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BULLETIN N° 212
ACADÉMIE EUROPEENNE INTERDISCIPLINAIRE DES SCIENCES
INTERDISCIPLINARY EUROPEAN ACADEMY OF SCIENCES

Lundi 6 février 2017:
à 17 h à la Maison de l'AX, 5 rue Descartes 75005 PARIS

Conférence du Pr Alberto OLIVIERO
Pr Émérite Psychobiologie / Faculté des Sciences / La Sapienza/Rome
" *La vie cachée du cerveau* "

Notre Prochaine séance aura lieu le lundi 6 mars 2017 à 16h30
5 rue Descartes 75005 PARIS
Elle aura pour thème

I. 16h30 :Présentation par notre collègue le Pr Anastasios-Jean.D. MÉTAXAS du Projet:
"*Rencontres Interdisciplinaires Franco-Helléniques*"
II. 17 h : Préparation du prochain colloque "Les signatures de la conscience":
Conférence du Pr Francis EUSTACHE
Université de Caen-Normandie
"*Neuropsychologie et Imagerie de la Mémoire Humaine*"

ACADÉMIE EUROPÉENNE INTERDISCIPLINAIRE DES SCIENCES
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TABLE DES MATIERES

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ACADEMIE EUROPEENNE INTERDISCIPLINAIRE DES SCIENCES
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5 rue Descartes 75005 PARIS

Séance du Lundi 6 février 2017 /Maison de l'AX 17h

La séance est ouverte à 17h **sous la Présidence de Victor MASTRANGELO** et en la présence de nos Collègues Gilbert BELAUBRE, Jean-Louis BOBIN, Gilles COHEN-TANNOUDJI, Sylvie DERENNE, Ernesto DI MAURO, Françoise DUTHEIL, Claude ELBAZ, Irène HERPE-LITWIN, Claude MAURY, Marie-Françoise PASSINI, Edith PERRIER, Jacques PRINTZ, Jean-Paul TEYSSANDIER.

Etaient excusés :François BEGON, Jean-Pierre BESSIS, Bruno BLONDEL, Michel CABANAC, , Alain CARDON, Juan-Carlos CHACHQUES, Alain CORDIER , Daniel COURGEAU, Jean-Felix DURASTANTI, Vincent FLEURY, Robert FRANCK, Jean -Pierre FRANCOISE, Michel GONDRAN, Jacques HENRI-ROBERT, Dominique LAMBERT, Valérie LEFEVRE-SEGUIN, Gérard LEVY, Antoine LONG, Pierre MARCHAIS, Anastassios METAXAS, Jacques NIO, Pierre PESQUIES, Jean SCHMETS , Michel SPIRO, Alain STAHL, Jean-Pierre TREUIL, Jean VERDETTI.

I. Présentation de notre conférencier le Pr Alberto OLIVIERO par notre Président Victor MASTRANGELO

Voici le CV résumé de notre conférencier Alberto OLIVERIO:

Après des études de médecine à l'Université de Rome et s'être spécialisé en pharmacologie du Système Nerveux Central, il a séjourné pendant de longues périodes à l'étranger:

- Département de Physiologie de l'Institut Karolinska à Stockholm,
- Institut de recherche sur le Cerveau de Los Angeles.

Ses principaux centres d'intérêt étaient l'action des drogues sur le comportement, sur la génétique comportementale et pharmaceutique. Au cours de différentes visites dans des labos de recherches aux USA tels que le Laboratoire Jackson à Bar Harbor, ou le Laboratoire des Primates à l'Université du Wisconsin à Madison où il a affiné ses approches de la génétique comportementale et s'est concentré sur différents modèles de mémorisation et d'apprentissage chez la souris.

Cursus Universitaire

- 1962 Docteur en Médecine et Chirurgie Université de Rome
- 1963-64 Chargé de Recherche à l'Institut Italien de Recherche sur la Santé à Rome. Recherche sur les neurotransmetteurs noradrénergiques et le métabolisme de la noradrénaline.
- 1964-65 Chargé de Recherche au Département de Physiologie de l'Institut Karolinska à Stockholm. Recherches sur la production d'adrénaline liée à une augmentation de l'activité nerveuse (avec U.S. Von EULER).
- 1965-67 Assistant de Recherche en Pharmacologie à la Faculté de Médecine d'UCLA et à l'institut de Recherche sur le Cerveau de Los Angeles, CA. Projet de Recherche sur la génétique comportementale et Psychopharmaceutique. Recherches sur l'apprentissage et la mémoire chez des

souches pures de souris. (Avec D.BOVET prix Nobel de Physiologie 1957 qui a travaillé à l'Institut Pasteur et JL. Mc GAUGH) .

- 1967-70 Chercheur en Pharmacologie à l'Université de Sassari en Italie. Recherche associée à un programme de psychobiologie et de pharmacologie. Recherches sur les mécanismes de génétique comportementale et sur les mécanismes impliqués dans les processus de mémorisation.
- 1969 Chercheur visiteur au Regional Primate Research Center à l'Université du Wisconsin à Madison (avec H.F. HARLOW).
- 1971 Directeur de Recherche à l'Institut de Psychologie et Psychopharmacologie, CNR (Centre National de la Recherche) à Rome. Génétique comportementale, rythmes circadiens , rôles principaux des agents cholinergiques. Collaboration avec le centre de neuro-chimie de Strasbourg
- 1972 Visiteur chercheur au Laboratoire Jackson à Bar Harbor, dans le Maine. Expériences sur des souches pures en recombinaison. (Avec D.W. BAILEY)
- 1973 Professeur agrégé en psychologie animale, Ecole de Psychologie, Université de Rome.
- 1975 Professeur de Psychologie physiologique, Université de Rome
- 1976-2002 Directeur de l'Institut de Psychobiologie et de Psychopharmacologie du CNR (CNRS Italien) à Rome. Etude sur la génétique du comportement - Corrélations neurobiologiques - Psycho-pharmacogénie
- 1978-2012 Professeur de Biopsychologie à la faculté des Sciences de la Sapienza à Rome (département de génétique et biologie moléculaire)
- 1982-1984 Doyen de l'Ecole des Sciences biologiques à la Sapienza de Rome.
- 1988-1990 Directeur du département de génétique et de biologie moléculaire à la Sapienza de Rome
- 1990 Visiteur chercheur au Centre de neurobiologie (Mémoire apprenante) à l'UC à Irvine
- 1994-2001 Président de l'Institut Italien d'Anthropologie.
- 2002-2007 Responsable du laboratoire de psychologie à l'Institut de Neurosciences du CNR Italien à Rome
- Depuis 2013: Professeur Emérite de Psychobiologie à l'Université de Rome, La Sapienza.

Publications:

Il est l'auteur de plus de 400 publications scientifiques et d'une vingtaine d'ouvrages de vulgarisation dont *l'Art de se souvenir*, *Explorer l'Esprit*, *Premières leçons de neurosciences etc....* Il a notamment publié auprès des revues: Comptes Rendus de la Société de biologie de Paris, Journal of Neuropharmacology, Biochemical Pharmacology, Life Sciences, Acta Physiologica Scandinavica, British Journal of Pharmacology, Neurosciences Letters etc...

Il fait partie du comité éditorial de nombreuses revues scientifiques. Il est cofondateur de la Société Italienne d'Éthologie, et de la Société Italienne des Neurosciences. Il a par ailleurs pris part à des congrès et des rencontres dans les domaines spécifiques de la biologie comportementale et des neurosciences.
Il a participé à de nombreuses conférences axées sur le rapport entre neurosciences et biologie .à l'Institut d'Aspen, à l'Académie Nationale des Lyncéens, à l'Institut de l'Encyclopédie Italienne, à la Communauté Économique Européenne, à l'Association Européenne des Neurosciences, auprès du gouvernement allemand lors du G8..

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II. Conférence du Pr Alberto OLIVIERO

Résumé en français de la présentation du Pr Alberto OLIVIERO:

La vie cachée du cerveau

Pr Dr Emerite. Alberto OLIVIERO
Pr Biopsychologie/ Faculté des Sciences / Université des Sciences / La Sapienza/Rome

Le cerveau possède une vie cachée; d'un ensemble allant de simples réflexes jusqu'à l'émotion, de la mémoire jusqu'aux décisions, notre esprit oscille entre des processus conscients ou inconscients. Lorsque des fonctions clés comme la mémoire, les décisions et la créativité sont concernées, nous devons garder à l'esprit le fait que d'un point de vue évolutif le développement du cortex préfrontal est concomitant avec celui d'une nouvelle structure de réseaux cognitifs dans lesquels les deux systèmes tels le cortex préfrontal et les anciens tels les noyaux gris centraux peuvent être activés en parallèle.

Ainsi, le "vieux" striatum, une des structures responsables de fonctions cognitives implicites chez les mammifères, est aussi impliqué dans des fonctions explicites et il interagit avec le cortex frontal lorsque de nouvelles réponses et stratégies sont requises. Par exemple, les structures du striatum ventral comme l'accumbens , sont impliquées dans la transition depuis diverses stratégies cognitives qui dépendent des contraintes et des conditions environnantes. Dans de nombreux cas le striatum prend en charge des fonctions explicites telles les fonctions linguistiques. Chez les mammifères le rôle du striatum ventral dans l'apprentissage spatial est similaire à celui impliqué dans la mémoire humaine déclarative (sémantique). En termes plus généraux, l'accumbens est impliqué dans l'adaptation du comportement à des situations instables et indéterminées. La plupart des activités du striatum se situent à un niveau inconscient.

Un compte-rendu détaillé sera prochainement disponible sur le site de l'AEIS , http://www.science-inter.com

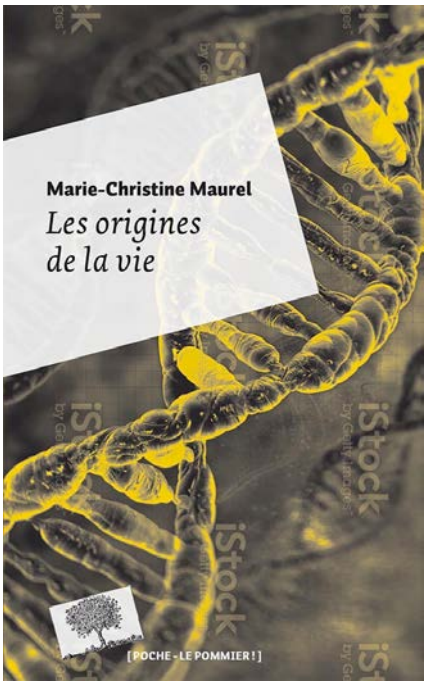
Annonces

I. **Quelques ouvrages papiers relatifs au colloque de 2014 " Systèmes stellaires et planétaires- Conditions d'apparition de la Vie" -**

- Prix de l'ouvrage :25€ .
- Pour toute commande s'adresser à :

Irène HERPE-LITWIN Secrétaire générale AEIS
39 rue Michel Ange 75016 PARIS
06 07 73 69 75
irene.herpe@science-inter.com

II. La Pr Marie-Christine MAUREL qui avait participé à notre colloque de 2014 " FORMATION DES SYSTÈMES STELLAIRES et PLANÉTAIRES CONDITIONS D'APPARITION de la VIE " nous fait part de la parution le 24 février chez "Le Pommier - Poche " de son ouvrage : **Les origines de la vie -** Prix 12€



Documents

- p. 08 Notre collègue Michel CABANAC Professeur à l'Université Laval de Québec nous a communiqué un article de Bjorn GRINDE publié dans Biol Theory (2013) 7:227–236 intitulé " The Evolutionary Rationale for Consciousness"

Pour compléter la conférence du Pr Alberto OLIVIERO nous vous proposons:

- p. 18 un article de Wikipedia intitulé "Behavioural Genetics"

Pour préparer la conférence du Pr Francis EUSTACHE nous vous proposons:

- p.29 Un article publié sous la direction du Pr EUSTACHE sur la mémoire sur le site http://www.inserm.fr/thematiques/neurosciencessciencescognitivesneurologiepsychiatrie/dossiersdinformation/

- p.34 Un article de Wikipedia sur le syndrome de Korsakoff

Biol Theory (2013) 7:227–236
DOI 10.1007/s13752-012-0061-3

LONG ARTICLE

The Evolutionary Rationale for Consciousness

Bjørn Grinde

Received: 16 April 2012 / Accepted: 7 August 2012 / Published online: 14 December 2012

Abstract To answer the question of why we have consciousness, I propose the following evolutionary trajectory leading to this feature: Nervous systems appeared for the purpose of orchestrating behavior. As a rule of thumb the challenges facing an animal concern either approach or avoidance. These two options were originally hard-wired as reflexes. Improvements in adaptability of response came with an expansion of the computational aspect of the system and a concomitant shift from simple reflexes to instinctual behavior, learning, and eventually, feelings. The assessment of positive and negative feelings allows organisms to weigh various options, but for this to be a viable strategy, an awareness of hedonic value is required. This was presumably the first neural attribute to evolve that required awareness, and thus the key force in the evolution of consciousness. The attribute first appeared in the early amniotes (the phylogenetic group comprising reptiles, birds and mammals). Support for this model in current accounts of the neurobiology of feelings and consciousness is discussed.

Keywords Amniotes · Consciousness · Emotions · Evolution · Mood modules · Self-awareness

Introduction

Terminology

For the human species, consciousness is what life is about; yet presumably it is a trait lacking in the vast majority of organisms as it is difficult to envisage this attribute in the absence of an advanced nervous system. At some point in our evolutionary history the trait evolved, and if we can understand the evolutionary rationale, i.e., the adaptive significance, behind this event, we stand a better chance of understanding what consciousness is about. I present a model for the evolution of consciousness suggesting that the feature first appeared for the purpose of experiencing feelings, and that the capacity to feel evolved as a strategy toward a more flexible and adaptive way of evaluating behavioral options.

Few topics in science have a more extensive, and varied, depiction than the phenomenon referred to as consciousness. In order to present a coherent model it is pertinent to first discuss a few key terms. The following outline reflects what is useful for the present purpose; a general overview of the literature is beyond the scope of this article.

Consciousness implies an ability to be aware of sensory input and thus be in a position to monitor aspects of both the external and internal environment. Besides the ability to experience life, this attribute entails a neurobiological flexibility that can be used to drive a variety of behavioral outputs. In an animal capable of consciousness, some types of behavior are driven by motivation based on feelings—rather than on more hard-wired responses such as fixed action patterns and innate or learned behavioral patterns. In the terminology of Edelman (2004), *primary consciousness* (i.e., sensory consciousness or awareness) can be defined as the ability to integrate observed events with memory to create awareness of the present and immediate past; while *secondary consciousness* includes additional features such as self-awareness and reflective thoughts and thus allows for "being conscious of being conscious." Primary consciousness is sufficient to turn key components of brain activity into a cohesive "film of life."

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Self-awareness (or self-recognition) implies an understanding of the "self" as a unique entity in the environment. The term suggests that the organism knows "who it is," i.e., it has concepts of "agent" and "agency." Self-awareness is generally assayed with the mirror test (or related methods), and appears to be restricted primarily to humans and apes (Kitchen et al. 1996); although other mammals, such as cetaceans (Reiss and Marino 2001), as well as certain birds (Prior et al. 2008) may possess rudimentary forms of self-awareness.

Feelings imply brain activity causing affect. They include emotions as well as any sensation that are made available to (or impact on) conscious experience and that tend to have a positive or negative connotation, i.e., pleasure or displeasure. Emotions typically have social (or extrovert) components, while sensations concern primarily oneself. The term feelings consequently includes affect caused by, e.g., physical pain and hunger, which are often not considered to be emotions. The parts of the brain involved in generating pleasure or displeasure may be referred to as *mood modules* (Grinde 2012). Feelings are, per definition, the conscious output of these modules. *Hedonic value* refers to the positive or negative aspect of feelings, as opposed to the particular type of sensation.

It should be noted that when employing words originally coined to describe human conditions in the characterization of animals, the question of appropriate use is necessarily somewhat arbitrary. Some people will, for example, claim that dogs have a nose, while others may say they do not possess a nose, but rather a snout. All living organisms have features in common with humans, but the features are unique to each species in their detailed structure and function. The snout and the nose are evolutionary homologous entities, but have evolved along different trajectories for a considerable amount of time. Similarly, the consciousness experienced by a dog is most likely different from that experienced by a human; but the two forms of consciousness are derived from a shared ancestor, which makes it reasonable to refer to them by the same term. In most cases, including consciousness, there is a somewhat arbitrary cutoff as to when the attribute possessed by an organism has the required similarity to the homologous (or analogous) human attribute to warrant the use of the same term.

Attributes of Consciousness

The feature of consciousness is one of many modules, or functions, that have been added to the mammalian brain over the course of evolution. It involves a select fraction of the processes taking place in the awake brain. The processes not brought to conscious awareness are referred to as *subconscious*. The subconscious activity has the capacity to direct the attention of the conscious brain in a fashion analogous to what, in the language of business, is referred to as "information given on a need-to-know basis." Thus, even information that impacts on our emotional life is not necessarily brought to conscious attention (Tamietto and de Gelder 2010). Presumably, consciousness is costly to operate, and only capable of handling one experience at the time; thus conveying too much information to the part of the brain responsible for consciousness could cause dangerous distractions.

Consciousness can be turned on or off, either by the power of control vested in the subconscious (as when falling asleep), by external means (as in anesthesia), or by damage to the brain (e.g., coma caused by a stroke). The various situations in which consciousness is off may be collectively referred to as *unconsciousness* (used here in a physiological, rather than Freudian, sense). The natural form of unconsciousness (sleep) is, however, different from anesthesia and coma in its capacity to generate dreams, and in that the subconscious retains the power to turn on awareness when needed, as when external stimuli suggest danger.

In humans, "accurate report" (e.g., in response to queries about a sensation or experience) may be used as a sign of consciousness (Seth et al. 2005), but in order to probe for a homologous feature in animals, we need to identify other defining qualities. A variety of neurobiological and behavioral correlates have been suggested, including: the presence of a thalamocortical complex, extensive "cross-talk" between dispersed nerve circuitry within this complex, a "default mode network" involving core activity in prefrontal and medial parietal regions of cortex, distinct sleep-wake cycling, behavioral flexibility (or behavior indicative of choice based on motivation rather than on hard-wired patterns), play behavior, signs of emotions or feelings, advanced communication, skill acquisition, and cultural transmission (for reviews, see Rossano 2003; Crick and Koch 2003; Butler 2008; Cabanac et al. 2009; Edelman and Seth 2009). The position taken here is that several of these features, but not necessarily all, should be present in order to ascribe consciousness to an organism within the vertebrate lineage.

There is reasonable evidence indicating the existence of primary forms of consciousness in mammals and birds (Butler and Cotterill 2006; Edelman and Seth 2009), and possibly in reptiles as well (Cabanac et al. 2009). Taken together, these observations suggest that the trait first evolved in the common ancestor of these three classes, collectively referred to as amniotes, some 300 million years ago. Excluding the reptiles would mean that it evolved independently in birds and mammals; and a model not requiring convergent evolution is, arguably, more parsimonious.

All amniotes have a complex behavioral repertoire, and at least birds and mammals appear to have cultural transmission (Laland and Galef 2009). Moreover, the amniotes (but apparently neither fish nor amphibians) display signs of emotion, such as tachycardia and fever upon handling, an increase in brain dopamine activity (the neurotransmitter most closely associated with reward-oriented behavior), and an apparent capacity to feel pain (Cabanac et al. 2009; Mosley 2011). Compared to lower vertebrates, amniotes have larger brains, and are thus presumably capable of a more complex response to the challenges of life. While it might be tempting to explain consciousness as an evolutionary strategy aimed at facilitating computational brainpower, or as a by-product of a sophisticated brain (Rosenthal 2008), advanced behavior—for example, communication in social insects—apparently does not require consciousness (Gould and Grant-Gould 1995) (and, one might add, neither do computers). Either presumed non-conscious species such as insects and fish do not possess a sufficiently sophisticated brain, or other factors beyond mere intricacy of response are required in order to explain the origin of consciousness. I shall argue in favor of the latter.

Amniotes were the first vertebrates to adapt to life on land. It has been discussed whether the complexity of terrestrial environments spurred the emergence of more complex behavior and consciousness (Cabanac et al. 2009). One would expect, however, that early terrestrial environments were a lot simpler, harboring a considerably lower diversity of life forms, compared to the oceans. Moreover, non-vertebrate animals, including annelids, arthropods and mollusks, colonized dry land at about the same time, or shortly after, without a similar expansion of the nervous system.

Interestingly, two of the most impressive escalations of brain capacity, i.e., in the molluscan class *Cephalopoda* (Edelman and Seth 2009) and the mammalian order *Cetacea* (Marino 2007), occurred in the ocean. In fact, cephalopods are the foremost candidates for consciousness in invertebrate animals (Mather 2008; Edelman and Seth 2009). The brains of these invertebrates are profoundly different as to neuroanatomical structures compared to amniotes. To the extent that they display signs of consciousness, a closer examination may therefore suggest general principles as to the underlying circuitry. Nevertheless, the presence of anything resembling consciousness in invertebrates would require convergent evolution, and has consequently limited relevance as to delineating the evolutionary trajectory leading to consciousness in humans. The present discussion will therefore focus on vertebrates.

A capacity for feelings, or emotions, are typically listed among the defining features of consciousness; however, even if consciousness were to be defined solely by other qualities, the current evidence suggests that the two features evolved concurrently (Cabanac et al. 2009; Denton et al. 2009; Mosley 2011). This observation may offer a more fruitful starting point for explaining the evolutionary scenario leading to vertebrate consciousness.

Evolution of Consciousness

The Rationale for Nervous Systems

The more primitive, decentralized nervous systems (e.g., in jellyfish and other members of the phylum *Cnidaria*) serve two functions: first, to collect information about the environment; and second, to initiate a response by activating muscles or glands. In more advanced, bilateral animals, nerve cells aggregate in ganglia or other centralized structures such as the vertebrate brain. These structures evolved for the purpose of a third function: to perform processing and evaluation of the information obtained prior to response.

While the most primitive nervous systems operate entirely on reflexes, or fixed action patterns, the expansion of processing implied a gradual shift toward learning and cognition. Nevertheless, even in humans, several types of external stimuli, and perhaps a majority of internal needs, are cared for by reflexive (subconscious) processing, exemplified by the adjustment of pupils in response to light and the heartbeat, respectively.

Nervous systems are associated with the management of behavior, and behavior is primarily a question of movement. Macroscopic plants are generally sedentary, and consequently have not evolved a nervous system. In the metazoans, however, nerve cells and their accompanying behavioral outputs were an evolutionary success. This success is founded on two pillars: One, neuronal circuitry allowed the organism to approach opportunities (e.g., nutrients and potential mates); and two, they made it possible to escape danger (e.g., toxins, inappropriate environments, and predators). This dichotomy—i.e., the pursuit of opportunities and the avoidance of aversive or dangerous conditions—is a core feature of all nervous systems.

Behavior that appears to be intelligent does not necessarily require consciousness, as (presumably) in the case of communication among social insects; and a response to sensual stimuli does not imply the sensation of feelings, as exemplified by the curling up of an earthworm in response to being poked. In other words, one should be careful about making assumptions as to the attributes of nervous systems based on observations of behavior alone.

The Rationale for Consciousness

Reflexes do not require extensive centralized processing. Brain power evolved gradually, presumably due to the advantages of integrating more information before executing a response, and being able to base that response on previous experience. The latter quality implies the ability to learn; but even relatively primitive animals, such as nematodes, may have this capacity (Zhang et al. 2005). Eventually, the response to the challenges of life was no longer simply an issue of whether or not to approach or escape, but rather, a matter of weighing the pros and cons in a decision-making process allowing a large number of finely tuned alternatives. The advantage came in the form of flexibility in dealing with the environment; i.e., behavior that adapts to variable conditions.

In order to implement an advanced form of behavioral response, a nervous system would need to evaluate the survival value of various expected outcomes. Early nervous systems must have already been tuned to the approach-or-avoid dichotomy of most situations; i.e., the outcome tends to be either positive or negative. However, in the case of more advanced animals, in order to effectively assess various alternatives a strategy for comparison was required. For example, how much pain, or risk, is it worth to try to lay down a prey? In order to respond optimally to this type of situation, the organisms needed a "common currency" for positive and negative, or "good" and "bad" (McFarland and Sibly 1975). The chosen currency is what I refer to as the hedonic value component of feelings, and is implicit in the terms "reward" and "punishment." The amniote brain considers the net outcome of various actions (the sum of positive and negative expectations), and hence the presumed optimal survival outcome (Cabanac 1992).

In other words, feelings presumably originated as a further elaboration of the neurobiological processing taking place between the sensory system and the executive branch of the nervous system. Feelings add value to the information obtained. The value is positive (pleasant) in the case where approach behavior is appropriate, and negative (painful or otherwise unpleasant) if avoidance is called for. The strength and duration of the expected feelings determine their worth. The score given to various options is based on a composite of innate tendencies and previous experience; e.g., humans may have an innate propensity to fear snakes (which implies a punitive feeling), though we can learn that certain snakes do not harm us.

Note that this strategy requires two attributes of the brain: one, to weigh alternatives based on hedonic value; and two, to translate the inference into action by generating motivation based on pleasure maximization (Cabanac 1992). It may be possible to conceive of ways to achieve similar performance without the use of feelings, but feelings appear to be a rational choice; moreover, it was presumably the choice opted for by evolution in the case of the amniotic lineage.

As to the present discussion, the core point is that for feelings to work, or make any sense as a currency to respond to, a capacity to assess (and hence experience) their positive and negative value is required. Most invertebrates respond to sensory input, but presumably not by weighing hedonic value. It is difficult to envision how feelings could function as "a currency for decision making" without an awareness component. *I surmise that the requirement for that awareness was the cue that engendered the emergence of consciousness.*

Why the Amniotes?

Evolution has moved in the direction of radically increased complexity of nervous systems primarily in three phyla: *Chordata* (vertebrates), *Arthropoda,* and *Mollusca*. The development can be seen as a consequence of an evolutionary "arms race": if one species improves its fitness by evolving more elaborate, or more flexible, behavior; interacting species needs to follow suit in order to survive. Feelings, compared to a more innate response, increased the flexibility and adaptability of behavior, though in the early stages not necessarily its complexity.

Although complex behavior is evident in present arthropods and mollusks, evolution may not have introduced consciousness. In other words, it seems a bit simplistic to assume that consciousness is a consequence of an increased computational capacity. The following presumed features of the early amniotes and their environment may help explain why the attribute emerged in terrestrial vertebrates:

1. At the time, the amniotes most likely possessed a more sophisticated central nervous system compared to the other two phyla mentioned above, and thus a better starting point for further elaborations.
2. They were relatively large animals with long generation times and small litters, which implies that they evolved slowly. Consequently, adaptation to novel environments relied to a greater extent on individual adaptability, rather than on genetic modification.
3. They evolved (advanced) lungs as an adaptation to terrestrial life. The brain is an expensive organ to operate, requiring a substantial portion of the energy (and oxygen) an organism can procure (Mink et al. 1981). Introducing a system of feelings, and concomitant awareness, as a strategy for complex decision-making presumably provided a considerable push in the direction of a larger and more demanding brain. The concentration of oxygen is much higher in air

compared to water, but of the terrestrial animals only amniotes developed an efficient breathing organ.
4. Although it seems likely that early terrestrial ecosystems were less complex than contemporary marine environments, the situation may have *changed* more rapidly on land, implying a greater selection pressure for behavioral flexibility.

I believe these four points may have contributed to the emergence of consciousness, but one should also take into account a possible stochastic element in the evolutionary process. As mentioned earlier, elaborate *non-conscious* behavior is possible, and a decision-making strategy employing feelings was almost certainly due, in part, to chance—or providence.

Further Elaborations of Consciousness

For the early amniotes, awareness presumably hinged on the assessment of behavioral options based on their hedonic value. The strategy proved to be successful, and evolution has since elaborated extensively on this first, simple version of (primary) consciousness. The elaborations adapted to the requirements of the various species; for example, olfactory signals play a prominent role in the conscious life of a dog.

In the human lineage, attributes such as self-awareness, culture, language, advanced cognitive power, and the curious sense of free will enhanced the experience of life. Concomitantly, the original function became less obvious, as the conscious brain evolved into a partly independent unit with "a life of its own." The subconscious presumably directed ever more information to the conscious brain, as more information would imply a better foundation for decision-making—limited primarily by available brain capacity. The original pleasure or displeasure dichotomy became obscured, as today the human experience of life is based on a smear of sensory input mixed with memories and thoughts that have none, or limited, hedonic value. Consciousness is often active even in the apparent absence of any (obvious) emotional valence. The integration of various sensory and cognitive information appears more important, and decisions are to a larger extent based on cognition, taking long term objectives into account, rather than on feelings alone.

Yet, consciousness has its shortcomings, which may explain why a substantial portion of the brain's processing capacity is retained by the unconscious. For example, only select parts of the sensory input meant to monitor internal and external environments are sent to the conscious brain, most of the signals received by sensory organs are filtered away. The constraints on consciousness also explain why following intuition sometimes (for example in the case of solving problems and in fine-tuned muscle movements) is a better strategy than exercising deliberate control.

The main drawbacks of consciousness are as follows:

1. It is a relatively slow process. Conscious perception of a stimulus requires 100-200 ms (Crick and Koch 2003).
2. It is probably energy intensive; thus, a more automated response conserves nutrients and oxygen in cases, such as the regulation of heartbeat, where awareness cannot add any meaningful input to the response.
3. While the subconscious most likely works as a parallel processor, organizing several tasks simultaneously (e.g., heartbeat and temperature regulation), the conscious brain can only handle one task at a time; if additional tasks require conscious input, it is necessary to shift back and forth between them (Baars 1997).
4. According to the present model, consciousness evolved for decision making, not for execution; thus the process does not have the power to deal with tasks such as how to orchestrate optimal performance of legs and arms.
5. Cognition is vulnerable to the whims of the individual. For the sake of the genes, flexibility comes with the price of uncertainty.
6. Feelings and awareness were only generated in cases where they made evolutionary sense. For example, we do not feel a tumor unless it happens to press on nerve cells installed for other purposes; because during our evolutionary history, being aware of a tumor would not have helped.

Due to these limitations, consciousness is not the sole, or even prime, "mover" of behavior; instead most human behavior stems from a mixture of conscious and subconscious processing (Kunde et al. 2003; Cabanac and Bonniot-Cabanac 2007; Pessiglione et al. 2008; Baumeister et al. 2011).

Neurobiological Support for the Present Model

Neural Correlates of Consciousness

The evolutionary scenario presented above suggests the following predictions: one, consciousness and feelings have related neurobiological features (as to neuroanatomy and/or neurochemistry), as they appeared at the same time and for a shared purpose; and two, if they evolved to care for the basal process of approach or avoidance, the core circuitry involved might be situated in the more ancient parts of the brain. It is worthwhile to consider whether these implications are supported by data.

The neurobiology of consciousness is elusive, presumably because it relies on constant communication between widely dispersed nerve circuits, rather than on the localized "off-or-on" activity of a particular center. One view that has gained broad acceptance is that the main anatomical components are within the thalamocortical complex, which may include the basal ganglia and possibly other parts of the forebrain (Crick and Koch 2003; Edelman and Seth 2009; Cabanac et al. 2009; Ward 2011). In this view, consciousness depends on the continuous chattering of circuits within the thalamocortical complex (Alkire et al. 2008; Noirhomme et al. 2010). More specifically, our experiences may reflect perturbations on a background of more regular, spontaneous activity (Buzsaki 2007); and attention may be a question of which of a variety of nascent, perturbation-causing nerve cell coalitions gain dominance at any given moment (Crick and Koch 2003).

Somewhat surprising is the recent suggestion that consciousness may be independent of either intact cortex or thalamus. Hydranencephalic children, i.e., humans born without cortex (or with minimal remnants thereof), appear to be conscious (Merker 2007; Beshkar 2008), as do animals in which cortex or (possibly) thalamus are removed (Panksepp et al. 1994; Alkire et al. 2008). In such instances, it is conceivable that remaining structures of the forebrain—particularly components of the basal ganglia such as the nucleus accumbens, ventral pallidum, and striatum—are sufficient for generating primary conscious states. Alternatively, the brain might compensate for the absence or loss of cortex by delegating functions to available nervous tissue.

A reasonable model based on the above discourse is that the functions regulating consciousness are associated with subcortical structures, perhaps in particular the intralaminar nuclei of the thalamus (Alkire and Miller 2005; Jones 2001). Here, direct injections of agonists to the generally inhibitory neurotransmitter GABA cause rapid sedation in rats (Miller and Ferrendelli 1990), a patient in minimal conscious state for 6 years improved drastically after stimulation of these nuclei by electrodes Schiff and Fins 2007), and thalamic damage in humans can result in a vegetative state, while restoration of consciousness is associated with restoration of functional connectivity between thalamus and (cingulate) cortex (Alkire et al. 2008). Moreover, the associated thalamic reticular nucleus has been implicated in schizophrenia, a disturbance of consciousness (Ferrarelli and Tononi 2011); and related structures in the hypothalamus apparently play a similar, central role in the regulation of sleep (Szymusiak and McGinty 2008; Gvilia 2010).

The cortex presumably adds substance and content, not only to conscious experience, but also to dreams (Nir and Tononi 2010). Other structures, such as the claustrum (Crick and Koch 2005), may help in the process of gathering and integrating information from different parts of the brain.

Neural Correlates of Feelings

As for feelings, it seems reasonable to divide the parts of the brain involved in generating hedonic value into three main modules: one for punishment, and two for rewards, i.e., seeking (or wanting) and liking (or consuming) (Panksepp 1998; Kringelbach and Berridge 2009). Recent data suggest that these three modules to a large extent use the same brain structures; that is, all types of punishment and reward—whether from food, sex, burns, social relations, etc.—converge on shared neural substrates for the generation of hedonic value (Leknes and Tracey 2008; Tabibnia et al. 2008; Lieberman and Eisenberger 2009; Takahashi et al. 2009; Berridge and Kringelbach 2011). Again, particular regions of the cortex (e.g., prefrontal, orbitofrontal, and insular cortex) may act as a sort of dashboard to add "flavor" and distinctiveness to various rewards and punishments, while subcortical structures—including areas associated with the basal ganglia, the amygdala, and thalamus—act more like a "motor," generating the hedonic quality (reviewed in (Grinde 2012)). The main "hedonic hotspots," in which direct stimulation can cause activation (in the form of enhanced pleasure) upon relevant stimulation (via electrodes or local injection of neurotransmitter modulators), are found in nucleus accumbens and pallidum (Pecina 2008; Smith et al. 2010); while stimulation of certain areas of the thalamus can inhibit pain (Bittar et al. 2005).

Comparison

Dopamine appears to play a central role in the seeking type of rewards (Barbano and Cador 2007; Leknes and Tracey 2008) as well as in consciousness (Lou 2011; Palmiter 2011). The considerable increase in telencephalic (the major part of the forebrain) dopamine receptors in reptiles compared to amphibians is taken as a further indication that consciousness first evolved in the amniotes (Cabanac et al. 2009).

The foregoing observations suggests that the core, or regulatory, circuitry for both feelings and consciousness is situated in basal parts of the brain; moreover, they point toward a considerable overlap between the neurobiology of emotions and that of consciousness, which accords with the notion that the two evolved together. Specifically, the neurobiology of the two converge in the basal ganglia, perhaps in the diencephalon (the minor part of the forebrain), in the function of dopamine, and, of course, in the use of the cortex for elaborating the experience.

It should be noted that even if the emergence of feelings spurred awareness, the two features have been molded by evolution for some 300 million years, which is ample time for considerable divergence in neurobiology. Moreover, a shared neurobiology in the early amniotes, while expected, is not required. Still it is interesting to note that, although cognitive capacity is lacking in hydranencephalic children, they do seem to experience feelings, including pleasure and pain (Merker 2007; Beshkar 2008). This observation lends credence to the idea of shared neurobiological features for feelings and consciousness; although one should consider that the presence of feelings is one of the criteria used to assess consciousness, which limits the validity of the argument. It is not obvious to what extent these children retain the basal ganglia, which may prove more crucial than either cortex or thalamus.

Discussion

Consciousness Evolved

I have outlined a model for the evolution of consciousness suggesting that the feature first appeared for the purpose of experiencing feelings. The capacity to feel evolved as a strategy toward a more flexible and adaptive way of evaluating behavioral options. The model is based on the following considerations:

1. The core function of a brain is to make behavioral decisions, and these were, in most of our evolutionary history, primarily a matter of either approach or avoidance. This dichotomy is a characteristic feature of all nervous systems.
2. In order to compare the survival value of various approach and avoidance options, a "common currency" for positive and negative salience, i.e., hedonic value, is required (McFarland and Sibly 1975). The ensuing assessment allows for a more flexible and sophisticated response compared to what innate or learned patterns of behavior can deliver.
3. Feelings, in the form of positive and negative incitements (e.g., reward and punishment), seem to be a reasonable choice of currency. The two are weighed against each other in order to create the right motivation, implying that the brain will motivate the individual to act according to the principle of pleasure maximization (Cabanac 1992).
4. For feelings to make any sense, an awareness of good and bad, pleasure and displeasure, is required. There seems to be no other obvious requirement for conscious experience in (early) amniote evolution, and consciousness is apparently not required for complex behavior.
5. Sensory input provides the primary source of relevant information for behavioral decisions, and would therefore be expected to play a dominant role in delivering reward and punishment, and in the conscious experience of life. On the other hand, only select sensations, those pertinent for advanced decision making, engage the mood modules. Adding hedonic value is not required for a sense organ to trigger behavior, as exemplified by reflexes.
6. Various lines of evidence suggest that awareness and feelings evolved concurrently in early amniotes.
7. The amniote form of awareness, or primary consciousness, has been further elaborated by the evolutionary process into the more advanced, secondary conscious experiences of humans.
8. Consciousness and feelings have neurobiological features in common, as expected if the two evolved together for a shared purpose.
9. The core, regulatory circuitry appears to be situated in the basal, sub-cortical parts of the brain; as would be expected for an evolutionary expansion of the core function of nervous systems—i.e., to make decisions about approach or avoidance. Expansion of the cortical mantle presumably occurred later, and caused enrichment of content as to both feelings and consciousness.

Starting with early vertebrates, it is theoretically possible to envision the evolution of advanced, human-like behavior without introducing feelings as a currency for weighing alternatives—a purely cognitive assessment of options would, for example, be conceivable. Evolution did not follow this trajectory, perhaps because: for one, cognition was not sufficiently advanced to make this a viable strategy; and two, moving from fixed action patterns to learned behavior, and then on to motivation based on feelings, is a more probable evolutionary scenario. This scenario is in line with how evolution is known to work; i.e., changes in the genome typically reflect indirect means to direct the body the genes reside into promote their propagation. For example, in mammals the sexual drive, rather than a desire to have children, is sufficient to ensure fertilization.

The evolutionary trajectory leading to the human brain may be considered providential in that it offers us an experience of life (Baars 1997), and a capacity for happiness (Grinde 2012). Fish and amphibians presumably lack this capacity; they respond to sensory stimuli, but may not *feel* pleasure or pain (the issue is discussed in Rose 2007; Cabanac et al. 2009; Sneddon 2009).

Human Consciousness

Dating back to the ancient Greek philosophers, there have been numerous ways to categorize and describe human

consciousness. I have mentioned the distinction between primary and secondary consciousness (Edelman 2004), as these terms are useful for the present model. Damasio (1999) prefers the term *self* as (partly) synonymous with secondary consciousness; i.e., as the personal experiences, thoughts and memories of an organism with the capacity for self-awareness. The self is further divided into core self and extended self; respectively, a stable representation of an individual's life, and the autobiographic information that accumulates in the mind. In the present biological model, however, this distinction seems somewhat arbitrary.

The following list is an attempt to use the present biological model to categorize the types of brain processes that are delegated to, and cared for by, the conscious part of the human brain:

1. Feelings (which here include the activity of the mood modules, as engaged by either emotions, sensations or cognition—i.e., all forms of affect).
2. Sensing (input from sensory organs that may or may not activate mood modules).
3. Cognition (thinking and related mental activity that may or may not activate mood modules).
4. Motivation and volition (initiators of actions based on the above three).

According to the present model, type 1 was the instigating rationale for the evolution of consciousness. The additional information deriving from sensory organs, i.e., type 2, may be brought to the conscious brain in order to secure that all relevant information is available for scrutiny. The subconscious does filter away the vast majority of signals reaching, for example, eyes and ears; but it would be difficult to install a filter that only left information of obvious relevance for making decisions, particularly as the conscious brain may be the best judge as to what constitutes relevant information. Cognition, type 3, evolved gradually to improve the process of decision making, but eventually, in the human lineage, took the shape of an "independent" feature of the brain. In fact, it has evolved to the point where decisions are made partly in the absence of, or in disregard of, the hedonic value of various options. The final type, number 4, is required as a link between feelings/cognition and actual behavior; but the relevant activity is not always brought to conscious attention.

It has been suggested that consciousness is simply an epiphenomenon, i.e., an incidental byproduct of selection in the direction of cognition and a more advanced brain (see, for example, Rosenthal 2008). In my mind, the epiphenomenon model is less attractive for the following reasons: One, consciousness is a rather distinct and noticeable feature of the brain, and conspicuous features are in general unlikely to appear unless selected for; and two, it is possible to outline a scenario that depicts why evolution opted for consciousness (as exemplified by the present text). With a reasonable evolutionary rationale available, selection offers a more compelling explanation compared to a model describing the feature as an epiphenomenon. These arguments, however, do not rule out the possibility that the evolutionary trajectory leading to consciousness was in part characterized by coincidental events.

Most bodily features, somatic as well as mental, evolve to various states of sophistication in different lineages. Their final complexity is primarily a question of survival value. The nose, for example, is considerably more advanced in dogs compared to humans; while both consciousness and emotions presumably display their most elaborate forms in humans. I have previously proposed that, if so, humans may have the propensity to be the most happy (and most miserable) of any animal (Grinde 2012).

One factor hampering our efforts to understand consciousness may simply be that the human version of the feature has progressed far beyond the original state. So much information has been added to our "film of life" that we do not easily sense the dichotomy of positive and negative feelings, which presumably dominated in the early amniotes. The neurobiology of the human brain reflects this advancement, making it difficult to identify the anatomical and neurochemical correlates of human consciousness. In this regard, reptilian brains may provide clues as to the nature of incipient substrates for early forms of primary consciousness.

Other Forms of Consciousness?

The success of combining feelings and consciousness in a strategy to generate sophisticated behavior begs the question of whether evolution may have opted for this combination more than once. The core elements of the nervous system—including the use of sensory cells, processing units, and muscles as effector organs—are present in most animals; thus convergent evolution in the direction of consciousness seems plausible. The three most successful metazoan phyla (*Chordata* (vertebrates), *Arthropoda* and *Mollusca*) all have sophisticated nervous systems and complex behavior. In fact, convergent evolution of advanced features is possible; eyes, for example, evolved independently (presumably from the shared starting point of light sensitive patches of skin) in these three phyla as a consequence of the obvious advantages of vision (Land and Nilsson 2002).

Among the invertebrates, the coleoid cephalopods (octopuses, squid, and cuttlefish) are considered prime candidates for consciousness (for reviews, see Mather 2008; Edelman and Seth 2009). These animals display advanced behavior, such as learning based on reward-like stimuli (Borrelli and Fiorito 2008), navigating mazes

(Moriyama and Gunji 1997), and possibly learning based on the observation of other members of the species (Fiorito and Scotto 1992). They can recognize a variety of objects and have considerable capacity for memory (Borrelli and Fiorito 2008; Hochner et al. 2006). In other words, their brains seem capable of a degree of processing and flexibility of behavior well beyond what one might expect from a collection of mere innate or learned behavioral patterns. Apparently they have evolved a level of sophistication, in terms of evaluating options, similar to that of amniotes. The key question as to whether they have anything resembling conscious experience may be whether evolution opted for the strategy of using feelings as a means to assess behavioral opportunities. Feelings seem to be a compelling choice, but there may be other options that are difficult for a human to conceive. If these creatures do possess an analogue to human consciousness, their "film of life" must be quite different from what we experience.

Final Comment

Smith (2010) notes that while we have made considerable progress in understanding most aspects of the natural sciences, when it comes to understanding consciousness, we are no closer today than at the time of Darwin. I believe we do have a better grasp today, but one problem may be in communicating what we know to a wider audience. The issue of human consciousness is easily distorted by emotional sentiments, including metaphysical or religious ideas. Pope John Paul II, for example, has supposedly claimed that while scientists may have the brain, the mind belongs to God (Lane 2009). Biological explanations face not only challenges from the clergy, but also the problem of disseminating ideas effectively to disparate scientific and cultural traditions such as philosophy and the social sciences.

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Behavioural genetics

From Wikipedia, the free encyclopedia

Behavioural genetics, also referred to as **behaviour genetics**, is a field of scientific research that uses genetic methods to investigate the nature and origins of individual differences in behaviour. While the name "behavioural genetics" connotes a focus on genetic influences, the field broadly investigates genetic and environmental influences, using research designs that allow removal of the confounding of genes and environment. Behavioural genetics was founded as a scientific discipline by Francis Galton in the late 19th century, only to be discredited through association with eugenics movements before and during World War II. In the latter half of the 20th century, the field saw renewed prominence with research on inheritance of behaviour and mental illness in humans (typically using twin and family studies), as well as research on genetically informative model organisms through selective breeding and crosses. In the late 20th and early 21st centuries, technological advances in molecular genetics made it possible to measure and modify the genome directly. This led to major advances in model organism research (e.g., knockout mice) and in human studies (e.g., genome-wide association studies), leading to new scientific discoveries.

Findings from behavioural genetic research have broadly impacted modern understanding of the role of genetic and environmental influences on behaviour. These include evidence that nearly all researched behaviors are under a significant degree of genetic influence, and that influence tends to increase as individuals develop into adulthood. Further, most researched human behaviours are influenced by a very large number of genes and the individual effects of these genes are very small. Environmental influences also play a strong role, but they tend to make family members more different from one another, not more similar.

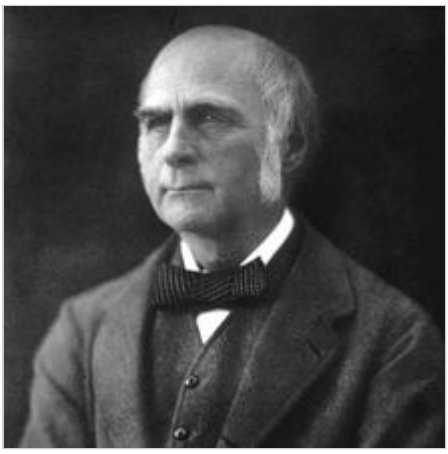
Contents

History

Selective breeding and the domestication of animals is perhaps the earliest evidence that humans considered the idea that individual differences in behaviour could be due to natural causes.[1] Plato and Aristotle each speculated on the basis and mechanisms of inheritance of behavioural characteristics.[2] Plato, for example, argued in *The Republic* that selective breeding among the citizenry to encourage the development of some traits and discourage others, what today might be called eugenics, was to be encouraged in the pursuit of an ideal society.[2][3] Behavioural genetic concepts also existed during the English renaissance, where William Shakespeare perhaps first coined the terms "nature" versus "nurture" in the The Tempest, where he wrote in Act IV, Scene I, that Caliban was "A devil, a born devil, on whose nature Nurture can never stick".[3][4]

Farmers with wheat and cattle - Ancient Egyptian art 1,422 BCE displaying domesticated animals.

Modern-day behavioural genetics began with Sir Francis Galton, a nineteenth-century intellectual and cousin of Charles Darwin.[3] Galton was a polymath who studied many things, including the heritability of human abilities and mental characteristics. One of Galton's investigations involved a large pedigree study of social and intellectual achievement in the English upper class. In 1869, 10 years after Darwin's Origin of the species, Galton published his results in *Hereditary Genius*.[5] In this work, Galton found that the rate of "eminence" was highest among close relatives of eminent individuals, and decreased as the degree of relationship to eminent individuals decreased. While Galton could not rule out the role of environmental influences on eminence, a fact which he acknowledged, the study served to initiate an important debate about the relative roles of genes and environment on behavioural characteristics. Through his work, Galton also "introduced multivariate analysis and paved the way towards modern Bayesian statistics" that are used throughout the sciences—launching what has been dubbed the "Statistical Enlightenment".[6]



Galton in his later years

The field of behavioural genetics, as founded by Galton, was ultimately undermined by another of Galton's intellectual contributions, the founding of the eugenics movement in 20th century society.[3] The primary idea behind eugenics was to use selective breeding combined with knowledge about the inheritance of behaviour to improve the human species.[3] The eugenics movement was subsequently discredited by scientific corruption and genocidal actions in Nazi Germany. Behavioural genetics was thereby discredited through its association to eugenics.[3] The field once again gained status as a distinct scientific discipline through the publication of early texts on behavioural genetics, such as Calvin S. Hall's 1951 book chapter on behavioural genetics, in which he introduced the term "psychogenetics",[7] which enjoyed some limited popularity in the 1960s and 1970s.[8][9] However, it eventually disappeared from usage in favour of "behaviour genetics".

The start of behavior genetics as a well-identified field was marked by the publication in 1960 of the book *Behavior Genetics* by John L. Fuller and William Robert (Bob) Thompson.[1][10] It is widely accepted now that many if not most behaviours in animals and humans are under significant genetic influence, although the extent of genetic influence for any particular trait can differ widely.[11][12] A decade later, in February 1970, the first issue of the journal *Behavior Genetics* was published and in 1972 the Behavior Genetics Association was formed with Theodosius Dobzhansky elected as the association's first president. The field has since grown and diversified, touching many scientific disciplines.[3][13]

Behavioural genetic research and findings have at times been controversial. Some of this controversy has arisen because behavioural genetic findings can challenge societal beliefs about the nature of human behaviour and abilities, other controversies have arisen due to misunderstandings of behavioural genetic research, whether by the lay public or the researchers themselves.[3] Major areas of controversy have included genetic research on topics such as racial differences, intelligence, violence, and human sexuality.[14]

Methods

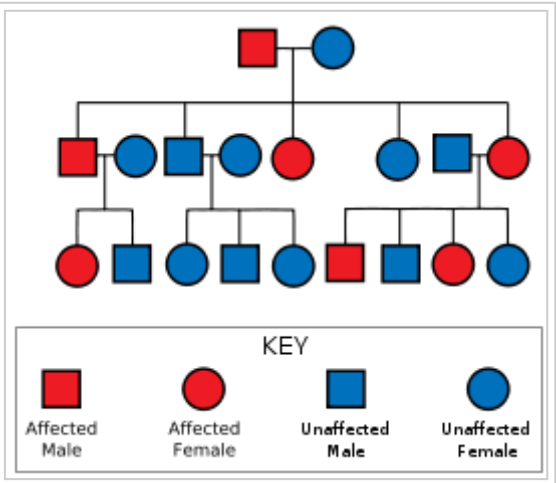
The primary goal of behavioural genetics is to investigate the nature and origins of individual differences in behaviour.[3] A wide variety of different methodological approaches are used in behavioral genetic research,[15] only a few of which are outlined below.

Animal studies

In animal research selection experiments have often been employed. For example, laboratory house mice have been bred for open-field behaviour,[16] thermoregulatory nesting,[17] and voluntary wheel-running behaviour.[18] A range of methods in these designs are covered on those pages.

Behavioural geneticists using model organisms employ a range of molecular techniques to alter, insert, or delete genes. These techniques include knockouts, floxing, gene knockdown, or genome editing using methods like CRISPR-Cas9.[19] These techniques allow behavioural geneticists different levels of control in the model organism's genome, to evaluate the molecular, physiological, or behavioural outcome of genetic changes.[20]

Twin and family studies



Pedigree chart showing an inheritance pattern consistent with autosomal dominant transmission. Behavioural geneticists have used pedigree studies to investigate the genetic and environmental basis of behaviour.

One research design used in behavioural genetic research are variations on family designs (also known as pedigree designs), including twin studies and adoption studies.[15] Quantitative genetic modelling of individuals with known genetic relationships (e.g., parent-child, sibling, dizygotic and monozygotic twins) allows one to estimate to what extent genes and environment contribute to phenotypic differences among individuals.[21] The basic intuition of the twin study is that monozygotic twins share 100% of their genome and dizygotic twins share, on average, 50% of their segregating genome. Thus, differences between the two members of a monozygotic twin pair can only be due to differences in their environment, whereas dizygotic twins will differ from one another due to environment as well as genes. Under this simplistic model, if dizygotic twins differ more than monozygotic twins it can only be attributable to genetic influences. An important assumption of the twin model is the equal environment assumption[22] that monozygotic twins have the same shared environmental experiences as dizygotic twins. If, for example, monozygotic twins tend to have more similar experiences than dizygotic twins—and these experiences themselves are not genetically mediated through gene-environment correlation mechanisms—then monozygotic twins will tend to be more similar to one another than dizygotic twins for reasons that have nothing to do with genes.[23]

Twin studies of monozygotic and dizygotic twins use a biometrical formulation to describe the influences on twin similarity and to infer heritability.[21][24] The formulation rests on the basic observation that the variance in a phenotype is due to two sources, genes and environment. More formally, $Var(P) = g + (g \times \epsilon) + \epsilon$, where P is the phenotype, g is the effect of genes, ϵ is the effect of the environment, and $(g \times \epsilon)$ is a gene by environment interaction. The g term can be expanded to include additive (a^2), dominance (d^2), and epistatic (i^2) genetic effects. Similarly, the environmental term ϵ can be expanded to include shared environment (c^2) and non-shared environment (e^2), which includes any measurement error. Dropping the gene by environment interaction for simplicity (typical in twin studies) and fully decomposing the g and ϵ terms, we now have $Var(P) = (a^2 + d^2 + i^2) + (c^2 + e^2)$. Twin research then models the similarity in monozygotic twins and dizogotic twins using simplified forms of this decomposition, shown in the table.[21]

Decomposing the genetic and environmental contributions to twin similarity.[21]

Type of relationship	Full decomposition	Falconer's decomposition
Perfect similarity between siblings	$1.0 = a^2 + d^2 + i^2 + c^2 + e^2$	$1.0 = a^2 + c^2 + e^2$
Monozygotic twin correlation(r_{MZ})	$r_{MZ} = a^2 + d^2 + i^2 + c^2$	$r_{MZ} = a^2 + c^2$
Dizygotic twin correlation (r_{DZ})	$r_{DZ} = \frac{1}{2}a^2 + \frac{1}{4}d^2 + (k)i^2 + c^2$	$r_{DZ} = \frac{1}{2}a^2 + c^2$
Where k is an unknown (probably very small) quantity.		

The simplified Falconer formulation can then be used to derive estimates of a^2, c^2, and e^2. Rearranging and substituting the r_{MZ} and r_{DZ} equations one can obtain an estimate of the additive genetic variance, or heritability, $a^2 = 2(r_{MZ} - r_{DZ})$, the non-shared environmental effect $e^2 = 1 - r_{MZ}$ and, finally, the shared environmental effect $c^2 = r_{MZ} - a^2$.[21] The Falconer formulation is presented here to illustrate how the twin model works. Modern approaches use maximum likelihood to estimate the genetic and environmental variance components.[25]

Measured genetic variants

The Human Genome Project has allowed scientists to directly genotype the sequence of human DNA nucleotides.[26] Once genotyped, genetic variants can be tested for association with a behavioural phenotype, such as mental disorder, cognitive ability, personality, and so on.[27]

- **Candidate Genes.** One popular approach has been to test for association candidate genes with behavioural phenotypes, where the candidate gene is selected based on some a priori theory about biological mechanisms involved in the manifestation of a behavioural trait or phenotype.[28] In general, such studies have proven difficult to broadly replicate[29][30] and there has been concern raised that the false positive rate in this type of research is high.[28][31]
- **Genome-wide association studies.** In genome-wide association studies, researchers test the relationship of millions of genetic polymorphisms with behavioural phenotypes across the genome.[27] This approach to genetic association studies is largely atheoretical, and typically not guided by a particular biological hypothesis regarding the phenotype.[27] Genetic association findings for behavioural traits and psychiatric disorders have been found to be highly polygenic (involving many small genetic effects).[32][33][34][35][36]
- **SNP heritability and co-heritability.** Recently, researchers have begun to use similarity between classically unrelated people at their measured single nucleotide polymorphisms (SNPs) to estimate genetic variation or covariation that is tagged by SNPs, using mixed effects models implemented in software such as Genome-wide complex trait analysis (GCTA).[37][38] To do this, researchers find the average genetic relatedness over all SNPs between all individuals in a (typically large) sample, and use Haseman-Elston regression or restricted maximum likelihood to estimate the genetic variation that is "tagged" by, or predicted by, the SNPs. The proportion of phenotypic variation that is accounted for by the genetic relatedness has been called "SNP heritability".[39] Intuitively, SNP heritability increases to the degree that phenotypic similarity is predicted by genetic similarity at measured SNPs, and is expected to be lower than the true narrow-sense heritability to the degree that measured SNPs fail to tag (typically rare) causal variants.[40] The value of this method is that it is an independent way to estimate heritability that does not require the same assumptions as those in twin and family studies, and that it gives insight into the allelic frequency spectrum of the causal variants underlying trait variation.[41]

Quasi-experimental designs

Some behavioural genetic designs are useful not to understand genetic influences on behaviour, but to control for genetic influences to test environmentally-mediated influences on behaviour.[42] Such behavioural genetic designs may be considered a subset of natural experiments,[43] quasi-experiments that attempt to take advantage

of naturally occurring situations that mimic true experiments by providing some control over an independent variable. Natural experiments can be particularly useful when experiments are infeasible, due to practical or ethical limitations.[43]

A general limitation of observational studies is that the relative influences of genes and environment are confounded. A simple demonstration of this fact is that measures of 'environmental' influence are heritable.[44] Thus, observing a correlation between an environmental risk factor and a health outcome is not necessarily evidence for environmental influence on the health outcome. Similarly, in observational studies of parent-child behavioural transmission, for example, it is impossible to know if the transmission is due to genetic or environmental influences, due to the problem of passive gene-environment correlation.[43] The simple observation that the children of parents who use drugs are more likely to use drugs as adults does not indicate *why* the children are more likely to use drugs when they grow up. It could be because the children are modelling their parents' behaviour. Equally plausible, it could be that the children inherited drug-use-predisposing genes from their parent, which put them at increased risk for drug use as adults regardless of their parents' behaviour. Adoption studies, which parse the relative effects of rearing environment and genetic inheritance, find a small to negligible effect of rearing environment on smoking, alcohol, and marijuana use in adopted children,[45] but a larger effect of rearing environment on harder drug use.[46]

Other behavioural genetic designs include discordant twin studies,[42] children of twins designs,[47] and Mendelian randomization.[48]

General findings

There are many broad conclusions to be drawn from behavioural genetic research about the nature and origins of behaviour.[3][49] Three major conclusions include: 1) all behavioural traits and disorders are influenced by genes; 2) environmental influences tend to make members of the same family more different, rather than more similar; and 3) the influence of genes tends to increase in relative importance as individuals age.[3]

Genetic influences on behaviour are pervasive

It is clear from multiple lines of evidence that all researched behavioural traits and disorders are influenced by genes; that is, they are heritable. The single largest source of evidence comes from twin studies, where it is routinely observed that monozygotic (identical) twins are more similar to one another than are same-sex dizygotic (fraternal) twins.[11][12]

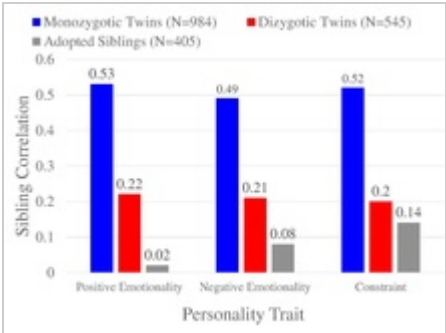
The conclusion that genetic influences are pervasive has also been observed in research designs that do not depend on the assumptions of the twin method. Adoption studies show that adoptees are routinely more similar to their biological relatives than their adoptive relatives for a wide variety of traits and disorders.[3] In the Minnesota Study of Twins Reared Apart, monozygotic twins separated shortly after birth were reunited in adulthood.[50] These adopted, reared-apart twins were as similar to one another as were twins reared together on a wide range of measures including general cognitive ability, personality, religious attitudes, and vocational interests, among others.[50] Approaches using genome-wide genotyping have allowed researchers to measure genetic relatedness between individuals and estimate heritability based on millions of genetic variants. Methods exist to test whether the extent of genetic similarity (aka, relatedness) between nominally unrelated individuals (individuals who are not close or even distant relatives) is associated with phenotypic similarity.[38] Such methods do not rely on the same assumptions as twin or adoption studies, and routinely find evidence for heritability of behavioural traits and disorders.[34][36][51]

Nature of environmental influence

Just as all researched human behavioural phenotypes are influenced by genes (i.e., are heritable), all such phenotypes are also influenced by the environment.[11][49] The basic fact that monozygotic twins are genetically identical but are never perfectly concordant for psychiatric disorder or perfectly correlated for behavioural traits, indicates that the environment shapes human behaviour.[49]

The nature of this environmental influence, however, is such that it tends to make individuals in the same family more different from one another, not more similar to one another.[3] That is, estimates of shared environmental effects (c^2) in human studies are small, negligible, or zero for the vast majority of behavioural traits and psychiatric disorders, whereas estimates of non-shared environmental effects (e^2) are moderate to large.[11] From twin studies c^2 is typically estimated at 0 because the correlation (r_{MZ}) between monozygotic twins is at least twice the correlation (r_{DZ}) for dizygotic twins. When using the Falconer variance decomposition ($1.0 = a^2 + c^2 + e^2$) this difference between monozygotic and dizygotic twin similarity results in an estimated $c^2 = 0$. It is important to note that the Falconer decomposition is simplistic.[21] It removes the possible influence of dominance and epistatic effects which, if present, will tend to make monozygotic twins more similar than dizygotic twins and mask the influence of shared environmental effects.[21] This is a limitation of the twin design for estimating c^2. However, the general conclusion that shared environmental effects are negligible does not rest on twin studies alone. Adoption research also fails to find large (c^2) components; that is, adoptive parents and their adopted children tend to show much less resemblance to one another than the adopted child and his or her non-rearing biological parent.[3] In studies of adoptive families with at least one biological child and one adopted child, the sibling resemblance also tends be nearly zero for most traits that have been studied.[11][52]

The figure provides an example from personality research, where twin and adoption studies converge on the conclusion of zero to small influences of shared environment on broad personality traits measured by the Multidimensional Personality Questionnaire including positive emotionality, negative emotionality, and constraint.[53]



Similarity in twins and adoptees indicates a small role for shared environment in personality.

Given the conclusion that all researched behavioural traits and psychiatric disorders are heritable, biological siblings will always tend to be more similar to one another than will adopted siblings. However, for some traits, especially when measured during adolescence, adopted siblings do show some significant similarity (e.g., correlations of .20) to one another. Traits that have been demonstrated to have significant shared environmental influences include internalizing and externalizing psychopathology,[54] substance use[55] and dependence,[46] and intelligence.[55]

Nature of genetic influence

Genetic effects on human behavioural outcomes can be described in multiple ways.[21] One way to describe the effect is in terms of how much variance in the behaviour can be accounted for by alleles in the genetic variant, otherwise known as the coefficient of determination or R^2. An intuitive way to think about R^2 is that it describes the extent to which the genetic variant makes individuals, who harbour different alleles, different from one another on the behavioural outcome. A complementary way to describe effects of individual genetic variants is in how much change one expects on the behavioural outcome given a change in the number of risk alleles an individual harbours, often denoted by the Greek letter β (denoting the slope in a regression equation), or, in the case of binary disease outcomes by the odds ratio OR of disease given allele status. Note the difference: R^2 describes the population-level effect of alleles within a genetic variant; β or OR describe the effect of having a risk allele on the individual who harbours it, relative to an individual who does not harbour a risk allele.[56]

When described on the R^2 metric, the effects of individual genetic variants on *complex* human behavioural traits and disorders are vanishingly small, with each variant accounting for $R^2 < 0.3\%$ of variation in the phenotype.[3] This fact has been discovered primarily through genome-wide association studies of complex behavioural phenotypes, including results on substance use,[57][58] personality,[59] fertility,[60] schizophrenia,[33] depression,[59][61] and endophenotypes including brain structure[62] and function.[63] There are a small handful of replicated and robustly studied exceptions to this rule, including the effect of *APOE* on Alzheimer's disease,[64] and *CHRNA5* on smoking behaviour,[57] and *ALDH2* (in individuals of East Asian ancestry) on alcohol use.[65]

On the other hand, when assessing effects according to the β metric, there are a large number of genetic variants that have very large effects on complex behavioural phenotypes. The risk alleles within such variants are exceedingly rare, such that their large behavioural effects impact only a small number of individuals. Thus, when assessed at a population level using the R^2 metric, they account for only a small amount of the differences between individuals. Examples include variants within *APP* that result in familial forms of severe early onset Alzheimer's disease but affect only relatively few individuals. Compare this to risk alleles within *APOE*, which pose much smaller risk compared to *APP*, but are far more common and therefore affect a much greater proportion of the population.[66]

Finally, there are classical behavioural disorders that are genetically simple in their etiology, such as Huntington's disease. Huntington's is caused by a single autosomal dominant variant in the *HTT* gene, which is the only variant that accounts for any differences among individuals in their risk for developing the disease, assuming they live long enough.[67] In the case of genetically simple and rare diseases such as Huntington's, the variant R^2 and the OR are simultaneously large.[56]

See also

- Adoption study
- *Behavior Genetics*
- Behavior Genetics Association
- Behavioural neurogenetics
- Biocultural evolution
- Evolutionary psychology
- *Genes, Brain and Behavior*
- Genome-wide association study
- Human behaviour genetics
- International Behavioural and Neural Genetics Society
- International Society of Psychiatric Genetics
- *Journal of Neurogenetics*
- Molecular genetics
- Nature versus nurture
- Psychiatric genetics
- *Psychiatric Genetics*
- Quantitative genetics
- Twin study

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- Institute for Behavioral Genetics at the University of Colorado Boulder (http://www.colorado.edu/ibg/)
- Virginia Institute for Psychiatric and Behavioral Genetics (http://vipbg.vcu.edu/)

Mémoire

Dossier réalisé en collaboration avec le Pr. Francis Eustache, Directeur de l'unité Inserm-EPHE-UCBN U1077 "Neuropsychologie et neuroanatomie fonctionnelle de la mémoire humaine" – Octobre 2014

La mémoire permet d'enregistrer des informations venant d'expériences et d'événements divers, de les conserver et de les restituer. Différents réseaux neuronaux sont impliqués dans différents types de mémorisation. La meilleure connaissance de ces processus améliorent la compréhension de certains troubles mnésiques et ouvrent la voie à des interventions possibles dans l'avenir.

La mémoire repose sur cinq systèmes de mémoire

La mémoire se compose de **cinq systèmes de mémoire impliquant des réseaux neuronaux distincts bien qu'interconnectés** :

La **mémoire de travail** (à court terme) est au cœur du réseau.
La **mémoire sémantique** et la **mémoire épisodique** sont deux systèmes de représentation consciente à long terme.
La **mémoire procédurale** permet des automatismes inconscients.
La **mémoire perceptive** est liée aux sens.

Cet ensemble complexe est indispensable à l'identité, à l'expression, au savoir, aux connaissances, à la réflexion et même à la projection de chacun dans le futur.

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Cette représentation de neuro-imagerie est un exemple de la technique dite de recalage interindividuel guidé par les sillons (DIffeomorphic Sulcal-based COrtical ou DISCO).

La mémoire de travail

La mémoire de travail (ou **mémoire à court terme**) est en fait **la mémoire du présent.** Elle permet de **retenir des informations pendant quelques secondes, voire quelques dizaines de secondes**. Nous la sollicitons en permanence à chaque instant, par exemple pour retenir un numéro de téléphone le temps de le noter. Dans la plupart des cas, les mécanismes neurobiologiques associés à la mémoire de travail ne permettent pas le stockage à long terme de ce type d'informations : leur souvenir est vite oublié. Néanmoins, il existe des **interactions entre le système de mémoire de travail et ceux de la mémoire à long terme**. Elles permettent la mémorisation de certains événements et, ainsi, de se remémorer des souvenirs anciens face à certaines situations présentes, afin de mieux s'adapter.

7, le nombre magique
Le chiffre 7 serait le "nombre magique" de la mémoire de travail. Il s'agit du **nombre d'éléments pouvant être mémorisés simultanément à court terme**, avec une marge de plus ou moins deux événements. En moyenne, nous sommes donc tous capables de retenir pendant quelques secondes entre 5 et 9 items. Par exemple, la suite [7, 9, 6, 4, 0, 9, 2] représente 7 chiffres. Elle peut aussi se lire [796, 409, 2] ce qui n'en représente plus que trois (et laisse la possibilité de retenir quatre autres items). De même, une suite de mots longs et compliqués comme [perroquet, colibri, araignée, diplodocus, chimpanzé, kangourou, ornithorynque] représente 7 mots que l'on peut retenir, bien qu'elle soit composée d'un bien plus grand nombre de lettres.
Divers **procédés mnémotechniques** utilisent cette propriété de notre cerveau pour élargir les capacités de la mémoire de travail.

La mémoire sémantique

La mémoire sémantique permet l'acquisition de connaissances générales sur soi (son histoire, sa personnalité) et le monde (géographie, politique, actualité, nature, relations sociales ou encore expérience professionnelle). C'est la **mémoire du savoir et de la connaissance.** Elle concerne des données personnelles accessibles à notre conscience et que l'on peut exprimer.

La mémoire épisodique

La mémoire épisodique est une forme de mémoire explicite. Elle permet de **se souvenir de moments passés (événements autobiographiques) et de prévoir le lendemain**. En effet, lorsqu'on demande à une personne d'évoquer un souvenir qui s'est déroulé au cours des derniers mois ou de penser aux prochaines vacances afin d'imaginer ce qui va s'y passer, ce sont les mêmes circuits cérébraux qui sont activés. Les détails des souvenirs épisodiques se perdent avec le temps (où, quand et comment l'événement s'est-il passé ?). Les traits communs aux différents événements vécus s'amalgament les uns aux autres pour devenir des connaissances qui ne sont plus liées à un événement particulier. **La plupart des souvenirs épisodiques se transforment donc, à terme, en connaissances générales**.

La mémoire procédurale

La mémoire procédurale est la **mémoire des automatismes.** Elle permet de conduire, de marcher, de faire du vélo ou du ski sans avoir à réapprendre à chaque fois. Cette mémoire est **particulièrement sollicitée chez les artistes ou encore les sportifs** pour

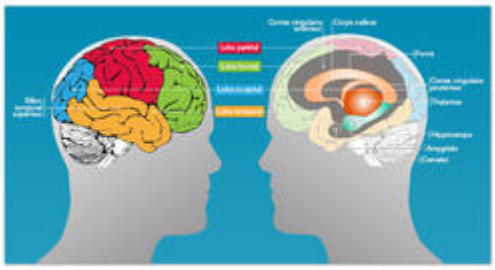
acquérir des procédures parfaites et atteindre l'excellence. Ces processus sont effectués **de façon implicite**, c'est à dire inconsciente. La personne ne peut pas vraiment expliquer comment elle procède, pourquoi elle tient en équilibre sur ses skis ou descend sans tomber. Les mouvements se font sans contrôle conscient et les circuits neuronaux sont automatisés.

La mémoire perceptive

La mémoire perceptive **dépend des modalités sensorielles, notamment de la vue** pour l'espèce humaine. Cette mémoire fonctionne beaucoup à l'insu de l'individu. Elle permet de retenir des images ou des bruits sans s'en rendre compte. C'est elle qui permet à une personne de rentrer chez elle par habitude, grâce à des repères visuels. Cette mémoire permet de **se souvenir des visages, des voix, des lieux**.

La mémoire fonctionne en réseaux

Du point de vue neurologique, **il n'existe pas "un" centre de la mémoire dans le cerveau.** Les différents systèmes de mémoire mettent en jeu **des réseaux neuronaux distincts,** observables par imagerie médicale au cours de tâches de mémorisation ou de récupération d'informations diverses. **Ces réseaux sont néanmoins interconnectés et fonctionnent en étroite collaboration** : un même événement peut avoir des contenus sémantique et épisodique et une même information peut être représentée sous forme explicite et implicite.



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Face latérale (à gauche) et face interne (à droite) de l'hémisphère cérébral droit.

La **mémoire procédurale** recrute des **réseaux neuronaux sous-corticaux** et dans le **cervelet**.

La **mémoire sémantique** implique des **réseaux neuronaux disséminés** dans des régions très étendues ainsi que dans les **lobes temporaux**, notamment dans leurs parties les plus antérieures.

La **mémoire épisodique** fait appel à des réseaux neuronaux dans l'**hippocampe** et plus largement dans la **face interne des lobes temporaux**.

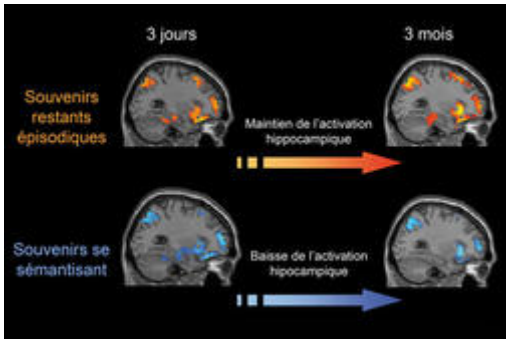
Enfin, la **mémoire perceptive** recrute des réseaux neuronaux dans **différentes régions corticales**, à proximité des aires sensorielles.

Des souvenirs multiples naissent les raisonnements
Les mémoires s'appuient les unes sur les autres ! Si vous savez qu'un 4x4 est une voiture, vous pouvez dire qu'un 4X4 a des freins, même si personne ne vous l'a dit et que vous ne les avez jamais vus. Vous déduisez cela du fait que toutes les voitures ont des freins. Ce type de raisonnement utile dans la vie quotidienne se fait essentiellement à partir des connaissances stockées en mémoire. Ainsi, plus les connaissances mémorisées sont importantes, plus il est facile de faire des analogies.

Encodage et stockage de l'information, une affaire de plasticité synaptique

Les processus de stockage sont difficiles à observer par imagerie cérébrale car ils relèvent de mécanismes de consolidation qui s'inscrivent dans la durée. Néanmoins, l'**hippocampe** semble jouer un **rôle central dans le stockage temporaire et plus durable des informations** explicites, en lien avec différentes structures corticales.

La **mémorisation** résulte d'une **modification des connexions entre les neurones d'un système de mémoire** : on parle de " **plasticité synaptique** " (les synapses étant les points de contacts entre les neurones). Lorsqu'une information parvient à un neurone, des protéines sont produites et acheminées vers les synapses afin de les renforcer ou d'en créer de nouvelles. Cela produit **un réseau spécifique de neurones associé au souvenir** qui se grave dans le cortex. Chaque souvenir correspond donc à une configuration unique d'activité spatio-temporelle de neurones interconnectés. Les représentations finissent par être réparties au sein de vastes réseaux de neurones d'une extrême complexité.



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L'activation de l'hippocampe se maintient pour les souvenirs épisodiques, mais baisse quand les souvenirs se sémantisent.

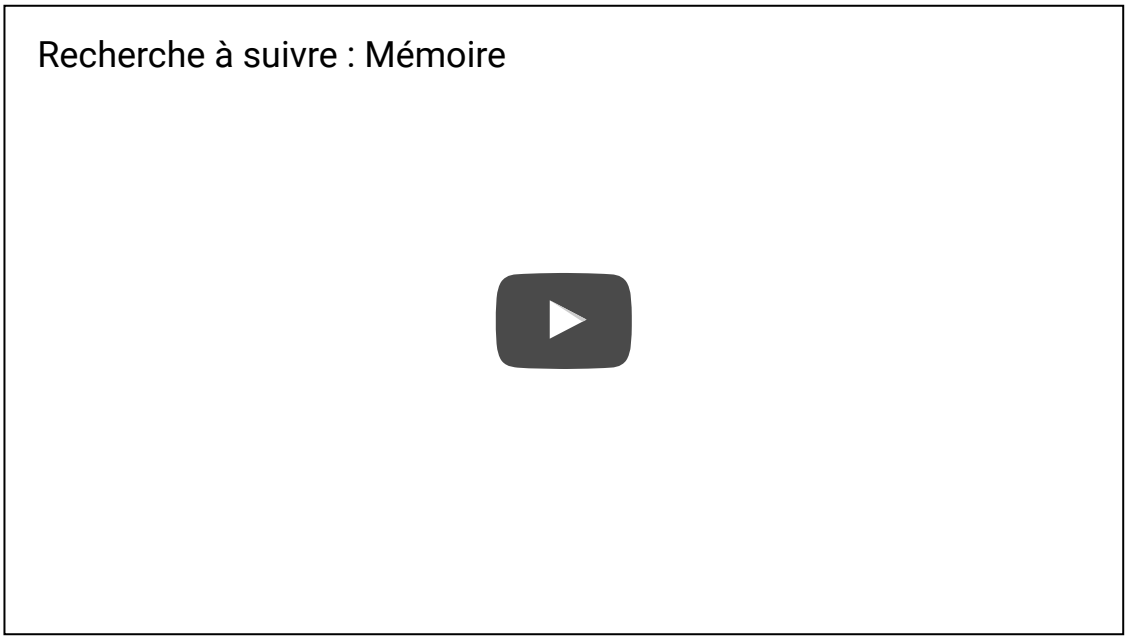
L'activation régulière et répétée de ces réseaux permettrait dans un second temps de **renforcer ou de réduire ces connexions, avec pour conséquence de consolider le souvenir ou au contraire de l'oublier**. Il est important de préciser que l'oubli est associé au bon fonctionnement de la mémoire en dehors de cas pathologiques. Des travaux suggèrent le rôle d'une molécule appelée **PKM zêta** dans le **maintien de la mémoire à long terme**. Chez l'animal, elle permet d'entretenir les molécules modifiées pendant l'encodage et d'empêcher qu'elles ne se dégradent avec le temps, consolidant ainsi les réseaux associés aux souvenirs.

La libération de neurotransmetteurs, notamment celle de **glutamate** et de **NMDA**, ainsi que l'expression d'une protéine qui augmente la libération de glutamate, la **syntaxine**, sont **associées à la plasticité synaptique.** Sur le plan morphologique, cette plasticité est associée à des **remaniements des réseaux neuronaux** : changement de forme et de taille des synapses, transformation de synapses silencieuses en synapses actives, croissance de nouvelles synapses.

Au cours du **vieillissement**, la plasticité des synapses diminue et les changements de connexions sont plus éphémères, pouvant expliquer des difficultés croissantes à retenir des informations. Par ailleurs, dans les rares formes familiales de la maladie d'Alzheimer, des mutations sont associées à des défauts de plasticité des synapses qui pourraient expliquer, dans ce cas, les troubles majeurs de mémoire.

Le sommeil consolide la mémoire
Une leçon s'apprend mieux le soir avant de dormir, c'est un fait ! Des expériences de rappel d'informations montrent que le fait de **dormir améliore la mémorisation**, et ce d'autant plus que la durée du sommeil est longue. A l'inverse, des privations de sommeil (moins de quatre ou cinq heures par nuit) sont associées à des troubles de la mémoire et des difficultés d'apprentissage. Par ailleurs, le fait de stimuler électriquement le cerveau (stimulations de 0,75 Hz) pendant la phase de sommeil lent (caractérisée par l'enregistrement d'ondes corticales lentes à l'encéphalogramme) améliore les capacités de mémorisation d'une liste de mots.
Plusieurs hypothèses pourraient expliquer ce phénomène : Pendant le sommeil, l'hippocampe est au repos et cela éviterait des interférences avec d'autres informations au moment de l'encodage du souvenir. Il se pourrait aussi que le sommeil exerce un tri, débarrassant les souvenirs de leur composante émotionnelle pour ne retenir que l'informationnelle, facilitant ainsi l'encodage.

Recherche à suivre : Mémoire



La réserve cognitive, soutien de la mémoire

Les chercheurs découvrent progressivement des facteurs qui accroissent les capacités de mémorisation et semblent stabiliser les souvenirs dans le temps. C'est le cas de **la réserve cognitive** : un phénomène associé à des connections fonctionnelles entre les neurones extrêmement nombreuses, résultant des apprentissages, d'une stimulation intellectuelle tout au long de la vie ou encore des relations sociales épanouies.

A ce jour les chercheurs ne savent pas précisément quels **ingrédients éducationnels et sociaux** participent précisément à la constitution de cette réserve cognitive. Des études menées chez les rongeurs montrent cependant que le séjour d'animaux dans des environnements complexes (dits " enrichis ") améliore leur capacité d'apprentissage et de mémoire. D'autres travaux, conduits chez l'Homme, indiquent que les personnes qui ont un haut degré d'éducation, développent les symptômes de la maladie d'Alzheimer plus tardivement que les personnes qui n'ont pas fait d'études. Ces résultats, issus de recherches en épidémiologie portant sur de très grands nombres de sujets, s'expliqueraient par la capacité du cerveau à compenser les dégénérescences neuronales liées à la maladie grâce à la mobilisation de circuits alternatifs, du fait d'un meilleur réseau de connexions entre les neurones chez les personnes qui ont un niveau d'éducation élevé.

D'autres facteurs contribuent à la consolidation de la mémoire sans que l'on en connaisse parfaitement les mécanismes : le **sommeil** (voir plus haut), l'**activité physique** ou encore une bonne **santé cardiovasculaire**. De façon générale une bonne **hygiène de vie** (sommeil, alimentation, activité physique) contribue à de bonnes capacités de mémorisation.

Les multiples troubles de la mémoire

Les troubles de la mémoire altèrent principalement la capacité à mémoriser un fait nouveau, à retrouver une information, ou les deux.

Les causes possibles

Certaines situations entrainent des **incapacités sévères** et des **amnésies durables.** Les causes possibles sont :

un **traumatisme** physique entrainant des lésions cérébrales,
un **accident vasculaire cérébral** hémorragique ou ischémique,
une **tumeur** du cerveau
ou encore une **dégénérescence neuronale** comme la maladie d'Alzheimer.

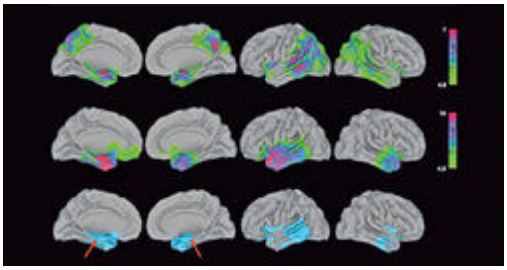
Dans d'autres cas, les troubles sont **moins sévères** et le plus souvent **réversibles.** Les causes possibles sont :

des maladies mentales comme la **dépression**,
le **stress** et l'**anxiété** ou la **fatigue**,
un **événement traumatisant** (deuil),
des effets indésirables de **médicaments** comme des somnifères, des anxiolytiques (d'autant plus fréquent que la personne est âgée),
l'usage de **drogues**.

Il existe aussi probablement des **origines biologiques** comme un déficit en certains neuromédiateurs ou une faible connectivité entre les réseaux cérébraux.

Une multitude de troubles

Les manifestations des troubles de la mémoire sont extrêmement variables selon l'origine du trouble et la localisation de la zone touchée. Les mécanismes sont éminemment complexes.



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Zones atrophiées dans la maladie d'Alzheimer (en haut), dans la démence sémantique (au milieu) et, de façon commune, dans ces deux pathologies. Les flèches rouges indiquent la région commune hippocampique affectée par ces démences.

Les travaux montrent par exemple que des patients atteints d'une **démence sémantique**, qui oublient des mots ou des informations, perdent également des souvenirs anciens alors qu'ils continuent à mémoriser de nouveaux souvenirs épisodiques (souvenirs " au jour le jour "). Ces troubles sont associés à une atrophie des lobes temporaux.

Chez d'autres patients présentant des **troubles de la mémoire épisodique**, les souvenirs anciens qui datent de l'adolescence sont épargnés plus longtemps que les souvenirs récents. C'est le cas chez les personnes souffrant de la maladie d'Alzheimer.

Les dégénérescences neuronales qui surviennent dans les **maladies de Parkinson ou de Huntington** provoquent d'autres types de **déficiences, affectant notamment la mémoire procédurale** avec la perte de certains automatismes.

Certaines personnes peuvent aussi présenter des **troubles de la mémoire du travail**, liées à des lésions du lobe frontal. L'individu a alors du mal à se concentrer et à faire deux taches en même temps.

Il existe aussi des troubles de la mémoire **sévères mais transitoires**, comme dans l'**ictus amnésique idiopathique** qui survient le plus souvent entre 50 et 70 ans. Il s'agit d'une amnésie soudaine et massive, qui dure environ six à huit heures, puis le patient recouvre sa mémoire. Pendant la phase aigue, le patient est incapable de se souvenir de ce qu'il vient de faire, sa mémoire épisodique est annihilée alors que sa mémoire sémantique est intacte : il peut répondre à des questions de vocabulaire et évoquer des connaissances générales.

A l'inverse, certaines personnes peuvent être atteintes d'**hypermnésie autobiographique**. Il s'agit d'une pathologie très rare qui se caractérise par des capacités de mémorisation exceptionnelles des détails d'événements personnels ou de l'actualité, survenus parfois plusieurs années avant. Il s'agit d'une pathologie de l'abstraction et de la généralisation du souvenir avec absence de tri, de synthèse et d'oubli de détails.

L'état de stress post-traumatique : une distorsion de la mémoire

L'état de stress post-traumatique survient chez une personne victime ou témoin impuissant d'un événement traumatique. Elle est ensuite hantée durablement par cet événement. Ce phénomène est lié à une distorsion profonde de l'encodage des événements. **Le souvenir est mémorisé à long terme mais de façon biaisée, avec une amnésie de certains aspects et une hypermnésie d'autres détails qui harcèlent le sujet**. Contrairement à un souvenir normal, il persiste au cours du temps sans s'édulcorer ni perdre de sa spécificité. Il s'impose à la victime face à des événements déclencheurs qui lui rappellent la scène. Cette distorsion de l'encodage est **associée à une décharge de glucocorticoïdes, hormone du stress, dans l'hippocampe au moment de l'événement**.

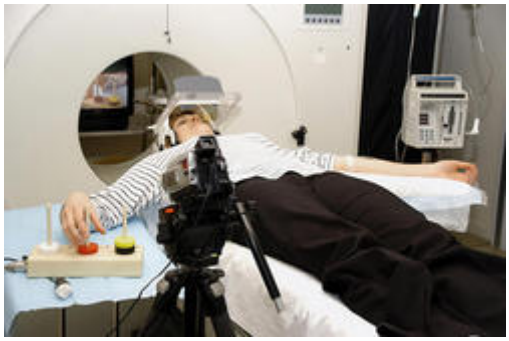
Une recherche pluridisciplinaire

La mémoire et ses troubles donnent lieu à de nombreuses recherches qui font appel à des expertises variées dans un cadre pluridisciplinaire : génétique, neurobiologie, neuropsychologie, électrophysiologie, imagerie fonctionnelle, épidémiologie, différentes disciplines médicales (neurologie, psychiatrie…), mais aussi sciences humaines et sociales.

L'**imagerie fonctionnelle** est très informative puisqu'elle permet de savoir quelles zones du cerveau s'activent pendant différentes taches de mémorisation et de restitution simples ou complexes (réciter une liste de mots, évoquer un souvenir précis dans le détail…). En parallèle les chercheurs étudient le cerveau " au repos " afin d'observer les réseaux cérébraux impliqués dans les

pensées internes et leurs interconnexions en dehors d'un effort de mémorisation. Des travaux ont montré qu'il est altéré notamment chez les patients atteints de la maladie d'Alzheimer.

L'**optogénétique** permet par ailleurs de mieux comprendre l'implication de certains neurones dans ces réseaux sur des modèles animaux. Cette technique qui associe génie génétique et optique permet " d'allumer " et " d'éteindre " des neurones sur commande et d'en observer l'effet sur la mémorisation, le stockage et la restitution des informations. Il devient donc possible de manipuler la mémoire et l'oubli expérimentalement pendant des tâches de mémorisation, pendant le sommeil, au repos, en réactivant ou en effaçant des souvenirs, ou encore en agissant sur la molécule PKM zêta qui serait responsable du maintien de la mémoire à long terme. Menés aux niveaux cellulaire et moléculaire, ces travaux ouvrent la voie à **des perspectives thérapeutiques, notamment pour les victimes de stress post-traumatique**.



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L'iimagerie cérébrale, tomographie par émission de positons, permet d'étudier le fonctionnement de la mémoire.

Les **sciences humaines et sociales**, comme l'histoire et la sociologie, s'intéressent à la mémoire collective, à comment celle-ci se construit progressivement pour conférer une identité à une communauté. Ces études sont rapprochées de celles menées en psychologie et en neurosciences, cette fois-ci au plan individuel, pour mettre en lumière les mécanismes à l'origine du maintien ou de l'oubli de certains événements.

Pour aller plus loin

Actualités

Les gènes de la mémoire sous les projecteurs (15 décembre 2014)
Les odeurs émotionnelles créent des souvenirs forts (24 juillet 2014)
Anesthésies répétées et troubles de la mémoire (23 février 2012)

Communiqués de presse

Les mitochondries sont essentielles à la mémoire (21 novembre 2016)
Augmenter les échanges hippocampe-cortex améliore la mémoire (17 mai 2016)
Should I stay or should I go? De l'importance des souvenirs aversifs et du système endocannabinoïde (24 septembre 2015)
Vieillissement du cerveau : des modifications génétiques identifiées (16 avril 2012)
Une inversion de l'activité du cerveau provoquée par les hormones du stress détermine l'Etat de stress post traumatique (24 février 2012)
Comment agit le cannabis sur la mémoire de travail ? (2 mars 2012)
Le déclin cognitif apparait dès 45 ans (5 janvier 2012)
Comment le cerveau cartographie et mémorise notre environnement pour nous permettre de nous orienter (14 avril 2011)
Le sommeil permet de trier les informations importantes de celles qui ne le sont pas ! (15 février 2011)

Les associations de malades

Inserm-Associations - la base Inserm Associations

A lire aussi sur inserm.fr

Dossier d'information sur la maladie d'Alzheimer
Cerveau, le secret de l'apprentissage, dossier du magazine Science&Santé n°4 (sept/oct 2011)
Vieillissement, quand l'âge fait perdre la tête, dossier du magazine Science&Santé n°21 (sept/oct 2011)

A lire sur d'autres sites

Au cœur de la mémoire, sur le site " Le cerveau à tous les niveaux ", Instituts de recherche en santé du Canada
Troubles de la mémoire, dossier de l'Assurance maladie (ameli-sante.fr)
Consultations mémoire - Fédération nationale des Centres mémoire de ressources et de recherche (CMRR)
A la découverte du cerveau, sur le site de la Fédération pour la recherche sur le cerveau

Livres

Alzheimer : fatalité ou espoir ? de Francis Eustache et collaborateurs, éditions Le Muscadier/Inserm (2014)
Mémoire et oubli de Francis Eustache, Jean-Gabriel Ganascia, Robert Jaffard, Denis Peschanski et Bernard Stiegler, éditions Le Pommier (2014)
Les Chemins de la mémoire de Francis Eustache et Béatrice Desgranges, éditions Le Pommier/Inserm (2012)

Multimédias

Mémoire et oubli un couple inséparable, conférence *Santé en questions* avec Bruno Dubois et Francis Eustache (mai 2014)
Les secrets de la mémoire, dossier du site allodocteurs.fr
La mémoire enfin démasquée ? Interview de Francis Eustache, Universcience.Tv (2010)

Syndrome de Korsakoff

Le **syndrome de Korsakoff** (ou **syndrome amnésique avec fabulations** ou **psychose de Korsakoff** ou **démence de Korsakoff**) est un trouble neurologique d'origine multifactorielle dont une carence en thiamine (vitamine B_1) au niveau du cerveau. Il se manifeste par des troubles neurologiques notamment de la cognition (oublis).

Sa survenue est souvent liée à l'alcoolisme chronique. Elle peut être due plus rarement à certaines formes de sévères malnutritions. C'est une complication de l'encéphalopathie de Wernicke, bien que chez certains patients la maladie soit passée totalement inaperçue. Victor *et al.* ont rapporté un syndrome de Korsakoff chez 84 % de leurs patients alcooliques préalablement atteints d'encéphalopathie de Wernicke[1].

Ce syndrome a été décrit par le neuropsychiatre russe Sergei Korsakoff à la fin du XIX^e^ siècle[2].

Syndrome de Korsakoff

Spécialité	Psychiatrie
CIM-10	F04 (http://apps.who.int/classifications/icd10/browse/2008/fr#/F04) F10.6 (http://apps.who.int/classifications/icd10/browse/2008/fr#/F10.6)
CIM-9	291.1 (http://www.icd9data.com/getICD9Code.ashx?icd9=291.1) 294.0 (http://www.icd9data.com/getICD9Code.ashx?icd9=294.0)
OMIM	277730 (http://www.ncbi.nlm.nih.gov/omim/277730)
DiseasesDB	14107 (http://www.diseasesdatabase.com/ddb14107.htm)
eMedicine	288379
MeSH	D020915 (http://www.nlm.nih.gov/cgi/mesh/2012/MB_cgi?field=uid&term=D020915)

Mise en garde médicale

Sommaire

Épidémiologie

Une enquête épidémiologique du syndrome de Korsakoff effectuée à La Haye, Pays-Bas, en 1987 révèle une prévalence de 4,8 pour 10 000 habitants. L'âge moyen des patients était de 62 ans. Soixante-quinze pour cent de tous les patients avaient déjà bénéficié d'au moins une hospitalisation parfois de longue durée[3]. Ce trouble semble sous-diagnostiqué. Il existe une grande différence entre la maladie diagnostiquée cliniquement et des autopsies systématiques[4].

Causes

- Alcoolodépendance
- Kyste du *septum pellucidum*[Note 1, 5]
- Vomissements fréquents dont les femmes enceintes qui ont des vomissements excessifs (*hyperemesis gravidarum*)[6, 7]
- SIDA avec encéphalopathie à cytomégalovirus (CMV)[8]
- Régime très restrictif / troubles du comportement alimentaire [réf. nécessaire]
- Autre cause de carence en vitamine B_1 comme les suites de gastrectomie[9]

Diagnostic

Clinique

Les symptômes majeurs du syndrome de Korsakoff sont[10] :

- une amnésie antérograde ;
- une désorientation temporo-spatiale c'est-à-dire une incapacité de se repérer par rapport au temps et à l'espace. En général, la désorientation temporelle précède la désorientation spatiale[11] ;
- une difficulté à la restructuration perceptive (insight);
- une anosognosie (méconnaissance/déni de la pathologie);
- une amnésie rétrograde des dernières années de sa vie (l'individu ne se souvient plus de son passé -mais a tendance à se souvenir de son passé lointain- et ne peut plus acquérir de nouvelles informations en mémoire à long terme) ;
- la répétition immédiate est conservée ;
- fabulations et fausses reconnaissances ;
- des persévérations (radotage)
- une apathie et un émoussement émotionnel.

Dans les cas les plus typiques, il n'y a pas d'autres troubles cognitifs. Cependant, une altération des fonctions exécutives est fréquente avec une diminution des performances globales[10].

Plus que d'une typologie spécifique du syndrome de Korsakoff, certains auteurs, à la suite à R.S. Ryback[12], préfèrent parler d'un *continuum* entre les troubles cognitifs des patients alcooliques non-korsakoff et ceux des patients Korsakoff, continuum allant de l'encéphalopathie de Wernicke au syndrome de Korsakoff en passant par un syndrome intermédiaire, le syndrome de Wernicke-Korsakoff. Cette théorie du *continuum* postule que l'alcool affecte le cerveau et la cognition de manière légère à modérée chez les alcooliques non-Korsakoff jusqu'aux déficits sévères du syndrome de Korsakoff[10,13]. Il existe des troubles de la mémoire de travail aussi bien chez les patients avec un syndrome de Korsakoff que chez les patients alcooliques sans complications neurologiques. La mémoire sémantique (apprentissage d'un nouveau vocabulaire, de concepts) est partiellement altérée chez les patients avec une alcoolodépendance chronique et ces troubles sont encore plus marqués chez les patients atteints d'un syndrome de Korsakoff[13].

Pathologies associées

Conséquences de l'alcoolodépendance

- Polyneuropathie (polynévrite) axonale carentielle (vitamines B_1 et B_6) de type sensitivo-motrice sévère et/ou névrite optique rétro-bulbaire[14]
- Encéphalopathie de Wernicke
- Cancers, notamment cancers ORL
- Cardiomyopathie dilatée

Examens complémentaires

Imagerie

- Scanner

« Le scanner a permis de faire plusieurs observations importantes en relation avec l'alcoolisation :

> - présence d'une atrophie corticale globale et d'une dilatation ventriculaire chez les alcooliques chroniques, partiellement réversible, et dont le mécanisme (perte cellulaire ou variation de l'hydratation ou de la myélinisation) reste discuté ;

- possibilité d'une atteinte plus spécifique du lobe frontal et des régions diencéphaliques, ces anomalies étant, elles, mieux corrélées aux déficits cognitifs[15]. »

- IRM morphologique (classique)

Une IRM peut retrouver une lésion dans le système limbique, au niveau des corps mamillaires, des noyaux thalamiques dorso-médian et antérieur, ainsi qu'aux noyaux septaux. Pour cela, on a décrit ce syndrome comme un syndrome amnésique touchant le diencéphale. Mais il est souvent associé à une atrophie cérébrale généralisée avec dilatation ventriculaire, une atteinte des lobes temporaux internes, une perte de volume de l'hippocampe, du cortex frontal, du cervelet, du corps calleux, du pont, du mésencéphale et surtout une atteinte du cortex cingulaire[13,16].

Vue 3D des corps mamillaires (en rouge)
Cliquer pour l'animation

L'atteinte du pont pourrait être en rapport avec une forme infraclinique de syndrome de myélinolyse centro-pontine[13].
L'atteinte du corps calleux pourrait être en rapport avec une forme infraclinique de syndrome de Marchiafava-Bignami[13].

- IRM fonctionnelle

Pendant une expérience d'apprentissage, une étude sur un seul patient aurait montré une absence d'activation de l'hippocampe lors de l'encodage et de la récupération des visages en IRM fonctionnelle[17].

- PET scan

Le PET scan montre qu'il y a une diminution du métabolisme du sucre dans les régions frontales (précuneus), pariétales [réf. nécessaire] et cingulaires chez les patients avec un syndrome de Korsakoff[18]. Ce n'est pas un examen fait en routine.

Sanguin

L'analyse sanguine retrouve un déficit en thiamine[10]. Ce dosage est corrélé aux performances mnésiques ($r=0,39$; $p=0,04$)[19].

Mécanisme / Physiopathologie

Biologique

Le syndrome de Korsakoff apparaît à la suite d'épisodes d'encéphalopathie de Wernicke répétés.

Carence en thiamine

Les conditions qui entraînent un déficit en vitamine B_1 sont l'alcoolisme chronique et la malnutrition sévère[10].
L'alcoolisme peut être un indicateur de mauvaise nutrition qui, associée à l'inflammation gastrique, un déficit de stockage de la thiamine et une diminution de la phosphorylation de la thiamine en forme activée (thiamine diphosphate) cause la carence en thiamine[19].

Toxicité directe de l'alcool

L'alcool active les récepteurs du GABA, inhibiteurs, et inhibe les récepteurs du glutamate, excitateurs. Ces mécanismes expliquent son effet sédatif. Mais ces anomalies semblent réversibles[10]. Ils pourraient avoir un rôle dans un processus inflammatoire[10] ou modifier la plasticité synaptique.

Psychologique

Classiquement, le syndrome de Korsakoff est décrit comme un syndrome amnésique diencéphalique avec une impossibilité d'apprendre des évènements récents. En réalité, on observe une impossibilité d'établir une stratégie, d'organiser un comportement (syndrome dysexécutif), une conservation de la mémoire du langage (mémoire sémantique) et de la mémoire procédurale[13] avec possibilité d'apprendre des comportements procéduraux (comme faire du vélo) mais sans le souvenir d'avoir appris ces comportements[20].

Au début, on pensait que les patients avec un syndrome de Korsakoff utilisaient les fabulations pour combler les trous de mémoire. Cependant, on a montré que la fabulation et l'amnésie ne sont pas nécessairement présentes toutes les deux. Des études ont montré qu'il y a une dissociation entre les fabulations provoquées, des fabulations spontanées et des fausses mémoires. Ainsi, les patients peuvent être amenés à croire des choses qui ne sont pas arrivées comme d'autres personnes qui ne sont pas atteintes de ce syndrome[21].

Troubles de la mémoire

Le syndrome de Korsakoff est classiquement décrit comme un déficit disproportionné de la mémoire comparativement aux autres sphères de la cognition[21]. L'amnésie antérograde, c'est-à dire l'impossibilité d'apprendre de nouvelles choses, est donc l'atteinte cognitive au premier plan dans cette pathologie.

Différentes hypothèses explicatives ont été avancées. La première propose l'existence d'un déficit des capacités de récupération des informations en mémoire épisodique[22]. Cependant les troubles de récupération des patients amnésiques sont parfois considérés comme une simple conséquence de l'amnésie plutôt que comme son origine.

Une autre hypothèse propose un déficit des capacités d'encodage en mémoire épisodique[21] lié notamment à l'utilisation de stratégies d'encodage superficielles et donc inefficaces ne permettant pas de retrouver ultérieurement l'information de manière efficace dans une tâche de reconnaissance[23].

Troubles visuo-constructifs

Les patients Korsakoff sont décrits comme présentant des performances altérées aussi bien dans les tâches visuo-perceptives[24] que visuo-spatiales[25]. L'apprentissage perceptif serait quant à lui préservé lorsqu'il n'implique pas de fonctions cognitives coûteuse[26] ou lorsque le délai entre l'apprentissage et le test est court[27]. Un délai d'une journée entre la fin des sessions d'apprentissage et le test suffirait à entrainer des performances déficitaires chez les patients atteints du syndrome de Korsakoff[27].

Troubles des fonctions exécutives

L'ensemble des études décrit une atteinte des capacités d'organisation, d'inhibition, de flexibilité, de mise à jour, de classement, d'estimation cognitive et de prise de décision[25].

Troubles de la mémoire autobiographique

Tout comme l'avait noté Korsakoff dès ses premières descriptions, l'amnésie rétrograde dans le syndrome de Korsakoff s'étend sur plusieurs années ou même plusieurs décennies. Selon Kopelman, le dysfonctionnement frontal présent dans le syndrome de Korsakoff pourrait être à l'origine des déficits de récupération des informations autobiographiques dans cette pathologie[21].

Traitement et prise en charge

Préventif

- Information de la population sur les conséquences de l'abus d'alcool et supplémentation des aliments en vitamine B1 par les industriels (déjà proposée pour la bière ou la farine en Australie)[28].
- Prise en charge addictologique.
- Supplémentation par vitaminothérapie intraveineuse lors des hospitalisations des patients alcoolodépendants.
- Détection précoce d'un syndrome de Korsakoff lors d'un épisode d'encéphalopathie de Gayet-Wernicke[29].

Une fois le trouble installé

Médicamenteux

Le traitement consiste en des injections intraveineuses ou intramusculaires de thiamine, associées à une bonne nutrition et hydratation. Ce traitement est largement recommandé mais l'évaluation de ce traitement (le rythme et la posologie) ne sont pas suffisamment étudiés d'après la collaboration Cochrane[30]

Cependant, les lésions cérébrales et l'amnésie ne répondent pas toujours à la thérapie. Dans certains cas, un traitement prolongé est nécessaire. Le traitement du patient nécessite de prendre de la thiamine par la bouche de 3 à 12 mois, bien que seulement 20 pour cent des cas soient réversibles[31]. Si le traitement est un succès, l'amélioration apparait dans les deux ans bien que la récupération soit lente et souvent incomplète [réf. nécessaire].

Psychologique

Les patients atteints du syndrome de Korsakoff d'origine éthylique peuvent bénéficier d'une prise en charge neuropsychologique des troubles mnésiques qui permet une amélioration de leur qualité de vie[32]. Cette rééducation spécifique se fonde sur un bilan cognitif et écologique, sur l'apprentissage de l'utilisation d'orthèses mnésiques et sur l'exploitation des capacités préservées de mémoire implicite et procédurale. La remédiation cognitive est destinée à agir spécifiquement sur l'altération des processus attentionnels, mnésiques, langagiers et exécutifs, de manière à permettre une action indirecte sur les déficits fonctionnels affectant la vie quotidienne. Elle ne se place pas en concurrent des traitements médicamenteux ou de la psychothérapie mais elle est conçue comme une nouvelle modalité thérapeutique venant compléter leurs effets[33].

Prise en charge sociale

On a longtemps cru que les patients souffrant de syndrome de Korsakoff ont besoin de soin permanents. C'est souvent le cas, mais la réhabilitation [Laquelle ?] ne peut apporter qu'un certain niveau, souvent limité, d'indépendance.

- La réorientation et la simplification de l'environnement pourrait être utile [réf. nécessaire].

Histoire et société

Histoire

Le syndrome de Korsakoff a été décrit par le neuropsychiatre Sergueï Korsakoff en 1889[2]. Il présente le premier cas de névrite multiple en 1889 où il détaille l'association d'une polyneuropathie et de ce qui deviendra un syndrome de Korsakoff chez des patients alcooliques[34, 35] [réf. insuffisante],[36].

Cas célèbres

Une célèbre histoire à propos d'un cas a été rapportée par le neurologue Oliver Sacks : *Le marin perdu* et *Une question d'identité* sont rapportés dans son livre *L'Homme qui prenait sa femme pour un chapeau*[37].

Certaines personnes célèbres ont souffert de ce syndrome : le comédien allemand Harald Juhnke **(en)**, l'artiste australien Charles Blackman et le présentateur australien Graham Kennedy.

Voir aussi

- Alcoolisme
- Amnésie
- Démence
- Démence alcoolique **(en)**
- Encéphalopathie de Wernicke
- Malabsorption
- Maladie de Marchiafava-Bignami
- Syndrome de Wernicke-Korsakoff

Notes et références

Notes

1. Le *septum pellucidum* est la membrane séparant les deux ventricules latéraux (voir aussi dysplasie septo-optique)

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