

Acta Medica Mediterranea, 2017, 33: 1279

### A MINIREVIEW ABOUT SPORTING PRACTICE IN EPILEPTIC CHILDREN

VINCENZO MONDA<sup>1,8</sup>, MARIA RUBERTO<sup>2,8</sup>, INES VILLANO<sup>18</sup>, ANNA VALENZANO<sup>38</sup>, ANNACLAUDIA RICCIARDI<sup>4</sup>, BEATRICE GALLAI<sup>5</sup>, ROSA MAROTTA<sup>6</sup>, FRANCESCO LAVANO<sup>6</sup>, SERENA MARIANNA LAVANO<sup>6</sup>, AGATA MALTESE<sup>7</sup>, GABRIELE TRIPI<sup>8,9</sup>, PALMIRA ROMANO<sup>4</sup>, MARGHERITA SALERNO<sup>10</sup>

<sup>1</sup>Department of Experimental Medicine, Section of Human Physiology and Unit of Dietetic and Sport Medicine, Università degli Studi della Campania "Luigi Vanvitelli", Italy - <sup>2</sup>Department of Medical-Surgical and Dental Specialties, Università degli Studi della Campania "Luigi Vanvitelli", Italy - <sup>3</sup>Department of Clinical and Experimental Medicine University of Foggia, Foggia, Italy - <sup>4</sup>Clinic of Child and Adolescent Neuropsychiatry; Department of Mental Health and Physical and Preventive Medicine, Università degli Studi della Campania "Luigi Vanvitelli", Italy - <sup>5</sup>Department of Surgical and Biomedical Sciences, University of Perugia, Perugia, Italy - <sup>6</sup>Department of Medical and Surgery Sciences, University "Magna Graecia", Catanzaro, Italy - <sup>7</sup>Department of Psychological, Pedagogical and Educational Sciences, University of Palermo, Italy - <sup>8</sup>Department PROSAMI, University of Palermo, Italy - <sup>9</sup>Childhood Psychiatric Service for Neurodevelopmental Disorders, CH Chinon, France - <sup>10</sup>Sciences for Mother and Child Health Promotion, University of Palermo, Italy

§Vincenzo Monda, Maria Ruberto, Ines Villano and Anna Valenzano contributed equally for manuscript

# ABSTRACT

Movement is important for neuropsycho-physical development, ensuring the correct growth and giving many benefits from childhood to adulthood. Motor activity plays a pivotal role in psychological, educational and social terms: sport practice induces harmonious physical development with common important benefits independently from sport type and each sport imposes rules respect that children learns to know and respect step by step improving the social skills and cognitive abilities. Sport has a very important role in the growth of children and adolescents. Sport and physical activity work as a moral laboratory to practice decision-making and problem-solving skills, as well as teamwork and cooperation. In many pathological conditions, the sport practice is strongly discouraged, as in epileptic patients for the negative consequences on their physical condition and psychic. In general, several studies reported that physical activity has positive influence on seizure frequency and severity. As a result, attitudes regarding sports and epilepsy have changed considerably in the last decades and presently, the risk of convulsive seizures during sports practice is minimal in case of well-managed epilepsy. Evaluating the control of convulsive disease is therefore a key point to allow sports in the children and adolescents.

Keywords: exercise, synaptic-plasticity, hippocampus, epilepsy.

DOI: 10.19193/0393-6384\_2017\_2s\_197

Received November 30, 2016; Accepted May 20, 2017

## Introduction

Movement is important for neuropsycho-physical development, ensuring the correct growth and giving many benefits from childhood to adulthood. In general, motor activity plays a pivotal role in psychological, educational and social terms. Certainly, sport practice induces harmonious physi-

cal development with common important benefits independently from sport type. On the other hand, each sport imposes rules respect that children learns to know and respect step by step improving the social skills and cognitive abilities, because regular physical exercise has been demonstrated to beneficially effect neural health and function and reduce the risk of various neurological diseases.

Rodent studies demonstrate that exercise improved spatial learning and memory co-occurring with changes in hippocampal plasticity, including increased neurogenesis, enhanced long-term potentiation (LTP), and elevated expression of brainderived neurotrophic factors (BDNF). BDNF seems to play a prominent role in the survival, growth, and maintenance of neurons during development and modulation of synaptic-plasticity in the adult brain. Also reelin, an extracellular glycoprotein, seems to be crucially important in the developmental organization of neurons in the brain, mainly expressed in interneurons residing primarily in the hilar region of dentate gyrus, and in the molecular stratum lacunosum-layer of hippocampus<sup>(1-25)</sup>.

Epilepsy is a common and prevalent neurologic disease found in 2% of the population, affecting people of all ages and characterized by a predisposition to promote seizures as well as neurobiological, psychological, cognitive, and social consequences. Due to their condition, patients with epilepsy may develop other medical problems such as heart disease, cognitive decline or dementia, insulin resistance, obesity, atherosclerosis, internalizing problems such as anxiety and depression. Commonly, individuals with epilepsy tend to have a sedentary lifestyle which leads to poor physical fitness.

Consequently, individuals with epilepsy have low levels of maximal oxygen uptake and cardiorespiratory fitness and poor levels of strength and flexibility. The lower aerobic fitness observed in people with epilepsy may be associated with their sedentary habits. Physical activity should be encouraged in this group, as previous studies have reported a number of positive effects of physical exercise in people with epilepsy. However, the correct management and prescription of physical exercise programs in epilepsy patients depends on health professionals' knowledge<sup>(26-30)</sup>.

Regular physical exercise, when prescribed at the correct dose and type, can promote quality of life and well-being, improve cardiovascular fitness and strength, increase maximal aerobic capacity, elevate work capacity, promote weight and body fat reduction, and help in the management of seizure frequency. Taken together, this broad body of evidence indicates that patients with epilepsy should be encouraged to practice regular physical exercise, as this is beneficial for their health and does not exacerbate seizure frequency.

In this light, sporting activities can be the right time for the child development, while training and working-out allows the child to mature skills and social abilities(31-35). Sport practice means also understanding the importance of training and constancy: even the most troublesome children or those who feel less wary than their comrades will be able to achieve brilliant results thanks to their training. This will help them understand that they can achieve goals that they would not have imagined at first, even in other contexts. Furthermore, team sports do not allow children to be selfish, enhancing mainly the social skills. Sport has a very important role in the growth of children and adolescents. Sport and physical activity work as a moral laboratory to practice decision-making and problem-solving skills, as well as teamwork and cooperation. In fact, many studies explored the possibility of teaching life skills in the contest of sport and physical activity programs(33-37).

Particularly, sporting can improve four areas of life skills:

- playing well, referring to skills that deal with being more physically active, improving levels of sport skills and enjoying physical activities and sport;
- connecting well, referring to work with and for other people, learning the importance of caring for others;
- coping well that refers to the life skill required to deal with stress, problems or conflicts in a constructive way, -dreaming well, that refers to skill related to exploring future lives and setting specific goals to achieve a future dreams.

Despite of all these advantages and benefits derived by regular physical activity, in many pathological conditions, the sport practice is strongly discouraged, as in epileptic patients. The relationship between epilepsy and physical exercise is debated. In the past the epileptic children was discouraged by sporting activities with negative consequences on their physical condition (less stress resistance, Increased body mass index, Increased cardiovascular risk) and psychic (isolation, reduced self- But, anxiety, depression)<sup>(38-43)</sup>.

On the other hand, we have to consider the presence of many precipitating factors in children and adolescents affected by epilepsy during the sport practice. Potentially, many seizure precipitating factors exist in relation to physical exercise, fatigue, stress, repeated head injury during contact sports, excessive aerobic exercise, hyperventilation,

changes in the metabolism of antiepileptic drugs (AEDs), and ionic/metabolic disturbances (44-50). In general, seizures seem to rarely be triggered by physical activity. In a study encompassing 400 PWE, only two were able to identify physical activity as a precipitant. No link has been established between post exercise fatigue and increased seizure frequency. Stress has been identified as a seizure trigger in a considerable number of patients, suggesting that intense athletic activity may increase seizures. In addition, physical stress and neurosteroids appear to be linked in epilepsy. In response to stress induced by physical exercise, it has been demonstrated, both in human and animal models, that the activation of the hypothalamic-pituitaryadrenal axis affects adrenal steroids and neurosteroids and increases the seizure susceptibility. However, the same stress may also activate hypothalamic corticotrophin-releasing hormone, which in turn stimulates deoxycorticosterone production in the adrenal gland. Increased levels of allotetrahydrodeoxycorticosterone synthesized in the liver and brain by circulating deoxycorticoster- one activates GABAA receptors in certain brain regions, with decreased seizure susceptibility(51-60).

Further studies are needed to elucidate the exact role of the physical stress in the control of seizures. It is well known that hyperventilation at rest triggers absence seizures; therefore one might assume that the same would apply during exercise. However during exercise, hyperventilation is a physiological response to an increased metabolic demand, a compensatory response to prevent hypercapnia. On the other hand, resting hyperventilation leads to hypocapnia and vasocon-striction. Furthermore, exercise-induced hyperventilation, as an adaptive reaction to acidosis, may even produce suppression of interictal abnormalities<sup>(61-65)</sup>.

Therefore, hyperventilation during exercise appears to deter seizure onset. Exercise is thought to increase liver-enzyme metabolism and so could also increase the metabolism of several AEDs, particularly the "old generation" ones. Greater drug clearance and competi-tion for protein (albumin) binding sites are factors that may account for a decrease in their serum levels. A prospective study on the effect of physical training on serum levels of AEDs, however, failed to show any correspondent decrease or abnormality of the metabolism rate (63-64).

Another study showed only slight variations in serum levels, especially for phenytoin (small decrease) and valproic acid and phenobarbital (small increase) between the exercise and pre-exercise periods, not statistically relevant and with no repercussion on seizure frequency, as it was a small sample conclusions must be drawn with caution<sup>(65-68)</sup>.

Despite this contradictory evidence, we would only recommend checking serum levels of AEDs in PWE practicing sports when clinically indicated. Finally, hypoxia (mainly altitude-related), hyperhydration, hyperthermia, hypoglycemia and hyponatremia are all distur-bances linked to physical activity and known to trigger seizures, although, at least some of them, may correspond to acute symptomatic seizures. There are no studies showing a link between these metabolic disturbances and the increase of true epileptic seizures, nor that PWE are more susceptible to them than athletes without epilepsy.8 However, it is also true that robust studies have not yet been carried out<sup>(69-71)</sup>.

The reasons that more were frequently adduced to justify the contraindication to the Physical exercise in the epileptic babies were numerous: for example, it was hypothesized that recurrent minor cranial traumas, induced by contact sports or collision, could worse generalized epilepsy.

Tonic-clonic seizures can cause unexpected falls and subjects suffering from epilepsy-absence, can have difficulties in mantaining balance, losing the ability to protect themselves while practicing contact sports (i.e. box, hockey and basket)<sup>(69-71)</sup>.

#### **Discussion**

In general, several studies reported that physical activity has positive influence on seizure frequency and severity. As a result, attitudes regarding sports and epilepsy have changed considerably in the last decades and presently, the risk of convulsive seizures during sports practice is minimal in case of well-managed epilepsy. Evaluating the control of convulsive disease is therefore a key point to allow sports in the children and adolescents. In case of well-controlled epilepsy both team sports and contact or collision sports are allowed, with an appropriate equipment, educating both parents and coaches. These data are not applicable in subjects with epileptic encephalopathies or in case or not controlled seizures or pharmacoresistant epilepsy(72-75).

Patients with epilepsy who wish to participate in sports represent a challenging population to counsel and manage because their condition puts them at risk for possibly life-threatening events; however, most of these risks are manageable. Highrisk activities for this population include water sports and any water-related activity. The athlete with epilepsy who participates in such activities should have constant supervision by a responsible adult or a "buddy" who can provide immediate assistance and maximally reduce the risk of drowning, which is never negligible. The athlete's frequency of seizures is also a factor in determining whether his or her participation in high-risk activities is advisable. Patients with frequent seizures should be guided toward activities in which loss of consciousness or bodily control is not life threatening. Athletes with known seizure disorders have not been reported to exhibit a higher incidence of seizures in comparison with their baseline frequencies when they play contact sports.

Collision sports associated with a greater number of and more forceful impacts resulting in a higher rate of concussions may place the brain at risk of seizures secondary to the increase in excitatory neurotransmitters during the acute phase of the injury, as has been described in animal models of brain injury. Clinical experience to date demonstrates that low-impact injuries typically seen in most competitive sports do not put athletes with epilepsy at increased risk for seizures<sup>(76-81)</sup>.

About the effects of AEDs in sporting practice by children affected by epilepsy, in general AEDs can slow mental processing, trigger physiologic changes, and cause imbalance and fatigue with reduced endurance, all of which negatively affect competitive performance. Consequently, athletes who notice these drops in performance may limit their compliance with these medications. Appetite can also be affected by the use of medications, with anorexia causing a diminution of adequate nutrition that affects strength and endurance and increases risk of seizures.

Carbamazepine and oxcarbazepine have been noted to cause hyponatremia, which may be compounded by excessive perspiration. 25Y28 careful monitoring is strongly encouraged when initiating medications and during increased physical training. Participation in organized sports provides many physical and psychological benefits for patients with epilepsy and can be safely incorporated into their lives. By providing appropriate education and encouragement, a neurologist can ensure that patients are properly equipped to make the right

choices and manage any complications that occur while they are participating in activities.

In conclusion, physical exercise has a positive effect on epilepsy and is associated with reduced epileptiform discharges and increased seizure threshold, and seizures are unlikely to occur during incremental physical effort to exhaustion. These findings are strengthened by studies in animal models of seizures and epilepsy, in which aerobic exercise training was found to retard the epileptogenic process, to reduce seizure frequency, and to promote favorable plastic changes in the hippocampus<sup>(82-100)</sup>.

#### References

- Chieffi S, Messina A, Villano I, Valenzano AA, Nigro E, Marra ML, Cibelli G, Monda V, Salerno M, Tafuri D, Carotenuto M, Cipolloni L, Mollica MP, Monda M, Messina G. The use of velocity information in movement reproduction. Frontiers in Psychology, 2017, 8 (JUN), art. no. 983, DOI: 10.3389/fpsyg.2017.00983.
- Chieffi S, Messina G, Messina A, Villano I, Monda V, Ambra FI, Garofalo E, Romano F, Mollica MP, Monda M, Iavarone A. Memory for spatial locations in a patient with near space neglect and optic ataxia: Involvement of the occipitotemporal stream. Frontiers in Neurology, 2017, 8, art. no. 231, DOI: 10.3389/fneur.2017.00231.
- 3) Chieffi S, Carotenuto M, Monda V, Valenzano A, Villano I, Precenzano F, Tafuri D, Salerno M, Filippi N, Nuccio F, Ruberto M, Luca VD, Cipolloni L, Cibelli G, Mollica MP, Iacono D, Nigro E, Monda M, Messina G, Messina A. Orexin system: The key for a healthy life. Frontiers in Neurology, 2017, 8, art. no. 357. DOI: 10.3389/fphys.2017.00357.
- 4) Chieffi S, Messina G, Villano I, Messina A, Valenzano A, Moscatelli F, Salerno M, Sullo A, Avola R, Monda V, Cibelli G, Monda M. Neuroprotective effects of physical activity: Evidence from human and animal studies. Frontiers in Neurology, 2017, 8, art. no. 188, DOI: 10.3389/fneur.2017.00188.
- Chieffi S, Villano I, Iavarone A, Messina A, Monda V, Viggiano A, Messina G, Monda M. Manual asymmetry for temporal and spatial parameters in sensorimotor synchronization. Experimental Brain Research, 2017, 235 (5), pp. 1511-1518. DOI: 10.1007/s00221-017-4919-2.
- 6) Monda V, Villano I, Messina A, Valenzano A, Esposito T, Moscatelli F, Viggiano A, Cibelli G, Chieffi S, Monda M, Messina G. Exercise modifies the gut microbiota with positive health effects. Oxidative Medicine and Cellular Longevity, 2017, art. no. 3831972. DOI: 10.1155/2017/3831972.
- 7) Panico A, Messina G, Lupoli GA, Lupoli R, Cacciapuoti M, Moscatelli F, Esposito T, Villano I, Valenzano A, Monda V, Messina A, Precenzano F, Cibelli G, Monda M, Lupoli G. Quality of life in over-

- weight (Obese) and normal-weight women with polycystic ovary syndrome. Patient Preference and Adherence, 2017, 11, pp. 423-429. DOI: 10.2147/PPA.S119180.
- 8) Triggiani AI, Valenzano A, Ciliberti MAP, Moscatelli F, Villani S, Monda M, Messina G, Federici A, Babiloni C, Cibelli G. Heart rate variability is reduced in underweight and overweight healthy adult women. Clinical Physiology and Functional Imaging, 2017, 37 (2), pp. 162-167. DOI: 10.1111/cpf.12281.
- Messina G, Valenzano A, Moscatelli F, Salerno M, Lonigro A, Esposito T, Monda V, Corso G, Messina A, Viggiano A, Triggiani AI, Chieffi S, Guglielmi G, Monda M, Cibelli, G. Role of autonomic nervous system and orexinergic system on adipose tissue. Frontiers in Physiology, 2017, 8, art. no. 137. DOI: 10.3389/fphys.2017.00137.
- 10) 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. Exercise influence on hippocampal function: Possible involvement of orexin-a. Frontiers in Physiology, 2017, 8, art. no. 85. DOI: 10.3389/fphys.2017.00085.
- 11) 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. Basal forebrain cholinergic system and orexin neurons: Effects on attention. Frontiers in Behavioral Neuroscience, 2017, 11, art. no. 10. DOI: 10.3389/fnbeh.2017.00010.
- 12) Precenzano F, Ruberto M, Parisi L, Salerno M, Maltese A, Vagliano C, Messina G, Folco AD, Filippo TD, Roccella M. Executive functioning in preschool children affected by autism spectrum disorder: A pilot study. Acta Medica Mediterranea, 2017, 33 (1), pp. 35-39. DOI: 10.19193/0393-6384\_2017\_1\_005.
- 13) Parisi L, Faraldo M, Ruberto M, Salerno M, Maltese A, Folco AD, Messina G, Filippo TD, Roccella M. Life events and primary monosymptomatic nocturnal enuresis: A pediatric pilot study. Acta Medica Mediterranea, 2017, 33 (1), pp. 23-27. DOI: 10.19193/0393-6384\_2017\_1\_003.
- 14) Parisi L, Salerno M, Maltese A, Tripi G, Romano P, Folco AD, Filippo TD, Messina G, Roccella M. Emotional Intelligence And Obstructive Sleep Apnea Syndrome In Children: Preliminary Case-Control Study. Acta Medica Mediterranea, 2017, 33, pp. 485-496. DOI: 10.19193/0393-6384\_2017\_3\_072.
- 15) Fiorelli A, Messina G, Chiodini P, Costanzo S, Viggiano A, Monda M, Vicidomini G, Santini M. Cardiac Autonomic Changes After Thoracic Sympathectomy: A Prospective, Randomized Study. Annals of Thoracic Surgery, 2017, 103 (1), pp. 216-224. DOI: 10.1016/j.athoracsur.2016.10.055.
- 16) De Fusco C, Messina A, Monda V, Viggiano E, Moscatelli F, Valenzano A, Esposito T, Chieffi S, Cibelli G, Monda M, Messina G. Osteopontin: Relation between Adipose Tissue and Bone Homeostasis. Stem Cells International, 2017, art. no. 4045238. DOI: 10.1155/2017/4045238.
- 17) Messina A, Monda V, Avola R, Moscatelli F, Valenzano AA, Villano I, Ruberto M, Monda E, La Marra M, Tafuri D, Chieffi S, Cibelli G, Monda M, Messina G. Role of the orexin system on arousal, attention, feeding

- behaviour and sleep disorders. Acta Medica Mediterranea, 2017, 33 (4), pp. 645-649. DOI: 10.19193/0393-6384\_2017\_4\_096
- 18) Precenzano F, Ruberto M, Parisi L, Salerno M, Maltese A, Verde D, Tripi G, Romano P, Folco AD, Filippo TD, Messina G, Roccella M. Sleep habits in children affected by autism spectrum disorders: A preliminary case-control study. Acta Medica Mediterranea, 2017, 33, pp. 405-409. DOI: 10.19193/0393-6384\_2017\_3\_059
- 19) Messina A, Monda V, Nigro E, Valenzano AA, Villano I, Ruberto M, Monda G, Ascione A, Chieffi S, Cibelli G, Messina G, Monda M. An allied health: The pasta. Acta Medica Mediterranea, 2017, 33 (4), pp. 641-644. DOI: 10.19193/0393-6384\_2017\_4\_095
- 20) Messina G, Viggiano E, Monda V, Messina A, Moscatelli F, Valenzano A, Tafuri D, de Luca V, Cibelli G, Monda M. Re: Neuroprotection and acidosis induced by cortical spreading depression. Neuropsychiatric Disease and Treatment, 2016, 12, pp. 3193-3194.
- 21) Moscatelli F, Messina G, Valenzano A, Petito A, Triggiani AI, Messina A, Monda V, Viggiano A, De Luca V, Capranica L, Monda M, Cibelli G. Differences in corticospinal system activity and reaction response between karate athletes and non-athletes. Neurological Sciences, 2016, 37 (12), pp. 1947-1953. DOI: 10.1007/s10072-016-2693-8
- Messina G, Di Bernardo G, Viggiano A, De Luca V, Monda V, Messina A, Chieffi S, Galderisi U, Monda M. Exercise increases the level of plasma orexin A in humans. Journal of Basic and Clinical Physiology and Pharmacology, 2016, 27 (6), pp. 611-616. DOI: 10.1515/jbcpp-2015-0133
- 23) Esposito T, Lobaccaro JM, Esposito MG, Monda V, Messina A, Paolisso G, Varriale B, Monda M, Messina G. Effects of low-carbohydrate diet therapy in overweight subjects with autoimmune thyroiditis: Possible synergism with ChREBP. Drug Design, Development and Therapy, 2016. 10, pp. 2939-2946. DOI: 10.2147/DDDT.S106440.
- 24) Messina A, De Fusco C, Monda V, Esposito M, Moscatelli F, Valenzano A, Carotenuto M, Viggiano E, Chieffi S, De Luca V, Cibelli G, Monda M, Messina G. Role of the orexin system on the hypothalamus-pituitary-thyroid axis. Frontiers in Neural Circuits, 2016, 10 (AUG), art. no. 66. DOI: 10.3389/fncir.2016.00066.
- Viggiano E, Monda V, Messina A, Moscatelli F, Valenzano A, Tafuri D, Cibelli G, de Luca B, Messina G, Monda M. Cortical spreading depression produces a neuroprotective effect activating mitochondrial uncoupling protein-5. Neuropsychiatric Disease and Treatment, 2016, 12, pp. 1705-1710. DOI: 10.2147/NDT.S107074.
- 26) Coaccioli S, Varrassi G, Del Giorno R, Pace MC, Sansone P, Angelucci D, Paladini A, Moscatelli F, Messina A, Monda V, Messina G, Monda M, Aurilio C. Meditation as a useful chance for chronic pain decrease. African Journal of Psychiatry (South Africa), 2016, 19 (3), art. no. 1000369. DOI: 10.4172/2378-5756.1000369.
- 27) Moscatelli F, Messina G, Valenzano A, Monda V, Viggiano A, Messina A, Petito A, Triggiani AI, Ciliberti MAP, Monda M, Capranica L, Cibelli G. Functional assessment of corticospinal system excitability in

- karate athletes. PLoS ONE, 2016, 11 (5), art. no. e0155998. DOI: 10.1371/journal.pone.0155998.
- 28) Moscatelli F, Valenzano A., Petito A, Triggiani AI, Ciliberti MAP, Luongo L, Carotenuto M, Esposito M, Messina A, Monda V, Monda M, Capranica L, Messina G, Cibelli G. Relationship between blood lactate and cortical excitability between taekwondo athletes and non-athletes after hand-grip exercise. Somatosensory and Motor Research, 2016, 33 (2), pp. 137-144. DOI: 10.1080/08990220.2016.1203305.
- 29) Valenzano A, Moscatelli F, Triggiani, AI, Capranica L, De Ioannon G, Piacentini MF, Mignardi S, Messina G, Villani S, Cibelli G. Heart-rate changes after an ultraendurance swim from Italy to Albania: A case report. International Journal of Sports Physiology and Performance, 2016, 11 (3), pp. 407-409. DOI: 10.1123/ijspp.2015-0035.
- 30) Messina G, Chieffi S, Viggiano A, Tafuri D, Cibelli G, Valenzano A, Triggiani AI, Messina A, De Luca V, Monda M. Parachute jumping induces more sympathetic activation than cortisol secretion in first-time parachutists. Asian Journal of Sports Medicine, 2016, 7 (1), art. no. e26841, 5 p. DOI: 10.5812/asjsm.26841.
- 31) Ruberto M, Precenzano F, Parisi L, Salerno M, Maltese A, Messina G, Roccella M. Visuomotor integration skills in children affected by obstructive sleep apnea syndrome: A case-control study. Acta Medica Mediterranea, 2016, 32 (5), pp. 1659-1663. DOI: 10.19193/0393-6384\_2016\_5\_146.
- 32) Precenzano F, Ruberto M, Parisi L, Salerno M, Maltese A, D'Alessandro I, Grappa MF, Magliulo RM, Messina G, Roccella M. Borderline intellectual functioning and parental stress: An italian case-control study. Acta Medica Mediterranea, 2016, 32 (6), pp. 1762-1765. DOI: 10.19193/0393-6384\_2016\_6\_160.
- 33) Mazzeo F, Santamaria S, Monda V, Tafuri D, Dalia C, Varriale L, De Blasio S, Esposito V, Messina G, Monda M. Dietary supplements use in competitive and non-competitive boxer: An exploratory study. Biology and Medicine, 2016, 8 (4), art. no. 1000294. DOI: 10.4172/0974-8369.1000294.
- 34) Mazzeo F, Monda M, Messina G, Santamaria S, Messina A, Montesano M, Monda V, Tafuri, D. Doping in Italy: An analysis of its spread in ten years. Biology and Medicine, 2016, 8 (1), art. no. 1000263. DOI: 10.4172/0974-8369.1000263.
- 35) Piombino L, Messina A, Piombino L, Monda V, Moscatelli F, Valenzano AA, Esposito T, Monda G, Cibelli G, Messina G, Monda M. An assessment of body composition and lifestyle in children aged from 8 to 10 years. Biology and Medicine, 2016, 8 (4), pp. 1-5. DOI: 10.4172/0974-8369.1000298.
- 36) Precenzano F, Lombardi P, Ruberto M, Parisi L, Salerno M, Maltese A, D'Alessandro I, Della Valle I, Magliulo RM, Messina G, Roccella M. Internalizing symptoms in children affected by childhood absence epilepsy: A preliminary study. Acta Medica Mediterranea, 2016, 32 (6), pp. 1749-1753. DOI: 10.19193/0393-6384\_2016\_6\_158.
- 37) Precenzano F, Ruberto M, Parisi L, Salerno M, Maltese A, D'alessandro I, Della Valle I, Visco G, Magliulo RM, Messina G, Roccella M. Adhd-like symptoms in children affected by obstructive sleep apnea syndrome: A case-control study. Acta Medica Mediterranea, 2016,

- 32 (6), pp. 1756-1759. DOI: 10.19193/0393-6384\_2016\_6\_159.
- 38) Monda V, Valenzano A, Moscatelli F, Messina A, Piombino L, Zannella C, Viggiano E, Monda G, De Luca V, Chieffi S, Villano I, Tafuri D, Russo L, Dalia C, Viggiano A, Cibelli G, Messina G, Monda M. Modifications of activity of autonomic nervous system, and resting energy expenditure in women using hormone-replacement therapy. Biology and Medicine, 2016, 8 (5), art. no. 1000306. DOI: 10.4172/0974-8369.1000306.
- 39) Chieffi S, Villano I, Messina A, Monda V, La Marra M, Messina G, Monda M. Involvement of orexin in sleep disorders and neurodegenerative diseases. Current Topics in Peptide and Protein Research, 2015, 16, pp. 49-54.
- 40) 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. Coexistence of childhood absence epilepsy and benign epilepsy with centrotemporal spikes: A case series. Eur J Paediatr Neurol. 2017 May; 21(3): 570-575. doi:10.1016/j.ejpn.2017.02.002.
- 41) 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. Survey on treatments for primary headaches in 13 specialized juvenile Headache Centers: The first multicenter Italian study. Eur J Paediatr Neurol. 2017 May; 21(3): 507-521. doi: 10.1016/j.ejpn.2016.12.009.
- 42) 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. 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. 2016 Sep; 172(3): 288-95. doi: 10.1002/ajmg.c.31513.
- 43) Carotenuto M, Esposito M, Cortese S, Laino D, Verrotti A. Children with developmental dyslexia showed greater sleep disturbances than controls, including problems initiating and maintaining sleep. Acta Paediatr. 2016 Sep; 105(9): 1079-82. doi: 10.1111/apa.13472.
- 44) Morandi A, Bonnefond A, Lobbens S, Carotenuto M, Del Giudice EM, Froguel P, Maffeis C. A girl with incomplete Prader-Willi syndrome and negative MS-PCR, found to have mosaic maternal UPD-15 at SNP array. Am J Med Genet A. 2015 Nov; 167A(11): 2720-6. doi: 10.1002/ajmg.a.37222.
- 45) Pasquali D, Carotenuto M, Leporati P, Esposito M, Antinolfi L, Esposito D, Accardo G, Carella C, Chiovato L, Rotondi M. Maternal hypothyroidism and subsequent neuropsychological outcome of the progeny: a family portrait. Endocrine. 2015 Dec; 50(3): 797-801. doi: 10.1007/s12020-015-0564-3.
- Esposito M, Precenzano F, Sorrentino M, Avolio D, Carotenuto M. A Medical Food Formulation of Griffonia simplicifolia/Magnesium for Childhood Periodic Syndrome Therapy: An Open-Label Study on Motion Sickness. J Med Food. 2015 Aug; 18(8): 916-

- 20. doi: 10.1089/jmf.2014.0113.
- 47) Esposito M, Gallai B, Roccella M, Marotta R, Lavano F, Lavano SM, Mazzotta G, Bove D, Sorrentino M, Precenzano F, Carotenuto M. Anxiety and depression levels in prepubertal obese children: a case-control study. Neuropsychiatr Dis Treat. 2014 Oct 3; 10: 1897-902. doi: 10.2147/NDT.S69795.
- 48) Verrotti A, Cusmai R, Laino D, Carotenuto M, Esposito M, Falsaperla R, Margari L, Rizzo R, Savasta S, Grosso S, Striano P, Belcastro V, Franzoni E, Curatolo P, Giordano L, Freri E, Matricardi S, Pruna D, Toldo I, Tozzi E, Lobefalo L, Operto F, Altobelli E, Chiarelli F, Spalice A. Long-term outcome of epilepsy in patients with Prader-Willi syndrome. J Neurol. 2015 Jan; 262(1): 116-23. doi:10.1007/s00415-014-7542-1.
- 49) 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). Clinical guidelines in pediatric headache: evaluation of quality using the AGREE II instrument. J Headache Pain. 2014 Sep 1; 15: 57. doi:10.1186/1129-2377-15-57;
- 50) Verrotti A, Carotenuto M, Altieri L, Parisi P, Tozzi E, Belcastro V, Esposito M, Guastaferro N, Ciuti A, Mohn A, Chiarelli F, Agostinelli S. Migraine and obesity: metabolic parameters and response to a weight loss programme. Pediatr Obes. 2015 Jun; 10(3): 220-5. doi: 10.1111/ijpo.245.
- 51) Carotenuto M, Parisi P, Esposito M, Cortese S, Elia M. Sleep alterations in children with refractory epileptic encephalopathies: a polysomnographic study. Epilepsy Behav. 2014 Jun; 35: 50-3. doi: 10.1016/j.yebeh.2014.03.009.
- 52) Perillo L, Esposito M, Caprioglio A, Attanasio S, Santini AC, Carotenuto M. Orthodontic treatment need for adolescents in the Campania region: the malocclusion impact on self-concept. Patient Prefer Adherence. 2014 Mar 19; 8: 353-9. doi: 10.2147/PPA.S58971.
- 53) Santamaria F, Esposito M, Montella S, Cantone E, Mollica C, De Stefano S, Mirra V, Carotenuto M. Sleep disordered breathing and airway disease in primary ciliary dyskinesia. Respirology. 2014 May; 19(4): 570-5. doi: 10.1111/resp.12273.
- 54) Esposito M, Marotta R, Roccella M, Gallai B, Parisi L, Lavano SM, Carotenuto M. Pediatric neurofibromatosis 1 and parental stress: a multicenter study. Neuropsychiatr Dis Treat. 2014 Jan 22; 10: 141-6. doi: 10.2147/NDT.S55518.
- 55) Esposito M, Ruberto M, Gimigliano F, Marotta R, Gallai B, Parisi L, Lavano SM, Roccella M, Carotenuto M. Effectiveness and safety of Nintendo Wii Fit Plus™ training in children with migraine without aura: a preliminary study. Neuropsychiatr Dis Treat. 2013; 9: 1803-10. doi: 10.2147/NDT.S53853.
- 56) Carotenuto M, Esposito M, Di Pasquale F, De Stefano S, Santamaria F. Psychological, cognitive and maternal stress assessment in children with primary ciliary dyskinesia. World J Pediatr. 2013 Nov;9(4):312-7. doi:10.1007/s12519-013-0441-1.
- 57) Di Filippo T, Orlando MF, Concialdi G, La Grutta S, Lo Baido R, Epifanio MS, Esposito M, Carotenuto M, Parisi L, Roccella M. The quality of life in developing age children with celiac disease. Minerva Pediatr. 2013

- Dec; 65(6): 599-608;
- 58) Esposito M, Parisi L, Gallai B, Marotta R, Di Dona A, Lavano SM, Roccella M, Carotenuto M. Attachment styles in children affected by migraine without aura. Neuropsychiatr Dis Treat. 2013; 9: 1513-9. doi: 10.2147/NDT.S52716.
- 59) Esposito M, Gimigliano F, Ruberto M, Marotta R, Gallai B, Parisi L, Lavano SM, Mazzotta G, Roccella M, Carotenuto M. Psychomotor approach in children affected by nonretentive fecal soiling (FNRFS): a new rehabilitative purpose. Neuropsychiatr Dis Treat. 2013; 9: 1433-41. doi: 10.2147/NDT.S51257.
- 60) Esposito M, Roccella M, Gallai B, Parisi L, Lavano SM, Marotta R, Carotenuto M. Maternal personality profile of children affected by migraine. Neuropsychiatr Dis Treat. 2013; 9: 1351-8. doi: 10.2147/NDT.S51554.
- 61) Perillo L, Esposito M, Contiello M, Lucchese A, Santini AC, Carotenuto M. Occlusal traits in developmental dyslexia: a preliminary study. Neuropsychiatr Dis Treat. 2013;9:1231-7. doi: 10.2147/NDT.S49985.
- 62) Esposito M, Marotta R, Gallai B, Parisi L, Patriciello G, Lavano SM, Mazzotta G, Roccella M, Carotenuto M. Temperamental characteristics in childhood migraine without aura: a multicenter study. Neuropsychiatr Dis Treat. 2013; 9: 1187-92. doi: 10.2147/NDT.S50458.
- 63) Esposito M, Antinolfi L, Gallai B, Parisi L, Roccella M, Marotta R, Lavano SM, Mazzotta G, Precenzano F, Carotenuto M. Executive dysfunction in children affected by obstructive sleep apnea syndrome: an observational study. Neuropsychiatr Dis Treat. 2013; 9: 1087-94. doi: 10.2147/NDT.S47287.
- 64) Esposito M, Gallai B, Parisi L, Roccella M, Marotta R, Lavano SM, Mazzotta G, Patriciello G, Precenzano F, Carotenuto M. Visuomotor competencies and primary monosymptomatic nocturnal enuresis in prepubertal aged children. Neuropsychiatr Dis Treat. 2013; 9: 921-6. doi: 10.2147/NDT.S46772;
- 65) Esposito M, Parisi P, Miano S, Carotenuto M. Migraine and periodic limb movement disorders in sleep in children: a preliminary case-control study. J Headache Pain. 2013 Jul 1; 14: 57. doi: 10.1186/1129-2377-14-57.
- 66) Gallelli L, Avenoso T, Falcone D, Palleria C, Peltrone F, Esposito M, De Sarro G, Carotenuto M, Guidetti V. Effects of acetaminophen and ibuprofen in children with migraine receiving preventive treatment with magnesium. Headache. 2014 Feb; 54(2): 313-24. doi: 10.1111/head.12162.
- 67) Carotenuto M, Gimigliano F, Fiordelisi G, Ruberto M, Esposito M. Positional abnormalities during sleep in children affected by obstructive sleep apnea syndrome: the putative role of kinetic muscular chains. Med Hypotheses. 2013 Aug; 81(2): 306-8. doi: 10.1016/j.mehy.2013.04.023.
- 68) Esposito M, Gallai B, Parisi L, Roccella M, Marotta R, Lavano SM, Mazzotta G, Carotenuto M. Primary nocturnal enuresis as a risk factor for sleep disorders: an observational questionnaire-based multicenter study. Neuropsychiatr Dis Treat. 2013; 9: 437-43. doi: 10.2147/NDT.S43673.
- 69) Carotenuto M, Esposito M. Nutraceuticals safety and efficacy in migraine without aura in a population of

- children affected by neurofibromatosis type I. Neurol Sci. 2013 Nov; 34(11): 1905-9. doi: 10.1007/s10072-013-1403-z.
- 70) Esposito M, Carotenuto M. Intellectual disabilities and power spectra analysis during sleep: a new perspective on borderline intellectual functioning. J Intellect Disabil Res. 2014 May; 58(5): 421-9. doi: 10.1111/jir.12036.
- 71) Esposito M, Gallai B, Parisi L, Roccella M, Marotta R, Lavano SM, Gritti A, Mazzotta G, Carotenuto M. Maternal stress and childhood migraine: a new perspective on management. Neuropsychiatr Dis Treat. 2013; 9: 351-5. doi: 10.2147/NDT.S42818.
- 72) Esposito M, Roccella M, Parisi L, Gallai B, Carotenuto M. Hypersomnia in children affected by migraine without aura: a questionnaire-based case-control study. Neuropsychiatr Dis Treat. 2013; 9: 289-94. doi: 10.2147/NDT.S42182.
- 73) Parisi L, Di Filippo T, La Grutta S, Lo Baido R, Epifanio MS, Esposito M, Carotenuto M, Roccella M. Sturge-weber syndrome: a report of 14 cases. Ment Illn. 2013 Jun 3; 5(1): e7. doi: 10.4081/mi.2013.e7;
- 74) Carotenuto M, Gallai B, Parisi L, Roccella M, Esposito M. Acupressure therapy for insomnia in adolescents: a polysomnographic study. Neuropsychiatr Dis Treat. 2013; 9: 157-62. doi: 10.2147/NDT.S41892.
- 75) Esposito M, Pascotto A, Gallai B, Parisi L, Roccella M, Marotta R, Lavano SM, Gritti A, Mazzotta G, Carotenuto M. Can headache impair intellectual abilities in children? An observational study. Neuropsychiatr Dis Treat. 2012; 8: 509-13. doi: 10.2147/NDT.S36863.
- 76) Carotenuto M, Esposito M, Parisi L, Gallai B, Marotta R, Pascotto A, Roccella M. Depressive symptoms and childhood sleep apnea syndrome. Neuropsychiatr Dis Treat. 2012; 8: 369-73. doi: 10.2147/NDT.S35974.
- 77) Esposito M, Verrotti A, Gimigliano F, Ruberto M, Agostinelli S, Scuccimarra G, Pascotto A, Carotenuto M. Motor coordination impairment and migraine in children: a new comorbidity? Eur J Pediatr. 2012 Nov; 171(11): 1599-604. doi: 10.1007/s00431-012-1759-8.
- 78) Verrotti A, Agostinelli S, D'Egidio C, Di Fonzo A, Carotenuto M, Parisi P, Esposito M, Tozzi E, Belcastro V, Mohn A, Battistella PA. Impact of a weight loss program on migraine in obese adolescents. Eur J Neurol. 2013 Feb; 20(2): 394-7. doi: 10.1111/j.1468-1331.2012.03771.x.
- 79) Elia M, Amato C, Bottitta M, Grillo L, Calabrese G, Esposito M, Carotenuto M. An atypical patient with Cowden syndrome and PTEN gene mutation presenting with cortical malformation and focal epilepsy. Brain Dev. 2012 Nov; 34(10): 873-6. doi: 10.1016/j.braindev.2012.03.005.
- 80) Esposito M, Ruberto M, Pascotto A, Carotenuto M. Nutraceutical preparations in childhood migraine prophylaxis: effects on headache outcomes including disability and behaviour. Neurol Sci. 2012 Dec; 33(6): 1365-8. doi: 10.1007/s10072-012-1019-8.
- 81) Carotenuto M, Esposito M, D'Aniello A, Rippa CD, Precenzano F, Pascotto A, Bravaccio C, Elia M. Polysomnographic findings in Rett syndrome: a case-control study. Sleep Breath. 2013 Mar; 17(1): 93-8. doi: 10.1007/s11325-012-0654-x.
- 82) Guzzetta A, D'Acunto MG, Carotenuto M, Berardi N,

- Bancale A, Biagioni E, Boldrini A, Ghirri P, Maffei L, Cioni G. The effects of preterm infant massage on brain electrical activity. Dev Med Child Neurol. 2011 Sep;53 Suppl 4: 46-51. doi: 10.1111/j.1469-8749.2011.04065.x.
- 83) Carotenuto M, Esposito M, Precenzano F, Castaldo L, Roccella M. Cosleeping in childhood migraine. Minerva Pediatr. 2011 Apr; 63(2): 105-9.
- 84) Esposito M, Carotenuto M, Roccella M. Primary nocturnal enuresis and learning disability. Minerva Pediatr. 2011 Apr;63(2):99-104.
- 85) Esposito M, Carotenuto M. Ginkgolide B complex efficacy for brief prophylaxis of migraine in school-aged children: an open-label study. Neurol Sci. 2011 Feb; 32(1): 79-81. doi: 10.1007/s10072-010-0411-5.
- 86) Esposito M, Carotenuto M. Borderline intellectual functioning and sleep: the role of cyclic alternating pattern. Neurosci Lett. 2010 Nov 19; 485(2): 89-93. doi: 10.1016/j.neulet.2010.08.062.
- 87) Carotenuto M, Esposito M, Pascotto A. Migraine and enuresis in children: An unusual correlation? Med Hypotheses. 2010 Jul; 75(1): 120-2. doi:10.1016/j.mehy.2010.02.004.
- 88) Carotenuto M, Esposito M, Pascotto A. Facial patterns and primary nocturnal enuresis in children. Sleep Breath. 2011 May; 15(2): 221-7. doi:10.1007/s11325-010-0388-6.
- 89) Guzzetta A, Pizzardi A, Belmonti V, Boldrini A, Carotenuto M, D'Acunto G, Ferrari F, Fiori S, Gallo C, Ghirri P, Mercuri E, Romeo D, Roversi MF, Cioni G. Hand movements at 3 months predict later hemiplegia in term infants with neonatal cerebral infarction. Dev Med Child Neurol. 2010 Aug; 52(8): 767-72. doi: 10.1111/j.1469-8749.2009.03497.x.
- 90) Carotenuto M, Santoro N, Grandone A, Santoro E, Pascotto C, Pascotto A, Perrone L, del Giudice EM. The insulin gene variable number of tandemrepeats (INS VNTR) genotype and sleep disordered breathing in childhood obesity. J Endocrinol Invest. 2009 Oct; 32(9): 752-5. doi: 10.3275/6398.
- 91) Elia M, Falco M, Ferri R, Spalletta A, Bottitta M, Calabrese G, Carotenuto M, Musumeci SA, Lo Giudice M, Fichera M. CDKL5 mutations in boys with severe encephalopathy and early-onset intractable epilepsy. Neurology. 2008 Sep 23; 71(13): 997-9. doi: 10.1212/01.wnl.0000326592.37105.88.
- 92) Carotenuto M, Bruni O, Santoro N, Del Giudice EM, Perrone L, Pascotto A. Waist circumference predicts the occurrence of sleep-disordered breathing in obese children and adolescents: a questionnaire-based study. Sleep Med. 2006 Jun;7(4):357-61.
- 93) Carotenuto M, Guidetti V, Ruju F, Galli F, Tagliente FR, Pascotto A. Headache disorders as risk factors for sleep disturbances in school aged children. J Headache Pain. 2005 Sep; 6(4): 268-70.
- 94) Coppola G, Auricchio G, Federico R, Carotenuto M, Pascotto A. Lamotrigine versus valproic acid as first-line monotherapy in newly diagnosed typical absence seizures: an open-label, randomized, parallel-group study. Epilepsia. 2004 Sep; 45(9): 1049-53.
- 95) Coppola G, Licciardi F, Sciscio N, Russo F, Carotenuto M, Pascotto A. Lamotrigine as first-line drug in child-hood absence epilepsy: a clinical and neurophysiological study. Brain Dev. 2004 Jan; 26(1): 26-9.

- 96) Capovilla G, Beccaria F, Montagnini A, Cusmai R, Franzoni E, Moscano F, Coppola G, Carotenuto M, Gobbi G, Seri S, Nabbout R, Vigevano F. Short-term nonhormonal and nonsteroid treatment in West syndrome. Epilepsia. 2003 Aug; 44(8): 1085-8.
- 97) D'Agostino, D., Man, A., Santacroce, L. Current trends in cardiac surgery: Clinical experience in the treatment of mediastinitis with sterna wound infection through negative pressure therapy Acta Medica Mediterranea, 2016, 32, pp. 1905-1910. DOI: 10.19193/0393-6384 2016 6 181.
- 98) Salehi N, Saidi M, Rai A, Moheghi S, Tadbiri H. Right ventricular diastolic function in patients with pulmonary arterial hypertension vs. healthy individual based on echocardiography findings. Acta Medica Mediterranea, 2016, 32 (Special Issue2), pp. 927-931.
- 99) Yilmaz MD, Eyigori H, Osma U, Selçuk OT, Renda L, Pirtik I, Yalcin AD. Prevalence of allergy in patients with benign lesions of the vocal folds. Acta Medica Mediterranea, 2016, 32 (1), pp. 195-201. DOI: 10.19193/0393-6384\_2016\_1\_30.
- 100) Hashemian K, Talebi M. The relationship between dissociative experiences and childhood trauma in adolescent offenders residing in Tehran correction and rehabilitation center. Acta Medica Mediterranea, 2016, 32 (Special Issue2), pp. 1051-1053.

Corresponding author
MARGHERITA SALERNO, MD
Sciences for Mother and Child Health Promotion
University of Palermo
(Italy)