Review

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The multifaceted and complex hypermobility syndrome (a.k.a. Ehlers-Danlos Syndrome Hypermobility Type): Evaluation and management through a rehabilitative approach

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Abstract

Joint hypermobility syndrome (JHS) is a hereditary disorder of connective tissue recently considered the one and the same as the Ehlers-Danlos Syndrome Hypermobility Type (EDS-HT).

The JHS/EDS-HT is mainly characterized by joint hypermobility, chronic pain and a variable skin involvement. Clinical manifestations expressed by patients are multiple and varied. The rehabilitative approach may play a fundamental role in the understanding and management of symptoms and clinical manifestation. Aim of this study is to make a literature revision of all the aspects of this not so rare disease.
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Key words: *Ehlers-Danlos, hypermobility, posture, proprioception, rehabilitation*

Introduction

Joint hypermobility syndrome (JHS) is a hereditary disorder of connective tissue that comprises symptomatic hypermobility which predisposes to arthralgia, soft tissue injury and joint instability (1). JHS was firstly described by Kirk in 1967 (2) and was defined as the occurrence of musculoskeletal symptoms in the presence of joint hypermobility in healthy individuals. Joint hypermobility (JHM) can be described as having an excessive range of movement in any given joint, above and beyond what would be considered the normal Gaussian range (3, 4). It seems that most people have an awareness of their hypermobility, or "being loose jointed" and have no problem or difficulties with their joints. Hypermobility, that may be described as a useful asset to dancers and performing artists, has a high prevalence among gymnasts, acrobats, musicians and dancers, with up to 70 per cent particularly within ballet and contemporary dance communities (5). The first clinical description of hypermobility is attributed to Hippocrates who, in the fourth century B.C., described in Scythians, a race of Iranian horse-riding, as having humidity, flabbiness and atony such that they were unable to use their weapons; their main problem was that hyperlaxity of the elbow and the shoulder joints prevented them from drawing their bows effectively (6). The first report of association between joint laxity and rheumatologic symptoms emanated from Sutro (7) who described effusion and pain associated to hypermobile joints; similar observations were made by Kirk (2) who firstly coined the JHS term.

JHS needs to be distinguished from other disorders that share many common features, such as Marfan Syndrome, Ehlers-Danlos syndrome and Osteogenesis Imperfecta which together form the group of the Hereditary Connective Tissue Disorders (8).

The last 50 years have seen the recognition of this syndrome and many are the articles published concerning all the different aspects of this syndrome; our aim is to analyze what emerges and what still needs to be studied from a rehabilitative point of view.

Assessing hypermobility

Before seeing a specialist able to make the diagnosis, it might be possible to identify hypermobility by answering five diagnostic questions (see Table1), that are particularly helpful for more mature patients since hypermobility declines (9).

The Beighton score is the most frequently used method of diagnosing hypermobility; it was devised in the 1970 to measure hypermobility and was devised to be a rapid assessment while clinically simple to measure (10). The Beighton score is a 9-point evaluation with attribution of one point in the presence of any of the following: (1) forward flexion of the trunk with the knees extended and the palms resting flat on the floor, (2) hyperextension of the elbow beyond 10° (one point for each arm), (3) hyperextension of the knees beyond 10° (one point for each leg), (4) passive apposition of the thumb to the flexor aspect of the forearm (one point for each hand), (5) passive dorsiflexion of the V finger beyond 90° (one point for each hand) (Fig. 1). It is now accepted that a score about four gives a diagnosis of generalized hyper-

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Table 1. Five item screening questionnaire for BJHS.

1	Can you now (or could you ever) place your hands flat on the floor without bending your knees?
2	Can you now (or could you ever) bend you thumb to touch your forearm
3	As a child did you amuse your friends by contorting your body into strange shapes or could you do splits?
4	As a child or teenager did your shoulder or kneecap dislocate on more than one occasion?
5	Do you consider yourself double jointed?
Answer in the affirmative to two or more items suggests hypermobility.	

mobility and this is a major criteria for hypermobility. This score reduced to three out of nine for those over 50 years old since hypermobility declines with age.

Diagnosis and epidemiology

The Revised Brighton criteria (11) promulgated by the British Society for Rheumatology Special Interest Group of the Hereditary disorders of Connective Tissue in the 1998 represents a validated set of Classification Criteria for JHS. Like set of Criteria for Ehlers-Danlos syndrome (12), the Brighton criteria comprise sets of major and minor criteria (see Table 2) that are met when either two major, or one

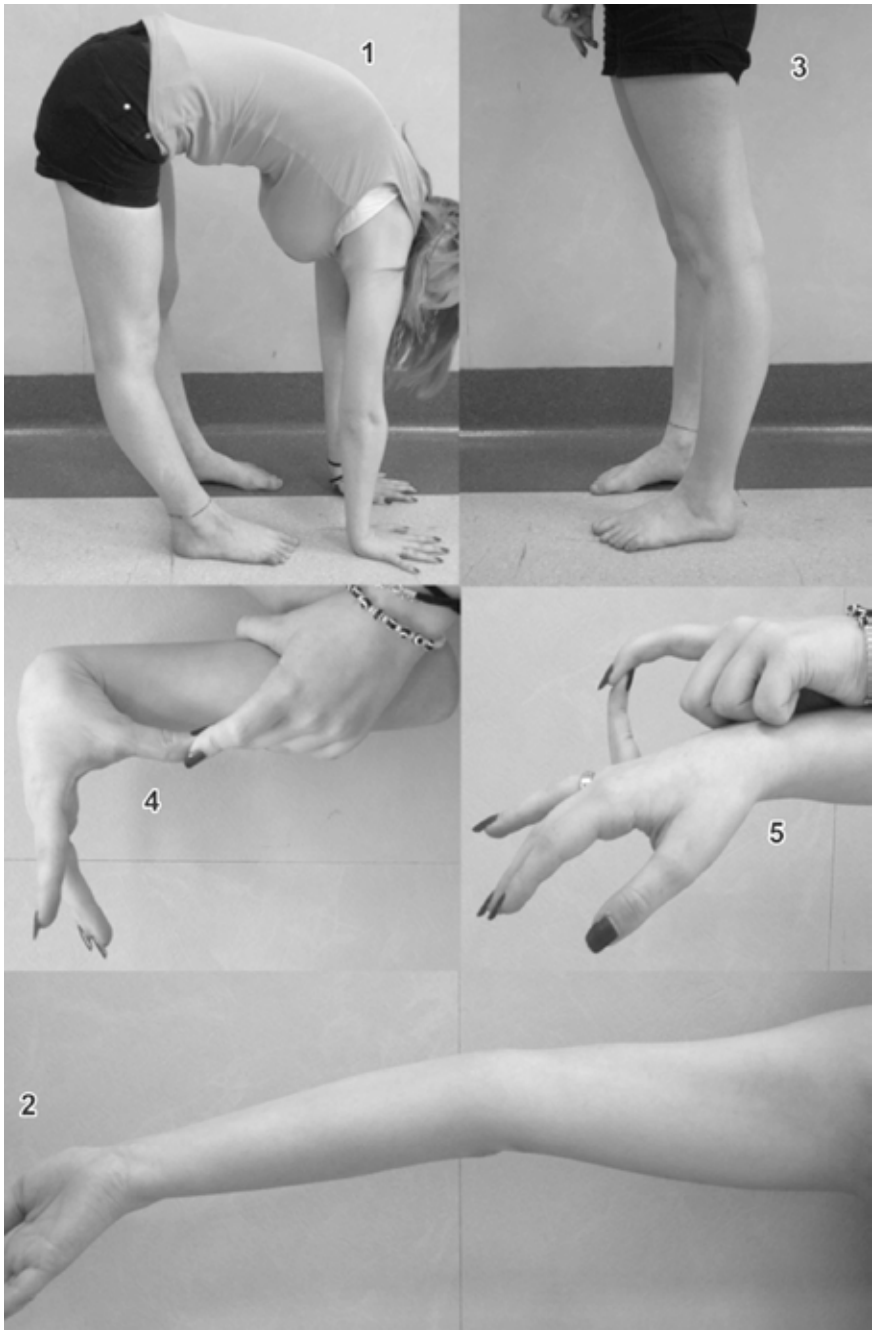

Fig. 1. The Beighton test for evaluate hypermobility.

Table 2. The Brighton Criteria.

Revised diagnostic criteria for JHS	
Major criteria	A Beighton score of 4/9 or greater (Either currently or historically)
	Arthralgia for longer than three months in four or more joints.
Minor criteria	A Beighton score of 1,2,or 3/9 (0,1,2,or 3 if aged 50+)
	Arthralgia (over three months) in one to three joints or back pain (over three months), spondylosis, spondylolysis/spondylolisthesis
	Dislocations/subluxations in more than one joint, or in one joint or more than one occasion
	Soft tissue rheumatism with more than three lesions (e.g. epicondylitis, tenosynovitis, bursitis)
	Marfanoid habitus: tall, slim, span/height ratio >1.03, upper: lower segment ratio less than 0.89, arachnodactyly (positive Steinberg/wrist sign)
	Abnormal skin: striae, hyperextensibility, thin skin, papyraceous scarring
	Eye signs: drooping eyelids or myopia or antimongoloid slant.
	Varicose veins or hernia or uterine/rectal prolapse.
JHS is diagnosed in the presence of two major criteria, or one major and two minor criteria, or four minor criteria. Two minor criteria will suffice where there is an unequivocally affected first degree relative.	

major and two minor, or four minor are satisfied. Recently there has been a lively debate as to whether JHS and the hypermobility type of the Ehlers-Danlos syndrome (EDS-HT) are the one and same, or whether they represent two phenotypically related conditions. This remains an area of contentious debate among clinical experts but currently it has been clearly and unequivocally expressed that JHS and EDS-HT represent the same phenotypic group of patients that can be differentiated from other HCTD, but not distinguished from each other (13).

Ehlers-Danlos syndrome (also known as "cutis hyperelastica") is a group of inherited connective tissue disorders caused by a deficit in the synthesis of collagen (14). The syndrome is named by two doctors, Edvard Ehlers of Denmark and Henri-Alexandre Danlos of France, who identified it at the turn of the 20th century. From the 10 types of subforms of Ehler-Danlos syndrome (EDS), in 1997 a group of researchers proposed a simple classification of six major forms (see Table 3) characterized by different gene mutation; except for the hypermobility type, whose diagnosis is only clinical, the specific mutations involved have been identified and can be done by genetic testing.(12)

The absence of a genetic test and of an accurate description on how to perform the clinical tests used to make the clinical diagnoses, urgent need to develop a standard protocol for the assessment of joint mobility taking age, gender and ethnic origin into consideration; it is also necessary to consider other aspects like the predominance of females in the affected group, the presence of signs and symptoms of dysautonomia in an apparent subset, the emergence of unexplained pain that did not match the overt findings, gastrointestinal involvement and the association of other psychological features (15).

Accordingly, based on registered data on the frequency of generalized JHM in various populations and the assumption of an ~10% chance of developing symptoms according to the Brighton criteria for "double-jointed" people, a presumed frequency of 0.75-2% has been proposed for JHS. As general JHM is rarer among Caucasians compared to other populations such as Africans (16), a frequency of 0.2–0.6%, with the lowest value better fitting for men and the highest for females, appears more realistic in Europe and USA. However, no systematic study accurately investigated these aspects (17).

Clinical aspects

JHS relates to the faulty collagen proteins that affect the body systemically. This implies that symptoms may be varied and may interest not only the musculoskeletal system.

In particular there are three major types of hypermobility and any one person will have varying combinations of these types with one that may be predominant: the bony hypermobility, the collagen- related hypermobility and the neuropathic hypermobility (5) and any one will have varying combinations of these types of hypermobility but one type may be predominate (18).

The Bony Hypermobility is mainly characterized by shallow joint sockets that might dislocate easily and the involvement of joint articular surfaces; the collagen-related hypermobility show signs like stretchy skin, weak bladder, bowel lung and cardiac symptoms; the neuropathic hypermobility occurs with proprioceptive defects, clumsy gait and late walkers when children, core instability (5).

Three clinical phases have been described in this syndrome (19). The hypermobility phase with marked ligamentous laxity begins during the first months of life. The pain phase starts during the second decade and is characterized by a relative decrease in hypermobility and the development of joint muscle and back pain. Chronic pain and joint instability progressively limit daily activities. The stiffness phase with progressive limitation of joint motion develops later (19).

We will try to analyze everyone aspects and manifestations of this syndrome in a rehabilitative point of view, attempt to give a preventive approach and management.

Orthopedics manifestations

Firstly described by Ainsworth and Aulicino in 1993 (20), the musculoskeletal manifestations of EDS-HT are varied and are quite often the first symptoms reported. Patients often report back and neck pain, scoliosis, joint pain associated or not with swelling and dislocations, limited function at lower and upper limbs, difficulties in walking and climbing stairs (21).

Beighton in the 1969 observed among the orthopedics aspects, that the most common foot deformity was severe pes planus (52%), which was usually asymptomatic (22).

Table 3. The Villefranche six forms of Ehlers-Danlos syndrome.

TYPE	CLINICAL MANIFESTATIONS		Protein	IP	Gene
	Major criteria	Minor criteria			
Classic (Type I/II)	Skin hyperextensibility Widened atrophic scarring Joint hypermobility	Easy bruising Smooth and velvety skin Molluscoid pseudotumours Subcutaneous spheroids Muscular hypotonia Complications of joint Hypermobility Surgical complications Positive family history	Type V procollagen (~50%)	AD	Col5a1 Col5a2
Hypermobility (Type III)	Generalized joint hypermobility Mild skin involvement	Recurring joint dislocations Chronic joint pain Positive family history	Tenascin X (~5%)	AD	Tnx-B
Vascular (Type IV)	Excessive bruising Thin, translucen skin Arterial/intestinal/uterin fragility or rupture Characteristic facial appearance	Acrogeria Early onset varicose veins Hypermobility of small joints Tendon and muscle rupture Arteriovenus or carotid-cavernous sinus fistula Pneumo(hemo)thorax Positive family history, sudden death in close relative(s)	Type III procollagen	AD	Col3a1
Kyphoscoliotic (type VI)	Sever muscular hypotonia at birth Generalized joint laxity Kyphoscoliosis at birth Scleral fragility and rupture of the globe	Tissue fragility including atrophic scars Easy bruising Arterial rupture Marfanoid habitus Microcornea Osteopenia	Type VIa: lysyl-hydrohylase 1 Type VIB: not known	AR	LH-1
Arthrochalasis (type VII A)	Severe generalized joint hypermobility with recurrent subluxations Congenital bilateral hip dislocation	Skin hyperextensibility Tissue fragility, including atrophic scars Easy bruising Muscular hypotonia Kyphoscoliosis Mild osteopenia	Type I procollagen	AD	Col1a1 Col1a2
Dermatosparaxis (type VIIC)	Severe skin fragility Sagging, redundant skin Excessive bruising	Soft, doughy skin texture Premature rupture of membranes Large hernia	Procollagen-N-proteinase	AR	Adamts-2

Recently Berglund (23) showed that individuals' with EDS endure difficulties with their mobility due to their foot problems but no specific information about foot were described. Galli (24) and Pau (25) have investigated the different type of foot in JHS/EDS-HT patients using baropodometric platform and shows an high incidence of pes cavus during upright position. These results are useful to identify the most effective treatment to reduce the pain caused by foot's problems.

JHM is also considered (26) a risk factor for temporomandibular joint (TMJ) disorders. Since constitutional hypermobility can affect all joints, which would include the TMJ, a correlation exists between JHM and temporomandibular dysfunction (TMD) and is shown by different studies.

In particular JHM can influence the physiological movement of the TMJ causing secondary problems; Ancillao et al (27) showed that EDS-HT/JHS subjects have poor control and stability of the mandible while opening and closing; moreover, the medio-lateral RoM of the chin in EDS-HT/JHS group resulted higher than controls; the ratio between right and left RoMs of the condyles was higher in EDS-HT/JHS group suggesting a significant asymmetry in the mandible movement. A possible explanation is that the lack of proprioception may also influence this joint (see later).

Osteoarthritis is described as premature and associated with an increased risk of articular dysfunction, in particular, regarding the temporomandibular joint, the knee and the hand in JHS/EDS-HT patients (28). Different are the determinants in the developing of osteoarthritis and are the most unknown.

A study conducted to evaluate lower limb dysfunction and the correlations with age, Beighton score and pain intensity in a group of JHS/EDS-HT patients, demonstrated that the extent of lower limb dysfunction is remarkable and comparable with a population of patients with OA (29); there is a correlation between intensity of pain and lower

limb dysfunction and the degree of disability increases with age and decreases with the Beighton score. From this data it can be inferred that higher degree of JHM is a good indicator for high functionality of the lower limbs and the maintenance of hypermobility may be a protective factor to prevent osteoarthritis.

Gait abnormalities

Patients with JHS/EDS-HT display a constellation of musculoskeletal complaints, but no longer show overt joint hypermobility. In fact, hypermobility not only determines passive hyperextension of joints but, more importantly, is likely to cause complex and still poorly understood biomechanical consequences on movement patterns. JHS/EDS-HT individuals showed non-physiological gait pattern. In particular Galli et al. (30) showed low values of anterior step length, an high excursion of pelvic tilt during the gait cycle, with no differences in terms of pelvic position on the frontal and transversal plane; hip and knee joint revealed physiological values while the ankle joint shows the feet in a plantarflexed position at initial contact with a reduced dorsiflexion during stance and swing phase; peak plantarflexion moment and power generated at ankle joint in the terminal stance showed reduced values suggestive of reduced ability to generate ankle power during gait cycle.

Hypotonia and ligament laxity, which are major features of JHS/EDS-HT are very probably the most important factors influencing reduced joint stiffness; the reduced plantarflexion at initial contact and reduced dorsiflexion ability may suggest a tibialis anterior weakness and reduced calf muscle strength of the triceps surae (30), mostly responsible for the generation of ankle power, may ineffectively contract during terminal stance. These features imply, that in JHS/EDS-HT patients, the rehabilitation program should be focused on ankle strategy improvement to optimize gait pattern and prevent the onset of compensatory strategies (31).

Rehabilitation aspects

Fatigue

Fatigue is considered the reduced capacity to sustain force or power output (physiological) reduced capacity to perform multiple tasks over time (psychological) and simply a subjective experience of feeling exhausted, tired, weak or lacking of energy (32). The perception of fatigue is subjective and no exact definition exists because of overlap between the lay notion of tiredness and the clinically relevant symptom of fatigue (33).

Voermans (34) showed that fatigue is a frequent and clinically relevant problem in EDS related to sleep disturbances, concentration problems, social functioning, self-efficacy concerning fatigue, and pain. Besides concentration problems, which are likely a result of chronic fatigue, all the remaining are possible causes for fatigue combining together in different ways case by case. Furthermore, muscle weakness has been recently outlined as a contributing factor to fatigue in EDS (35).

Overall it is not clearly defined what the determinants are in the development of fatigue in EDS-HT/JHS patients that is, more than pain, disabling (Celletti, unpublished data) and the major determinants for such severe deterioration of the quality of life in these individuals (36).

The intensity of fatigue has been demonstrated to be correlated with the peak of vertical component of ground reaction force during walking (37); the negative correlation gives evidence that the higher the fatigue is, the more reduced force there is during gait. These data may suggest that muscle fatigue may be associated with a loss of proprioceptive acuity in various lower limb muscles, that means a peripheral component in generating fatigue that should be treated with an appropriate rehabilitation approach. The reduced generated force during gait may also be a consequence of the foot pain and of difficulties with their mobility due to their foot problems (38); the high frequency of flexible flat foot in JHS/EDS-HT patients (unpublished data) should itself unfold this problem.

Kinesiophobia

"Kinesiophobia" or movement phobia is defined as "an excessive, irrational and debilitating fear of physical movement and activity resulting from a feeling of vulnerability to painful injury or re-injury", and it has been reported as a common feature of patients with CFS (39), fibromyalgia and chronic low back pain (40). Pain-related fear can be defined as the fear that emerges when stimuli that are related to pain are perceived as a main threat. People with EDS-HT/JHS suffer chronic pain that is often made worse by any kind of movement as a management strategy; but avoiding movement leads to muscle deconditioning, which is detrimental in patients with unstable joints, and further contributes to pain increase.

Kinesiophobia is a common symptom in JHS/EDS-HT, in association with pain and fatigue, but the probable correlation with the severity of fatigue rather than the intensity of pain shows that kinesiophobia may contribute to the progression and, perhaps, onset of fatigue by bodily disuse secondary to decreased physical effort (41).

Presence of Kinesiophobia may be evaluated using the Tampa Scale for Kinesiophobia that is a scale translated into and validated in different languages including Italian (42).

Rehabilitative management may take into consideration the presence of this symptom in order to establish type, intensity and frequency of exercises, in particular, in the initial phase of return to physical exercises.

Postural instability

Postural stability is defined as the ability to maintain or control the center of mass (COM) in relation to the base of support (BOS) to prevent falls and complete desired movements. Balancing is the process by which postural stability is maintained. The ability to maintain a posture such as balancing in a standing or sitting position, is operationally defined as *static balance*. The ability to maintain postural control during other movements, such as when reaching for an object or walking across a lawn, is operationally defined as dynamic balance. Both static and dynamic postural

controls are thought to be important and necessary motor ability (43).

Patients with JHS/EDS-HT presented some difficulties in the goal of maintaining Centre Of Pression (COP) inside the base of support. Normally, during standing, ankle and hip joint work in a co-contraction manner in order to limit the degrees of freedom that postural structures have to control, thanks to the integration of visual, vestibular and proprioceptive system. Since JHS/EDS-HT patients present impairments related to hyperlaxity and consequently muscle weakness, their joints result unstable increasing their mobility. This means that they increased the COP excursion during standing. Moreover they present a significant increasing of COP excursion during standing with closed eyes that means the impairment of the proprioceptive system correlated to the lack of visual information in the integration process of postural stability (44).

EDS-HT patients have a degraded postural control and act in negative sense on somatosensory postural control feedback, increasing the attentional demands of visual and vestibular feedback systems: this is translated in less automaticity of the postural system, evidenced by a lower value of entropy (45).

In general, it has been observed that JHS/EDS-HT patients present difficulties in controlling COP displacements, trying to keep it inside the base of support using the plantarflexor muscles (ankle strategy) alone, and pointing out that EDS-HT patients must rely also on hip strategy in order to avoid the risk of falling (45).

Proprioception

Proprioception is a term coined by Charles Sherrington in 1906 that means the perception of one's self; this is a sensory modality based on receptors densely packed in the muscles and in tendons and called the "secret sixth sense". Proprioceptors precisely measure physical proprieties, such as muscle length, tendon tension, joint angle and deep pressure. Signals from this sensory orchestra are sent by afferent nerves through the spinal cord to the somatosensory, motor and parietal cortices of the brain, where the continuously feed and update the sensory-motor maps of the body (45).

A poor sense of proprioception could explain why people with JHS become injured, having a lack of sensation of the joint at the end of the range. In hypermobile people the proprioceptors are basically not given the right feedback. The reason underlying why JHS patients have poor proprioception may be the tissue laxity of the soft tissue; proprioceptors are unable to give the right feedback (47) and the body is continuously getting the "wrong" motor information about where it should be. Impaired proprioception has been described in various joints of JHS/EDS-HT patients (48-50). More interestingly, the entire postural control and balance seems disrupted in JHS (51).

Gastroenterology aspects

Patients with JHS/EDS-HT often complain of gastrointestinal symptoms like gastro-esophageal reflux, poor digestion, bloating and altered defecation (constipation and/or diarrhea), symptoms of delayed gastric emptying, recurrent abdominal pain. The potential pathophysiological factor is the laxity of the supporting ligamentous structures that may have a role also in the digestive system. Patients often referred also to swallowing difficulties and occasionally dysphagia. Unpublished data (Badiali) reveal that these symptoms are probably due to a muscular incoordination that, like what happens in the other districts, is responsible for dysfunctions and related symptoms.

A recent study demonstrating an increased rate of celiac disease in JHS/EDS-HT adds complexity to the study of connections between connective tissue and bowel function (52).

Cardiologic manifestations

Cardiovascular involvement is a feature of many connective disorders including JHS/EDS-HT. In addition to a known mitral, tricuspid, and aortic valve mild regurgitation, an instrumental evaluation of cardiac functioning in JHS/EDS-HT patients show different abnormalities; in particular the electrocardiographic data shows an electrical disturbance involving the automatism, the inter-atrial and the atrio-ventricular conduction; the Holter analysis shows a more evident atrio-ventricular conduction disturbances during the night (I and II degree atrio-ventricular blocks) and the origin of the impulse in the sino-atrial node (ectopic atrial rhythm, sinus arrhythmia, sin-atrial block). (Danese unpublished data).

Moreover patients with JHS/EDS-HT described symptoms like tachycardia, light-headedness, nausea, headache and syncope that are caused by an autonomic nervous system alteration named POTS, postural orthostatic tachycardia syndrome (53).

Pain

Pain is a complex experience that depends strongly on cognitive, emotional, and educational influences. In particular, pain can be categorized into three types: inflammatory or nociceptive, neuropathic and dysfunctional pain (54). Inflammatory or nociceptive pain can arise from an injury to integrity of tissue either by trauma or infection, and associated conditions include headaches, arthritis and appendicitis; neuropathic pain is defined by trauma or pathological changes in the central or peripheral nervous system and often responds poorly to standard pain treatment; the dysfunctional pain can be ascribed to nerve dysfunction and is thought to underlie conditions such as fibromyalgia and migraine, and is often poorly characterized by non-localized diffuse pain which is not accompanied by overt tissue inflammation or nerve pathology (54).

Pain is a prominent component of many rheumatologic conditions and it is the result of a complex physiologic interaction of central and peripheral nervous system signaling that results in a highly individualized symptom complex (55). Chronic pain (a pain that generally is more than 3 months' duration) is not simply acute pain that has lasted longer; it is more likely influenced by input from the central nervous system, whereas acute pain is often attributable primarily to inflammation and/or damage in peripheral structures. There are also central factors that alter pain processing by setting

the "gain" such that when peripheral input is present, it is processed against a background of central factors that can enhance or diminish the experience of pain (55).

JHS is a condition wherein pain is the major problem. Pain appears following a trauma with acute features and quite often remains indefinitely, becoming chronic. The reasons why some hypermobile people present pain and exhibit the syndrome while others remain asymptomatic is still unclear. There is no doubt that the most hypermobile people quite often have no pain; hypermobility can cause pain but there is not a direct relationship. People who are fitter physically and take part in sport seem to be better protected than those who take less exercise.

Pain in JHS has been described to be chronic, nociceptive or neuropathic (56). Recently it has been shown, using specific scales to evaluate the kind of pain, that EDS-HT/JHS patients frequently have a neuropathic chronic pain (57). This implies that the pathophysiology of pain in EDS may be more complex than expected, and that musculoskeletal involvement cannot explain the entire spectrum of pain.

In recent years, neurobiology of pain is increasingly understood and is suggested cortical reorganization to be as a consequence of central plasticity (i.e. changes that occur in the nervous system) in chronic pain; neuroplasticity is related to the propagation of pain, long after the original cause is gone, depriving pain of its functional role and becoming the disease itself (58).

Another hypothesis may explain the presence of chronic pain in EDS-HT/JHS patients: it's known that the discordance between awareness of motor intention, muscle and joint proprioception and vision may result in feeling pain like what happened in patients with phantom limb (59). Parietal cortex is the brain structure that receives convergent information from sensory receptors, and is involved in constructing a unified body image. Like what happen in different chronic pathology (lower back pain, foot cramps in runner etc.), the incongruence between motor intention, proprioception and vision, limited as a consequence of the disease, causes the appearance of pathological pain (59).

The rehabilitative approach needs to treat pain not only with traditional techniques (analgesics, anti-inflammatories, physical therapies, etc.), but also with therapies directed at restoring the integrity of the cortical information processing.

Peripheral neuropathy

Peripheral nerves are vulnerable to trauma secondary to hypermobility and the entrapment neuropathies are found to be more common in JHS/EDS-HT patients (60). These conditions are responsible for symptoms such as numbness, tingling and burning pain.

Conversely an extensive clinical, neurophysiological and ultrasonographic (US) examination of the involvement of the peripheral nervous system, with particular attention to entrapment syndromes, JHS/EDS-HT patients showed an inconsistency between symptoms and neurophysiological and ultrasound evidences of focal or diffuse nerve involvement (61). The study showed instead an increase of incidence in the occurrence of ulnar nerve subluxation and luxation at elbow in the JHS/EDS-HT patients that could be explained by the presence of Osborne ligament laxity. Probably more than a nerve disease, patients with JHS/EDS-HT may have a very mild and transient nerve involvement.

Cephalalgia

Headache is a highly disabling form of pain in EDS (62). In JHS/EDS-HT, migraine seems the most common form of headache (63). A study the aim of which was to describe the prevalence, frequency and main characteristic of migraine headache in an Italian population of JHS/HT-EDS patients, comparing it with a control population of migraine patients attending an outpatients headache clinic and to assess possible differences regarding clinical aspects of migraine, founded that JHS/EDS-HT patients have a substantially stronger headache syndrome in respect to normal migraineurs, regarding both headache frequency and its characteristics. In fact JHS/EDS-HT patients seem to be significantly more phonophobic, have a stronger mean intensity and higher frequency of migraine days per month, as well as an earlier onset of the disease, usually in a childhood age. Nonetheless, ED patients tend to assume significantly less pain medication/per month than the control group, and not because drugs are less efficient. Most patients in the EDS group seem to be simply more accustomed to pain, as they directly explain.(unpublished data)

Psychiatric aspects

Anxiety disorders have been associated with JHS/EDS-HT, probably because a high rate of medically unexplained symptoms and chronic pain is observed in these patients (64); other studies reported a very high rate of panic disorder (41.4%) (65) and other anxiety disorders (66, 67) in these patients.

In a single-center case-control study a psychiatric evaluation based on the structured clinical interview for DSM-IV criteria using the SCID-I and the SCID-II showed an unexpected high prevalence of personality disorders (21%), and of Axis-I disorders (38%), mostly depressive; they did not observe a high rate of panic disorders, as previous studies reported (68). Even though panic disorder is a complex condition not reducible to somatic anxiety, the role of dysautonomia might be a confounding factor as previously discussed by the other authors (66, 69).

Pediatric manifestations

A greater range of joint motion is present in children than adults, and the frequency of musculoskeletal disorders arising from such hypermobility in childhood is quite variable (70). Children with JHS have been recognized to have potentially pathological consequences of hypermobility. As early as birth, specific problems related to hypermoblility are the congenital dislocation of the hip and the congenital (benign) hypotonia or "floppy infant syndrome"; later, children with JHS/EDS-HT may present clumsiness and/or poor coordination, a delay in walking, growing pain and recurrent joint sprain (71). Speech and learning difficulties were founded during childhood (71) and perceptive/attentional disorders and apraxia are often present (unpublished data).

Not infrequently children present pain and fatigue in the hand when they start writing at school or difficulty in tasks such as music lessons. When they start sport activities, not infrequently, they complain of back pain due to the typical adolescent posture characterized by exaggerated lumbar lordosis and compensated thoracic kyphosis, giving the typical round-shouldered appearance. Joint pain may be referred to the shoulders, the hips, the knees and the elbows, the metacarpophalangeal joints and the ankles.

The successful management includes the early recognition of all these symptoms that child may present at different ages and that may become chronic and disabling if not correctly treated.

Principles of Rehabilitative approach

Patients with JHS/EDS-HT show a "poor posture" that means that they have a tendency to rest at the end of joint range and have a poor postural alignment (72); they have difficulties in standing or sustaining a position for a long time and they prefer to take a position which requires decreased muscle work like standing with hyperextended knee, lumbar hyper lordosis, ankle joint held in plantarflexion; moreover they use a "bracing" pattern with breath holding in attempt to improve stability and produce more force with the consequence of increasing abdominal pressure, that may be responsible of some symptoms previously described (72). In addition to this, patients suffer from instability and reduced proprioception (both joint position sense and detention of movement are impaired) that progressively determine a reduced movement and secondary deconditioning. For a rehabilitative program, the first goal to obtain is to improve proprioception and to reduce the fear of movement.

An approach to improve proprioception may be the use of repetitive muscle vibration that may minimize the consequences of an interruption of visual input on posture control. Focal muscle vibration was demonstrated as a highly selective stimulus for Ia spindle afferents. In fact, vibratory stimulation with specific parameters (i.e., frequency of 100 Hz, peak-to-peak amplitude of 0.20–0.50 mm) may activate different mechanoceptors, in particular spindle afferents and Golgi tendon organs. Activation of peripheral contractile elements strongly influences the activity of the γ-motoneuron system, and therefore the muscle spindle in providing afferent information. The tonic spindle activation is able to induce long-term primary motor cortex reorganization, characterized by an enduring increase of intracortical and cortical reciprocal inhibition (73). Also if evaluated in a single case, the application of focal muscle vibration shows to be able to increase joint stability by improving muscle strength in order to facilitate muscle cocontraction; in particular, it was hypothesized that the dynamic stabilization process of co-contraction may be inhibited by abnormal firing of afferent mechanoreceptors. Repetitive muscle vibration may be a good alternative also for patients in an advanced stage of the disease in order to improve proprioception and, consequently, increase stamina (73).

Another possible approach may be the use of Neuromuscular Taping (NMT) that has been proved to be effective in various musculoskeletal conditions. Although its precise working mechanism has yet to be fully understood, it is believed to interact with neuromuscular function through mechanoceptor activation (74). NMT is elastic tape that differs from the traditional cotton non-elastic tape because of its ability to stretch up to 140% of its original length, thereby providing a constant shear force on the skin. NMT was conceived to be therapeutic and, according to its creators, yields the following results: it corrects muscle function by strengthening weak muscles; it improves blood and lymph circulation by eliminating tissue fluid or bleeding beneath the skin through muscle movement; it reduces pain through neurological suppression; it corrects misaligned joints by relieving muscle spasm (75).

Even Hydrotherapy may be particularly useful to improve proprioception and reduce muscle spasm (4).

Also Feldenkrais Method balance classes may be effective in improving balance; current theories of motor skill acquisition and postural control, provide a sound theoretical basis for the effectiveness of the Feldenkrais approach in improving balance (76) and may be effective in JHS/EDS-HT patients .

Generally, JHS/EDS-HT patients refer to a specialist when a history of chronic pain (secondary or not to recurrent sprain or joints lesions) associated with fatigue and consequently deconditioning has been occurring. Usually a specific rehabilitation treatment is not necessary or may be non-resolving thought it can be temporarily effective; occasionally the condition tends to self-resolve. Sometimes a specific rehabilitation treatment may even deteriorate the situations for a wide variety of reasons.

A rehabilitative approach has to consider firstly the treatment of the back problems: in fact, almost all patients complain of lower back pain and clinically present core instability; paravertebral muscles are hypotonic and the spinals processes are always painful. Core stability exercise is the name given to the strengthening of the corset of muscles surrounding the back and abdomen. These muscles are also known as the 'core' or powerhouse muscles and provide a solid base upon which all other muscles can work upon to initiate movement. The principle muscles involved are the trasversus abdominus, multifidis muscles, the diaphragm and the pelvic floor muscles.

In particular, the diaphragm is the muscle that contributes to the intra-abdominal pressure modulation and plays an important role in spine stability; therefore an insufficient function and/or poor coordination of this muscle may affect how the trunk is stabilized, especially during postural activity (77).

Secondly in all patients present, associated to hypermobility and hypotonic muscles, contracted muscles that are frequently very painful; for example evaluating lower limb strength it is frequently observed that the quadriceps femoral is weak and the tensor's fascia lata is painful to the touch, and needs to be stretched and can often cause the hip to click.

In the acute phase may be usefull to normalize the spine working with the Fascia (78).

When patients have to restart exercises or movements they have to consider a progression program and every activity they want to start they have to think of as a "Bradipo" (Camerota personal communication). In order to avoid fatigue they have to estimate the baseline of activity (that may

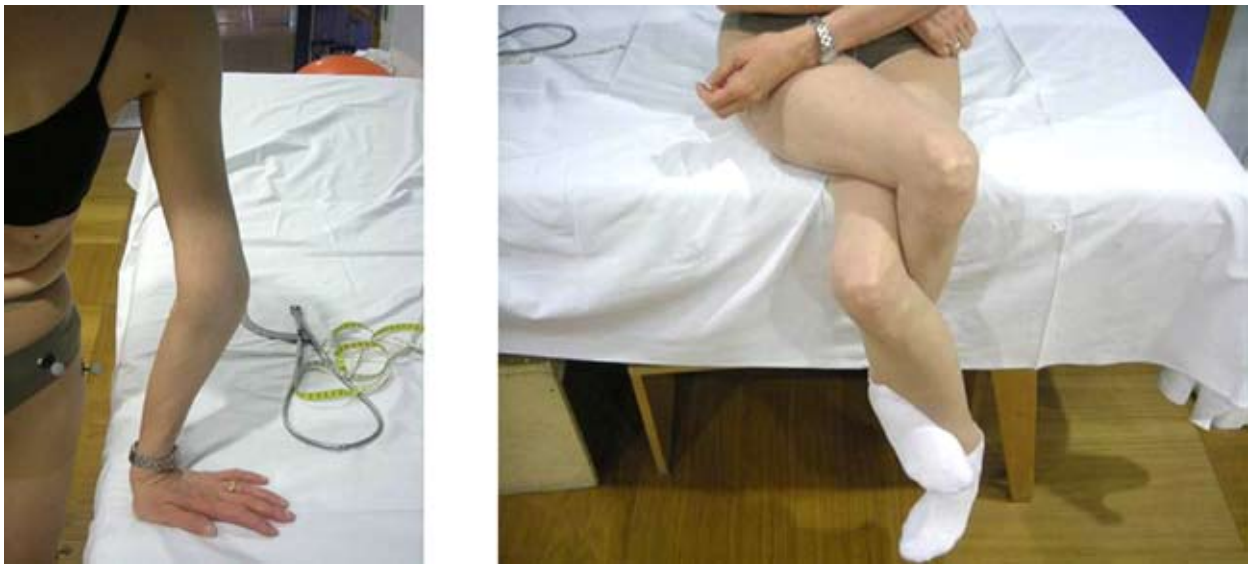

Fig. 2. Patient's contortionism.

be walking or standing or doing a specific exercise or sport activity); to get the baseline they have to measure the time tolerance (time that does not imply pain or fatigue) in two consecutive days, adding it, divide by two and minus 20 per cent. The time obtained is the activity baseline, and every day, a patient may increase the activity by only 1 unit. This measurement is also valid for the exercise number.

Patients have to avoid all treatment which requires maintaining a posture for a long period because this may be responsible for fatigue and pain.

Conclusion

JHS/EDS-HT is a complex and multifaced syndrome that involves all the systems, with particular involvement of the musculoskeletal one. Management of this syndrome is multidisciplinary, considering all the symptoms referred by patients but the role of the rehabilitation is of particularly interest: fatigue, pain, joint instability, functional limitations are all conditions that may benefit from a correct rehabilitative approach.

Muscle strengthening, controlled exercises, a world built on their body would bring out extraordinary qualities from these patients like: excellent dancers, athletes, gymnasts and riders; it is enough to remember Paganini whose hand transformed a growth into a violin bow.

The extraordinary nature of the hypermobility patients, that often seems to be contortionist (see figure 2), can be traced back to the Scythian legendary origin, to the Greek Heracle hero who joined Echidna, a serpent-woman with a hypermobile body.

The correct management of this syndrome may change the clinical history of these patients helping them to use their hypermobility.

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