

Addiction

ISSUE 9



SureScreen Diagnostics Ltd
Cutting Edge Biotechnology

Addiction isn't just about drink and drugs, or the images that come to mind of drunks, beggars, prostitutes and organised crime etc. Addiction is a disease of any recurring misuse of **any activity** which has harmful consequences to the individual's health, mental state or social life. This may include drugs, foods/overeating, gambling, sex/pornography, exercise/thrill-seeking sports, shopping, video games/internet addiction, self-harm/cutting, vandalism, or even religion. In this bulletin we will focus on **drug and alcohol** addiction.

Types of addiction

The DSM-IV TR psychiatric manual defines drug addiction as "substance dependence":

"Substance dependence may be diagnosed, when an individual persists in use of alcohol or other drugs despite problems related to use of the substance. Compulsive and repetitive use may result in tolerance to the effect of the drug and withdrawal symptoms when use is reduced or stopped. This, along with substance abuse are considered substance use disorders..."

There are two types of substance dependence which are of interest to drug researchers and drug workers:

Physical dependence is characterised by a clear-cut abstinence syndrome, which occurs when the removal of drug is accompanied by **physical withdrawal symptoms**, such as cramps, sweating, increased heart rate, dilated pupils, pain, excitement, hallucinations, seizures, etc. Physically addicting drugs like opiates, benzodiazepines, barbiturates, alcohol and nicotine may initially induce pleasure, but that changes over time because of **tolerance** (having to increase the dose to get the same effect). Avoiding the unpleasant withdrawal symptoms, tolerance causes compulsive use.

Nicotine's initial pharmacological effects, for example, quickly give way to a rapid tolerance, and so any subsequent "pleasure" derived from the drug thereafter consists mainly in alleviating its own withdrawal symptoms. In the case of opiates like heroin, this is extremely uncomfortable, but rarely life-threatening, whilst in the case of depressant drugs like alcohol, barbiturates or benzodiazepines, can lead to seizures and even death. Some non-addicting medicines like cortisone, beta blockers and most antidepressants (which are not designed to be euphoricants) can still cause tolerance, physical dependence, and withdrawal symptoms if abruptly discontinued.

Psychological dependence is a more complex phenomenon than physical dependence, and has much more importance in the genesis of compulsive drug-taking. It occurs when the drug produces psychological reinforcement, and its removal is accompanied by impaired psychological function such as cravings, irritability, anger, insomnia, anxiety, difficulty concentrating, depression, anorexia, etc. Most psychologically-addicting drugs, including heroin, morphine, cocaine, amphetamines, alcohol and nicotine produce a **reward-reinforcement** effect in the dopaminergic system of the brain (or its accessory structures), which, when suspended, cuts off the "anti-stress" neurotransmitter dopamine (DA), and produces unpleasant withdrawal symptoms. For this reason experimentally addicted rats will press a lever up to 2000 times per hour for stimulation of certain brain areas that release dopamine. But because the brain, like the body, exists in a natural state of *homeostasis* (acting to minimise the effect of external changes), chronic artificial elevation of DA by alcohol, or recreational drugs (or even brain electrodes), eventually results in a reflex decrease in the number, size and sensitivity of brain DA receptors available in a process known as **down-regulation**. This makes dopamine neurones less excitable in response to the drug, and leads to **tolerance**. By this time the brain may have become so **dependent** on the drug that it has stopped producing its own natural neurotransmitters, and started producing opposing, or antagonistic substances to minimise the effects of the drug. When the addictive substance is then withdrawn, the brain cannot restart its functions, leading to the emergence of unpleasant symptoms known as psychological withdrawal symptoms, inverse to the pleasure response.

What causes addiction?

Addiction is a **multifactorial disease**, caused by a complex interplay of genetic, neurochemical, medical, psychosocial, cultural and spiritual factors. How quickly addiction becomes established depends on the substance used, how often it is taken, how it is taken, the intensity of the pleasure it produces, and probably most importantly the individual's genetic, medical and psychological susceptibility to use again. Some individuals may show signs of addiction from the first moment of exposure to a particular substance, whereas others may use them socially without ever becoming addicted to them. Addiction can rarely be cured, it can only be controlled, but the desire and risk of relapse remain. These controls are nowadays called 'harm reduction measures'.

1. Drug choice and addiction

Drugs known to cause addiction include **illegal drugs** like amphetamine, methamphetamine, cocaine, crack cocaine, heroin as well as some **prescription** (POM) or **over-the-counter** (OTC) drugs such as the sedative/hypnotic barbiturates, tranquillizers like benzodiazepines, methaqualone, analgesics like morphine and codeine, oxycodone, hydromorphone, fentanyl, pethidine, methadone and **recreational substances** like alcohol, caffeine and nicotine which, incidentally, are the most common addictions in society.

Some drugs, however, are more addictive than others. Alcohol and codeine, for instance, typically require repeated exposures to addict their users, while drugs like heroin or crack cocaine can create dependence after first use. **Generally, the most addictive drugs are those which act the quickest and produce the strongest euphoria. The most addictive drugs create the most intensive cravings, and withdrawal symptoms.**

"Addiction isn't just about drugs and alcohol."

Methamphetamine ("crystal meth", "ice" "crank" etc), for instance, is probably the most potent, long-acting and hence habit-forming stimulant on the black market, and according to recent BBC news reports, has superseded heroin and crack in popularity in the **"Golden Triangle"** drug-producing areas of Thailand, Burma and Laos. Although it is not physically addictive it can be **smoked** and produces a rapid exhilaration and intense **euphoria** which gives it huge psychological addiction potential.

Nicotine is an exception to the "pleasure" rule; its reputation as one of the most addictive drugs is not so much owed to its pleasure-inducing action (often described as a mild "calming euphoric effect"), as it is the **rapid tolerance and intense cravings** that develop to its milder effects. Tolerance almost immediately increases the dose required to achieve the desired effect, which in turn increases the likelihood of addiction. Once hooked, smokers find themselves cheated of any appreciable pleasure, and stuck in a vicious craving cycle, smoking only to allay the onset of withdrawal symptoms. No wonder some heroin addicts rate the urge to smoke as equal to or stronger than the urge to take heroin!

The addiction potential of a particular drug will also depend on how quickly the body physically reacts to remove it. The **biological half life** of a drug is the time taken for the amount of the drug in the body to decrease by 50%. **Generally the shorter the half life, the quicker the development of tolerance, and the sooner the withdrawal symptoms are felt.** For example, drugs like heroin and morphine with half lives of 4-6 hours require administration several times a day, and have a greater addiction potential than their longer lasting counterpart methadone whose half life is 30 hours. They also produce more severe withdrawal symptoms, which unlike methadone's long withdrawal, their resolution is much quicker. Nicotine's very short half life of less than 2 hours requires even more frequent administration to stop withdrawal.

Neurobiology of addiction

Addiction may arise because of low DA activity (hypodopaminism) in the

final “pleasure-reward” circuit of the brain. Hypodopaminism can be chemically induced, by recreational drugs and other substances or be an inherited genetic problem (which paradoxically often leads into drug-seeking behaviour to correct the problem). The former case involves a number of discrete neurobiological and biochemical adaptations in the mesolimbic system.

Initial exposure to drugs will cause DA-responsive cells in the “pleasure-reward” pathway of the mesolimbic system to raise levels of a signalling molecule cyclic AMP (cAMP), which in turn activates the genetic transcription factor cyclic AMP response element binding protein (CREB). Immediately after a drug “high”, CREB protein levels rise and cut off DA release, which temporarily inhibits the pleasure-reward circuit. This neurobiological safeguard basically sets a “ceiling effect” to how much pleasure-reward the drug can give between “hits”. Chronic repeated drug use however, causes a *sustained* activation of CREB which, accompanied by the proliferation of “neuroadaptive” N-methyl d-aspartate (NMDA)-glutamate receptors, dampens the pleasure-reward circuitry, inducing **tolerance** to the effects and all other natural goal-motivated rewards, rendering the addict depressed, unmotivated and disinterested in their surroundings. If the addict abstains, his CREB levels will return to normal, and his mesolimbic system will reset. This should, theoretically, be the end of the problem. But as any addict will tell you, stopping is easier than abstaining.

Even though CREB is switched off after a few days of abstinence, it doesn't explain the chronic grip that some drugs have over the brain. Certain brain alterations can cause addicts to return to a substance after years or even decades of abstinence. For instance, if the drug supply is disconnected from an animal dispenser, addicted monkeys continue to press its lever at a high rate, and it takes months for the response to be extinguished, implying that in monkeys, as in man, the reinforcing effect of the drug greatly outlasts the duration of the physical abstinence syndrome. This is owed to the phenomenon of **sensitisation**, which is a process that makes the addict's brain more sensitive to a particular drug long term. It involves the strengthening of learned drug-associated behaviours at the expense of adaptive responses to natural rewards like food, sex or a job well done.

“addicts take drugs to feel normal.”

The neurobiological process underlying sensitisation is thought to involve increased expression of the “neuroadaptive” NMDA-glutamate receptor which governs the brain process of “learning” to become more (or less) sensitive to a drug over time, and two genetic transcription factors delta FosB and G-protein signalling 9-2 (RGS 9-2) proteins, responsible for long term molecular changes in the pleasure-reward circuit. Whilst altered glutamate sensitivity strengthens the neuronal pathways that link memories of drug-taking experiences (particularly the amygdala which is the brain's seat of emotional memories) with high reward, they feed the desire to seek the drug. FosB and RGS 9-2 go to work sensitising the mesolimbic system's VTA and NA to their inputs. As long as CREB activity is high, tolerance to the drug dominates, but as soon as the addict abstains, CREB levels decline and the hardwired effects of sensitisation take over leading to cravings and drug seeking behaviour. At this stage even the sight of drug paraphernalia or familiar sights, sounds and smells associated with past drug use can trigger pleasurable emotional memories in the amygdala and cause relapse. Interestingly, experimental animals lacking the RGS 9-2 transcription factor show a lack of responsiveness to cocaine and amphetamines and don't seem to get addicted. Their brains literally don't “learn” to become addicted.

2. Neurochemical factors and addiction

Natural or genetic hypodopaminism consists of neurochemical factors predisposing a first time user to addiction. They are thought to involve a breakdown in the complex cascade of events leading to the activation of the final common “pleasure-reward pathway” in the brain's mesolimbic system which starts in the ventral tegmental area (VTA), and ends in the nucleus accumbens (NA) involving several neurotransmitters and neuro-anatomical structures.

The firing of the “pleasure reward” pathway begins outside in the “starter motor area” of the brain's hypothalamus with the activation of serotonin (5-HT) releasing neurones. These neurones project to the precipice of the reward pathway at the VTA where liberation of 5-HT triggers the release of “amplifier” neurones containing one of the brain's natural pain-killers methionine-enkephalin (ME). When this reaches a critical point it “lifts the brake” of the inhibitory gamma-aminobutyric acid neurones, originating in the Substantia Nigra's A9 region, which ordinarily prevent the release of dopamine (DA) from the VTA. The liberation of DA that follows and its final interaction with D-2 receptors on the cell bodies of neurones at the NA, produces a pleasure-reward-reinforcement effect, which results in feelings of well-being, satisfaction and stress reduction. This cascade can

be polygenically faulty **at any, or all** of its four levels such as the 5-HT neurones of the “starter motor” area of the hypothalamus, the “amplifier system” of the ME neurones, the “braking system” of the GABA neurones, or the DA neurones of the final “pleasure-reward” circuit of the mesolimbic system.

3. Genetic factors and addiction

The most common defect to the cascade system is a genetic loss of sensitivity and numbers of dopamine D-2 receptors (hypodopaminergic trait) in the final segment of the “pleasure-reward” pathway; known as the Tac A1 allele. Other genetic polymorphisms like the VNTR intron 1 mutant, actually slow down the dopamine manufacturing enzyme Tyrosine hydroxylase (TH), leading to lowered transmitter levels, whereas the SLC6A3-9 mutant affects the dopamine transporter, impairing dopamine release. The A48G, S9G and VNTR (tandem repeat in exon 3) mutants affect other important classes of DA receptors.

The “starter motor” area of the 5-HT neurones can also be adversely affected by the same genetic polymorphisms, such as the L279 mutant which damages the 5-HT manufacturing enzyme Tryptophan Hydroxylase, and at least two 5-HT transporter mutants which impair transmitter release. 5-HT receptor defects are as varied as the receptor subclass themselves and include the G861C, T102C, G1438A, C238 and P158 mutants.

The ME “amplifier system” of the VTA can be damaged by defects to the u-opioid receptor and the GABA “braking mechanism” by multiple genetic polymorphisms of its receptor subunits too numerous to list here. (For a good review see Tyndale RF, *Genetics of alcohol and tobacco use in humans* Ann Med 2003, 35: 94-121).

One or more interruptions to this complex cascade lead to a dulling of the final reward pathway and this results in an inability to feel pleasure known as **anhedonia**, often observed in established addicts. It manifests in an form of sensory deprivation of the brain's pleasure mechanism which produces a biochemical inability to derive reward from ordinary, everyday, activities. Drug researchers call it **Reward Deficiency Syndrome (RDS)**. Some individuals can suffer with it all their lives never knowing why they don't feel “normal”. When the levels of dopamine in the VTA or the number of receptors in the NA are genetically below par in this way, symptoms of anxiety, anger, fear, impulsiveness, compulsiveness, substance craving and the behavioural rituals which alleviate these negative emotions become manifest in the personality. Substance-seeking behaviour which temporarily restores dopamine levels in the mesolimbic system and alleviates associated unpleasant emotions is often the result. **These addicts take drugs to feel normal.**

Drug addiction and alcoholism are heavily determined by these genetic factors. Back in the 50s the American psychologist L. Mirone found that, given a choice, certain mice preferred alcohol to water. More recently this research has led to the inbreeding through successive generations of an alcohol-preferring C57 strain mouse which tends to confirm that alcoholism has a genetic basis. Alcoholism is also **4-5 times more common in the biological children of alcoholic parents** than in those of non-alcoholic parents, and 3 times as common, even when the child is adopted to non-alcoholic parents early in life. All of this tends to be confirmed by the latest genetic research which shows that 69% of alcoholics carry the Tac A1 allele of the D-2 receptor gene, as compared with 20% of non-alcoholics. Parental alcoholism is also associated with an increased tendency toward drug abuse in the children. Likewise about 52% of cocaine addicts have the Tac A1 allele as compared with only 21% of non-addicts. This figure rises strikingly to 87% if the individual had an alcoholic or drug-using parent who used high potency cocaine and a history of childhood conduct disorder.

Genetic polymorphisms are not always bad and can sometimes be beneficial. Orientals are less likely to develop alcoholism than their western counterparts because around 90% of them possess a mutant alcohol dehydrogenase isoenzyme (ADH2/2), which breaks down alcohol into Acetaldehyde (AH) 30-40% faster than their western counterparts. At least 40-50% of them also possess a mutant Aldehyde dehydrogenase (ALDH2/1) enzyme which can only break down the AH very slowly. The result is an accumulation of AH and an unpleasant flushing reaction similar to that produced by the alcoholic prescription drug antabuse™, which deters them from drinking to excess and developing alcoholism.

Full blown alcoholics on the other hand may present with one or more overlapping biotypes each with its own pattern of drink abuse.

Alcohol Biotypes

While most people drink alcohol occasionally and many drink it regularly there are some who become dependent on it and frequently descend into alcoholism. A person is considered to be dependent on alcohol when they have experienced:

- A strong urge to drink
- Difficulty controlling drinking
- Physical withdrawal symptoms
- A growing tolerance to alcohol
- General neglect of other activities
- Persistent drinking despite it causing harm

Problem drinking occurs when they drink enough to cause physical or psychological harm, but without being dependent. Currently, alcohol misuse is defined as 60 grams of alcohol or more each day. Alcohol affects people in different ways, depending on their biotype:

Biotype 1:

The TH1Q biotype is lacking liver isoenzymes which otherwise encourage the accumulation of the drink-deterrant AH. Overtime, their runaway drinking habits produce more AH than the brain can handle, and it condenses with neurotransmitters to yield addictive morphine-like substances called tetrahydroisoquinolines (THIQs) and anxiety-provoking tetrahydro-beta-carbolines (THBCs), keeping locked into an energetic anxious-addictive cycle.

These are the big drinkers who can consume alcohol all day, and who stay on a high with little signs of inebriation or negative effects. They have a high tolerance for alcohol and after many years of drinking are more prone to develop liver problems than psychiatric symptoms.

Biotype 2:

The allergic-addicted biotype is addicted to the grapes, grains, cereals and "congeners" (fermentation byproducts) in alcohol responsible for liberating his brain's stores of natural opioids, often at the cost of volatile drunken behaviour and toxic hangovers.

Often arising from Northern European or American Indian ancestors, this category is made up of the typical "bad-starters" who learn how to drink. They are often moody, changeable and unpredictable alcoholics who experience very bad hangovers and who may become socially disruptive, engaging in fights and arguments, dangerous driving, irrational or bizarre behaviour and even criminal acts after drinking.

Biotype 3:

The PGE1 deficient biotype suffers with lifelong depression resulting from a genetic shortage of the neurotransmitter prostaglandin E1 (PGE1). Alcohol temporarily banishes depression by liberating PGE1 but this is followed by rebound and often suicidal depression when building up a tolerance to the drug.

Often arising from Scottish, Welsh, Irish, and Scandinavian ancestors this category is made up of lifelong sombre, introverted and depressed individuals who visibly cheer up after drinking. They drink to banish their depression and may become suicidal once a tolerance builds up to the effects of the drug.

Biotype 4:

The hypoglycaemic biotype is addicted to the sugars in alcohol because the body produces too much insulin which starves his brain of the glucose it needs. Alcohol temporarily gives him a lift before his body overreacts with reflex hypoglycaemia and symptoms of light-headedness, spaciness, confusion, weakness, sleepiness and lack of co-ordination, resembling acute alcohol intoxication (even at low intakes).

This category is made up of individuals who cannot handle too much alcohol and who despite feeling a temporary increase in well-being after a drink or two, quickly show signs of neuroglycopenia (brain glucose starvation) resembling intoxication.

Biotype 5:

The dopamine deficient biotype brings us back to carriers of the A1 allele with RDS who are not sufficiently rewarded by stimuli that normal people find satisfying or calming. It tends to be made up of risk takers, gamblers, sexually promiscuous, compulsive overeaters, drug takers, and of course alcoholics who possess a lifelong propensity for antisocial behaviour, conduct disorders, violent behaviour, and criminal tendencies.

This category is made up of people who may possess a general lifelong genetic propensity for antisocial behaviour, conduct disorders, violent behaviour and criminal tendencies. Many prisoners and re-offenders will probably fall into this category.

4. Brain damage and addiction

Some researchers believe that addiction as a disease may also involve brain damage leading to a failure of the higher rational inhibitory centres in the brain, like the orbitofrontal cortex, to send "stop" signals to the instinctive emotional lower brain centres involved in the generation of pleasure-reward responses; such as the mesolimbic system and the seat of

emotional memories the amygdala. Experimentally depressed animals, for instance, will forgo food, sleep and sex for continued access to a lever that administers psychoactive drugs which tends to indicate a failure in the higher brain centres to delay gratification for more important goal driven behaviour. Brain imaging has confirmed this in human cocaine addicts who have decreased activity, as compared with non-addicts, in the same area of the pre-frontal cortex in response to the presentation of stimuli associated with natural rewards. This explains the chaotic lives led by some addicts.

5. Medical disorders and addiction

Psychiatric disorders:

Statistically a greater number of addicts present with psychiatric disorders than non-addicts. Anxious individuals and atypical depressives may become psychologically dependent on alcohol or, worse still, prescription tranquillizers for their confidence-enhancing properties before becoming physically hooked. They may also **resort to sugar and carbohydrate bingeing for a mood boost** (many addicts binge on pizza), and by stimulating the release of insulin from the pancreas to withdraw the larger amino acids from the blood stream. This allows the selective build up of l-tryptophan, and hence the body's natural antidepressant, Serotonin (5-HT) in the brain. Crude **"self-medication"** in this way can often mean the beginning of addiction. Stressed-out individuals also tend to convert their DA reserves into the stress transmitter Norepinephrine (NE) too rapidly, which has the twofold effect of releasing the master stress hormone corticotropin-releasing factor (CRF) and lowering DA levels (hypodopaminism) associated with drug-seeking behaviour. In experimentally stressed rats, CRF blockers and CRF receptor antagonists decrease the self-administration of addictive substances. Both hyperactive boys and anorexic girls may also run the risk of stimulant abuse in later life to tackle the Tac 1A allele-associated hypodopaminism in the former case and as a misbegotten attempt to lose weight in the latter.

"Alcohol affects people in different ways, depending on their biotype."

Hypoglycaemia:

Individuals who suffer with poor blood glucose control (hypoglycaemia) have lower levels of brain 5-HT in their hypothalamus (which we have seen is involved in the final "pleasure-reward" circuit), and are more likely to develop carbohydrate addiction and alcoholism than those who don't. Because they tend to overproduce insulin (hyperinsulinism) and suffer with low blood glucose symptoms of irritability, tiredness, confusion, disorientation, forgetfulness and depression after eating sucrose or refined carbohydrates (insulin shock), hypoglycaemics quickly learn that **a sugary snack or glass of beer can temporarily raise their blood sugar and bring their neuroglycopenic (glucose-starved) brain back to life**. According to 6-hour glucose tolerance testing, between 70-90% of alcoholics are hypoglycaemic, many of whom will have unconsciously started drinking for a sugar fix. Unfortunately animal studies show that even repetitious non-drug rewards like sucrose consumption (or excessive wheel running in laboratory mice) raises levels of the "addiction protein" delta FosB in the brain's NA, leading to the development of sensitisation and possibly addiction to a range of rewarding stimuli. Unlike a high-protein snack, which gently raises blood sugar in a sustainable way, both **sugar and alcohol can be especially addictive to hypoglycaemics**.

Adrenal insufficiency:

This can often be the start of caffeinism, smoking or more serious stimulant abuse. Individuals who live fast-paced, high stress, fear-based lifestyles running on **"emergency mode"** all the time can eventually start to experience adrenal burnout associated with low secretion of the stress hormones cortisol, adrenaline and a host of unpleasant symptoms like chronic fatigue, anxiety, low blood sugar and irritability. When the stress hormones fall, the liver's manufacture of the copper-binding protein ceruloplasmin falls too, and free copper levels start to rise and wreak havoc on brain function by inhibiting DA-forming enzymes like DOPA decarboxylase and stimulating enzymes involved in the breakdown of DA and 5-HT like Dopamine Beta Carboxylase, 5-hydroxytryptophan decarboxylase and Monoamine Oxidase (MAO). A cigarette (containing the copper antagonist cadmium), an espresso or something stronger like cocaine or prescription stimulants like Ritalin™, will often whip the adrenals back into action and shift the brainfog and **fatigue that results from a build up of unbound copper in the blood**. Overtime, however, the body becomes tolerant to these substances and addiction creeps in.

Food allergy often starts with a "leaky" gut which admits partially digested food particles to the blood stream, provoking immune and behavioural reactions. Gluten exorphin B5 protein found in wheat, barley, rye and oats and alphaS1 casein protein or alpha S1 casomorphin, as it is also known, in cow's milk are known as **exorphins** for their

ability, when improperly digested in this way, to mimic the brain's own natural pain killers (enkephalins) by activating a special class of opioid receptors in the brain. Individuals with a leaky gut often experience a short-lived high and a longer-lived withdrawal phase after consuming foods high in these substances, which keeps them stuck in a recurring cycle of food addiction. Heroin addicts routinely resort to pints of milk or milk chocolate snacks between fixes for precisely the same reason

Heavy metal toxicity

Subclinical chronic lead intoxication from exposure to leaded fuels, paints, water pipes, or from living in environmentally unfriendly older homes has been linked to the development of hyperactivity (ADHD), low IQ's, psychopathy, criminal behaviour, alcoholism and substance abuse and the damage is thought to be irreversible. By weakening the brain's inhibitory processes and impairing its detoxification-capacity, lead exposure enhances the effects of alcohol, drugs and other toxins, encouraging addiction. Although it predominantly affects Black and Hispanic children living in substandard conditions, it is not really known to what extent the effects of long term industrial lead pollution is having on the population at large.

Acetaldehyde intoxication can occur from exposure to perfumes, flavours, dyes, plastics, synthetic rubber, alcohol, cigarette smoke or from fungal yeast infections as a sugar fermentation by-product. AH is an addictive narcotic hydrocarbon which can trigger sugar, alcohol and cigarette cravings in those affected, in order to keep its blood levels maintained.

Bacterial infections

According to American researchers at the Great Plains laboratory, *Clostridia* and *Pseudomonas* bacterial infections of the bowel can produce their own psychoactive end-products like the amino acid L-tyrosine analogue 2,3 Dihydroxyphenylpropionic acid (DHPPA), which acts as a false neurotransmitter and lowers endogenous (natural) DA formation, leading to symptoms of hyperactivity (ADHD), and stimulant craving. Pharmaceutical companies cottoned-on to this decades ago and started prescribing addictive DA-raising amphetamines to treat the disorder. Today, the pharmaceutical drug Ritalin™, considered the front-line in ADHD treatment, has the same effect on the brain as cocaine. Unfortunately both strategies have serious drawbacks.

Chronic pain disorders can often be the occasion of iatrogenic (clinically induced) addiction to painkillers like morphine and diacetylmorphine (heroin). Statistically 2 million Americans use prescription opioid painkillers like these every year, and although the risk of addiction is quite small at around 0.01% or around 200 new cases a year, it is thought to be much higher in those who have a genetic predisposition to hypodopaminism or a history of substance abuse.

6. Diet and addiction

The 21st Century diet consists more than ever of refined sugars and cereal grains, which disrupt blood sugar, rob the body of vital brain nutrients, and cause psychiatric illness. These foods are likely to encourage obesity, food and drug addiction. Sucrose (table sugar) itself is an addictive substance which produces fluctuations in 5-HT turnover, which in turn sharply influences dopamine levels. Glucose receptors in the hypothalamus are directly connected to dopamine release in the mesolimbic system via inputs to the ME amplifier neurones of the "pleasure-reward" circuit, which, over time, can develop tolerance to dietary sugar, leading to obesity and addiction. As with hypoglycaemics, individuals addicted to sucrose are much more likely then to turn to other substances that give them the same high they are looking for. High consumption of caffeine-containing foodstuffs like coffee, tea, chocolate and fizzy drinks which, like sucrose, raises dopamine, is also addictive and once the body has built up a tolerance to it can encourage those affected to seek stronger alternatives. Nutritional deficiencies of amino acids like the 5-HT precursor L-Tryptophan, the DA precursors L-Tyrosine and L-Phenylalanine, and the GABA precursor L-Glutamine, and any of the many cofactors required for neurotransmitter biosynthesis (manufacture), such as vitamins B1, B3, B6, B12, folic acid, vitamin C and minerals like zinc, magnesium, iron and chromium, can predispose an individual to psychiatric disorders, anhedonia, and substance abuse; although this is somewhat of a chicken and egg situation as we shall see in the second bulletin on addiction.

7. Cultural and social factors

Factors such as childhood experience, parental attitudes, social policies, and culture strongly affect the vulnerability to addiction. Drug addiction is

prevalent across all socioeconomic strata, including age, demographics, economic, social, political, religious, and livelihood, although unemployed individuals in poorer socio-economic groups are also more likely to become addicted to drugs especially where drugs are affordable. The classic "Rat Park" experiment, of Bruce K Alexander showed that addiction in rats only took hold when the rats had no other options. When their environment was enriched with other behavioural opportunities, the rats developed more complex behaviours. The same is true in human society.

It is well reported that over half of all patients diagnosed as alcoholic are born into families where alcohol is heavily used, suggesting that familial influence, genetic factors, or more likely both, play a role in the development of addiction. Less often mentioned is that children raised by adoptive parents who's consumption of alcohol is high, are also more likely to become alcoholics. In Saudi Arabia, for instance, where obtaining alcohol is difficult and using it is prohibited, alcoholism is rarely seen. This suggests that familiarity with alcohol, or alcohol availability can also encourage alcoholism. Interestingly addiction is also more likely in permissive families, where moderation is not taught as part of childhood education.

8. Spiritual factors

With the advent of liberal democracies, the increase in materialism and weakening of stabilising moral influences in western societies over the last couple of hundred years, there has been a radical shift in human behaviour away from leading moral lives, to enjoyment and indulging pleasure, to excess in all its forms, good and bad. According to scientists, this is a disturbing trend because neurochemical studies are showing that pleasure-seeking behaviour is a common denominator of addiction to alcohol, drugs, and carbohydrates. Certainly this neo-liberal notion, born out of a superabundance of material wealth in the west, has no doubt encouraged the growth of addictive disorders in the genetically predisposed and curious to a degree unknown. Traditional values are viewed by most of today's youth as out of date, and tend to be fuelled by the mass media's epithet that religion is "the enemy of freedom and pleasure". On the contrary, it is precisely this sort of "moderation in all things" (temperance) which produces happier, healthier people, free of the need to be satisfied by stimulants. Christian rehab programmes like Cenacolo for ex-drug addicts, for instance, have a 93% success rate which greatly surpasses that for most medical treatments. If nothing else history has taught us that decadence and moral corruption cannot be sustained.

Conclusions

Addiction is a complex subject, and isn't just confined to drug and alcohol use. Indeed most stimulants, edibles, routines and activities that trigger a feeling of well-being can become addictive. Such addictions are not usually as dangerous as drugs or alcohol, and unless chronic, don't cause serious damage to the body or have the same social or economic implications.

Addicted people can be genetically predisposed to addiction, and others can become addicted through the body's need to stabilise mood after repeated stimulation.

Substances such as alcohol, drugs and food can alter the mood of the user, and therefore when addicted, taking these extinguishes the craving, withdrawal symptoms, and normalises the mood. Many addicts, for example smokers, feel 'normal' when under the influence of their addicted substance.

Addicted eaters must really struggle, because the food that they are addicted to, such as carbohydrates, may form part of their daily diet. We also know that associated activities can instigate cravings; so eating alone could start a craving for the very thing they are trying to avoid.

Craving triggers can be as diverse as:

- Associated routine activity
- Smells
- Sight
- Sound
- Medication

Next Issue: Testing Solid Drugs and Paraphernalia

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