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Editorial

Neurological "soft signs" in children and adolescents

Paola Iannetti*, Mario Mastrangelo and Sara Di Netta
Pediatric Neurology Unit, Department of Pediatrics, University of Rome "La Sapienza", Italy

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1. Introduction

Neurological "soft signs" (NSS) are defined as minor abnormalities in the neurological examination in subjects with no other features of fixed or transient neurologic disorders [1]. These clinical disabilities are often associated with behavior, coordination and learning difficulties. The prevalence of motor examination abnormalities among a normal pediatric population is unknown; about this aspect, studies performed have given different results in children examined at seven and seventeen years [2]. In this issue of JPN, Wu et al. [3] investigated the frequency of motor abnormalities in a random sample of healthy 5-year-old children, and then they examined the relationship between these motor abnormalities and standardized measures of cognition and motor performance. Based on their findings they have concluded that motor examination abnormalities in otherwise healthy 5-year-old children may be more common than previously thought. However, the proportion of children with motor examination abnormalities who have an unrecognized neurologic disorder remains unknown [3].

The main factors that may determine the appearance of NSS are:

- *Genetic predisposition* to hereditary neurological diseases. These congenital conditions are very numerous and not always severe and manifest in early ages;
- *Neonatal and perinatal diseases* as prenatal Cytomegalovirus and Toxoplasma infections, perinatal ischemia and/or asphyxia. Moreover, a high incidence of minor neurological signs, perceptual motor difficulties and fine motor skills abnormalities have been observed in prematurely born babies, low-birth weight infants and in malnutrition. There is a high rate of preterm children who shows minor neurological signs and/or perceptual motor difficulties in the absence of major neurological impairment [4]. It appears that NSS may emerge as a result of general developmental disability associated with the complications of pregnancy and failure to grow at expected rates [5]. The involvement of early malnutrition in the manifestation of NSS is, instead, mainly due to moderate or severe protein-energy uptake deficiency [6];
- Environmental causes including social and economic situations;
- *Psychological aspects:* mainly learning disabilities and Attention Deficit Hyperactivity Disorder (ADHD).

The principal NSS in "normal" pediatric population are:

- The inability to recognize the familiar objects with tactile manipulation: *astereognosis*;

*Correspondence: Prof. Dr. Paola Iannetti, La Sapienza University, Division of Pediatric Neurology, Viale Regina Elena 324, 00161 Roma, Italy. Fax: +39 6 49979312; E-mail: paola.iannetti@uniroma1.it.

- The lack of ability to understand numbers or letters written on the skin: *dysgraphesthesia*;
- Incapability to perform purposeful movement in the absence of paresis, ataxia, disturbance of muscular tone, or sensation: *apraxia*;
- Inability to perform alternating rapid movements with fingers and hands: *dysdiadochokinesis*;
- Decreased resistance to passive movement as assessed by the examiner: *hypotonia*;
- Reduced ability and slowing in the coordination motor tests: clumsiness in normal school children. The term "clumsiness" is used to describe children at low level of competence in motor skills without evidences of neurological disease. "Clumsy" children, in fact, have a significantly lower score, in relation to the others, in various motor performances [7];
- Involuntary movements:
  a) *choreiform movements:* fast, purposeless, asymmetrical and arrhythmic, frequently localized at the extremities with inability for 30–40 seconds to stand motionless with feet close each other, eyes closed and supinated arms outstretched.
  b) *mirror movements* which appear in a corporeous segment in a synchronous and specular way to the intentional movements of the controlateral one and during finger apposition. These movements represent another form of presentation of a minor neurological dysfunction. They may be present in healthy children as a feature of progressive maturation and myelination of specific brain structures, especially the corpus callosum. In case of persistence of their symptomatology it is necessary to search for Klippel-Feil [8], cleft spine, Chiari Malformations, neurological hereditary pathologies [9] such as Usher syndrome and phenylketonuria, pyramidal lesions and various behavior disturbances.

Special attention is to be paid to:

- *ADHD*, frequently observed in children with minor neurological signs and which can be considered as a chronic disorder with high prevalence in school ages: its typical symptoms are inattention, impulsivity and hyperactivity. Recently it has been described its connection with a central nervous system (CNS) myelination delay and developmental derangements (e.g. mega cisterna magna) and even its link with fetal alcohol spectrum disorder [10]. In absence of an improvement of the clinical presentation during the growth it can be managed through pharmacological, psychosocial, environmental and psychoeducational therapy;
- *Autism*, among mild neurological disorders should be taken into account since children who fail to speak or understand spoken language may have motor and coordination deficits due to underlying structural neurological lesions;
- *Endocrinological modifications and the onset of puberty.* Puberty is the transition period between the sexually immature state and potentially fertile stage during which secondary sexual characteristics become evident [11]. Adolescence is also used as a synonym for puberty [12,13]. The major neuronal structures involved in the initiation puberty have been indicated in the complex relationship at the hypothalamic-pituitary axis level. The major modifications are a rise in growth hormone (GH) and gonadal hormone levels and the increased T4 utilization [14]. The effects of GH and T4 on the estrogens and testosterone result in the stimulation of muscular tissue and in the increment of strength, which possibly may reduce hypotonia. T4 also acts on myelination and interferes with some signs of incomplete myelination such as the mirror movements. It has also been demonstrated a negative association between tardive dyskinesia and estrogens level and a positive correlation between estradiol level and fine motor performance.

It is possible that soft signs persist after puberty because of a fixed but unrecognized focal or global brain injury; in this case it is required the execution of other diagnostic probe because this fact denies the idea that they could have been a maturational lag. Neurological soft signs, which persist in to puberty seems to be more clearly related to perinatal factors than the ones, which disappears in this period [15]. It has been described several cases of children born after a difficult gestation or affected by prenatal/perinatal complications who evidenced fine manipulative disability and various coordination problems. The role of perinatal lesions is also confirmed by the frequent manifestation of choreiform movement in subjects who had suffered of asphyxia at birth.

Social behaviors have a great role on the performance during the neurological examination. The possibility to evidence the minor neurological deficit is, in fact connected to the attention and willingness to co-operate of the patients and his family [16]. Subtle neurological abnormalities are also associated with the psycholog-

ical and cognitive features of the child affected [17]. Different studies have showed the lower performance in motor and IQ tests of the patient that evidenced soft motor abnormalities. Nevertheless, even if several authors have reported a decreasing in neurological "soft signs" during puberty, how the hormonal changes of this period affect the neurological impairments is unclear.

In conclusion, neurological "soft signs" are defined as abnormal performance on a neurological examination by children not mentally retarded and without focal neurological deficits connected to brain tissue lesions. If metabolic or structural CNS abnormalities are hypothesized, a certain number of neurological diseases need to be considered for differential diagnosis. Usually, during adolescence progressive neurological dysfunctions may improve.

It is also interesting to recall the possibility to find in healthy children, not only clinical neurological abnormalities but also epileptiform electroencephalographic alterations (spike and slow waves discharges, multiple spike and slow wave complexes, midtemporal spikes, rolandic or parietal spikes, occipital and multifocal spikes) that disappear during the school age or, at the latest, during the adolescence [18]. It is possible that these alterations express difficulties in affective or motor adaptation during childhood.

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