. Neuropsychopharmacology. 2018; 43: 2350-2360.
46. Kantak KM. Adolescent-onset vs. adult-onset cocaine use: Impact on cognitive functioning in animal models and opportunities for translation. Pharmacol Biochem Behav. 2020; 196: 172994.
47. Koob GF. A role for brain stress systems in addiction. Neuron. 2008; 59: 11-34.
48. Koob GF. Addiction is a Reward Deficit and Stress Surfeit Disorder. Front Psychiatry. 2013; 4: 72.
49. DePoy LM, Noble B, Allen AG, et al. Developmentally divergent effects of Rho-kinase inhibition on cocaine- and BDNF-induced behavioral plasticity. Behav Brain Res. 2013; 243: 171-175.
50. Gourley SL, Koleske AJ, Taylor JR. Loss of dendrite stabilization by the Abl- related gene (Arg) kinase regulates behavioral flexibility and sensitivity to cocaine. Proc Natl Acad Sci U S A. 2009; 106: 16859-16864.
51. Gourley SL, Olevska A, Warren MS, et al. Arg kinase regulates prefrontal dendritic spine refinement and cocaine-induced plasticity. J Neurosci. 2012; 32: 2314-2323.
52. Gourley SL, Swanson AM, Jacobs AM, et al. Action control is mediated by prefrontal BDNF and glucocorticoid receptor binding. Proc Natl Acad Sci U S A. 2012; 109: 20714-20719.
53. Pitts EG, Taylor JR, Gourley SL. Prefrontal cortical BDNF: A regulatory key in cocaine- and food-reinforced behaviors. Neurobiol Dis. 2016; 91: 326-335.