



Gait Analysis in Uner Tan Syndrome Cases with Key Symptoms of Quadrupedal Locomotion, Mental Impairment, and Dysarthric or No Speech

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[ILLUSTRATION 2](#)

[ILLUSTRATION 3](#)

[ILLUSTRATION 4](#)

[ILLUSTRATION 5](#)

[ILLUSTRATION 6](#)

Gait Analysis in Uner Tan Syndrome Cases with Key Symptoms of Quadrupedal Locomotion, Mental Impairment, and Dysarthric or No Speech

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Abstract

Introduction: Uner Tan syndrome (UTS) consists of quadrupedal locomotion (QL), impaired intelligence and dysarthric or no speech. Previously, I described the walk of cases with UTS as diagonal sequence (DS) because of ipsilateral limb interference, mostly observed in nonhuman primates with DS QL. The only gait analysis performed for UTS were a few cases with lateral sequence (LS) QL. The current work presents a gait analysis of UTS in more families.

Methods: Hip and knee angles during quadrupedal standing were measured in UTS cases, healthy controls with requested QL, and nonhuman primates. Limb phases were assessed from video footages, as the percent of the hind limb's stride durations.

Results: UTS cases and nonhuman primates exhibited quadrupedal standing with straight legs nearly perpendicular to the ground. Healthy individuals could not walk quadrupedally like UTS cases. They could perform QL only with flexed legs. UTS cases and healthy individuals with free (flexed-leg) QL used predominantly lateral sequence-diagonal couplet (LSDC) walks. Terrestrial primates preferred DS gaits. The healthy individuals with free QL were similar to arboreal primates in quadrupedal posture.

Conclusions: Although these results do not seem to support the thesis of locomotor evolution in reverse, nobody knows with certainty who our ancestors were or how they walked, and so the possibility of UTS as an example for the ancestral reappearance of QL in human beings cannot be positively excluded. This locomotor evolution in reverse was supported by experimental evidence, which proved reverse evolution as a scientific fact.

Introduction

In 1887, Eadweard Muybridge reported the first case of a person walking on all fours, in a child with a paralyzed leg [1]. In this context, Price [2] noted "...not only was the regular system of limb movements used, but the support of the body devolved, in their proper

sequence, on the lateral and on the diagonals." This child typically exhibited straight legs during quadrupedal standing.

A man with healthy legs walking on all fours was discovered by Childs [3] in Turkey, 1917. Childs [3] described this man as follows: "I saw that he was without thighs; that the knee-joint was at the hip, the leg rigid, and only half the usual length. With his grim bearded face thrust upwards, and the odd movements of his little legs, he lacked only a stump of tail to make me think I had come upon a satyr in life." This man exhibited habitual QL with straight legs. He had tattered and torn trousers (**Illustration 1**). Habitual QL, mental impairment, and poverty were the characteristics of all of the UTS cases [4].

About a century later, in the years 2004-2005, Turkish media reported five siblings of a consanguineous family with 19 children, residing in a village near Iskenderun beneath the Syrian border. The five siblings exhibited habitual QL, accompanied by severe mental retardation, and dysarthric speech. At the time the discovery attracted little interest among scientists.

Because I was deeply interested in, and had worked on, the extensor and flexor motor systems since 1960, I visited this family and investigated the affected siblings neurologically, radiologically, and cognitively with my colleagues [4]. After an "Aha!" experience [5], I realized the affected siblings were affected by a novel syndrome. This was called Uner Tan syndrome (UTS) after its discoverer [6,7]. I described the condition as "locomotor evolution in reverse in humans," or in short, "locomotor devolution" [6,7], to highlight the reappearance of an ancestral locomotion in human beings.

Despite obtaining extensive video recordings, I performed no quantitative gait analysis of the UTS cases. Instead, I made simple gait analyses by observing that the still photos showed ipsilateral limb interferences. I therefore described their walk as (DS) because ipsilateral limb interferences frequently occur in nonhuman primates with DS walking, and indeed, the ipsilateral limb interference is a potential drawback of a diagonal walk [8-10]. "DS gaits often result in limb interference [11, 12]," as noted by Young et al. [13]; "a diagonal sequence/diagonal couplet walking gait

creates a strong potential for interference between the ipsilateral hind and forelimbs" [12]; "...its associated ipsilateral limb interference in DS gait." [10]; "ipsilateral interlimb interference is very high for DSDC walking" [14], in which the hind foot touchdowns are followed by the contralateral fore foot touchdowns. In a lateral sequence (LS) walking gait, the hind foot touchdowns are followed by the ipsilateral fore foot touchdowns [13].

The idea that nonhuman primates exclusively prefer the DS walking gait is not in accord with the scientific literature. Namely, Sellers et al. [15] found a mixture of DS and LS gaits in nonhuman primates when they used a computer simulation of chimpanzee locomotion, suggesting a mixture distribution of the DS and LS walking in these primates. Hildebrand [8] and Cartmill et al. [9], early experts in gait analysis, also found a broad spectrum of gaits with footfall overlaps in nonhuman primates.

In humans, Shapiro et al. [16] carried out a biomechanical gait analysis of a few UTS cases belonging to a single family and a few healthy individuals requested to use QL. They reported the UTS cases exhibited LS walks almost exclusively, unlike the DS walking gaits of nonhuman primates. Consequently, these authors suggested the UTS cases may not reflect a locomotor reappearance of ancestral human QL. That is, Tan's theory of reverse locomotor

evolution in humans [6,7] would not be tenable, provided that nonhuman primates were our ancestors [16]. However, I had discovered 33 cases in 10 families since finding the first family with UTS in 2005 [17]. Thus, more families with UTS cases needed to be subjected to a quantitative gait analysis, to be conclusive about their type of QL.

The essential questions to be answered by a more comprehensive study of cases from the 10 families were: (i) do the UTS cases use LS and/or DS walking gait?; (ii) how might the locomotion of UTS cases be related to that of nonhuman primates?; (iii) are the UTS cases examples of a locomotor evolution in reverse, provided that present-day nonhuman primates could be considered to be similar to our ancestors, at least with regard to locomotion. In the present work, a postural and locomotor gait analysis was performed on videos of a larger sample of UTS cases, with healthy individuals with requested and free QL, and nonhuman primates, to answer these questions.

Methods

To assess the quadrupedal posture while standing on four extremities, the hip and knee angles were measured using the "Universal Desktop Ruler v3.6.3481" software. These measurements were performed on photographs of the UTS cases (Group 1, n = 32), adults with requested straight-leg QL (Group 2, n = 27), adults with free (flexed-leg) QL (Group 3, n = 53), adult terrestrial primates (Group 4, n = 24: bonobos, baboons, chimps, gorillas, and rhesus monkeys), and adult arboreal primates (Group 5, n = 31): loris, lemur, propithecus, and marmoset), as depicted in **Illustration 2**.

The UTS cases (Group 1, n = 32) from 10 families voluntarily took part in the study, and video footages of them were used for the gait analyses. Group 2 included 27 healthy individuals asked to use QL keeping their legs straight; the adult terrestrial primates constituted Group 3 (n = 53); healthy individuals using flexed-leg QL included Group 4 (n = 24); adult arboreal primates constituted Group 5 (n = 31).

. A gait analysis was performed on videos of UTS cases and other groups. The UTS cases were filmed with a digital video camcorder at 25 frames/sec.

Limb phases were measured from the video footage, "as the percentage of a hind limb's stride duration that the touchdown of a forelimb follows that of the hind limb on the same side of the body", following Shapiro et al. [16]. Gait numbers (limb phases), were as follows: 0 (or 100) corresponds to a pace, 1-24 represents LSLC, 25: LSSF, 26-49: LSDC, 50: trot (diagonal limbs landing simultaneously), 51-74: DSDC, 75: DSSF, and 76-99: DSLC. LS, LC, DS, SF, and DC were abbreviations for lateral sequence, lateral couplet, diagonal sequence, single foot, and diagonal couplet, respectively. Sequence meant the order of footfalls in time. In a DS walk, a reference hind limb touches the ground and then the contralateral forelimb touches the ground. In an LS walk, a reference hind limb touches the ground and then the ipsilateral forelimb touches the ground [16]. Gait analysis included only the symmetrical walking strides between 40 and 60% for the fore and hind limbs [11].

Informed and written consent was taken from a responsible person before the investigations. The study was approved by the ethics committee of the Cukurova University, following the Helsinki declaration. Statistical analyses were performed using SPSS V. 22 (IBM Corp., 2012, USA).

Results

Hip and knee angles during standing on all fours

Illustration 2 depicts quadrupedal standing postures of the UTS cases (**A1-A3**), healthy individuals with requested straight-leg QL (**B1-B3**), terrestrial nonhuman primates (**C1-C3**), humans with free quadrupedal standing (**D1-D3**), and arboreal primates (**E1-E3**). The UTS cases stood on all fours with straight legs nearly perpendicular to the ground. The healthy individuals with requested straight-leg quadrupedal posture could not bend at the hip as much as the UTS cases. The terrestrial nonhuman primates were able to stand on all fours with straight legs like the UTS cases. The healthy individuals with free QL used flexed legs, i.e., bent at the knees, contrary to the UTS cases and nonhuman primates, but similar to the arboreal primates with a bent-knee quadrupedal posture and mostly similar hip angles.

Hip and knee angles during standing on all fours

Means with SDs of the hip and knee angles of the UTS cases (Group 1), healthy individuals with requested QL using straight legs (Group 2), adult terrestrial primates (Group 3), healthy individuals with free quadrupedal standing using flexed legs (Group 4), and adult arboreal primates (Group 5) were presented in **Illustration 3**.

Univariate ANOVA showed the mean hip Angle (dependent variable) was significantly different between groups ($F_{1,162} = 86.7$, $p < .000$), but multiple comparison tests indicated no significant difference between the mean hip angles of the UTS cases (Group 1) and terrestrial primates (Group 3), and between the mean hip angles of the healthy individuals with free QL (flexed-legs), and arboreal primates: $p = 1.000$. Multiple comparisons further indicated the mean hip angle was significantly greater in healthy individuals with straight-legged quadrupedal standing (Group 2) than UTS cases (Group 1), $p < .000$. The mean hip angle was significantly greater in UTS cases than healthy individuals with free QL (flexed-leg): $p < .000$, also being significantly greater than that of the arboreal primates with $p < .05$. **Illustration 4** depicts the mean hip (open circles) and knee angles (filled circles) in UTS cases (UTS), healthy individuals with requested QL (HEALTHY1), terrestrial primates (PRIMATES1), healthy individuals with free QL (HEALTHY2), and arboreal primates (PRIMATES2). Univariate ANOVA indicated the mean knee angle, as the independent variable, significantly associated with groups ($F_{1,62} = 200.8$, $p < .000$).

Multiple comparisons yielded the following results: UTS cases > healthy individuals with free QL (flexed-legs); UTS cases > arboreal primates; healthy individuals with requested QL > healthy individuals with free QL and arboreal primates; terrestrial primates > healthy individuals with free QL and arboreal primates. healthy individuals with free QL < UTS cases, healthy individuals with requested straight-leg QL, < terrestrial primates.

Gaits

The univariate ANOVA test of between subjects effects indicated significant associations of the mean limb phase values with groups ($F_{4,84} = 37.1$, $p < .000$). **Illustration 5** shows the mean limb phase values (%) with their ± 2.0 SDs for the UTS cases (UTS), healthy individuals with requested QL (forced QL), and free QL (free QL), babies (babies QL), and terrestrial primates (primates QL). The single groups entirely below and above the 50% reference line were the healthy individuals with requested QL (FORCED QL) and terrestrial primates (PRIMATES QL), respectively. Otherwise, the mean limb phase value was significantly greater in UTS cases than the healthy individuals with requested QL, but significantly smaller than the healthy individuals with free QL, babies with free QL, and the terrestrial primates ($p < .000$).

Illustration 6 presents the stride numbers and percentages of the LSDC and DSDC walks, including minimum and maximum limb phase values (%) in all 5 groups. Accordingly, the limb phase values of the UTS cases mainly exhibited LSDC gaits (94.9%) with a small percentage of DSDC gaits (5.1%), but the healthy individuals with requested QL exclusively exhibited LSDC gaits. The individuals with free QL exhibited a mixture of walking gaits: 67.6% of the strides LSDC, and 32.4% DSDC gait. Babies with free QL exhibited a similar gait pattern to the healthy individuals with free QL, being 70.0% LSDC and 30.0% DSDC. On the contrary the terrestrial primates exclusively exhibited only DSDC gait.

Discussion

The quintessential question this study sought to answer was whether the quadrupedal locomotion characteristics of UTS cases were more similar to those of healthy humans or to those of nonhuman primates. Shapiro et al [16] found that individuals with UTS nearly exclusively used LS gaits, contrary to nonhuman primates with DS gaits, and claimed "*the quadrupedalism exhibited by individuals with UTS resembles that of healthy adult humans.*" The results

of the present work, however, did not entirely support this claim. Although the UTS cases predominantly used an LSDC walking style, and primates used exclusively DSDC, the quadrupedal standing postures were the same in UTS cases and terrestrial primates. Furthermore, the healthy individuals requested to walk on all fours could not reproduce the UTS style of walking, with straight legs nearly perpendicular to the ground, or the standing posture of the UTS cases. The neural mechanisms of this postural behavior would be the same throughout the tetrapods. In this context, Stuart [18] wrote: "*Neural mechanisms that integrate posture with movement are widespread throughout the central nervous system.*"

Quadrupedal standing in humans and nonhuman primates

The individuals with UTS kept their legs straight during quadrupedal standing and even locomotion, a fact that had not been reported previously. Healthy individuals were asked to walk on all four extremities with straight legs to imitate the UTS cases but were almost unable to do so. They instead made very small steps and only with great difficulty, despite being given a warm-up period of five minutes. Shapiro et al. [16] compared the gaits in a few UTS cases with healthy individuals, but they did not report if their healthy participants walked freely with bent (flexed) or straight (extended) legs. They also did not include any pictures or video recordings exhibiting the quadrupedal standing posture or locomotion of their healthy participants. In light of the extreme difficulty of adopting UTS-like locomotion it seems likely that they analyzed the gaits in healthy individuals with flexed legs. Thus, their conclusion: "*...although the habitual use of quadrupedalism by adults with UTS is unusual, the form of this quadrupedalism resembles that of healthy adults and is thus not at all unexpected*" is not justified.

The mean hip angles were not significantly different between the UTS cases and nonhuman primates. Statistical analyses also found no significant differences between the hip and knee angles of the UTS cases and the terrestrial primates. Thus, the UTS cases and the terrestrial primates exhibited similar postural characteristics while standing on all fours. As expected, the mean hip and knee angles were significantly smaller in the healthy individuals with flexed legs than in the UTS cases and terrestrial primates. Thus, the healthy individuals freely standing on all fours-with flexed legs-did not resemble the UTS cases or the terrestrial primates.

The mean hip and knee angles were not significantly different between the healthy individuals freely standing on all fours with flexed legs and the arboreal

primates also with flexed legs. So, the quadrupedal standing posture of arboreal primates was similar to that of healthy individuals freely standing on all fours.

These results add support to the hypothesis that bipedal locomotion in human beings originated from arboreal primate life. Schmitt [19] emphasized the importance of stiff-leg (extended) locomotion and the role of arboreal life in the emergence of bipedal locomotion of human beings with the following statements: "*...the evolution of bipedalism in humans involved a simple transition from a relatively stiff-legged quadrupedalism ...laboratory based studies of primates also suggest that human bipedalism arose not from a terrestrial ancestor but rather from a climbing, arboreal forerunner.*" The results of the present study, indicating similarities between the flexed-leg quadrupedal posture of the healthy human individuals and the arboreal primates, support these statement.

Gaits in humans and nonhuman primates

The UTS cases primarily used LSDC walking gaits (92.4%) with the remainder being DSDC. The healthy individuals with straight leg QL used only LSDC walking gaits, but the mean limb phase was significantly different to that of the UTS cases; the distribution of the mean limb phase value in healthy individuals using free QL was also significantly different to that of the UTS cases, contrary to the conclusions of Shapiro et al [16]. The overall results of the present study showed UTS was unique in several QL characteristics, as shown above.

The limb phase values showed overlaps among groups. In nonhuman primates all limb phase values were greater than 50, indicating exclusively DSDC walking gaits. The UTS cases, healthy individuals with free QL, and babies, shared many limb phase values with nonhuman primates, with 42.9% of babies exhibiting LSDC, and 57.1% DSDC, for example. Trettien [20] also found a mixture distribution of walking gaits in human babies, with 50% using diagonal crawling on hands and knees, 20% lateral crawling on hands and knees, and 9% diagonal crawling on hands and feet. Righetti et al. [21] reported crawling on hands and knees in infants was very similar to the locomotion in nonhuman primates. Patrick et al. [22] found infants on hands and knees all inclined to move the diagonal limbs together, and concluded: "*human crawling shares features both with other primates and with nonprimate quadrupeds, suggesting similar underlying mechanisms.*" Using hands and feet instead of hands and knees, the babies in the present study constituted a different group from the UTS cases, with a significantly greater

percentage of DSDC walking gaits and significantly greater mean limb phases. These results also suggest the UTS cases belong to a unique group, contrary to Shapiro et al.'s [16] claim that their locomotion was not remarkable.

A small percentage of the UTS cases shared limb phase values with those of nonhuman primates. This suggests UTS may share some gait characteristics with nonhuman primates, possibly as traces from human ancestors using DSDC gaits, and as the reappearance of some primate locomotor traits. Our ancestors probably also used a mixture of the walking gaits as found in UTS. The supraspinal motor control mechanisms and the spinal motor control are also shared among human adults [23,24], infants [25,26], and all quadrupeds [27], with primates constituting a more or less distinct group because their upper limbs are specialized for skilled hand movements with specific supraspinal motor control [23]. In essence, "*rhythmic arm movements are under the control of cervical forelimb generators in quadrupeds as well as in humans*," suggesting phylogenetic conservation of the preserved spinal network organization [28], which may play a role in the re-emergence of quadrupedalism in humans under certain genetic, epigenetic, and/or environmental conditions [29].

The characteristics of quadrupedal locomotion among tetrapods vary, depending upon adaptive locomotor changes [30]. In this context, Ivanenko et al. [31], for instance, concluded: "*human quadrupedalism is a behavior that can result from adaptive processes triggered by disorders in postural tone and environmental cues*." With regard to the neural mechanisms of human quadrupedalism [32], Patrick et al. [22] concluded that the shared features of the crawling of humans and quadrupeds suggested the existence of similar underlying mechanisms. Dietz [32] and Righetti et al. [21] also concluded that similar supraspinal and spinal locomotor controls exist in human infants, adults, and quadrupeds.

In a study by Zampagni et al. [33], human expert climbers exhibited a prominent diagonal gait resembling the diagonal walking gait of nonhuman primates as an adaptive phenomenon. Human beings use a mixture of the limb phase patterns dominated by LSDC, but with the DS gait used if necessary. Similarly, nonhuman primates do not always use purely LS or DS but also exhibit a mixed pattern in diagonality. Primates alternating between DS and LS gaits have been reported in several studies [8,34,35]. Wallace and Demes [10] investigated the walking gaits of two primates (*Cebus apella*) as they moved across terrestrial and simulated arboreal substrates, and also

found they used DS gait on the arboreal substrate and LS gait on the ground. In light of these results, the locomotion of the UTS cases, with dominantly LS walking gaits on the ground, resembles that of arboreal primates on the ground, supporting the notion of the reappearance of ancestral QL in humans with UTS.

Locomotor evolution in reverse; Darwinian medicine

In their gait analysis, Shapiro et al [16] rejected the idea that the reappearance of quadrupedalism in contemporary human beings in the UTS cases represented locomotor evolution in reverse in humans or, in brief, "human locomotor devolution" [4]. The idea of evolution in reverse can also be considered within the framework of evolutionary or Darwinian medicine [36], a foundation for all medicine [37], which was proposed to answer the question why serious diseases still exist despite natural selection. Besides UTS, a recently recognized pathological condition, a number of diseases were considered as Darwinian disorders, such as tuberculosis, Huntington's disease, depression, obesity, anxiety, pain, nausea, cough, fever, vomiting, fatigue, epilepsy, obsessive compulsive disorder, and schizophrenia [38,39,40,41]. Alzheimer's disease was also considered to be a "*phylogenetic regression*" or phylogenetic disease. In this context, Ghika [42] stated "*The highest level of gait disorders including Uner Tan syndrome, with its simian-like gait and posture or apraxia, i.e., the re-emergence of old automatism of pre-human gait, may also be considered under these phylogenetic diseases*." These considerations are in accord with the theory of "human locomotor evolution in reverse" [4].

This theory was criticized by Shapiro et al [16], who rejected the hypothesis that human quadrupedalism appeared in UTS as an ancestral trait by comparing the gait characteristics of a few UTS cases with living nonhuman primates, as if the primates were our ancestors. I would like to make two points: (i) they experimentally tested my theory of "human locomotor evolution in reverse" or, in short "human locomotor devolution" as a scientific theory, since a theory is scientific only if it is falsifiable or testable, and if not it is unscientific, according to Popper [43]; (ii) they appeared to consider living primates as our ancestors. I agree with the first point with pleasure, but I do not agree with the second point, since even though our ancestors are not known with certainty they are not the living primates. In this context, Huxley [44] stated: "*..the stock whence two or more species have sprung, need in no respect be intermediate between those species*." Indeed, the paleontological discoveries

made on African fossils have not yet identified with certainty our proposed common ancestors [45]. Consequently, any gait analysis on living nonhuman primates would not be sufficient to reach an acceptable conclusion about the walking patterns of our ancestors. Although Shapiro et al. [16] compared the locomotor characteristics of UTS cases with those of living primates to evaluate Tan's devolution hypothesis, Dawkins [46] pointed out that a theory has been proposed that, "*chimpanzees and gorillas descend from more human-like, even bipedal ancestors, and have reverted to all fours more recently,*" suggesting an evolutionary route contrary to our general knowledge. In brief, living primates cannot constitute a model to study our ancestors' locomotor characteristics, contrary to Shapiro et al. [16].

Conclusions

The locomotor characteristics of UTS, healthy individuals with forced and free QL, human babies, and nonhuman primates were the main subjects of the present work. Individuals with UTS stood and walked on all four extremities with straight legs almost perpendicular to the ground, but healthy individuals asked to use straight leg QL could not mimic the QL of UTS cases, indicating that quadrupedal locomotion in healthy human individuals is not at all similar to the UTS cases and the UTS quadrupedal style is unique. The quadrupedal standing of UTS cases was similar to that of terrestrial primates, suggesting an evolutionary proximity between quadruped humans and terrestrial primates. On the other hand, the quadrupedal standing of the healthy individuals with free (flexed-leg) QL showed similarities to the arboreal primates, suggesting the arboreal locomotor origins of prehumans.

The analysis of the locomotor characteristics in the UTS cases demonstrated this syndrome may constitute a unique group among healthy individuals with or without requested QL. Accordingly, Guertin [47] also described UTS as "*a recently identified, and uniquely different neurological disorder.*"

Similarities between locomotor characteristics of human quadrupeds with UTS and terrestrial nonhuman primates suggest a reappearance of the quasi ancestral QL in our present time, in line with the theory of "human locomotor evolution in reverse," but it should be noted that no one is certain who our real ancestors were, which makes it impossible to be conclusive in this context. The evolution in reverse is a scientifically proven fact shown by experiments in animals.

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Figure legends

Illustration 1: First discovered man with habitual QL in Turkey in 1917 [3]. Notice the hip (1) and knee (2) angles.

Illustration 2: Quadrupedal postures in the UTS cases (**A1-A3**), healthy individuals with straight- leg quadrupedal posture (**B1-B3**), nonhuman primates (**C1**: chimpanzee, **C2**: macaca mulatta, **C3**: macaque), healthy individuals with free (natural) quadrupedal postures (**D1-D3**), and nonhuman primates with arboreal QL (**E1**: slow loris, **E2**: grey mouse lemur, **E3**: propithecus. Notice primates with large (**C**: terrestrial) and small (**E**: arboreal) bodies.

Illustration 3: Means and SDs of the hip and knee angles

Illustration 4: Error bars with ± 2.0 SD for the hip (open circles, red) and knee (filled circles, black) angles of the UTS cases (UTS), healthy individuals with requested QL, straight legs (FORCED QL), terrestrial primates with free quadrupedal standing (PRIMATE1), healthy individuals with free (flexed legs) QL (NORM QL), and arboreal primates with free

quadrupedal standing (PRIMATE2).

Illustration 5: Mean limb phases with ± 2.0 SDs for five study groups. UTS cases (UTS); FORCED QL: healthy individuals with requested straight-leg QL; FREE QL: healthy individuals with free QL; BABIES QL: babies with QL; PRIMATES QL: terrestrial nonhuman primates QL. Notice the differences and similarities in these subgroups.

Illustration 6: Percentages and minimum-maximum limb phase values for five study groups

Cover letter

Dear Editor:

I would like to submit my revised paper entitled "**Gait Analysis In Uner Tan Syndrome With Quadrupedal Locomotion, Mental Impairment, And Dysarthric Or No Speech,**

for possible publication in the Journal of WebmedCentral).

Uner Tan syndrome was first identified in 2005 as a unique syndrome characterized by the habitual use of quadrupedal locomotion, severe truncal ataxia, dysarthric or no speech, and severely impaired intellectual abilities. No quantitative gait analysis was carried on these cases until 2014, when the QL was characterized by others as lateral sequence similar to healthy human adults, but in a small sample size from only one family. The submitted work included a representative sample size from 10 families hitherto discovered in Turkey, and reports a new quantitative gait analysis of Uner Tan syndrome cases, healthy human infants, healthy human individuals and nonhuman primates. It addresses the fact that UTS cases walk with straight rather than flexed legs, and the results show that while the QL is mostly lateral sequence, there are similarities in gait characteristics with terrestrial primate locomotion, whereas the QL in healthy individuals had similarities with arboreal primate locomotion. These findings have implications in the evolution of bipedal locomotion in human beings and in the quadrupedal locomotion in UTS cases.

I hope the findings and conclusions in the paper all make this manuscript worthy of publishing.

Yours faithfully,

Prof. Dr. Uner Tan, M.D., Ph.D.

Honorary member of the Turkish Academy of Sciences, Ankara, Turkey

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Illustrations

Illustration 1

First discovered man with habitual QL in Turkey in 1917 [3]. Notice the hip (1) and knee (2) angles

ILLUSTRATION1



Illustration 2

Quadrupedal postures in the UTS cases (A1-A3), healthy individuals with straight- leg quadrupedal posture (B1-B3), nonhuman primates (C1: chimpanzee, C2: macaca mulatta, C3: macaque), healthy individuals with free (natural) quadrupedal postures (D1-D3), and nonhuman primates with arboreal QL (E1: slow loris, E2: grey mouse lemur, E3: propithecus). Notice primates with large (C: terrestrial) and small (E: arboreal) bodies.

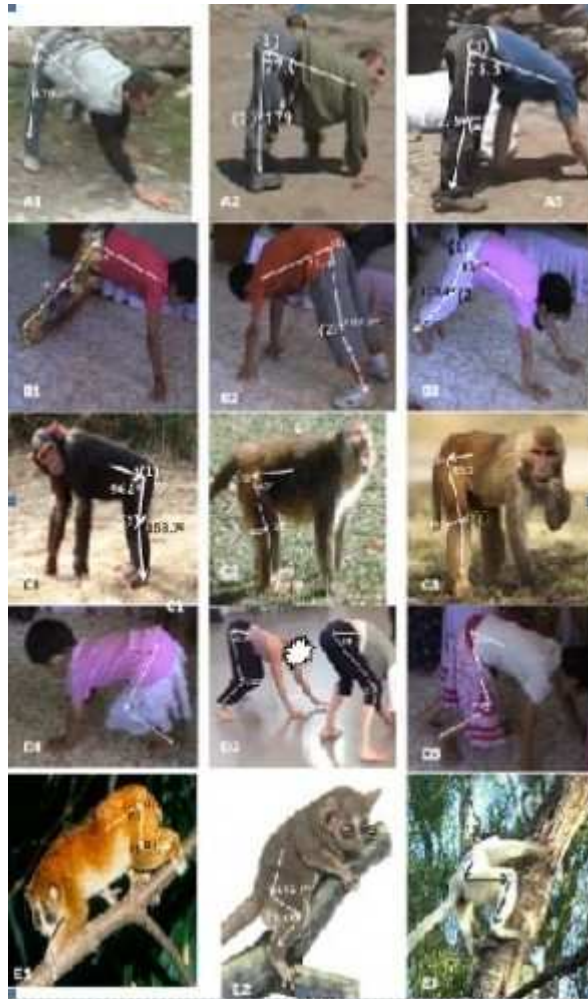


Illustration 3

Means and SDs of the hip and knee angles

ILLUSTRATION3

Means and SDs of the hip and knee angles

Groups	N	Hip Angle		Knee Angle	
		Mean	SD	Mean	SD
1: UTS	32	69.6	12.2°	171.8	5.5°
2: Healthy1	27	120.6	19.0°	173.7	2.6°
3: Primates1	53	74.8	12.0°	169.8	6.3°
4: Healthy2	24	52.0	11.7°	115.1	16.0°
5: Primates2	31	57.2	18.1°	106.8	24.4°

SD: standard deviation; 1: UTS cases; 2: (Healthy1): healthy individuals with requested quadrupedal standing with straight legs; 3 (Primates1): terrestrial primates; 4: (Healthy2) healthy individuals with flexed-leg (free) quadrupedal standing; 5: (Primates2): arboreal primates.

Illustration 4

Error bars with $\hat{A} \pm 2.0$ SD for the hip (open circles, red) and knee (filled circles, black) angles of the UTS cases (UTS), healthy individuals with requested QL, straight legs (FORCED QL), terrestrial primates with free quadrupedal standing (PRIMATE1), healthy individuals with free (flexed legs) QL (NORM QL), and arboreal primates with free quadrupedal standing (PRIMATE2)

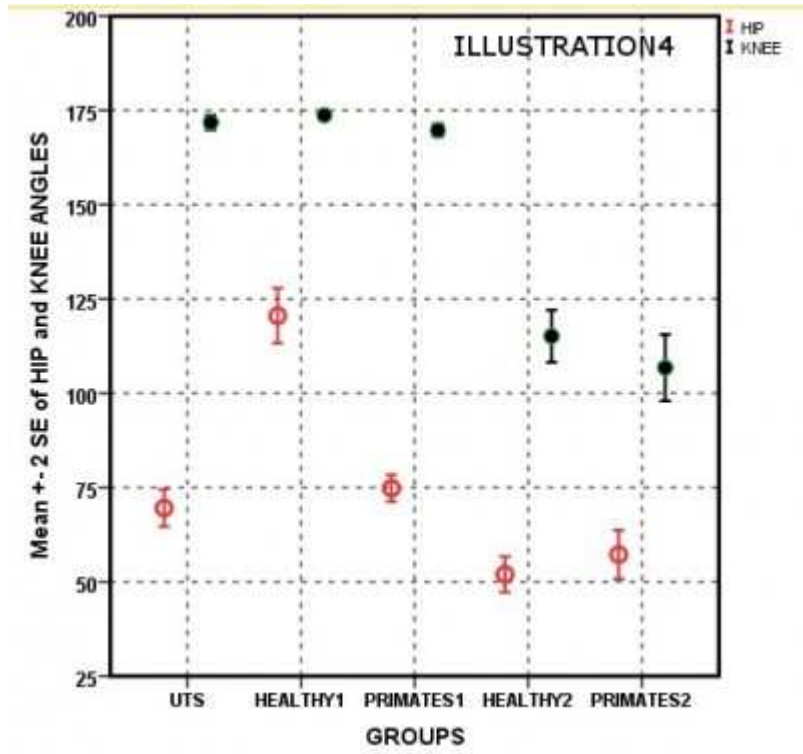


Illustration 5

Mean limb phases with ± 2.0 SDs for five study groups. UTS cases (UTS); FORCED QL: healthy individuals with requested straight-leg QL; FREE QL: healthy individuals with free QL; BABIES QL: babies with QL; PRIMATES QL: terrestrial nonhuman primates QL. Notice the differences and similarities in these subgroups

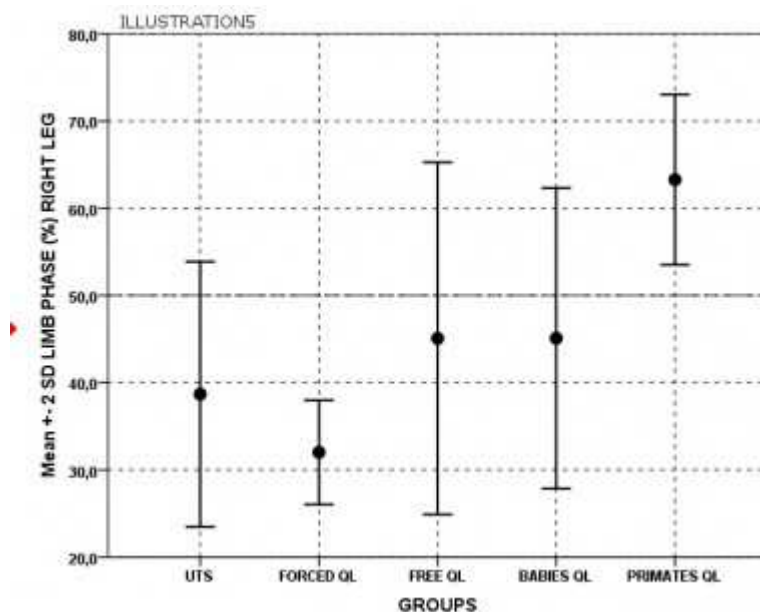


Illustration 6

Percentages and minimum-maximum limb phase values for five study groups

Illustration 6: Percentages and ranges of the limb phases in five study groups

Groups	N	Strides	LSDC		DSDC		Min	Max
			N	%	N	%		
1: UTS	32	336	319	94.9	17	5.1	25.6	59.2
2: Forced QL	27	254	254	100.0	0.0	0.0	25.9	39.0
3: Free QL	53	71	48	67.6	23	32.4	25.3	74.5
4: Babies	24	70	49	70.0	21	30.0	31.0	74.4
5: Primates	31	122	0	0.0	122	100.0	52.1	73.9