ARTICLE

Neurobiological and epigenetic perspectives on hedonism, altruism and conscience

Prasanna N. De Silva

Prasanna N. De Silva is an old age psychiatrist with Cumbria, Northumberland, Tyne and Wear NHS Trust, based at Monkwearmouth Hospital, Sunderland, UK. He has previously published on the dopamine reward system and on the pathophysiology of synaptic pruning.
Correspondence Dr Prasanna N. De Silva. Email prasanna.desilva@cntw.nhs.uk

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SUMMARY

This article examines notions of hedonism, altruism and conscience in relation to the activity of four neurotransmitter pathways: the dopamine reward, noradrenaline fight or flight, serotonin calming and glutamine learning pathways. Associated brain areas that modulate behaviour are highlighted: the prefrontal cortex (activity planning, risk mitigation), the hippocampus (memory retrieval) and the insular cortex (integration of information to decide on action). Putative epigenetic changes influencing adult behaviours after childhood privation are discussed. Pharmacological and psychological means of mitigating harmful behaviours are summarised, alongside the ethics of epigenetic screening to predict future addictive and violent tendencies.

LEARNING OBJECTIVES

After reading this article you will be able to:

- understand the neurobiology of conscience and how hedonism and altruism are mediated through the dopamine reward pathway
- recognise the impact of childhood privation on adult behaviour through epigenetic modifications
- understand current approaches to mitigate damaging hedonistic impulses, including lessons learned from prolonged dopamine agonist use.

KEYWORDS

Hedonism; altruism; conscience; dopamine; glutamate.

Hedonistic behaviours potentially causing harm to self and to others have been described in various religious and secular texts, such as the Ten Commandments (Skeel 2011), the Buddhist path to enlightenment (Rahula 1959) and contemporary secular versions pertaining to academic life (Franke 2013). These include suppressing impulses to kill, steal, speak untruths, use intoxicating substances and become involved in sexual misdemeanours (Table 1).

The notion of an inborn tendency to hedonism ('original sin' in Christian theology) suggests potential for these behaviours from childhood. The restraining influence, one's 'conscience', is also considered to be innate, albeit seen as a gradually maturing facility (Timpe 2021).

The dopamine reward pathway

The brain's reward pathway is based on the neurotransmitter dopamine, which is produced at the substantia nigra (Koob 2010) (Fig. 1). On receipt of sensory stimuli via the thalamus, dopamine is transported to the prefrontal areas of the brain to motivate activity. Dopamine is also directed at the mesolimbic system in the mid-brain, comprising the ventral tegmental area and the nucleus accumbens. This joint structure experiences reward as a 'thrill', with the hippocampus recording the stimuli and response for future use.

Repetitive thrill-seeking behaviour can lead to both tolerance – needing more intense stimuli – and dependence – needing escalating frequency of activity, with features of withdrawal if discontinued (Miller 1987). There is increasing evidence that humans can move from one reward-inducing behaviour to another if the original activity is thwarted: cross-sensitisation between sweetened drinks, alcoholic beverages and stimulants, for example (de Silva 2019).

Altruistic thoughts and actions also produce a dopamine-induced reward experience (Sonne 2018), leading to repetition of such behaviours. Swapping between different altruistic acts can also occur, with the possibility of addiction to them, as can happen in blood donation, for example (Piliavin 1982).

The adrenergic 'fight, freeze or flight' system

The main neurochemical pathway associated with 'fight, freeze or flight' is the adrenergic pathway (McCorry 2007). The source chemical noradrenaline is produced in the locus ceruleus in the brainstem and supplied to the motor areas (frontal and

TABLE 1 Summary of three ethical codes, with possible contemporary applications

The Ten Commandments of Abrahamic faiths	The eight-fold path of Buddhism	The seven academic sins (described by Franke 2013)
• You shall have no other gods before me (celebrity worship?) • You shall not make idols (smart phone dependency?) • You shall not take the name of the Lord God in vain ('OMG'?) • Keep the Sabbath day holy (work/rest imbalance?) • Honour your father and mother (neglect of older parents?) • You shall not murder (cancel culture?) • You shall not commit adultery (accessing pornography?) • You shall not steal (tax avoidance?) • You shall not bear false witness (social media speculation?) • You shall not covet (perusing social status?)	• Right understanding (critical analysis) • Right thought (avoiding biases) • Right speech (avoiding insults) • Right action (avoiding aggression, intoxication) • Right livelihood (avoiding drugs, arms, sex trades) • Right effort (persistence) • Right mindfulness • Right concentration	• Sloth (plagiarism, including 'cut and paste') • Gluttony (alcohol and substance misuse) • Lust (sexual relationships with students) • Greed (financial conflicts of interest in research) • Pride (inability to retract one's theories) • Envy (of others' grant income) • Wrath (retaliation towards academic opponents)

parietal cortices) as well as to the amygdala, which is situated in front of the hippocampus.

Amygdala activation causes a sensation of fear, with the prefrontal cortex assisting the insula to decide whether to fight, freeze or escape. The fight response can secondarily release dopamine and be perceived as a thrill, habituating aggressive behaviours.

The serotonergic 'calming' system

The serotonergic (5-HT) system can downregulate both dopamine and noradrenaline (Lowry 2005). Over 80% of 5-HT is produced by the gut microbiota, although a local supply is produced by the raphe nucleus of the brain-stem, and it is distributed to prefrontal and limbic areas. The vagus nerve, which links the gut, heart and brain-stem, also modulates the adrenergic and dopaminergic supply.

Learning via glutamate and synaptic pruning

Glutamate is available from embryonic life onwards, prior to the formation of dopamine and noradrenaline pathways. Unlike dopamine, noradrenaline and

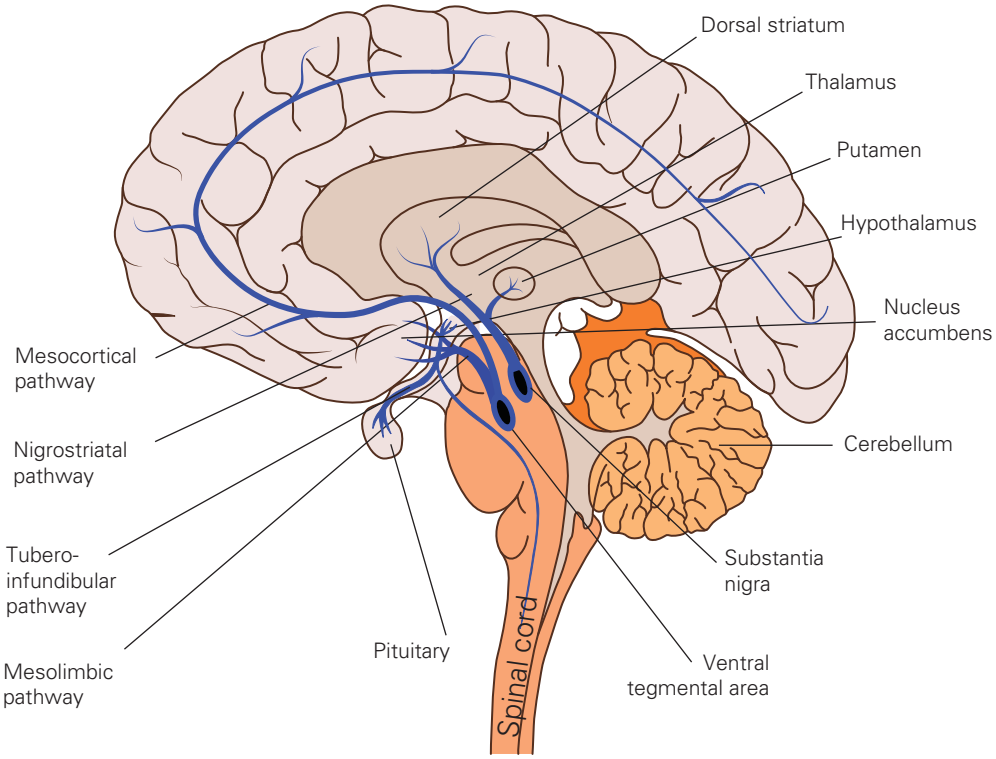

FIG 1 The dopamine pathway (Patrick J. Lynch, https://en.wikipedia.org/wiki/Dopaminergic_pathways#/media/File:Dopaminergic_pathways.svg).

5-HT, glutamate is locally sourced through the central nervous system, mainly in astrocytes which surround and support neurons (Meldrum 2000). It reinforces synapses devoted to recalling behaviour appropriate to a stimulus (Riedel 2003). Repeated practice of behaviours is also accommodated via glutamate to ensure efficiency and lack of errors in application.

Assisting glutamate to hardwire learning, synaptic pruning is carried out by microglia phagocytosing unused synapses (Faust 2021). Synaptic pruning typically occurs at particular periods: a whole brain prune between the ages of 8 and 11 (learning to avoid physical injury) and a selective prefrontal prune between the ages of 18 and 25 (learning to live and work collaboratively).

In keeping with the presence of glutamate from embryonic life, it appears that 'caring behaviours' are learned and hardwired during the first 2 years of life in reaction to parental nurturing (Upshaw 2015), with neglect associated with more harmful behaviours in later life (Bland 2018).

Behavioural epigenetics

Evidence of early childhood privation leading to hedonistic and antisocial behaviours in adult life was raised over 30 years ago (Farringdon 1993). Animal studies have shown that epigenetic mechanisms, specifically gene silencing via DNA methylation, provide a link between childhood neglect and later life behaviours: silencing at the glucocorticoid receptor gene appears to alter the cortisol responsiveness to stress in later life (Weaver 2004).

The other area of epigenetic interest is intergenerational transmission of addictive behaviours (Vassoler 2014), with the potential for altering the epigenome during early childhood (for example using micro-RNA or gene editing) to mitigate transmission of such behaviours.

Brain regions advising choice of behaviour

The prefrontal cortex (PFC) is responsible for planning and sequencing activity (St Onge 2010), as well as assisting the cerebellum and basal ganglia to smoothen motor and emotional activity. Subcomponents of the PFC have additional roles. The ventromedial prefrontal cortex (VMPFC) is involved in predicting and mitigating risks associated with proposed actions. The dorsolateral prefrontal cortex (DLPFC) is responsible for recognising others' motivations, ensuring success of one's actions.

Functional imaging has revealed a reverberating circuit that perpetuates behaviour (Lipton 2019). This consists of the VMPFC, thalamus, anterior cingulate and hippocampus. Various compulsive behaviours (self-harm, ritualistic cleaning, bulimia and addictions) appear to share this circuit.

The insula

The site responsible for integrating and ultimately making choices on behaviour is buried under the surface of the frontotemporal cortex and is known as the insula (Gogolla 2017). This site creates a three-dimensional representation of the self in relation to the environment, to assist selection of action. However, the likelihood of a particular response is influenced by previous episodes and consequences (information supplied by the hippocampus) as well as areas of the brain associated with conscience.

Conscience – the intrinsic modulator of hedonism

The main restraint on hedonistic impulses is one's 'conscience', an instinctive awareness that certain behaviours are unhelpful to others and, given time, to oneself (Schalkwijk 2018). The experience of being protected and nurtured by adults during early childhood, alongside moral teaching and modelling of other humans, should develop one's conscience (Kochanska 2010). DLPFC-associated learning about how others experience one's behaviour, the so-called 'theory of mind' (Astington 1995), would also assist maturation of conscience.

Neurochemically, conscience can be seen as glutaminergic suppression of excess dopaminergic/adrenergic drives, with further kindling achieved by gaining religious insights or utilising psychological techniques such as mindfulness (Schuman-Olivier 2020). Alternatively, mitigation of hedonistic activity could potentially be induced via prayer to a 'higher power' (Arnaud 2015).

One interesting aspect of conscience is the presence of 'guilt' or 'shame' before and after a hedonistic act is contemplated. Two pilot studies (Takahashi 2004; Michl 2014) involving functional imaging suggest that guilt and shame share similar sites of activation involving prefrontal, temporal and limbic areas, with specific activation of the amygdala and insula when experiencing guilt and activation of the anterior cingulate and parahippocampal areas during the experience of shame. It is possible that guilt and shame activate the reverberating circuit described above, resulting in compulsive behaviours.

Potential extrinsic modulators of hedonistic behaviours

Optimal functioning of the gut biome (Mohajeri 2018) and subsequent vagal nerve input to the brain-stem can have a modulating influence on fear-mediated behaviour (Breit 2018). Indeed,

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improvements in the gut biome involving dietary fibre (prebiotics) and bacterial species supplementation (probiotics), alongside faecal transplantation, are being considered for behaviour modification (Meyyappan 2020).

Another approach to gaining insight is by using psychedelics such as psilocybin, which can produce enhanced awareness of mental activity (Lowe 2021). However, these can result in 'bad trips' involving frightening hallucinations. Repurposed drugs such as ketamine can increase expression of glutamate at the frontal cortex (Abdallah 2018), thereby modulating dopamine release. Ketamine is being considered for treatment of addictive disorders (Jones 2018).

The main psychological approach used to modulate behaviour is a combination of progressive muscular relaxation coupled with guided imagery for slowing thought processes, which leads to improved awareness of one's thoughts, emotions and impulses (Toussaint 2021). This allows the person to gain insight about triggers and motivations for behaviour.

Forced hedonism: effects of dopamine agonist use

Three clinical syndromes are associated with prolonged use of dopamine agonists (such as pramipexole, cabergoline, ropinirole). These drugs are used for symptomatic treatment of Parkinsonism, restless legs syndrome and, of late, treatment-resistant depression.

Impulse control disorder

Up to 15% of patients on dopamine agonists experience hedonistic impulses (O'Sullivan 2009), for example to shop or gamble excessively, become hypersexualised or access proscribed internet sites. These behaviours can lead to financial losses or criminal prosecution. Previous illicit drug use or a family history of addictions increase the risk of impulse control disorder.

Dopamine dysregulation syndrome

This associated condition is characterised by escalating dopamine agonist consumption (including levodopa for Parkinson's disease), psychomotor agitation, euphoria, drug-related dyskinesias and resistance to dose reduction (Lawrence 2003). Discontinuation of these drugs can result in dopamine agonist withdrawal syndrome, characterised by agitation, panic attacks, generalised pain, orthostatic hypotension, insomnia and, at times, suicidality, with symptoms lasting months (Nirenberg 2013) even with gradual tapering. Patients who have experienced impulse control disorder are particularly at risk.

Punding behaviours

Punding is a stereotyped behaviour characterised by an intense fascination with a complex, repetitive activity without necessity (Fasano 2010). Examples include repetitive cleaning, dismantling electrical equipment and, arguably, constantly trawling social media. Punding has mainly been studied in people with Parkinson's disease prescribed dopamine agonists long term and among people addicted to cocaine or amphetamine. Drugs interacting with dopamine type 1 and 2 receptors are especially implicated. Individuals are aware of their behaviour, but reluctant to discontinue, as they experience punding as calming.

Religious approaches to modulating behaviour

The Abrahamic religions (Judaism, Christianity and Islam) regard hedonistic behaviour as being detrimental to faith in, and respect for, God the creator of humans, and therefore consider it 'sinful' (Weldon 2010). The expectation is to seek repentance for one's hedonistic impulses, minimising accessibility of environmental cues and being watchful of potential relapses. This approach of avoidance and vigilance is also used by secular organisations such as Alcoholics Anonymous, with similar faith in a 'higher power' based on an understanding that addictive behaviour cannot be controlled by one's will.

These religions hold contradictory opinions on altruistic behaviours: Christianity decries 'carrying out good works', believing this is not the path to communing with God, whereas the other two do believe in maximising altruistic behaviour. Perhaps the idea that altruistic behaviours are potentially as addictive as hedonistic tendencies owing to the shared dopamine reward pathway might be relevant in this debate.

Conclusions

Neuroscience provides an understanding of the physiological processes involved in reward-driven behaviour, both of an altruistic and harmful nature, via the dopamine reward pathway. Current neuroscience findings also suggest that the insula is the probable site of coordination and, in effect, the final decision maker. Current functional imaging suggests that the mind and brain 'co-produce' hedonistic impulses.

A 'sensitive period' during the first 2 years of life for experiencing privation (abuse, domestic disharmony or neglect) suggests an epigenetically mediated predisposition to harmful behaviour in later life. However, nurturing parental care can lead to more altruistic behaviours in adulthood, perhaps a more nuanced interpretation of 'original sin'.

MCQ answers
1 d 2 b 3 a 4 d 5 c

The possibility that compulsive or addictive behaviours could be modified by intervening in epigenetic processes in early childhood is intriguing but raises ethical problems. Furthermore, epigenetic signatures suggesting a predisposition to addiction or violence (for example to alcoholism or domestic violence) raises issues of 'pre-crime' described in the film *Minority Report*.

Clinically, pragmatic research is needed to compare the effectiveness of various religious and secular approaches to combat harmful compulsive hedonistic behaviours and to develop the conscience. Design of future studies should include the value of synergism in combining approaches and the influence of personal preferences.

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Declaration of interest

None.

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MCQs

Select the single best option for each question stem

1 The dopamine 'reward' supply:
- a originates in the locus ceruleus
- b preferentially supplies the mesolimbic system
- c does not lead to tolerance
- d can produce cross-sensitisation between behaviours
- e does not involve altruistic behaviours.

2 The serotonergic pathway:
- a is experienced as a 'thrill' sensation
- b originates at the raphe nucleus
- c is inhibited by vagal nerve input
- d is not influenced by the gut biome
- e activates the dopamine pathway.

3 Glutamate in the brain:
- a is the main 'learning from experience' system
- b is expressed from childhood onwards
- c inhibits synaptic pruning periods
- d activates microglia
- e is predominantly produced in the brain-stem.

4 Behavioural epigenetics:
- a involves DNA cleavage
- b is mediated through demethylation
- c can result in better maternal care
- d can influence cortisol response to stress
- e has no effect on adult behaviour.

5 Impulse control disorder:
- a is associated with dopamine antagonists
- b is seen in 5% of dopamine agonist users
- c is more likely when a family history of addiction is present
- d does not include excess shopping
- e is not related to dopamine agonist withdrawal syndrome.