

# Managing the Pandemic of Obesity: Siding with the Fox or the Hedgehog?

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## Key Words

Obesity · Treatment · Prevention · Public health · Cognitive therapy

## Summary

Obesity is a major public health problem of pandemic proportion. Despite its high prevalence and widespread distribution (consistent with a common underlying etiology), clinical psychologists and primary care physicians routinely approach the problem with individualized but often ineffective treatments like psychotherapy and pharmacotherapy, or propose alterations to specific components of the ‘toxic environment’, cultural influences, and psychosocial factors purported to cause overeating. This paper presents an alternative perspective and proposes a potential framework for assisting health professionals in developing rational approaches to education about and preventive treatment of obesity based on the role of factors in early life that contribute to personality and behavior and which over time lead to obesity and its maintenance.

## Introduction

Although the current pandemic of obesity is said to have been driven by environmental factors, in reality the latter are dependably fueled by some simple personal choices: the inability to alter the food selection (e.g., more fat and sugar) and the size of intake (e.g., bigger portions), and a decrease in physical activity in the everyday routine. Those who wish to reduce weight are traditionally torn between two opposite tendencies: pharmacotherapy and lifestyle changes, mostly di-

rected by cognitive-behaviorally oriented therapies. None is fully successful, mostly because no therapy is ever as nuanced as the paths leading to obesity, environmentally, psychologically or genetically.

Genetics of obesity that one day might hopefully provide therapeutically relevant insights is not a theory, but rather a body of ideas, models, and methods directed to predict, estimate, understand and optimize the search of genes and proteins controlling different aspects of feeding behaviors. None of the monogenic variants of obesity is of importance for its garden variety [1], so that patients with varied etiologies have been lumped together by the ‘thrifty genes’ theory of obesity [2] into a pool of genetic victims of natural selection. The latter is a popular cliché that maintains that obesity is a ‘spillover’ of aggressive ‘thriftiness’ from a domain in which it was beneficial in our remote past. An important corollary of this idea is that natural selection must have favored a ‘thrifty behavioral phenotype’ to match the thrifty metabolic machinery to secure the ‘survival of the fittest’ [3, 4]. The major component of human environment is social interaction, such that commenting on the ‘thrifty’ hypothesis, Hockaday and Yajnik [3] indicated that genetic control of the ability to maintain weight in the face of environmental disadvantages would affect many domains needed to succeed in securing scarce food: motivation, drive, reward dependence, and expectancies when processing environmental and mnemonic signals.

Perhaps, such determination in actively pursuing environmental niches and seizing the right opportunity at the right time, as well as in manipulating the environment or resisting it, was envisioned by Bateson [5] who coined the term *envirotypes*. Envirotypes may be defined as ‘selfish phenotype’ uncoupling it from its ‘selfish genes’, or as culturally based cognitive pragmatics, the ‘software’ of the mind [6]. In the social domain, it is in keeping with Bandura’s notion of ‘reciprocal determinism’ [7]. The latter implies that the world and individual behaviors

mold one another; that the way people think, feel and behave informs and alters their environment; that environmental influences and cognitive and other personal factors (self-beliefs) create interactions that result in a *triadic reciprocity of cognition, behavior and environment* [8]. Whether this metaphor is accepted or not, the advantage of the enviotype is in sensitizing us to the dictum of a French poet, Rene Char (1907–1988): ‘Develop your legitimate strangeness’ since the tenacity of the famished is expected to morph into diverse neuropsychological ‘individual pathway(s) to obesity’ [9] that have been targeted by cognitive-behavioral therapies. This emphasis on diverse neuropsychological and lifestyle factors reflects a profound ambivalence in weight management between the hope of future discoveries of the safe and efficacious anti-obesity agents as opposed to a reliance on control of the gamut of environmental events and self-control, neither of which can be easily phrased in the language of molecular machinery.

In the following, some aspects of this neuropsychological reductionism are reviewed in order to show that individually focused behavioral remediation of obesity is unlikely to contain the current epidemic.

### Neuropsychological Reductionism

#### *‘Tyranny of the Urgent’: Reward Discounting*

In keeping with terms of evolutionary ecology [10], individuals tend to control consumption impulses if convinced that a delay of gratifying the whim is worthy. Eating behaviors of the Paleolithic hunter were dependent on the ‘myopic’ rule that eating should not be delayed since food supply was never granted. Uncertainty leads to an error in the original goal value and a degree of its ‘markdown’ associated with numerous personal and extrapersonal circumstances. Such gradual devaluation of reinforcers with time is labeled time discounting. Time discounting refers to any reason for caring less about the future, from a diminished reinforcement value of expected benefits due to changing tastes or to health attrition [11]. It may conceivably describe individual variability in eating behaviors, particularly concerning delayed penalty of overeating. Accordingly, greedy ‘myopic’ impulses are in keeping with ‘thrifty genes’ programming, and have the advantage of drawing attention to the utility of immediately available smaller and less rewarding victuals when the rate of feeding is random [12]. Stephens [13] observed that birds presented with a choice of getting a small food reward immediately or waiting a short moment for a bigger one could not be trained to wait, even after a thousand repetitions. The work may apply to humans, he suggested, because taking rewards without hesitation may have paid off for our foraging ancestors [12], as memorialized in the aphorism ‘a bird in hand is worth two in the bush’.

People do not randomly choose food items since preference stems from efforts to maximize pleasure [14], and there

is a reluctance to change established behaviors in order to comply with therapeutic demands. Operationally, addiction is defined through behaviors initiated ‘to produce pleasure and to provide relief from internal discomfort’ [15]. Dependence on eating may thus be paraphrased after the Diagnostic and Statistical Manual of Mental Disorders (DSM)-III-R criteria regarding psychoactive substance dependence, as ‘... a cluster of cognitive, behavioral, and physiologic symptoms that indicate that the person has impaired control over eating and continues it in undesirable quantity despite adverse consequences.’ Thus defined, however, ‘food addiction’ is a feat of medicalization in that this characterization justifies the conviction that we are all fundamentally gamblers living in a chancy world [16].

The similarity between compulsive overeating and food addiction, and parallels of both to addiction disorders such as substance abuse, is frequently pointed out [17]. That is, addiction sets in when expectations (drives) are fulfilled or even exceeded, thus leading to a pleasurable experience. In turn, both categories of individuals are compared to compulsive gamblers. In fact, in a structured psychological environment, healthy adult women with obesity as reflected in high BMI manifest an impaired performance at computerized gambling tasks [18–20]. Although decisions to take a bet in a gambling game are not directly related to the food domain, they do provide support for the hypothetical link between obesity and neuronal processes, which regulate one’s ability to inhibit short-term rewards when the long-term consequences are deleterious [19]. Choices made by obese individuals in the gambling task are believed to be reminiscent of a ‘decision-making disorder’ of patients with a prefrontal cortex defect that implies difficulties in ‘veto’ functions, e.g., inhibition of excessive food intake [20]. Patients with ventromedial prefrontal damage do behave as if they are insensitive to future social penalties, being primarily guided by immediate rewards that ultimately lead to a net financial loss, and do not develop anticipatory autonomic responses [21] (see, however, alternative interpretations in ref. [22]). Evidence for impairments in eating behavior following isolated prefrontal lesions acquired in adulthood is still lacking.

#### *Loss of ‘Experience of Ownership’*

Although cognitive-behavioral group treatment programs emphasize stimulus-control techniques and reinforcement techniques, and help with cognitive restructuring, self-observation is at the heart of these therapeutic techniques [23]. However, the judgment of potential effects of eating may be less self-referential in obese individuals. Self-reported dietary records or accounts of physical activity can be erratic in obese individuals [24–28] as though showing that misbelief (self-deception) is beneficial for their coping style [29]. Up to 46% of people who are overweight or obese underestimate what they eat by about 300–400 kcal/day, studies show. Such miscalculation can easily thwart an individual’s weight loss efforts [30].

How can we reconcile those erroneous self-perceptions with the fact that people are generally concerned with what they eat? Perhaps they do not have access to their episodic memory. Alternatively, as with patients with ventromedial prefrontal damage, they have deficient metacognitive faculties (meta-memory, insight, and awareness of one's own mental states) or they understand diet dilemmas and restrictions when the problem is spelled out verbally, but fail in real-life settings. Since successful restraint (will-power) is believed to require cognitive efforts [31], another reason might be that people are less attentive to the quantity of food consumed. Preconsciously, they choose to avoid food-related imagery by engaging strategically with diverse aspects of their environment and, in so doing, disrupt the unity of their experience [32].

The *unity of self* is experienced when our mind supplies us with timely previews of actions that turn out to be accurate when we observe the actions that ensue [33]. Gain of weight provides neither an accurate nor a timely feedback. In most cases, it is immensely gradual and delayed. A common cliché is that butter added to a cake or a cookie contains more energy than a similar weight of an explosive, such as trinitrotoluene (TNT), except that the energy of butter is released slowly (through metabolism). Consequently, the causal effect of a couple of extra cookies a day may not be associated with the *experience of authorship* or *ownership*, i.e. the sense that weight gain a few years later was caused by one's own behavior.

#### *Magical Thinking*

The scenario of magical thinking, also known as the self-torturer puzzle of Warren Quinn [34], is a continuation of the previous theme. As the puzzle's scenario goes, a person is given a chance to collect a thousand dollars by self-delivery of electrical currents through a medical device implanted on his body. The current dial permits advancing just one setting a day or leaving it where it was and getting nothing. Such 'self-stimulation' could continue day by day for 10 years. The sensations were so mild initially that the 'player' felt as though the device is harmless. After a decade of so doing, the pain becomes much too great to bear. It follows from the moralistic Faustian logic of the puzzle that perfectly conscious and rational individuals, by accepting presumably innocuous and tempting rewarding contracts, would reach beyond the range of desirable outcomes. Andreou [35] explains that the 'self-torturer' is not alone in his predicament. The accumulation of trifling weight gain after ingesting a scoop of ice cream per week distributed over a few years could easily lead to a considerable weight gain in well-informed people. An often-cited example is that ingestion of only 8 kcal/day more, expended over 30 years, could lead to an increase of 10 kg in body weight. Not many think of this increment when young, but that is the average amount of weight gained by American adults from 25 to 55 years of age [36]. Some individuals will not be convinced to diet or exercise because their overweight is a risk factor for somatic or neurodegenerative disorders that far beyond their

prospective horizon. Even if risk is acknowledged, according to Weinstein's [37] seminal idea, people have a tendency to claim that one is less at risk than one's peers.

The self-torturer's paradox may be interpreted as a particular deficit in high-level planning routine when people cannot prepare themselves for future challenges or rather have difficulties to cognitively time travel in their episodic memory when planning for the future. Such ability entails the coupling of future-oriented executive operations or visualizing oneself in a specific future event while juxtaposing the future with relevant episodic memories. A model of such a process has been proposed elsewhere in discussing prospective memory or memory for intentions [38].

#### *Impulsiveness*

Many obese and weight-gaining people assert that their eating impulses escape their ability to control them [39]. That is why the construct of impulsivity (lack of cognitive restraint, disinhibition and disregard of planning, attentional and motor rashness) has gained interest as a sign of decision-making impairments in otherwise normal eating patterns as well as in eating-disordered populations. Impulsivity could secure higher fitness when competition is intense, but would put one at a disadvantage when competition is relaxed and slow exploration of potential options and their delay works well. The trait is singled out as a crucial personality characteristic for the development and maintenance, as well as treatment, of obesity [40, 41]. It is most resistant to management as compared to other personality traits; it remains a dominant symptom after surgery for morbid obesity whereas other personality features gradually normalize in proportion to the magnitude of weight loss [42]. Obese women showed deficits in response inhibition on objective behavioral measures while they did not appear impulsive on self-report measures [43]. In laboratory studies, impulsivity might be easily validated by scoring the rate of commission errors (failures to withhold responses to non-target stimuli) in versions of the continuous performance test (CPT). With regard to impulsivity, it should be noted that the majority of impulses for eating are not hunger related [44], justifying a distinction between physiological and psychological hunger [45].

#### *Environmental Cue Dependency*

To a degree, environmental food cues determine the desire for food, the onset of eating, and the magnitude of energy intake. According to the psychological principle known as Thorndike's Law of Effect [46], individuals tend to repeat and subsequently learn responses to signals that lead to tension reduction and the completion of motivated activity. Essentially, with regard to tension created by appetite, we are 'programmed' to immediately ingest whatever we see as edible ('a Tootsie Roll in the hand is almost a Tootsie Roll in the mouth') [47] and spit it later (if the piece is found to be unpalatable). Because of the limited information-processing

capacity of the visual system, attention has the power to 'wrap around' a target signal, thereby excluding other cues that are potentially competing for interest [48], so that food cues narrow the focus of consciousness en route to a desirable item (into a sort of perceptual 'tunnel'). When confronted with a large number of food cues, such as is offered in a buffet dinner, even weight- (health-)conscious people may abandon the 'Take-the-Best' heuristic [49]. The point is that food may prompt a kind of 'environmental dependency syndrome'; when in a buffet environment, people simply maximize the amount of food on the plate in order to sample all they see [50, 51]. Part of this environmental cue dependency may be associated with impulsivity. Experimentally, however, impulsive choice and cue hypersensitivity may dissociate [52], and probably should be managed separately.

Kennedy [53] noted that the principle of diversifying foods derives from the need to achieve nutritional adequacy. Perhaps that is how we tend to rationalize the need for assortment, but its biological and cognitive origins are worlds apart from our nutritional objectives. Is more choice in food always preferable? Is dietary assortment good or bad for weight gain? The answer is that a smorgasbord-style of dining is more likely to encourage eating in the absence of hunger [54]. The common phenomena of stimulus-specific satiety and novelty seeking [55] imply that monotonous diets are aversive. The amount of food people tend to select is a function of its diversity and the 'unit' in which food is offered [47, 56]. Sensory-specific satiety predicts that diversifying foods intensifies their hedonic ratings by causing oral or visual dishabituation [55]. Ultimately, the greater dietary variety is associated with increased body weight. By contrast, food sameness decreases its hedonic ratings by causing monotony. One might wonder whether limiting the visual food variety, particularly in people eating together, and maintaining this monotony over an extended time would be a viable technique in weight loss interventions [57].

The social component of eating in humans determines why vision may dominate olfaction. The shared experience of seeing other eaters and even reactions to their manners of enjoyment, their facial expression or body language, are irresistible triggers or, to the contrary, inhibitors of appetite. The way other participants behave has partial control over aspects of eating, such as its pace, the size of meal consumed, choices of food made, and length to termination [58]. A simpler human example of an adaptive social heuristic is to copy the choice of meal of someone who is more familiar with the restaurant [49].

In the absence of sight, the attractiveness of food or hurriedness of ingestion is anticipated to be significantly lessened. The research literature provides some support for this prediction. Blind people are forced to replace the missing information with other senses, but a creation of what might be called an acoustic or olfactory image of food space would be still deficient without visual food-related cues. The microstructure

of eating behavior of the blind may seem similar to that of normal-sight controls. Only when controls were requested to eat with a blindfold, some differences emerged. When blindfolded, they ate 22% less food and had significantly shorter meal durations. Despite a smaller amount of food consumed, they reported a feeling of fullness identical to that after the larger serving ingested when seeing the meal, thereby suggesting that sight could have reduced the dependence on internal signals, and so eating blindfolded might be useful to those whose threshold for overeating is decided by the sight [59]. Alternatively, the benefit could be in eating slowly, increasing the likelihood of successful satiety signaling and avoiding the metabolic disadvantages of increased meal frequency.

#### *Homo Chronocentricus and Sleep*

Organisms exhibit cyclic variations in a variety of other essential functions, including reproduction, which in part is secondary to the daily alternation of darkness and light. The pathophysiology of obesity took a new turn with the recognition of sleep deficit as still another catalyst of obesity [60–63]. Homozygous Clock mutant mice, which have a greatly attenuated diurnal feeding rhythm, appear to be hyperphagic and obese and develop a metabolic syndrome of hyperleptinemia, hyperlipidemia, hepatic steatosis, hyperglycemia, and hypoinulinemia [64, 65]. Chronic sleep deficit is now believed to contribute to the visceral form of obesity that underlies the metabolic syndrome [66]. In Sweden, ~6,400 men who were healthy at baseline were followed for almost 15 years. Difficulty in sleeping at baseline significantly predicted development of type 2 diabetes after controlling for a number of variables, such as age, BMI at screening, physical activity, family history of diabetes, smoking, social class, alcohol intake and others [67].

In mammals, the photoperiod is communicated by a primitive visual system distinct from the image-forming primary visual system; it projects via the retinohypothalamic tract to the 'master clock' located in the hypothalamic suprachiasmatic nucleus. However, our entire temporal identity is an interpretive framework within which we construe the world around us; our worldview has become hopelessly colored by 'chronocentrism' [68] when food availability becomes conditioned by other timed cues, i.e. when anticipatory behaviors and appraisal of the future rewards during foraging happen to be uncoupled from light/dark information.

#### *Physical Indolence*

Indolence is not synonymous to a conscious refusal to burn up energy through purposeful exercise. It is a non-volitional or subconscious activity, such as fidgeting or shifting in one's seat and spending time in purposeless moving (standing and ambulating) [69]. This involuntary activity is poorly characterized; the neuronal systems controlling it are virtually unknown. Recent studies by Levine and associates [70, 71] revealed that obese individuals were seated, on average, 2 h a day longer

than were lean individuals. Posture allocation did not change when the obese individuals lost weight or when lean individuals gained weight, suggesting that it is biologically determined. It was predicted that the addition of non-volitional activity to daily behaviors might expend an additional 350 kcal/day.

### The Fox or the Hedgehog Strategy?

Diet and lifestyle changes are likely to remain the major tools of treatment for the near future, despite the fact that people are surprisingly deficient at predicting the degree to which their inclinations will last [72], and it is not unreasonable to be skeptical of the individuals' ability to keep up with a rigorous routine of dieting. Deservedly or not, these difficulties as well as a considerable investment of therapists' time have fueled anti-dieting sentiments in recent years [45]. Under the best of circumstances, therapeutic goals imply the need for numerous steps. These are:

- early identification of individuals at risk for developing obesity,
- early recognition of potential long-term metabolic problems,
- establishing endocrinological/neurochemical characteristics that covary with specific environments,
- profiling potential responders and non-responders of scheduled clinical interventions,
- determining individual paths of pharmacotherapy and behavioral obesity management,
- predicting tolerance to pharmacotherapy as well as the possibility of side effects and noncompliance,
- initiating well-tolerated pharmacopsychotherapy of affordable cost that impacts selective aspects of behavior.

Admittedly, those individualized behavioral maneuvers were relevant in the period of relative stability of the US population weight (e.g., until 1980 [73]) when overweight could have been handled as sporadic episodes that were fought with individual cognitive-behavioral approaches (along with psychotherapy). However needed, they cannot be a strategy for successfully dealing with an epidemic when it is believed to have already afflicted over 60% of the population. In addition, obesity remains in the category of treatment-resistant disorders when no single treatment has been able to contain it [74]. The obesity epidemic has grown into a 'syndemic', a term coined in the early 1990s by the anthropologist Merrill Singer [reviewed in 75] to catalog diverse co-morbidities and environmental factors (e.g., diet, socioeconomic status, and 'toxic environments') in the context of their synergistic relations.

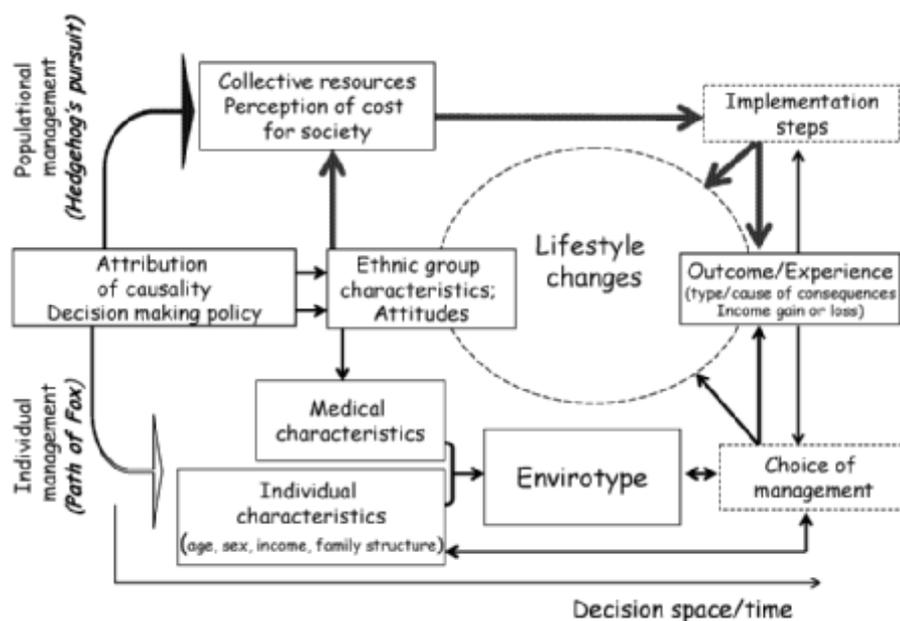
A famous British philosopher, Sir Isaiah Berlin [76], is credited with refreshing in his essay an ancient Greek parable: 'The fox knows many things, but the hedgehog knows one big thing.' In the present context, the miscellaneous knowledge of the fox would be synonymous to the term 'multifactorial'. The latter style of thinking is preferred when we feel that the 'one

big thing' in managing a problem, such as obesity, is hardly possible, that more than one factor is in play and our explanation must be more nuanced such that a student or practicing clinician would be better prepared to confront individual behavioral or clinical problems. In this spirit, a recurrent trend in medicine is often to split rather than lump disease phenotypes into multiple components. With it, the tricks of 'fox knowledge' could presumably apply. The fox strategy is behind the temptation to split obesity into a number of components that might differ neuropsychologically and neurochemically.

The second paradigm affirms that awareness of the magnitude of obesity's social and economic costs could provide support for the magnitude of resources necessary for science to work towards development and implementation of a 'hedgehog plan' to contain this puzzling increase in the rates of obesity or to manage it preventively. Its major effort is delegated to the perinatal period and early childhood, since adult interventions in general have proven to be of limited effectiveness.

The frequency of diverse disorders in children born at low birth weight increased sharply in about 1980, but the cause of the condition is still poorly researched [77]. The prevalence of overweight among US children changed relatively little from the early 1960s through to 1980. However, since 1980 it has increased sharply. This coincidence is suggestive. Collectively, pathological changes due to pre- or perinatal stressors were designated almost half a century ago as 'reproductive casualty' [78]. Nowadays, these early ideas evolved into the notion of latent 'functional teratogenesis' [79], which is actively discussed as part of the 'fetal' or 'Barker programming hypothesis' [80]. Prospective studies exploring this possibility are wanting, but the critical roles of intrauterine abnormalities (nutritional, neuroendocrine, hemodynamic, metabolic, and toxic) as well as a suboptimal early environment in the dysregulation of pathologies of adolescence or adulthood are increasingly recognized [reviewed in 81–85]. The major benefit in tracing the origin of the pathway to obesity from very early life periods is in the ability to itemize structural and molecular components of pathways that can predispose individuals to obesity in later life [86]. One example of the role of prenatal programming is that of rarefaction, which may be an early event in obesity, but could well be programmed prenatally or genetically. Compared with lean subjects, overweight/obese individuals appear to have 44% lower capillary density, suggesting that rarefaction could drive obesity via hypoxia and inflammation [87] cooperating in producing reactive oxygen species. The importance of both factors is in that they may be misattributed to obesity, but could be easily caused by pre- or perinatal pathology [88].

Harvey et al. [89] recently reproduced experimentally lymphatic vasculature dysfunction as a cause of adult-onset obesity by showing that functional inactivation of a single allele of the homeobox gene *Prox1* led to lymphedema with consequent hypertrophy or hyperplasia of adipocytes. At 6–12



**Fig. 1.** General steps in obesity management based on alternative attributions of causality.

months of age, these mice were noticeably heavier than their wild-type littermates. The discovery of the role of *Prox1* inaugurated the new field in obesity research. An indication of the importance of this pathway was illustrated by showing that most severely dilated lymphatic vessels in *Prox1*<sup>+/-</sup> mice were in the intestinal lymphatic network and mesentery, which were a likely source of visceral obesity. It is possible that in capillary-dearth environments, an increased exit of plasma that cannot be effectively cleared up by deficient lymphatic vessels would contribute to adipogenesis in tissues.

We pay little attention to the role of the intestinal microbiota as a significant factor of postnatal development of the intestine's blood vascular system [90]. The intestine of the premature infant also has poor motility and is predisposed to bacterial overgrowth [reviewed in 91]. Gordon's group [92] reported that, in contrast to mice with a gut microbiota, germ-free animals are protected against obesity that develops after consuming a Western-style, high-fat, sugar-rich diet. Does microbiota manipulation promise to become an alternative therapeutic target for the prevention or treatment of obesity? The answer has yet to come. According to some optimistic ideas, there might be a 'nutraceutical angle' when commensal epitopes are offered as optional genetically engineered food additives [93].

Psychology is not left out in the hedgehog strategies. Strong environmental exposures might reverse or alter epigenetic programming of genes regulating human behavior. Numerous studies indicate that parental care early in life can affect gene expression, leaving lasting traces that program alterations in behavior and morbidity in adulthood [94–96]. In humans, the effect may be illustrated by aberrations of social-emotional prosody disrupting maternal communications with their infants [97]. Notably, children suffering from serious obesity and their mothers show a reduced ability to decode nonverbal expression of emotions [98].

Successfully nurturing distressed neonates requires, in Ryle's [99] terminology, both 'knowledge-how' (procedural skills) as well as 'knowledge-that' (declarative knowledge). Even after successfully acquiring the former, caretakers may be guessing about the latter, and thus their default reaction may well be based on a 'false positive error', i.e. abandoning the search for the 'why' of an infant's distress and promptly initiating feeding, regardless of whether the infant's distress is hunger related or not [100]. In most cases, feeding will reliably reduce arousal and calm irritability. Consequently, a child learns to exploit a caretaker's conviction of accurate empathy to assure feeding *ad libitum*.

When mothers of obese children were compared with mothers of normal-weight children, the former showed a significant prevalence of the insecure attachment style (66.6 vs. 38.5%). They idealized their own role as parents and the efficiency of the care (including feeding) they provide for their children [101]. In effect, such mothers add to obesity programming by reinforcing behaviors that pave the road to future 'stress-eating'.

These ideas have changed the field in several important ways. The major one is that the programming hypothesis has liberated obesity from the stigma of a disease of overindulgence; its 'hedgehog advantage' is in that it shifts the focus from the lifestyle of obese adults to that of their infancy and their caretakers. It sends the message that investing in pre- and perinatal care may be the best way of managing an epidemic of adult obesity. Finally, it gives hope for deliverance from a whimsical individualized one-on-one long-term care of obesity to the reliability of standardized care.

Figure 1 compares two paradigm streams in obesity management based on the attribution of causality and decision-making policy: individual management and population-based management. Both have strong and weak points; the question

is not which one is possible, but which one best applies to the situation at hand. The steps are arranged in two streams (paradigms). The bottom stream treats obesity as a chronic individual problem, exploring individual paths to obesity [9]. The individual variables such as age, sex, occupation, education, income, ethnic origin, religion and the level of morbidity affect the eventual choices for behavioral or drug intervention. To emphasize the complexity of the bottom path, the flow of decision-making was marked to turn around at each step of the path, since in managing obesity, things can always go wrong, and commonly will. The distinction between a mere intermittent 'symptom' and a stable 'cognitive aberration' demanding a specific behavioral therapy is vague, but vital in practical implementations. An alternative model represented by the top stream proposes tackling obesity before it develops at the population level of decision-making and management. At a minimum, it denotes the need to work with expectant mothers, supporting healthy attachment, implementing strategies for maintaining healthy weight in preschoolers and other actions that begin before significant weight gain. The schematic does not ignore the 'Change lifestyle' that is shared by either strategy, such that the top path includes under this heading perinatal care, infant nutrition, as well as other traditional lifestyle amendments. The population-targeting approach is expected to be more transparent and, ultimately, cost effective. The 'Outcome/experience' button shown as a feedback station for both streams is established to empirically assess that claim. Evidence for greater cost and lower efficacy of the individualized approach would support shifting resources to the top-stream approach.

## Conclusions and Future Directions

The word obesity is a recognized synecdoche, a figure of speech in which the whole may stand for a part: a particular cause (e.g., hyperphagic obesity), cosmetic problems, local expansion of adiposity (e.g. visceral obesity), genetics of obesity or 'obesity related diseases', for which no individual medical solution could be easily found. Public belief that adverse health events of overweight allegedly threaten to occur in the future is limited [73].

The behavioral syndrome logic of obesity aberrations might provide a neurobiological rationale for specifying relevant brain areas or molecular components, as well as their interconnections, to a range of biologically plausible conditions. A rigorous test of this possibility is still remote and requires specifying the model in more detail than is currently possible. No particular cerebral locus supports the reviewed scenarios that drive anticipatory behaviors, appraisal of current and future rewards, learning, and memory, circadian regulation of functions, locomotor activity, and vigilance. Said differently, the obesity-related neural network resides in so many areas of the brain that its neuronal network could be defined as

'*utopia*', meaning in the precise translation of the word (from Greek) 'no place'.

Its fundamentally 'utopic' (distributed) character has defied thus far the pharmacological mastery of obesity. It is a rare example of a field in which the gain in understanding of interactions of orexigenic and anorexigenic circuits has *not* been paralleled by innovative paradigms for managing obesity. No single drug against obesity is expected to be effective in most patients. Rather, varieties of drugs are needed to produce an efficacious *cocktail*. This would emphasize the utility of (cognitive) activity-directed drug disposition as 'pharmacopsychotherapy' advocated elsewhere [102, 103] when the notion of *envirotpe* may be helpful in stratifying patient populations for clinical trials.

The principal characteristic of biological systems, and weight regulation is one of them, is that they are always multifarious [104]. A therapeutic hypothesis, to be practically useful when confronted by complexity, should consider every possibility that foretells the pathogenic trajectory of an organism in real life, because all possible pathological events may not be symptomatic or cannot be fully defined in terms of their probabilities. That accounts for the high cost and low efficacy of personalized care. In theory, pharmacotherapy of obesity faces the same dilemma. Yet, it is unrealistic to expect that, when designing a drug affecting central targets for the control of food intake and energy expenditure in humans, the pharmaceutical industry would conduct its clinical trials in patients with diverse cognitive profiles. That is why an admonition by Müller and Hebebrand [74] that the contemporary fear of the epidemic may create a therapeutic climate that, if implemented, would exceed the bounds of scientific and pragmatic possibilities is so pertinent. Given that medical costs are increasingly borne by governments, Neel [105] provocatively asked: 'To what extent should governments go to ensure that their citizenry lead lives more in keeping with their genetic endowment, presumably thereby decreasing medical costs?' (p. 18).

Obesity probably represents the final common pathway for a number of different processes. This perspective suggests that behavior modification along with diet, exercise and drug therapy would remain the province of the fox's trial-and-error antiobesity measures and that, when it comes to an epidemic of obesity, the hedgehog strategy of early intervention may be more gainfully employed. If the list of pathological processes triggered in utero becomes self-perpetuating in adult life, the preventive path should be taken, for it focuses on the mediation of epigenetic effects that otherwise have the potential to be transmitted to more than the immediately succeeding generation. The proof of this approach, of course, lies in empirical validation of successful intervention through prospective longitudinal trials. As a first step, increased epidemiological investigation of perinatal and puerperal factors associated with adult obesity may provide a naturalistic experiment to shed light on promising strategies for future intervention trials.

## Acknowledgements

We are grateful to two anonymous reviewers for numerous useful suggestions. All remaining errors the reader might detect were produced without an outside help.

## Disclosure

No financial interest has influenced the position taken in this manuscript.

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