When speaking of mood disturbance or disorders, in the broad sense of chronic changes in emotions, one should recognize that all intimate and relational events are bathed in emotions, such as sadness, happiness, or anger. Our perception of the world is not emotionally neutral: it may taste bitter, it may be colored black, it may weigh a ton, or, on the contrary, it may have a rosy summery hue. These perceptual “tastes” can be broken down into biological, behavioral, and subjective components in which subjects express verbally how they experience their lives.

Ethology—the science of behavior from a biological and psychological point of view—approaches mood disturbance along phylogenetic lines and is based on observing the evolution of species. It then analyzes the ontogenesis of a given mood disturbance in the growth of an individual member of that species. Finally, it evaluates how the language competence of humans, by constructing a world of verbal representations, can lead to feelings of a lighter or, on the contrary, heavier “taste” of the world.

Animal ontogenesis

Mice with Lesch-Nyhan syndrome interpret all information as aggression, to which they respond by defensive aggression. In this X-chromosome–linked recessive syndrome, there is a deficiency of the enzyme hypoxanthine guanine phosphoribosyl transferase (HPRT), which does not degrade uric acid properly. In these conditions, the basal ganglia and the amygdala can be permanently activated by too much uric acid, an otherwise useful antioxidant. The slightest external stimulus prompts a reaction of rage and self-injury. This is a clear instance of a mood disturbance being induced by an endogenous substance. Another chromosomal abnormality, Down’s syndrome, which is common in monkeys, induces a very different
development, where the affected animal is easygoing and behaves like a “superbaby.” This triggers mothering responses from many females and even some males. The first example, among many others, reminds us how mood states are sometimes massively shaped by the biology of the brain, independently of the environment. However, the example below illustrates how the environment interacts with the genes.

In his paradigmatic protocol from the early 1960s, Harlow used partial or total sensory deprivation and showed that this induced severe developmental disturbances. Eight very young rhesus monkeys were separated from their mother and raised in isolation in cages containing two surrogate mothers: one made of wire incorporating a nipple that gave milk; the other covered in terry cloth with no nipple, thus giving no milk. At each stress, in the form of mechanical teddy bear beating a drum, the baby monkeys were startled and leapt for reassurance onto the terry-cloth mother. As soon as they made contact with this secure base, the monkeys lost their anxiety. But, in the absence of the terry-cloth mother, they would run in every direction, whimper, and stop eating or sleeping. In summary, they were soothed by contact with the soft mother surrogate and panic-stricken in its absence.

Each species reacts differently to the deprivation of a mother. Some are barely affected, whereas others are arrested in their development. Thus, there are genetic determinants for the sensitivity to this type of situation. There is also variation within a given species. Although most baby rhesus monkeys are impaired in their development, some even fatally, a few pursue their growth as if they had no need of the secure base of a mother. Monkeys with the short form of the 5-hydroxytryptamine (serotonin, 5-HT) transporter (5-HTT) gene appear less able to cope with inadequate mothering. Those with the long form of the 5-HTT allele, on the other hand, do not experience the inadequate mothering as a deprivation or as a cause for anxiety, and they continue their normal development. The long form of the 5-HTT allele leads to the synthesis of more 5-HT in the synapses and interstitial fluid.

These observations are synchronic, meaning that they refer to a single point in time. The same maternal failing plunges the baby monkey with the short form of the 5-HTT allele into mood disturbances, but the baby monkey with the long form of the 5-HTT allele will not experience the same information as a loss. Thus, the same environmental fact can prompt opposing interpretations: “I perceive defective mothering that impairs my mood,” would say one baby monkey; while another would say “I perceive the same defective mothering, but it makes me seek out a sensory surrogate in my environment to maintain my peace of mind.”

The changes in physiological regulation (homeostasis) that occur with mood changes should also be analyzed through longitudinal observation. This diachronic dimension reveals that, through repetition of a given interpretation of the sensory information, the monkey with the short form of the 5-HTT allele eventually develops a distinctive style of existence. Every encounter involves trauma and this monkey avoids socializing play and experiences all unexpected information as an alarm, often responding by fight or flight; its path in life is littered with emotional alerts, dazed mood, and interaction difficulties.

However, such genetic predisposition to vulnerability does not constitute an inexorable destiny. Thus, when a vulnerable baby monkey is raised by a competent mother, it acquires a style of attachment that is secure, calm, and confident. An environment with stable developmental tutors enables it to mature in security with a decline in vulnerability. On the other hand, a baby monkey with the long form of the 5-HTT allele, although less vulnerable to emotional loss, may have developmental difficulties in an overstable environment. A female rat stressed during the last part of pregnancy will give birth to a litter with durable increased biological correlates of stress, such as enhanced corticosterone secretion.

All these results from studies in observational and experimental ethology suggest that the same genetic pattern can produce emotional vulnerability in an unstable setting or emotional strength in a stable setting.

**Human ontogenesis**

The model of baby monkey development mentioned above associated synchronic phenomena with diachronic adaptation. This model can also be applied to the development of children.
At the embryonic stage, interactions are essentially physicochemical. However, long before birth, a baby responds to sensory information. As its memory develops, the baby manifests habituation in the cognitive sense of the term, in that it decreases its response to tactile or auditory inputs that have become familiar through repetition. The emergence of memory has made it possible for a present perception to be modified by—or after—comparison with a similar perception from the past.

Absence of appropriate sensory stimulation during this stage of intense fetal neuronal and synaptic development could impair the organization of information circuits. After birth and during the first years of life, this could lead to a failure to give a form to the perceived world, and to the fact that all information is flagged with an alert status because it does not fit into a circuit that would permit an appropriate response. All information, even if purely physiological, thus becomes a stressor.

In 1946, clinical neurologists observed a very high frequency of frontal lobe and limbic system atrophy in the gas encephalograms of Holocaust survivors, which they explained by a vitamin deficiency according to the scientific myth prevailing at the time. After the fall of the Iron Curtain in 1989, computed tomography scans of Romanian orphans institutionalized under catastrophic conditions of sensory deprivation demonstrated the same frontal lobe and limbic system atrophy. On this occasion, however, the prevailing scientific interpretation took ethology into account, and this sometimes massive cerebral atrophy was attributed to sensory deprivation. Modern neurobiology can now describe stages and conditions of nervous system development where given stimuli can result in atrophy, normality, or repair. To take the example of light-deprived kittens, sensory deprivation abolishes traffic across physiological synaptic pathways. Not only does the corresponding brain area then fail to develop the dendrites that would normally have filled their allotted space, but also any subsequent visual physiological stimulus and information will be interpreted as a stress. With functional imaging techniques, one observes that these light-deprived kittens, when later exposed to visual stimuli, have a profusion of occipital neuron activation, despite failing to process the visual information properly. In contrast, when a neuronal circuit has been adequately trained by the repetition of normal sensory stimulation, it can handle information at a lower energy cost, i.e., neurons are not overly activated.

Emotional deprivation might have toxic effects on brain development that make the individual more or less incapable of processing emotional information. Even the banal and everyday fact of being touched by another person or a simple glance or word unleashes aggression. Affected children bite themselves when somebody smiles at them or bang their head on the floor when somebody looks at them. The interpretation of these sensory stimuli as being threats to oneself is accompanied by an increase in secretion of glucocorticoids. This might lead to neuronal damage and death, in particular in the pyramidal cells of the CA3 area in the hippocampus. During the early phases of the dazzlingly fast development of the brain, external information can participate in dendrite formation: an environment of sensory impoverishment substantially decreases brain mass in the area of the hippocampus. A large number of other factors also influence brain maturation. Some of these factors are physical, such as the secretion of hormones. Physical factors interact with the environment. For example in 1057 people followed from birth to the age of 26 years, neither life stress nor the polymorphism of the 5-HTT alone was able to predict the occurrence of a major depressive episode. However, the combination of a high load in life stressors and having the short form of the 5-HTT allele did serve as a predictor. Stress had no influence on people who had the long form of the 5-HTT allele. This suggests that the 5-HTT polymorphism determines the “taste” of the world for the individual as well as temperamental dispositions, such as harm avoidance. Other factors are social and cultural, for example, the beliefs or myths about how to best take care of newborn babies and children. All these factors converge onto individual developing neurons and neuronal circuits.

Memory traces

Imprinting is a process readily observed in nature and equally readily demonstrated in the laboratory. It differs from other forms of learning by becoming established with great rapidity at a very early stage in development. At a particular time and a sensitive stage in its growth, the body becomes highly sensitive to all external information reaching it. In this way, auditory, olfactory, or visual objects become imprinted in memory, in the limbic system, sensitizing the individual preferentially to a type of information. From then on, it is with heightened sensitivity that the individual perceives a particular
maternal body language—or a song, intonation, landscape, or smell—because this sensory object for the individual stands out from all others. From this stage of development onwards, the individual’s world is categorized into hyperfamiliar imprinted objects, which induce a feeling of security that allows him or her to explore the environment and hence lead to other forms of learning. By contrast, in a world deprived of imprinted objects, the individual experiences all information as aggression. He or she responds with alert reactions (discharge of catecholamines and cortisol; cerebral arousal) and disorganized fight or flight behavior. Prisoners of the moment, such individuals become unable to learn.

The plasticity of the human nervous system, the length of its development, makes it impossible to speak of imprinting in humans. This does not exclude astonishing receptivity in the early years and a huge potential for rapid learning. Moreover, an apparently identical external fact could have completely different effects, depending on the development stage and the memories already acquired. Although one cannot talk of imprinting in the sense of the early and automatic affiliation that was studied by Konrad Lorenz, one can talk of phases of sensitization. These phases, together with the keen memory of humans, explain why early interaction could mold temperaments, through incorporation into implicit memory of preferential sensitivity (the “taste” of perception) and relationship skill (the style of attachment). The imprinting of sensory objects thus tailors the nervous system to perceive a particular type of world, select certain items of information, and create a personal representation of oneself interacting with others. Bowlby called this imprinted representation the “internal working model.” Several lines of research show that the experiences and the environment encountered during critical periods of development can lead to long-term changes in the expression of the genome. For example, female rats who lick their newborn offspring more often during the first week of life induce in them a lesser responsivity to stressors, lasting into adulthood. These behavioral changes are accompanied by a higher number of glucocorticoid receptors in the hippocampus due to an epigenetic modification of a transcription factor of this receptor.

Feelings and words

The above facts could induce resignation (“we are the puppets of our genes and environment; we are molded by our experiences”), were there not the option of reworking our representation through speech. How we talk about our past, and the stories we tell ourselves about our present and our future, reflect our feelings and emotions. The same facts can induce different feelings because each person has a different history, and does not attribute the same emotion to the same verbal representation. The fact that the emotional response to the same story differs between listeners invites the speaker to make the effort of empathy, by which he or she looks at himself or herself from the outside. This cognitive leap can act upon and transform the initial emotion.

This use of speech—this rhetoric—expresses the emotions of the inner world, organizes the behavioral consequences of these emotions, and thus explains the possibility of mental transmission. Between molecular biology on the one hand and emotion-structuring speech on the other, mood stands at a confluence of determinants, and is subject to modification by each.

REFERENCES

1. Harlow HF, Harlow MK. Social deprivation in monkeys. Sci Amer. 1962;207:157-146.
2. Suomi SJ. A biobehavioral perspective on developmental psychopathology: excessive aggression and serotoninergic dysfunction in monkeys. In: Sameroff AJ, Lewis M, Miller S, eds. Handbook of Developmental Psychopathology. New York, NY: Plenum Press; 2000:237-256.
3. Bennett AJ, Lech K, Heils A, et al. Early experience and serotonin transporter gene variation interact to influence primate CNS function. Mol Psychiatry. 2002;7:118-122.
4. Higley JD, King ST, Hasert MF, Champaign M, Suomi SJ, Linnoila M. Stability of interindividual differences in serotonin function and its relationship to severe aggression and competent social behavior in rhesus macaque females. Neuropsychopharmacology. 1996;14:67-76.
5. Henry C, Kabbaj M, Simon H, Le Moal M, Maccari S. Prenatal stress increase the hypothalamo-pituitary-adrenal axis response in young and adult rats. J Neuroendocrinol. 1994;6:341-345.
6. Abalan F, Bourgeois M. Les conséquences neuropsychiques de la déportation. Synapse. 1995;119.
7. Abalan F, Martínez-Gallardo R, Bourgeois M. Neuropsychological sequences of deportation to the Nazi concentration camps during the Second World War [in Spanish]. Actas Luso Esp Neurol Psiquiatr Cienc Afines. 1989;17:36-43 and 1989;17:365-372.
8. LeDoux JE, Romanski LM, Xagoraris AE. Indelibility of subcortical emotional memories. J Cogn Neurosci. 1999;22:105-122.
9. McEwen BS. Stress and hippocampal plasticity. Annu Rev Neurosci. 1999;22:105-122.
10. Hubel DH, Wiesel TN. Receptive fields of single neurons in the cat’s striate cortex. J Physiol. 1959;148:574-591.
La etología y los correlatos biológicos del humor

La comprensión de la etología –la ciencia de la conducta animal desde una perspectiva biológica y psicológica– fue incorporada en los años 1950 por el psiquiatra inglés experto en desarrollo, John Bowlby, en su teoría del apego. Esta teoría argumenta que una base afectiva segura en la infancia es crítica para el normal desarrollo de la percepción, la cognición, el aprendizaje y la emoción, además de los parámetros físicos. La teoría fue ilustrada por los experimentos pioneros de Harlow en crías de monos: las que crecían con una “madre” hecha de alambre no tenían un desarrollo exitoso en comparación con el desarrollo más normal de aquéllas que recibían un contacto confortable de una madre sustituta confeccionada en tela de toalla. Las modernas técnicas de neurociencias han confirmado que la ausencia de la estimulación sensorial durante períodos de máxima expresión sináptica proporciona el sustrato para un posterior trastorno del ánimo. La etología ofrece una original aproximación de “lo natural más lo adquirido” en el desarrollo del ánimo anormal y como blanco para el tratamiento.

Éthologie et corrélations biologiques de l’humeur

Dans les années 1950, le spécialiste britannique de la psychiatrie du développement, John Bowlby, a intégré la compréhension de l’éthologie, étude du comportement des animaux d’un point de vue biologique et psychologique, à sa théorie de l’attachement. Cette théorie stipule qu’une base affective sûre dans l’enfance est déterminante pour le développement normal de la perception, de la cognition, de l’apprentissage et de l’émotion, auxquels s’ajoutent les paramètres physiques. Pionnier, Harlow a illustré cette théorie par des expériences avec les bébés singes : ceux qui ont été élevés avec une mère substitutive en fil de fer ne se sont pas bien développés, tandis que ceux qui ont grandi au contact confortable d’un tissu éponge en guise de substitut maternel se sont développés plus normalement. Les techniques modernes des neurosciences ont confirmé que l’absence de stimulation sensorielle pendant les périodes de développement maximal des synapses conduit à l’élaboration du substrat induisant les futurs troubles de l’humeur. L’éthologie offre une nouvelle approche « inné plus acquis » au développement de l’humeur pathologique, ainsi qu’une cible pour le traitement.

11. Caspi A, Sugden K, Moffitt TE, et al. Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene. Science. 2003;301:386-389.
12. Immelman K. Dictionnaire de l'éthologie. Brussels, Belgium: Pierre Mardaga; 1990:100-103.
13. Chapouthier G. La biochimie de l’empreinte. La Recherche. 1977;83:994-995.
14. Bowlby J. The role of childhood experience in cognitive disturbance. In: Mahoney MJ, Freeman A, eds. Cognition and Psychotherapy. New York, NY: Plenum; 1985:181-200.
15. Pierrehumbert B. Modèle interne opérant. In: Dictionnaire de psychopathologie de l’enfant et de l’adolescent. Paris, France: Presses Universitaires de France; 2000:422-424.
16. Weaver IC, Cervoni N, Champagne FA, et al. Epigenetic programming by maternal behavior. Nat Neurosci. 2004;7:847-854.
17. Main M, Kaplan N, Cassidy J. Security in infancy, childhood and adulthood: a move to the level of representations. In: Bretherton I, Waters E, eds. Growing Points in Attachment Theory and Research. Ann Arbor, Mich: Society for Research in Child Development; 1985;50:66-104.