

## Biophysical Parameters Mediate the Relationship between Anxiety and Gait Characteristics: A Sub-Analysis

Ron Feldman<sup>1\*</sup>, Shaul Schreiber<sup>2,3,4</sup>, Chaim G. Pick<sup>1,4,5</sup>, Ella Been<sup>1,6</sup>

<sup>1</sup>Department of Anatomy and Anthropology, Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel

<sup>2</sup>Department of Psychiatry, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

<sup>3</sup>Tel-Aviv University Sackler Faculty of Medicine, Tel-Aviv, Israel

<sup>4</sup>Sagol School of Neuroscience, Tel Aviv University, Tel Aviv, Israel

<sup>5</sup>The Dr. Miriam and Sheldon G. Adelson Chair and Center for the Biology of Addictive Diseases, Tel-Aviv University, Tel-Aviv, Israel

<sup>6</sup>Department of Sports Therapy, Faculty of Health Professions, Ono Academic College, Kiryat Ono 55107, Israel

\*Corresponding author: Ron Feldman, Department of Anatomy and Anthropology, Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, 69978, Israel

**Citation:** Feldman R, Schreiber S, Pick CG, Been E (2021) Biophysical Parameters Mediate the Relationship between Anxiety and Gait Characteristics, a Sub-Analysis. Yoga Phys Ther Rehabil 6: 1080. DOI: 10.29011/2577-0756.001080

**Received Date:** 03 February, 2021; **Accepted Date:** 18 February, 2021; **Published Date:** 22 February, 2021

### Abstract

**Background:** Gait disturbances are common in psychiatric population and in patients with anxiety. Even though people with anxiety show slower walking velocity, the effect of the biophysical factors on their gait characteristics has not been examined. This study examines whether pain, balance, muscle strength and general joint hypermobility (GJH) mediate the relationship between anxiety and gait.

**Methods:** A sub-analysis was conducted on a recent one-year observational study, which was conducted at a psychiatric outpatient unit, in a large Israeli general hospital.

**Results:** Pain and static balance were found to mediate the relationship between anxiety and gait velocity and step length. The relationship between anxiety and step length was also mediated by GJH. The findings suggest that both pain, balance and GJH affect gait velocity and step length in people with anxiety.

**Limitations:** The study did not randomize subjects into groups nor enlisted a blind procedure for the researcher or the participants.

**Conclusions:** It is thus recommended to consider these components, specifically pain, and balance when planning a physical gait assessment and intervention for people with anxiety.

**Keywords:** Pain; Balance; General joint hypermobility (GJH); Gait velocity; Step length; Mental health.

### Highlights

- Biophysical elements influence gait characteristics in people with anxiety.
- Pain and balance mediate the relationship between anxiety and gait velocity.

- GJH, pain and balance mediate the relationship between anxiety and step length.
- Balance and pain are major mediators that effects the relationship between anxiety and gait.

### Introduction

Human gait is a fundamental function that enables us to move from one place to another. In healthy individuals, the most

influential factors on gait velocity include pain, balance, muscle strength, and GJH [1-6]. Asymmetrical gait pattern and slow gait velocity were found in individuals suffering from musculoskeletal pain [7-10]; Patients with balance dysfunction often demonstrate gait disturbances and slow gait velocity, thus suggesting that balance plays a major role in maintaining normal walking speed [11-13]; weak lower limb and trunk muscles can lead to slow walking velocity [6,14,15]; and Generalized Joint Hypermobility (GJH) is associated with slower walking velocity and increased incidence of musculoskeletal injury [1,16], probably as a result of pain and joint instability that is more common in individuals with GJH [5,17].

Gait disturbances are common in the psychiatric population and were recently reported in patients with anxiety [18-22]. These disturbances are thought to reflect impaired cortical and subcortical function [23,24].

Although a number of studies have examined gait in the context of anxiety disorder [18,19,21,25,26], and the biophysical components affecting walking speed in humans is well documented [2,4,6,27,28], to the best of our knowledge, no study examined the biophysical factors that influence gait characteristics in patients with anxiety.

Therefore, the current study aims to evaluate which biophysical components (pain, balance, muscle strength and GJH) affect gait characteristics (velocity, step length and cadence) in a group of people with anxiety. To do so, we will (a) assess group differences in gait and biophysical parameters between people with anxiety and healthy individuals; (b) examine the relationship between biophysical components (pain, balance, GJH, and muscle strength) and gait characteristics; and (c) evaluate whether these biophysical components mediate the relationship between anxiety and gait characteristics.

## Method

### Study Setting, Design and Population

This is a sub-analysis of a former observational study from our lab (Feldman et al., 2019), where we examined a group of individuals suffering from anxiety symptoms (rather than a diagnosed anxiety disorder) and a healthy control group of individuals without anxiety. The study was approved by the hospital's IRB (Approval number 0447-16-TLV). A total of 93 participants were divided into two groups: An anxiety group consisting of 48 participants (27 female, 21 male), who were being treated and examined at the Tel Aviv Sourasky Medical Center's psychiatric outpatient clinic, and a control group of 45 participants (25 female, 20 male), who were under examination at the Department of Anatomy and Anthropology, Sackler Faculty of Medicine at Tel-Aviv University. Both groups consisted of various ages and mixed genders. The observations and data collection were conducted between January 2017 and May 2018. For further information on study participants, please see Feldman et al., (2019) [21].

### Inclusion Criteria

The following criteria served as a prerequisite to participation in the study:

**Research group:** Patients (men and women, 18-65 years of age) at a psychiatric outpatient clinic who displayed anxiety symptoms ( $\geq 14$  on the Hamilton Anxiety Rating Scale) and possessed sufficient knowledge of the Hebrew language (needed to comprehend and complete the research questionnaires).

**Control group:** Volunteers (men and women, 18-65 years of age) without anxiety symptoms ( $\leq 5$  on the Hamilton Anxiety Rating Scale), recruited from Tel-Aviv University, who possessed sufficient knowledge of the Hebrew language (needed to comprehend and complete the research questionnaires).

### Exclusion Criteria

The following exclusionary criteria were enforced: Any pre-existing psychotic condition, any major affective condition (either mania or depression), a neurological or neuropsychological disorder (e.g., head injury), an orthopedic disorder that causes gait difficulties, vestibular issues or dizziness, cardiovascular disease, inability to comprehend questions on the research instruments, fever at the time of participation or trauma that may cause pain. No one was excluded based on the HAM-A score. Exclusion criteria for the anxiety group were decided upon according to their medical records, and the group was kept under the control and supervision of the head of the psychiatric outpatient clinic at Tel Aviv Sourasky Medical Center, whereas the exclusion criteria for the control group were based on self-report.

### Procedure

Participants were asked to fill a consent form, and then answer the following three questionnaires:

- A socio-demographic and medical questionnaire (see Table 1);
- The Hamilton Anxiety Rating Scale (HAM-A) [29]. The top cut-off point in the scale is 14 points and the bottom cut-off point is 5. A score greater than or equal to 14 suggests clinical anxiety, which classifies the participant in the anxiety group. A score lower than or equal to 5 classifies the participant as healthy. A score between 5 and 14 suggests that the person has partial and nonclinical anxiety symptoms.
- Pain intensity was rated on the numeric rating scale (NRS) with a score range between 0 (no pain) and 10 (high-intensity pain) [30,31].

Participants underwent a series of physical examinations following the questionnaire.

Variables	Control group (N = 45)	Anxiety group (N = 48)	p
Gender (M/F)	25/20	27/21	0.95
Age (years)	40.8 (12.62)	40.3 (12.84)	0.85
Weight (kg)	67.3 (14.95)	72.5 (22.01)	0.19
Height (m)	1.6 (0.09)	1.7 (0.14)	0.65
BMI (Kg/m <sup>2</sup> )	23.9 (4.17)	24.9 (5.95)	0.60
Education (years)	13.3 (1.82)	12.4 (1.77)	0.14
HAM-A (score)	2.2 (1.75)	35.9 (11.92)	<0.001
Hand dominance (RT/LT)	39/6	44/4	0.32

Frequencies and descriptive statistics of study participants. The first six variables are presented as means, with standard deviations provided in parentheses. The last two variables (hand dominance) are presented as frequencies (n). Kg – Kilogram; BMI – Body Mass Index; HAM-A – Hamilton Anxiety Rating Scale; Hand Dominance: RT – Right; LT – Left.

**Table 1:** Baseline participant characteristics.

### Physical examination

The principal researcher, a certified physiotherapist, conducted the physical assessment.

A 10 MWT (10-meter walking test) was used to measure spatiotemporal gait parameters. The test was conducted in a 20-meter long corridor and consisted of a 14-meter path. Participants were asked to walk 10 meters, with an added 2 meters for acceleration and another 2 for deceleration. Four points along the course were marked with adhesive tape, denoting the two ends of the 10-meter walkway, and the acceleration and deceleration point. The acceleration and deceleration points were disregarded in the data collection. Verbal instructions (in Hebrew) were given before the test: “I will say: ready, set, go. When I say ‘go’, walk as safely as you can in your normal, comfortable speed until I say stop.” Time was measured with a stopwatch from the moment the participants crossed the starting line, up to the moment they passed the 10-meter mark, completing a 10-meter walk at a comfortable pace. Walking time and the number of steps were used to determine spatiotemporal gait parameters. The average time and number of steps in three paths were documented [32-36]. Eventually, mean gait velocity (m/sec), step length (m) and cadence (steps/sec) were calculated for each participant.

The Unipedal Stance Test (UST) was used to assess static balance. Participants were asked to stand barefoot on one foot, cross their arms over their chest, then raise their other leg toward the ankle of their weight-bearing leg without touching it. The participants were asked to focus on a spot on the wall in front of them, at eye level. A stopwatch was used to measure the duration of time the participant was able to stand on one foot, from the moment the participant raised their foot off the floor until the moment the participant either: (1) used their arms (i.e., uncrossed them); (2) used their raised foot (moved it toward or away from the standing leg or

touched the floor); (3) moved the weight-bearing foot to maintain balance (i.e., rotated foot on the ground); or (4) a maximum of 45 seconds had elapsed. The process was repeated three times. The average duration of all three trials was recorded [37,38].

GJH was evaluated using the Beighton Criteria, a standard assessment tool employed in clinical settings that was used in multiple studies in the evaluation of joint hypermobility presence. It assesses participants’ ability to perform nine maneuvers, which helps evaluate the joint range of motion at five separate areas in the body: right and left passive dorsiflexion of the pinky toe at 90° or more; right and left passive opposition of the thumb to the flexor aspect of the forearm; right and left elbow hyperextension at 10° or more; right and left knee hyperextension at 10° or more; and forward flexion of the torso, with knees extended and both palms laid flat on the floor. Points were allocated for completion of each maneuver, with the maximum score being 9 (successful completion of all 9 items) and the minimum being 0 [5,39]. A Beighton score of 4 or higher signified GJH [5,39-41], and was therefore used as the cutoff point according to which outcomes were assessed.

JAMAR Hand Grip Dynamometer was used to evaluate muscle strength. It should be acknowledged that hand grip, an instrumental muscle strength measure, can be used as a tool for the rapid indication of general body muscle strength [42,43]. Participants were asked to sit with their shoulders adducted and neutrally rotated, elbow flexed at 90°, forearm in a neutral position, and wrist between 0° and 30° dorsiflexion and between 0° and 15° ulnar deviation. Once properly positioned, the participants were given specific verbal instructions (in Hebrew): “Squeeze as hard as you can, harder! Harder! And relax.” The score of three successive trials for each hand was recorded. The average score of the three trials compared to the normative data was measured in kg [42-45].

**Statistical Analysis**

The statistical analysis was conducted using SPSS v24 (IBM Corp., Armonk, NY, USA), with a p-value of <0.05 defined as statistically significant. Normality of distribution was assessed using the Kolmogorov-Smirnov test. Step length and all distributions of the biophysical parameters were not normal. Differences between study groups in terms of socio-demographic and anthropometric variables and in-study variables were explored using t,  $\chi^2$  and Mann-Whitney tests, according to variables' scales and normality. Linear relationships between gait characteristics and biophysical parameters were evaluated using Spearman correlations. Mediation models were tested using Process command [46] Model 4. Process command estimates the 95% confidence interval (CI) of the indirect effect of the independent variable (IV) (i.e., anxiety) on the dependent variable (DV) (i.e., gait characteristics), by comparing the observed indirect effect against a bootstrapped distribution constructed from 1,000 parallel data sets. Each simulated parallel data set was constructed by randomly sampling from the observed data set with replacement. If the CI does not include zero, the in-

direct (mediated) effect is significantly different than zero [46,47].

**Results**

The results presented here include our new findings regarding pain, GJH, correlations and mediation effect combined with our previous findings regarding gait, balance, and muscle strength (see: Feldman et al., 2019) [21]. No significant differences were found between the two groups in terms of socio-demographic and anthropometric variables (Table 1). Furthermore, as expected, the anxiety group scored significantly higher on the Hamilton Anxiety Rating Scale than the control group (p<.001) (Table 1).

Group differences were found in all three-gait characteristics and three out of four biophysical components (Table 2). In the anxiety group, gait velocity and cadence were lower, step length was shorter, the pain was stronger, and the UST score was lower (indicating shorter time spent standing on one leg), Beighton score was higher (indicating GJH), compared to the control group. The groups did not differ in muscle strength in either right or left hands (Table 2).

	Control group (N=45)		Anxiety group (N=48)		Group difference
	M	SD	M	SD	
Gait velocity	1.42	0.13	1.12	0.17	t(91)=9.48***
Step length	0.69	0.08	0.63	0.08	U=664.50***
Cadence	124.56	10.67	106.93	9.7	t(91)=8.34***
Pain	0.64	1.82	5.85	3.44	U=261.00***
UST	44.23	2.3	28.18	14.48	U=367.00***
GJH	1.6	1.56	4.52	2.21	U=322.50***
Hand grip RT	29.49	10.60	26.93	12.87	U=919.00
Hand grip LT	27.35	10.97	25.21	12.46	U=950.00

UST – Unipedal Stance Test; GJH – Generalized Joint Hypermobility; RT – Right; LT – Left; \*\*\*p≤.001.

**Table 2:** Group differences in gait and biophysical parameters.

Table 3 presents the relationships between gait characteristics and biophysical parameters. As can be seen in the table, in the entire sample, biophysical parameters were significantly correlated to gait characteristics, with one exception: The correlations between muscle strength measures and cadence were insignificant.

	Gait velocity	Step length	Cadence
Pain	-.67***	-.43***	-.52***
UST	.66***	.52***	.47***
GJH	-.52***	-.33***	-.35***
Hand grip RT	.30**	.64***	-.13
Hand grip LT	.30**	.66***	-.14

UST – Unipedal Stance Test; GJH – Generalized Joint Hypermobility; RT – Right; LT – Left; \*\*p<.005, \*\*\*p≤.001.

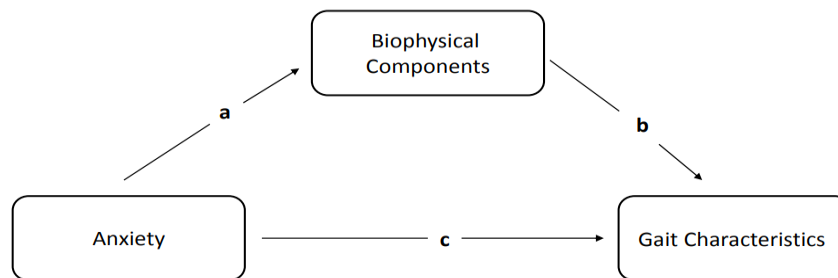
**Table 3:** Correlations between gait and biophysical parameters.

Mediation effects of biophysical parameters on the relationship between anxiety and gait characteristics were explored using Process command, model 4, on SPSS. The basic mediation model is presented in Figure 1. The unstandardized path coefficients indicating the effects of anxiety on the mediators – biophysical parameters (path a), the effects of the mediators on gait characteristics (path b) and the direct effect of anxiety on gait characteristics (path c) are presented in Table 4. The estimations of the indirect effects, including the bootstrapping CIs, are also presented in Table 4.

DV	Mediator	Path a		Path b		Path c		Indirect effect (bootstrapping)	
		B (SE)	T	B (SE)	t	B (SE)	t	B (SE)	95% CI
Gait velocity	Pain	5.19 (0.58)	8.91***	-0.02 (0.00)	-3.44***	-0.20 (0.04)	-4.85***	-0.10 (0.03)	-0.17; -0.05
	UST	-16.05 (2.19)	-7.34***	0.00 (0.00)	3.05***	-0.23 (0.04)	-5.98***	-0.07 (0.02)	-0.12; -0.02
	GJH	2.92 (0.40)	7.32***	-0.01 (0.01)	-1.34	-0.27 (0.04)	-6.74***	-0.03 (0.03)	-0.11; 0.02
	Hand grip RT	-2.56 (2.45)	-1.04	0.00 (0.00)	3.91***	-0.29 (0.03)	-9.71***	-0.01 (0.01)	-0.05; 0.01
	Hand grip LT	-2.15 (2.44)	-0.88	0.01 (0.00)	4.15***	-0.29 (0.03)	-9.86***	-0.01 (0.01)	-0.04; 0.01
Step length	Pain	5.19 (0.58)	8.91***	-0.01 (0.00)	-2.95**	-0.01 (0.02)	-0.72	-0.04 (0.01)	-0.08; -0.02
	UST	-16.05 (2.19)	-7.34***	0.00 (0.00)	2.79**	-0.02 (0.02)	-1.27	-0.03 (0.01)	-0.05; -0.01
	GJH	2.92 (0.40)	7.32***	-0.01 (0.00)	-2.12*	-0.03 (0.02)	-1.63	-0.03 (0.01)	-0.06; -0.01
	Hand grip RT	-2.56 (2.45)	-1.04	0.00 (0.00)	7.02***	-0.05 (0.01)	-3.68***	-0.01 (0.01)	-0.03; 0.01
	Hand grip LT	-2.15 (2.44)	-0.88	0.00 (0.00)	7.69***	-0.05 (0.01)	-3.90***	-0.01 (0.01)	-0.03; 0.01
Cadence	Pain	5.19 (0.58)	8.91***	-0.33 (0.39)	-0.85	-15.76 (2.93)	-5.38***	-1.71 (2.06)	-5.75; 2.32
	UST	-16.05 (2.19)	-7.34***	0.06 (0.10)	0.6	-16.65 (2.68)	-6.22***	-0.98 (1.49)	-3.60; 2.34
	GJH	2.92 (0.40)	7.32***	0.51 (0.56)	0.92	-19.12 (2.66)	-7.18***	1.50 (1.79)	-2.34; 4.94
	Hand grip RT	-2.56 (2.45)	-1.04	-0.22 (0.09)	-2.49**	-18.18 (2.07)	-8.80***	0.56 (0.69)	-0.36; 2.41
	Hand grip LT	-2.15 (2.44)	-0.88	-0.24 (0.09)	-2.71**	-18.14 (2.05)	-8.84***	0.51 (0.71)	-0.49; 2.32

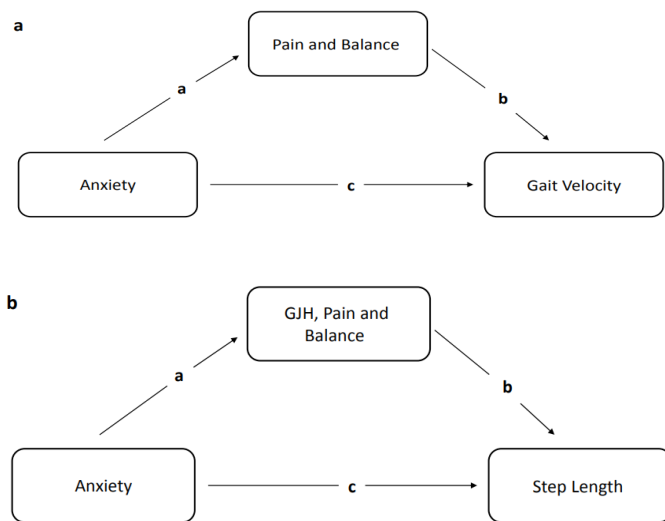
DV- Dependent Variable (gait velocity, step length, cadence); UST – Unipedal Stance Test; GJH – Generalized Joint Hypermobility; RT – Right; LT – Left; \*p<.05, \*\*p<.01, \*\*\*p<.001, #p=.06. Path a= effect of anxiety on the mediator; Path b= effect of the mediator on the DV; Path c= direct effect of anxiety on the DV. The coefficients are unstandardized.

**Table 4:** Single mediation models for the relationship between anxiety and gait characteristics.



**Figure 1:** Mediation model; Path a= effect of anxiety on the mediator; Path b= effect of the mediator on dependent variables (DV); Path c= direct effect of anxiety on the DV.

Anxiety had a direct effect on all gait characteristics, i.e. velocity, cadence and step length (path c). On top of that, as can be seen in Table 4, pain and UST mediated the relationship between anxiety and gait velocity, and the relationship between anxiety and step length (Figure 2a+b). The relationship between anxiety and step length was also mediated by GJH (Figure 2b). Thus, anxiety was related to higher levels of pain and GJH, and lower levels of balance, which in turn were related to lower gait velocity and step length (Table 4). Cadence was not mediated by biophysical parameters.



**Figure 2:** Mediation models for the relationship between anxiety and gait characteristics; a. Gait velocity model, b. Step length model.

## Discussion

While the previous study demonstrated the differences in gait characteristics between people with anxiety to healthy individuals [21], the current study reveals the biophysical parameters that contribute to these differences. Our findings indicate that anxiety is related to higher levels of pain and GJH, and lower levels of balance, which in turn are related to lower gait velocity and step length. Specifically, the significant components that influence gait velocity were pain and balance; and the significant components that influence step length were pain, balance and GJH. Cadence was only affected directly by anxiety, with no mediation of biophysical components. Therefore, the differences in gait velocity and step length between healthy individuals and people with anxiety stem from a combination of the anxiety itself and poor balance, higher level of pain and higher levels of GJH found in these patients. This should not come as a surprise to us, since balance, pain and GJH are known to influence gait characteristics in healthy individuals. On the other hand, while in healthy individuals muscle

strength has an important role in gait velocity, we found no such relationship in people with anxiety.

Balance is a dominant factor that influences gait in people with anxiety, as a deficit in balance is expressed in slow walking speed and short step length. This is in agreement with previous studies, which showed that balance impairment may lead to walking speed declines and shorter steps [2,11-13,48-51]. It is also in agreement with studies that showed a strong relationship between balance disorders and anxiety in a number of young and adult populations [11,52-54]. Anxiety can, directly and indirectly, influence balance control, either by producing an ineffective balance response or by masking or modifying underlying balance deficits.

Pain had a significant correlation with all three gait characteristics. It was therefore not surprising to find that pain was a dominant mediator influencing the relationship between anxiety and walking speed. Pain appears to be a unique domain as a cause of disablement. Given the fundamental nature of walking and the fact that it is an oft-prescribed activity for patients with anxiety [55], it is important to have a better understanding of the effect of pain on walking [4]. Just as the relationship between pain and spatiotemporal gait parameters is well documented in chronic orthopedic disorders [8,9,20,56], so is the relationship between pain and anxiety [57,58]. Pain is an important domain in people with anxiety [57], and is often overlooked by practitioners when it comes to patients with mental disorders [59,60]. Our results suggest that when aiming to improve gait in people with anxiety, pain should be taken into consideration.

Studies propose a number of mechanisms that may explain this relationship [58,61,62]. Hayashi et al. (2016) [20] suggest that a vicious cycle of fear-avoidance may be initiated when the pain prompts dysfunctional interpretations. Anxiety and avoidance of activity lead to deteriorated muscle strength and, consequently, limited activity, e.g., gait. Pain-related fear and anxiety-induced responses (e.g., avoidance, hypervigilance, disuse, disability) may in turn lower the threshold at which subsequent pain will be experienced.<sup>20</sup> Respectively, it can be assumed that people with anxiety are more prone to pain disturbances, which in turn, influence their gait characteristics, i.e., they tend to walk slower and have a shorter step length.

The results of the study demonstrate a direct relationship between anxiety and GJH, as measured by the Beighton score. A moderate and significant positive correlation was found between GJH and gait velocity, revealing a correlation between a high score on the Beighton scale and slow gait in people with anxiety. Finally, GJH has a strong mediation effect on decreasing step length. These results are consistent with previous studies that reported a strong relationship between joint hypermobility syndrome and anxiety disorders, from young children to older adults [63-67]. GJH is associated with reduced trunk stability, slow walking velocity,

higher joint moments during walking and increased incidence of musculoskeletal injury and pain [1,5,16,68].

Although there is no definitive evidence in the literature of the efficacy of a specific training regimen for people with GJH [69], it has recently been found that an 8-week training program that emphasizes spinal stabilization exercises is essential for pain reduction, spinal stability, and increase the endurance of thoracic strength among women with GJH [70]. Such an exercise regimen could potentially be beneficial to people with anxiety.

In accordance with previous studies that support the notion of muscle strength as a major biophysical component affecting spatiotemporal gait characteristics in humans [6,14,71], we found similar a relationship between muscle strength and gait characteristics in our sample group. On the other hand, the results presented here indicate that muscle strength has a negligible effect on gait characteristics in people with anxiety. This gap can be explained by the fact that the anxiety group had a large variance in muscle strength scores compared to healthy individuals.

## Limitations

It is important to note that the study was observational rather than a randomized and clinically controlled study, and there was no randomization of the subjects. Therefore, it did not allow to examine whether a certain physical characteristic was the cause of anxiety or the anxiety disorder was the cause of the physical deficiency. Further clinical research on these topics, with emphasis on gait and balance, and the relationship between these components and mental illnesses, such as anxiety, is needed.

## Conclusions

In conclusion, the results of this study highlight the major biophysical components that mediate the relationship between gait characteristics (walking speed and step length) and anxiety. While there is a direct influence of anxiety on gait characteristics (pass c), there is also a more complex route through mediation (pass a+b): Pain and balance influence gait velocity, while GJH, pain and balance influence step length. Given that biophysical elements influence gait characteristics, clinicians are advised to consider these biophysical components when assessing and treating a patient who is suffering from anxiety. These mostly refer to pain, balance and GJH, and a lesser extent to muscle force. When coupled with appropriate treatment, proper identification and treatment of these biophysical components can potentially contribute to improved functioning and participation in people with anxiety.

**Conflict of Interest:** No conflicts of interest were encountered in this study.

## References

1. Rombaut L, Malfait F, De Wandele I, et al. (2011) Balance, gait, falls, and fear of falling in women with the hypermobility type of ehlers-danlos syndrome. *Arthritis Care Res*.
2. Hak L, Houdijk H, Steenbrink F, et al. (2012) Speeding up or slowing down?: Gait adaptations to preserve gait stability in response to balance perturbations. *Gait Posture*.
3. Bandelow B, Zohar J, Hollander E, et al. (2008) World Federation of Societies of Biological Psychiatry guidelines for the pharmacological treatment of anxiety, obsessive-compulsive and post-traumatic stress disorders - first revision. *World J Biol Psychiatry*. 9: 248-312.
4. Simmonds MJ, Lee CE, Etnyre BR, Morris GS (2012) The influence of pain distribution on walking velocity and horizontal ground reaction forces in patients with low back pain. *Pain Res Treat*.
5. Simonsen EB, Tegner H, Alkjær T, et al. (2012) Gait analysis of adults with generalised joint hypermobility. *Clin Biomech*.
6. van der Krogt MM, Delp SL, Schwartz MH (2012) How robust is human gait to muscle weakness? *Gait Posture*.
7. Zeni JA, Higginson JS (2009) Differences in gait parameters between healthy subjects and persons with moderate and severe knee osteoarthritis: A result of altered walking speed? *Clin Biomech*.
8. Debi R, Mor A, Segal O, et al. (2009) Differences in gait patterns, pain, function and quality of life between males and females with knee osteoarthritis: A clinical trial. *BMC Musculoskelet Disord*.
9. Marcum ZA, Zhan HL, Perera S, Moore CG, Fitzgerald GK, et al. (2014) Correlates of gait speed in advanced knee osteoarthritis. *Pain Med (United States)*.
10. Rosenbaum S, Tiedemann A, Sherrington C, Curtis J, Ward PB (2014) Physical Activity Interventions for People With Mental Illness. *J Clin Psychiatry* 75: 964-974.
11. Bolmont B, Gangloff P, Vouriot A, Perrin PP (2002) Mood states and anxiety influence abilities to maintain balance control in healthy human subjects. *Neurosci Lett* 329: 96-100.
12. Bolbecker AR, Hong SL, Kent JS, Klaunig MJ, O'Donnell BF, et al. (2011) Postural control in bipolar disorder: Increased sway area and decreased dynamical complexity. *PLoS One* 6.
13. Espy DD, Yang F, Bhatt T, Pai YC (2010) Independent influence of gait speed and step length on stability and fall risk. *Gait Posture*.
14. Willén C, Stibrant Sunnerhagen K, Ekman C, Grimby G (2004) How is walking speed related to muscle strength? A study of healthy persons and persons with late effects of polio. *Arch Phys Med Rehabil*.
15. Flansbjerg UB, Downham D, Lexell J (2006) Knee Muscle Strength, Gait Performance, and Perceived Participation After Stroke. *Arch Phys Med Rehabil*.
16. Wolf JM, Cameron KL, Owens BD (2011) Impact of joint laxity and hypermobility on the musculoskeletal system. *J Am Acad Orthop Surg*.
17. Schmid S, Luder G, Mueller Mebes C, et al. (2013) Neuromechanical gait adaptations in women with joint hypermobility - An exploratory study. *Clin Biomech*.

18. Young WR, Wing AM, Hollands MA (2012) Influences of state anxiety on gaze behavior and stepping accuracy in older adults during adaptive locomotion. *Journals Gerontol - Ser B Psychol Sci Soc Sci*.
19. Staab JP, Balaban CD, Furman JM (2013) Threat assessment and locomotion: Clinical applications of an integrated model of anxiety and postural control. *Semin Neurol*.
20. Hayashi K, Kako M, Suzuki K, et al. (2016) Gait speeds associated with anxiety responses to pain in osteoarthritis patients. *Pain Med (United States)*. 17: 606-613.
21. Feldman R, Schreiber S, Pick CG, Been E (2019) Gait, balance, mobility and muscle strength in people with anxiety compared to healthy individuals. *Hum Mov Sci* 67.
22. Feldman R, Schreiber S, Been E (2020) Gait, Balance and Posture in Major Mental Illnesses: Depression, Anxiety and Schizophrenia .
23. Lemke MR (1999) Motor phenomena in depression. *Nervenarzt*: 70.
24. Sanders RD, Gillig PM (2010) Gait and its assessment in psychiatry. *Psychiatry (Edgmont)* 7: 38-43.
25. Davis JR, Campbell AD, Adkin AL, Carpenter MG (2009) The relationship between fear of falling and human postural control. *Gait Posture*.
26. Staab JP (2014) The influence of anxiety on ocular motor control and gaze. *Curr Opin Neurol* 27: 118-124.
27. Kang HG, Dingwell JB (2008) Effects of walking speed, strength and range of motion on gait stability in healthy older adults. *J Biomech*.
28. Viccaro LJ, Perera S, Studenski SA. (2011) Is timed up and go better than gait speed in predicting health, function, and falls in older adults? *J Am Geriatr Soc*.
29. Maier W, Buller R, Philipp M, Heuser I (1988) The Hamilton Anxiety Scale: reliability, validity and sensitivity to change in anxiety and depressive disorders. *J Affect Disord* 14: 61-68.
30. Ferreira-Valente MA, Pais-Ribeiro JL, Jensen MP (2011) Validity of four pain intensity rating scales. *Pain*.
31. Hjermstad MJ, Fayers PM, Haugen DF, et al. (2011) Studies comparing numerical rating scales, verbal rating scales, and visual analogue scales for assessment of pain intensity in adults: A systematic literature review. *J Pain Symptom Manage*.
32. Bohannon RW, Andrews A, Thomas MW (1996) Walking speed: reference values and correlates for older adults. *J Orthop Sports Phys Ther* 24: 86-90.
33. Bohannon RW, Williams Andrews A (2011) Normal walking speed: A descriptive meta-analysis. *Physiotherapy* 97: 182-189.
34. Marques A, Cruz J, Quina S, Regencio M, Jacome C (2015) Reliability, Agreement and Minimal Detectable Change of the Timed Up & Go and the 10-Meter Walk Tests in Older Patients with COPD. *COPD*: 1-9.
35. Peters DM, Fritz SL, Krotish DE (2013) Assessing the reliability and validity of a shorter walk test compared with the 10-Meter Walk Test for measurements of gait speed in healthy, older adults. *J Geriatr Phys Ther* 36: 24-30.
36. Wolf SL, Catlin P a, Gage K, Gurucharri K, Robertson R, et al. (1999) Establishing the reliability and validity of measurements of walking time using the Emory Functional Ambulation Profile. *Phys Ther* 79: 1122-1133.
37. Hurvitz EA, Richardson JK, Werner RA, Ruhl AM, Dixon MR (2000) Unipedal stance testing as an indicator of fall risk among older outpatients. *Arch Phys Med Rehabil* 81: 587-591.
38. Springer BA, Marin R, Cyhan T, Roberts H, Gill NW (2007) Normative Values for the Unipedal Stance Test with Eyes Open and Closed. *J Geriatr Phys Ther* 30: 8-15.
39. Gullo TR, Golightly YM, Flowers P, et al. (2019) Joint hypermobility is not positively associated with prevalent multiple joint osteoarthritis: A cross-sectional study of older adults. *BMC Musculoskelet Disord*.
40. Boyle KL, Witt P R-KC (2003) Intrarater and interrater reliability of the Beighton and Horan Joint Mobility Index. *J Athl Train* 38: 281-285.
41. Smits-Engelsman B, Klerks M, Kirby A (2011) Beighton score: A valid measure for generalized hypermobility in children. *J Pediatr*.
42. Moraes Gonçalves M, Marson RA, Sá Rego Fortes M de, Borba Neves E, Rodrigues Neto G, et al. (2018) The relationship between handgrip strength and total muscle strength in the Brazilian army military personnel. *Med dello Sport*.
43. Wind AE, Takken T, Helders PJM, Engelbert RHH (2010) Is grip strength a predictor for total muscle strength in healthy children, adolescents, and young adults? *Eur J Pediatr*.
44. Hamilton GF, McDonald C, Chenier TC (1992) Measurement of grip strength: validity and reliability of the sphygmomanometer and jamar grip dynamometer. *J Orthop Sports Phys Ther* 16: 215-219.
45. Massy-Westropp NM, Gill TK, Taylor AW, Bohannon RW, Hill CL (2011) Hand Grip Strength: Age and gender stratified normative data in a population-based study. *BMC Res Notes* 4.
46. Hayes AF (2013) Chapter 1: Introduction. *Introd to Mediat Moderation, Cond Process Anal A Regression-Based Approach*.
47. Preacher KJ, Hayes AF (2008) Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. In: *Behavior Research Methods*.
48. Morio Y, Izawa K, Omori Y, et al. (2019) The Relationship between Walking Speed and Step Length in Older Aged Patients. *Diseases*.
49. Hak L, Houdijk H, Beek PJ, Van Dieë JH (2013) Steps to take to enhance gait stability: The effect of stride frequency, stride length, and walking speed on local dynamic stability and margins of stability. *PLoS One*.
50. Helbostad JL, Moe-Nilssen R (2003) The effect of gait speed on lateral balance control during walking in healthy elderly. *Gait Posture*.
51. Shkuratova N, Morris ME, Huxham F (2004) Effects of age on balance control during walking. *Arch Phys Med Rehabil*.
52. Balaban CD, Thayer JF (2001) Neurological bases for balance-anxiety links. *J Anxiety Disord* 15: 53-79.
53. Kogan E, Lidor R, Bart O, Bar-Haim Y, Mintz M (2008) Comorbidity between balance and anxiety disorders: Verification in a normal population. *J Psychol Interdiscip Appl*.
54. Yardley L, Redfern MS (2001) Psychological factors influencing recovery from balance disorders. *J Anxiety Disord* 15: 107-119.
55. Merom D, Phongsavan P, Wagner R, et al. (2008) Promoting walking as an adjunct intervention to group cognitive behavioral therapy for anxiety disorders-A pilot group randomized trial. *J Anxiety Disord*.
56. Al-Obaidi SM, Al-Zoabi B, Al-Shuwaie N, Al-Zaabie N, Nelson RM (2003) The influence of pain and pain-related fear and disability beliefs on walking velocity in chronic low back pain. *Int J Rehabil Res*.
57. Gerrits MMJG, Vogelzangs N, Van Oppen P, Van Marwijk HWJ, Van Der Horst H, et al. (2012) Impact of pain on the course of depressive and anxiety disorders. *Pain*.



58. Gerrits MMJG, van Marwijk HWJ, van Oppen P, van der Horst H, Penninx BWJH (2015) Longitudinal association between pain, and depression and anxiety over four years. *J Psychosom Res* 78: 64-70.
59. Gureje O, Von Korff M, Kola L, et al. (2008) The relation between multiple pains and mental disorders: Results from the World Mental Health Surveys. *Pain*.
60. Vigo D, Thornicroft G, Atun R (2016) Estimating the true global burden of mental illness. *The Lancet Psychiatry*.
61. de Heer EW, Gerrits MM, Beekman AT, et al. (2014) The association of depression and anxiety with pain: a study from NESDA. *PLoS One* 9: e106907.
62. Tegethoff M, Belardi A, Stalujanis E, Meinschmidt G (2015) Comorbidity of Mental Disorders and Chronic Pain: Chronology of Onset in Adolescents of a National Representative Cohort. *J Pain* 16: 1054-1064.
63. Bulbena-Cabr e A, Rojo C, Pailhez G, Buron Maso E, Mart n-Lopez LM, et al. (2017) Joint hypermobility is also associated with anxiety disorders in the elderly population. *International Journal of Geriatric Psychiatry*.
64. Bulbena A, Gago J, Pailhez G, Sperry L, Fullana MA, et al. (2011) Joint hypermobility syndrome is a risk factor trait for anxiety disorders: A 15-year follow-up cohort study. *Gen Hosp Psychiatry* 33: 363-370.
65. Bulbena A, Agull o A, Pailhez G, et al. (2004) Is joint hypermobility related to anxiety in a nonclinical population also? *Psychosomatics* 45: 432-437.
66. Garcia-Campayo J, Asso E, Alda M (2011) Joint hypermobility and anxiety: The state of the art. *Curr Psychiatry Rep* 13: 18-25.
67. Sanches SB, Os rio FL, Louzada-Junior P, Moraes D, Crippa JAS, et al. (2014) Association between joint hypermobility and anxiety in Brazilian university students: Gender-related differences. *J Psychosom Res* 77: 558-561.
68. Falkerslev S, Baag  C, Alkj er T, et al. (2013) Dynamic balance during gait in children and adults with Generalized Joint Hypermobility. *Clin Biomech*.
69. Palmer S, Bailey S, Barker L, Barney L, Elliott A (2013) The effectiveness of therapeutic exercise for joint hypermobility syndrome: a systematic review. *Physiotherapy* 100: 220-227.
70. Toprak Celenay S, Ozer Kaya D (2017) Effects of spinal stabilization exercises in women with benign joint hypermobility syndrome: a randomized controlled trial. *Rheumatol Int* 37: 1461-1468.
71. Muehlbauer T, Granacher U, Borde R, Hortob gyi T (2017) Non-Discriminant Relationships between Leg Muscle Strength, Mass and Gait Performance in Healthy Young and Old Adults. *Gerontology*.