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Clinical short communication

Clinically visible but often unperceived: Low awareness of fasciculations in amyotrophic lateral sclerosis

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ABSTRACT

Background: Fasciculations are a key clinical sign of amyotrophic lateral sclerosis (ALS) but also occur in other conditions such as benign fasciculation syndrome. Patients often present with perceived twitching fearing ALS; however, the extent to which ALS patients themselves perceive fasciculations has not been systematically examined. We therefore aimed to clarify how often ALS patients are aware of fasciculations that are clinically visible.

Methods: We prospectively studied 34 ALS patients. First, a structured questionnaire assessed initial symptoms, chief complaints, and awareness of twitching. Then, the frequency and concordance between objective fasciculations and subjective awareness of fasciculations (twitching) were analyzed across five body regions (bilateral upper and lower limbs and trunk) based on simultaneous visual observation and patient reports.

Results: In the questionnaire, only one of the 34 patients (3 %) reported twitching as the initial symptom, and none presented with twitching as the chief complaint. More than half (19, 56 %) had never noticed twitching. In the fasciculation analysis, patients showing objective fasciculations without subjective awareness were most common (21/34, 62 %), whereas those with objective fasciculations accompanied by subjective awareness were fewer (10/34, 29 %), indicating relatively low concordance between visible fasciculations and patient awareness. No patient exhibited subjective awareness without objective fasciculations. These findings suggest that the majority of visible fasciculations in ALS are not perceived by patients.

Conclusion: Fasciculations in ALS are rarely the initial or presenting symptom and are often unperceived by patients despite being clinically visible.

1. Introduction

Fasciculations are spontaneous muscle contractions that appear as brief, localized twitches visible beneath the skin. Physiologically, they represent spontaneous depolarizations of a single motor unit or a portion thereof, rather than contractions of an entire muscle fascicle [1]. They are a well-recognized clinical sign of amyotrophic lateral sclerosis (ALS), although not unique to the disease. Previous studies have reported their occurrence even in healthy individuals, with up to 70 % noticing them at some point in life—a phenomenon referred to as benign fasciculation syndrome (BFS) [2,3]. In daily neurological practice, a subset of patients present with "twitching" as their chief complaint, often fearing the onset of ALS. Many such cases are ultimately diagnosed as BFS or fasciculation anxiety syndrome—highlighting that subjective twitching does not necessarily indicate neurodegeneration [4,5]. More recently, Montalvo et al. (2021) confirmed the benign nature of BFS through long-term clinical and neurophysiological observations, showing no progression to ALS even in patients with minor chronic neurogenic changes in electromyography (EMG) [5]. With the growing influence of internet-based symptom searching, patients linking isolated twitching to ALS and later diagnosed with BFS are increasingly common [5].

From the perspective of ALS, however, evidence remains scarce regarding fasciculations as an initial symptom or as the chief complaint at presentation. Apart from a single retrospective review of 312 cases, in which fasciculations were the first symptom in only 21 patients (6.7 %) [6], additional reports are limited to isolated case descriptions [7–9].

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More importantly, no previous study has systematically investigated how frequently fasciculations are perceived by ALS patients, despite their frequent visibility on examination.

Considering these unresolved issues, this study prospectively evaluated how often fasciculations constitute the initial symptom of ALS and the concordance between patients' subjective awareness and objective detection through direct visual observation. Clarifying these features may help distinguish ALS from BFS in which subjective twitching is typically the main complaint.

2. Methods

2.1. Participants

Patients were prospectively enrolled if they met all of the following inclusion criteria:

(1) A diagnosis of ALS was confirmed within two weeks prior to the study evaluation according to the revised El Escorial criteria for clinically definite, clinically probable, or clinically probable laboratory-supported ALS. As part of this diagnostic workup, all patients had already undergone needle electromyography that included at least the trapezius, triceps brachii, vastus medialis, and tibialis anterior muscles. (2) Age 18 years or older. (3) Ability to provide informed consent and to participate in the observation protocol. Eligible patients were consecutively recruited at Teikyo University Hospital between April 2023 and August 2025. All participants provided written informed consent, and the study was approved by the institutional ethics committee (Approval No. 0427–4).

2.2. Questionnaire survey of symptom profile

Before observation, all participants completed a structured questionnaire addressing the interval from symptom onset to evaluation, initial symptom, chief complaint at the first neurological visit, and history of twitching awareness. Patients were asked whether twitching occurred as the first symptom, concurrent with other neurological symptoms, or after their onset, and its frequency was also recorded. A one-month period was used to define recent twitching and simultaneous onset with other symptoms. The full questionnaire is shown in Supplementary Table S1.

2.3. Fasciculation assessment

2.3.1. Observation area

Each patient underwent a standardized fasciculation screening in five regions: bilateral upper limbs, bilateral lower limbs, and the trunk. For the upper limbs, the examiner observed the muscles mainly from an oblique superior angle while standing lateral to the musculature, allowing visualization of the anterolateral surface of the upper arm and the dorsal surfaces of the forearm and hand, with the arm placed in a slightly pronated position. For the lower limbs, the anterior surfaces from the thigh to the foot were examined. The trunk was observed from the dorsal side (posterior neck and back).

2.3.2. Observation procedure

Fasciculations were assessed simultaneously by two examiners with predefined roles: Examiner A (K.H.) evaluated objective fasciculations (O), and Examiner B (the treating neurologist) independently recorded subjective awareness (S) reported by the patient in real time. When a patient reported subjective awareness that was temporally and anatomically concordant with an objective fasciculation, Examiner A provisionally recorded it as objective fasciculation with subjective awareness (O + S, OS). The concordance of these provisional OS events was later verified using Examiner B's independent log of subjective awareness.

Each of the five predefined body regions (bilateral upper limbs, bilateral lower limbs, and the trunk) was evaluated separately for 60 s. Throughout the examination, patients were instructed to keep their body fully relaxed and to immediately report any perceived twitching by pointing to its location. To standardize reporting, anatomical regions were predefined as follows: upper limbs (shoulder, upper arm, forearm, hand); lower limbs (thigh, lower leg, foot); and trunk (neck, back), and patients were familiarized with these terms before the examination. During each observation, patients were instructed to report any twitching only within the region currently being observed, thereby preventing cross-site interference (e.g., reporting leg twitching during arm observation). All examinations were performed at the bedside under comparable ceiling lighting conditions.

2.3.3. Role of examiner a in assessing objective fasciculations (O)

Examiner A observed each region for 60 s from approximately 50 cm away, ensuring a clear view of the musculature and focusing on detecting objective fasciculations (O), defined as spontaneous, visible twitches on the body surface. Examiner A continuously counted all fasciculations observed during the session. When a patient reported subjective awareness (S) of a fasciculation during observation, Examiner A temporarily timestamped the corresponding visible fasciculation (O) and noted its anatomical site as a "provisional O + S (OS)" for later confirmation through cross-checking with Examiner B's records.

2.3.4. Role of examiner B in assessing subjective awareness (S)

Subjective awareness was defined as twitching reported by the patient during observation.

Examiner B independently recorded all episodes of subjective awareness in real time, noting the anatomical site and timing with timestamps. Before the examination, patients were instructed: "If you feel any twitching, immediately point to the location."

This independent recording by Examiner B allowed Examiner A to focus on visual assessment and ensured that Examiner B accurately timestamped each episode of subjective awareness, thereby improving the objectivity of judging concordance.

2.3.5. Concordance of objective fasciculations with subjective awareness (OS)

Concordance between objective fasciculations and subjective awareness was determined using a two-step approach. First, Examiner A provisionally recorded OS during the observation. After each 60-s session, Examiner A's provisional OS marks (timestamped during the session) were compared with Examiner B's independent log of subjective awareness, which had been recorded simultaneously during the same 60-s observation.

If both timestamps and anatomical sites corresponded within $\leq$1 s, the provisional mark was confirmed as a definite concordant event (O + S, OS). The 1-s window was defined as the temporal tolerance for matching between Examiner A's provisional OS marks and Examiner B's independent records of subjective awareness (S), and was determined based on the temporal characteristics of fasciculations observed by muscle ultrasound (M-mode)—specifically, their brief duration ($\approx$0.2–0.5 s), recurrence frequency (0.25–2 Hz), and the practical feasibility of manual timing [10].

2.3.6. Analysis of fasciculations

Fasciculation findings were analyzed at two levels:

- **Observation-site level**: Each of the five body sites was independently assessed for objective fasciculations (O), subjective awareness (S), and objective fasciculations with subjective awareness (OS). A site was classified as positive if at least one event was detected during the 60-s observation.
- **Patient level**: Each fasciculation type (O, S, OS) was considered present if detected in at least one site.

For the main analysis, sites and patients were classified into four primary categories:

(1) **O only** (only objective fasciculations were identified);
(2) **S only** (only subjective awareness was identified);
(3) **OS** (objective fasciculations with simultaneous subjective awareness were identified); and.
(4) **None** (neither objective nor subjective fasciculations were identified).

2.4. Statistical analysis

Continuous variables were summarized as mean ± SD, and categorical variables as counts and percentages. At the observation-site and patient levels, distributions of fasciculations were described. At the patient level, concordance between O and S was assessed using McNemar's test.

3. Results

3.1. Patient characteristics

A total of 34 patients with ALS were enrolled. The mean age at evaluation was 69.0 ± 12.2 years (range, 46–85), and 22 were men and 12 were women. The mean disease duration from symptom onset to evaluation was 12.3 ± 7.0 months.

3.2. Questionnaire survey

Among the 34 enrolled patients, only one patient (3 %) reported twitching as the first symptom, and none presented with twitching as the chief complaint at the first neurological consultation. Fifteen patients (44 %) noticed twitching within one month of evaluation, whereas the remaining 19 (56 %) had never been aware of twitching. Among those with awareness, 14 of the 15 (93 %) reported that twitching emerged after the onset of other ALS symptoms, with a mean delay of 6.5 ± 4.6 months. Regarding frequency, the most common category was "once every few hours" ($n = 9$, 57 %), followed by "once every few days" ($n = 3$, 21 %), "once a day" ($n = 2$, 14 %), and "once every hour" ($n = 1$, 7 %).

3.3. Analysis of fasciculations

Fasciculation findings were summarized using four primary categories: O only, S only, OS, and None. The detailed eight mutually exclusive subcategories (A–H), defined by combinations of fasciculation types, are provided in Table 1 for reference. The frequency of the four primary categories (O only, S only, OS, and None) at the observation-site and patient levels is shown in Fig. 1.

Across 170 observation sites (34 patients × 5 body regions), the distribution of fasciculations was as follows: O only in 78 sites (78/170, 46 %), OS in 21 (12 %), S only in 1 (1 %), and None in 70 (41 %) (Fig. 1A). Among the 100 fasciculation-positive sites, the majority were O only (78/100, 78 %). Event counts varied widely, with some sites showing frequent O only events (up to 62) and OS events (up to 12), whereas S only events remained rare (Supplementary Table S2).

At the patient level ($n = 34$), the distribution was as follows: O only in 21 patients (62 %), OS in 10 (29 %), S only in 0 (0 %), and None in 3 (9 %) (Fig. 1B). Thus, patients with O only were more common than those showing any subjective awareness (62 % vs. 29 %). McNemar's test confirmed that O only cases significantly outnumbered S only cases (21 vs. 0; $p < 0.001$), indicating relatively low concordance mainly due to a high proportion of unperceived visible fasciculations.

Table 1
Distribution of fasciculation categories (A–H) at the observation-site and patient levels.

Category	Definition	Observation-site level (n = 170)	%	Patient level (n = 34)	%
A	O only	78	46	21	62
B	S only	1	1	0	0
C	O only + S only (no OS)	0	0	0	0
D	OS only	1	1	0	0
E	OS + O only (no S only)	14	8	6	17
F	OS + S only (no O only)	0	0	0	0
G	OS + O only + S only	6	3	4	12
H	None	70	41	3	9
Total		170	100	34	100

(1) **O only**, only objective fasciculations were identified.
(2) **S only**, only subjective awareness was identified.
(3) **OS**, objective fasciculations with simultaneous subjective awareness were identified.
(4) **None**, neither objective nor subjective fasciculations were identified.

4. Discussion

The present study is, to our knowledge, the first to systematically evaluate the subjective awareness of fasciculations and its concordance with clinically visible fasciculations in patients with ALS. Our results indicate that fasciculations are frequently observed but often go unperceived by patients.

From the questionnaire, 19 of the 34 patients (56 %) had never noticed twitching, and only one (3 %) reported it as the first symptom. None presented with twitching as the chief complaint at their first neurological consultation. Even among patients who did perceive fasciculations, awareness typically followed the onset of other neurological symptoms after several months (93 %, 14 of 15). These findings suggest that fasciculations seldom represent the initial or presenting symptom of ALS, in contrast to BFS, where twitching is typically the main complaint [2–4].

Fasciculation assessments also demonstrated low patient awareness of fasciculations in ALS. At the site level, the majority of fasciculation-positive sites showed O only (78 %, 78/100). At the patient level ($n = 34$), patients with O only were the most common (62 %, 21/34), whereas those with subjective awareness were less frequent (29 %, 10/34), and none exhibited subjective awareness alone. Importantly, McNemar's test confirmed a significant predominance of objective fasciculations over isolated subjective awareness (21 vs. 0, $p < 0.001$). These findings indicate that fasciculations in ALS are often visible but not perceived by patients.

Previous studies have shown that patients with BFS often present with isolated subjective awareness of fasciculations (twitching) as their chief complaint, usually exhibit normal or only minor EMG abnormalities, and rarely progress to ALS during long-term follow-up [2–5]. In this context, our findings complement these observations from the perspective of ALS, suggesting a contrasting pattern: fasciculations in ALS are typically visible but often unperceived by patients, indicating that isolated subjective twitching is an uncommon feature of the disease.

The mechanism underlying this low awareness remains unclear. One plausible explanation is that early fasciculations, before substantial reinnervation, are of small magnitude and insufficient to activate muscle spindles or cutaneous receptors to a perceivable degree [11]. Another possible mechanism may involve pathological and functional changes in muscle proprioceptive afferents, particularly group Ia and II fibers, recently reported in ALS [12,13].

Overall, our findings demonstrate that fasciculations are often unrecognized in ALS patients and seldom represent the initial or presenting symptom. Nevertheless, rare cases have been reported in which fasciculations precede other ALS manifestations [6–9], and our cohort also included one such case. Based on our results, because other neurological

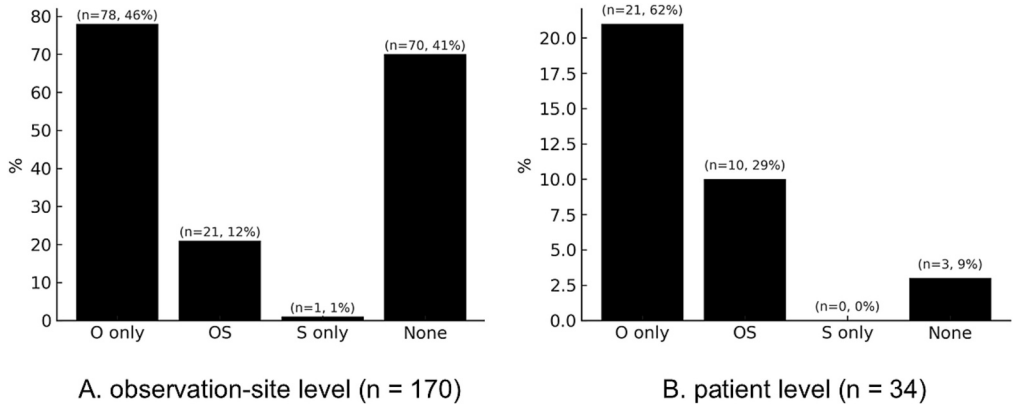

Fig. 1. Distribution of fasciculation categories at the observation-site and patient levels in ALS.
Fasciculation findings were analyzed at two levels: the observation-site level (five body sites per patient, $n = 170$, Panel A) and the patient level ($n = 34$, Panel B). For the main analysis, sites and patients were classified into four categories:
(1) O only (only objective fasciculations were identified);
(2) S only (only subjective awareness was identified);
(3) OS (objective fasciculations with simultaneous subjective awareness were identified); and.
(4) None (neither objective nor subjective fasciculations were identified).
At both levels, O only cases are more prevalent than OS and S only cases, suggesting that the majority of visible fasciculations in ALS are not perceived by patients.

symptoms usually preceded twitching, careful assessment for accompanying neurological signs and appropriate follow-up are recommended when a patient presents with isolated twitching.

5. Limitations

First, this single-center study included a relatively small cohort ($n = 34$), which limits generalizability. Nevertheless, methodological consistency under standardized conditions and the inclusion of only confirmed ALS cases strengthen the internal validity of our findings. Second, subjective awareness was based on patient self-report and may be subject to recall bias. However, the over-reporting of fasciculations as an initial symptom, previously raised as a concern, was not observed in our cohort [6]. Finally, fasciculations were assessed during a single 60-s visual observation, and several methodological constraints should be noted. Because the observation field was limited to the anterolateral surface of the upper arm, the dorsal surface of the forearm and hand, and the dorsal trunk, some muscles that frequently show fasciculations (e.g., the pectoralis) may have been missed. In addition, low-frequency or deep-seated fasciculations might also have been overlooked. Nevertheless, this approach closely reflects routine clinical practice and therefore supports the validity of our findings.

6. Conclusion

Our study demonstrates that fasciculations in ALS are rarely the initial or presenting symptom and are often unperceived by patients. Isolated twitching without other neurological deficits is therefore unlikely to indicate ALS. These features contrast with BFS, where twitching is typically the main complaint, and may help reassure patients presenting with isolated twitching.

CRediT authorship contribution statement

Keiichi Hokkoku: Writing – original draft, Validation, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Masato Inoue:** Writing – review & editing, Methodology, Investigation, Data curation. **Saya Yamada:** Writing – review & editing, Investigation. **Hiroto Namba:** Writing – review & editing, Investigation, Data curation. **Kiyoshi Matsukura:** Writing – review & editing, Investigation, Data curation. **Taiji Mukai:** Writing – review & editing, Investigation, Data curation. **Takashi Chiba:** Writing – review & editing, Investigation, Data curation. **Yuki Hatanaka:** Writing – review & editing, Supervision, Investigation. **Shunsuke Kobayashi:** Writing – review & editing, Supervision, Project administration. **Masahiro Sonoo:** Writing – review & editing, Supervision, Conceptualization.

Ethical compliance

The present study was conducted in accordance with the guidelines of the Declaration of Helsinki. Informed consent was obtained from all patients for this report.

Declaration of competing interest

The authors declare no conflicts of interest. K.H. was supported by the Touko Fujii Academic Research Encouragement Fund (No. 24) from Teikyo University School of Medicine.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jns.2025.123764.

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