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Decision making

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Abstract

Decision making is one of the most, if not the most, important allostatic strategies of human being. Allostatic capacity is the capability to restore homeostasis after a stressful event at the cellular or systemic level within a time-dependent concept. Stress alters energy allocation of almost all organs and systems of the modern human, being the brain the most important organ. The fact that stress alters the choice of energy resources and significantly increases energy demand makes stress an evolutionary "expensive" trait. A fact which polished the stress-systems of all primates in general and especially of the homo sapiens. Making the right decision is the most effective way to relax stress axes; a capability which is influenced by factors such as nutrition, genetic background, evolutionary trade offs, exercise, urban living, culture and economical level. The uncertain times of today's society make "the right decision making" a hazardous task. If decision making is an allostatic system, there should exist something like a human decision making brain-area or areas. Dopaminergic areas seem to be involved and probably determine decision making procedures in the brain. The utility theory is the basis for decision making neurobiology. Dopamine, acetylcholine, serotonin, testosteron and oxytocine interact in the biochemistry of making the right decision. Dopamine anatomy has evolved during the hominid evolution; intelligence seems to be dependent of dopamine-sensible neurons, with acetylcholine permitting cognitive flexibility. Dopaminergic neurons possibly express a range of dopamine receptors (D1-D5). The two most important receptors for decision making are D1 and D2 receptors. D1 and D2 exhibit different functions in a cooperative way. Health and decision making are related by the rate between D1 and D2 receptors; a rate dependent on nutritional factors (omega 3 fatty acids), urban population, future decision making pressure, tyrosine containing nutrients, refined carbohydrates, exercise and meal size/frequency.
This paper will describe the neuro-anatomical and biochemical factors related with decision making, cognitive flexibility, executive function and the way nutritional interventions could influence and improve these essential tasks of the human brain.

Introduction

We routinely encounter situations requiring us to deal with unexpected changes in our environments. Many times, certain actions that led to rewards in the past are no longer effective for obtaining our goals, and we must enact novel modes of responding to achieve our objectives. For example, when trying to make your morning coffee, you may find that your spouse has reorganized the kitchen so that the coffee container which always used to be in the freezer is now located on one of the cupboard shelves. You may find that for the first few days (or weeks) you automatically (and now, erroneously) reach for the freezer rather than the cupboard for your coffee. Over time, your behavior eventually

adapts (a process referred to as "reversal learning"), but every once and a while, you regress back to your old habits and reach for the freezer before correcting yourself. Imagine a more complex situation where a local take-out eatery that you frequent has closed down. Obtaining a new source of your favorite dish requires you to look at your neighborhood a bit differently (maybe checking out side streets rather than main roads) and take a number of steps to change your foraging strategy. First, stop going to the old location (i.e., stop perseverating), next search around for a reasonable substitute restaurant, and then in the future, make sure you don't subconsciously drift over to the old place when you're having a craving for just ***that pizza*** (or whatever you have). Our ability to behave in a flexible manner and adjust actions to adapt to these types of changes is an essential survival skill that taps multiple cognitive operations, requiring inhibition of outmoded responding, searching for novel effective strategies and then maintaining these new strategies. It is well established that the frontal lobes play a fundamental role in enabling these different forms of behavioral flexibility. Patients with damage to prefrontal cortical regions can acquire novel skills or rules with relative ease.
However, they have great difficulty when they must change their behavior in response to changes in reinforcement contingencies, both in real-life settings and in laboratory tests of behavioral flexibility such as the Wisconsin Card Sorting task. Damage to the frontal lobes typically leads to perseverative deficits, suggesting that these regions play a key role in suppressing the use of old, ineffective behaviors. Moreover, a number of neuropsychiatric disorders have also been associated with impairment in behavioral flexibility, including schizophrenia, obsessive-compulsive disorder and attention deficit and hyperactivity disorder. As such, understanding the neural circuitry that facilitates this form of executive functioning can provide insight into the brain pathology that may underlie impairments in the functions associated with these diseases. Not only individuals with diagnosed pathology can suffer from behavioral rigidity; in normal healthy people behavioral/cognitive flexibility varies greatly (Stocco 2012).

Executive function; choosing right prevents disease

Executive functions (EFs), a set of cognitive abilities that facilitate top-down control of behavior, emotion, and cognition, can be considered as basic for understanding behavioral medicine (Hall 2010). Executive abilities are a collection of related cognitive operations that comprise inhibition ("behavioral inhibition"), maintenance, and updating of the contents of active memory ("working memory"), and switching between tasks efficiently ("task switching"; Myaki 2000). Individual differences in EF are characterized by a high degree of temporal stability and a strong genetic component. For example, a recent adoptive twin study using latent variable modeling of the relative contribution of genes versus environment estimated that individual differences in EF were approximately 99% genetic in origin. Though this does not preclude malleability of performance on individual tests of EF among those who are subject to age-related cognitive decline, it does suggest that, among cognitively intact individuals, much of the variability around the population mean is attributable to genetic influences or a combination of gene x environment selection factors.

Executive control has long been considered a unitary, general-purpose ability that can be measured with a single complex "frontal lobe" task such as the Wisconsin Card Sorting Test. Recent behavioral and neuropsychological evidence indicates, however, that executive control may be more accurately characterized as a collection of related but separable abilities (Baddeley, 1996; Collette et al., 2005; Friedman et al., 2006), a pattern referred to as the "unity and diversity" of executive functions (Duncan, Johnson, Swales, & Freer, 1997; Miyake et al., 2000; Teuber, 1972). Researchers often disagree on what the underlying components of executive functions might be, but arguably the three most frequently studied executive functions are response inhibition (the ability to inhibit dominant, automatic, or prepotent responses), updating working memory representations (the ability to monitor incoming information for relevance to the task at hand and then appropriately update by replacing old, no longer relevant information with newer, more relevant information), and set shifting (the ability to flexibly switch back and forth between tasks or mental sets). Other executive functions have been examined, such as dual-tasking (e.g., Logie, Cocchini, Della Sala, & Baddeley, 2004; Salthouse, Atkinson, & Berish, 2003) and resisting proactive interference (Friedman & Miyake, 2004), but the three executive functions mentioned above have dominated recent executive function research.

In resume we state that the three most important tasks related with executive function are:

1. response inhibition
2. updating working memory representations and
3. set shifting.

On a theoretical level, EFs have potential significance to the field of behavioral medicine, given that they could facilitate a number of behaviors that have implications for morbidity and mortality. To date, EFs have been shown to predict treatment adherence, substance use, stress regulation, rehabilitation behaviors, physical activity, and eating behavior (Pruimboom 2011). EF can predict mortality in people with chronic disease (Hall 2009) but also the possibility of developing disease in adlut life (Friedman 2008).

Several tests have been developed to measure cognitive flexibility, executive function and decision making (table 1, Chang 2012). Not all tests are needed to determine executive function or cognitive flexibility. A few tests, including the Wisconsin card sorting test (WCST) and the digit symbol substitution test (DSST), are so called wide spectrum tests and should be used basically. Other tests (table 1) are needed for verification and scientific in depth research. The digit symbol substitution test is very simple (takes only 5 minutes) and has shown a very high validity and sensibility to measure executive function in healthy and brain damaged individuals (Akbar 2011, Hall 2010). The DSST (see annexo) can even predict future disease susceptibility in persons form 7 – 20 years old (Rosano 2008).
The WCST method is simple. Initially, a number of stimulus cards are presented to the participant. The shapes on the cards are different in color, quantity, and design. The cards are to be matched first by color, then by design and then by

quantity. The participant is given a stack of additional cards and asked to match each one to one of the stimulus cards, thereby forming separate piles of cards for each. The participant is not told how to match the cards; however, he or she is told whether a particular match is right or wrong. During the course of the test the matching rules are changed and the time taken for the participant to learn the new rules, and the mistakes made during this learning process are analysed to arrive at a score. Clinically, the test is widely used by neuropsychologists, clinical psychologists, neurologists and psychiatrists in patients with acquired brain injury, neurodegenerative disease, or mental illness such as schizophrenia. It has been considered a measure of executive function because of its reported sensitivity to frontal lobe dysfunction. As such, the WCST allows the clinician to assess the following "frontal" lobe functions: strategic planning, organized searching, utilizing environmental feedback to shift cognitive sets, directing behavior toward achieving a goal, and modulating impulsive responding. The test can be administered to those 6.5 years to 89 years of age. Figure 1 shows a test example of the WCST (Deveney 2006).

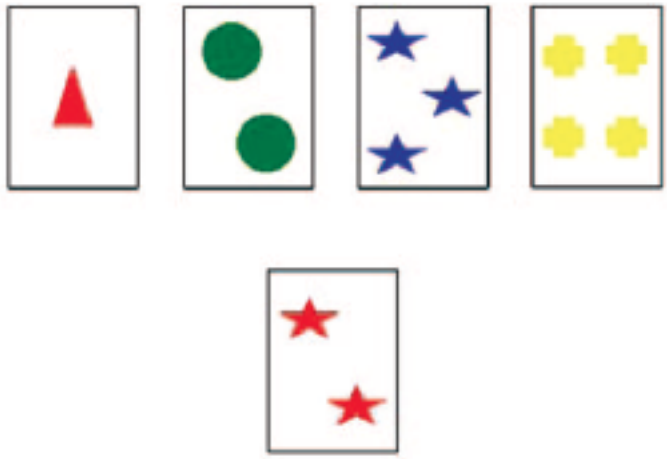
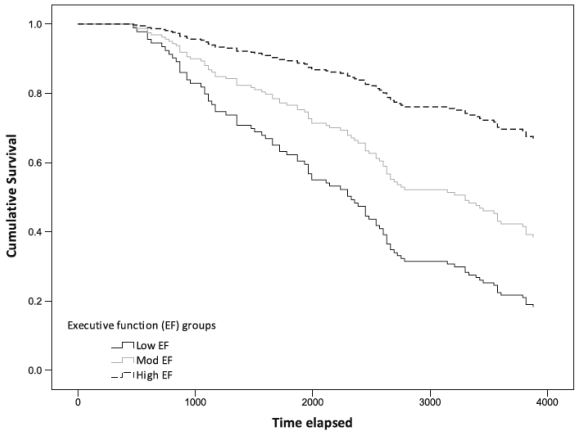


Figure 1 An example of the WCST

Executive function predicts several important clinical topics such as mortality probability when individuals suffer from chronic disease, drug adherence, food choice and engagement in exercise (Friedman 2008, Friedman, 2006, Insel 2006, Hinkin 2002). Hall (Hall 2010) showed that EF is an independent predictor of survival in chronic diseased individuals in spite of sex, race, age or other confounding factors (figure 2)

Figure 2
Survival curve for Low (−1SD), Moderate (mean), and
High (+1SD) EF groups. Log-Rank Test: $\chi 2=21.245$ ($p<0.001$); time elapsed is in days; y-axis indicates survival
probability; x-axis indicates survival time in days


Cumulative Survival
1.0
0.8
0.6
0.4
0.2
0.0
0
1000
2000
3000
4000
Time elapsed
Executive function (EF) groups
Low EF
Mod EF
High EF

1. Information processing
   a. Finger tapping
   b. Visual search task
   c. Stroop word or Stroop color
   d. Digit symbol substitution
   e Anticipation/coincident timing task
   f. Rotor task
   g. Tracking task
   h. Draw a line task
   i. Visual field
   j. Wechsler Intelligence Scale for Children — coding
   k. Number cancelation task
2. Reaction time
   a. Simple pre-motor time
   b. Choice pre-motor time
   c. Simple reaction time
   d. Choice reaction time
3. Attention
   a. PASAT
   b. Woodchuck–Johnson test of concentration
4. Crystallized intelligence
   a. Addition and subtraction (Math)
   b. WAIS
   c. MMSE
   d. Eysenck IQ: verbal
   e. Eysenck's IQ: numerical ability
   f. Eysenck's IQ: visuospatial
   g. Kbit
5. Executive function
   a. Erickson flankers task
   b. Trail making test
   c. Verbal fluency/word fluency
   d. Decision making
   e. Incompatible reaction time
   f. Stroop interference
   g. Alternate uses task
   h. Random number generation
   i. Digit span (backward)
   j. Wisconsin card sorting task
   k. Raven's progressive matrices
   l. Math problem solving
   m. Logical reasoning
6. Memory
   a. Free recall
   b. Visual short-term memory
   c. Verbal working memory
      (Auditory Verbal Learning Test or
      California Verbal Learning Test)
   d. Digit span (forward)
   e. Figural learning test
   f. Sequential memory
   g. Paired associate

Table 1
The total spectrum of cognitive tasks and cognitive tasks categories. The most

Executive function and cognitive flexibility (CF) should be considered the two basic necesities when analizing decision making capacity and its possible improvement. Both EF and CF develop early in life depending on the interaction of the newborn with its parents.

Oxytocin, vasopressin, prolactin and morphin; bonding as the optimal start for decision making capacity in the future

Human babies are born helpless, needing to be entirely cared for and protected. Luckily, they are born with all the necessary tools and "instructions" to attain such care for themselves, and to become a loved and loving part of their family and society. The ingrained neural and hormonal interactions provided for parent and child to assist them in this process are among the most powerful in nature.
The hormonal cues are clear and compelling and our instincts can provide us with all the appropriate responses. Without taking great efforts to avoid and ignore such urges, parents will naturally follow the advice of their neurons and hormones, nurturing their babies and maintaining physical closeness with them. Once born, baby's hormonal control systems and brain synapses begin to permanently organize according to the human interactions she experiences. Unneeded brain receptors and neural pathways are disposed of, while those appropriate to the given environment are enhanced (Bruer 1999).

Love as the driving force behind neurological development

Love is a complex neurobiological phenomenon, relying on trust, belief, pleasure and reward activities within the brain, i.e., limbic processes. Th ese processes critically involve oxytocin, vasopressin, dopamine, and serotonergic signaling. Moreover, endorphin and endogenous morphinergic mechanisms, coupled to nitric oxide autoregulatory pathways, play a role. Naturally rewarding or pleasurable activities are necessary for survival and appetitive motivation, usually governing beneficial biological behaviors like eating, sex, and reproduction. Yet, a broad basis of common signaling and benefi cial neurobiological features exists with connection to the love concept, thereby combining physiological aspects related to maternal, romantic or sexual love and attachment with other healthy activities or neurobiological states. Medical practice can make use of this concept, i.e., mind/ body or integrative medicine. Thus, love, pleasure, and lust have a stress-reducing and health-promoting potential, since they carry the ability to heal or facilitate benefi cial motivation and behavior. In addition, love and pleasure ensure the survival of individuals and their species. After all, love is a joyful and useful activity that encompasses wellness and feelings of well-being (Esch 2005).

Food choice, overeating and non-engaging in exercise

Oxytocin (OT), a nonapeptide primarily synthesized in the hypothalamus, released within the brain or (via the posterior pituitary) to the general circulation, has been implicated in a variety of processes, including social bonding, sexual behavior, pain perception, lactation, and parturition. Importantly, OT has been linked with inhibition of consummatory behavior

(Olszewski 2010).
Initial experiments showed that intraventricular infusion of OT and OT receptor agonists produced a dose-dependent decrease in food consumption in schedule- fed rats as well as in rats refed after food deprivation of moderate length. The anorexigenic effect was similar in males and females. Although some authors observed mild hypophagia upon peripheral administration of OT, it could be achieved only with very high doses. Therefore, a consensus has been reached that the central rather than peripheral pool of OT regulates food intake. It was later discerned that OT's anorexigenic effect stems from the involvement of this peptide in many mechanisms, such as gastric motility, and control of gastric distention, responses to increased plasma osmolality that often accompanies food intake, as well as with the role of OT in termination of feeding upon consumption of aversive tastants and avoidance of such tastants upon subsequent presentations. The actual state of science shows that OT is responsible for the inhibition of carbohydrate intake; therefore, OT neuro-anatomy development in early life is essential for later food-choice and carbohydrate intake inhibition (Olszewski 2010[a], Mitra 2010). Surprisingly so is the fact that chronic sugar intake increases the need for sweet and endogenous morphin production. The latter is responsible for inhibition of oxytocin production and even possible loss of oxytocin neurons/receptors (Olszewski 2010b). Oxytocin can be considered as one of the most important regulators of food intake with higher oxytocin sensibility in the hypothalamus leading to lower carbohydrate intake, higher protein and fat intake and maintenance of body weight (Olszewski 2010b). Figure 3 and 4 show the influence of oxytocin on satiety processes and food choice; one of the major topics in modern society where food choice is ad libidum and obesity an pandemia. As shown it is oxytocin facilitating flexible macronutrient choice, leading to optimal diet and body weight.

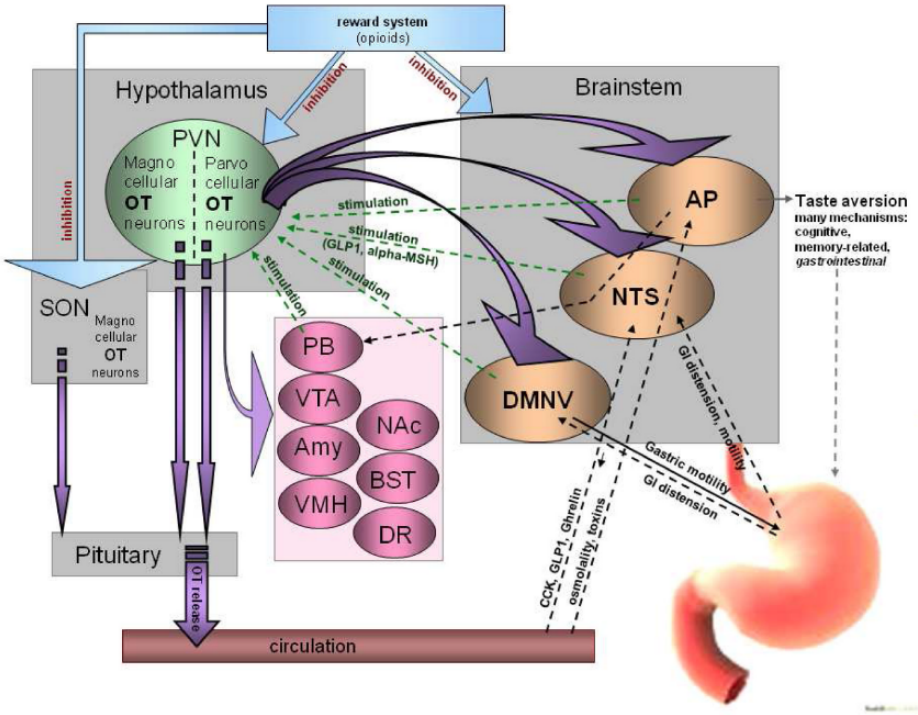


Figure 3 OT neurons project from parvocellular PVN neurons in the hypothalamus to brainstem sites known to regulate feeding (NTS, AP, DMNV) and to the pituitary, where OT is released to the general circulation. While the brainstem-hypothalamus pathways have been extensively studied in relation to OT's involvement in anorexigenic responses stemming from peripheral parameters, such as GI tract distension, osmolality of the blood, etc., many other feeding-related sites that contain OT terminals or OT receptors have not been comprehensively evaluated in relation to anorexigenic action of OT. These include areas involved in reward (ventral tegmental area, VTA; nucleus accumbens, NAc; bed nucleus of the stria terminalis, BST), affect (dorsal raphe nucleus, DR), energy homeostasis (ventromedial hypothalamic nucleus, VMH) and stress (amygdala, Amy; and parabrachial nucleus; PB, adapted from Olszewski 2010)

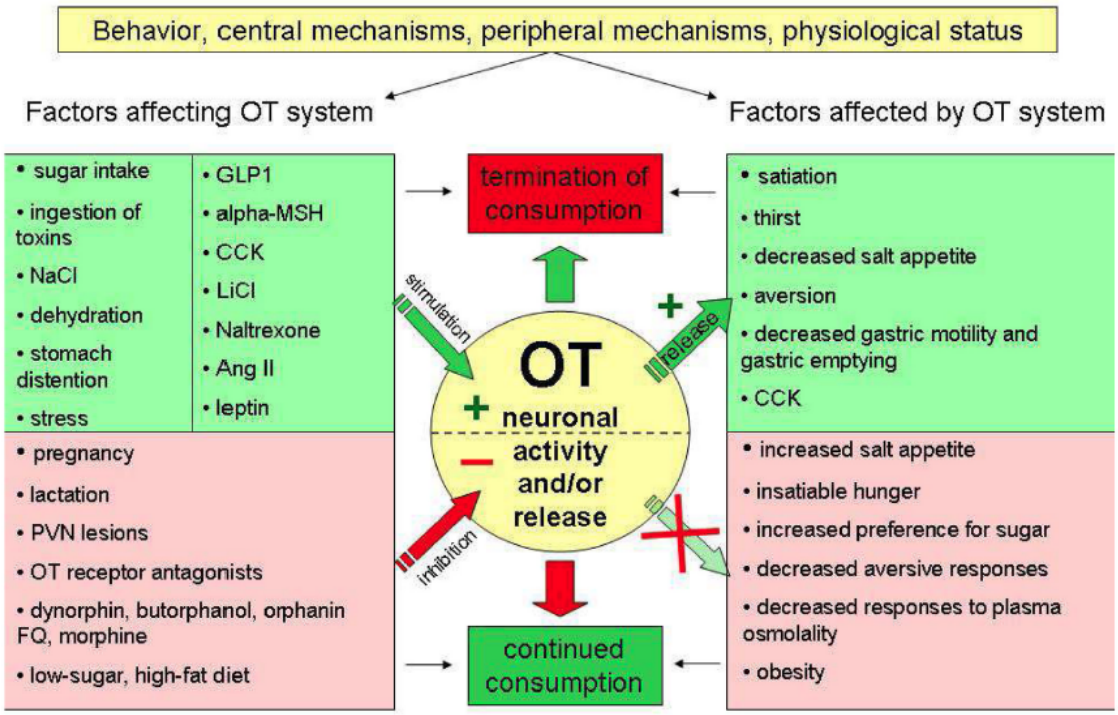


Figure 4 Oxytocin signalling as central pathway of food choice.

It seems that food and its palatability are capable of overdriving the natural inhibition of overeating. Eating for palatability can therefore lead to craving, food addiction and compulsivity (Alsiö 2012). Food reward, not hunger, has become the main driving force for eating in the modern society. We seek pleasure derived from consumption of rewarding foods that usually combine palatability and high energy density, even though overeating promotes body weight gain. Weight control programs aimed at reducing the intake of palatable food suffer from poor long-term compliance and food craving appears to be a critical factor underlying relapse to overeating. Importantly, craving for palatable calories has many similarities

with drug craving observed in addiction, and obese as
well as lean individuals often develop addictive-like overeating behavior. Regulating the neuro-functional pathways leading to "wrong" food choices should preceed the prohibition of food and other soft drugs. Prohibition will only lead to more severe craving behavior (Alsio 2009); if palatibility of food produces hedonic overeating (without cognitive control), than perhaps pharmacological interventions recovering normal "food homeostasis" should be considered. People dieting show higher craving behavior than non-dieting individuals. This craving behavior can lead to further disturbances in their neuro-endocrinological pathways responsible for regulation of food intake. The ultimate consquence is more weight gain than loss after the dieting period (Massey 2012).
Figure 5 shows the proposed model for food craving and food addiction in humans by the group of Olszewski (Alsio 2012).

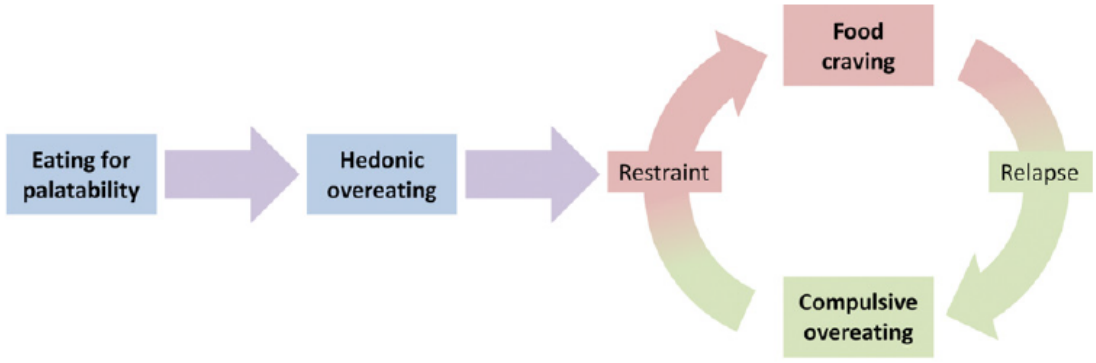


Figure 5 From palatability to addiction

The neuro-endocrinological changes leading to food craving, addiction and compulsive overeating are complex and affect many parts of the neuro-endocrinological organs in the central and peripheral nervous system (figure 6, Alsio 2012).

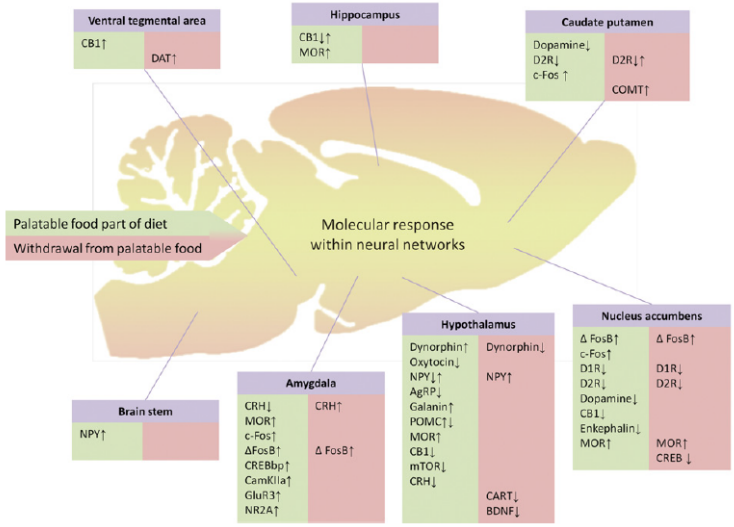


Figure 6 Signaling molecules implicated in food reward, hunger and satiety contribute to the positive feedback loop that drives eating behavior from a pleasurable experience to craving and compulsivity. AgRP, agouti-related peptide; BDNF, brainderived neurotrophic factor; CamKII**α**, Ca2+/calmodulin-dependent protein kinase alpha; CART, cocaine- and amphetamine-regulated transcript; CB1, type 1 cannabinoid receptor; COMT, catechol-O-methyl transferase; CREB, cAMP response element-binding protein; CREBbp, CREB binding protein; CRH, corticotropin-releasing hormone; DAT, dopamine transporter; D1R and D2R, types 1 and 2 dopamine receptor; GluR3, glutamate receptor 3; MOR, mu opioid receptor; mTOR, mammalian target of rapamycin; NR2a, NMDA receptor 2A; NPY, neuropeptide Y; POMC, proopiomelanocortin. " denotes higher levels or activity; ; denotes reduced activity; "# denotes that both upregulated and down-regulated activity have been reported (Alsio 2012)

Oxytocin, and many other substances seem to interact in food choice, executive function, cognitive flexibility, engagement in exercise (Pruimboom 2011) and many other functions. Oxytocin neuro-anatomy develops during early life and is essential for future decision making. The use of oxytocin and vasopressin (see further) are therefore interesting interventions for people with overweight, dementia and even neurodegenerative disorders and psychiatric diseases (Finger 2011, Netherton 2011).

Oxytocin: A Bonding Hormone but also a regulator of food intake

Oxytocin, as stated is a chemical messenger released in the brain chiefly in response to social contact, food intake, odors, but its release is especially pronounced with skin-to-skin contact.
In addition to providing health benefits, this hormone-like substance promotes bonding patterns and creates desire for further contact with the individuals inciting its release. When the process is uninterrupted, oxytocin is one of nature's chief tools for creating a mother. Roused by the high levels of estrogen ("female hormone"). When the process is uninterrupted, oxytocin is one of nature's chief tools for creating a mother. Roused by the high levels of estrogen ("female hormone") during pregnancy, the number of oxytocin receptors in the expecting mother's brain multiplies dramatically near the end of her pregnancy. This makes the new mother highly responsive to the presence of oxytocin. These receptors increase in the part of her brain that promotes maternal behaviors. Oxytocin's first important surge is during labor. If a cesarean birth is necessary, allowing labor to occur first provides some of this bonding hormone surge (and helps ensure a final burst of antibodies for the baby through the placenta).
Passage through the birth canal further heightens oxytocin levels in both mother and baby. High oxytocin causes a mother to become familiar with the unique odor of her newborn infant, and once attracted to it, to prefer her own baby's odor above all others'. Baby is similarly imprinted on mother, deriving feelings of calmness and pain reduction along with mom. When the infant is born, he is already imprinted on the odor of his amniotic fluid. This odor imprint

helps him find mother's nipple, which has a similar but slightly different odor. In the days following birth, the infant can be comforted by the odor of this fluid Gradually over the next days, baby starts to prefer the odor of his mother's breast, but continued imprinting upon his mother is not food related. In fact, formula-fed infants are more attracted (in laboratory tests) to their mother's breast odor than to that of their formula, even two weeks after birth .
By influencing maternal behavior and stimulating milk "let down" (allowing milk to flow) during nursing, oxytocin helps make the first attempts at breastfeeding feel natural. Attempts at nursing during the initial hour after birth cause oxytocin to surge to exceptional levels in both mother and baby. Mothers who postpone nursing lose part of the ultimate hormone high provided for immediately after birth. Powerful initial imprinting for mother and baby is intended to occur chiefly so that mother and baby will be able to find and recognize each other in the hours and days after birth.
Yet a lifetime opportunity for bonding and love is not lost if this initial window is missed. Beyond birth, mother continues to produce elevated levels of oxytocin as a consequence of nursing and holding her infant, and the levels are based on the amount of such contact. This hormonal condition provides a sense of calm and well being. Oxytocin levels are higher in mothers who exclusively breastfeed than in those who use supplementary bottles. Under the early influence of oxytocin, nerve junctions in certain areas of mother's brain actually undergo reorganization, thereby making her maternal behaviors "hard-wired."

As long as contact with the infant remains, oxytocin causes mother to be more caring, to be more eager to please others, to become more sensitive to other's feelings, and to recognize nonverbal cues more readily. Continued nursing also enhances this effect. With high oxytocin, mother's priorities become altered and her brain no longer signals her to groom and adorn herself in order to obtain a mate, and thus a pregnancy. Now that the child has already been created, mom's grooming habits are directed toward baby. High oxytocin in the female has also been shown to promote preference for whatever male is present during its surges (one good reason for dad to hang around during and after the birth). Prolonged high oxytocin in mother, father, or baby also promotes lower blood pressure and reduced heart rate as well as certain kinds of artery repair, actually reducing lifelong risk of heart disease .
Although baby makes her own oxytocin in response to nursing, mother also transfers it to the infant in her milk. This provision serves to promote continuous relaxation and closeness for both mother and baby. A more variable release of oxytocin is seen in bottle-fed infants, but is definitely higher in an infant who is "bottle-nursed" in the parents' arms rather than with a propped bottle.
Persistent regular body contact and other nurturing acts by parents produce a constant, elevated level of oxytocin in the infant, which in turn provides a valuable reduction in the infant's stress-hormone responses.

Multiple psychology studies have demonstrated that, depending on the practices of the parents, the resulting high or low level of oxytocin will control the permanent organization of the stress-handling portion of the baby's brain -- promoting lasting "securely attached" or "insecure" characteristics in the adolescent and adult. Such insecure characteristics include anti-social behavior, aggression, difficulty forming lasting bonds with a mate, mental illness,

and poor handling of stress. When an infant does not receive regular oxytocin-producing responsive care, the resultant stress responses cause elevated levels of the stress hormone cortisol. Chronic cortisol elevations in infants and the hormonal and functional adjustments that go along with it are shown in biochemical studies to be associated with permanent brain changes that lead to elevated responses to stress throughout life, such as higher blood pressure and heart rate. Mothers can also benefit from the stress-reducing effects of oxytocin-women who breastfeed produce significantly less stress hormone than those who bottle-feed .

Nor are fathers left out of the oxytocin equation. It has been shown that a live-in father's oxytocin levels rise toward the end of his mate's pregnancy. When the father spends significant amounts of time in contact with his infant, oxytocin encourages him to become more involved in the ongoing care in a selfperpetuating cycle. Oxytocin in the father also in-creases his interest in physical (not necessarily sexual) contact with the mother. Nature now provides a way for father to become more interested in being a devoted and satisfied part of the family picture through his involvement with the baby.
With all of its powers, oxytocin is but one of a list of many chemicals that nature uses to ensure that baby finds the love and care he needs.

Vasopressin & Protection

Although present and active during bonding in the mother and infant, vasopressin plays a much bigger role in the father. This hormone promotes brain reorganization toward paternal behaviors when the male is cohabitating with the pregnant mother. The father becomes more dedicated to his mate and expresses behaviors of protection.
Released in response to nearness and touch, vasopressin promotes bonding between the father and the mother, helps the father recognize and bond to his baby, and makes him want to be part of the family, rather than alone. It has gained a reputation as the "monogamy hormone." Dr. Theresa Crenshaw, author of The Alchemy of Love and Lust, says, "Testosterone wants to prowl, vasopressin wants to stay home." She also describes vasopressin as tempering the man's sexual drive.
Vasopressin reinforces the father's testosterone-promoted protective inclination regarding his mate and child, but tempers his aggression, making him more reasonable and less extreme. By promoting more rational and less capricious thinking, this hormone induces a sensible paternal role, providing stability as well as vigilance.

Prolactin & Behavior

Prolactin is released in all healthy people during sleep, helping to maintain reproductive organs and immune function. In the mother, prolactin is released in response to suckling, promoting milk production as well as maternal behaviors.
Prolactin relaxes mother, and in the early months, creates a bit of fatigue during a nursing session so she has no strong desire to hop up and do other things.
Prolactin promotes caregiving behaviors and, over time, directs brain

reorganization to favor these behaviors . Father's prolactin levels begin to elevate during mother's pregnancy, but most of the rise in the male occurs after many days of cohabitation with the infant.
As a result of hormonally orchestrated brain reorganization during parenthood, prolactin release patterns are altered. It has been shown that fathers release prolactin in response to intruder threats, whereas childless males do not. On the other hand, nursing mothers do not release prolactin in response to loud noise, whereas childless females do. In children and non-parents, prolactin surges are related to stress levels, so it is generally considered a stress hormone. In parents, it serves as a parenting hormone. Elevated prolactin levels in both the nursing mother and the involved father cause some reduction in their testosterone levels, which in turn reduces their libidos (but not their sexual functioning). Their fertility can be reduced for a time as well.
This reduction in sexual activity and fertility is entirely by design for the benefit of the infant, allowing for ample parental attention and energy. When the father is intimately involved with the infant along with the mother, there should be some accord between the desires of the two, and oxytocin and other chemicals provide for heightened bonding and non-sexual interest in each other, which serves to retain a second devoted caretaker for the infant.

Opioids & Rewards

Opioids (pleasure hormones) are natural morphine-like chemicals created in our bodies. They reduce pain awareness and create feelings of elation. Social contacts, particularly touch-especially between parent and child- induce opioid release, creating good feelings that will enhance bonding. Odor, taste, activity, and even place preferences can develop as the result of opioid release during pleasant contacts, and eventually the sight of a loved one's face stimulates surges. Opioid released in a child's brain as a conditioned response to a parent's warm hugs and kisses can be effective for helping reduce the pain from a tumble or a disappointment.
Parents "learn" to enjoy beneficial activities such as breastfeeding and holding, and infants "learn" to enjoy contact such as being held, carried, and rocked, all as a response to opioid release. Babies need milk, and opioids are nature's reward to them for obtaining it, especially during the initial attempts. The first few episodes of sucking organize nerve pathways in the newborn's brain, conditioning her to continue this activity. This is the reason that breastfed babies sometimes have trouble if they are given bottles in the newborn nursery-early exposure to bottles creates a confusing association of pleasure with both bottle nipples and the mother's breast. In fact, any incidental sensations experienced during rocking, touching, and eating that aren't noxious can become part of a child's attachment and will provide comfort.
It could be the warmth of mother's body, father's furry chest, grandma's gentle lullaby, a blanket, or the wood-slatted side of a crib. Prolonged elevation of prolactin in the attached parent stimulates the opioid system, heightening the rewards for intimate, loving family relationships, possibly above all else. Just as with codeine and morphine, tolerance to natural opioids can occur, which will reduce the reward level for various activities over time. But this is not a problem for attached infants and parents, because higher levels of oxytocin, especially when created through frequent or prolonged body contact, actually inhibit

opioid tolerance , protecting the rewards for maintaining close family relationships. On the other hand, consuming artificial opioid drugs replaces the brain's need for maintaining family contacts.

Once a strong opioid bonding has occurred, separation can become emotionally upsetting, and in the infant possibly even physically uncomfortable when opioid levels decrease in the brain, much like the withdrawal symptoms from cocaine or heroin. When opioid levels become low, one might feel like going home to hold the baby or like crying for a parent's warm embrace, depending on your point of view. Sometimes alternate behaviors are helpful. For instance, thumb-sucking can provide some relief from partial or total withdrawal from a human or rubber nipple and can even provide opioid-produced reminiscences for a time.

Norepinephrine & Learning

Breastfeeding also causes dopamine and its product, norepinephrine (adrenaline), to be produced, which help maintain some of the effects of the early bonding.
They enhance energy and alertness along with some of the pleasure of attachment. Norepinephrine helps organize the infant's stress control system, as well as other important hormonal controls in accordance with the nature of the early rearing experiences. It promotes learning about the environment-especially learning by memorization that is carried out by oxytocin, opioids, and other chemical influences.

Pheromones & Basic Instincts

How does the man's body know to initiate hormonal changes when he is living with a pregnant female? How can an infant accurately interpret mother's "odors" that adults often can barely detect? The answer is pheromones. Among other things, pheromones are steroid hormones that are made in our skin and interact with MHC antigenes. Our bodies are instinctually programmed to react accordingly when we detect these pheromones around us. Newborns are much more sensitive to pheromones than adults. Unable to respond to verbal or many other cues, they apparently depend on this primitive sense that controls much of the behavior of lower animals. Most likely the initial imprinting of baby to odors and pheromones is not just a matter of preferring the parents' odors, but is a way nature controls brain organization and hormonal releases to best adapt baby to its environment.
Baby's earliest, most primitive experiences are then linked to higher abilities such as facial and emotional recognition. Through these, baby most likely learns how to perceive the level of stress in the caretakers around her, such as when mother is experiencing fear or joy. Part of an infant's distress over separation may be caused by the lost parental cues about the safety of her environment. Of course the other basic sensation an infant responds to well is touch, and coincidentally, body odors and pheromones can only be sensed when people are physically very near each other.

What the World Needs Now . . .

Infants universally cry when laid down alone. If we allow ourselves to listen, our neurons and hormones encourage us in the proper response. Babies are designed to be frequently fed in a fashion that requires skin-to-skin contact, holding, and available facial cues. Beneficial, permanent brain changes result in both parent and infant from just such actions. Contented maternal behaviors grow when cues are followed. The enhancement of fatherhood is strongly provided for as well. A father's participation encourages his further involvement and creates accord between father and mother. Frequent proximity and touch between baby and parents can create powerful family bonding-with many long-term benefits. Sadly, over the last century parents have been encouraged by industry-educated "experts" to ignore their every instinct to respond to baby's powerful parenting lessons. Psychologists, neurologists, and biochemists have now confirmed what many of us have instinctually suspected: that many of the rewards of parenthood have been missed along the way, and that generations of children may have missed out on important lifelong advantages.

The adult making decisions

Decision making, as this article tempts to prove, is difficult, influenced by multiple biochemical pathways and regulated by different parts of the central nervous centre. DM is relative easy during low stress situations; stressful situations tend to produce decisions based on emotional values and therefore very "reward" proned. Direct reward-susceptibility can lead to binch-eating, compulsive drinking, "lazy" phenotype and higher risk of falls and accidental death (Liu-Ambrose 2012, Pruimboom 2011, Peters 2011, Schultz 2006). Stress-tolerance, dependent on multiple parameters such as physical condition, socia-economical status, professional occupation, nutritional state, early life experiences and even transgenerational factors, determines DM during stressful periods. People with high stress-tolerance can be considered resilient and will learn from their decision although it will not always be the best decision. Non-resilient people show a lower rate of flexibility and learning capacity, leading to circular behavior in which individuals repeat mistaken DM strategies although they "know" that it is the wrong strategy (Ortin 2012).
McEwen showed very recently how chronic psychosocial stress interacts with environmental toxins and how this interaction is responsible for low EF and higher mortality rate than expected (Figure 7, McEwen 2011).

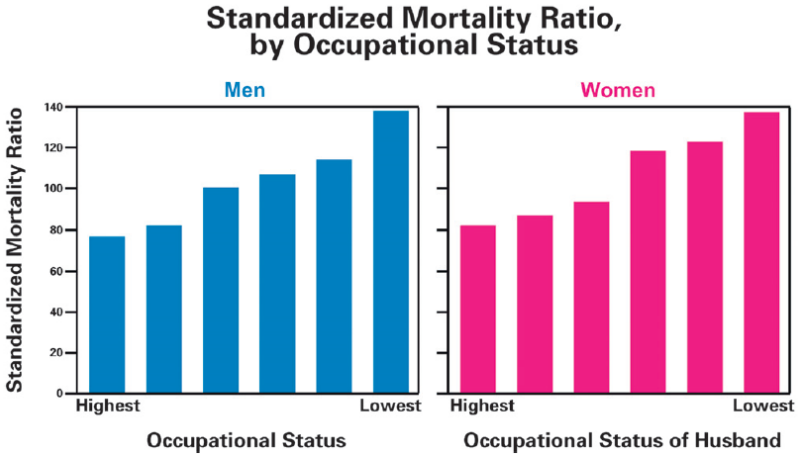


Figure 7 Inverse relationship between SES and mortality ratio in Whitehall Study.
SES = socioeconomic status. The standardized mortality ratio is the ratio of actual deaths to expected deaths. Note that there is an almost linear gradient with occupational status in the British Civil Service in which all persons have jobs and access to health care. The gradient indicates that there are aspects of income and education related to stress and lifestyle that are related to health and mortality.

Flexible, tolerant persons will provide decisions which will benefit themselves, their direct kins and other "loved/liked" individuals, whereas non-resilient individuals tend to choose direct reward related options with the purpose to inhibit the activity of central stress-axes (figure 8, McEwen 2011, Starcke 2010, Esch 2010).

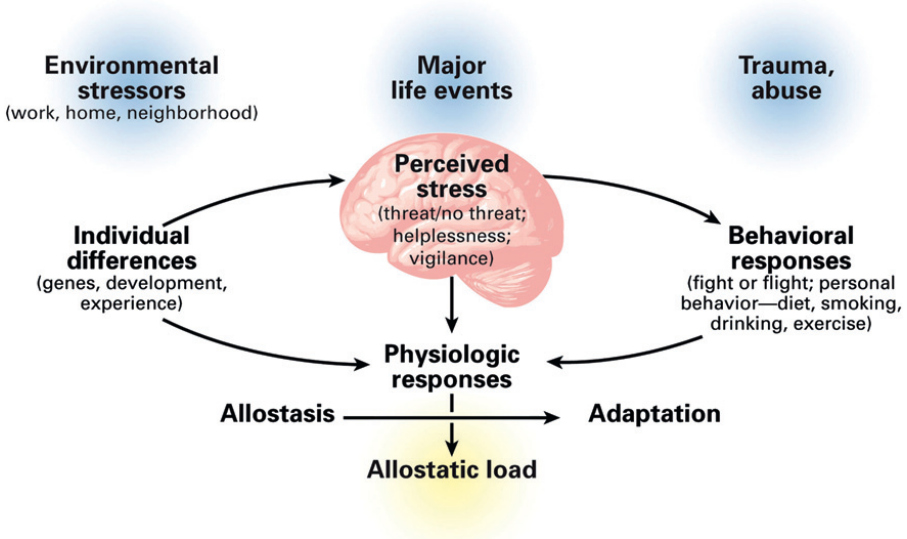


Figure 8 The brain at the center of decision making. It is all between the ears a psychologist would say (McEwen 2011).

DM is not a linear proces. The major difference between the human brain and even the biggest most powerful computer is that human DM can be unpredictable (but not necessarily so), whereas a computer decision probability can be almost countless but will always be predictable, because of the fact that every program is produced by humans (Sheppes 2011). Looking at DM as a network-proces every probability is possible (Figure 9, McEwen 2011).

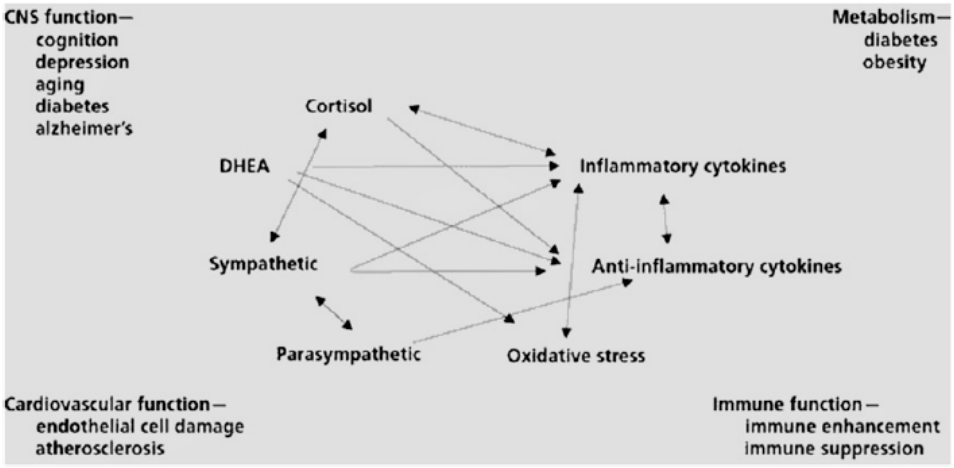


Figure 9 The network-proces involved with human decision making. The interaction of cell-cell and system-system communication makes making the right decision very difficult when predators are at the corner of the street (adapted from McEwen 2011).

It is interesting to see that human´s judgement about causal reasoning problems is normally better than statisctical methods or computerized algorythms (Trueblood 2012).
For example, Gopnik et al. (2001) demonstrated that individuals can infer causal relationships even when sample sizes are too small for statistical tests. Further, people can infer hidden causal structures that are difficult for computer scien- tists or statisticians to uncover (Kushnir et al., 2003). Even though people can infer rich causal representations of the world based on limited data, human causal reasoning is not infallible. Like many other types of subjective probability judgments, judgments about causal events often deviate from the normative rules of classic probability theory.
One of the oldest and most reliable findings regarding human inference is that the order in which evidence is presented affects the final inference (Hogarth and Einhorn, 1992). For example, a juror's belief that a criminal suspect is guilty might depend on the order of presentation of the prosecution and defense. More generally, an order effect occurs when a judgment about the probability of a hypothes is given as equence of information *A* followed by *B*, does not equal the probability of the same hypothesis when the given information is reversed, *B* followed by *A*. As numerous factors influence DM and DM is essential for maintaining human health, is seems vital that individuals learn to use their "free will" even when the circunstances in which they have to make their decision are severely stressful (Pruimboom 2008). When people are pre-

stressed, high emotional dilemmas produce predictable "egoistic" behavior as evidenced in recent research of the group of Starcke (figure 10, Starcke 2010).

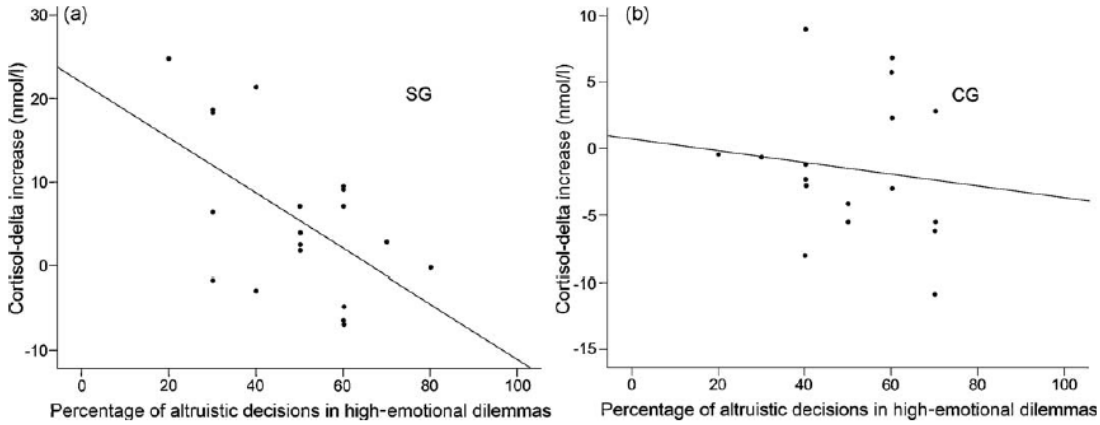


Figure 10 Pre-stress (given by pre-cortisol levels) and decision making when confronted with high-emotional dilemmas. Left stressed group, right control group (Starcke 2010)

In resume it can be stated that the effects of stress on decisions may be relevant to public health. The detrimental effects of stress on health are well documented. Stress is thought to increase the risk for cardiovascular, psychiatric and psychosomatic diseases, and it also encourages unhealthy lifestyle behaviors, such as smoking, drinking or unhealthy diet (Juster et al., 2010; McEwen, 2008; Schneiderman et al., 2005). Thus, stress may have direct and indirect effects on health and these effects may be mediated by the individual's suboptimal decisions, which offer immediate reward at the cost of long-term negative consequences (Starcke 2012).

Understanding the background and producing the intervention

EF and CF are the two basic parameters related with optimal decision making. EF and CF are influenced by emotional challenges, nutritional state, socio-economical status, professional occupation, sleep, level of exercise, early life experiences, culture, environmental toxins and transgenerational factors. All of these factors influence DM through changes of energy allocation to essential parts of the brain related with DM (figure 11, Starcke 2012).

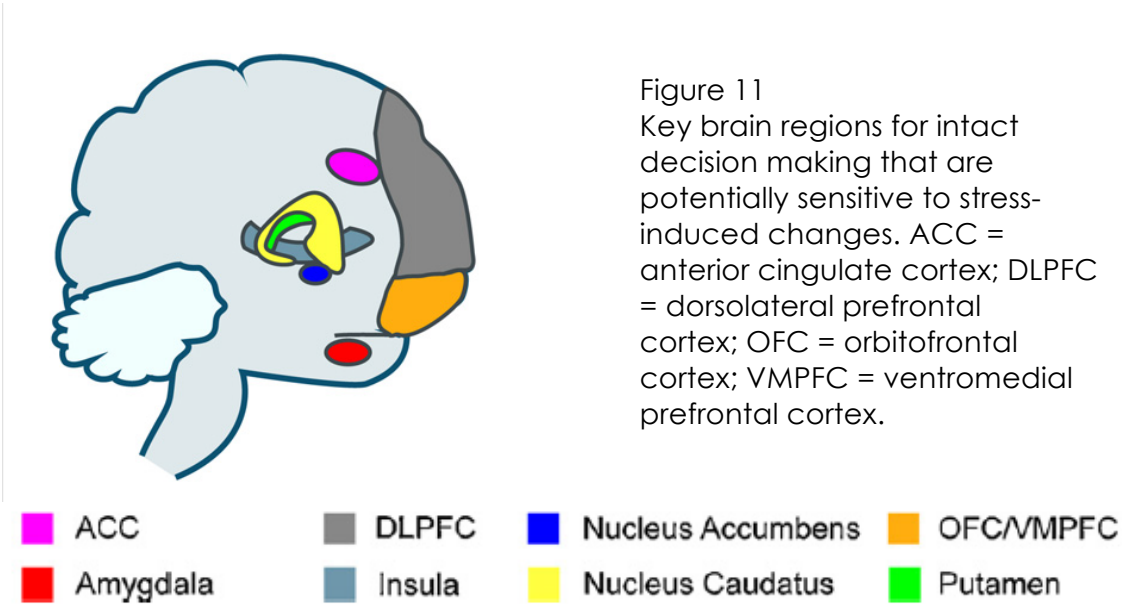


Figure 11
Key brain regions for intact decision making that are potentially sensitive to stress-induced changes. ACC = anterior cingulate cortex; DLPFC = dorsolateral prefrontal cortex; OFC = orbitofrontal cortex; VMPFC = ventromedial prefrontal cortex.

Energy allocation to the brain is a consequence of cerebral blood flow (CBF) facilitating oxigen and resource transport to the central nervous system. CBF is a dynamic proces regulated through the activity pattern of the two central stress axes, i.e. the sympathetic nervous system and the HPA-axis (Bosma 2012, Peters 2011, Zlokovic 2011, Eskes 2010). Peters et al. (Peters 2011, Peters 2010, Peters 2004) have shown that the brain is selfish at the level of energy and resource allocation even when other organs could suffer pathological consequences of this fundamental biological drive (Pruimboom 2012 submitted). The so-called pull/push equation between the brain pull – environmental push systems have arised to provide the brain with enough energy on the account of obesity, disease and, if necessary, the production of a non-permissive brain disorder (Pruimboom 2011).

Optimal functioning individuals use a energy brain-pull mechanism during stressful situations, facilitating DM, EF and CF. An intact stress-axis response increase CBF and energy allocation to the brain by activating brain-parts in a hierarchical sequence (figure 12, Peters 2011). Stressful situations induce CH craving (but not dependent on sweetness) which seems to prevent neuroglycopenic symptoms and bad mood after a stress challenge (Hitze 2010).

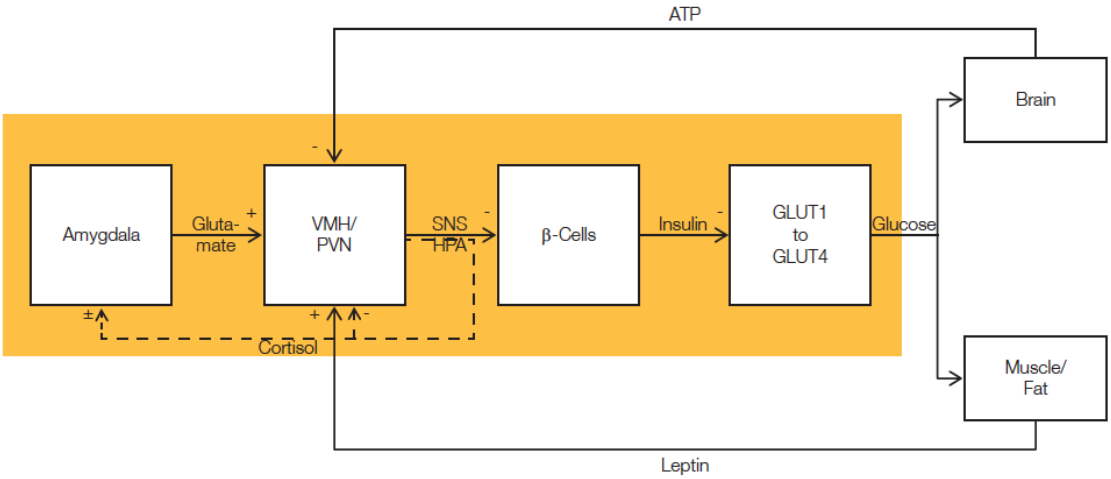


Figure 12 The hierarchically organized stress-system responsible for energy allocation to the brain in stressful situations. Optimal DM during stressful situations produces an energy demand of >12% to the brain compared with normal situations. Inhibition of insulin production drives the shift from GLUT4 (insulin dependent glucose uptake in fat and muscles) to GLUT1 (insulin independent glucose uptake BBB) receptors. The stress-system favors CBF and energy allocation to the central nervous system (Peters 2011)

Healthy individuals suffering from chronic psychoemotional stress show a maintained brain-pull system with higher sympathetic nervous system (SAM) activity and HPA responsiveness, in the end leading to weight loss and loss of apetite (Peters 2011). What happens when stress-axes loose their responsiveness through habituation to chronic activation of the stress axes?
A fascinating paper of Flaa et al (Flaa 2008) shows that individuals with a low SAM response after an acute stress test tend to gain more weight than individuals with a higher SAM response (figure 13, Flaa 2008).

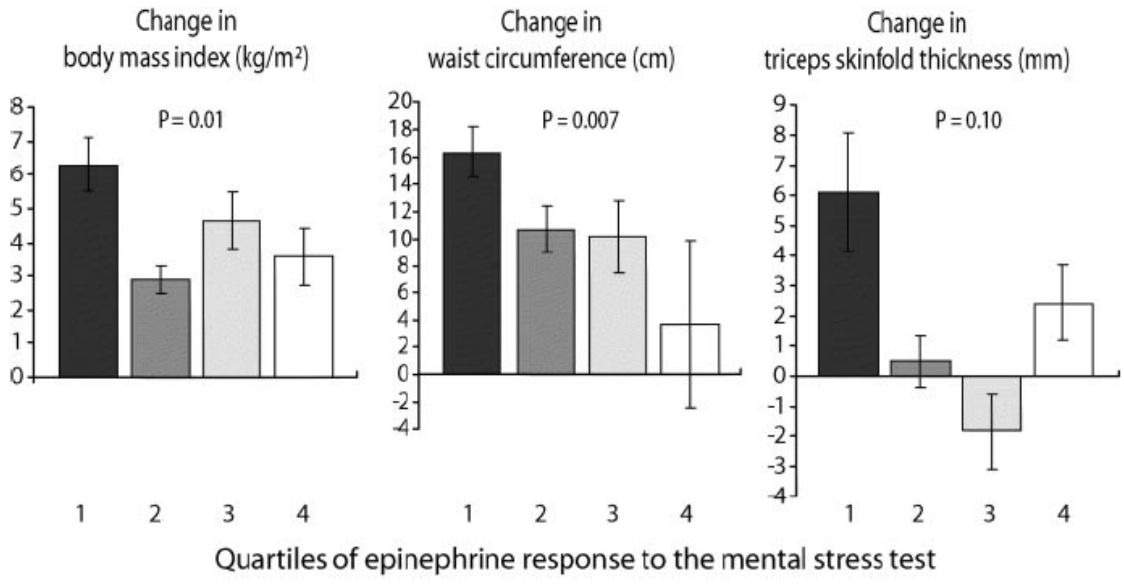


Figure 13 Mean (- SEM) changes in BMI, waist circumference, and triceps skinfold thickness over 18 y according to quartiles of epinephrine response. The mean (-SD) epinephrine responses were 11.3 - 19.7 pg/mL in quartile 1, 44.0 - 27.8 pg/mL in quartile 2, 100.1 - 54.7 pg/mL in quartile 3, and 146.0 - 75.7 pg/mL in quartile 4. P values represent Pearson correlation analyses between the change in BMI, waist circumference, and triceps skinfold thickness and epinephrine responses during mental stress as a continuous variable (Faa 2008)

The lower SAM response after acute stress could be explained by engagement in exercise (with heavy exercise > SAM response) and the higher rest level of noradrenalin and adrenalin in people with susceptibility to stress induced weight gain. This higher rest level seems to be caused by loss of negative feedback at the level of central SAM-regulation organs, causing a ***constant*** production of NA and A instead of the normal rhythmic activity (figure 14). The higher sympathetic tone in rest causes catecholamin resistance at the level of fat tissue and muscles, leading to lower lipolytic capacity and lack of gluconeogenesis (Bosma 2012, Faulds 2003, Hellstrom 1997). Food intake has to be increased (body pull – environmental push) to maintain basic metabolic rate of the brain which has lost its physiological pull-system (Peters 2011) Overeating will lead to storage of fuel in muscles and fat tissue, causing obesity and inflammation.

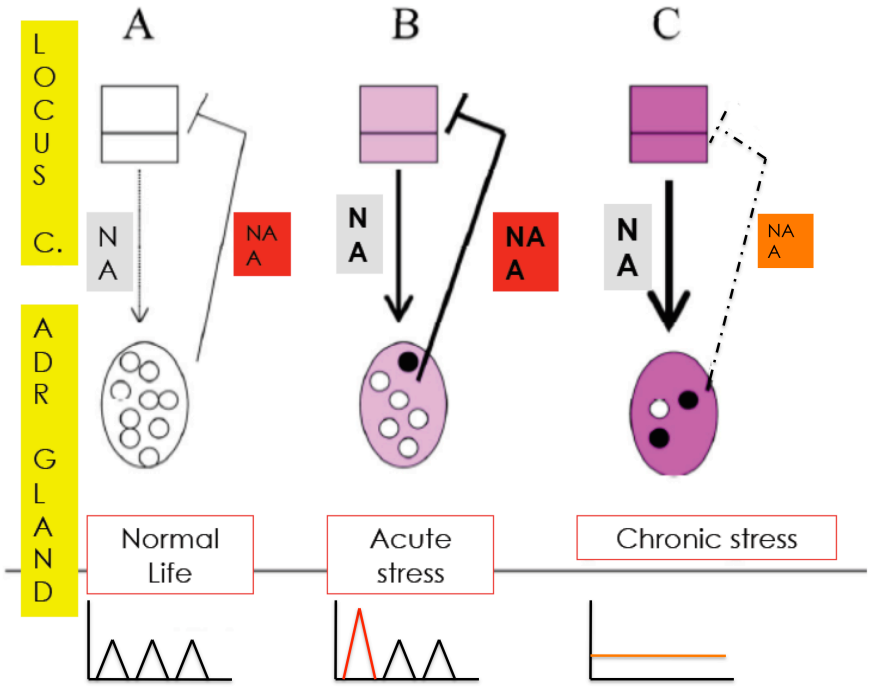


Figure 14 Chronic activation of the sympathetic nervous system starting in the locus coereleus (locus C.) leads to habituation and loss of acute stress responses. The loss of rhythmic activation leads to a higher sympathetic tone in rest (orange line) and the development of catecholamin resistance at the level of muscles

and fat tissue. Resistance to catecholamins decreases lipolysis causing an increased need of food intake, weight gain and lower metabolic rate.

As stated, DM, EF and CF depend on CBF during stressful situations and CBF is disturbed in people suffering from low EF and CF, such as in individuals suffering from Alzheimer, depression and dementia (Zlokoviz 2011). CBF response during stressful situations is a major drive to provide enough energy and resources to the essential parts of the brain related with solution-based behavior (Peterson 2011). The upregalutaion of CBF is called cerebrovascular reserve. Cerebrovascular reserve is the ability of cerebral blood vessels to respond to increased metabolic demand and chemical, mechanical or neural stimuli (Davenport 2012). CBF is regulated by several mechanisms proving the importancy of maintaining brain function is almost every situation (figure 15, Peterson 2011). NO plays the central role in cerebrovascular reserve. NO production is inhibited when people suffer from endothelial dysfunction, when free radical production is increased and with low l-arginine intake/higher use (Vita 2011). The use of NO inducing interventions should be considered as basic for the recovery of energy allocation to the brain, improvement of EF, CF and DM. The use of the amino acid l-arginine seems indicated using increased intake of arginine rich nutrients or as supplement (Cuevas 2004).

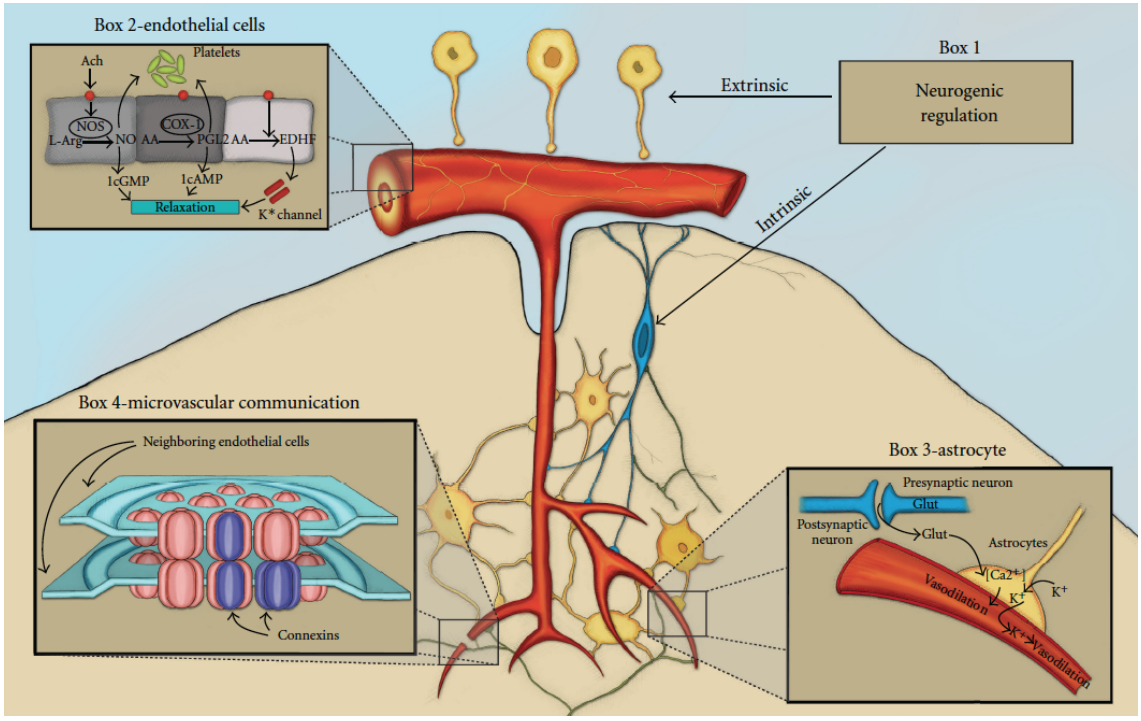


Figure 15 CBF maintained by several pathways; NO plays the central role in cerebrovascular reserve. NO production is inhibited when people suffer from endothelial dysfunction, when free radical production is increased and with low l-arginine intake/higher use (adapted from Peterson 2011)

The actual interventions

EF and CF can be improved by several interventions varying from single bout exercise, chronic exercise, specific food intake, psychotherapy, choline and magnesium supplementation (Davenport 2012, Chang 2012, Slutsky 2010, Zeisel 2009). Choline, omega 3 fatty acids and magnesium seem to hold the most promising effects when supplemented in sufficient high dosis (Zeisel 2009, Slutsky 2010). This is especially interesting for choline while choline (as precursor of acetylcholine) seems to regulate the production and sensibility of ***all*** other neurotransmitters influencing CF, Ef and DM (figure 16, do Santos Coura 2012).

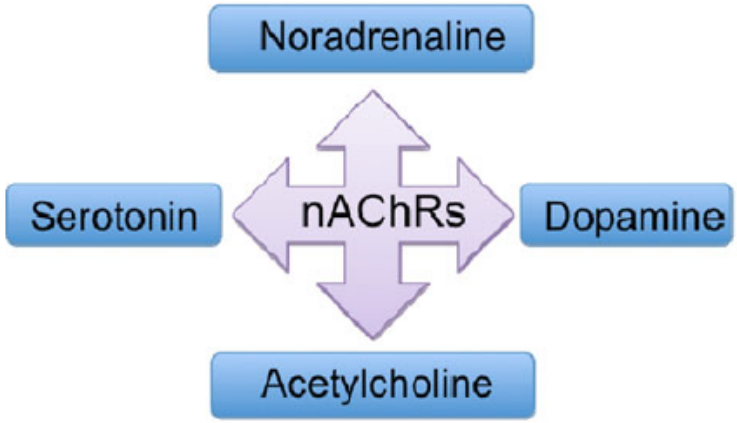


Figure 16 The nAChRs are the central regulators of EF, CF and decision making. Choline and its derivates (such as phosphatidylcholine) activate these receptors, producing flexibility in the use of neurotranmitters with a specific function (adapted from do Santos Coura 2012)

In this context it is choline and its derivates responsible for the majority of functions related with working memory, task shift and reversal learning (figure 17, do Santos Coura). Choline is considered a semi-essential nutrient with higher need in situations of prolonged stress (physical and emotional), disease, changing environment and increasing age (Zeisel 2009). The use of choline rich nutrients should therefore be considered as basic for the treatment of people suffering from low EF and CF, such as those suffering from obesity, overweight, auto-immune diseases, dementia, Alzheimer, CFS, FMS and other pathologies affecting brain homeostasis.
Low choline supply causes a choline distribution based on the model of hierarchical priorities; choline in kidney, lung and intestine will be redistributed to liver and brain, possible causing damage to these disposable organs for direct survival and reproduction (McCann 2011, Li 2008, Kirkwood 2008). Long term deficiency of choline intake can lead to severe damage of these organs and even to cerebral choline insufficiency provoking the onset of Alzheimer and other neurodegenerative diseases (Li 2008).
Choline is present in diferent nutritional sources and minimal daily need is 500 mg. The upper limit lays around 3,5 gr/day; higher dosis could produce fishy body odor, vomiting, increased salivation, increased sweating, and low blood

pressure (FDA 1998). Important sources of choline are egg yolk, fish, crustaceans, green leave vegetables and wild meat (figure 17).

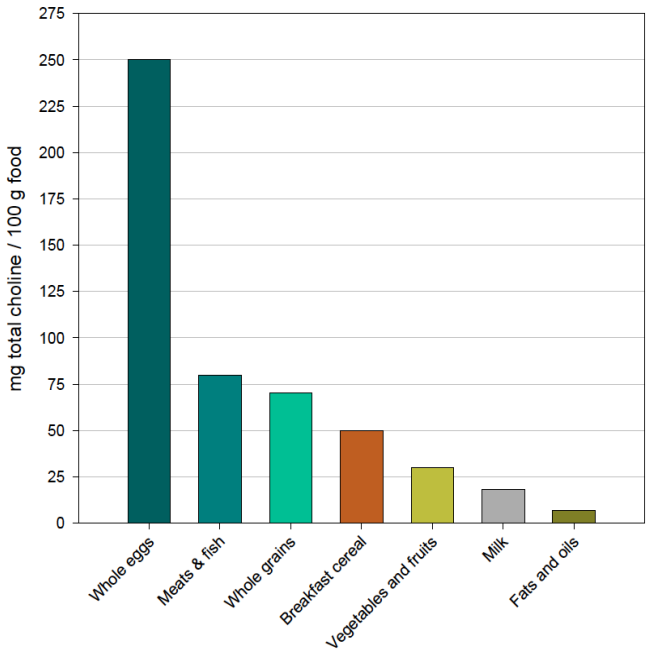


Figure 17

Choline rich foods. Eggs yolk has the highest content followed by fish and meat

The optimal treatment for low EF, CF and DM is an the use of an integrated program based on behavioral interventions, exercise, relaxation and nutrition (see Esch 2010, figure 18). Whole food treatment

B ehavior	>	including pleasurable activities, social interaction, social support, friendship, love, healthy communication, arts and creativity, pacing, cognitive behavioral therapy, motivational and positive psychology
E xercise	>	*aerobic* and anaerobic physical activity
R elaxation	>	including meditation, spirituality / belief, sleep hygiene
N utrition	>	diet, including supplements – if indicated

Figure 18 The BERN concept of stress management. The four columns of professional and integrative – i.e., multimodal – stress management programs such as BERN **[Esch, 2008a; Esch & Stefano, 2007b; Esch et al. 2006b; Esch et al. 2009a; Stefano et al. 2005d]** are a) behavior, b) exercise, c) relaxation, and d) nutrition; two further columns may be added (if not included,as above): social support and spirituality; cognitive behavioral interventions are critical ingredients i) of the behavioral column and ii) the underlying therapeutic model, i.e., mind-body medicine.

Omega 3 fatty acids have long be proven to be effective in treating patients with EF and CF disturbances (Yurko-Mauro 2010). The pathways of how omega 3 fatty acids may improve CF, EF, DM and overall functioning of the central

nervous system have recently been reviewed (Su 2010) and are resumed in figure 19.

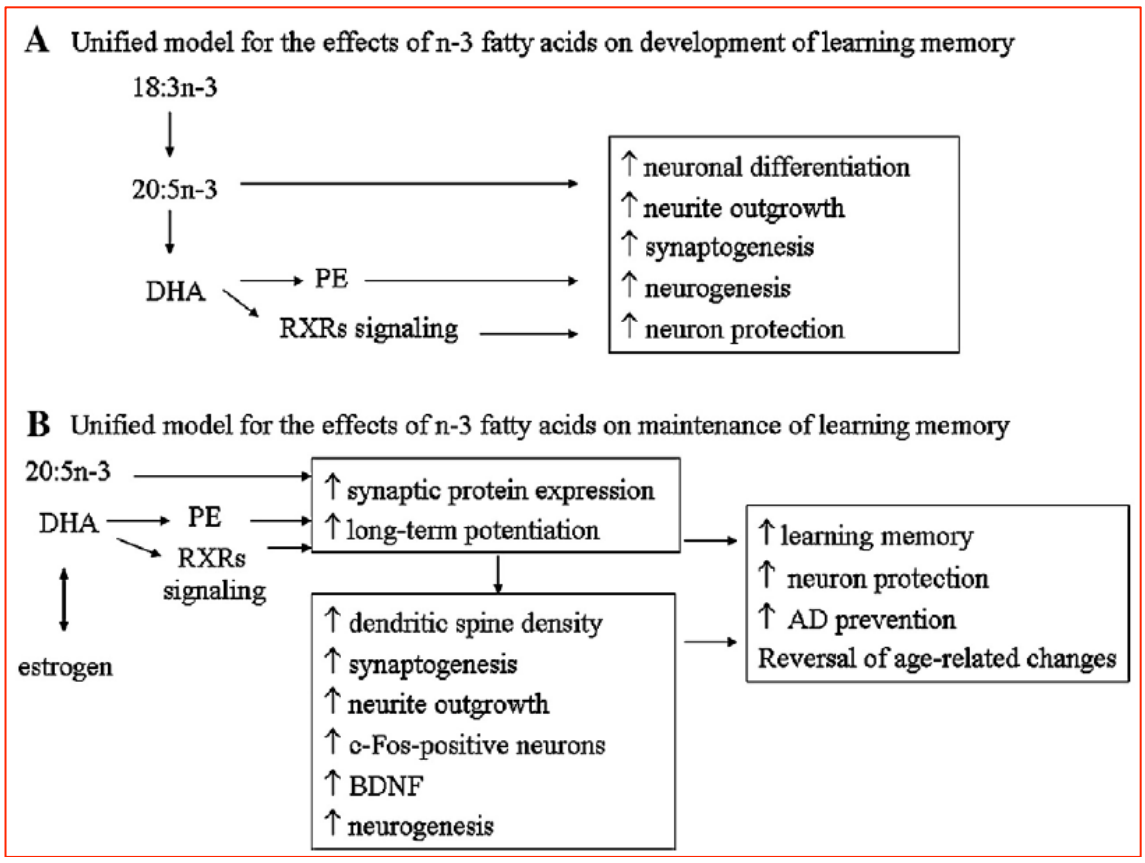


Figure 19 An unified model of the effects of n-3 fatty acids on the development and maintenance of learning memory performance. (A) Unified model for effects on the development of learning memory. It is proposed that the developing brain can carry out DHA biosynthesis and incorporated it into PE. n-3 fatty acids or DHA-RXRs signaling is involved in brain development. (B) Unified model for effects on maintenance of learning memory. It is proposed that the mature brain can take up DHA and incorporate it into neuron membrane PE fractions, where n-3 fatty acids or DHA-RXRs signaling strengthen synaptic plasticity, increase neuron protection and reverse age-related changes. There may be an interaction between the effects of DHA and estrogen.

Magnesium seems to be one of the most promising compounds to treat people with loss of cognitive function in general, but especially those individuals suffering from neurodegenerative pathologies (Abumaria 2011, Slutsky 2010). Magnesium deficiency can be considered the most important pro-inflammatory factor according to the inflammatory index of Cavicchia (Cavicchia 2009). More recently Weglicki (Weglicki 2012) showed that magnesium deficiency should also be considered as the major drive to develop inflammation in the central nervous system (figure 20). Magnesium rich

nutrients should therefore be part of the whole food treatment in people suffering from low EF and CF. Magnesium functions as the natural calcium antagonist, induces the production of NO, augments brain reserve and is highly anti-inflammatory. Magnesium rich foods are green vegetables (chlorophyl), nuts and carbage.

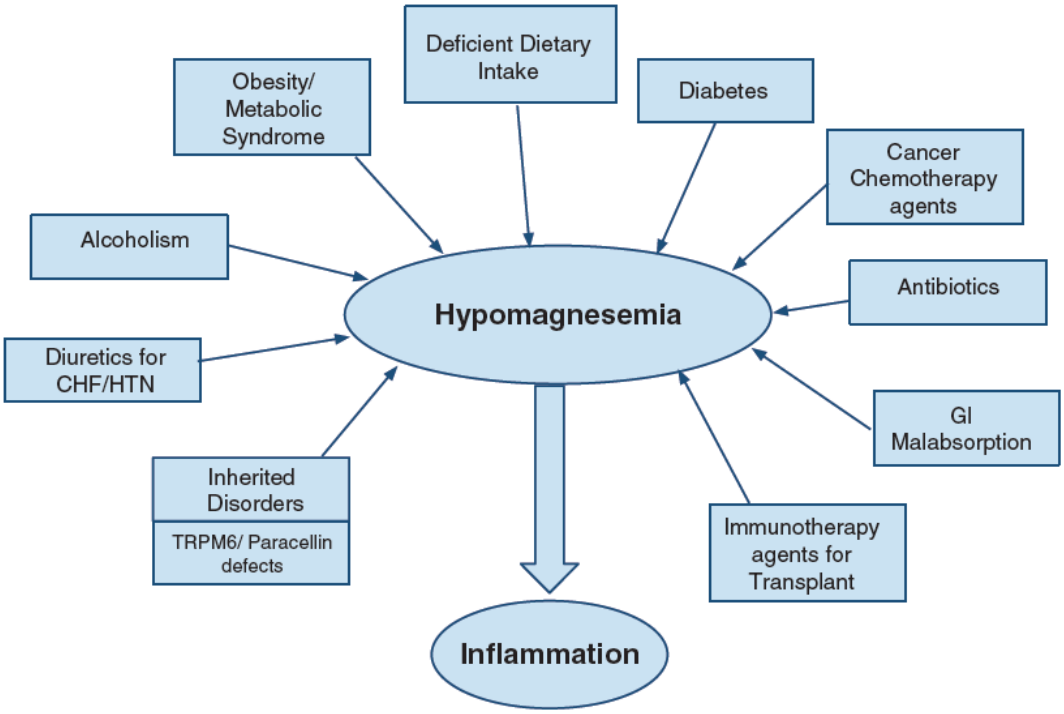


Figure 20 Clinical disorders leading to hypomagnesemia and inflammation. Shown here are multiple diseases and disorders associated with the development of hypomagnesemia and resulting inflammation. Abbreviations: CHF, congestive heart failure; GI, gastrointestinal; HTN, hypertension (Weglciki 2012).

Conclusion

Decision making is the most important allostatic capacity of homo sapiens. Choosing the right nutrient, engaging in physical activity, cooperate with others, altruistic behavior, diet adherence are all DM dependent. Factors such as nutrition, culture, early life experiences, micronutrient deficiency, exercise, gender and age influence DM through changes at the level of executive function and cognitive flexibility. Chronic disease is often the consequence of making incorrect decisions and suffering chronic disease makes individuals susceptible for low EF and CF. Treatment of all patients should start with measuring their EF and CF using validated instruments such as the Iowa gambling test, the wisconsin card sorting test and the digit symbol substitution test. If EF is affected than BERN based therapy should first improve DM and afterwarts disease specific treatment should be applied. Intervention

adherence depends on EF and therefore only EF can improve treatment compliance and its efficacy.