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NEUROBIOLOGY OF ANOREXIA NERVOSA

Milano Walter[1], Capasso Anna[2]

[1]U.O.S.D. Eating Disorder Unit ASL Napoli 2 Nord, Napoli, Italy

[2]Department of Pharmacy, University of Salerno, 84084-Fisciano, Italy

*wamilano@tin.it

Abstract

The present review was focused on the Anorexia Nervosa (AN), the role of neurotransmitters and peptides involved as well as the drugs used in the treatment of these diseases. For AN we intend a syndrome characterized by an persistent alteration of eating behavior and the conducts that cause an insufficient ingestion and/ or adsorption of aliments. The AN is complex conditions that arise from a combination of long-standing behavioral, emotional, psychological, interpersonal, and social factors. The neuronal circuits that control the ingestion of food is mainly related to catecholaminergic, serotoninergic and peptidergic systems. In this respect, while serotonin, dopamine and prostaglandin promote the ingestion of food, on the other side. neuropeptide Y, nor-epinephrine, GABA, opioid peptides inhibit it thus causing the insurgence of AN. The drugs mainly used in the treatment of AN are the antidepressants as the selective serotonin reuptake inhibitors and tricyclic antidepressant. Also, mood stabilizers (lithium), anxiolytics, serotonin and noradrenalin reuptake inhibitors and antipsychotic are often used in the treatment of AN.

Keywords: Anorexia Nervosa, eating behaviour, neurotransmitters, peptides

Introduction

The term "anorexia", that means loss of appetite, is inappropriate. In fact, even though these people refuse the food, generally they preserve their appetite and, like most people, they think excessively to the food.
The illness generally start by the first at the late adolescence, interesting for the 95% of cases the female sex. The loss of weight is due to the drastic reduction of the taking daily of food, that frequently is followed by self-induced vomiting, abuse of laxatives, diuretics ext. This impressive loss of weight is followed by a series of somatic symptoms that are due to the consequences of the poor state of health variable, to time of extreme level. The principal characteristic of AN is the refusal to preserve the normal corporeal weight, that is correlated to the extreme fear to fatten. The latest edition of DSM IV of 1994 expounds the diagnostic criteria of AN, specifying besides the possibility to divide the patients affected by AN in 2 subgroup, with or without purging behavioural [1-10]

Clinical picture.

Generally the premorbid characteristics are similar: timid, submissive, perfectionist and competitive children and adolescents; conscientious, aimed to obtain the maximum by all performance. The modality of beginning more frequent is that gradual and insidious: an adolescent really in overweight sometime, decides to begin a diet lose some kilo, tends progressively to depart herself by hers contemporary, often she makes on activity of study or work with obsessive determination, ignoring every other interest. Even if the beginning can be similar to innocuous dietetic slimming regime, what distinguishes anorexic patient by the contemporary to diet, are the tenacity with which the objective of to make lose weight is followed and the absolute rigidity by the dietetic regime. The meal begin early to becomes early a motive of anxiety so the patient tries to delay as much as possible the moment to sit down at table, he sometimes tills to subvert completely the hours, postponing all activities [1-10]
Many patients at the alimentary restriction associate physical activity whose very soon start increasing frequency and duration and they rapidly assume a compulsive modality.
In the phase of disorders, the worry for the weight assume obsessive characteristics, of predominant idea or even of delirious conviction. The amenorrhea appears very precociously, sometimes after that the loss of weight results evident. The latent hunger, even if denied, resurfaces both disguised as bulimic crisis, both by a constant presence of food at the centre of patient's. With advance of disorders, alimentation, practice of control of weight, styles of life, become more and more severe and stereotyped. In spite of the serious psycho-physical poor state of health, is unaltered the terror to become stout and the conviction to be in overweight for all the skinny aspect. At the objective examination appear signs and symptoms by the extreme malnutrition: patients lament constipation and abdominal algia, skin appears dies, dehydrate, with typical yellow coloration and appears both lanugo that alopecia [1-10]
ECG and EEG are modified as regards norm. Patients are hypotensive and bradycardie; hemato-chemical tests show alteration of the hematic crasis and the hepatic and renal functions.
In the anorexic patients any weight loss seem to be sufficient: also when are seriously underweight they continue to feel too much fat or to feel some part of body like too much fat. The distortion by bodily image is the psychopathological nuclear aspect more resistant in each attempt of confutation and in many patients it assumes the aspect of the delirium [1-10]
The course of AN is variable: it can be characterized by the remission more or less complete, in consequence of single episode, particularly in more young patients and with better pre-existing social or working adaptation. In the 50% of cases well remain residual symptoms or psychopathological sequence, like the presence of depressive symptoms or dependence by drugs. The mortality varies between 5-20%. Even if the normalization of the weight can be left anomaly of the alimentary pattern and the relation with the food can remain altered for a long time, with caloric restrictions, constant worry for the weight and bulimia [1-10]

Methods

Role of neurochemical and neuropeptides systems

The behaviours of search and ingestion of food or Alimentary Conducts (AC) can be interpreted as a final way resultant by the integration of exogenous and endogenous signals. The AC often shows quantitative or qualitative modifications in function of several environmental variables like ethnic-cultural, religious, climatic; but also inside of the same individual, there are alteration of AC that show clearly how is deep-rooted his adaptation homeostatic value, directed to preservation of the constancy of internal means in site variation of environmental conditions. The neurobiological research uses an integrated interdisciplinary approach to obtain information on determinants of ED [11-20]. The eating behaviour is regulated by several factors origin both exogenouses and endogenouses. The different informations coming both by internal and by external find their integration to hypothalamic level, also if today we prefer to speak about hypothalamus like centre of "satiety" and of "hunger". Clearly, besides this central function of hypothalamus there are in the Central Nervous System (CNS) also other specialized areas. Between these areas there is: (inferior tract of encephalic trunk and, particularly, the dorsal vagal complex) that receives and integrates the information that arrive by periphery autonomous endocrine organs and by different cerebral areas. Neuronal circuits of the mesencephalic trunk and of the thalamus interpret these information in relation to signals generated by the mechanical property of foods, that are obtained a different level of the gastrointestinal system [11-20]. The nucleus accumbens, the amygdale and the frontal cortex are responsible, instead, of more important functions that implicate the integration of cognitive information that regard the sensation of pleasantness or adversity to food. At the hypothalamic level, in virtue of its intense vascularization and of nervous projections by the inferior tract of the encephalic trunk, it happens an exact monitoring of the haematic levels of nutriments, of hormones and of the signal that arrive by the periphery. All these information have a deep impact on the activities of the neurochemical and neuroendocrine systems of hypothalamus that, in its turn, transfers signals act to influence the behavioural and metabolic processes [11-20]. All these neuronal systems, coordinating signals of several neurotransmitters and hormones as the amino acids, amines, peptides, and other steroidal hormones, are implicate in the control process of ingestion of food and of energy balance and so of the body weight. Naturally, these fine and precise neurochemical balances can be altered also by drugs that act on these modulators causing, in this way, alteration of the ED and consequently of the body weight. The control of ingestion of food results by the prevalence of factors to promoter action (neuropeptide Y, nor-epinephrine, GABA, opioid peptides) by inhibitory factors (serotonin, CRF, prostaglandin) that interact as a model to cascade. On this central system enters a peripheral system responsible to send of hormonal and nervous signals coming by the gastro enteric tract, by metabolic signals by adipose tissue and other generated by nutriments present in circulation. This model is made more complex by the modulating effect explained, particularly, by circulating levels of the some hormones like insulin, steroids, and thyroids hormones [11-20].

The neuronal circuits that controls the ingestion of food is mainly related to catecholaminergic, serotonergic signals and peptidergic systems; also opioids have a really important role in the control of appetite, but certainly an essential role in this complex mechanism is done by the neuropeptides that have an inhibitory or stimulating action and can act by they self or in synergy with other neuromodulators [11-20]. Regarding the catecholamines, it has been observed that both noradrenaline (NA) and adrenaline (A) at the level of paraventricular nucleus of hypothalamus (PVN) stimulate the ingestion of food. By contrast, A,NA and dopamine (D) exert an anorexic action when they act at level of adrenergic and dopaminergic receptors in the perifornical area of lateral hypothalamus [11-20]. The role of serotonergic system at the level of PVN and of arcuate nucleus (ARC) of hypothalamus is to produce satiety. From data we know how factors that act, stimulating or inhibiting, on these system of neurotransmission, are able to interfere on the regulation of the bringing of food, on the structure of meal and on the choice of nutriments. Apart from the neurotransmitters exist numerous peptides able to do inhibitory or stimulatory activities that can act

with a central or peripheral mechanism [11-20]. The anatomic seat of action of the neuropeptides at the central level is the same neuron modulating its action. The more effective stimulatory of appetite is certainly the neuropeptide Y (NPY); also the galanine and the opioid peptides are stimulatory of the ingestion of food. Besides peptides are able to determine the preference of certain nutriments, that is carbohydrates (NPY), carbohydrates and lipids (opioides); lipids (galanine). Other peptides like the cholecystokinin (CCK), the bombesin (BBS), the somatostatine, the glucagons and other, belong to a complex peripheral system of the satiety, that in part carries on its action thanks to the use of numerous fibre coming by the vagus. At the peripheral level, and particularly in the gastro enteric tract, are secreted the PYY (Peptide YY) and PP (Peptide P); these molecules, similar for structure to NPY, are potent stimulatory of the appetite if injected to the hypothalamus. Therefore the gastro enteric tract through the various stimulus conduct by vagus nerve, has certainly a relevant role in the regulation of the diet [11-20].
So we must to remember that recently is been cloned in the adipose tissue of mouse and in the man one the gene OB that codifies for the protein leptine, which reduces the ingestion of food and the weight increase with an action at hypothalamic level acting on the sensation of hunger, the energetic consumption and body temperature.

Adrenaline and Noradrenaline

Adrenalin and Noradrenalin control the adiposity and the energetic balance through several mechanisms: they promote the catabolism of triglycerides and glycogen, stimulate the ingestion of food when are injected in the CSN, activate the thermo genesis in the brown tissue and regulate the loss of calories through the modulation of the peripheral vasoconstriction. The stimulation aside of NA of α2-adrenergic hypothalamic receptors induces the ingestion of food through the increase of the quantity and duration of foods rich in carbohydrates. These response are anatomically localized at the level of paraventricular nucleus (PVN). In the perifornical area of lateral hypothalamus (LH), the NA and A, through the stimulation of β-adrenergic receptors, induce the suppression of ingestion of food delaying the beginning of meal, reducing the time spent to eat and the quantity of food introduced for meal. The amphetamine and similar, that induce a release both of NA that of dopamine, cause a strong stimulation of β-adrenergic and dopaminergic receptors. This kind of stimulation induces a reduction in particular in the ingestion of proteins [21-26].

Dopamine

The dopamine is able to suppress the ingestion of food through the activation of central dopaminergic receptors. In fact the systemic administration of dopaminergic agonists causes the reduction of the quantity of food ingested. As D as the agents that induce release of D reduce in particular the ingestion of foods rich in proteins and lipids, while have minor effect on the consumption of carbohydrates, the D attenuates the effect of galanine and of opiate on the ingestion of lipids [21-26].
The block of dopaminergic receptors in the lateral hypothalamus, through the injection of neuroleptic antagonist of dopaminergic receptors, provokes the opposite effects and, in particular an increased of consumption of proteins and lipids and so weight increase.
At last, we must to remember that recently is has been established a significant statistically correlation between the presence of a particular allele of D_2 receptors and some aspects of eating behaviours in obese patients [21-26].

Serotonin (5-HT)

Substances that increase the activity of the serotonergic system induce an immediate and prominent reduction of ingestion of food, while the serotonergic antagonists cause an increase of it**.** The serotonin reduces the ingestion of food interacting with 5-HT1b post-synaptic receptors that are concentrated in the medial hypothalamic nucleus and that are sensitive to the deprivation of food. The hypothalamic administration of 5-HT induces a pattern of ingestion of food contrary to that observed after α2-adrenergic stimulation. In fact we can note a reduction of the percentage of carbohydrates ingest respect to the proteins. We can see a similar pattern of taking of macronutrients

after injection of fluoxetine in PVN, that can stop the reuptake of 5-HT from pre-synaptic endings. The serotonin and the drugs that induce the release of it, reduce the quantity and duration of meal, while they have a low effect on number of consumed meal [21-26].
Besides is necessary remember that a reduced taking of food could alter the hypothalamic serotonergic activity: the diet particularly reduces the concentration of tryptophan, amino acid precursory of 5-HT. This reduce the level of cerebral tryptophan, reducing the synthesis of serotonin. So the reduced taking inhibiting the synthesis of 5HT hypothalamic could induce a compensatory up-regulation in the response of 5-HT2C receptors. Then the extreme dieting provoke a reduced signal of satiety induced by the same serotonin.
We know that repeated and prolonged diets are the most important causes of the beginning of eating disorders, like the bulimia nervosa, that is a state characterized by episodes of binge eating [21-26].

Gamma-Aminobutyric Acid (GABA)

The gamma-aminobutyric acid, if injected in the PVN, develops the consumption of food and, particularly that one rich of carbohydrates. The GABA carries on its action through the activation of GABA receptors. Probably, this amino acid operates by coordinator between metabolic and neuronal signals that modulate the taking of the carbohydrates. At last, has been showed that the benzodiazepine, agonists of receptors for the GABA, provoke an increase of ingestion of food [21-26].

Neuropeptide Y (NPY)

The neuropeptide Y is a polypeptides of 36 amino acids that belongs to the pancreatic polypeptides' family and was been isolated for the first time in the 1982. It is considered the most potent stimulator of appetite. It is situated in different zones of brain. It is stays in elevated concentrations in the cortex and in corpus striated, in structures limbic, in the adrenergic and noradrenergic neurons that project versus the hypothalamus and in neuron one's of hypothalamus. The NPY to perform its action must legate to specific receptors: Y1, Y2 and Y3. The SNC contains Y1 and Y2 receptors. The action of stimulate on the appetite is followed by the activation of Y1 receptor [21-26].

Galanin

The galanin is a polypeptide made up of 29 amino acids and it is amply distributed in everywhere of gastro enteric tract and in brain. An injection of galanin in PVN produce in way dose-dependent, an increase of taking of food. The galanin operates through α2-adrenergic receptors [21-26].

Opioids

Since a long time we know that the opioids stimulate the appetite and that an injection intracerebroventricular of β-endorfin increases the appetite but in a less marked way respect to NPY. Probably, opioids have a role also in process that regulate the use of energy interfering in particular on the thermo genetic processes. This data derives by the observation of patients who are in treatment with metadone: they are in fact most sub-weight, even if they preserving an caloric introit equal or also superior to the necessary for the preservation of ideal weight to cause of activation of processes of energetic dispersion [21-26].

Results

Treatment of Anorexia Nervosa

The first description of two probable cases of anorexia go back to 1689 when Richard Morton, in England, spoke of phthisis nervosa. He highlighted all the symptoms of current forms but without the worry to put on a lot weight. Two century in the 1868, W. Gull, described a patient with similar symptomatology, and he propose to call it hysteric apepsia. Some years later, in the 1873, Gull spoke more diffusely about a case with the same symptomatology but he preferred to call it "anorexia nervosa" and instead of hysteric, to underline the psychological component [27-29].
. Both Morton and Gull, later, raised questions on the therapy still present today, that is:

- the empiric character of the prescription;
- the large use of symptomatical, the use ,with or after, of drugs and moral indications relative to the diet and to the style of life;

- uncertainly of results and of outcome a long term;
- the refusal of treatment or, most precisely, of recovery.

They are problems with which still today we must deal.

Still the second middle of twentieth century, the psychopharmacology has done large progresses, by the synthesis, in the 1952 of the progenitor of the neuroleptics, the chlorpromazine, till neuroleptics of latest generation, the so called atypical and to the SSRI ext. Is important to underline that a large part of psychoactive drugs, gradually discovered had been tested in the treatment of AN [27-29].

But, in spite of much general progresses of the psychopharmacology, between the drugs identified as useful in the treatment of AN, BN and obesity, anyone has characters of wonder drugs, expression that means, the beginning of a drug of new, stupefying efficacy [27-29].

In fact the data in actual literature don't show the real efficacy of any drugs in this group of diseases, unless for limited time and only on some symptoms. The psychological treatments are, for now, the cornerstone of the therapy of these diseases. The same dietetic prescription, could be defined as a psychotherapeutic intervention not formalized:

- *psychotherapeutic*, because it tries to modify with psychical means (information, prescription, persuasion, ext) behaviours, complex personal and familiar equilibrium;
- *no formalized* because, generally, ii is not preceded by a precise psychological valuation and is not inspired by a theory or guided by a technique. Probably this defect is one of the most important causes of the failure collected by the diet-therapy. So drugs have a rule still limited, not decisive and not sufficient. But they is an aid more precious and more studies have demonstrated their utility. In the AN is field, necessary, as in some others fields of psychiatry and general medicine, to combine, case for case, the better pharmacological therapy possible with the appropriate case psychotherapeutic treatment, designing, from time to time, the strategy of intervention in function of the kind of pathology (indicator of diagnosis) and of the individual characteristics of single patient (clinics indicator)

Follow now a summary of drugs more used and more useful in the treatment of AN.

Antipsychotic

These drugs have represented, on empiric basis, the first systematic attempt of psychopharmacological intervention in AN. The rational of their used is bound to the hypothesis of a dopaminergic dysfunction in AN. Recent studies have valued that the use of the clozapine (antagonist D1/D4, D2/D3, agonist 5-HT2A/2C and 5-HT3) is potentially useful but, the tolerability and the necessity of frequent haematic check given, its use is an exception. Maybe the olanzapine (antagonist D1/D2/D4/5-HT2C) have more possibility of use for its grater handiness. However, according to some recent met-analysis, in AN's treatment, the use of antipsychotic drugs, hasn't induced significant benefit in the ED, of weight, of hyperactivity and, unfortunately, neither in the area of illness of body image [27-29].

Tricyclic Antidepressant (TC)

In the clinical practice, the antidepressant tricyclic with SSRI, are the psycho drugs most frequently used in the AN treatment. The target symptoms are the depressive manifestations and the anxiety with recover of weight. Their use respond to the hypothesis of disfunction of monoamine [27-29].

Cyproheptadine

It is the central agonist of serotonin and histamine, it acts reducing the central serotonergic activity and stimulates the ingestion of food. It possesses also sedative effects. The results of some studies have showed a better response in cases of restrictive anorexia, but it not exist evidence of the efficacy such to induce its use in the clinical practice [27-29].

Selective Serotonin Reuptake Inhibitors (SSRI)

This drugs are been used in first place for the aspect of comorbidity, as modulator of humour and control of impulses. Their use responds to hypothesis of a

serotonergic dysfunction in the AN. The SSRI act blocking the reuptake of serotonin in the synapses. The deficit of tryptophan (precursory of serotonin) caused by the malnutrition could make these drugs less efficacy, consequently hey must be given with an adequate nutritional counselling. Their use is supported by the elevated tolerability as regards antidepressant tricyclic with a greater or equal efficacy. Between the various SSRI the fluoxetine seems to be the molecule that has produced the most encouraging results. Some open studies have underlined that the fluoxetine seems to be able to promote the preservation in the time of the weight increase obtained during the acute phase of treatment and, then, to prevent the relapses. But remain some doubts about dosage, moment of prescription and total duration of therapy. Also the citalopram, that has a profile of more tolerability as regards to antidepressant tricyclic and also respect to others SSRI, has showed a specific effect on the increase of the appetite [27-29].

Lithium

The salts of lithium are used in AN as mood regulating and the common side effect that produce is the weight increase. These are only the anecdotal descriptions without evidence of efficacy [27-29].

Anxiolytics

The anxiety is a frequent symptoms in AN. It is associated in particular to the act of eat. Anyhow, the use of minor tranquilizer in AN must be occasional and limited in the time, because there are not evidences to the systematic use [27-29].

Is important to underline, then, that anorexic patients live the pharmacological intervention as an invasive and uncontrollable action, like a strong, toxic and aggressive treatment to witch patients oppose their self. The resistance to start the treatment is one of the pathologic characteristics more frequent in AN. A drug orally administered sometime represents a foreign body that introducing himself in the organism can have immediate and profound effects not only on the weight and figure but also on the character and liberty and, like the food, it is refused or vomited.

The therapy of AN consists to impose concurrent or sequential interventions, of individual and/or familiar, nutritional and pharmacological psychotherapy, since the symptoms of diseases are multi-determinate by biological, psychological and familiar factors. The pharmacological therapy is inserted in a polyphonic programme and it never is a single intervention. It must to be supported to the psychotherapy and to nutritional counselling. The first one will consider reasons of the treatment, resistance to the changer, of the importance of symptoms and, in particular, of the importance that have drugs on the patient is imaginary. The second one will give the necessary nutritious to the survival and functioning of drugs, but, without, promoting a sudden weight increase, cause frequently the interruption of treatment, also pharmacological [27-29].

Conclusions

In conclusion, in these last years the knowledge in the physiopathologist field of AN have increased and is probable that this will consent, in the distance future, to discover molecules most sure and aimed to the pharmacological treatment of AN and of the weight. The studies on leptin, de-coupled proteins, β3-adrenergic agonists, SSRI, are rich of expectations.

"Safer and better targeted medications for the drugs treatments of obesity and eating disorders can now be designed" Albert Stunkard 2000.

But the only biological evidences appear still distant to explain the complexity of AN. We know still little about integration between base's processes and superior mental functions in AN that we had to consider, for various aspects, a psychopathology. We think, for example, to communicative and social elements of the alimentation, at symbolic implications, at connections with the psychopathology of body's image, enjoyment, anxiety, wrong, shame, taste and disgust that modulate the report between man and food.

Waiting the wonder drug, we don't remain that continue to work, in a way most refined and unprejudiced, on the comparison and dialogue between body's and psyche's science, through the methodological line that Edgard Morin call complex thought, loved by experts and to neuroscience studious.

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References

[1] Sharan P, Sundar AS Eating disorders in women. Indian J Psychiatry. 2015 Jul;57(Suppl 2):S286-95.

[2] Val-Laillet D, Aarts E, Weber B, Ferrari M, Quaresima V, Stoeckel LE, Alonso-Alonso M, Audette M, Malbert CH, Stice E Neuroimaging and neuromodulation approaches to study eating behavior and prevent and treat eating disorders and obesity. Neuroimage Clin. 2015 Mar 24;8:1-31

[3] Yilmaz Z, Hardaway JA, Bulik CM Genetics and Epigenetics of Eating Disorders. Adv Genomics Genet. 2015;5:131-150

[4] Leslie A. Sim, PhD; Donald E. McAlpine, MD; Karen B. Grothe, PhD; Susan M. Himes, PhD; Richard G. Cockerill, BA; and Matthew M. Clark, PhD Identification and Treatment of Eating Disorders in the Primary Care Setting Mayo Clin Proc. 2010;85(8):746-751

[5] Favaro A, Tenconi E, Santonastaso P. Perinatal factors and the risk of developing anorexia nervosa and bulimia nervosa. Arch Gen Psychiatry 2006; 63: 82–88.

[6] Petra AI, Panagiotidou S, Hatziagelaki E, Stewart JM, Conti P, Theoharides TC Gut-Microbiota-Brain Axis and Its Effect on Neuropsychiatric Disorders With Suspected Immune Dysregulation. Clin Ther. 2015 May 1;37(5):984-95

[7] Mu C, Yang Y, Zhu W. Gut Microbiota: The Brain Peacekeeper. Front Microbiol. 2016 Mar 17;7:345

[8] Walter Kaye Neurobiology of anorexia and bulimia nervosa Physiology & Behavior 94 (2008) 121–135

[9] Jesse Roth, Alessandra L Szulc, and Ann Danoff 2011 Energy, evolution, and human diseases: an overview Am J Clin Nutr 2011;93(suppl):875S–83S

[10] Schwartz MW, Woods SC, Porte Jr D, Seeley RJ, Baskin DG. Central nervous system control of food intake. Nature 2000;404(6778):661–71.

[11] Kaye W, Strober M, Jimerson D. The neurobiology of eating disorders. In: Charney DS, Nestler EJ, editors. The neurobiology of mental illness. New York: Oxford Press; 2004. p. 1112–28.

[12] Palmiero Monteleone, Eloisa Castaldo, Mario Maj Neuroendocrine dysregulation of food intake in eating disorders Regulatory Peptides 149 (2008) 39–50

[13] Tong J, D'Alessio D Eating disorders and gastrointestinal peptides. Curr Opin Endocrinol Diabetes Obes. 2011 Feb;18(1):42-9.

[14] Angelica Lindén Hirschberg. Sex hormones, appetite and eating behaviour in women. Maturitas 71 (2012) 248– 256

[15] Alfonso Tortorella, Francesca Brambilla, Michele Fabrazzo, Umberto Volpe, Alessio Maria Monteleone, Daniele Mastromo & Palmiero Monteleone Central and Peripheral Peptides Regulating Eating Behaviour and Energy Homeostasis in Anorexia Nervosa and Bulimia Nervosa: A Literature Review Eur. Eat. Disorders Rev. 22 (2014) 307–320

[16] Cota D, Marsicano G, Lutz B, Vicennati V, Stalla GK, Pasquali RP, Pagotto U. Endogenous cannabinoid system as a modulator of food intake. Int J Obes Relat Metab Disord 2003;27:289–301.

[17] Phillips M, Drevets WR, Lane R (2003) Neurobiology of emotion perception I: the neural basis of normal emotion perception. Biol Psychiatry 54:504–514

[18] Walter H. Kaye, Angela Wagner, Julie L. Fudge, and Martin Paulus. Neurocircuity of Eating Disorders. Curr Topics Behav Neurosci, 2011

[19] Monteleone P, Maj M. Dysfunctions of leptin, ghrelin, BDNF and endocannabinoids in eating disorders: beyond the homeostatic control of food intake. Psychoneuroendocrinology. 2013 Mar;38(3):312-30

[20] Monteleone AM, Di Marzo V, Monteleone P, Dalle Grave R, Aveta T, Ghoch ME, Piscitelli F, Volpe U, Calugi S, Maj M. Responses of peripheral endocannabinoids and endocannabinoid-related compounds to hedonic eating in obesity. Eur J Nutr. 2016 Jun;55(4):1799-805

[21] Culbert KM, Racine SE, Klump KL Hormonal Factors and Disturbances in Eating Disorders. Curr Psychiatry Rep. 2016 Jul;18(7):65.

[22] Cassin S, Von Ranson K (2005) Personality and eating disorders: a decade in review. Clin Psychol Rev 25:895–916 42

[23] Schwartz MW, Woods SC, Porte Jr D, Seeley RJ, Baskin DG. Central nervous system control of food intake. Nature 2000; 404: 661–671.

[24] Giuliano C, Cottone P The role of the opioid system in binge eating disorder. CNS Spectr. 2015 Dec;20(6):537-45.

[25] Spanagel R, Weiss F. The dopamine hypothesis of reward: past and current status. Trends Neurosci 1999; 22: 521–527.
[26] Hoebel BG. Brain neurotransmitters in food and drug reward. Am J Clin Nutr 1985; 42: 1133–1150. |
[27] Capasso A. Petrella C and Milano W. (2009). Recent clinical aspects of eating disorders. Reviews on Recent Clinical Trials. Vol. 4. Pag.63-69
[28] A. Capasso, C. Petrella, W. Milano (2009) Pharmacological Profile of SSRIs and SNRIs in the Treatment of Eating Disorders. Current Clinical Pharmacology 4: 78-83
[29] Milano W, De Rosa M, Milano L, Riccio A, Sanseverino B, Capasso A (2013) The Pharmacological Options in the Treatment of Eating Disorders. ISRN Pharmacology 2013: 352865
[1] Sharan P, Sundar AS Eating disorders in women. Indian J Psychiatry. 2015 Jul;57(Suppl 2):S286-95.
[2] Val-Laillet D, Aarts E, Weber B, Ferrari M, Quaresima V, Stoeckel LE, Alonso-Alonso M, Audette M, Malbert CH, Stice E Neuroimaging and neuromodulation approaches to study eating behavior and prevent and treat eating disorders and obesity. Neuroimage Clin. 2015 Mar 24;8:1-31
[3] Yilmaz Z, Hardaway JA, Bulik CM Genetics and Epigenetics of Eating Disorders. Adv Genomics Genet. 2015;5:131-150
[4] Leslie A. Sim, PhD; Donald E. McAlpine, MD; Karen B. Grothe, PhD; Susan M. Himes, PhD; Richard G. Cockerill, BA; and Matthew M. Clark, PhD Identification and Treatment of Eating Disorders in the Primary Care Setting Mayo Clin Proc. 2010;85(8):746-751
[5] Favaro A, Tenconi E, Santonastaso P. Perinatal factors and the risk of developing anorexia nervosa and bulimia nervosa. Arch Gen Psychiatry 2006; 63: 82–88.
[6] Petra AI, Panagiotidou S, Hatziagelaki E, Stewart JM, Conti P, Theoharides TC Gut-Microbiota-Brain Axis and Its Effect on Neuropsychiatric Disorders With Suspected Immune Dysregulation. Clin Ther. 2015 May 1;37(5):984-95
[7] Mu C, Yang Y, Zhu W. Gut Microbiota: The Brain Peacekeeper. Front Microbiol. 2016 Mar 17;7:345
[8] Walter Kaye Neurobiology of anorexia and bulimia nervosa Physiology & Behavior 94 (2008) 121–135
[9] Jesse Roth, Alessandra L Szulc, and Ann Danoff 2011 Energy, evolution, and human diseases: an overview Am J Clin Nutr 2011;93(suppl):875S–83S
[10] Schwartz MW, Woods SC, Porte Jr D, Seeley RJ, Baskin DG. Central nervous system control of food intake. Nature 2000;404(6778):661–71.
[11] Kaye W, Strober M, Jimerson D. The neurobiology of eating disorders. In: Charney DS, Nestler EJ, editors. The neurobiology of mental illness. New York: Oxford Press; 2004. p. 1112–28.
[12] Palmiero Monteleone, Eloisa Castaldo, Mario Maj Neuroendocrine dysregulation of food intake in eating disorders Regulatory Peptides 149 (2008) 39–50
[13] Tong J, D'Alessio D Eating disorders and gastrointestinal peptides. Curr Opin Endocrinol Diabetes Obes. 2011 Feb;18(1):42-9.
[14] Angelica Lindén Hirschberg. Sex hormones, appetite and eating behaviour in women. Maturitas 71 (2012) 248– 256
[15] Alfonso Tortorella, Francesca Brambilla, Michele Fabrazzo, Umberto Volpe, Alessio Maria Monteleone, Daniele Mastromo & Palmiero Monteleone Central and Peripheral Peptides Regulating Eating Behaviour and Energy Homeostasis in Anorexia Nervosa and Bulimia Nervosa: A Literature Review Eur. Eat. Disorders Rev. 22 (2014) 307–320
[16] Cota D, Marsicano G, Lutz B, Vicennati V, Stalla GK, Pasquali RP, Pagotto U. Endogenous cannabinoid system as a modulator of food intake. Int J Obes Relat Metab Disord 2003;27:289–301.
[17] Phillips M, Drevets WR, Lane R (2003) Neurobiology of emotion perception I: the neural basis of normal emotion perception. Biol Psychiatry 54:504–514
[18] Walter H. Kaye, Angela Wagner, Julie L. Fudge, and Martin Paulus. Neurocircuity of Eating Disorders. Curr Topics Behav Neurosci, 2011
[19] Monteleone P, Maj M. Dysfunctions of leptin, ghrelin, BDNF and endocannabinoids in eating disorders: beyond the homeostatic control of food intake. Psychoneuroendocrinology. 2013 Mar;38(3):312-30
[20] Monteleone AM, Di Marzo V, Monteleone P, Dalle Grave R, Aveta T, Ghoch ME, Piscitelli F, Volpe U, Calugi S, Maj M. Responses of peripheral endocannabinoids and endocannabinoid-related

compounds to hedonic eating in obesity. Eur J Nutr. 2016 Jun;55(4):1799-805
[21] Culbert KM, Racine SE, Klump KL Hormonal Factors and Disturbances in Eating Disorders. Curr Psychiatry Rep. 2016 Jul;18(7):65.
[22] Cassin S, Von Ranson K (2005) Personality and eating disorders: a decade in review. Clin Psychol Rev 25:895–916 42
[23] Schwartz MW, Woods SC, Porte Jr D, Seeley RJ, Baskin DG. Central nervous system control of food intake. Nature 2000; 404: 661–671.
[24] Giuliano C, Cottone P The role of the opioid system in binge eating disorder. CNS Spectr. 2015 Dec;20(6):537-45.
[25] Spanagel R, Weiss F. The dopamine hypothesis of reward: past and current status. Trends Neurosci 1999; 22: 521–527.
[26] Hoebel BG. Brain neurotransmitters in food and drug reward. Am J Clin Nutr 1985; 42: 1133–1150. |
[27] Capasso A. Petrella C and Milano W. (2009). Recent clinical aspects of eating disorders. Reviews on Recent Clinical Trials. Vol. 4. Pag.63-69
[28] A. Capasso, C. Petrella, W. Milano (2009) Pharmacological Profile of SSRIs and SNRIs in the Treatment of Eating Disorders. Current Clinical Pharmacology 4: 78-83
[29] Milano W, De Rosa M, Milano L, Riccio A, Sanseverino B, Capasso A (2013) The Pharmacological Options in the Treatment of Eating Disorders. ISRN Pharmacology 2013: 352865.