Medical Hypotheses 78 (2012) 341–348

Contents lists available at SciVerse ScienceDirect

Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy

A new three-dimensional model for emotions and monoamine neurotransmitters

Hugo Lövheim *

Department of Community Medicine and Rehabilitation, Geriatric Medicine, Umeå University, SE-901 85 Umeå, Sweden

ARTICLE INFO

Article history:
Received 30 August 2011
Accepted 13 November 2011

ABSTRACT

The monoamines serotonin, dopamine and noradrenaline have a great impact on mood, emotion and behavior. This article presents a new three-dimensional model for monoamine neurotransmitters and emotions.

In the model, the monoamine systems are represented as orthogonal axes and the eight basic emotions, labeled according to Tomkins, are placed at each of the eight possible extreme values, represented as corners of a cube.

The model may help in understanding human emotions, psychiatric illness and the effects of psychotropic drugs. However, further empirical studies are needed to establish its validity.

Background

In this article a new explanatory model for emotions and monoaminergic neurotransmitters is presented. The model though rather simple contains much information and may help in the understanding of human emotions, psychiatric illness and the effects of psychotropic drugs.

The monoamine system

Consider first the monoamine neurotransmitter systems. The most important monoamine neurotransmitters are serotonin, noradrenaline and dopamine, which share many properties. They are all derived from one amino acid (hence the name monoamines) and are produced by relatively few neurons in small areas in the upper part of the brainstem. The main brain areas for the production of these monoamine neurotransmitters are the raphe nuclei for serotonin, ventral tegmental area and substantia nigra for dopamine and locus ceruleus for noradrenaline. The monoamine-producing nerve cells project their axons, and release their transmitter substances widely and diffusely throughout the cerebral cortex. Each monoamine binds to a whole family of receptors. Most, but not all, monoamine receptors are metabotropic, G-protein coupled, receptors that typically upon binding of their particular ligand do not elicit an action potential, but act to change the sensitivity of the postsynaptic cell to other signals. Most monoamine receptors are excitatory, i.e. increase the probability of an action potential starting in the postsynaptic cell [1–6]. All these features are consistent with the concept that the monoamine systems are regulating systems.

The monoamine transmitter systems are highly evolutionarily conserved. It has been found that monoamines are involved in behavioral control in various species such as nematodes, lobsters, desert locusts, mice, zebra finches and hens [7–14]. That monoamine control of behavior has been conserved throughout evolution indicates that it is a great advantage for survival if an organism is able to modify its behavior. The environment an organism encounters is very complex, therefore, a system of behavioral control cannot be specific to every possible situation; instead these systems have to be general in some way. The monoamine systems are probably also very dynamic, as the modification of behaviors and emotion has to be rather rapid and able to adjust to changes in the environment.

In humans, the important role of the monoamine systems in regulating emotions and behavior is illustrated, not least, by the fact that many psychotropic drugs, e.g. antidepressants and antipsychotics, act by interfering with the monoamine system [15]. It is suggested that monoaminergic systems are involved in human behavior [16–20], and in several psychiatric disorders such as depression, psychosis, attention-deficit hyperactivity disorder, anxiety, and behavioral disturbances among people with dementia [15,21–33].

The monoamine-releasing upper brain stem areas – raphe nuclei, ventral tegmental area and locus ceruleus – do not, however, ultimately control our emotions. There is a growing body of evidence suggesting a crucial role for the amygdala and other limbic structures in the synthesis of information and control of behaviors and emotions [34–44]. These structures handle the processing of emotion-eliciting information and trigger certain emotions in certain situations, and are projecting towards the monoaminergic nuclei which serve to deliver the message – the emotion – to the whole brain [5,41,43]. In other words, the monoamine transmitter systems might form one final pathway for the simultaneous delivery of emotional information to large and dispersed areas of the brain.

* Tel.: +46 90 785 88 59; fax: +46 90 13 06 23.
E-mail address: hugo.lovheim@germed.umu.se

0306-9877/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.mehy.2011.11.016

Many studies from different research fields support the belief that all three of the monoamines, serotonin, dopamine and noradrenaline are essential in the control of behaviors and emotions [7–14,16–31,45–56]. Furthermore, each of the monoamines seems to be involved in different aspects of emotion or behavior. People suffering from major depression and premenstrual dysphoric disorder appear to have low levels of serotonin, and common antidepressants act through blocking the serotonin transporter [15,26,51,54–56]. Low levels of serotonin have also been coupled to aggression [10,19,27,28,52,53]. The serotonin axis, therefore, seems to represent aspects such as self-confidence, inner strength and satisfaction. The dopamine axis has been found to be involved in reward, motivation and reinforcement [9,46,48,49,57–59], while noradrenaline has been coupled to the fight or flight response and to stress and anxiety, and appears to represent an axis of activation, vigilance and attention [4,5,33,45,47,50,60,61]. A brief overview of the monoaminergic systems is given in Table 1.

As each of these three monoamine systems probably represents a different aspect of emotion, a hypothetical three-dimensional space for possible combinations is formed. It is evolutionarily rational that the monoamine systems are mutually orthogonal as this maximizes the amount of information that can be transmitted, however, although likely, this needs to be further established empirically. It is important to note that as long as none of the monoamines transmit exactly the same information as any other (which seems unlikely), there will still be a three-dimensional space. For simplicity, in this article the monoamines axes have been depicted as mutually orthogonal.

In the model depicted in Fig. 1 serotonin is represented on the x-axis, noradrenaline on the y-axis and dopamine on the z-axis, in an orthogonal coordinate system. The origin represents a situation where no signal substances at all are released. The other end of each arrow represents the maximum effect of the specific neurotransmitter system. The corners of the cube thus represent the combination of the extreme values, either low or high on the three axes respectively. An infinite number of combinations of different levels of the three neurotransmitters are possible, but all lie within this space, and within the eight "extreme values", defined by the eight possible combinations of either zero or maximum effect of the three monoamine systems respectively.

That each monoamine neurotransmitter represents a different aspect of emotion should not, however, be interpreted to mean that the monoamines are independent. There are probably complex systems of feedback and reciprocal control where the monoamine systems interact and affect each other. These interactions probably contribute to the dynamics of the monoamine systems [62–66]. It is also noteworthy that the total "out-effect" in a monoamine axis is a function of the amount of signal substance that is released into the synaptic cleft, the rate of reuptake and degradation of the transmitter substance as well as the type, number, sensitivity and specificity of post-synaptic receptors. Complex feedback mechanisms regulate these factors.

Basic emotions theory

Keeping in mind the monoamines, let us now focus on the theory of basic emotions. Basic in this context means that certain

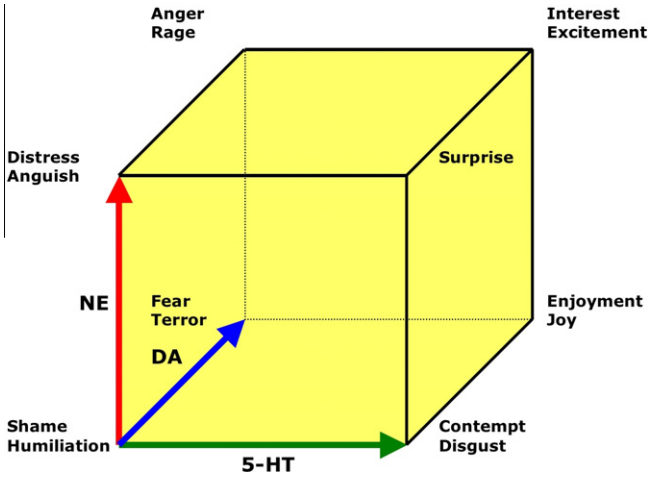

Fig. 1. A three-dimensional model for emotions and monoamine neurotransmitters. A three-dimensional model of emotion, with the eight basic emotions ordered in an orthogonal coordinate system of the three main monoaminergic axes. The axes represent serotonin (5-HT, 5-hydroxytryptamine), dopamine (DA) and noradrenaline (NE), and each end of the arrows represents low and high levels of signaling respectively. The eight basic emotions, located in each corner, are labeled according to Tomkins.

emotions are thought to be innate and universal, a theory sometimes referred to as the differential emotions theory (DET) [67,68]. In 1872 Charles Darwin published his groundbreaking work *The Expression of the Emotions in Man and Animals*, in which he listed over thirty emotions, ordered into seven clusters [69]. Later scientists have proposed different sets of basic emotions, although no final consensus has yet been reached concerning the exact number of basic emotions, or which emotions are basic. In fact, scientists have long argued over whether or not there is a finite number of basic emotions at all [70–74]. However, among those who adhere to the theory of basic emotions there seems to be a fair level of agreement that the number of basic emotions lies somewhere in the range of 5–10 [67,68,75–88].

For psychologists, the study of emotions has often originated from the study of facial expressions. By investigating facial expression in adults and newborn children, and in people from different cultures, common features have been found which seem to represent an innate palette of emotions, shared by all humans [67,69,78,89–92]. Recent evidence in support of the idea of basic emotions has also been gathered from brain imaging studies and investigations of autonomic responses, demonstrating unique patterns of activation associated with certain emotions [93–97].

Basic emotions might be viewed as the extremes of emotional expression. All emotions, including everyday tepid emotions, lie within the bounds of these basic emotions.

The aim of this article

Combining these two fields of research, my intention was to explore how different levels of monoamines are jointly linked to particular emotional states, and thereby to fit these emotions into the three-dimensional model comprising the monoamine

Table 1
The three main monoamines.

Monoamine	Derived from the amino acid	Area projecting to the cerebral cortex	Assumed axis representation
Serotonin (5-HT)	Tryptophan	Raphe nuclei	Self confidence, inner strength, satisfaction
Dopamine (DA)	Tyrosine	Ventral tegmental area[a]	Reward, reinforcement, motivation
Noradrenaline (NE)	Tyrosine	Locus ceruleus	Attention, vigilance, activity

[a] Neurons in substantia nigra also contain dopamine, however, these neurons do not project to the cerebral cortex.

axes. During the work, I discovered that the eight basic emotions, as described by Tomkins, could fit rather well into the eight corners of the cube model. In the following, the reasoning and some evidence for the placement of each basic emotion in its particular corner of the model will be presented. The choice of which basic emotion should be placed in which corner was made based on the literature of basic emotions theory, various aspects of monoamines and their relation to mood and behavior in humans and animals, and the known effects and side-effects of various psychotropic drugs.

Construction of the model

The psychologist Silvan Tomkins devoted his life to the study of emotions and developed an elaborate and comprehensive theory of basic emotions [85–87,89]. Tomkins identified eight basic emotions, which he labeled with one word for the emotion when it was of low intensity and another word for the same emotion at a higher intensity [98,99]. Tomkins referred to basic emotions as "innate affects" where affect, in his theory, stands for the "strictly biological portion of emotion" [83]. According to his theory, these are the eight basic emotions: Two positive: Interest/excitement and enjoyment/joy, one neutral: Surprise/startle, and five negative: Distress/anguish, fear/terror, shame/humiliation, contempt/disgust and anger/rage [98,99]. The basic emotions and their associated facial expressions, according to Tomkins, are summarized in Table 2. Tomkins originally labeled one basic emotion surprise/startle, however, Ekman later convincingly showed that the startle response was unrelated to the basic emotion of surprise [100], and the label surprise was therefore chosen.

Fear/terror and anger/rage

Both of the basic emotions, fear/terror and anger/rage, are supposedly high-dopaminergic and therefore coupled to reinforcement [9,101–104]. This seems logical when one considers the great evolutionary value of learning about those dangerous situations in which these negative basic emotions are triggered. It has been found that laboratory rats easily learn to avoid various stimuli presented simultaneously as something innately scary (such as a cat) [34]. The rewarding effect of these basic emotions might also possibly explain why certain people continue to seek so-called adrenaline rushes.

Patients with Parkinson's disease acutely withdrawn from dopamine replacement therapy have been found to have a selective impairment of the recognition of facial expressions of anger [105], and in another study patients with Parkinson's disease showed a blunted response to aversive stimuli [106]. Further, treatment with the dopamine receptor 2 antagonist sulpiride was found to lead to a selective disruption of the recognition of facial expressions of anger [107] and reduced striatal dopamine 1 (D1) receptor binding (indicative of increased release of dopamine) has been found among patients with major depression with anger attacks [108,109].

Both fear/terror and anger/rage are here further assumed to be low-serotonergic, as these emotions are triggered when the individual feels threatened or under pressure, and therefore probably has an inner feeling of weakness. Aggression has also been coupled to serotonergic deficit in many studies, supporting the placement of anger/rage on the low-serotonergic side [10,19,27,28,52,53]. Anger is also a rather common symptom in patients with depression [110–113], which lends further support to the idea that anger is low-serotonergic. Aggression among patients with Alzheimer's disease has been treated with selective serotonin re-uptake inhibitors (SSRI), antipsychotic drugs (dopamine antagonists) and noradrenergic β-blockers [24,114].

High-noradrenergic emotions are supposedly those where the individual is active and aroused, attentive, with a high pulse [5,33,45,47,50]. The basic emotion fear/terror has been placed in the low-serotonergic, low-noradrenergic, high-dopaminergic corner of the cube. This basic emotion should not be confused with the active "fight or flight" reaction; instead fear/terror is considered here the "white, cold" fear, when the heart almost stops beating. Darwin wrote that fear is expressed "...by trembling, the erection of the hair, cold perspiration, pallor, widely opened eyes, the relaxation of most muscles, and by the whole body cowering downwards or held motionless."[69] The so-called vasovagal syncope might be understood as this reaction, as can freezing behavior in mice. Considering these features, one might understand that fear/terror is probably low-noradrenergic. The "fight or flight" reaction, on the other hand, seems analogous with the basic emotion anger/rage i.e. high-noradrenergic, low-serotonergic, high-dopaminergic, in the model. The reddish face and high pulse associated with anger point towards this basic emotion being high-noradrenergic.

As mentioned above Tomkins labeled each basic emotion with two words, one for high intensity and one for lower intensity. In the model the corner should be understood as the extreme state and, therefore, the site for the basic emotion at maximum intensity. The lower intensity of the specific basic emotion is located within the cube, in the model, somewhere along the line between the corner and the centre of the cube (which represents a more or less neutral state).

Shame/humiliation and distress/anguish

The basic emotion of shame/humiliation has been placed in the corner where all three monoamines are low. Tomkins wrote that "...shame strikes deepest into the heart of man." and the individual feels "naked, defeated, alienated, lacking in dignity or worth."

Table 2
The basic emotions, facial expression and assumed monoamine levels.

Basic emotion[a]	Facial expression[a]	5-HT	DA	NE
Interest/excitement	Eyebrows down, eyes track, look, listen	High	High	High
Enjoyment/joy	Smile, lips widened up and out, smiling eyes (circular wrinkles)	High	High	Low
Surprise[b]	Eyebrows up, eyes blink	High	Low	High
Distress/anguish	Crying, arched eyebrows, mouth down, tears, rhythmic sobbing	Low	Low	High
Fear/terror	Eyes frozen open, pale, cold, sweaty, facial trembling, with hair erect	Low	High	Low
Shame/humiliation	Eyes down, head down	Low	Low	Low
Contempt/disgust	Sneer, upper lip up	High	Low	Low
Anger/rage	Frown, clenched jaw, eyes narrowed, red face	Low	High	High

Note: 5-HT = serotonin, DA = dopamine, NE = noradrenaline.
[a] According to Tomkins [98,99].
[b] Tomkins originally labeled this basic emotion surprise/startle, however, Ekman later convincingly showed that the startle response is unrelated to the basic emotion surprise [100], and the label surprise was therefore chosen.

[86] It seems rather clear, therefore, that this basic emotion belongs in this corner, considering the assumed properties of each axis.

Distress/anguish is placed in a corner close to shame/humiliation, as the active (and hence noradrenaline-high) analogue to shame/humiliation, i.e. where noradrenaline is supposedly high and dopamine and serotonin are low. The relation between shame and depression [115–117], and anxiety and depression [118] respectively, supports the placing of these two basic emotions on the low-serotonergic side, as do the effect of SSRI antidepressants on anxiety disorders [119], and an increased serotonin transporter binding in generalized social anxiety disorder [120,121]. The association between shame and anxiety supports the decision to place these two basic emotions close to each other [122,123].

A panic attack might be regarded as a model for the basic emotion distress/anguish. There is evidence to support an association between low dopamine activity and anxiety, particularly social phobia but also generalized anxiety disorder. Patients with Parkinson's disease often have concomitant anxiety [124,125], and the dopamine-low Val genotype of the Val158Met polymorphism of the catechol-*O*-methyltransferase (COMT) gene is associated with phobic anxiety [126,127]. Increased dopamine transporter binding has been found among patients with generalized social anxiety disorder [121]. Treatment with antipsychotics might also, in some cases, provoke acute social phobia [128], and one dopamine-enhancing drug, bupropion, has been found to be possibly useful in the treatment of social phobia [129].

Noradrenergic β-receptors have been found to be critical for the expression of cocaine-induced anxiety in mice [130], and high doses of caffeine might provoke panic attacks in patients with panic disorder or social phobia [131]. Tension-anxiety has been found to be associated with decreased β-adrenergic sensitivity [132] and noradrenergic β-blockers are sometimes used to treat uncomplicated performance anxiety [119]. Taken together this supports the view that distress/anguish is high-noradrenergic.

Interest/excitement and enjoyment/joy

Interest/excitement has been placed in the corner of the cube where all three monoamines are high. This basic emotion is, therefore, according to this model, active, reinforcing and coupled to a basic feeling of inner strength. One archetypal form of excitement is sexual excitement, but this basic emotion might accompany a wide range of events, perceptions or thoughts.

Considering the rewarding, motivating and reinforcing effects of the dopamine axis it seems logical for the basic emotion of interest to be high-dopaminergic. Dopamine plays an important role in drug addiction [133], in appetite [134–136], in exploratory activity [137], and in love [138] – which all represent interest in different ways.

That interest is a high-serotonergic basic emotion is supported by the effects of the serotonin-releasing agent 3,4-methylenedioxymethamphetamine (MDMA, "Ecstasy") [139–144], the finding that tryptophan supplementation or acute treatment with SSRI antidepressants induces a positive bias in the processing of stimuli [145–148], and the possibility of inducing mania by giving treatment with antidepressants [149]. The inability to experience interest, i.e. anhedonia, is also a key feature of major depression [150], and hence supports interest as a high-serotonergic basic emotion. Furthermore, the fact that ongoing treatment with SSRI antidepressants might lead to blunted positive emotions and sexual dysfunction [51,151,152], also supports interest as high-serotonergic, as a reduction of post-synaptic receptors following continuous treatment probably dampens serotonergic transmission in these cases.

Noradrenaline has been found to be elevated in relation to positive experiences of unexpected food reward [153] and sexual excitement [154], and in relation to the initiation of eating [155–158]. The classical experiment by Dutton and Aron where sexual attraction to an attractive interviewer was increased by locating the interview on a fear-arousing, high, suspension bridge as compared to a low bridge [159], also points towards interest being high-noradrenergic.

Enjoyment/joy is suggested as the low-noradrenergic analogue to interest/excitement. Another word for this basic emotion might be contentment, and compared to the basic emotion of interest/excitement the individual experiencing enjoyment/joy is calm and relaxed. These two basic emotions are considered the positive basic emotions according to Tomkins [98,99], and, according to the model, are defined by high levels of both serotonin and dopamine.

Contempt/disgust

When an individual experiences an emotion of contempt or disgust, there is also a nuance of superiority towards the object of the emotion. Therefore, this basic emotion has been placed in one high-serotonergic corner. Food-related disgust has been regarded as a core feature of disgust and if you continue to eat when you are already satisfied, you will eventually experience aversion towards the food, even though it was previously palatable. Disgust might, therefore, be somewhat related to satiety, in its extreme. This points towards disgust being high-serotonergic, as do the reduced ability to recognize disgusted faces found in healthy individuals after tryptophan depletion [160] and among patients with severe depression [161] or social anxiety disorder [162]. A serotonin 5-HT_{2C} receptor agonist has been shown to induce conditioned taste aversion [163] and blockade of 5-HT_3 receptors to lessen allergy-induced food aversion [164]. Nausea and vomiting are also often treated with antagonists of serotonin receptor type 3, e.g. ondasetron [165]. The relation between shame/humiliation and contempt/disgust has been described as self-contempt versus contempt for an object [86], and therefore, it seems logical that the difference between these basic emotions, according to the model, is the serotonergic state, assumed to be related to inner strength and self-confidence.

Disgust is supposedly low-dopaminergic as it is in many ways the direct opposite of reinforcement. Contempt/disgust is closely related to repulsion and withdrawal; we usually stop eating when we feel disgust. Dopamine-low individuals with the Val/Val genotype of the COMT Val158Met polymorphism have been found to be more sensitive to disgust [166], and individuals with chronic schizophrenia with anhedonia (functionally low in their dopamine axis] have also been found to experience more disgust than healthy controls [167,168]. In rats, it has been found that a conditioned taste aversion stimulus leads to a significant decrease in extracellular dopamine in the nucleus accumbens [169].

Surprise

Surprise has been placed in the high-serotonergic, low-dopaminergic, high-noradrenergic corner, and might thus be regarded as the non-reinforced analogue to excitement, which seems logical considering that surprise has been described as a neutral basic emotion. At the same time surprise is a highly focused, attentive state, and therefore logically high-noradrenergic. Also, according to the model, the individual experiencing surprise as compared to distress/anguish has a basic feeling of confidence and inner strength.

Discussion

The basic emotions can be observed in adults and in newborns and across different cultures [67,78,89–91]. Nathanson describes

the basic emotions as "the group of "hard-wired," preprogrammed, genetically transmitted mechanisms that exist in each of us and are responsible for the earliest forms of emotional life" [83]. Considering the great impact of the monoamine systems on mood and behavior, it seems likely that this "hard-wired" emotional control system is in fact the monoamine system.

Even if the monoaminergic axes might be represented in an orthogonal coordinate system, as suggested in this article, further studies are needed to confirm the relation between combinations of monoamine levels and different emotional states. There is also a need for further elucidation of the properties of each monoaminergic axis. More studies including registration of emotions and behavior, and/or registration of typical brain activation patterns using a PET scan, during pharmacological manipulation of the monoaminergic axes, either one by one or more than one at the time, would be valuable, as would more studies of emotional dysregulation and associated perturbations in the monoaminergic systems in people with various psychiatric disorders. Animal studies of emotion and behavior following systematic manipulation of the monoaminergic axes or during direct voltammetric measurements [170] of monoamine levels could also be used to test the validity of the model.

Interestingly, the model suggested in this article offers a theoretical explanation of why there might be exactly eight basic emotions, a number previously suggested as a result of various empirical investigations of emotion [82,99]. There is also, supposedly, an infinite number of intermediate states, located inside the cube model, that all correspond to certain inner states. This model might, therefore, also explain the formation of complex, or mixed, emotional states, as well as why certain emotions are "basic". Cognitive processes might also, most probably, modify the experience and emotional expression produced by a given monoaminergic combination, however, this does not invalidate the model as such.

In the field of psychology, some authors have previously described human emotions in terms of dimensions [71,171–187], and some have proposed three-dimensional systems [177–185,187]. In 1897 Wilhelm Max Wundt, the father of modern psychology, proposed three dimensions of emotion: "pleasurable versus unpleasurable", "arousing or subduing" and "strain or relaxation" [185]. Later, Schlosberg named three dimensions "pleasantness–unpleasantness", "attention–rejection" and "level of activation" [187]. These two theories bear some obvious similarities to the model presented in this article. However, the pleasantness dimension, which has been proposed in many articles following Wundt, is not identical to either one of the serotonergic or dopaminergic axes. These earlier models thus seem somewhat rotated compared to the model presented in this article. One potential bias in previous studies of the dimensionality of emotion is that the pleasantness dimension was often more or less taken for granted, and used when subsequently rating a variety of emotions.

Plutchik also developed a sort of three-dimensional model of emotion, in which the emotions are basically ordered in a circle based on similarity [82]. An intensity dimension is added to this polar, similarity-based model. Here Plutchik might have been misled by the fact that the model originated from a two-dimensional representation, a so-called circumplex model, which then might have led to the possibly false conclusion that the emotions could be ordered in opposing pairs. Therefore, Plutchik's model is not three-dimensional in the same sense as the model presented in this article.

The main advantage of the model presented in this article, compared to all these earlier models of the dimensionality of emotions, is its neurobiological correlate. The model presented in this article could, because of its direct relation to the monoamine systems, help in the understanding of psychiatric illness and the effect of psychotropic drugs. In certain psychiatric disorders the dynamics of one monoamine is thought to be impaired, e.g. serotonin in major depression [26]. If interpreted in terms of the model, in the case of depression, the serotonin axis is supposedly locked in the low-end of the scale and the emotional palette is therefore restricted to one side of the cube, the low-serotonergic side. The basic emotions that are within reach are shame/humiliation, fear/terror, distress/anguish and anger/rage. The primary depressive symptoms of sadness and lack of interest or pleasure [150], might be viewed as the inability to reach the basic emotions of enjoyment/joy and interest/excitement respectively, both located on the high-serotonergic side of the cube.

Other psychiatric disorders associated with disturbances of the monoamine systems might also be interpreted in terms of the model. Although this is speculative and needs to be empirically tested, consider, for example, whether the symptoms of an acute psychosis might be characterized by the supposedly high-dopaminergic basic emotions – an emotional palette restricted to the high-dopaminergic side of the cube – or possibly if symptoms of mania could be characterized as an emotional palette comprising high-serotonergic basic emotions only. If further studies could confirm the validity of this model, perhaps an inventory of the emotions expressed by the patient could serve as a guide to which monoamine disturbances are present. Further clarifying the relation between the emotions, the monoamines and the psychiatric disorders might contribute to a better understanding of emotional regulation in healthy as well as in mentally ill people, and possibly lead to more specific treatments with psychotropic drugs.

Conclusion

This article presents a new, explanatory, three-dimensional model for monoamine neurotransmitters and basic emotions. Further empirical studies are needed to establish its validity.

Conflict of interest

None declared.

References

[1] Purves D, Augustine GJ, Fitzpatrick D, Hall WC, LaMantia A, McNamarra JO, et al. Neuroscience. Sunderland: Sinauer Associates; 2004.
[2] Hannon J, Hoyer D. Molecular biology of 5-HT receptors. Behav Brain Res 2008;195:198–213.
[3] Hornung JP. The human raphe nuclei and the serotonergic system. J Chem Neuroanat 2003;26:331–43.
[4] Benarroch EE. The locus ceruleus norepinephrine system: functional organization and potential clinical significance. Neurology 2009;73:1699–704.
[5] Heimer L. The human brain and spinal cord. Functional neuroanatomy and dissection guide. New York: Springer-Verlag; 1995.
[6] Girault JA, Greengard P. The neurobiology of dopamine signaling. Arch Neurol 2004;61:641–4.
[7] Alenina N, Kikic D, Todiras M, Mosienko V, Qadri F, Plehm R, et al. Growth retardation and altered autonomic control in mice lacking brain serotonin. Proc Natl Acad Sci USA 2009;106:10332–7.
[8] Anstey ML, Rogers SM, Ott SR, Burrows M, Simpson SJ. Serotonin mediates behavioral gregarization underlying swarm formation in desert locusts. Science 2009;323:627–30.
[9] Couppis MH, Kennedy CH. The rewarding effect of aggression is reduced by nucleus accumbens dopamine receptor antagonism in mice. Psychopharmacology (Berl) 2008;197:449–56.
[10] Dennis RL, Chen ZQ, Cheng HW. Serotonergic mediation of aggression in high and low aggressive chicken strains. Poult Sci 2008;87:612–20.
[11] Huber R, Smith K, Delago A, Isaksson K, Kravitz EA. Serotonin and aggressive motivation in crustaceans: altering the decision to retreat. Proc Natl Acad Sci USA 1997;94:5939–42.
[12] Kabelik D, Kelly AM, Goodson JL. Dopaminergic regulation of mate competition aggression and aromatase-Fos colocalization in vasotocin neurons. Neuropharmacology 2010;58:117–25.
[13] Kravitz EA. Hormonal control of behavior: amines and the biasing of behavioral output in lobsters. Science 1988;241:1775–81.

[14] Sawin ER, Ranganathan R, Horvitz HR. *C. elegans* locomotory rate is modulated by the environment through a dopaminergic pathway and by experience through a serotonergic pathway. Neuron 2000;26:619–31.
[15] Stahl S. Stahl's essential psychopharmacology. Neuroscientific basis and practical applications. Cambridge: Cambridge University Press; 2008.
[16] Keltikangas-Jarvinen L, Salo J. Dopamine and serotonin systems modify environmental effects on human behavior: a review. Scand J Psychol 2009;50:574–82.
[17] Lakatos K, Nemoda Z, Birkas E, Ronai Z, Kovacs E, Ney K, et al. Association of D4 dopamine receptor gene and serotonin transporter promoter polymorphisms with infants' response to novelty. Mol Psychiatry 2003;8:90–7.
[18] Szekely A, Ronai Z, Nemoda Z, Kolmann G, Gervai J, Sasvari-Szekely M. Human personality dimensions of persistence and harm avoidance associated with DRD4 and 5-HTTLPR polymorphisms. Am J Med Genet B Neuropsychiatr Genet 2004;126B:106–10.
[19] Dolan M, Anderson IM, Deakin JF. Relationship between 5-HT function and impulsivity and aggression in male offenders with personality disorders. Br J Psychiatry 2001;178:352–9.
[20] Ebstein RP, Benjamin J, Belmaker RH. Personality and polymorphisms of genes involved in aminergic neurotransmission. Eur J Pharmacol 2000;410: 205–14.
[21] Krause J, La Fougere C, Krause KH, Ackenheil M, Dresel SH. Influence of striatal dopamine transporter availability on the response to methylphenidate in adult patients with ADHD. Eur Arch Psychiatry Clin Neurosci 2005;255: 428–31.
[22] Dougherty DD, Bonab AA, Spencer TJ, Rauch SL, Madras BK, Fischman AJ. Dopamine transporter density in patients with attention deficit hyperactivity disorder. Lancet 1999;354:2132–3.
[23] Gur RE, Keshavan MS, Lawrie SM. Deconstructing psychosis with human brain imaging. Schizophr Bull 2007;33:921–31.
[24] Herrmann N, Lanctot KL, Eryavec G, Khan LR. Noradrenergic activity is associated with response to pindolol in aggressive Alzheimer's disease patients. J Psychopharmacol 2004;18:215–20.
[25] Hesse S, Ballaschke O, Barthel H, Sabri O. Dopamine transporter imaging in adult patients with attention-deficit/hyperactivity disorder. Psychiatry Res 2009;171:120–8.
[26] Kalia M. Neurobiological basis of depression: an update. Metabolism 2005;54:24–7.
[27] Lai MK, Tsang SW, Francis PT, Esiri MM, Keene J, Hope T, et al. Reduced serotonin 5-HT1A receptor binding in the temporal cortex correlates with aggressive behavior in Alzheimer disease. Brain Res 2003;974:82–7.
[28] Lanctot KL, Herrmann N, Eryavec G, Van Reekum R, Reed K, Naranjo CA. Central serotonergic activity is related to the aggressive behaviors of Alzheimer's disease. Neuropsychopharmacology 2002;27:646–54.
[29] Marks DM, Pae CU, Patkar AA. Triple reuptake inhibitors: the next generation of antidepressants. Curr Neuropharmacol 2008;6:338–43.
[30] Ruhe HG, Mason NS, Schene AH. Mood is indirectly related to serotonin, norepinephrine and dopamine levels in humans: a meta-analysis of monoamine depletion studies. Mol Psychiatry 2007;12:331–59.
[31] Sharp SI, Ballard CG, Ziabreva I, Piggott MA, Perry RH, Perry EK, et al. Cortical serotonin 1A receptor levels are associated with depression in patients with dementia with Lewy bodies and Parkinson's disease dementia. Dement Geriatr Cogn Disord 2008;26:330–8.
[32] Meisenzahl EM, Schmitt GJ, Scheuerecker J, Moller HJ. The role of dopamine for the pathophysiology of schizophrenia. Int Rev Psychiatry 2007;19:337–45.
[33] Tanaka M, Yoshida M, Emoto H, Ishii H. Noradrenaline systems in the hypothalamus, amygdala and locus coeruleus are involved in the provocation of anxiety: basic studies. Eur J Pharmacol 2000;405:397–406.
[34] Phelps EA, LeDoux JE. Contributions of the amygdala to emotion processing: from animal models to human behavior. Neuron 2005;48:175–87.
[35] Berntson GG, Bechara A, Damasio H, Tranel D, Cacioppo JT. Amygdala contribution to selective dimensions of emotion. Soc Cogn Affect Neurosci 2007;2:123–9.
[36] Pare D, Quirk GJ, Ledoux JE. New vistas on amygdala networks in conditioned fear. J Neurophysiol 2004;92:1–9.
[37] Klüver H, Bucy P. Psychic blindness and other symptoms following bilateral temporal lobectomy in Rhesus monkeys. Am J Physiol 1937;119:352–3.
[38] Adolphs R, Baron-Cohen S, Tranel D. Impaired recognition of social emotions following amygdala damage. J Cogn Neurosci 2002;14:1264–74.
[39] Davidson RJ. Affective neuroscience and psychophysiology: toward a synthesis. Psychophysiology 2003;40:655–65.
[40] Terzian H, Ore GD. Syndrome of Kluver and Bucy; reproduced in man by bilateral removal of the temporal lobes. Neurology 1955;5:373–80.
[41] LeDoux J. Emotion circuits in the brain. Annu Rev Neurosci 2000;23: 155–84.
[42] Talarovicova A, Krskova L, Kiss A. Some assessments of the amygdala role in suprahypothalamic neuroendocrine regulation: a minireview. Endocr Regul 2007;41:155–62.
[43] Phillips AG, Ahn S, Howland JG. Amygdalar control of the mesocorticolimbic dopamine system: parallel pathways to motivated behavior. Neurosci Biobehav Rev 2003;27:543–54.
[44] Sprengelmeyer R, Rausch M, Eysel UT, Przuntek H. Neural structures associated with recognition of facial expressions of basic emotions. Proc Biol Sci 1998;265:1927–31.
[45] De Martino B, Strange BA, Dolan RJ. Noradrenergic neuromodulation of human attention for emotional and neutral stimuli. Psychopharmacology (Berl) 2008;197:127–36.
[46] Egerton A, Mehta MA, Montgomery AJ, Lappin JM, Howes OD, Reeves SJ, et al. The dopaminergic basis of human behaviors: a review of molecular imaging studies. Neurosci Biobehav Rev 2009;33:1109–32.
[47] Flugge G, Van Kampen M, Mijnster MJ. Perturbations in brain monoamine systems during stress. Cell Tissue Res 2004;315:1–14.
[48] Haber SN, Knutson B. The reward circuit: linking primate anatomy and human imaging. Neuropsychopharmacology 2010;35:4–26.
[49] Hikosaka O, Bromberg-Martin E, Hong S, Matsumoto M. New insights on the subcortical representation of reward. Curr Opin Neurobiol 2008;18:203–8.
[50] McGaughy J, Ross RS, Eichenbaum H. Noradrenergic, but not cholinergic, deafferentation of prefrontal cortex impairs attentional set-shifting. Neuroscience 2008;153:63–71.
[51] Price J, Cole V, Goodwin GM. Emotional side-effects of selective serotonin reuptake inhibitors: qualitative study. Br J Psychiatry 2009;195:211–7.
[52] Seo D, Patrick CJ, Kennealy PJ. Role of serotonin and dopamine system interactions in the neurobiology of impulsive aggression and its comorbidity with other clinical disorders. Aggress Violent Behav 2008;13:383–95.
[53] Silva H, Iturra P, Solari A, Villarroel J, Jerez S, Vielma W, et al. Serotonin transporter polymorphism and fluoxetine effect on impulsiveness and aggression in borderline personality disorder. Actas Esp Psiquiatr 2007;35:387–92.
[54] Tops M, Russo S, Boksem MA, Tucker DM. Serotonin: modulator of a drive to withdraw. Brain Cogn 2009;71:427–36.
[55] Landen M, Erlandsson H, Bengtsson F, Andersch B, Eriksson E. Short onset of action of a serotonin reuptake inhibitor when used to reduce premenstrual irritability. Neuropsychopharmacology 2009;34:585–92.
[56] Pearlstein T. Premenstrual dysphoric disorder: out of the appendix. Arch Womens Ment Health 2010;13:21–3.
[57] Bressan RA, Crippa JA. The role of dopamine in reward and pleasure behaviour–review of data from preclinical research. Acta Psychiatr Scand Suppl 2005:14–21.
[58] Ikemoto S, Panksepp J. The role of nucleus accumbens dopamine in motivated behavior: a unifying interpretation with special reference to reward-seeking. Brain Res Brain Res Rev 1999;31:6–41.
[59] Fields HL, Hjelmstad GO, Margolis EB, Nicola SM. Ventral tegmental area neurons in learned appetitive behavior and positive reinforcement. Annu Rev Neurosci 2007;30:289–316.
[60] Foote SL, Aston-Jones G, Bloom FE. Impulse activity of locus coeruleus neurons in awake rats and monkeys is a function of sensory stimulation and arousal. Proc Natl Acad Sci USA 1980;77:3033–7.
[61] Aston-Jones G, Rajkowski J, Kubiak P. Conditioned responses of monkey locus coeruleus neurons anticipate acquisition of discriminative behavior in a vigilance task. Neuroscience 1997;80:697–715.
[62] Leggio GM, Cathala A, Neny M, Rouge-Pont F, Drago F, Piazza PV, et al. In vivo evidence that constitutive activity of serotonin2C receptors in the medial prefrontal cortex participates in the control of dopamine release in the rat nucleus accumbens: differential effects of inverse agonist versus antagonist. J Neurochem 2009;111:614–23.
[63] Jenner P, Sheehy M, Marsden CD. Noradrenaline and 5-hydroxytryptamine modulation of brain dopamine function: implications for the treatment of Parkinson's disease. Br J Clin Pharmacol 1983;15(Suppl 2):277S–89S.
[64] Millan MJ, Dekeyne A, Gobert A. Serotonin (5-HT)2C receptors tonically inhibit dopamine (DA) and noradrenaline (NA), but not 5-HT, release in the frontal cortex in vivo. Neuropharmacology 1998;37:953–5.
[65] Mejias-Aponte CA, Drouin C, Aston-Jones G. Adrenergic and noradrenergic innervation of the midbrain ventral tegmental area and retrorubral field: prominent inputs from medullary homeostatic centers. J Neurosci 2009;29:3613–26.
[66] Fink KB, Gothert M. 5-HT receptor regulation of neurotransmitter release. Pharmacol Rev 2007;59:360–417.
[67] Izard C. Human emotions. New York: Plenum Press; 1977.
[68] Izard C. Basic emotions, relations among emotions, and emotion-cognition relations. Psychol Rev 1992;99:561–5.
[69] Darwin C. The Expression of the emotions in man and animals. London: Penguin Group 2009; 1890.
[70] Ortony A, Turner TJ. What's basic about basic emotions? Psychol Rev 1990;97:315–31.
[71] Posner J, Russell JA, Peterson BS. The circumplex model of affect: an integrative approach to affective neuroscience, cognitive development, and psychopathology. Dev Psychopathol 2005;17:715–34.
[72] Turner TJ, Ortony A. Basic emotions: can conflicting criteria converge? Psychol Rev 1992;99:566–71.
[73] Schachter S, Singer J. Cognitive, social, and psychological determinants of emotional state. Psychol Rev 1962;69:379–99.
[74] Scherer KR, Ellgring H. Are facial expressions of emotion produced by categorical affect programs or dynamically driven by appraisal? Emotion 2007;7:113–30.
[75] Kemper T. How many emotions are there? Wedding the social and the autonomic components. Am J Sociol 1987;93:263–89.
[76] Ekman P. Are there basic emotions? Psychol Rev 1992;99:550–3.
[77] Hennenlotter A, Schroeder U. Partly dissociable neural substrates for recognizing basic emotions: a critical review. Prog Brain Res 2006;156: 443–56.

[78] Izard C. Innate and universal facial expressions: evidence from developmental and cross-cultural research. Psychol Bull 1994;115: 288–99.
[79] Panksepp J. A critical role for "affective neuroscience" in resolving what is basic about basic emotions. In resolving what is basic about basic emotions. Psychol Rev 1992;99:554–60.
[80] Panksepp J. Affective consciousness: core emotional feelings in animals and humans. Conscious Cogn 2005;14:30–80.
[81] Tracy JL, Robins RW, Schriber RA. Development of a FACS-verified set of basic and self-conscious emotion expressions. Emotion 2009;9:554–9.
[82] Plutchik R. The psychology and biology of emotion. New York: HarperCollins College Publishers; 1994.
[83] Nathanson D. Affect, sex, and the birth of the self, Norton & Company. New York: Norton & Company; 1992.
[84] Allport F. Social psychology. Cambridge: The Riverside Press; 1924.
[85] Tomkins S. Affect imagery consciousness volume I the positive affects. New York: Springer Publishing Company; 1962.
[86] Tomkins S. Affect imagery consciousness volume II the negative affects. New York: Springer Publishing Company; 1963.
[87] Tomkins S. Affect imagery consciousness volume III the negative affects anger and fear. New York: Springer Publishing Company; 1991.
[88] Panksepp J. Affective neuroscience. The foundations of human and animal emotions. New York: Oxford University Press; 1998.
[89] Tomkins S. The quest for primary motives: biography and autobiography of an idea. J Pers Soc Psychol 1981;41:306–29.
[90] Ekman P, Friesen WV. Constants across cultures in the face and emotion. J Pers Soc Psychol 1971;17:124–9.
[91] Ekman P, Sorenson ER, Friesen WV. Pan-cultural elements in facial displays of emotion. Science 1969;164:86–8.
[92] Matsumoto D, Willingham B. Spontaneous facial expressions of emotion of congenitally and noncongenitally blind individuals. J Pers Soc Psychol 2009;96:1–10.
[93] Rainville P, Bechara A, Naqvi N, Damasio AR. Basic emotions are associated with distinct patterns of cardiorespiratory activity. Int J Psychophysiol 2006;61:5–18.
[94] C.L. Stephens, I.C. Christie and B.H. Friedman, Autonomic specificity of basic emotions: Evidence from pattern classification and cluster analysis, *Biol Psychol* (2010).
[95] K. Vytal and S. Hamann, Neuroimaging Support for Discrete Neural Correlates of Basic Emotions: A Voxel-based Meta-analysis, *J Cogn Neurosci* (2009).
[96] Fusar-Poli P, Placentino A, Carletti F, Landi P, Allen P, Surguladze S, et al. Functional atlas of emotional faces processing: a voxel-based meta-analysis of 105 functional magnetic resonance imaging studies. J Psychiatry Neurosci 2009;34:418–32.
[97] Collet C, Vernet-Maury E, Delhomme G, Dittmar A. Autonomic nervous system response patterns specificity to basic emotions. J Auton Nerv Syst 1997;62:45–57.
[98] Tomkins S. Affect theory. In: Ekman P, Friesen W, Ellsworth P, editors. Emotions in the human face. Cambridge: Cambridge University Press; 1982. p. 355–95.
[99] Tomkins S, McCarter R. What and where are the primary affects? Some evidence for a theory. Percept Mot Skills 1964;18:119–58.
[100] Ekman P, Friesen WV, Simons RC. Is the startle reaction an emotion? J Pers Soc Psychol 1985;49:1416–26.
[101] Fadok JP, Dickerson TM, Palmiter RD. Dopamine is necessary for cue-dependent fear conditioning. J Neurosci 2009;29:11089–97.
[102] Ponnusamy R, Nissim HA, Barad M. Systemic blockade of D2-like dopamine receptors facilitates extinction of conditioned fear in mice. Learn Mem 2005;12:399–406.
[103] de Oliveira AR, Reimer AE, Brandao ML. Role of dopamine receptors in the ventral tegmental area in conditioned fear. Behav Brain Res 2009;199: 271–7.
[104] Fadok JP, Darvas M, Dickerson TM, Palmiter RD. Long-term memory for pavlovian fear conditioning requires dopamine in the nucleus accumbens and basolateral amygdala. PLoS One 2010;5:e12751.
[105] Lawrence AD, Goerendt IK, Brooks DJ. Impaired recognition of facial expressions of anger in Parkinson's disease patients acutely withdrawn from dopamine replacement therapy. Neuropsychologia 2007;45:65–74.
[106] Bowers D, Miller K, Mikos A, Kirsch-Darrow L, Springer U, Fernandez H, et al. Startling facts about emotion in Parkinson's disease: blunted reactivity to aversive stimuli. Brain 2006;129:3356–65.
[107] Lawrence AD, Calder AJ, McGowan SW, Grasby PM. Selective disruption of the recognition of facial expressions of anger. Neuroreport 2002;13:881–4.
[108] Dougherty DD, Bonab AA, Ottowitz WE, Livni E, Alpert NM, Rauch SL, et al. Decreased striatal D1 binding as measured using PET and (11C)SCH 23, 390 in patients with major depression with anger attacks. Depress Anxiety 2006;23:175–7.
[109] Cannon DM, Klaver JM, Peck SA, Rallis-Voak D, Erickson K, Drevets WC. Dopamine type-1 receptor binding in major depressive disorder assessed using positron emission tomography and (11C)NNC-112. Neuropsychopharmacology 2009;34:1277–87.
[110] Pasquini M, Picardi A, Biondi M, Gaetano P, Morosini P. Relevance of anger and irritability in outpatients with major depressive disorder. Psychopathology 2004;37:155–60.
[111] Painuly N, Sharan P, Mattoo SK. Antecedents concomitants and consequences of anger attacks in depression. Psychiatry Res 2007;153:39–45.
[112] Rosenbaum JF, Fava M, Pava JA, McCarthy MK, Steingard RJ, Bouffides E. Anger attacks in unipolar depression, Part 2: Neuroendocrine correlates and changes following fluoxetine treatment. Am J Psychiatry 1993;150:1164–8.
[113] Fava M, Rosenbaum JF, Pava JA, McCarthy MK, Steingard RJ, Bouffides E. Anger attacks in unipolar depression, Part 1: clinical correlates and response to fluoxetine treatment. Am J Psychiatry 1993;150:1158–63.
[114] Barak Y, Plopski I, Tadger S, Paleacu D. Escitalopram versus risperidone for the treatment of behavioral and psychotic symptoms associated with Alzheimer's disease: a randomized double-blind pilot study. Int Psychogeriatr 2011:1–5.
[115] Luby J, Belden A, Sullivan J, Hayen R, McCadney A, Spitznagel E. Shame and guilt in preschool depression: evidence for elevations in self-conscious emotions in depression as early as age 3. J Child Psychol Psychiatry 2009;50:1156–66.
[116] Orth U, Berking M, Burkhardt S. Self-conscious emotions and depression: rumination explains why shame but not guilt is maladaptive. Pers Soc Psychol Bull 2006;32:1608–19.
[117] Vikan A, Hassel AM, Rugset A, Johansen HE, Moen T. A test of shame in outpatients with emotional disorder. Nord J Psychiatry 2010;64:196–202.
[118] Pollack MH. Comorbid anxiety and depression. J Clin Psychiatry 2005;66(Suppl 8):22–9.
[119] Schneier FR. Clinical practice. Social anxiety disorder. N Engl J Med 2006;355:1029–36.
[120] Maron E, Kuikka JT, Ulst K, Tiihonen J, Vasar V, Shlik J. SPECT imaging of serotonin transporter binding in patients with generalized anxiety disorder. Eur Arch Psychiatry Clin Neurosci 2004;254:392–6.
[121] van der Wee NJ, van Veen JF, Stevens H, van Vliet IM, van Rijk PP, Westenberg HG. Increased serotonin and dopamine transporter binding in psychotropic medication-naive patients with generalized social anxiety disorder shown by 123I-beta-(4-iodophenyl)-tropane SPECT. J Nucl Med 2008;49:757–63.
[122] Tangney JP, Wagner P, Gramzow R. Proneness to shame, proneness to guilt, and psychopathology. J Abnorm Psychol 1992;101:469–78.
[123] Fergus TA, Valentiner DP, McGrath PB, Jencius S. Shame- and guilt-proneness: relationships with anxiety disorder symptoms in a clinical sample. J Anxiety Disord 2010;24:811–5.
[124] Walsh K, Bennett G. Parkinson's disease and anxiety. Postgrad Med J 2001;77:89–93.
[125] Dissanayaka NN, Sellbach A, Matheson S, O'Sullivan JD, Silburn PA, Byrne GJ, et al. Anxiety disorders in Parkinson's disease: prevalence and risk factors. Mov Disord 2010;25:838–45.
[126] Hettema JM, An SS, Bukszar J, Van den Oord EJ, Neale MC, Kendler KS, et al. Catechol-*O*-methyltransferase contributes to genetic susceptibility shared among anxiety spectrum phenotypes. Biol Psychiatry 2008;64:302–10.
[127] McGrath M, Kawachi I, Ascherio A, Colditz GA, Hunter DJ, De Vivo I. Association between catechol-O-methyltransferase and phobic anxiety. Am J Psychiatry 2004;161:1703–5.
[128] Scahill L, Leckman JF, Schultz RT, Katsovich L, Peterson BS. A placebo-controlled trial of risperidone in Tourette syndrome. Neurology 2003;60:1130–5.
[129] Emmanuel NP, Brawman-Mintzer O, Morton WA, Book SW, Johnson MR, Lorberbaum JP, et al. Bupropion-SR in treatment of social phobia. Depress Anxiety 2000;12:111–3.
[130] Schank JR, Liles LC, Weinshenker D. Norepinephrine signaling through beta-adrenergic receptors is critical for expression of cocaine-induced anxiety. Biol Psychiatry 2008;63:1007–12.
[131] Nutt DJ, Bell CJ, Malizia AL. Brain mechanisms of social anxiety disorder. J Clin Psychiatry 1998;59(Suppl 17):4–11.
[132] Yu BH, Kang EH, Ziegler MG, Mills PJ, Dimsdale JE. Mood states, sympathetic activity, and in vivo beta-adrenergic receptor function in a normal population. Depress Anxiety 2008;25:559–64.
[133] Ross S, Peselow E. The neurobiology of addictive disorders. Clin Neuropharmacol 2009;32:269–76.
[134] A.C. Galvao, R.C. Kruger, P.D. Campagnolo, V.S. Mattevi, M.R. Vitolo and S. Almeida, Association of MAOA and COMT gene polymorphisms with palatable food intake in children, J Nutr Biochem (2011).
[135] Faure A, Reynolds SM, Richard JM, Berridge KC. Mesolimbic dopamine in desire and dread: enabling motivation to be generated by localized glutamate disruptions in nucleus accumbens. J Neurosci 2008;28:7184–92.
[136] Berridge KC. Food reward: brain substrates of wanting and liking. Neurosci Biobehav Rev 1996;20:1–25.
[137] Mallo T, Alttoa A, Koiv K, Tonissaar M, Eller M, Harro J. Rats with persistently low or high exploratory activity: behaviour in tests of anxiety and depression and extracellular levels of dopamine. Behav Brain Res 2007;177:269–81.
[138] Ortigue S, Bianchi-Demicheli F, Patel N, Frum C, Lewis JW. Neuroimaging of love: fMRI meta-analysis evidence toward new perspectives in sexual medicine. J Sex Med 2010;7:3541–52.
[139] Tancer M, Johanson CE. The effects of fluoxetine on the subjective and physiological effects of 3, 4-methylenedioxymethamphetamine (MDMA) in humans. Psychopharmacology (Berl) 2007;189:565–73.
[140] Nichols DE. Differences between the mechanism of action of MDMA, MBDB, and the classic hallucinogens. Identification of a new therapeutic class: entactogens. J Psychoactive Drugs 1986;18:305–13.
[141] Cami J, Farre M, Mas M, Roset PN, Poudevida S, Mas A, et al. Human pharmacology of 3, 4-methylenedioxymethamphetamine ("ecstasy"): psychomotor performance and subjective effects. J Clin Psychopharmacol 2000;20:455–66.

[142] Curran HV, Rees H, Hoare T, Hoshi R, Bond A. Empathy and aggression: two faces of ecstasy? A study of interpretative cognitive bias and mood change in ecstasy users. Psychopharmacology (Berl) 2004;173:425–33.
[143] Bedi G, Hyman D. H. de Wit, Is ecstasy an "empathogen"? Effects of +/-3, 4-methylenedioxymethamphetamine on prosocial feelings and identification of emotional states in others. Biol Psychiatry 2010;68:1134–40.
[144] Parrott AC. Human psychopharmacology of Ecstasy (MDMA): a review of 15 years of empirical research. Hum Psychopharmacol 2001;16:557–77.
[145] Orosco M, Rouch C, Beslot F, Feurte S, Regnault A, Dauge V. Alpha-lactalbumin-enriched diets enhance serotonin release and induce anxiolytic and rewarding effects in the rat. Behav Brain Res 2004;148:1–10.
[146] Murphy SE, Longhitano C, Ayres RE, Cowen PJ, Harmer CJ. Tryptophan supplementation induces a positive bias in the processing of emotional material in healthy female volunteers. Psychopharmacology (Berl) 2006;187:121–30.
[147] Kemp AH, Gray MA, Silberstein RB, Armstrong SM, Nathan PJ. Augmentation of serotonin enhances pleasant and suppresses unpleasant cortical electrophysiological responses to visual emotional stimuli in humans. Neuroimage 2004;22:1084–96.
[148] Norbury R, Taylor MJ, Selvaraj S, Murphy SE, Harmer CJ, Cowen PJ. Short-term antidepressant treatment modulates amygdala response to happy faces. Psychopharmacology (Berl) 2009;206:197–204.
[149] Tondo L, Vazquez G, Baldessarini RJ. Mania associated with antidepressant treatment: comprehensive meta-analytic review. Acta Psychiatr Scand 2010;121:404–14.
[150] American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision, American Psychiatric Association, Washington, DC (2000).
[151] Corona G, Ricca V, Bandini E, Mannucci E, Lotti F, Boddi V, et al. Selective serotonin reuptake inhibitor-induced sexual dysfunction. J Sex Med 2009;6:1259–69.
[152] Opbroek A, Delgado PL, Laukes C, McGahuey C, Katsanis J, Moreno FA, et al. Emotional blunting associated with SSRI-induced sexual dysfunction Do SSRIs inhibit emotional responses? Int J Neuropsychopharmacol 2002;5:147–51.
[153] Young EJ, Williams CL. Valence dependent asymmetric release of norepinephrine in the basolateral amygdala. Behav Neurosci 2010;124:633–44.
[154] Rodriguez-Manzo G, Fernandez-Guasti A. Participation of the central noradrenergic system in the reestablishment of copulatory behavior of sexually exhausted rats by yohimbine, naloxone, and 8-OH-DPAT. Brain Res Bull 1995;38:399–404.
[155] Ventura R, Latagliata EC, Morrone C, La Mela I. Prefrontal norepinephrine determines attribution of "high" motivational salience. PLoS One 2008;3:e3044.
[156] Hoebel BG, Hernandez L, Schwartz DH, Mark GP, Hunter GA. Microdialysis studies of brain norepinephrine Serotonin, and dopamine release during ingestive behavior. Theoretical and clinical implications. Ann N Y Acad Sci 1989;575:171–91. discussion 192-173.
[157] Hagemann LF, Costa CV, Zeni LZ, Freitas CG, Marino-Neto J, Paschoalini MA. Food intake after adrenaline and noradrenaline injections into the hypothalamic paraventricular nucleus in pigeons. Physiol Behav 1998;64:645–52.
[158] Wellman PJ. Norepinephrine and the control of food intake. Nutrition 2000;16:837–42.
[159] Dutton DG, Aron AP. Some evidence for heightened sexual attraction under conditions of high anxiety. J Pers Soc Psychol 1974;30:510–7.
[160] Aan Het Rot M, Coupland N, Boivin DB, Benkelfat C, Young SN. Recognizing emotions in faces: effects of acute tryptophan depletion and bright light. J Psychopharmacol 2010;24:1447–54.
[161] Douglas KM, Porter RJ. Recognition of disgusted facial expressions in severe depression. Br J Psychiatry 2010;197:156–7.
[162] Montagne B, Schutters S, Westenberg HG, Van Honk J, Kessels RP, De Haan EH. Reduced sensitivity in the recognition of anger and disgust in social anxiety disorder. Cogn Neuropsychiatry 2006;11:389–401.
[163] Mosher TM, Smith JG, Greenshaw AJ. Aversive stimulus properties of the 5-HT2C receptor agonist WAY 161503 in rats. Neuropharmacology 2006;51:641–50.
[164] Zarzana EC, Basso AS, Costa-Pinto FA, Palermo-Neto J. Pharmacological manipulation of immune-induced food aversion in rats. Neuroimmunomodulation 2009;16:19–27.
[165] Patanwala AE, Amini R, Hays DP, Rosen P. Antiemetic therapy for nausea and vomiting in the emergency department. J Emerg Med 2010;39:330–6.
[166] Kang JI, Kim SJ, Namkoong K, An SK. Association of DRD4 and COMT polymorphisms with disgust sensitivity in healthy volunteers. Neuropsychobiology 2010;61:105–12.
[167] Ille R, Schony M, Kapfhammer HP, Schienle A. Elevated disgust proneness in schizophrenia. J Clin Psychol 2010;66:1090–100.
[168] Suslow T, Roestel C, Ohrmann P, Arolt V. The experience of basic emotions in schizophrenia with and without affective negative symptoms. Compr Psychiatry 2003;44:303–10.
[169] Mark GP, Blander DS, Hoebel BG. A conditioned stimulus decreases extracellular dopamine in the nucleus accumbens after the development of a learned taste aversion. Brain Res 1991;551:308–10.
[170] Mas M, Fumero B, González-Mora JL. Voltammetric and microdialysis monitoring of brain monoamine neurotransmitter release during sociosexual interactions. Behav Brain Res 1995;71:69–79.
[171] Russell J. A Circumplex Model of Affect. J Pers Soc Psychol 1980;39:1161–78.
[172] Izard C, Nunnally J. Evaluative responses to affectively positive and negative facial photographs: factor structure and construct validity. Educ Psychol Meas 1965;25:1061–71.
[173] Frijda NH, Philipszoon E. Dimensions of recognition of expression. J Abnorm Soc Psychol 1963;66:45–51.
[174] Russell J. Pancultural aspects of the human conceptual organization of emotions. J Pers Soc Psychol 1983;45:1281–8.
[175] Schlosberg H. A scale for the judgment of facial expressions. J Exp Psychol 1941;29:497–510.
[176] Schlosberg H. The description of facial expressions in terms of two dimensions. J Exp Psychol 1952;44:229–37.
[177] Abelson RP, Sermat V. Multidimensional scaling of facial expressions. J Exp Psychol 1962;63:546–54.
[178] Block J. Studies in the phenomenology of emotions. J Abnorm Psychol 1957;54:358–63.
[179] Bush 2nd LE. Individual differences multidemensional scaling of adjectives denoting feelings. J Pers Soc Psychol 1973;25:50–7.
[180] Osgood C. Dimensionality of the semantic space for communication via facial expressions. Scand J Psychol 1966;7:1–30.
[181] Thompson DF, Meltzer L. Communication of emotional intent by facial expression. J Abnorm Psychol 1964;68:129–35.
[182] Triandis HC, Lambert WW. A restatement and test of Schlosberg's theory of emotion with two kinds of subjects from Greece. J Abnorm Psychol 1958;56:321–8.
[183] Osgood C. Studies on the generality of affective meaning systems. Am Psychol 1962;17:10–28.
[184] Russell J. Evidence for a three-factor theory of emotions. J Res Pers 1977;11:273–94.
[185] W.M. Wundt, Outlines of Psychology. In: Classics in the history of psychology. http://psychclassics.asu.edu/index.htm, York University 2010, Toronto (1897).
[186] Watson D, Wiese D, Vaidya J, Tellegen A. The two general activation systems of affect: structural findings. Evolutionary considerations, and psychobiological evidence. J Pers Soc Psychol 1999;76:820–38.
[187] Schlosberg H. Three dimensions of emotion. Psychol Rev 1954;61:81–8.