CHAPTER 11

Neurochemistry and Pharmacology of Addictions: An African Perspective

Andrew G. Mtewa, Serawit Deyno, Emmanuel L. Peter, Annu Amanjot, Lucrèce Y. Ahovegbe, and Duncan C. Sesaazi

11.1 Introduction

Neurochemistry deals with the chemistry of nervous system molecules such as neurotransmitters, autacoids, hormones and neuropeptides that direct functions of neurons. These chemicals modulate the central and peripheral nervous systems. Neurochemistry provides a platform for pharmacological and psychological understanding of addictions—their

A. G. Mtewa (✉)
Malawi University of Science and Technology, Blantyre, Malawi

PHARMBIOTRAC, Mbarara University of Science and Technology, Mbarara, Uganda
e-mail: amtewa@must.ac.mw

E. L. Peter
National Institute for Medical Research (NIMR), Dar es Salaam, Tanzania

PHARMBIOTRAC, Mbarara University of Science and Technology, Mbarara, Uganda
e-mail: epeter@std.must.ac.ug

Y. Ndasauka, G. M. Kayange (eds.), *Addiction in South and East Africa*, https://doi.org/10.1007/978-3-030-13593-5_11

pro-genesis, prognoses, progressions and remediations. Neurochemistry interfaces with pharmacology, which is basically the study of uses, effects and mechanisms of drug actions.

Addictions are loosely repeated exposure episodes to substances or behaviours that modify the nervous system chemistry and physiology to the point of loss of control (Nestler 2013). These exposures are stimuli that work on the receptors of the nervous system at a microscopic scale, which, with time, completely alter the response system of the mechanism, leading to a bio-psychological condition called addiction (Bettinardi-Angres and Angres 2010). To understand the occurrence and treatment of addictions, there is a need to get familiar with the neuroscience of addictions, which involves at least three disciplines of chemistry, biology and pharmacology. This field encompasses both neurological and neuro-psychiatric disorders (George-Carey et al. 2012). Africa and persons of African descent have been reported to be more vulnerable to addiction, for various reasons, which will be discussed in the next sections. Research shows that Africa had its own ways of dealing with the disease, mainly through the use of spiritual interventions and herbal therapy. This chapter outlines historical perspectives of the study of neuroscience, with a focus on addictions in the African community, scientific mechanisms involved in addictions, African interventions and research on addictions.

11.2 Neurochemistry in Africa, a Brief Historical Perspective

Neuroscience has been practised in Africa, dating back to the Middle Ages, particularly in the northern part (El-Khamlichi 1996). It particularly began in the form of neurosurgery and neuro-anatomy some 5000 years ago in ancient Egypt (Russell 2017). Imhotep, a physician and a high priest of the Sun God Ra, is believed to have authored the earliest records on neuroscience around 2620 BC (Elhadi et al. 2012). Significant advances in the science was observed from around 332 BC, after Egypt was conquered by Alexander the Great (Elhadi et al. 2012). It was being taught

S. Deyno • A. Amanjot • L. Y. Ahovegbe • D. C. Sesaazi
PHARMBIOTRAC, Mbarara University of Science and Technology, Mbarara, Uganda
e-mail: dserawit@std.must.ac.ug; lahovegbe@std.must.ac.ug; dsesaazi@must.ac.ug

and practised by traditional healers from various tribes, leading to different specializations and focus, such as neurosurgery, among others. In eastern Africa, neuroscience was already being studied in the 1940s (Qureshi and Oluoch-Olunya 2010). The practice and knowledge of neuroscience in Africa and the Arabic region contributed much to the development of medicine during the European renaissance period (El-Khamlichi 1996).

11.3 Addiction amongst People of the African Descent

Incidences of substance abuse are well reported for Africa; however, the epidemiology of neurological and neuropsychiatric disorders, including addictions, has not been widely explored on the African continent (Quansah and Karikari 2016). Although persons of all races are prone to getting addicted to some stimuli, studies have shown that there is a genetic basis in the vulnerability to some neurotic disorders between African and non-Africans (Blanckenberg et al. 2013; Karikari and Aleksic 2015). Research shows that those of African descent are more susceptible to addictions due to proximity to factors that drive them towards addictions. It is reported that addiction, mainly to drugs, is rampant on the African continent (Sevenzo 2015). These include easy access to stimuli (e.g. drugs, pornography, gambling, etc.), mental illnesses, discrimination and racism, poverty, violence, crime and traumatic experiences (Gibbons et al. 2004; Wallace and Muroff 2002; Van-Niekerk 2011). This proximity could be by choice but with a large influence from daily life experiences. The factors associated with addictions, according to some literature (UNODC 2004; Bettinardi-Angres and Angres 2010), have been outlined below.

Genetic Predisposition

Research shows that there is a group of people who are more vulnerable to getting addicted from minor exposures to environmental factors than others under the same conditions. Despite the whole African race being relatively genetically vulnerable, there are some within the group who are more prone to getting addicted. This is the reason that proper institutionalization, management and research on the continent, spearheaded by Africans themselves, are highly recommended. If not well managed, addictions may cripple the development of the continent in one way or another.

Access to Stimuli

Largely, a society with rampant subjection to various substances and habits is more likely to have its young members, as well as the old, experiment with the same at various levels than societies with less of those stimulants. The society could be as small as a family unit, a small chat group or a community at large. Uncontrolled circulation of drugs of abuse, pornographic content and sniffing chemicals in the African continent can produce addictive stimuli to the society. Lack of employment may be one of the factors that subject individuals, who mostly have nothing to do on any particular day, to experiment and engage themselves with addictive substances and behaviour.

Mental Illness

These illnesses manifest in a variety of ways, including anxiety, depression and bipolar disorders. Traumatic experiences in the physical and emotional sense often lead to post-traumatic stress disorders (PTSD), which when untreated, remain a persistent source of stress. As indicated by the Right Addiction Recovery centre (Guarnotta 2018), there are none to limited treatment options in African communities for most of these illnesses, which force the patients to resort to addictive substances and behaviour in order to cope with illness challenges. Seemingly simple matters such as marital cheating to more complex experiences and natural mental disorders are rampant on the African continent, with almost no proper structures to monitor and check their ramifications on consequent human behaviour. In the end, an unfortunate outcome, where the victim is forced to get solace in addictive stimuli, is taken as a normal thing in most communities and not as a matter of urgency.

Discrimination and Racism

Discrimination and racism are one of the leading causes of low self-esteem and inferiority amongst a community that believes that life draws a line for opportunities based on race and other descriptive characteristics. Those who are regarded inferior are likely to seek redress from drugs and repetitive habits that will see them off on an addictive path requiring recovery.

Poverty

Sometimes, addicted individuals or those who think they are getting addicted to things and behaviour would wish to get treatment, but lack of community or national facilities and/or personal finances may hinder them from accessing appropriate treatment. They therefore continue on the road of addiction as part of their normal lives. This situation continues to push individuals deep into poverty.

Repetitive behaviour and use of substances to cope with mental challenges naturally affect the neuro-response system. This, in effect, heavily loads the nervous system to the point that it becomes laden, causing abnormal physiological responses due to changes in the chemical imbalance of the system. The next section discusses the general chemistry and physiology that occurs during addiction and while on the path to recovery.

11.4 Chemical and Pharmacological Descriptions of Addiction Episodes in Neurosciences

For convenience, this section will discuss drugs as an example of various stimuli that come the way of the neurosystem. Drugs, commonly abused substances, are structurally diverse and produce different behavioural effects in the user. Yet, all share the common feature that they can modulate the brain reward system that is fundamental to initiating and maintaining behaviours that are important for survival. It was first proposed that specific neural circuits within the brain were involved in the regulation of reward processes when studies demonstrated that reinforcing effects of commonly abused prescription opioids in rats are diminished following nerve injury and alleviation of mechanical allodynia with non-opioid analgesics do not appear to stimulate limbic dopamine pathways originating from the ventral tegmental area (VTA) (Ewan and Martin 2011). The medial forebrain bundle (MFB), which connects the VTA to the nucleus accumbens (NAc), was the site first identified in this way. Other neurotransmitter pathways projecting from the VTA and the NAc that innervate additional limbic system—for example, the amygdale and cortical areas of the brain, which are important for the expression of emotions, reactivity to conditioned cues, planning and judgement—have also been associated in reward. The dopaminergic projection has been most closely associated with reward, though the MFB consists of neurons that contain dopamine, noradrenaline and 5-hyrdoxytryptamine (5-HT).

Natural and artificial rewards (food, sex, drugs of abuse) have been shown to activate this dopaminergic pathway, also known as the mesolimbic dopamine pathway, causing an increase in dopamine levels within the NAcc (Nutt et al. 2015).

Drugs of abuse exert influence over the brain reward pathway, either by directly influencing the action of dopamine within the system or by altering the activity of other neurotransmitters that exert a modulatory influence over the mesolimbic dopaminergic pathway (Lewis 2011). γ-aminobutyric acid (GABA), opioid, serotonergic, cholinergic and noradrenergic neurotransmitter pathways have all been shown to interact at various points along the mesolimbic dopaminergic pathway and to modulate its activity. The major neurotransmitters involved in addiction are thus dopamine, serotonin, norepinephrine and opioids (Tomkins and Sellers 2001). These neurotransmitters are discussed below.

Dopamine in Addiction

Dopamine is majorly a neurotransmitter and also a hormone involved in the regulation of body functions such as behaviour, mood, weight, temperature, reproduction, sex and movement, among others. One scientific writer described dopamine as “love, lust, adultery, motivation, attention, feminism and in general dopamine is addiction” (Brookshire 2013) emphasizing its greater influence on behaviour. Dopamine is synthesized from tyrosine, which enters the neuron by active transport. In the neuronal cytosol, tyrosine hydroxylase converts tyrosine to dihydroxyphenylalanine (dopa). The enzyme aromatic L–amino acid decarboxylase, sometimes termed dopadecarboxylase, finally converts to dopamine. Dopamine is also actively transported into storage vesicles, where it is converted to norepinephrine by dopamine-hydroxylase (Gnegy 2012). Although research on African gene make up is concerned with dopamine, little research has been conducted, which is not enough for a better understanding to direct any robust interventions in the modulation of dopamine response.

Dopamine was originally considered merely a precursor to norepinephrine; however, latter studies revealed distinct regions of the CNS for dopamine and norepinephrine distribution (Gnegy 2012). Indeed, more than half the CNS content of catecholamine is dopamine and extremely large amounts are found in the basal ganglia in the caudate nucleus, the nucleus accumbens, the olfactory tubercle, the central nucleus of the amygdala, the median eminence and restricted fields of the frontal cortex. Of these connections, projections between the major dopamine-containing nuclei in the substantia nigra and ventral tegmentum and their targets in the striatum, in the limbic zones of the cerebral cortex, and in other major limbic regions have received greater attention. At the cellular level, the actions of dopamine depend on receptor subtype expression and the convergent actions of other transmitters to the same target neurons (Volkow et al. 2012). As it appears, the African race must have a significant level of dopamine activity in various environmental subjections.

The dopaminergic system is highly involved in neural reward processes and substance abuse (Nutt et al. 2015). Dopamine is released in the NAc from neurons originating in the VTA (Small et al. 2003). Neural changes results from repeated dopamine enhancement; addiction and abstention are not choices made freely and flexibly. Momentary states of dopamine enhancement, triggered by a narrow range of cues, shut down intertemporal flexibility. Brain changes that accumulate with the recurrence of this cycle send it further out of reach. Yet, addiction is not one monolithic brain state; rather, it is a sequence of transitory states underlying impulse, reflection and emotions that include embarrassment and repentance. The recursive nature of this sequence provides windows of opportunity for the present self to influence future decisions—such as the decision to quit based on fluctuations in brain state, emotion, and cognitive functioning. Addiction comprises a recurrent series of brain states underlying a recurrent set of choices, whereby habit is interspersed with unexpected opportunities for change (Lewis 2011).

In the addiction stage, the dopaminergic system recruits specific neural networks and corresponds to the level of adaptation of molecular and cellular mechanisms and environmental associations made with drug use. Drug addiction involves the ascription of distorted weights onto key elements of the neurocircuitry underlying the processing of motivationally relevant events. First, the recruitment of the mesolimbic dopamine system, which originates in the VTA and projects to extended amygdala, is required to produce the acute reinforcing properties of drugs of abuse. In contrast, the symptoms of acute withdrawal, such as negative affect and increased anxiety, are related to decreases in function of the extended amygdala system and the recruitment of brain stress circuits (Everitt and Robbins 2005).

Norepinephrine in Addiction

Norepinephrine is synthesized from dopamine by dopamine-hydroxylase, where dopamine is actively transported into storage vesicles and converted by the enzyme within the storage vesicle (Gnegy 2012). In noradrenergic neurons, the end product is norepinephrine, while in the adrenal medulla, the synthesis is carried one step further by the enzyme phenylethanolamine N-methyltransferase, which converts norepinephrine to epinephrine. The human adrenal medulla contains 80% epinephrine and 20% norepinephrine. The absence of this enzyme in noradrenergic neurons accounts for the absence of significant amounts of epinephrine in noradrenergic neurons (Rush and Geffen 1980).

Two types of adrenergic receptors (α and β) and their subtypes have been described in the CNS; all are G-protein coupled receptors (GPCRs). The β adrenergic receptors are coupled to stimulation of adenylyl cyclase activity. The *α1* adrenergic receptors are associated predominantly with neurons, while a_2 adrenergic receptors are more characteristic of glial and vascular elements. The a_1 receptors couple to G_q to stimulate phospholipase C. The a_1 receptors on noradrenergic target neurons of the neocortex and thalamus respond to norepinephrine with prazosin-sensitive, depolarizing responses due to decreases in K^+ conductances (Gnegy 2012). There is need for in-depth studies towards understanding the nature and response rate of norepinephrine among Africans from different regions of the continent and the world as exposure to different environmental and social factors would have a contribution.

Serotonin in Addiction

Serotonin (5-hydroxytryptamine or 5HT) is present in the brain as well as in the periphery. Brain serotonin has been implicated as a potential neurotransmitter in the mediation of a wide variety of phenomena in several aspects of behaviour, including sleep, pain perception, depression, sexual activity, aggressiveness, mood, behaviour, satiety and addiction. Serotonin also may be involved in temperature regulation and in the hypothalamic control of the release of pituitary hormones. Most of the serotonin in the brain is in the brainstem, specifically in the raphe nuclei; considerable amounts also are present in areas of the hypothalamus, the limbic system and the pituitary gland (Jorgensen 2007).

Dietary tryptophan is initially hydroxylated to form 5-hydroxytryptophan by tryptophan hydroxylase to form 5-hydroxytryptophan. Decarboxylation of 5-hydroxytryptophan by L-amino acid decarboxylase results in the formation of serotonin. Much of the serotonin released in the brain at synapses is taken back into the initial neuron by an active reuptake mechanism, to be released again (Ren et al. 2017). The serotonergic (5-HT) system is involved in the establishment of drug use–associated behaviours and the transition and maintenance of addiction to drugs such as cocaine, amphetamine, methamphetamine, MDMA (ecstasy), morphine/heroin, cannabis, alcohol and nicotine. There is a crucial and distinct involvement of the 5-HT system in both processes with considerable overlap between psychostimulant, opioids and alcohol. Functional model suggests specific adaptations in the 5-HT system, which coincides with the establishment of controlled drug use–associated behaviours. These serotonergic adaptations render the nervous system susceptible to the transition to compulsive drug use behaviours and often overlap with genetic risk factors for addiction, a new trajectory by which serotonergic neuro-adaptations induced by first drug exposure pave the way for the establishment of addiction (Muller and Homberg 2015). The serotonin (5-HT) neurotransmitter system provides fundamental modulatory regulation of the limbic-corticostriatal circuitry known to be vital in the development of addiction as well as the aspects of addiction that hinder recovery and contribute to relapse (Jorgensen 2007). Most of the research on serotonin in Africans is limited only to African Americans, which makes it difficult to understand its activities and responses in Africans on the African continent.

Opioid Peptides in Addiction

Opioid peptides are the most common neurotransmitters in the hypothalamus. They are far more potent than any other neurotransmitters. Three distinct families of classical opioid peptides have been identified: the enkephalins, endorphins and dynorphins (Beaumont 1983). Each family derives from a distinct precursor protein and has a characteristic anatomical distribution. These precursors—prepro-opiomelanocortin (POMC), preproenkephalin and preprodynorphin—are encoded by three corresponding genes. Each precursor is subject to complex cleavages and post-translational modifications, resulting in the synthesis of multiple active peptides (Ozaki 2016). The opioid peptides share the common amino-terminal sequence of Tyr-Gly-Gly-Phe-(Met or Leu), which has been called the opioid motif. This motif is followed by various C-terminal extensions, yielding peptides ranging from 5 to 31 residues. Endogenous opioid peptides appear to function as neurotransmitters, modulators of neurotransmission or neurohormones; the full extent of their physiological role is not completely explored. The elucidation of the physiological roles of the opioid peptides has been made more difficult by their frequent coexistence with other putative neurotransmitters within a given neuron (Mosberg et al. 1988). The genetic basis of addiction in Africa can be connected to the changes in these receptors and signal transduction system. Future studies characterizing receptors in African population is highly needed. There is a dire need among Africans living on different parts of the continent to understand how peptides of opioid nature interact with other peptides, especially over addiction episodes.

11.5 Withdrawal Symptoms in Drug Addiction

Withdrawal is a vital manifestation of dependence and motivates relapse. It is a cohesive collection of symptoms that emerge during drug deprivation and decline with either the passage of time or reinstatement of drug use, may be inadequate to explain scientific findings or fit with modern theories of addiction (Piper 2015). Withdrawal symptoms include depression, increased appetite, abdominal cramping, diarrhoea and headache. Withdrawal syndrome occurs in non-availability of the abused drug. The symptoms of withdrawals, such as craving for drugs and increased anxiety, are related to decreases in function of the extended amygdala system and the recruitment of brain stress circuits (Everitt and Robbins 2005). Coping with withdrawal symptoms is often the most challenging part of addiction cessation.

11.6 Treatment Approaches to Addictions

Pharmacological Approaches

African governments are conscious about addiction as a serious issue, right at policy formulation level. The governments of South Africa and Tanzania are just a few of many other examples that have guidelines for the treatment of addictions (URT 2013). Pharmacological approaches to addiction treatment are focused on the underlying neurotransmitters affected by addictions and are aimed at reducing drug reward or alleviating withdrawal states (Forray and Sofuoglu 2014). The components of the 5-HT system had been researched for novel targets for the development of pharmacological treatments for psychostimulant dependence, which is associated with significant deviations in dopamine neurotransmission. Two key modulators of dopamine signalling within the limbic-corticostriatal circuit are the 5-HT(2A) receptor (5-HT(2A)R) and the 5-HT(2C)R. These receptors are known to control the neurochemical and behavioural effects of psychostimulants, and in particular, the *in vivo* effects of cocaine (Bubar and Cunningham 2008). Agonist replacement therapy in the treatment of drug addiction, either in a low-dose or slow-release formulation, alleviates craving and blocks the reward effects while having little or no abuse potential of its own. D-amphetamine is used as an agonist-like medication in the treatment of amphetamine addiction. Methadone (Robertson and Daniels 2012) and nicotine (Stead et al. 2012) replacement therapy are substitution therapies for opioid and nicotine addiction respectively.

Different drugs are used to treat different withdrawal symptoms. Some of the drugs include benzodiazepines, antidepressants and clonidine. Benzodiazepines reduce anxiety and irritability. Anxiety is a common symptom of withdrawal from many drugs, including cocaine and opiates such as heroin. Benzodiazepines have a sedative effect, which helps ease alcohol withdrawals (Perry 2014). Caution should be taken as they are addictive themselves. Antidepressants help relieve depression feelings until the brain is able to produce biogenic amines. Clonidine is used to treat alcohol and opiate withdrawals; reduces sweating, cramps, muscle aches, anxiety and also stops tremors and seizures (Fresquez-Chavez and Fogger 2015).

Community-Based Approaches

National responsible gambling programme supported by industry and the community is used to achieve redress to addictions (Collins et al. 2011) by getting input from various sectors of the communities. Partnership between the academic and the industry is also another approach that is being used in some parts of Africa, including South Africa (Stein 2015).

Spiritualism

Religion is reported to be playing a central role among the African population, varying only in extents from region to region due to cultural differences (Mattis and Jagers 2001). Its role is in both treatment and preventive purposes. Religion has, for a long time, been documented to be instrumental in dealing with substance abuse pattern treatments (Chitwood et al. 2008). It has also been shown by research to play a protective role against addiction (Hodge et al. 2001; Rote and Starks 2010).

Phytotherapy

The use of herbs to treat addiction and its withdrawal symptoms has been practised in African communities for some time. A Congolese and Gabon plant called *Tabernanthe iboga* was reported to contain an alkaloid, ibogaine, which is effective against addictions (Schenberg et al. 2014; Lavaud and Massiot 2017). Most chemical dependencies are treatable with ibogaine by body cleansing and the resetting of the neurochemistry of the brain. Prolonged use of ibogaine induces serious adverse effects, including irregular cardiac rhythms (Alper et al. 2008) and sleep repression (González et al. 2018). Other plants from which ibogaine is found include *Catharanthus roseus*, which has two alkaloids of the iboga group, catharanthine and coronaridine (Lavaud and Massiot 2017). In West Africa, a plant, Voacanga Africana is also one of the plants with extracts used against psychoactivities of Indian hemp principally (Kitajima et al. 2011).

11.7 Neuroscience Research and Training in Modern-Day Africa

Modern-day neuroscience studies are considered to have been introduced and developed around 1960 in African countries, with teaching in many universities in the continent starting between the years 1960 and 1970 (El-Khamlichi 1996). Folk medicine practice and African physiotherapy against addictions has so much informed modern research and studies on plant-based chemical compounds to come up with conventionally optimized drugs. Despite research being carried out to find treatment agents against addictions, gaps still remain, particularly in the synthesis of derivatives of previously known active molecules. For example, catharanthine and coronaridine are yet to be biosynthesized (Lavaud and Massiot 2017; Kries and O'Connor 2016). The active principle in Voacanga Africana of West Africa was found to be voacangalactone, which acts as an antagonist to cannabinoid receptor CB_1 in hemp addictions (Kitajima et al. 2011).

African research in neurosciences, including addictions to substance abuse, has been very low. A systematic review of research in the field for two decades (1995–2015) (Quansah and Karikari 2016) reported a lack of clinical and experimental research data, which shows that most of the research being conducted in Africa in neurosciences are survey-based. About 60% of the articles retrieved in the same research were reported to have been published between 2008 and 2015, which is a good indicator of the development and growing interest in more recent times.

There is generally both a lack of interest and low training opportunities in Africa in the field of neurosciences (Karikari et al. 2016) which significantly limits proper ways of handling addictions and other neuro-diseases. Strides being made in Ghana are still crippled by lack of trained neuroscientists (Quansah and Karikari 2016). Currently, various disciplines in neurosciences have been bundled up together with the facilitation of professional networks in the field such as the Society of Neuroscientists of Africa (SONA) and the Southern African Neuroscience Society (SANS) (Howells and Womersley 2018).

Neuroscience studies in Africa are envisaged to sustainably progress well in future with proper engagement and communication amongst stakeholders amidst various challenges (Karikari et al. 2016). The use of implants to counter addictions in South Africa, for example, indicates the positive direction in which African science is heading.

In Nigeria, animal models and herbal research have been conducted for interventions in various neurological and neuropsychotic disorders (Akinyemi et al. 2018). Africa's ability to undertake high-impact research in neurosciences is hindered by lack of funding, facilities and technology (Awenva et al. 2010). Today, most of the following countries have registered at least 20 research publications in neurosciences by 2017 from the south to the northern part of Africa: South Africa, Tanzania, Kenya, Cameroon, Nigeria, Morocco, Algeria and Tunisia (Russell 2017). This is a good indication of the interest African researchers have in the topic, but more can be done.

11.8 Conclusion

Africa has high cases of neurological and neuropsychiatric disorders, including addictions. The impact that these cases have on the lives and socio-economic development of individuals and communities is significantly high. Knowing that these disorders are genetic and environment-dependent, it is tricky to manage them without understanding neuroscience mechanisms of individual genetic sets as well as individual environmental dispositions. Unfortunately, poor resources and governance impede high-impact scientific research, training and policy formulations to make significant contributions towards managing addictions, in particular. In-depth studies are required for customized groups of people and regions of Africa to make meaningful scientific impact. This work recommends deliberate budgetary allocations specifically to develop areas in this field of science through funding various research projects and establishment of graduate academic and industrial study programmes. More collaborative interdisciplinary work in this field is sure to make a difference. The research has to focus on the genetic basis of addiction in Africa. Other ways through which a robust intervention in the field can be achieved in Africa is by deliberate capacity-building policies and programmes that should be monitored and reviewed regularly. Early stage scientists can be engaged by professionals and drilled in specific research areas to improve approaches as well as techniques suitable for the context.

Early childhood interventions, mainly in the prevention of addictions and determination of early signs and traits towards addictions as alarms for possible interventions, need to be instituted in a formal way. This could be by incorporating the filed-in mainstream early learners' school curriculum, community engagement and civic education. Community engagement is one of the best ways through which locally effective addiction therapies can be understood and perfected in a professional way for better and sustainable outcomes.

In schools, "Watch-buddy" approach could also help detect early traits towards addictions. This is an approach where students can have accountability partners who can be working together with a third party, on mutual consent, to assist one another against addictive paths.

Lastly, a formidable multi-disciplinary approach amongst scientists will help in finding customized solutions in both research and direct victim support.

References

Akinyemi, A.J., G. Oboh, O. Ogunsuyi, A.O. Abolaji, and A. Udofia. 2018. Curcumin-Supplemented Diets Improve Antioxidant Enzymes and Alter Acetylcholinesterase Genes Expression Level in Drosophila Melanogaster Model. *Metabolic Brain Disease* 33: 369–375.

Alper, K.R., H.S. Lotsof, and C.D. Kaplan. 2008. The Ibogaine Medical Subculture. *Journal of Ethnopharmacology* 115: 9–24.

Awenva, A.D., U.M. Read, A.L. Ofori-Attah, V.C. Doku, B. Akpalu, A.O. Osei, and A.J. Flisher. 2010. From Mental Health Policy Development in Ghana to Implementation: What Are the Barriers? *The African Journal of Psychiatry* 13: 184–191.

Beaumont, A. 1983. Putative Peptide Neurotransmitters: The Opioid Peptides. *International Review of Experimental Pathology* 25: 279–305.

Bettinardi-Angres, K., and D.H. Angres. 2010. Understanding the Disease of Addiction. *Journal of Nursing Regulation* 1 (2): 31–37.

Blanckenberg, J., S. Bardien, B. Glanzmann, N.U. Okubadejo, and J.A. Carr. 2013. The Prevalence and Genetics of Parkinson's Disease in Sub-Saharan Africans. *Journal of the Neurological Sciences* 335: 22–25.

Brookshire, B. 2013. *Dopamine Is ____. Is it love? Gambling? Reward? Addiction?* [Online]. Available: http://www.slate.com/articles/health_and_science/science/2013/07/what_is_dopamine_love_lust_sex_addiction_gambling_motivation_reward.html. Accessed 7 Jun 2018.

Bubar, M.J., and K.A. Cunningham. 2008. Prospects for Serotonin 5-HT2R Pharmacotherapy in Psychostimulant Abuse. *Progress in Brain Research* 172: 319–346.

Chitwood, D.D., M.L. Weiss, and C.G. Leukefeld. 2008. A Systematic Review of Recent Literature on Religiosity and Substance Use. *Journal of Drug Issues* 38: 649–652.

Collins, P., D.J. Stein, A. Pretorius, H. Sinclair, D. Ross, G. Barr, A. Hofmeyr, C. Sharp, D. Spurrett, J. Rousseau, G. Ainslie, A. Dellis, H. Kincaid, and N. Bak. 2011. Addressing Problem Gambling: South Africa's National Responsible Gambling Programme. *South African Medical Journal* 101: 722–723.

Elhadi, A.M., S. Kalb, L. Perez-Orribo, A.S. Little, R.F. Spetzler, and M.C. Preul. 2012. The Journey of Discovering Skull Base Anatomy in Ancient Egypt and the Special Influence of Alexandria. *Neurosurgical Focus* 33 (2): E2.

El-Khamlichi, A. 1996. African Neurosurgery. 1: Historical Outline. *Neuro-Chirurgie* 42: 312–320.

Everitt, B.J., and T.W. Robbins. 2005. Neural Systems of Reinforcement for Drug Addiction: From Actions to Habits to Compulsion. *Nature Neuroscience* 8: 1481–1489.

Ewan, E.E., and T.J. Martin. 2011. Rewarding Electrical Brain Stimulation in Rats After Peripheral Nerve Injury: Decreased Facilitation by Commonly Abused Prescription Opioids. *Anesthesiology* 115: 1271–1280.

Forray, A., and M. Sofuoglu. 2014. Future Pharmacological Treatments for Substance Use Disorders. *British Journal of Clinical Pharmacology* 77: 382–400.

Fresquez-Chavez, K.R., and S. Fogger. 2015. Reduction of Opiate Withdrawal Symptoms With Use of Clonidine in a County Jail. *Journal of Correctional Health Care* 21: 27–34.

George-Carey, R., D. Adeloye, K.Y. Chan, A. Paul, I. Kolcić, H. Campbell, and I. Rudan. 2012. An Estimate of the Prevalence of Dementia in Africa: A Systematic Analysis. *Journal of Global Health* 2: 1–13.

Gibbons, F.X., M. Gerrard, M.J. Cleveland, T.A. Wills, and G. Brody. 2004. Perceived Discrimination and Substance Use in African American Parents and Their Children: A Panel Study. *Journal of Personality and Social Psychology* 86: 517.

Gnegy, M.E. 2012. Catecholamines A2. In *Basic Neurochemistry*, ed. G.J. Siegel, R.W. Albers, and D.L. Price, 8th ed. New York: Academic Press.

González, J., J.P. Prieto, P. Rodríguez, M. Cavelli, L. Benedetto, A. Mondino, M. Pazos, G. Seoane, I. Carrera, C. Scorza, and P. Torterolo. 2018. Ibogaine Acute Administration in Rats Promotes Wakefulness, Long-Lasting REM Sleep Suppression, and a Distinctive Motor Profile. *Frontiers in Pharmacology* 9: 1–11.

Guarnotta, E. 2018. *A Guide to Addiction and Recovery for African Americans*. The Right Addiction Recovery Center.

Hodge, D.R., P. Cardenas, and H. Montoya. 2001. Substance Use: Spirituality and Religious Participation as Protective Factors Among Rural Youths. *Social Work Research* 25: 153–160.

Howells, F.M., and J.S. Womersley. 2018. Progress in Neuroscience in Africa: Editorial. *Metabolic Brain Disease* 33: 357–358.

Jorgensen, H.S. 2007. Studies on the Neuroendocrine Role of Serotonin. *Danish Medical Bulletin* 54: 266–288.

Karikari, T.K., and J. Aleksic. 2015. Neurogenomics: An Opportunity to Integrate Neuroscience, Genomics and Bioinformatics Research in Africa. *Applied & Translational Genomics* 5: 3–10.

Karikari, T.K., N.A. Yawson, and E. Quansah. 2016. Developing Science Communication in Africa: Undergraduate and Graduate Students Should be Trained and Actively Involved in Outreach Activity Development and Implementation. *Journal of Undergraduate Neuroscience Education* 14: E5–E8.

Kitajima, M., M. Iwai, R. Kikura-Hanajiri, Y. Goda, M. Iida, H. Yabushita, and H. Takayama. 2011. Discovery of Indole Alkaloids with Cannabinoid CB1 Receptor Antagonistic Activity. *Bioorganic & Medicinal Chemistry Letters* 21: 1962–1964.

Kries, H., and S.E. O'Connor. 2016. Biocatalysts from Alkaloid Producing Plants. *Current Opinion in Chemical Biology* 31: 22–30.

Lavaud, C., and G. Massiot. 2017. The Iboga Alkaloids. In *Progress in the Chemistry of Organic Natural Products*, ed. A. Kinghorn, H. Falk, S. Gibbons, and J. Kobayashi. Cham: Springer.

Lewis, M.D. 2011. Dopamine and the Neural "Now": Essay and Review of Addiction: A Disorder of Choice. *Perspectives on Psychological Science* 6: 150–155.

Mattis, J.S., and R.J. Jagers. 2001. A Relational Framework for the Study of Religiosity and Spirituality in the Lives of African Americans. *Journal of Community Psychology* 29: 519–539.

Mosberg, H.I., R.C. Haaseth, K. Ramalingam, A. Mansour, H. Akil, and R.W. Woodard. 1988. Role of Steric Interactions in the Delta Opioid Receptor Selectivity of [D-Pen2, D-Pen5]Enkephalin. *International Journal of Peptide and Protein Research* 32: 1–8.

Muller, C.P., and J.R. Homberg. 2015. The Role of Serotonin in Drug Use and Addiction. *Behavioural Brain Research* 277: 146–192.

Nestler, E.J. 2013. Cellular Basis of Memory for Addiction. *Dialogues in Clinical Neuroscience* 15: 431–443.

Nutt, D.J., A. Lingford-Hughes, D. Erritzoe, and P.R. Stokes. 2015. The Dopamine Theory of Addiction: 40 Years of Highs and Lows. *Nature Reviews. Neuroscience* 16: 305–312.

Ozaki, M. 2016. Characteristics and Functional Roles of Opioids Originally Present in Vivo. *Yakugaku Zasshi* 136: 591–605.

Perry, E.C. 2014. Inpatient Management of Acute Alcohol Withdrawal Syndrome. *CNS Drugs* 28: 401–410.

Piper, M.E. 2015. Withdrawal: Expanding a Key Addiction Construct. *Nicotine & Tobacco Research* 17: 1405–1415.

Quansah, E., and T.K. Karikari. 2016. Neuroscience-Related Research in Ghana: A Systematic Evaluation of Direction and Capacity. *Metabolic Brain Disease* 31: 11–24.

Qureshi, M.M., and D. Oluoch-Olunya. 2010. History of Neurosurgery in Kenya, East Africa. *World Neurosurgery* 73: 261–263.

Ren, L.Q., M. Chen, H. Hultborn, S. Guo, Y. Zhang, and M. Zhang. 2017. Heterogenic Distribution of Aromatic L-Amino Acid Decarboxylase Neurons in the Rat Spinal Cord. *Frontiers in Integrative Neuroscience* 11 (31): 1–19.

Robertson, J.R., and A.M. Daniels. 2012. Methadone Replacement Therapy: Tried, Tested, Effective? *The Journal of the Royal College of Physicians of Edinburgh* 42: 133–138.

Rote, S.M., and B. Starks. 2010. Racial/Ethnic Differences in Religiosity and Drug Use. *Journal of Drug Issues* 10: 729–754.

Rush, R.A., and L.B. Geffen. 1980. Dopamine Beta-Hydroxylase in Health and Disease. *Critical Reviews in Clinical Laboratory Sciences* 12: 241–277.

Russell, V.A. 2017. Notes on the Recent History of Neuroscience in Africa. *Frontiers in Neuroanatomy* 11: 1–8.

Schenberg, E.E., M.A.C. Comis, B.R. Chaves, and D.X. Da-Silveira. 2014. Treating Drug Dependence with the Aid of Ibogaine: A Retrospective Study. *Journal of Psychopharmacology* 28: 993–1000.

Sevenzo, F. 2015. Drug Addiction in Africa. *The Africa Report*, 20 May 2015.

Small, D.M., M. Jones-Gotman, and A. Dagher. 2003. Feeding-Induced Dopamine Release in Dorsal Striatum Correlates with Meal Pleasantness Ratings in Healthy Human Volunteers. *NeuroImage* 19: 1709–1715.

Stead, L.F., R. Perera, C. Bullen, D. Mant, J. Hartmann-Boyce, K. Cahill, and T. Lancaster. 2012. Nicotine Replacement Therapy for Smoking Cessation. *Cochrane Database of Systematic Reviews* 14: 11.

Stein, D.J. 2015. Academic-Industry Partnerships in Alcohol and Gambling: A Continuum of Benefits and Harms. *Israeli Journal of Psychiatry and Related Sciences* 52: 81–84.

Tomkins, D.M., and E.M. Sellers. 2001. Addiction and the Brain: The Role of Neurotransmitters in the Cause and Treatment of Drug Dependence. *CMAJ* 164: 817–821.

UNODC. 2004. *Conducting Effective Substance Abuse Prevention Work Among the Youth in South Africa*. Pretoria: United Nations Office on Drugs and Crime.

URT. 2013. *Standard Treatment Guidelines and Essential Medicines List*. Dar-es-salaam: Ministry of Health and Social Welfare, The United Republic of Tanzania.

Van-Niekerk, J.P. 2011. Addiction. *South African Medical Journal* 101: 673.

Volkow, N.D., G.J. Wang, J.S. Fowler, and D. Tomasi. 2012. Addiction Circuitry in the Human Brain. *Annual Review of Pharmacology and Toxicology* 52: 321–336.

Wallace, J.M., and J.R. Muroff. 2002. Preventing Substance Abuse Among African American Children and Youth: Race Differences in Risk Factor Exposure and Vulnerability. *The Journal of Primary Prevention* 22: 235–261.