

## AUTONOMIC REGULATION IN AUTISM SPECTRUM DISORDERS

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**ABSTRACT**

**Introduction:** The sinactive developmental model provides suggests a different way for the brain study by observing the children behavior. In all neurodevelopmental disorders, we can observe autonomic alteration comprising sleep disorders, meal behaviour alteration and self-regulatory impairment. These alterations/impairment are very frequent in autism spectrum disorders (ASD) (1-12). Aim of the present preliminary study is the assessment of metabolic rate in children affected by ASD.

**Material s and methods.** 5 males affected by ASD aged 7-10 years (mean age  $6.73 \pm 3.39$ ), were recruited. The average score at the ADOS scale was 12.24 (SD  $\pm 3.29$ ). The control group consisted of 5 males typically developing children (TDC) aged 7 to 11 years (mean age  $7.92 \pm 3.23$ ).

**Autonomic/Metabolic evaluation:** Free-living daily physical activity was measured using either the SenseWear Armband in order to calculate the total energy expenditure (TEE), baseline (REE) and the metabolic physical activity for prolonged periods of time. In general, the SenseWear Armband allows objective monitoring of the lifestyle including duration and sleep efficiency.

**Results:** ASD subjects show values of total energy expenditure ( $p = 0.0047$ ) and active energy expenditure ( $p = 0.044$ ) significantly higher compared to control subjects (Table 1). In addition, ASD children have a metabolic intermediate significantly higher than healthy subjects ( $p=0.015$ ). (Table 1). Finally, the ASD children show a significant reduction of sleep time ( $p = 0.027$ ) (Table 1).

**Conclusion:** ASD can represents a very significant risk factor for developing sleep disorders and to high energy expenditure, although further studies are needed in this respect.

**Keywords:** autonomic regulation, autism spectrum disorders, SenseWear Armband.

DOI: 10.19193/0393-6384\_2017\_3\_073

Received November 30, 2016; Accepted March 20, 2017

**Introduction**

The sinactive developmental model provides ways of access to the brain study by observing the children behavior, the first way of communicating for the newborn<sup>(1-8)</sup>.

According to this theory, the development process is an interactive and hierarchical process including five subsystems: the autonomic nervous system, motor system, the behavioural system, the attention-interaction system and the self-regulation

system. be a hint of aging, but the facilities are needed<sup>(9-11)</sup>.

In all neurodevelopmental disorders, we can observe autonomic alteration comprising sleep disorders, meal behaviour alteration and self-regulatory impairment. These alterations/impairment are very frequent in autism spectrum disorders (ASD)<sup>(1-12)</sup>.

Therefore, aim of the present preliminary study is the assessment of metabolic rate in children affected by ASD.

## Materials and methods

### Population

5 males affected by ASD aged 7-10 years (mean age  $6.73 \pm 3.39$ ), were recruited.

The average score at the ADOS scale was 12.24 (SD  $\pm 3.29$ ).

Exclusion criteria were the following: overweight ( $z\text{-BMI} > 85$  pc) and obesity ( $z\text{-BMI} > 95$  pc), cognitive disability (IQ  $< 70$ ), neurological disorders (ie headaches, epilepsy), chromosomal syndromes (eg. Down, Prader-Willi, Crouzon, Pierre-Robin, trisomy 18), psychiatric illness (ie. mood disorders, anxiety disorders, psychosis) and specific neuropsychological disorders<sup>(13-38)</sup>.

The control group consisted of 5 males typically developing children (TDC) aged 7 to 11 years (mean age  $7.92 \pm 3.23$ ). The subjects of both groups are all Caucasians, recruited in the same urban area and similar socio-economic status.

### Autonomic/Metabolic evaluation

Free-living daily physical activity was measured using either the SenseWear Armband. Participants were requested to wear the SWA on their upper arm 24 h a day, with the exception of swimming or showering/bathing. Moreover, the specific characteristics of the instrument makes it suitable pediatric age. In fact, the tool is handy, small, light is worn on the upper part of his right arm, the triceps area of the posterior. It has a low weight (80 g) allows the data storage of up to 2 weeks of continuous monitoring of all the physiological signals. Allows the calculation of "objectively" the total energy expenditure (TEE), baseline (REE) and the metabolic physical activity for long periods of time. It allows objective monitoring of the "lifestyle" including duration and sleep efficiency.

### Statistics

t-Test for comparison between the two populations. p values  $\leq 0.05$  were considered significant.

## Results

The two groups were similar for age ( $p = 0.585$ ). The ASD subjects show values of total energy expenditure ( $p = 0.0047$ ) and active energy expenditure ( $p = 0.044$ ) significantly higher compared to control subjects (Table 1). In addition, the ASD children have a metabolic intermediate in the 24 hours significantly higher than in healthy sub-

jects ( $p = 0.015$ ). (Table 1). Finally, the ASD children show a significant reduction of sleep time ( $p = 0.027$ ) (Table 1).

	ASD N=5	TDC N=5	P
Age	6.73 $\pm$ 3.39	7.92 $\pm$ 3.23	0.585
Total expenditure (Joule)	7048.58 $\pm$ 1126.36	5398.18 $\pm$ 1094.25	0.047
Active expenditure (Joule)	3506.75 $\pm$ 714.91	2189.63 $\pm$ 1003.49	0.044
Mean Metabolic rate (METs)	5.396 $\pm$ 0.141	3.971 $\pm$ 1.026	0.015
Total sleep time (min)	346.48 $\pm$ 75.16	453.25 $\pm$ 45.72	0.027

**Table 1:** shows comparison between means and standard deviation among children affected by autism spectrum disorders (ASD) and typical developing children (TDC) for ArmBand evaluation. t-Test was applied; p values  $< 0.05$  were considered as statistical significant.

## Discussion

The results of the autism spectrum disorders represent a complex disease and articulated in several respects. Besides the core symptoms, in fact, there are many other complications that the clinician, therapist and parents are forced to face. The neurodegenerative disorders are, among these, the key for feeding difficulties notes, to pain and sensory perception. The sleep of people with ASD is impaired and disturbed at any age and independently of the severity of impaired social and communicative sphere, but not the level of development. In our study, we excluded cases of mental retardation.

What emerges from the results of our survey shows that ASD is a very significant risk factor for developing sleep disorders, although the report could also be interpreted in the opposite manner or that have a disturbed sleep can be an aggravating factor in the nuclear symptoms ASD subjects, although further studies are needed in this respect<sup>(39-50)</sup>.

## References

- 1) 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.
- 2) 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.
- 3) 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.
- 4) 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.
  - 5) 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.
  - 6) 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.
  - 7) 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.
  - 8) 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.
  - 9) Carotenuto M, Esposito M, Precenzano F, Castaldo L, Roccella M. Cosleeping in childhood migraine. *Minerva Pediatr*. 2011 Apr; 63(2): 105-9.
  - 10) Esposito M, Carotenuto M, Roccella M. Primary nocturnal enuresis and learning disability. *Minerva Pediatr*. 2011 Apr; 63(2): 99-104.
  - 11) 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.
  - 12) 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.
  - 13) 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.
  - 14) Precenzano F, Ruberto M, Parisi L, Salerno M, Maltese A, Vagliano C, Messina G, Di Folco A, Di Filippo T, Michele Roccella. 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.
  - 15) 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.
  - 16) 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: 1755-1759; DOI: 10.19193/0393-6384\_2016\_6\_159.
  - 17) 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.
  - 18) 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.
  - 19) 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.
  - 20) 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.
  - 21) 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.
  - 22) 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.
  - 23) 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.
  - 24) 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.
  - 25) 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.
  - 26) 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.
  - 27) 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.
  - 28) Maltese A, Pepi A, Scifo L, Roccella M. Referential communication skills in children with Down Syndrome. *Minerva Pediatr*. 2014 Feb; 66(1):7-16.
  - 29) 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.
  - 30) Alesi M, Battaglia G, Roccella M, Testa D, Palma A, Pepi A. Improvement of gross motor and cognitive abilities by an exercise training program: three case reports. *Neuropsychiatr Dis Treat*. 2014 Mar 14; 10:479-85. doi:

- 10.2147/NDT.S58455.
- 31) 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 overweight (obese) and normal-weight women with polycystic ovary syndrome. *Patient Prefer Adherence*. 2017 Mar 2; 11: 423-429.
  - 32) Precenzano F, Ruberto M, Parisi L, Salerno M, Maltese A, Gallai B, Marotta R, Lavano SM, Lavano F, Roccella M. Visual-spatial training efficacy in children affected by migraine without aura: a multicenter study. *Neuropsychiatr Dis Treat*. 2017 Jan 27; 13: 253-258. doi: 10.2147/NDT.S119648
  - 33) Epifanio, M.F., Genna, V., Di Marco, S., Furnari, M.L., Pardo, F., Collura, M., Roccella, M., La Grutta, S. Quality of life, affect regulation and resilience in adult patients with cystic fibrosis. *Gazzetta Medica Italiana Archivio per le Scienze Mediche*, 2013 172 (9), pp. 705-711.
  - 34) 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.
  - 35) 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.
  - 36) 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.
  - 37) 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.
  - 38) 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. *Front Neural Circuits*. 2016 Aug 25 ;10: 66. doi: 10.3389/fncir.2016.00066.
  - 39) 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.
  - 40) 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.
  - 41) Pasquali D, Carotenuto M, Loporati 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.
  - 42) Morandi A, Bonnefond A, Lobbens S, Carotenuto M, Del Giudice EM, Froguel P, Maffei 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.
  - 43) 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.
  - 44) 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.
  - 45) Franzoni E, Matricardi S, Di Pisa V, Capovilla G, Romeo A, Tozzi E, Pruna D, Salerno GG, Zamponi N, Accorsi P, Giordano L, Coppola G, Cerminara C, Curatolo P, Nicita F, Spalice A, Grosso S, Pavone P, Striano P, Parisi P, Boni A, Gobbi G, Carotenuto M, Esposito M, Cottone C, Verrotti A. Refractory absence seizures: An Italian multicenter retrospective study. *Eur J Paediatr Neurol*. 2015 Nov; 19(6): 660-4. doi: 10.1016/j.ejpn.2015.07.008.
  - 46) 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.
  - 47) 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.
  - 48) 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.
  - 49) 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.
  - 50) Carotenuto M, Esposito M, D'Aniello A, Ripa 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.

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