A BRIEF REVIEW ABOUT ANXIETY AND AGGRESSIVE BEHAVIOR IN PEDIATRIC AGE

MARIA GRIECO¹, MARGHERITA SALERNO², GABRIELE TRIPI^{3,4}, FRANCESCO LAVANO⁵, PALMIRA ROMANO⁶, DANIELA RUSSO⁷, SERENA MARIANNA LAVANO⁵, DAVIDE TESTA⁸, FRANCESCO CERRONI⁹, ROSA MAROTTA⁵, LUCREZIA D'ORO

RO¹⁰, MICHELE SORRENTINO¹¹, ANNABELLA DI FOLCO⁸, ROSARIA MARTINA MAGLIULO¹², BEATRICE GALLAI¹³, GABRIELLA MARSALA¹⁴, ANGELO MONTANA¹⁵, SABRINA FRANCO¹⁵, DIEGO GERACI¹⁵, MARIO GIUSEPPE CHISARI¹⁶, ELISABETTA PICCIOCCHI^{17,18}, GIUSEPPE CIBELLI¹⁷, ANNA VALENZANO¹⁷, ANNA NUNZIA POLITO¹⁹, PAOLO MURABITO²⁰, PASQUALE GIUGLIANO²¹ LUCIA PARISI⁸

¹Presidio di Riabilitazione Diocleziano, Napoli, Italy - ²Sciences for Mother and Child Health Promotion, University of Palermo, Italy - ³Department PROSAMI, University of Palermo, Italy - ⁴Childhood Psychiatric Service for Neurodevelopmental Disorders, CH Chinon, France - 5Department of Health Sciences, University "Magna Graecia", Catanzaro, Italy - Centro di Riabilitazione LARS, Sarno, Italy - Centro di Riabilitazione La Filanda LARS; Sarno, Italy - *Department of Psychology, Educational Science and Human Movement, University of Palermo, Italy - ⁹Centro Manzoni s.r.l., Napoli, Italy - ¹⁰Centro Ambulatoriale Santo Stefano, Pesaro, Italy - "NICU -Preterm and High Risk Newborn Neurodevelopmental Follow-up Service; Pineta Grande Hospital Castel Volturno (CE), Italy - 12Centro Studi Della Scoliosi S.R.L, Italy - 13Department of Surgical and Biomedical Sciences, University of Perugia, Perugia, Italy - 14Struttura Complessa di Farmacia, Azienda Ospedaliero-Universitaria, Ospedali Riuniti di Foggia, Foggia, Italy - 15Department of Medical, Surgical and Advanced Technology Sciences G.F. Ingrassia, University of Catania, Catania, Italy - 16 Istituto nazionale della previdenza sociale (INPS), Catania, Italy - ¹⁷Department of Clinical and Experimental Medicine, University of Foggia, Foggia, Italy - 18 Casa di Cura Villa dei Fiori Acerra, Napoli, Italy -¹⁹Complex Structure of Neuropsychiatry Childhood-Adolescence of Ospedali Riuniti of Foggia, Foggia, Italy - ²⁰Università degli Studi di Catania, Catania, Italy - ²¹UOC Medicina Legale; Azienda Ospedaliera Sant'Anna e San Sebastiano di Caserta

ABSTRACT

Anxiety can be considered a normal experience of the human being and as such also of the child. It manifests itself in different ways according to the level of development: in the smaller the child, the more anxiety is expressed with manifestations that involve the whole organism, becoming evident either with motor excitement or with physical discomfort. As the psychic apparatus is structured, anxiety is experienced as an inner phenomenon and is experienced as an unpleasant state. Fortunately, we are all a bit anxious, even if there are some people who are more, others less.

Keywords: pediatric anxiety, aggressive behaviour, pediatric age.

Received July 17, 2018; Accepted Septemper 20, 2018

Introduction

Anxiety can be considered a normal experience of the human being and as such also of the child. It manifests itself in different ways according

to the level of development: in the smaller the child, the more anxiety is expressed with manifestations that involve the whole organism, becoming evident either with motor excitement or with physical discomfort. As the psychic apparatus is struc-

tured, anxiety is experienced as an inner phenomenon and is experienced as an unpleasant state. Fortunately, we are all a bit anxious, even if there are some people who are more, others less.

In reality, everything depends on the behavior: if it is just mentioned, it does not disturb and can also be accepted and useful. The pathology appears when the person, for example, is excessively attentive to personal hygiene spending most of the day washing and washing, or when he is so distressed by the idea of taking a disease and terrified of viruses; or even when the anxiety for the illness of the loved one is unmotivated and at the same time continues, and absorbs all the energies as well as causing harm to the patient(1-7). It is true that the emotionally healthy person always coexists with a fair amount of anxiety to act efficiently, but these tensions are kept under control: the cares are therefore not dumped onto others and there is no need to be encouraged in all circumstances. Anxiety, under normal conditions, is a state of activation, of psychological and organic charge that allows to face the daily problems with a determination necessary to solve them. It is a positive, creative tension at the base of intelligence. Anxiety then, is very similar to fear, only that the latter is an "apprehensive tension or restlessness that arises from a threat or danger that is clear to our conscience and external". Anxiety and stress then, indicate two sides of the same coin and have many characteristics in common: there are in fact both a good anxiety and a bad anxiety, so also a good stress and a bad one. Only when anxiety and stress exceed a certain level, things start to get worse⁽⁸⁻¹⁵⁾.

The most relevant aspect of all emotional experiences is the physiological activation state, which represents the energetic, stimulating component of emotion, connected to the work of certain areas of the brain, the autonomic nervous system and the endocrine system. The autonomic nervous system regulates the autonomous organic functions, that is independent of our will, such as the heart pulsations or the contractions of the stomach. These changes are due to stimulations that derive from two structures in antagonism: parasympathetic and sympathetic nervous system⁽¹⁶⁻²⁰⁾.

The main causes of anxiety are mainly related to three addresses:

- Constitutionalist;
- Psychoanalytic;
- Behavioral. The classical conception gives importance to constitutional factors, identifiable in

a predisposition on a genetic basis, which manifests itself through particular modalities of neuropsychological functioning. According to the psychoanalytic theory, anxiety and the disorders related to it, define a group defined as neurosis. The neurotic disorders, apparently incomprehensible, find an explanation in early relational experiences⁽²¹⁻²⁵⁾. The behavioral theory instead, refers to the classic Pavlovian conceptions on neurosis (Figure 1). Subsequent elaborations of this theory have then proposed that the anxious symptoms should be interpreted as unadapt behavioral models⁽²⁶⁻³⁵⁾.



Figure 1: shows the reproduction of Pavlovian experi-

Anxiety is therefore a normal response to the reality of illness, aging, death, and the fragility of our human being(36-45). The unconscious defenses of the ego In order to cope with the various external and internal problems, our organism carries out a series of psychological processes that operate unconsciously, spontaneously, and tend to defend the ego from anxious tension: it is about "defenses of anxiety". They act in groups, reinforcing each other, are present and working in everyone, just because we all have more or less anxiety. The primary task of these processes is to defend ourselves from the experience of anxiety, retain the emotional stability that is needed as organic stability; increase personal safety and esteem of us, contribute to efficiency and satisfaction of life.

We can distinguish the ego's defenses in two groups: the immature or neurotic ones and the mature and realistic ones.

The main defenses of the neurotic ego can be classified as follows:

- Removal: involuntary and automatic defense with which we reject unacceptable thoughts and impulses in the unconscious;
- Projection: involuntary and automatic defense with which we reflect aspects rejected by us on other people;
- Identification: involuntary and automatic defense with which we try to make ourselves simi-

lar to another person, lived as important;

- Rationalization: involuntary and automatic defense thanks to which we try to justify tendencies, needs, feelings, unacceptable behavior or we try to transform them in others more acceptable;
- Regression: involuntary and automatic defense that allows you to return, in a more or less symbolic way, to a kind of life that is now passed or preferable;
- Compensation: involuntary and automatic defense with which we tend to counterbalance, ie compensate for our defects;
- Reactive training: involuntary defense and automatic with which we exhibit feelings and behaviors that are exactly contrary to those we would tend to have, but which are unacceptable from personal and social points of view.

Among mature, adaptive defenses, we understand:

- Humor: direct expression of our intimate feelings without experiencing discomfort or embarrassment and without arousing the disapproval of others:
- Sublimation: process by which we direct unacceptable impulses towards ways of expressing ourselves acceptable for ourselves and for society;
- Altruism: tendency to care for others, which substitutes constructively and gratifying other unconscious tendencies. It is the pleasure of doing to others what we would like others to do to ourselves⁽²⁶⁻⁴⁵⁾.

All children are able to express their hostility with different forms and intensities, depending on each person's personal history, their behavioral and educational models, their feelings and their more or less unconscious fantasies (46-54).

Generally, the motivations of the appearance of aggressive behavior are not easily definable, because they are mixed, one with the other, becoming the course of the "conflict". Exemplary, in this sense, is the "common ground" identified by Isaacs between aggression and guilt.

The sense of guilt acts as an engine of aggressive behavior: the more the child is displaced by shame, the more he attacks those who have generated this feeling in him. Often the sense of guilt is the result of the activation of more motives than those indicated above. The reason of possession originates from the impulsive childish desire to possess, in an exclusive way, an object, an idea, a role.

Another important characteristic of this motive is the absolute refusal, on the part of the child, to await his turn for the possession of what he desires: the time that separates him from the realization of his desire is an infinite time, an eternity to which he does not intend to surrender. The reason of power originates from the child's desire to exercise power, to do to others "... what he feels has been done to him ...". In these cases, the child becomes aggressive in reacting to interference from others, adults and children: he opposes these obstacles by demanding for himself a position of supreme control over others, through an aggressive, verbal or physical act.

The situations of rivalry that can be observed are of two types: rivalry towards other children and rivalry against an adult. In the first years of life all children live the other children as fearful and powerful rivals. From a certain relational point of view this experience testifies to the actual ability of a child to fit into a social group: it is as if the aggressive behavior towards the other children constituted a sort of "experimental game", an attempt to discover who the others are, a way of recognizing their social existence.

However, rivalry for adults (and especially parents) affection is the first and true cause of childhood hostility: it is precisely the child's dependence on the love of adults that makes them experience the presence of another child as a terrible threat.

Another threat to the child is represented by the mutual love of the parents: he lives their love as an enemy that separates him from the total and definitive possession of those adults who loves so much. In these cases, child behavior is aimed at determining a contrast between adults: the two parents must be separated at all costs and made aware of the needs and the need for unique and exclusive love experienced by the child. This strong ambivalence (loving and hating the same person at the same time) puts the child in a situation of tension, where often the way out is offered by the manifestation of a hostile and aggressive behavior that "temporarily" alienates one of the adults and "reassures" the child, because he can continue to love and be loved without limiting intrusion(50-60).

Regarding to general anxiety, it is expressed in a prevalently verbal and playful aggressiveness: anxiety is alleviated through joking aggressive attacks, the only ones allowed by the community and by adults in particular. Emblematic in this sense is the child's tendency to destroy any other children's creative product, because of his own feeling of inadequacy and inefficiency, for which he is convinced that he cannot do what others do. Once again it is not a circumscribed fact to generate hostility, but a pre-existing chronic psychological condition to aggressive attack, persistent even after this. The forms in which aggression manifests itself: many bites, spitting, kicking, pulling of hair, scratches, throwing of objects, damaging the work of others, appropriation, verbal expressions of contempt, threats and boycotts. The manifestations of hostility, arrogance and aggressiveness must be faced and contained by the adult, even without repressive attitudes; only in this way will the child feel more protected from his own aggressive impulses and from the anxiety that such impulses entail. The external control guaranteed by the adult reassures the child and gives him the opportunity to learn to control his hostility and to adapt his desires to the reality that surrounds him (55-60).

Aggressive behaviour

Aggression can be defined as a "defense mechanism" of the whole individual, responsible for maintaining and restoring the balance of the brain, just as our immune system does. It is a "system" that is activated gradually, unlike what can be believed. It can be activated by any stimulus (thermal sensation, words or provocative gestures, negative thoughts) that threatens the psychophysical integrity of the individual, freeing what are commonly called "inhibitory brakes". In particular, it is the activation of the reticular system, the so-called "alarm system" that causes aggression. It is an interweaving of neurons along the brainstem, whose functionality is precisely that of filtering sensory stimuli.

In practice, an internal or external stimulus reaches our senses, so that our emotional brain - consisting of thalamus and amygdala - perceives that stimulus and responds directly and immediately⁽⁶¹⁻⁶²⁾ (Figure 2).

Therefore, depending on the neuroanatomical pathway taken by the stimulus, somatic and behavioral reactions are established that in the brain produce summation effects between stimuli, experiences and previous memories. It is precisely for this reason that the immediate response can be far superior to the actual stimulus, both in intensity and in direction. Aggression can present itself through two different and distinguished modes, which however can in some cases present themselves simultaneously:

- Somatization: in some cases rabies is not acted because the non-external subject defenses, somatizing the aggressive behavior and causing to the person, in a self-injury perspective, consequences just somatic such as ulcers, gastrointestinal attacks, skin eczema etc. that in evolutionary age they appear rather in the form of eye tics, visual grimaces, sense of continuous excitement, painful abdomen, asthma attacks etc. The subject internalizes every possible reaction to any stimulant triggering aggression, somatizing without externalising, up to a true paralysis of becoming.
- Acting Out: with punches, slaps, kicks, verbal vehemence, against oneself, against the other or against things. It is precisely this mode that often alarms because it can not be shared socially.

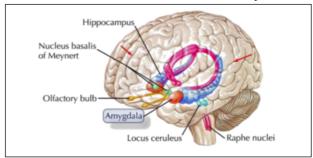


Figure 2: show the neuronatomical allocation of amygdala

It is first of all essential to keep in mind that when the brain is agitated, it is impossible to attempt mediations or request evaluations. It is therefore appropriate, in the phase immediately following the aggressive act, to proceed with the distension, reassurance and decolpitation of that subject, so as to gradually facilitate the activation of the Neocortex which, through increasingly more and more conscious modes, inhibits the limbic system. Aggression, like any other expression of hardship and difficulty, can not and should not be blamed but always decolpized, trying to understand the reasons behind that specific behavior. We should therefore understand more than the mechanism of aggression, the causes behind it (60-70).

It is frequent to find in the literature a directly proportional correlation between children exposed to pathological behavioral modalities and their acquisition. We are often faced with aggressive children, children of parents who are aggressive in turn. Also, it is more and more frequent to observe adults who absently listen to what their child is saying, without bothering to send him a demonstrative feedback of adequate listening and effective understanding.

The risk is that the child himself will cease to require attention, turning in on himself and using distorted ways to communicate with the environment around him. One should always have the foresight to show the child attention, giving him the importance he has, without any reward or punishment. The child, just like the adult needs to feel respected, in order to increase self-esteem⁽⁷¹⁻⁸⁰⁾.

In conclusion, aggressive and anxiety may be considered as frequent and normal behavior during certain ages of life, mainly childhood and adolescence although may considered also induced by many other exogenous factors such as chronic illnesses and drugs⁽⁸¹⁻⁹⁹⁾.

References

- Esposito M, Gallai B, Roccella M, Marotta R, Lavano F, Lavano SM, Mazzotta G, Bove D, Sorrentino M, Precenzano F, Carotenuto M. (2014) Anxiety and depression levels in prepubertal obese children: a case-control study. Neuropsychiatr Dis Treat. Oct 3; 10: 1897-902. doi: 10.2147/NDT.S69795
- Chieffi S, Messina G, Villano I, Messina A, Esposito M, Monda V, Valenzano A, Moscatelli F, Esposito T, Carotenuto M, Viggiano A, Cibelli G, Monda M. (2017) Exercise Influence on Hippocampal Function: Possible Involvement of Orexin-A. Front Physiol. Feb 14; 8: 85. doi: 10.3389/fphys.2017.00085
- Esposito M, Carotenuto M. (2010) Borderline intellectual functioning and sleep: the role of cyclic alternating pattern. Neurosci Lett. Nov 19; 485(2): 89-93. doi: 10.1016/j.neulet.2010.08.062
- 4) Esposito M, Ruberto M, Pascotto A, Carotenuto M. (2012) Nutraceutical preparations in childhood migraine prophylaxis: effects on headache outcomes including disability and behaviour. Neurol Sci. Dec; 33(6): 1365-8. doi: 10.1007/s10072-012-1019-8
- Esposito M, Verrotti A, Gimigliano F, Ruberto M, Agostinelli S, Scuccimarra G, Pascotto A, Carotenuto M. (2012) Motor coordination impairment and migraine in children: a new comorbidity? Eur J Pediatr. Nov; 171(11): 1599-604. doi: 10.1007/s00431-012-1759-8.
- 6) Carotenuto M, Santoro N, Grandone A, Santoro E, Pascotto C, Pascotto A, Perrone L, del Giudice EM. (2009) The insulin gene variable number of tandem repeats (INS VNTR) genotype and sleep disordered breathing in childhood obesity. J Endocrinol Invest. Oct; 32(9): 752-5. doi: 10.3275/6398.
- Carotenuto M, Guidetti V, Ruju F, Galli F, Tagliente FR, Pascotto A. (2005) Headache disorders as risk factors for sleep disturbances in school aged children. J Headache Pain. Sep; 6(4): 268-70
- 8) Carotenuto M, Esposito M, Cortese S, Laino D, Verrotti A. (2016) Children with developmental dyslexia showed greater sleep disturbances than controls, including problems initiating and maintaining sleep. Acta Paediatr. Sep; 105(9): 1079-82. doi: 10.1111/apa.13472

- 9) Carotenuto M, Esposito M, D'Aniello A, Rippa CD, Precenzano F, Pascotto A, Bravaccio C, Elia M. (2013) Polysomnographic findings in Rett syndrome: a case-control study. Sleep Breath. Mar; 17(1): 93-8. doi: 10.1007/s11325-012-0654-x. Epub 2012 Mar 7. Erratum in: Sleep Breath. 2013 May; 17(2): 877-8
- 10) Verrotti A, Agostinelli S, D'Egidio C, Di Fonzo A, Carotenuto M, Parisi P, Esposito M, Tozzi E, Belcastro V, Mohn A, Battistella PA. (2013) Impact of a weight loss program on migraine in obese adolescents. Eur J Neurol. Feb; 20(2): 394-7. doi: 10.1111/j.1468-1331.2012.03771.x
- 11) Esposito M, Carotenuto M. (2014) Intellectual disabilities and power spectra analysis during sleep: a new perspective on borderline intellectual functioning. J Intellect Disabil Res. May; 58(5): 421-9. doi: 10.1111/jir.12036
- 12) Esposito M, Roccella M, Gallai B, Parisi L, Lavano SM, Marotta R, Carotenuto M. (2013) Maternal personality profile of children affected by migraine. Neuropsychiatr Dis Treat. 9: 1351-8. doi: 10.2147/NDT.S51554
- Carotenuto M, Esposito M, Precenzano F, Castaldo L, Roccella M. (2011) Cosleeping in childhood migraine. Minerva Pediatr. Apr; 63(2): 105-9
- 14) Esposito M, Marotta R, Gallai B, Parisi L, Patriciello G, Lavano SM, Mazzotta G, Roccella M, Carotenuto M. (2013) Temperamental characteristics in childhood migraine without aura: a multicenter study. Neuropsychiatr Dis Treat. 9:1187-92. doi: 10.2147/NDT.S50458
- Esposito M, Gallai B, Parisi L, Castaldo L, Marotta R, Lavano SM, Mazzotta G, Roccella M, Carotenuto M. (2013) Self-concept evaluation and migraine without aura in childhood. Neuropsychiatr Dis Treat. 9: 1061-6. doi: 10.2147/NDT.S49364
- 16) Esposito M, Parisi L, Gallai B, Marotta R, Di Dona A, Lavano SM, Roccella M, Carotenuto M. (2013) Attachment styles in children affected by migraine without aura. Neuropsychiatr Dis Treat. 9:1513-9. doi: 10.2147/NDT.S52716
- 17) Carotenuto M, Gallai B, Parisi L, Roccella M, Esposito M. (2013) Acupressure therapy for insomnia in adolescents: a polysomnographic study. Neuropsychiatr Dis Treat. 9: 157-62. doi: 10.2147/NDT.S41892
- 18) Carotenuto M, Gimigliano F, Fiordelisi G, Ruberto M, Esposito M. (2013) Positional abnormalities during sleep in children affected by obstructive sleep apnea syndrome: the putative role of kinetic muscular chains. Med Hypotheses. Aug; 81(2): 306-8. doi: 10.1016/j.mehy.2013.04.023
- 19) Coppola G, Licciardi F, Sciscio N, Russo F, Carotenuto M, Pascotto A. (2004) Lamotrigine as first-line drug in childhood absence epilepsy: a clinical and neurophysiological study. Brain Dev. Jan; 26(1): 26-9
- 20) Esposito M, Pascotto A, Gallai B, Parisi L, Roccella M, Marotta R, Lavano SM, Gritti A, Mazzotta G, Carotenuto M. (2012) Can headache impair intellectual abilities in children? An observational study. Neuropsychiatr Dis Treat. 8: 509-13. doi: 10.2147/NDT.S36863.
- Esposito M, Gallai B, Parisi L, Roccella M, Marotta R, Lavano SM, Gritti A, Mazzotta G, Carotenuto M. (2013) Maternal stress and childhood migraine: a new

- perspective on management. Neuropsychiatr Dis Treat. 9: 351-5. doi: 10.2147/NDT.S42818.
- 22) Esposito M, Parisi P, Miano S, Carotenuto M. (2013) Migraine and periodic limb movement disorders in sleep in children: a preliminary case-control study. J Headache Pain. Jul 1; 14: 57. doi: 10.1186/1129-2377-14-57
- 23) Esposito M, Gallai B, Parisi L, Roccella M, Marotta R, Lavano SM, Mazzotta G, Patriciello G, Precenzano F, Carotenuto M. (2013) Visuomotor competencies and primary monosymptomatic nocturnal enuresis in prepubertal aged children. Neuropsychiatr Dis Treat. 9: 921-6. doi: 10.2147/NDT.S46772
- 24) Esposito M, Carotenuto M. (2011) Ginkgolide B complex efficacy for brief prophylaxis of migraine in school-aged children: an open-label study. Neurol Sci. Feb; 32(1): 79-81. doi: 10.1007/s10072-010-0411-5
- 25) Esposito M, Roccella M, Parisi L, Gallai B, Carotenuto M. (2013) Hypersomnia in children affected by migraine without aura: a questionnaire-based case-control study. Neuropsychiatr Dis Treat. 9: 289-94. doi: 10.2147/NDT.S42182
- 26) Carotenuto M, Esposito M, Pascotto A. (2011) Facial patterns and primary nocturnal enuresis in children. Sleep Breath. May; 15(2): 221-7. doi: 10.1007/s11325-010-0388-6
- 27) Carotenuto M, Esposito M. (2013) Nutraceuticals safety and efficacy in migraine without aura in a population of children affected by neurofibromatosis type I. Neurol Sci. Nov; 34(11):1905-9. doi: 10.1007/s10072-013-1403-z
- 28) Carotenuto M, Esposito M, Parisi L, Gallai B, Marotta R, Pascotto A, Roccella M. (2012) Depressive symptoms and childhood sleep apnea syndrome. Neuropsychiatr Dis Treat. 8: 369-73. doi: 10.2147/NDT.S35974
- 29) Carotenuto M, Bruni O, Santoro N, Del Giudice EM, Perrone L, Pascotto A. (2006) Waist circumference predicts the occurrence of sleep-disordered breathing in obese children and adolescents: a questionnaire-based study. Sleep Med. Jun; 7(4): 357-61
- 30) Esposito M, Carotenuto M, Roccella M. (2011) Primary nocturnal enuresis and learning disability. Minerva Pediatr. Apr; 63(2): 99-104
- 31) Perillo L, Esposito M, Contiello M, Lucchese A, Santini AC, Carotenuto M. (2013) Occlusal traits in developmental dyslexia: a preliminary study. Neuropsychiatr Dis Treat. 9:1231-7. doi: 10.2147/NDT.S49985
- 32) Esposito M, Marotta R, Roccella M, Gallai B, Parisi L, Lavano SM, Carotenuto M. (2014) Pediatric neurofibromatosis 1 and parental stress: a multicenter study. Neuropsychiatr Dis Treat. Jan 22;10:141-6. doi: 10.2147/NDT.S55518.
- 33) Carotenuto M, Esposito M, Pascotto A. (2010) Migraine and enuresis in children: An unusual correlation? Med Hypotheses. Jul; 75(1): 120-2. doi: 10.1016/j.mehy.2010.02.004
- 34) Verrotti A, Carotenuto M, Altieri L, Parisi P, Tozzi E, Belcastro V, Esposito M, Guastaferro N, Ciuti A, Mohn A, Chiarelli F, Agostinelli S. (2015) Migraine and obesity: metabolic parameters and response to a weight loss programme. Pediatr Obes. Jun;10(3): 220-5. doi: 10.1111/ijpo.245

- 35) Esposito M, Precenzano F, Sorrentino M, Avolio D, Carotenuto M. (2015) A Medical Food Formulation of Griffonia simplicifolia/Magnesium for Childhood Periodic Syndrome Therapy: An Open-Label Study on Motion Sickness. J Med Food. Aug; 18(8): 916-20. doi: 10.1089/jmf.2014.0113
- 36) Esposito M, Ruberto M, Gimigliano F, Marotta R, Gallai B, Parisi L, Lavano SM, Roccella M, Carotenuto M. (2013) Effectiveness and safety of Nintendo Wii Fit Plus™ training in children with migraine without aura: a preliminary study. Neuropsychiatr Dis Treat. 9: 1803-10. doi: 10.2147/NDT.S53853
- 37) Di Filippo T, Orlando MF, Concialdi G, La Grutta S, Lo Baido R, Epifanio MS, Esposito M, Carotenuto M, Parisi L, Roccella M. (2013) The quality of life in developing age children with celiac disease. Minerva Pediatr. Dec: 65(6): 599-608.
- 38) Carotenuto M, Parisi P, Esposito M, Cortese S, Elia M. (2014) Sleep alterations in children with refractory epileptic encephalopathies: a polysomnographic study. Epilepsy Behav. Jun; 35: 50-3. doi: 10.1016/j.yebeh.2014.03.009
- 39) Esposito M, Gimigliano F, Ruberto M, Marotta R, Gallai B, Parisi L, Lavano SM, Mazzotta G, Roccella M, Carotenuto M. (2013) Psychomotor approach in children affected by nonretentive fecal soiling (FNRFS): a new rehabilitative purpose. Neuropsychiatr Dis Treat. 9: 1433-41. doi: 10.2147/NDT.S51257
- 40) Parisi L, Di Filippo T, La Grutta S, Lo Baido R, Epifanio MS, Esposito M, Carotenuto M, Roccella M. (2013) Sturge-weber syndrome: a report of 14 cases. Ment Illn. Jun 3; 5(1):e7. doi: 10.4081/mi.2013.e7
- 41) Coppola G, Auricchio G, Federico R, Carotenuto M, Pascotto A. (2004) Lamotrigine versus valproic acid as first-line monotherapy in newly diagnosed typical absence seizures: an open-label, randomized, parallel-group study. Epilepsia. Sep; 45(9): 1049-53
- 42) Perillo L, Esposito M, Caprioglio A, Attanasio S, Santini AC, Carotenuto M. (2014) Orthodontic treatment need for adolescents in the Campania region: the malocclusion impact on self-concept. Patient Prefer Adherence. Mar 19;8:353-9. doi: 10.2147/PPA.S58971
- 43) Esposito M, Antinolfi L, Gallai B, Parisi L, Roccella M, Marotta R, Lavano SM, Mazzotta G, Precenzano F, Carotenuto M. (2013) Executive dysfunction in children affected by obstructive sleep apnea syndrome: an observational study. Neuropsychiatr Dis Treat. 9: 1087-94. doi: 10.2147/NDT.S47287
- Villano I, Messina A, Valenzano A, Moscatelli F, Esposito T, Monda V, Esposito M, Precenzano F, Carotenuto M, Viggiano A, Chieffi S, Cibelli G, Monda M, Messina G. (2017) Basal Forebrain Cholinergic System and Orexin Neurons: Effects on Attention. Front Behav Neurosci. Jan 31; 11:10. doi: 10.3389/fnbeh.2017.00010
- 45) Verrotti A, Greco M, Varriale G, Tamborino A, Savasta S, Carotenuto M, Elia M, Operto F, Margari L, Belcastro V, Selicorni A, Freri E, Matricardi S, Granata T, Ragona F, Capovilla G, Spalice A, Coppola G, Striano P. (2018) Electroclinical features of epilepsy monosomy 1p36 syndrome and their implications. Acta Neurol Scand. Aug 14. doi: 10.1111/ane.13006
- 46) Gallelli L, Cione E, Caroleo MC, Carotenuto M, Lagana P, Siniscalchi A, Guidetti V. (2017) microRNAs

- to Monitor Pain-migraine and Drug Treatment. Microrna. Dec 6; 6(3): 152-156. doi: 10.2174/2211536606666170913152821
- 47) Matricardi S, Darra F, Spalice A, Basti C, Fontana E, Dalla Bernardina B, Elia M, Giordano L, Accorsi P, Cusmai R, De Liso P, Romeo A, Ragona F, Granata T, Concolino D, Carotenuto M, Pavone P, Pruna D, Striano P, Savasta S, Verrotti A. (2018) Electroclinical findings and long-term outcomes in epileptic patients with inv dup (15). Acta Neurol Scand. Jun; 137(6): 575-581. doi: 10.1111/ane.12902
- 48) Smirni D, Beadle JN, Paradiso S. (2018) An Initial Study of Alexithymia and Its Relationship With Cognitive Abilities Among Mild Cognitive Impairment, Mild Alzheimer's Disease, and Healthy Volunteers. J Nerv Ment Dis, 206 (8): 628-636. doi:10.1097/NMD.0000000000000853
- 49) Esposito M, Messina A, Monda V, Bitetti I, Salerno F, Precenzano F, Pisano S, Salvati T, Gritti A, Marotta R, Lavano SM, Lavano F, Maltese A, Parisi L, Salerno M, Tripi G, Gallai B, Roccella M, Bove D, Ruberto M, Toraldo R, Messina G, Carotenuto M. (2017) The Rorschach Test Evaluation in Chronic Childhood Migraine: A Preliminary Multicenter Case-Control Study. Front Neurol. Dec 12; 8: 680. doi: 10.3389/fneur.2017.00680
- 50) Messina A, Monda V, Sessa F, Valenzano A, Salerno M, Bitetti I, Precenzano F, Marotta R, Lavano F, Lavano SM, Salerno M, Maltese A, Roccella M, Parisi L, Ferrentino RI, Tripi G, Gallai B, Cibelli G, Monda M, Messina G, Carotenuto M. (2018) Sympathetic, Metabolic Adaptations, and Oxidative Stress in Autism Spectrum Disorders: How Far From Physiology? Front Physiol. Mar 22;9:261. doi: 10.3389/fphys.2018.00261
- 51) Sperandeo R, Monda V, Messina G, Carotenuto M, Maldonato NM, Moretto E, Leone E, De Luca V, Monda M, Messina A. (2017) Brain functional integration: an epidemiologic study on stress-producing dissociative phenomena. Neuropsychiatr Dis Treat. Dec 19; 14: 11-19. doi: 10.2147/NDT.S146250
- Messina A, Bitetti I, Precenzano F, Iacono D, Messina G, Roccella M, Parisi L, Salerno M, Valenzano A, Maltese A, Salerno M, Sessa F, Albano GD, Marotta R, Villano I, Marsala G, Zammit C, Lavano F, Monda M, Cibelli G, Lavano SM, Gallai B, Toraldo R, Monda V, Carotenuto M. (2018) Non-Rapid Eye Movement Sleep Parasomnias and Migraine: A Role of Orexinergic Projections. Front Neurol. Feb 28; 9: 95. doi: 10.3389/fneur.2018.00095.
- 53) Esposito M, Gimigliano F, Barillari MR, Precenzano F, Ruberto M, Sepe J, Barillari U, Gimigliano R, Militerni R, Messina G, Carotenuto M. (2017) Pediatric selective mutism therapy: a randomized controlled trial. Eur J Phys Rehabil Med. Oct 53(5): 643-650. doi: 10.23736/S1973-9087.16.04037-5
- 54) Esposito M, Gallai B, Parisi L, Roccella M, Marotta R, Lavano SM, Mazzotta G, Carotenuto M. (2013) Primary nocturnal enuresis as a risk factor for sleep disorders: an observational questionnaire-based multicenter study. Neuropsychiatr Dis Treat. 9: 437-43. doi: 10.2147/NDT.S43673
- Monda V, La Marra M, Perrella R, Caviglia G, Iavarone A, Chieffi S, Messina G, Carotenuto M, Monda M, Messina A. (2017) Obesity and brain illness:

- from cognitive and psychological evidences to obesity paradox. Diabetes Metab Syndr Obes. Nov 21; 10:473-479. doi: 10.2147/DMSO.S148392
- Parisi P, Vanacore N, Belcastro V, Carotenuto M, Del Giudice E, Mariani R, Papetti L, Pavone P, Savasta S, Striano P, Toldo I, Tozzi E, Verrotti A, Raucci U; "Pediatric Headache Commission" of Società Italiana di Neurologia Pediatrica (SINP). (2014) Clinical guidelines in pediatric headache: evaluation of quality using the AGREE II instrument. J Headache Pain. Sep 1; 15: 57. doi: 10.1186/1129-2377-15-57
- 57) Toldo I, Rattin M, Perissinotto E, De Carlo D, Bolzonella B, Nosadini M, Rossi LN, Vecchio A, Simonati A, Carotenuto M, Scalas C, Sciruicchio V, Raieli V, Mazzotta G, Tozzi E, Valeriani M, Cianchetti C, Balottin U, Guidetti V, Sartori S, Battistella PA. (2017) Survey on treatments for primary headaches in 13 specialized juvenile Headache Centers: The first multicenter Italian study. Eur J Paediatr Neurol. May; 21(3): 507-521. doi: 10.1016/j.ejpn.2016.12.009
- Verrotti A, Casciato S, Spalice A, Carotenuto M, Striano P, Parisi P, Zamponi N, Savasta S, Rinaldi VE, D'Alonzo R, Mecarini F, Ritaccio AJ, Di Gennaro G. (2017) Coexistence of childhood absence epilepsy and benign epilepsy with centrotemporal spikes: A case series. Eur J Paediatr Neurol. May; 21(3): 570-575. doi: 10.1016/j.ejpn.2017.02.002
- 59) Matricardi S, Spalice A, Salpietro V, Di Rosa G, Balistreri MC, Grosso S, Parisi P, Elia M, Striano P, Accorsi P, Cusmai R, Specchio N, Coppola G, Savasta S, Carotenuto M, Tozzi E, Ferrara P, Ruggieri M, Verrotti A. (2016) Epilepsy in the setting of full trisomy 18: A multicenter study on 18 affected children with and without structural brain abnormalities. Am J Med Genet C Semin Med Genet. Sep; 172(3): 288-95. doi: 10.1002/ajmg.c.31513
- Gallelli L, Avenoso T, Falcone D, Palleria C, Peltrone F, Esposito M, De Sarro G, Carotenuto M, Guidetti V. (2014) Effects of acetaminophen and ibuprofen in children with migraine receiving preventive treatment with magnesium. Headache. Feb; 54(2): 313-24. doi: 10.1111/head.12162
- 61) Elia M, Amato C, Bottitta M, Grillo L, Calabrese G, Esposito M, Carotenuto M. (2012) An atypical patient with Cowden syndrome and PTEN gene mutation presenting with cortical malformation and focal epilepsy. Brain Dev. Nov; 34(10): 873-6. doi: 10.1016/j.brain-dev.2012.03.005
- 62) Pomara, C., D'Errico, S., Riezzo, I., De Cillis, G.P., Fineschi, V. Sudden cardiac death in a child affected by Prader-Willi syndrome. (2005) International Journal of Legal Medicine, 119 (3), pp. 153-157. DOI: 10.1007/s00414-004-0513-9
- 63) Fineschi, V., Neri, M., Di Donato, S., Pomara, C., Riezzo, I., Turillazzi, E. An immunohistochemical study in a fatality due to ovarian hyperstimulation syndrome. (2006) International Journal of Legal Medicine, 120 (5), pp. 293-299. DOI: 10.1007/s00414-006-0104-
- 64) Turillazzi, E., Baroldi, G., Silver, M.D., Parolini, M., Pomara, C., Fineschi, V. A systematic study of a myocardial lesion: Colliquative myocytolysis. (2005) International Journal of Cardiology, 104 (2), pp. 152-157. DOI: 10.1016/j.ijcard.2004.10.051

- 65) Mazzeo F, Motti ML, Messina G, Monda V, Ascione A, Tafuri D, et al. Use of nutritional supplements among south Italian students of physical training and sport university. Curr Top Toxicol. 2013; 9: 21-6;
- 66) Messina G, Monda V, Moscatelli F, Valenzano AA, Monda G, Esposito T, et al. Role of orexin system in obesity. Biol Med. 2015;7(4);
- 67) Messina G, Di Bernardo G, Viggiano A, De Luca V, Monda V, Messina A, et al. Exercise increases the level of plasma orexin A in humans. J Basic Clin Physiol Pharmacol. 2016; 27(6): 611-6;
- 68) Messina G, Palmieri F, Monda V, Messina A, Dalia C, Viggiano A, et al. Exercise causes muscle GLUT4 translocation in an insulin-independent manner. Biol Med. 2015; 7(Special issue);
- 69) Messina G, Viggiano A, Tafuri D, Palmieri F, De Blasio S, Messina A, et al. Role of orexin in obese patients in the intensive care unit. J Anesth Clin Res. 2014; 5(3)
- 70) Monda M, Viggiano A, Viggiano A, Viggiano E, Messina G, Tafuri D, et al. Quetiapine lowers sympathetic and hyperthermic reactions due to cerebral injection of orexin A. Neuropeptides. 2006; 40(5): 357-63
- 71) Chieffi S, Messina G, Villano I, Messina A, Esposito M, Monda V, et al. Exercise influence on hippocampal function: Possible involvement of orexin-a. Front Physiol. 2017; 8
- 72) Valenzano A, Moscatelli F, Triggiani AI, Capranica L, De Ioannon G, Piacentini MF, et al. Heart-rate changes after an ultraendurance swim from Italy to Albania: A case report. Int J Sports Physiol Perform. 2016; 11(3): 407-9
- 73) Viggiano E, Monda V, Messina A, Moscatelli F, Valenzano A, Tafuri D, et al. Cortical spreading depression produces a neuroprotective effect activating mitochondrial uncoupling protein-5. Neuropsychiatr Dis Treat. 2016; 12: 1705-10
- 74) Rinaldi B, Guida F, Furiano A, Donniacuo M, Luongo L, Gritti G, et al. Effect of Prolonged Moderate Exercise on the Changes of Nonneuronal Cells in Early Myocardial Infarction. Neural Plast. 2015; 201;
- 75) Monda V, Valenzano A, Moscatelli F, Salerno M, Sessa F, Triggiani AI, et al. Primary motor cortex excitability in karate athletes: A transcranial magnetic stimulation study. Front Physiol. 2017; 8
- 76) Triggiani AI, Valenzano A, Ciliberti MAP, Moscatelli F, Villani S, Monda M, et al. Heart rate variability is reduced in underweight and overweight healthy adult women. Clin Physiol Funct Imaging. 2017; 37(2): 162-7
- 77) Messina G, Di Bernardo G, Viggiano A, De Luca V, Monda V, Messina A, et al. Exercise increases the level of plasma orexin A in humans. J Basic Clin Physiol Pharmacol. 2016; 27(6): 611-6-
- 78) De Luca V, Viggiano E, Messina G, Viggiano A, Borlido C, Viggiano A, et al. Peripheral amino acid levels in schizophrenia and antipsychotic treatment. Psychiatry Investig. 2008; 5(4):2 03-8-
- 79) Messina G,Dalia C,Tafuri D, Monda V, Palmieri F, Dato A, et al. Orexin-A controls sympathetic activity and eating behavior.Front Psychol. 2014; 8(5)997;
- 80) Messina A, Monda V, Avola R, Moscatelli F, Valenzano A, Ruberto M, et al. Role of the orexin system on arousal, attention, feeding behaviour and sleep disorders. Acta Medica Mediterr. 2017; 33(4): 645-649;
- 81) Monda M, Viggiano A, Viggiano E,

- Messina G, Tafuri D, et al. Sympathetic and hyperthermic reactions by orexin A: role of cerebral cate-cholaminergic neurons. Regul Pept. 2007; 139(1-3): 30.44
- 82) Monda M, Messina G, Scognamiglio I, Lombardi A, Martin GA, Sperlongano P, et al. Short term diet and moderate exercise in young overweight men modulate cardiocyte and hepatocarcinoma survival by oxidative stress. Oxid Med Cell Longev. 2014; 2014: 131024
- 83) Monda M, Messina G, Vicidomini C, Viggiano A, Mangoni C, De Luca B. Activity of autonomic nervous system is related to body weight in pre-menopausal, but not in post-menopausal women. Nutr Neurosci. 2006; 9(3-4): 141-5
- 84) Di Bernardo G, Messina G, Capasso S, Del Gaudio S, Cipollaro M, Peluso G, et al. Sera of overweight people promote in vitro adipocyte differentiation of bone marrow stromal cells. Stem Cell Res Ther. 2014; 5(1): 4
- 85) Chieffi S, Carotenuto M, Monda V, Valenzano A, Villano I, Precenzano F, et al. Orexin System: The Key for a Healthy Life. Front Physiol. 2017; 31(8): 357
- 86) Panico A, Messina G, Lupoli GA, Lupoli R, Cacciapuoti M, Moscatelli F, et al. Quality of life in overweight (Obese) and normal-weight women with polycystic ovary syndrome. Patient Prefer Adherence. 2017; 11: 423-9
- 87) Viggiano A, Chieffi S, Tafuri D, Messina G, Monda M, De Luca B. Laterality of a second player position affects lateral deviation of basketball shooting. J Sports Sci. 2014; 32(1): 46-52.
- 88) Moscatelli F, Messina G, Valenzano A, Petito A, Triggiani AI, Ciliberti MAP, et al. Relationship between RPE and blood lactate after fatiguing handgrip exercise in taekwondo and sedentary subjects. Biol Med. 2015; 7(Special issue)
- 89) Chieffi S, Iachini T, Iavarone A, Messina G, Viggiano A, Monda M. Flanker interference effects in a line bisection task. Exp Brain Res. 2014; 232(4): 1327-34
- 90) Parisi L, Faraldo M, Ruberto M, Salerno M, Maltese A, Di Folco A, et al. Life events and primary monosymptomatic nocturnal enuresis: A pediatric pilot study. Acta Medica Mediterr. 2017; 33(1), 23-27
- 91) Parisi L, Salerno M, Maltese A, Tripi G, Romano P, Di Folco A, et al. Emotional intelligence And Obstructive Sleep Apnea Syndrome In Children: Preliminary Case-Control Study. Acta Medica Mediterr. 2017; 33: 485-489
- 92) Moscatelli F, Messina G, Valenzano A, Monda V, Viggiano A, Messina A, et al.Functional Assessment of Corticospinal System Excitability in Karate Athletes. PLoS One. 2016; 24(5):e0155998;
- 93) Turillazzi E, Greco P, Neri, M., Pomara, C., Riezzo, I., Fineschi, V. Anaphylactic latex reaction during anaesthesia: The silent culprit in a fatal case. (2008) Forensic Science International, 179 (1), pp. e5-e8. DOI: 10.1016/j.forsciint.2008.03.021;
- 94) Turillazzi, E., Riezzo, I., Neri, M., Pomara, C., Cecchi, R., Fineschi, V. The diagnosis of fatal pulmonary fat embolism using quantitative morphometry and confocal laser scanning microscopy. (2008) Pathology Research and Practice, 204 (4), pp. 259-266. DOI: 10.1016/j.prp.2007.12.010;
- 95) Turillazzi, E., Neri, M., Cerretani, D., Cantatore, S., Frati, P., Moltoni, L., Busardò, F.P., Pomara, C.,

- Riezzo, I., Fineschi, V. Lipid peroxidation and apoptotic response in rat brain areas induced by long-term administration of nandrolone: The mutual crosstalk between ROS and NF-kB. (2016) Journal of Cellular and Molecular Medicine, 20 (4), pp. 601-612. DOI: 10.1111/jcmm.12748;
- 96) Li Volti G, Ientile R, Abraham NG, Vanella A, Cannavò G, Mazza F, Currò M, Raciti G, Avola R, Campisi A. Immunocytochemical localization and expression of heme oxygenase-1 in primary astroglial cell cultures during differentiation: effect of glutamate. Biochem Biophys Res Commun. 2004 Mar 5; 315(2): 517-24;
- 97) Rizzo M, Abate N, Chandalia M, Rizvi AA, Giglio RV, Nikolic D, Marino Gammazza A, Barbagallo I, Isenovic ER, Banach M, Montalto G, Li Volti G. Liraglutide reduces oxidative stress and restores heme oxygenase-1 and ghrelin levels in patients with type 2 diabetes: a prospective pilot study. J Clin Endocrinol Metab. 2015 Feb; 100(2): 603-6. doi: 10.1210/jc.2014-2291;
- 98) Santillo A, Kelly AL, Palermo C, Sevi A, Albenzio M. Role of indigenous enzymes in proteolysis of casein in caprine milk. International Dairy Journal. 2009 19: 655-660;
- 99) Santillo A, Albenzio M, Quinto M, Caroprese M, Marino RM Sevi. A. Probiotic in Lamb Rennet Paste Enhances Rennet Lipolytic Activity, and CLA and Linoleic Acid Content in Pecorino Cheese. Journal of Dairy Science 2009 92: 1330-1337

Corresponding author
LUCIA PARISI, MD
Department of Psychology, Educational Science
and Human Movement
University of Palermo
(Italy)