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Posted Date: 6 January 2025

doi: 10.20944/preprints202501.0328.v1

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Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 6 January 2025 doi:10.20944/preprints202501.0328.v1

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The Experience of Pain in Hypermobility Ehlers Danlos Syndrome: Having No Words for Feelings and Sharing Emotions. The Alexithymia Role

Filippo Camerota [1,*], Rachele Mariani [2], Giada Petronelli [3], Beatriz Rabissi [2], Marta A.S. Vizzini [2], Michela Di Trani [2], Valentina Roselli [4], Massimo Pasquini [5], Alessia Renzi [2] and Claudia Celletti [6]

[1] Physical Medicine and Rehabilitation Division, Umberto I University Hospital, Rome, Italy
[2] Department of Dynamic and Clinical Psychology and Health Studies, "Sapienza" University of Rome, Via degli Apuli 1, 00185 Rome, Italy
[3] Health Professions of Rehabilitation Sciences Degree, Sapienza University of Rome
[4] Department of Neurosciences and Mental Health, Umberto I Policlinic, Rome 00185, Italy
[5] Department of Human Neurosciences, Sapienza University, Rome 00185, Italy
[6] Department of Life Science, Health, and Health Professions, Link Campus University, Rome, Italy
* Correspondence: filippo.camerota@uniroma1.it

Abstract: Background: Hypermobility Ehlers Danlos syndrome (hEDS) is a clinical condition characterized by hypermobility and tissue fragility and associated to chronic pain**.** The present study aimed to investigate the associations between affect regulation, pain perception and psychophysical dimensions. **Methods:** Twenty-five hEDS patients completed tests assessing pain experience, pain intensity, emotion regulation, alexithymia and quality of life. A regression analysis was performed on the total sample, in order to investigate the relationship between alexithymia, pain, emotional regulation and perception of quality of life. **Results:** A high percentage of alexithymia emerged**.** Negative significant associations emerged between quality-of-life scale and both emotion regulation scale and scales as well as with alexithymia scale and difficulties in identifying and describing feelings. Moreover, a relationship between hEDS and psychological variables concern the time of diagnosis appear. **Discussion:** Patients with hEDS seems to refer alexithymia; pain seems to interfere with practical aspects of daily life, and may reduce an individual's awareness of their emotional capabilities. Perception of heightened pain has a stronger impact on emotional resources when it interferes with affective life, rather than with practical life. Finally, delayed diagnoses of hEDS entail psychological consequence such as alexithymia. **Conclusion:** All these aspects may interfere with the possibility of patients to be understood for clinicians and a particular attention is needed also to define the rehabilitative approach.

Keywords: alexithymia; Ehlers Danlos syndrome; emotion; pain; quality of life; rehabilitation

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1. Introduction

Ehlers-Danlos syndrome are an heterogenous group of hereditary connective tissue disorders mainly characterized by hypermobility and tissue fragility [1]. The International Classification of EDS and related disorders published in 2017 identifies thirteen clinical subtypes, which are distinguished according to the differential expression of the main phenotypical hallmarks, presence of additional distinctive features and/or inheritance pattern [2].

A fourteenth type of EDS resembling classic EDS but inherited in an autosomal recessive pattern was described associated with biallelic variants in the AEBP1 gene [3].

doi:10.20944/preprints202501.0328.v1

The most common type is hypermobile Ehlers-Danlos syndrome (hEDS; formerly EDS type III) characterized by joint hypermobility, chronic musculoskeletal pain, and skin abnormalities and easy bruising.

Associated to all these symptoms, often patients complain severe pain [4] that influence quality of life and contribute to exhibit personality disorders [5]. Different studies report a considerable excess of emotional symptoms and psychological distress, and somatosensory amplification [6].

Research indicates that affect regulation—namely, the ability to manage the experience and expression of emotions—plays a significant role in understanding the manifestation of symptoms in different medical conditions [7]. Affect dysregulation is considered a risk factor for the development of both physical and mental health diseases as well as for the severity of the disorders [8]. As specifically regards the psycho-physical health, a broader literature confirms the presence of higher levels of affect regulation deficits in several somatic and mental conditions compared to healthy controls [9–11]. Moreover, variations in emotional awareness and affect regulation capabilities may be connected to the experience of pain in chronic conditions [10,12]. Several constructs within this area have been explored and debated and among them one specific is the alexithymia, that has garnered significant theoretical and empirical focus over the past few decades [12] . Alexithymia is a multidimensional construct characterized by challenges in recognizing and articulating emotions, limited imaginative processes, and a tendency toward an externally focused cognitive style [11,13]. More recently, it has been redefined as an emotion-dysregulation disorder, encompassing difficulties in using imagination to manage painful emotions, finding creative solutions to problems, or effectively communicating needs to others to gain social support [9,11]. In general, people showing difficulties in the emotional regulation abilities tend to report an increased number of somatic symptoms especially in stressful, negative or threatening situations as may be considered suffering from hEDS [14,15]. As a consequence of this, individuals with high alexithymia-affect dysregulation, often experience stronger clinical pain in afflicting situations [16–19]. A systematic review with meta-analysis revealed that alexithymia was significantly and positively associated with pain intensity and physical interference in chronic pain samples, but when controlled for negative affect-related measures alexithymia was no longer significantly related to pain intensity or interference [12]. Accordingly, the association between alexithymia and pain intensity and interference may be may be accounted for by negative affect. A recent study revealed greater difficulty in identifying and describing emotions among patients with somatoform pain and depression: while this challenge is partly influenced by elevated levels of depressive feelings, it also persists independently of negative affect [15]. Therefore, Lankes et collegue [15] concluded that affect regulation difficulties may worsen the burden of pain and may contribute to a poorer outcome. The association between affect regulation and pain is still controversial producing contrasting results and thus needing to be further explored. To the best of the Authors’ knowledge no previous studies exploring the affect regulation construct in association to psychophysical health, pain and disabilities in patients suffering from hEDS have been realized.

The general aim of present study is to explore the associations between affect regulation, pain perception and psychophysical dimensions in patients affected by EDS. All of this with the broader aim of enriching the knowledge on this clinical population suffering from a rare and difficult to diagnose condition.

The hypothesis is that to greater difficulties in affect regulation, as evaluated by both high alexithymia and affect regulation deficits, will correspond a greater perception of pain as well as a worsen psycho-physical health.

2. Methods

All patients studied have attended a multidisciplinary service dedicated to Hereditary Connective Tissue Disorders and were followed into the “joint hypermobility” outpatient clinic in the Division of Physical Medicine and Rehabilitation of the Umberto I University Hospital (Rome, Italy). They have been included into this study if they have met the 2017 criteria for diagnosis of hEDS, if other neurological conditions have been excluded.

Patients has been clinically evaluated and different scale have been administered in a period of totally 3 months.

The following measures has been used to evaluate these patients:

- *Socio-Demographic Questionnaire*: A socio-demographic questionnaire was specifically designed to collect information concerning age, gender, education level, social status, occupation, and information about the disease.
- *Difficulties in Emotion Regulation Scale (DERS)* [20,21]. It is a 36-item self-report questionnaire designed to evaluate challenges in emotion regulation, particularly those associated with negative emotions. The scale includes six subscales: Nonacceptance of Negative Emotional Responses (6 items), Difficulties Engaging in Goal-Directed Behavior When Distressed (5 items), Difficulties Controlling Impulsive Behaviors When Distressed (6 items), Lack of Emotional Awareness (6 items), Limited Access to Effective Emotion Regulation Strategies (8 items) and Lack of Emotional Clarity (5 items). Each item is rated on a 5-point scale, ranging from 1 (almost never) to 5 (almost always), and subscale scores are obtained by summing the respective items. The DERS has demonstrated robust psychometric properties. It shows strong test–retest reliability and high internal consistency across clinical and nonclinical populations [22–24].
- *20-item Toronto Alexithymia Scale (TAS-20)* [25,26] It is the most widely employed self-report measure to assess alexithymia through 20 item divided into three distinct dimensions: difficulty identifying feelings (DIF), difficulty describing feelings (DDF), and externally oriented thinking (EOT). Participants respond to each item using a 5-point Likert scale ranging from "strongly disagree" (1) to "strongly agree" (5). The scale yields a total score as well as scores for the three subscales, with total scores ranging between 20 and 100, higher scores indicate higher alexithymia level. The TAS-20 cut-off scores are as follows: ≤ 51 no alexithymia, 52–60 borderline alexithymia, ≥ 61 alexithymia. The TAS-20 has demonstrated satisfactory psychometric properties, including internal consistency and strong test–retest reliability.
- *The Short Form 36 (SF-36)* is a generic, widely used, multidimensional tool divided into 8 scales, designed to assess overall health status and captur the impact of a disease on various dimensions of quality of life, e Physical Component Summary (PCS) and Mental Component Summary (MCS) were calculated according to the method developed by Ware et al. [27,28] The SF-36 measures eight domains of Health-related quality of life including: Physical Functioning (PF), Role-Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role-Emotional (RE), and Mental Health (MH). For each domain, a score was calculated and was transformed to a value from 0 to 100.
- *Brief Pain Inventory (BPI)* [29,30] it is a well-recognized tool used to evaluate the severity of pain and its impact on various aspects of a patient's daily life. BPI is a patient self-reported 11-point numerical rating scale that measures the severity of pain and the interference of pain on function. There are 4 questions assessing worst pain, least pain, average pain, and pain right now. The scores range from 0 (no pain) to 10 (pain as severe as you can imagine). The BPI measures both the intensity of pain (sensory dimension) and interference of pain in the patient's life (reactive dimension) that are activity and affective sub-dimensions (stanhope 2016). It also queries the patient about pain relief, pain quality, and patient perception of the cause of pain. The BPI is a self-administered measure of the sensory and reactive dimensions of pain—that is the severity or intensity of the pain and the level of interference it has on various aspects of life.

3. Statistical Analyses

The statistical analyses for the present study were executed by means of the Statistical Package for Social Science—24 (SPSS version 24, Armonk, NY). Continuous variables are described as means and standard deviations whereas the discrete variables were reported as percentages and frequency. Pearson's correlation analysis was employed to evaluate the associations between affect regulation measures, pain disabilities and health measures as well as age and time since the diagnosis. A p value < .05 was considered significant.

4. Results

Twenty-eight patients have been recruited, but 3 of them have not fully completed the questionaries; among the 25 patients have studied, only two were male; the mean age at the evaluation was 38.2 ± 17.03.

The socio-anamnestic characteristics of the sample as well as the means and standard deviation to all the measures administered are reported respectively in Tables 1 and 2.

Table 1. Socio demographic characteristics.

TabSocio-anamnestic characteristics		
Variables	**M/ n.**	**SD/ %**
Age	38.32	17.01
Time since diagnosis	9.08	6.16
Employment status		
Unemployed	4	16
Employed	15	60
Student	6	24
Educational Qualification		
Middle School Diploma	3	12
High School Diploma	15	60
Bachelor's degree	5	20
Postgraduate degree	2	8
Marital status		
Single	14	56
Cohabiting	3	12
Married	7	28
Separated	1	4
Children		
Yes	14	56
No	11	44

Table 2. Participants' psychophysical measures investigated.

Variables	**M**	**SD**
Difficulties in Emotion Regulation Scale		
Total score	92.24	36.80
Non Acceptance	16.84	8.00
Goals	14.80	5.88
Impulse	14.92	8.14
Awareness	15.12	6.42
Strategies	18.48	9.11
Clarity	12.08	5.49
20-item Toronto Alexithymia Scale		
Total score	53.36	12.92
DDF Difficulty Describing Feelings	21.28	8.03
DIF Difficulty Identifing Feelings	15.12	4.72
EOT Externally-Oriented Thinking	16.96	4.85
Short Form-36 item health survey		
Physical Functioning	56.40	24.85

Role Physical	19.00	27.27
Role Emotional	44.00	38.15
Vitality	33.60	15.31
Mental Health	56.80	19.86
Social Functioning	48.50	22.62
Bodily Pain	38.80	16.75
General Health	26.20	16.85
Brief Pain Inventory		
Pain Intensity	5.01	2.13
Pain Interference	4.64	2.39
Activity pain interference	4.93	2.40
Affective pain interference	4.65	2.64

Considering the different scale administered, TAS-20 results showed a 28% of patients with alexithymia and 36 % with borderline value for alexithymia. Regarding the SF 36 scale the Role Physical and Vitality elements showed the worst perception.

Correlational analysis revealed several significant associations between affect regulation measures and the other dimensions investigated (see Table 3). Psychophysical health, as evaluated trough the SF-36 instrument's dominions, showed several significant associations with both affect regulation measures employed. Specifically, several negative significant associations emerged between SF-36 scales and both DERS total and scales as well as with TAS-20 total and difficulties in identifying and describing feelings (see Table 3).

Table 3. Associations between affect regulation dimensions and psycho-physical and anamnestic variables.

	DERS Total	**DERS Non-Acceptance**	**DERS Goals**	**DERS Impulse**	**DERS Awareness**	**DERS Strategies**	**DERS Clarity**	**TAS-20 Total**	**TAS-20 DIF**	**TAS-20 DDF**	**TAS-20 EOT**
SF-36 Physical Functioning	0.266	0.217	0.153	0.291	.403*	0.154	0.142	0.373	0.277	0.243	0.298
SF-36 Role Physical	-0.157	0.265	-0.237	-0.205	-0.293	-0.176	0.177	-0.340	-0.358	-0.180	-0.215
SF-36 Role Emotional	0.010	0.325	-.674**	-.558**	-.701**	-.462*	-0.272	-.719**	-.752**	-.476*	-.559**
SF-36 Vitality	-0.178	0.001	-0.343	0.007	-0.199	-0.219	-0.241	-0.215	-0.090	-.406*	-0.029
SF-36 Mental Health	-.732**	-.687**	-.618**	-.560**	-.460*	-.763**	-.609**	-.680**	-.605**	-.480*	-0.340
SF-36 Social Functioning	-0.232	-0.154	-0.221	-0.221	-0.013	-0.267	-0.305	-0.084	-0.118	-0.139	0.109
SF-36 Pain	-0.045	-0.080	-0.062	0.102	0.132	-0.165	-0.149	-0.133	-0.110	-0.114	-0.060
SF-36 General Health	-0.266	-0.051	-.426*	0.011	-0.321	-0.271	-.444*	-0.153	-0.070	-0.303	0.003
BPI Intensity	-0.168	-0.062	-0.070	-0.225	-0.392	-0.111	0.018	-0.084	0.062	-0.240	-0.093

BPI Interference	0.148	0.187	0.190	0.039	-0.251	0.307	0.242	0.160	0.356	-0.027	-0.137
Bpi activity interference	-0.059	0.029	0.031	-0.154	-.439*	0.124	0.066	-0.012	0.206	-0.140	-0.237
Bpi affective interference	0.307	0.298	0.322	0.170	-0.041	.421*	0.372	0.310	.448*	0.133	-0.046
Time since diagnosis	-.530**	-.466*	-.546**	-.618**	-.190	-.435*	-.419*	-.180	-.472*	-.138	.453*

BPI intensity of pain scale showed only a significant and negative association with DERS difficulties engaging in goal-directed behaviour when distressed whereas no significances emerged as regards the BPI scale pain interference with daily life (see Table 3).

As specifically regards the anamnestic variables explored significances emerged for both age and time since the diagnosis. Specifically, age resulted negatively associated to SF-36 pain scale (r= -.530; p=.026). The time since the diagnosis resulted negatively associated to both DERS total and several dominions and TAS- 20 difficulties in describing feelings as well as a positive association with externally orientated thinking (see Table 3).

4. Discussion

Our study aimed to examine the relationship between pain and quality of life in relation to specific psychological variables in patients with hEDS. Our research question focused on understanding how pain is experienced by these patients and its role in the organization of their daily lives. To the best of our knowledge, this is the first study to address this aspect. We hypothesized that difficulties in affect regulation, as indicated by high levels of alexithymia and deficits in emotional regulation, would be associated with a greater perception of pain and poorer psycho-physical health.

Upon analysing the correlations between the pain scales and the alexithymia and affect regulation scales, we observed that the relationship between pain and emotional regulation appeared to be independent. Specifically, the two pain scales, measuring intensity and overall interference, did not show significant correlations with emotional regulation. However, the BPI-Practice subscale revealed a significant negative correlation with the emotional regulation awareness strategy. This finding suggests that when pain interferes with practical aspects of daily life, it may reduce an individual's awareness of their emotional capabilities.

This insight highlights the intricate interplay between physical pain and emotional regulation, particularly in the context of hEDS, and underscores the importance of addressing both physical and emotional dimensions in therapeutic interventions.

In a different direction, a correlation emerged between emotional regulation capabilities, specifically the ability to find strategies, and pain perception interfering with affective life. This positive correlation indicates that as pain is increasingly felt in the emotional domain, greater coping abilities are required. This finding suggests that the perception of heightened pain has a stronger impact on emotional resources when it interferes with affective life, rather than with practical life.

Notably, the higher the affective perception of pain, the more it is associated with a reduction in emotional awareness. This result aligns with previous research demonstrating that negative emotions amplify pain perception and, conversely, that heightened pain perception can exacerbate negative emotional states [31]. While there is no significant relationship between pain intensity and emotional regulation, similar results were found regarding the relationship between alexithymia and pain. There was no significant correlation between alexithymia factors and pain intensity; however, a positive correlation was observed between pain perception that interferes with affective life and the alexithymia factor "Difficulty Identifying Feelings." These results suggest that pain perception interfering with emotional life may be a risk factor for psychological health.

The findings between emotional regulation, alexithymia, and quality of life reveal inverse correlations for the factors of Mental Health and Role of Emotion [32]. The negative significant correlations show that the higher the quality of emotional life and mental health, the greater the ability to regulate emotions and stay in touch with one's feelings. This result is consistent with the idea that a good ability to navigate one's emotional world is possible when it is not impaired by pain perception. In fact, a positive correlation was found between physical function quality and difficulty in being aware of one's emotional strategies.

Finally, the most intriguing results from this first study examining the relationship between hEDS and psychological variables concern the time of diagnosis. As we know, a critical factor for these patients is the time it takes to diagnose their condition, with the average time to diagnosis being at least 10 years [33]. Our results show that the longer the time since diagnosis, the greater the ability to emotionally regulate and recognize one's own emotions. This finding underscores the importance of early diagnosis to better understand one's physical functioning and learn to manage chronic pain.

However, a counterintuitive result emerged: the time since diagnosis correlates positively with the alexithymia factor of externally oriented thinking. This suggests that knowledge of one's illness and the development of emotional awareness may trigger defensive strategies, leading to distraction and less constant reflection on one's inner world. Instead, coping strategies are often more focused on the practical and concrete aspects of life.

The major limitation of this study is the little number of patients; however, we decided to obtain data only from patients directly evaluated; considering an overall prevalence of the disorder of one in 5000, our results are representative for a population of 125.000 individuals and, therefore, can be considered quite significant.

Studies on a larger population related also with major clinical data are desirable to confirm and better explain our results.

In conclusion, we have found the presence of alexithymia in hEDS population like in other conditions of chronic pain (for example fibromyalgia), and that alexithymia has a strictly relation with pain. Patients have always an impairment in the recognition of their own emotions that make often difficult to describe their situation and to be understood in particular from clinicians. These results also confirm the utility of metaphors [34] as a tool for examining illness experience able to help clinicians in understanding patient perception and in particular for helping them in the management of pain [35].

Author Contributions: All authors have substantially contributed to this work and have approved this manuscript version. Conceptualization F.C., R.M, C.C; Methodology, A.R., G.P., B.R.; Software, A.R, M.V.; Validation, V.R., M.P., R.M.; Formal Analysis, A.R, M.D.T.; Investigation, G.P., B.R.; Data Curation, R.M., C.C., A.R.; Writing—Original Draft Preparation, F.C., R.M., A.R., C.C., ; Writing—Review & Editing, F.C., R.M., M.P., C.C.; Visualization, G.P., B.R., M.V., M.D.T., V.R.; Supervision, F.C., R.M., C.C.".

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflicts of interest.

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