

THE CEREBRAL LOCALIZATION OF EXECUTIVE FUNCTIONS

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ABSTRACT

Executive Functions (EFs) are a complex neuropsychological tool that can lead all action of daily-life independently from age. The attempt to associate specific regions of the central nervous system (CNS) with specific sensory functions, motor and cognitive skills is one of the most recurring themes in the history of neuroscience. The concept of cerebral localization of mental activities started from the formulations of beginning phrenologists in Nineteenth century, passing through the holistic conceptions and antilocalization that marked some periods of the Twentieth century, until the beginning of the new millennium, characterized by the enormous popularity of the techniques of functional neuroimaging and the success of research programs aiming to create a real functional cartography of the human cerebral cortex.

Keywords: *Executive Functions, frontal lobes, cortical areas, neuropsychology.*

DOI: 10.19193/0393-6384_2018_4_141

Received November 30, 2017; **Accepted** January 20, 2018

Introduction

Executive Functions (EFs) are a complex neuropsychological tool that can lead all action of daily-life independently from age. The attempt to associate specific regions of the central nervous system (CNS) with specific sensory functions, motor and cognitive skills is one of the most recurring themes in the history of neuroscience. The concept of cerebral localization of mental activities started from the formulations of beginning phrenologists in Nineteenth century, passing through the holistic conceptions and antilocalization that marked some periods of the Twentieth century, until the beginning of the new millennium, characterized by the enormous populari-

ty of the techniques of functional neuroimaging and the success of research programs aiming to create a real functional cartography of the human cerebral cortex⁽¹⁻⁵⁾.

Certainly, 150 years after Paul Broca's discovery, conventionally regarded as the birth certificate of neuropsychology, the consensus is unanimous on the fact that selective lesions of different areas of the human cerebral cortex can produce cognitive and behavioral disturbances equally selective. However, the debate about the limits of this selectivity is still on. In particular, it remains the question of whether faculties such as intelligence or high-level cognitive processes can be allocated with a certain precision in specific areas of the cortex⁽¹⁻⁵⁾.

In this context, the case of the EFs is paradigmatic, but also in some paradoxical ways. In this case, the location of the function historically precedes the same formulation of the construct.

If indeed the notion of EFs has established itself relatively recently, the disorders we call today Dysexecutive were already known and labeled as frontal lobe syndrome with the clear implication of an explicit localization in the frontal cortex, and in particular in its anterior part, the cortex prefrontal. Indeed, it can be said that in the last twenty years the consensus on an inevitable correspondence between disorders dysexecutive and prefrontal lesions both went hand in hand. Today it is believed rather that the EFs are implemented in multiple distributed circuits, each of which includes connections to some portion of the prefrontal cortex⁽¹⁻⁵⁾.

The idea of the prefrontal cortex as a control system can be traced back to Lurija, who considers the higher mental faculties as the result of the operation of functional systems that involve multiple areas interconnected cortical and subcortical. In this regard, the prefrontal cortex is part, together with the cerebellum e to some subcortical nuclei, a system for planning, regulating and monitoring actions voluntary. This idea was based however on clinical observations about the relationship between frontal lesions and disorders of these integrative and control functions. Despite the validity of these evidences has been questioned, above all for their qualitative nature, Lurija's ideas have influenced the subsequent cognitive models of the front operation and in the prefrontal cortex the possible location of the supervisory system supervisor (SAS); the dysexecutive symptoms of the frontal patients are then attributed the inability of a damaged SAS to generate new plans and new voluntary actions in all those situations not habitual, in which the routine and automatic selection of actions is not satisfactory (Figure 1).

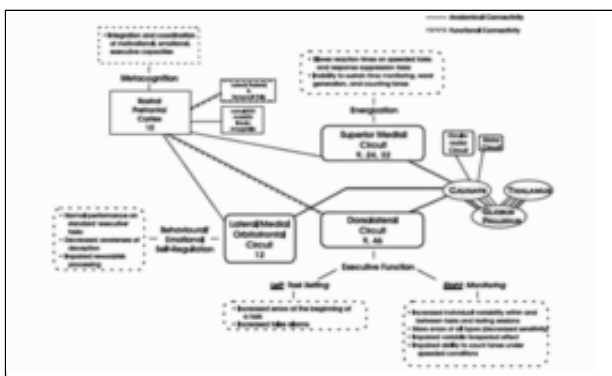


Figure 1: shows the frontal cortical-basal ganglia-thalamic circuits, supporting the fractionation of the frontal functional regions.

The idea of one direct correspondence between frontal cortex and SAS is based on evidence that only those with lesions fronts fail in classic EFs tests such as the Wisconsin Card Sorting Test (WCST), the Stroop test and the Tower of London⁽¹⁻¹²⁾. However, there are good theoretical and empirical reasons for dissociating at least partially the concept of executive function from the functioning of the prefrontal cortex. In 1988 it has been proposed the term dis-executive syndrome in place of that of lobe frontal syndrome frontal, to allow to study the nature and cognitive-behavioral characteristics of patients with executive disorders separately from the delicate problem of the possible cerebral localization of EFs⁽¹²⁻¹⁵⁾.

On the other hand, patients with focal frontal lesions do not necessarily show impaired performance in these tasks, while abnormal performance can be found in patients without evidence of frontal damage. In fact, although the activation of different components of the prefrontal cortex is verify with a certain regularity, other regions are also constantly activated, including the parietal cortex lateral and medial-posterior and various subcortical centers. So, although it is indisputable that the frontal lobe is involved in the EFs, it is risky to consider the prefrontal cortex as such as the executive center of the brain, because it is more plausible that the EFs are the result of the operation of several interconnected circuits, which include different areas of the frontal cortex with their cortical and subcortical connections. The simplistic equation between EFs and prefrontal cortex functions has therefore been criticized. basic considerations of empirical order, but there are two observations to make⁽¹⁶⁻²⁸⁾.

The prefrontal cortex constitutes about 30% of the entire cortex; the earlier frontal areas are specifically developed in the human brain, but their greater volume seems to be due to an increase in the size of the white substance, rather than the gray substance⁽²⁹⁻³⁵⁾. In addition, the neurons of the prefrontal cortex have the distinction of having a greater density of spines and dendrites than the other cortical areas⁽³⁶⁻⁴⁸⁾. These differences in volume and density are the reason for the complexity of human cognition, in particular of executive functions.

In man the period of childhood and adolescence is more protracted in all other living species and it is in this period that the development of the frontal lobe, in particular of the prefrontal buck, is more active. The different organizational models of the prefrontal areas all propose an unsustainable func-

tional segregation of the cortical areas occupying the three surfaces of the cortex: lateral, orbital and medial⁽⁴⁹⁻⁵³⁾. The lateral prefrontal cortex is the neural substrate of the following executive processes: set-shifting (active and cognitive flexibility), working memory - ability to keep active a mental representation (perceptive verbal) to perform complex tasks -, planning, strategic behavior, categorization (abstraction). Although the working memory is a conceptual construct connected to a network of both front and back structures, the crucial anatomical portion for this process is the lateral cortex.

Furthermore, the lateral prefrontal areas are also involved in attenuating through a modulation of the posterior cortical areas. The orbital portion of the prefrontal cortex is instead connected to activities in which the subject has to make a choice between a series of possible alternatives. It is divided into two portions, medial and lateral: the medial portion is involved in maintaining in memory the association between a family stimulus and a gratifying response, while the lateral portion has a specific role in suppressing a habitual behavioral response, persuading it with a response different more suited to the context⁽⁵⁴⁻⁶⁰⁾.

This portion of the prefrontal cortex is connected to the limbic system and the subcortical structures, therefore it has a fundamental role in the management of primary thrusts, instincts and in the emotional sphere. The medial prefrontal region has among its functions that of detect errors and resolve divergent trainings conflicts. The circuits of the medial prefrontal cortex are important to the sustained attention, but above all in the behavioral initiative. The medial lesions of the frontal lobes are those that constitute the cortical apparatus that regulates the state of activity and allow the initiative. The same ones play a fundamental role in the maintenance of some conditions of human conscious activity: the preservation of the necessary cortical tone and the modification of the state n basis for the immediate tasks of the subject. All these data are supported by anatomo-clinical evidence in which the effects, in part specific, of the frontal lesions have been studied. Orbitofrontal syndrome. An orbitofrontal damage is associated with disinhibition, inappropriate behavior, personality changes, irritability, emotional lability, absence of touch and distractibility⁽⁶¹⁻⁶⁹⁾.

They are subjects incapable of responding appropriately to social stimuli. Furthermore, orbitofrontal exposure is phylogenetically and ontogenetically earlier than development.

It is linked to basic adaptation tasks: emotional regulation and behavioral inhibition⁽⁷⁰⁻⁷⁴⁾.

Moreover, when the dorsolateral circuit is compromised, there is an inability to organize a behavioral response to new and complex stimuli. Several researchers have noted that this syndrome is characterized by perseverations, syndrome of utilization (difficulty to make functional use of the object evoked by its presence), echopraxis and echolalia. Numerous experimental evidences suggest that there is at least another cortical region involved as well as the prefrontal area and the related cortical and subcortical circuits. This area is the posterior parietal cortex, which is considered relevant in the reconfiguration of the associations between stimuli and responses or in the management of stimulus-guided behavioral adjustments⁽⁷⁵⁻⁸⁰⁾.

In a recent neuroimaging study for example, the implementation of cognitive control in response to the interchange of the experimental task produced significant modulations in the dorsolateral prefrontal cortex, in the anterior cingulum and in the posterior parietal cortex. The type of conflict, at the level of stimulus or response representation, selectively modulated the parietal cortex and the anterior cingulate, independently of the prefrontal cortex. Compatibly with the idea that the parietal cortex, together with the cingulum, has a role in detecting the conflict in signaling it to the lateral prefrontal cortex in order to increase cognitive control, increase the activity in the parietal cortex and in the cingulate predicted an increase in activity in the prefrontal cortex and an improvement in performance in subsequent trials⁽⁸¹⁻⁸⁷⁾.

To date, knowledge the neurological development allow us to highlight only the macroevolution ontogenetics of neural circuits; moreover, the localizations of the cognitive processes are rather sketched and they are also modified according to the peculiar characteristics of each person. It is believed that in the future developmental neuroscience will try to grasp the relationship between cognitive and neurological development in an integrated way, through neuroimaging tools and experimental neuropsychology⁽⁸¹⁻⁸⁷⁾.

References

- 1) Burgess PW, Stuss DT. Fifty Years of Prefrontal Cortex Research: Impact on Assessment. *J Int Neuropsychol Soc.* 2017 Oct; 23(9-10): 755-767. doi: 10.1017/S1355617717000704

- 2) Craik FIM, Bialystok E, Gillingham S, Stuss DT. Alpha Span: A Measure of Working Memory. *Can J Exp Psychol.* 2017 Nov 27. doi: 10.1037/cep0000143
- 3) Salmon DP, Stuss DT. Executive functions can help when deciding on the frontotemporal dementia diagnosis. *Neurology.* 2013 Jun 11; 80(24): 2174-5. doi: 10.1212/WNL.0b013e318296ea38
- 4) Stuss DT. Functions of the frontal lobes: relation to executive functions. *J Int Neuropsychol Soc.* 2011 Sep; 17(5): 759-65. doi: 10.1017/S1355617711000695;
- 5) Stuss DT, Alexander MP. Is there a dysexecutive syndrome? *Philos Trans R Soc Lond B Biol Sci.* 2007 May 29; 362(1481): 901-15
- 6) Precenzano F, Ruberto M, Parisi L, Salerno M, Maltese A, Vagliano C, Messina G, Di Folco A, Di Filippo T, Roccella M. Executive functioning in preschool children affected by autism spectrum disorder: a pilot study. *Acta Medica Mediterranea,* 2017, 33: 35-39; DOI: 10.19193/0393-6384_2017_1_005
- 7) 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: 1749-1753; DOI: 10.19193/0393-6384_2016_6_158
- 8) 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: 1761-1765; DOI: 10.19193/0393-6384_2016_6_160
- 9) 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: 1659; DOI: 10.19193/0393-6384_2016_5_146
- 10) Parisi L, Ruberto M, Precenzano F, Di Filippo T, Russotto C, Maltese A, Salerno M, Roccella M. The quality of life in children with cerebral palsy. *Acta Medica Mediterranea,* 2016, 32: 1665; DOI: 10.19193/0393-6384_2016_5_147;
- 11) Epifanio, M.S., Genna, V., De Luca, C., Roccella, M., La Grutta, S. Paternal and maternal transition to parenthood. The risk of postpartum depression and parenting stress. *2015 Pediatric Reports,* 7 (2), pp. 38-44
- 12) Parisi, L., Di Filippo, T., Roccella, M. The child with Autism Spectrum Disorders (ASDs): Behavioral and neurobiological aspects. *Acta Medica Mediterranea,* 2015, 31 (6), pp. 1187-1194
- 13) Vecchio D, Salzano E, Vecchio A, Di Filippo T, Roccella, M. A case of femoral-facial syndrome in a patient with autism spectrum disorders. *Minerva Pediatrica,* 2011, 63 (4), pp. 341-344
- 14) Parisi, L., Di Filippo, T., Roccella, M. Hypomelanosis of Ito: Neurological and psychiatric pictures in developmental age. *Minerva Pediatrica,* 2012, 64 (1), pp. 65-70
- 15) Di Filippo, T., Parisi, L., Roccella, M. Psychological aspects in children affected by Duchenne de Boulogne muscular dystrophy. *Mental Illness,* 2012, 4 (1), pp. 21-24
- 16) Epifanio MS, Genna V, Vitello MG, Roccella M, La Grutta S. Parenting stress and impact of illness in parents of children with coeliac disease. *Pediatr Rep.* 2013 Dec 19; 5(4): e19. DOI: 10.4081/pr.2013.e19
- 17) 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: case-control study. *Acta Medica Mediterranea,* 2016, 32: 1755-1759; DOI: 10.19193/0393-6384_2016_6_15
- 18) Parisi L, Salerno M, Maltese A, Tripi G, Romano P, Di Folco A, Di Filippo T, Roccella M. Anxiety levels in mothers of children affected by X-fragile syndrome. *Acta Medica Mediterranea,* 2017, 33: 495; DOI: 10.19193/0393-6384_2017_3_074
- 19) Parisi L, Salerno M, Maltese A, Tripi G, Romano P, Di Folco A, Di Filippo T, Roccella M. Autonomic regulation in autism spectrum disorders. *Acta Medica Mediterranea,* 2017, 33: 491; DOI: 10.19193/0393-6384_2017_3_073
- 20) Parisi L, Salerno M, Maltese A, Tripi G, Romano P, Di Folco A, Di Filippo T, Messina G, Roccella M. Emotional intelligence and obstructive sleep apnea syndrome in children: preliminary case-control study. *Acta Medica Mediterranea,* 2017, 33: 485; DOI: 10.19193/0393-6384_2017_3_072
- 21) Parisi L, Salerno M, Maltese A, Tripi G, Romano P, Di Folco A, Di Filippo T, Roccella M. Paternal shift-working and sleep disorders in children affected by primary nocturnal enuresis. *Acta Medica Mediterranea,* 2017, 33: 481; DOI: 10.19193/0393-6384_2017_3_071
- 22) Moscatelli F, Valenzano A, Monda V, Ruberto M, Monda G, Triggiani AI, Monda E, Chieffi S, Villano I, Parisi L, Roccella M, Messina A. Transcranial Magnetic Stimulation (TMS) application in sport medicine: A brief review. *Acta Medica Mediterranea,* 2017, 33: 423; Doi: 10.19193/0393-6384_2017_3_062
- 23) Parisi L, Faraldo Ma, Ruberto M, Salerno M, Maltese A, Di Folco A, Messina G, Di Filippo T, Roccella M. Life events and primary monosymptomatic nocturnal enuresis: a pediatric pilot study. *Acta Medica Mediterranea,* 2017, 33: 23; DOI: 10.19193/0393-6384_2017_1_003
- 24) Precenzano F, Ruberto M, Parisi L, Salerno M, Maltese A, Verde D, Tripi G, Romano P, Di Folco A, Di Filippo T, Messina G, Roccella M. Sleep habits in children affected by autism spectrum disorders: a preliminary case-control study. *Acta Medica Mediterranea,* 2017, 33: 405; DOI: 10.19193/0393-6384_2017_3_059
- 25) Parisi L, Fortunato MR, Salerno M, Maltese A, Di Folco A, Di Filippo T, Roccella M. Sensory perception in preschool children affected by autism spectrum disorder: A pilot study. *Acta Medica Mediterranea,* 2017, 33: 49; DOI: 10.19193/0393-6384_2017_1_007
- 26) Maltese A, Salerno M, Tripi G, Romano P, Ricciardi A, Di Folco A, Di Filippo T, Parisi L. The Angelman Syndrome: A Brief Review. *Acta Medica Mediterranea,* 2017, 33: 667; DOI: 10.19193/0393-6384_2017_4_100
- 27) Salerno M, Maltese A, Tripi G, Romano P, Di Folco A, Di Filippo T. Separation anxiety in pediatric migraine without aura: A Pilot Study. *Acta Medica Mediterranea,* 2017, 33: 621; DOI: 10.19193/0393-6384_2017_4_092
- 28) Maltese A, Salerno M, Tripi G, Romano P, Ricciardi A,

- Sessa G, Di Folco A, Di Filippo T, Parisi L. Rehabilitative treatment proposals in pediatric non-verbal syndrome. *Acta Medica Mediterranea*, 2017, 33: 675; DOI: 10.19193/0393-6384_2017_4_101
- 29) Monda V, Nigro E, Ruberto M, Monda G, Valenzano A, Triggiani Ai, Moscatelli F, Monda E, Villano I, Roccella M, Parisi L, Messina A. Synergism or competition between zinc and chromium dietary levels on insulin action mechanism. A method to investigate. *Acta Medica Mediterranea*, 2017, 33: 581; DOI: 10.19193/0393-6384_2017_4_085
- 30) 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: 645; DOI: 10.19193/0393-6384_2017_4_096
- 31) 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. eCollection 2014
- 32) 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
- 33) Carotenuto M, Santoro N, Grandone A, Santoro E, Pascotto C, Pascotto A, Perrone L, del Giudice EM. The insulin gene variable number of tandem repeats (INS VNTR) genotype and sleep disordered breathing in childhood obesity. *J Endocrinol Invest*. 2009 Oct;32(9):752-5. doi: 10.3275/6398
- 34) 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
- 35) 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.S4281836
- 36) 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;
- 37) 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
- 38) 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
- 39) 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
- 40) 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
- 41) 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;
- 42) Esposito M, Gallai B, Parisi L, Castaldo L, Marotta R, Lavano SM, Mazzotta G, Roccella M, Carotenuto M. Self-concept evaluation and migraine without aura in childhood. *Neuropsychiatr Dis Treat*. 2013; 9: 1061-6. doi: 10.2147/NDT.S49364;
- 43) 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;
- 44) 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. *Somatosens Mot Res*. 2016 Jun; 33(2): 137-44. doi: 10.1080/08990220.2016.1203305
- 45) 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
- 46) 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
- 47) Perillo L, Esposito M, Contiello M, Lucchese A, Santini AC, Carotenuto M. Oculusal traits in developmental dyslexia: a preliminary study. *Neuropsychiatr Dis Treat*. 2013; 9: 1231-7. doi: 10.2147/NDT.S49985
- 48) 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
- 49) 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
- 50) 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
- 51) 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. Erratum in: *Epilepsia*. 2004 Jul; 45(7): 887
- 52) 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. eCollection 2014
- 53) 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
- 54) 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. *Front Physiol*. 2017 Feb 14;8:85. doi: 10.3389/fphys.2017.00085
- 55) Sperandeo R, Maldonato MN, Messina A, Cozzolino P, Monda M, Cerroni F, Romano P, Salerno M, Maltese A, Roccella M, Parisi L, Tripi G, Moscatelli F, Sessa F, Salerno M, Cibelli G, Messina G, Monda V, Chieffi S, Villano I, Monda E, Ruberto M, Marsala G, Marotta R, Valenzano A. Orexin system: network multi-tasking. *Acta Medica Mediterranea*, 2018, 34: 349. DOI: 10.19193/0393-6384_2018_2_55
- 56) Maldonato MN, Sperandeo R, Dell'orco S, Iennaco D, Cerroni F, Romano P, Salerno M, Maltese A, Roccella M, Parisi L, Tripi G, Moscatelli F, Sessa F, Monica S, Cibelli G, Messina G, Monda M, Chieffi S, Villano I, Monda V, Messina A, Ruberto M, Marsala G, Valenzano A, Marotta R. Mind, brain and altered states of consciousness. *Acta Medica Mediterranea*, 2018, 34: 357. DOI: 10.19193/0393-6384_2018_2_56
- 57) Maltese A, Gallai B, Marotta R, Lavano F, Lavano SM, Tripi G, Romano R, D'oro L, Salerno M. The synactive theory of development: the keyword for neurodevelopmental disorders. *Acta Medica Mediterranea*, 2017, 33: 1257. DOI: 10.19193/0393-6384_2017_2s_194
- 58) Maltese A, Romano P, D'Oro L, Gallai B, Marotta R, Lavano F, Lavano SM, Tripi G, Salerno M. Anger in children: A minireview. *Acta Medica Mediterranea*, 2017, 33: 1233. DOI: 10.19193/0393-6384_2017_2s_191
- 59) Gallai B, Valentini V, Barbanera F, Marotta R, Lavano F, Lavano SM, Maltese A, Tripi G, Romano R, Salerno M, Di Folco A. The Behavioral Parenting Interventions (BPT) for support and mandatory integrative therapy for children and adolescents affected by disruptive behavioural disorders: a brief review. *Acta Medica Mediterranea*, 2017, 33: 1205. DOI: 10.19193/0393-6384_2017_2s_187
- 60) Gallai B, Valentini V, Barbanera F, Marotta R, Lavano F, Lavano SM, Maltese A, Tripi G, Romano P, Salerno M. Behavioural disorders in children and adolescents: a conceptual review about the therapeutic alliance with family and school. *Acta Medica Mediterranea*, 2017, 33: 1181. DOI: 10.19193/0393-6384_2017_2s_184
- 61) Gallai B, Valentini V, Barbanera F, Marotta R, Lavano F, Lavano SM, Maltese A, Tripi G, Romano P, Salerno M. Review about comorbidities of behavioural disorders in children and adolescents: the focus on attention-deficit/hyperactivity disorder. *Acta Medica Mediterranea*, 2017, 33: 1197. DOI: 10.19193/0393-6384_2017_2s_186
- 62) Monda M, Ruberto R, Villano I, Valenzano A, Ricciardi A, Gallai B, Marotta R, Lavano F, Lavano SM, Maltese A, Tripi G, Romano P, Salerno M. A minireview about sporting practice in epileptic children. *Acta Medica Mediterranea*, 2017, 33: 1279. DOI: 10.19193/0393-6384_2017_2s_197
- 63) Maltese A, Gallai B, Marotta R, Lavano F, Lavano SM, Tripi G, Romano P, D'oro L, Salerno M. Neurosciences and attachment theory: A brief review. *Acta Medica Mediterranea*, 2017, 33: 1249. DOI: 10.19193/0393-6384_2017_2s_193
- 64) Maltese A, Gallai B, Romano P, D'oro L, Marotta R, Lavano F, Lavano SM, Tripi G, Salerno M. The dynamic maturative model for attachment. *Acta Medica Mediterranea*, 2017, 33: 1265. DOI: 10.19193/0393-6384_2017_2s_195
- 65) 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. Non-Rapid Eye Movement Sleep Parasomnias and Migraine: A Role of Orexinergic Projections. *Front Neurol*. 2018 Feb 28; 9: 95. doi: 10.3389/fneur.2018.00095
- 66) 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. Electroclinical findings and long-term outcomes in epileptic patients with inv dup (15). *Acta Neurol Scand*. 2018 Jan 23. doi: 10.1111/ane.12902
- 67) 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. The Rorschach Test Evaluation in Chronic Childhood Migraine: A Preliminary Multicenter Case-Control Study. *Front Neurol*. 2017 Dec 12; 8: 680. doi: 10.3389/fneur.2017.00680
- 68) Carotenuto M, Messina A, Monda V, Precenzano F, Iacono D, Verrotti A, Piccorossi A, Gallai B, Roccella M, Parisi L, Maltese A, Lavano F, Marotta R, Lavano SM, Lanzara V, Ferrentino RI, Pisano S, Salerno M, Valenzano A, Triggiani AI, Polito AN, Cibelli G, Monda M, Messina G, Ruberto M, Esposito M. Maternal Stress and Coping Strategies in Developmental Dyslexia: An Italian Multicenter Study. *Front Psychiatry*. 2017 Dec 22; 8: 295. doi: 10.3389/fpsyt.2017.00295;
- 69) Monda V, Salerno M, Sessa F, Bernardini R, Valenzano A, Marsala G, Zammit C, Avola R, Carotenuto M, Messina G, Messina A. Functional Changes of Orexinergic Reaction to Psychoactive Substances. *Mol Neurobiol*. 2018 Jan 6. doi: 10.1007/s12035-017-0865-zM
- 70) Sperandeo R, Monda V, Messina G, Carotenuto M,

- Maldonato NM, Moretto E, Leone E, De Luca V, Monda M, Messina A. Brain functional integration: an epidemiologic study on stress-producing dissociative phenomena. *Neuropsychiatr Dis Treat*. 2017 Dec 19; 14: 11-19. doi: 10.2147/NDT.S146250
- 71) Monda V, La Marra M, Perrella R, Caviglia G, Iavarone A, Chieffi S, Messina G, Carotenuto M, Monda M, Messina A. Obesity and brain illness: from cognitive and psychological evidences to obesity paradox. *Diabetes Metab Syndr Obes*. 2017 Nov 21;10:473-479. doi: 10.2147/DMSO.S148392. eCollection 2017
- 72) Monda V, Valenzano A, Moscatelli F, Salerno M, Sessa F, Triggiani AI, Viggiano A, Capranica L, Marsala G, De Luca V, Cipolloni L, Ruberto M, Precenzano F, Carotenuto M, Zammit C, Gelzo M, Monda M, Cibelli G, Messina G, Messina A. Primary Motor Cortex Excitability in Karate Athletes: A Transcranial Magnetic Stimulation Study. *Front Physiol*. 2017 Sep 12;8:695. doi: 10.3389/fphys.2017.00695
- 73) Chieffi S, Carotenuto M, Monda V, Valenzano A, Villano I, Precenzano F, Tafuri D, Salerno M, Filippi N, Nuccio F, Ruberto M, De Luca V, Cipolloni L, Cibelli G, Mollica MP, Iacono D, Nigro E, Monda M, Messina G, Messina A. Orexin System: The Key for a Healthy Life. *Front Physiol*. 2017 May 31;8:357. doi: 10.3389/fphys.2017.00357
- 74) Maltese A, Salerno M, Tripi G, Romano P, Ricciardi A, Di Folco A, Di Filippo T, Parisi L. Internalizing problems are related to sleep patterns disorder in children affected by primary headache. *Acta Medica Mediterranea*, 2017, 33: 729. DOI: 10.19193/0393-6384_2017_5_107;
- 75) Maltese A, Salerno M, Romano P, Ricciardi A, Di Filippo T, Tripi G. Ketogenic diet as antiepileptic therapy: historical perspective. *Acta Medica Mediterranea*, 2017, 33: 769. DOI: 10.19193/0393-6384_2017_5_113
- 76) Maltese A, Salerno M, Romano P, Ricciardi A, Di Filippo T, Tripi G. Ketogenic diet as antiepileptic therapy: neurotransmission effects. *Acta Medica Mediterranea*, 2017, 33: 777. DOI: 10.19193/0393-6384_2017_5_114
- 77) Maltese A, Salerno M, Romano P, Ricciardi A, Di Filippo T, Tripi G. Ketogenic diet as antiepileptic therapy: administration and formulas. *Acta Medica Mediterranea*, 2017, 33: 737. DOI: 10.19193/0393-6384_2017_5_108
- 78) Maltese A, Gallai B, Romano P, D'oro L, Marotta R, Lavano F, Lavano SM, Tripi G, Salerno M. Motion sickness in childhood migraine. *Acta Medica Mediterranea*, 2017, 33: 1241. DOI: 10.19193/0393-6384_2017_2s_192
- 79) Smirni D, Smirni P, Di Martino G, Cipolotti L, Oliveri M, Turriziani P. Standardization and validation of a parallel form of the verbal and non-verbal recognition memory test in an Italian population sample. *Neurol Sci*. 2018 May 4. doi: 10.1007/s10072-018-3433-z
- 80) Pisano S, Coppola G, Catone G, Carotenuto M, Iuliano R, D'Esposito V, Cabaro S, Miraglia Del Giudice E, Bravaccio C, Formisano P. Differences in Metabolic Factors Between Antipsychotic-Induced Weight Gain and Non-pharmacological Obesity in Youths. *Clin Drug Investig*. 2018 Feb 12. doi: 10.1007/s40261-018-0627-3
- 81) Maltese A, Salerno M, Cerroni F, Romano P, Di Folco A, Di Filippo T, Tripi G. The transcranial stimulation with direct currents (TDCS): an historical and conceptual minireview. *Acta Medica Mediterranea*, 2018, 34: 697. DOI: 10.19193/0393-6384_2018_3_107
- 82) 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. *Front Behav Neurosci*. 2017 Jan 31;11:10. doi: 10.3389/fnbeh.2017.00010
- 83) A, Tafuri D, Capranica L, Cibelli G, Monda M. Relationship between RPE and blood lactate after fatiguing handgrip exercise in taekwondo and sedentary subjects. *Biology and Medicine*, 2015 7 (Specialissue3), art. no. S3008)
- 84) Messina A, Monda M, Valenzano A, Messina G, Villano I, Moscatelli F, Cibelli G, Marsala G, Polito R, Ruberto M, Carotenuto M, Monda V, Viggiano A, Daniele A, Nigro E. Functional Changes Induced by Orexin A and Adiponectin on the Sympathetic/Parasympathetic Balance. *Front Physiol*. 2018 Mar 22;9:259. doi: 10.3389/fphys.2018.00259
- 85) M. Use of nutritional supplements among south Italian students of physical training and sport university. *Current Topics in Toxicology*, 2013 9, pp. 21-26
- 86) 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 and Carotenuto M. Sympathetic, Metabolic Adaptations, and Oxidative Stress in Autism Spectrum Disorders: How Far From Physiology? *Front. Physiol*. 2018; 9: 261. doi: 10.3389/fphys.2018.00261
- 87) Valenzano A, Monda V, Messina A, Precenzano F, Cibelli G, Monda M, Lupoli G. Quality of life in overweight (obese) and normal-weight women with polycystic ovary syndrome. *Patient Prefer Adherence*. 2017 Mar 2;11:423-429. doi: 10.2147/PPA.S119180

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