Comparison between ^{18}F -FDG PET/CT and EMG Mapping for Identifying Dystonic Superficial Muscles in Primary Cervical Dystonia: Preliminary Results

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Abstract

Purpose This study was conducted to compare ^{18}F -FDG PET/CT and electromyography (EMG) mapping in patients with primary cervical dystonia (PCD) to find dystonic superficial cervical muscles.

Methods Ten consecutive patients with PCD (M:F=5:5, age 44 ± 13 years) whose dystonic posture was not relieved with conventional muscle relaxant therapy were included. Target cervical muscles for the comparison between ^{18}F -FDG PET/CT and EMG mapping were four representative superficial bilateral cervical muscles: splenius capitis muscle, sternocleidomastoid muscle, upper trapezius muscle, and levator scapulae muscle. The diagnostic efficacy was compared between ^{18}F -FDG PET/CT and EMG mapping using physical exam and measurement of rotation angle as the gold standard.

Results Among 80 muscles evaluated, there were 21 (26%) dystonic superficial cervical muscles assessed with physical

exam and motion analysis. The sensitivity, specificity, and accuracy for localizing dystonic muscles were 76, 92, and 88% for ^{18}F -FDG PET/CT, and 95, 66, and 74% for EMG mapping, respectively. The sensitivity of EMG mapping was significantly higher than that of ^{18}F -FDG PET/CT. In contrast, ^{18}F -FDG PET/CT was significantly superior to EMG mapping for specificity and accuracy.

Conclusions ^{18}F -FDG PET/CT is more specific and accurate than EMG mapping for finding superficial dystonic cervical muscles. The high sensitivity of EMG mapping suggests that ^{18}F -FDG PET/CT and EMG mapping are complementary for finding dystonic superficial cervical muscles.

Keywords Primary cervical dystonia · Spasmodic torticollis · ^{18}F -FDG · PET/CT · Electromyography

Introduction

Primary (or idiopathic) cervical dystonia (PCD), sometimes referred to as spasmodic torticollis, is characterized by an abnormal head and neck posture due to involuntary tonic or phasic contractions of the neck muscles [1]. Various options are available for treating patients with PCD, and although no universally accepted treatment protocol exists, chemodenervation with botulinum toxin (BT) is regarded as a first-line treatment for PCD [1, 2]. However, 10–30% of patients do not respond to BT injection [2–4]. The poor localization of target muscles is a major cause of treatment failure [1, 5]. Once it is determined that dystonia is present, history, physical examination and, if necessary, laboratory tests must exclude secondary dystonia [1]. However, due to the lack of a specific diagnostic test, neurophysiologic techniques such as surface electromyography are recom-

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mended to document functional abnormalities in patients with dystonia and assist in differential diagnosis, evaluation of the pathophysiology, and directing treatment with botulinum toxin injections [6]. Mapping based on needle electromyography (EMG) is the most widely used method for identifying dystonic muscles in PCD. Needle EMG can detect the abnormal firing of the motor unit action potentials (MUAP) of dystonically contracting muscles [6, 7]. However, deep cervical muscles may be beyond reach with a conventional 37-mm needle electrode for EMG [8]. Also, the use of motion analysis systems has allowed the extraction of kinematics parameters in a quantitative and reliable way [9–12].

Application of PET images to evaluate muscular metabolic activity has been reported to be a useful strategy [13–16]. A recent study showed ^{18}F -fluorodeoxyglucose (FDG) PET/CT could be effectively applied to localize dystonic muscles in PCD patients [17], however, ^{18}F -FDG PET/CT was not compared with the EMG mapping data in this study. Comparison of ^{18}F -FDG PET/CT with EMG mapping to localize dystonic superficial cervical muscles is needed. It is well-known that glucose metabolism and ^{18}F -FDG uptake are enhanced in contracting skeletal muscles [13–15], and thus, it has been suggested that the degree of ^{18}F -FDG uptake might be associated with the contraction strength of skeletal muscles [13–15]. Moreover, a recently developed integrated PET/CT method was found to provide both metabolic and anatomic information on hypermetabolic lesions. A recent report suggested that ^{18}F -FDG PET/CT was potentially useful for identifying dystonic cervical muscles for BT therapy in patients with PCD [17]. However, there was no direct comparison between ^{18}F -FDG PET/CT and EMG for localizing PCD to find dystonic superficial cervical muscles.

Materials and Methods

Subjects

The inclusion criteria used for this study were as follows: (1) All subjects had PCD without any evidence of an identifiable cause of secondary dystonia. (2) Extra-nuchal area was not affected by the dystonia. (3) Dystonic posture was not relieved despite conventional muscle relaxant therapy consisting of anticholinergics (trihexyphenidyl), benzodiazepines (clonazepam), and baclofen. Ten consecutive patients with PCD who visited our hospital met the study criteria and were included in this study. The ethics review committee at our institute approved the study protocol.

Determination of Dystonic Superficial Cervical Muscles

Target cervical muscles for the comparison between ^{18}F -FDG PET/CT and EMG mapping were four representative

superficial bilateral cervical muscles: splenius capitis muscle (SPC), sternocleidomastoid muscle (SCM), upper trapezius muscle (uTz), and levator scapulae muscle (LS). The dystonic activities in these four superficial muscles could be objectively determined by physical exam and measurement of rotation angle, which were used as the gold standard in this study because they are considered the current best practical diagnostic tests to evaluate superficial cervical muscles in PCD [1, 8–12].

Physical examinations were performed by a single investigator. Bilateral SPC, SCM, uTz, and LS muscles were inspected and palpated. Hypertrophic muscles or muscles with visible or palpable contraction on inspection and palpation were defined as dystonic. Maximum rotation angles of dystonic postures were determined using a motion analysis system (Vicon 612 motion analysis system, Oxford Metrics, Oxford, UK). Patients sat on a chair, without a backrest, while clinical scores and rotation angles were determined. Patients were instructed not to resist abnormal head and neck postures. Rotation angles of dystonic posture were measured two dimensionally using six light-reflecting markers attached to the anterior/posterior and left/right sides of a helmet and to both acromioclavicular joints. A motion analysis system detected the positions of the markers while seated patients wore the helmet. Rotation angle was defined as the angle between the line connecting markers on bilateral acromioclavicular joints and the line connecting the anterior and posterior helmet markers (Fig. 1). Dystonic muscle was determined based on the results of both physical exam and measurement of rotation angle.

^{18}F -FDG PET/CT

All patients were fasted for at least 6 h prior to the PET/CT study but were allowed water and muscle relaxant medications. To prevent nonspecific ^{18}F -FDG uptake by muscles not related to PCD, muscle relaxants consisting of anticholinergics (trihexyphenidyl), benzodiazepines (clonazepam), and baclofen were administered to all patients before PET/CT. PET/CT scans were performed using a Discovery LS PET/CT scanner (GE Healthcare, Milwaukee, WI). CT scanning from head to upper chest was performed using a continuous spiral technique on an 8-slice helical CT with 80 mAs, 140 KeV, at a 5 mm section width, and at a table feed rate of 5 mm per rotation. An emission scan was performed after CT scans from head to upper chest at 4 min per frame, 45 min after the administration of 370 MBq ^{18}F -FDG i.v. Patients maintained a sitting position with head and neck in the adopted abnormal involuntary posture during the ^{18}F -FDG uptake period without making any effort to correct this posture [17]. Attenuation-corrected PET images using CT data were reconstructed using an ordered subsets

Fig. 1 Measurement of rotation angle in dystonic posture. Six light-reflecting markers were located on the anterior/posterior and left/right sides of a helmet and on both acromioclavicular joints. The rotation angle was defined as the angle between the line connecting markers on bilateral acromioclavicular joints and the line connecting the anterior and posterior helmet markers

expectation maximization algorithm (28 subsets, two iterations). Using an Xeleris workstation, CT and PET scan data were accurately co-registered. Standardized uptake values (SUVs) were acquired using attenuation-corrected images, and the amount of ^{18}F -FDG injected, patient body weight, and cross-calibration factors between PET and the dose calibrator were recorded. CT, PET, fused PET/CT, and maximum-intensity-projection (MIP) PET images were reviewed by one nuclear medicine physician. When increased ^{18}F -FDG uptake was observed in bilateral SPC, SCM, uTz, and LS muscles, maximum SUV and the name of each hypermetabolic muscle were recorded.

EMG Mapping

The SPC, SCM, uTz, and LS muscles were studied bilaterally using a monopolar needle electrode (37 mm long, 27 gauge) and an EMG system (band pass 20–10,000 Hz, gain 200 $\mu\text{V}/\text{div}$, sweep speed 1 s/div) (Synergy, Oxford Instruments, Oxfordshire, UK). EMG electrode placements were made using standard anatomic landmarks. SCM muscle recordings were made at mid-belly of visible muscle. SPC recordings were made with the needle inserted 1–2 cm inferior and posterior to the SPC attachment to the mastoid process. LS recordings were made at mid-belly of the muscle after palpation during ipsilateral scapular elevation. To record the uTz muscle, the electrode was introduced at the front edge of the trapezius's horizontal portion 2 cm removed from the medial angle of the shoulder. The electrode positions were tested by maximum innervation during rotation, flexion, extension, lateral flexion, and unilateral scapular elevation. No other cervical muscles were explored because it was difficult to place the needle tip accurately into targeted muscles. A single test was defined as a continuous 5 s monitoring period, and five tests were conducted on each muscle. A "turn" was defined as a reversal of slope separated from the

previous reversal and the following reversal by an amplitude change of $> 100 \mu\text{V}$. The number of turns per second over the 5 s test periods was determined for each muscle studied, and a muscle was defined as displaying dystonic activity if the average number of turns per second exceeded 100 (Fig. 2). [7, 18–22]. EMG mapping was either carried out after ^{18}F -FDG PET/CT scanning on the same day (eight patients) or within 4 days (two patients).

Statistical Analysis

To compare diagnostic efficacy between ^{18}F -FDG PET/CT and EMG mapping, McNemar test was used. $P < 0.05$ was considered statistically significant.

Fig. 2 Maximum intensity projection volume-rendering PET image of a 30-year-old male patient with right PCD. Hypermetabolism was found in right splenius capitis muscle, right levator scapulae muscle, left trapezius muscle, and bilateral sternocleidomastoid muscles. All hypermetabolic muscles were dystonic based on physical exam and measurement of rotation angle

Table 1 Clinical characteristics of patients

Characteristics	Values
Male/female	5/5
Age (years)	44±13 (22–64)
Age of onset (years)	43±12 (22–62)
Duration of dystonia (min)	13±17 (2–60)
Direction of rotation (right/left)	7/3

Values are numbers or mean ± SD (range)

Results

Clinical characteristics of patients are summarized in Table 1. Half of subjects were male. Mean age was 44±13 years (range: 22–64 years). Among 80 muscles evaluated, there were 21 (26%) dystonic superficial cervical muscles assessed with physical exam and motion analysis (Table 2). Based on EMG mapping (Table 3), there were 40 dystonic muscles (50%). In contrast, there were 22 hypermetabolic muscles (28%) on ^{18}F -FDG PET/CT (Table 4). Most commonly involved muscles were the ipsilateral splenius capitis and contralateral sternocleidomastoid muscles both on EMG and ^{18}F -FDG PET/CT. False positive results of EMG analysis occurred most frequently in ipsilateral levator scapulae (25%) and contralateral upper trapezius (25%) muscles. Three out of five false positive results on ^{18}F -FDG PET/CT occurred in the contralateral upper trapezius muscle. The sensitivity, specificity, and accuracy were 76, 92, and 88% for ^{18}F -FDG PET/CT and 95, 66, and 74% for EMG mapping, respectively (Table 2). The sensitivity of EMG mapping was significantly higher than that of ^{18}F -FDG PET/CT. In contrast, ^{18}F -FDG PET/CT was superior to EMG mapping in terms of specificity and accuracy. Maximum SUVs in

dystonic muscles as determined by ^{18}F -FDG PET/CT fell in the range of 1.5 to 19.4.

Discussion

There are reliable clinical rating scale systems such as the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS). However, they may not be discriminating enough to estimate significant changes in cervical dystonia patients [12, 23]. As the availability of reasonably effective symptomatic treatment such as botulinum toxin injection has stimulated the development of various approaches to select candidate muscles, electrophysiologic and goniometric analysis has gained popularity. Although mapping based on needle electromyography (EMG) is the most widely used method for identifying dystonic muscles in PCD, the poor localization of target muscles is a major cause of treatment failure [1, 5]. Application of PET images to evaluate muscular metabolic activity has been reported to be a useful strategy [13–16]. A recent study showed ^{18}F -FDG PET/CT could be effectively applied to localize dystonic muscles in PCD patients [17], however, ^{18}F -FDG PET/CT was not compared with the EMG mapping data in this study.

In the present study, we compared ^{18}F -FDG PET/CT with EMG mapping for the purpose of localizing dystonic superficial cervical muscles. ^{18}F -FDG PET/CT showed higher specificity and accuracy than EMG mapping. High specificity is important to find dystonic cervical muscles because the permitted dose of BT injection is limited and BT is an expensive drug. The sensitivity was higher in EMG mapping than the ^{18}F -FDG PET/CT. The specificity of EMG analysis can be compromised by intermittent symptoms, dystonia involving deep muscles that were not recorded by the surface electromyogram, or difficulties in

Table 2 Result of electromyography mapping of each patient

Patients (sex/age)	1 (F/46)	2 (F/22)	3 (M/43)	4 (M/35)	5 (M/30)	6 (F/51)	7 (M/63)	8 (M/64)	9 (F/42)	10 (F/48)
Ipsilateral^a										
SPC	P ^c	P	P	P	P	P	P	P	P	P
SCM	N	N	N	P	P	N	N	N	N	N
LS	P	N	P	N	P	N	P	P	P	P
uTz	N	N	N	P	P	N	N	N	N	N
Contralateral										
SPC	N	P	N	N	P	N	N	N	P	P
SCM	N	P	P	N	P	P	P	P	P	P
LS	N	P	N	N	P	N	N	N	P	P
uTz	P	P	N	P	P	P	N	P	N	N

SPC Splenius capitis muscle, SCM sternocleidomastoid muscle, LS levator scapulae muscle, uTz upper trapezius muscle, P EMG positive dystonic muscle, N EMG negative nondystonic muscle

^a The side where the head is rotated

Table 3 Standardized uptake values of each hypermetabolic dystonic muscle measured on ^{18}F -FDG PET/CT

Patient no.	1	2	3	4	5	6	7	8	9	10
Ipsilateral ^a										
SPC	5.7	6.8	4	3.4	19.4	N	3.6	2.7	6.6	4.6
SCM	N	N	N	4.4	6.4	N	N	N	N	N
LS	3.2	N	N	N	11.2	N	N	N	N	N
uTz	1.5	N	N	2.1	N	N	N	N	N	N
Contralateral										
SPC	N	N	N	N	N	N	N	N	N	N
SCM	N	N	N	N	16.3	1.9	4.6	N	4.8	9
LS	N	N	N	N	N	N	N	N	N	N
uTz	N	1.6	N	N	10.9	N	N	N	5.6	1.6

SPC Splenius capitis muscle, SCM sternocleidomastoid muscle, LS levator scapulae muscle, uTz upper trapezius muscle, N ^{18}F -FDG PET/CT negative nondystonic muscle

^a The side where the head is rotated

reproducing the dystonic symptoms during the examination [24]. This relative lower specificity of EMG mapping suggests that the electrical abnormality of cervical muscles is not always correlated with dystonic muscles causing dystonic posture. In contrast, metabolic abnormality may be more correlated with clinically significant dystonic superficial muscles causing dystonic posture. This result suggests ^{18}F -FDG/PET and EMG mapping can be reliably adopted as complementary tools for the detection of dystonic cervical muscles in PCD patients and as aids to establish an effective therapeutic plan. In this study, all patients underwent PET/CT while maintaining a sitting position during ^{18}F -FDG uptake; this was shown to be the optimum posture for improving the sensitivity of PET/CT [17]. Also, all measurements were performed before BT therapy, which excludes the possible influence of muscle denervation owing to prior BT therapy.

This study had several limitations. First, the small number of subjects was a major limitation. Second, a comparison of the responses to BT therapy was not included. The response prediction for BT therapy is clinically more important. The detection of dystonic muscles in PCD patients with ^{18}F -FDG PET/CT before and after therapy needs to be compared with EMG mapping, and feasibility as a therapy monitoring tool should also be determined. Therefore, this study presents preliminary results. Currently, we are undergoing clinical trials on a larger number of patients to substantiate the results of the present study, and we are including BT response data.

In conclusion, ^{18}F -FDG PET/CT is more specific and accurate than EMG mapping for finding superficial dystonic cervical muscles. High sensitivity of EMG mapping suggests that ^{18}F -FDG PET/CT and EMG mapping complement each other for finding dystonic superficial cervical

Table 4 Diagnostic efficacy for detecting of dystonic superficial cervical muscles between EMG mapping and ^{18}F -FDG PET/CT

Dystonic muscles (n)		^{18}F -FDG PET/CT			EMG mapping		
		Sensitivity	Specificity	Accuracy	Sensitivity	Specificity	Accuracy
Ipsilateral ^a							
SPC	9	89% (8/9)	100% (1/1)	90% (9/10)	100% (9/9)	0% (0/1)	90% (9/10)
SCM	1	100% (1/1)	89% (8/9)	90% (9/10)	100% (1/1)	89% (8/9)	90% (9/10)
LS	2	100% (2/2)	100% (8/8)	100% (10/10)	100% (2/2)	38% (3/8)	50% (5/10)
uTz	0	NA	100% (10/10)	100% (10/10)	NA	100% (10/10)	100% (10/10)
Contralateral							
SPC	0	NA	100% (10/10)	100% (10/10)	NA	60% (6/10)	60% (6/10)
SCM	8	50% (4/8)	50% (1/2)	50% (5/10)	88% (7/8)	50% (1/2)	80% (8/10)
LS	0	NA	100% (10/10)	100% (10/10)	NA	70% (7/10)	70% (7/10)
uTz	1	100% (1/1)	60% (6/9)	70% (7/10)	100% (1/1)	44% (4/9)	50% (5/10)
Overall	21	76% (16/21)*	92% (54/59)*	88% (70/80)*	95% (20/21)*	66% (39/59)*	74% (59/80)*

SPC Splenius capitis muscle, SCM sternocleidomastoid muscle, LS levator scapulae muscle, uTz upper trapezius muscle

* $P < 0.05$

^a The side where the head is rotated

muscles. Further comparative studies using a larger number of subjects and therapeutic response data are necessary.

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