

## Prevalence and clinical features of non-motor symptoms of essential tremor in Shanghai rural area



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### ABSTRACT

**Objective:** Few studies regarding the epidemiology of essential tremor (ET) and its non-motor symptoms (NMS) have been conducted to date. We thus conducted a door-to-door survey to investigate the ET and its NMS and their clinical manifestations in a rural area of Shanghai, China.

**Methods:** We recruited 19,614 residents ( $\geq 50$  years old), living in Malu town, Shanghai. Investigations were divided into two steps. In first step, trained physicians conducted door-to-door surveys and reported probable ET subjects to movement disorder specialists. In the second step, participants with suspected ET had their diagnosis confirmed by movement disorder specialists. We randomly selected 123 subjects from those adults who screened negative for neurological conditions as healthy controls for the study of NMS.

**Results:** The prevalence of ET in individuals ( $\geq 50$  years old) was 0.306% (PR = 3.06 per 1000). The mini-mental state examination (MMSE) scores were lower in ET patients than in controls ( $25.81 \pm 4.20$  vs.  $26.63 \pm 3.14$ ,  $P = 0.024$ ). Complaints of restless legs reported by ET patients were significantly higher than those in controls ( $P < 0.05$ ). In contrast, we did not observe a significant difference for other NMS between ET patients and controls, including olfactory function ( $P = 0.82$ ), depression ( $P = 0.94$ ), and rapid eye movement sleep behavior disorder (RBD) ( $P = 0.71$ ).

**Conclusions:** The prevalence of ET in people  $\geq 50$  years old in a rural area of Shanghai China is low. Prevalence of certain NMSs was higher among participants with ET relative to health controls.

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### 1. Introduction

Essential tremor (ET) is characterized by tremor (postural and/or kinetic) predominantly in both upper limbs and may also involves other body sites [1,2]. Previously, the modifier "benign" was used to indicate the favorable prognosis of the condition, but it is now widely acknowledged that ET can result in marked physical and psychosocial disabilities in affected individuals. Furthermore,

the traditional view that ET is a mono-symptomatic tremorgenic disorder has been challenged. Emerging evidences in recent years suggest that ET is possibly associated with several non-motor symptoms (NMS), including cognitive impairment, anxiety, depression and olfactory dysfunction [3–11]. However, upon reviewing the literature to date, there is no epidemiological study covering the natural spectrum of NMS featured in ET. Therefore, we conducted a population-based, door-to-door survey to assess the prevalence of NMS in ET in a Chinese rural area. The main purpose of study is to broaden the recognition and deepen the understanding of NMS in ET.

ET is considered to be one of the most common adult-onset movement disorders. Yet, there are significant discrepancies among the reported prevalence of ET (from 0.01% to 1.6% in all ages)

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as reported by different surveys [12]. Previous studies have demonstrated that the prevalence of ET in Asian countries is lower than that in their Western counterparts, which could be due to certain genetic or environmental variations [13]. Our study also aims to further contribute to the epidemiological data of ET in China, as only two published articles had presented the prevalence of ET in a Chinese population to date [14,15].

## 2. Methods

A population-based study was conducted from April 2011 to October 2013 to identify subjects with ET through a 2-step door-to-door survey. This study was approved by the local authority and the Research Ethics Committee; Ruijin Hospital affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China. Written informed consent was obtained from the subjects prior to the survey interview.

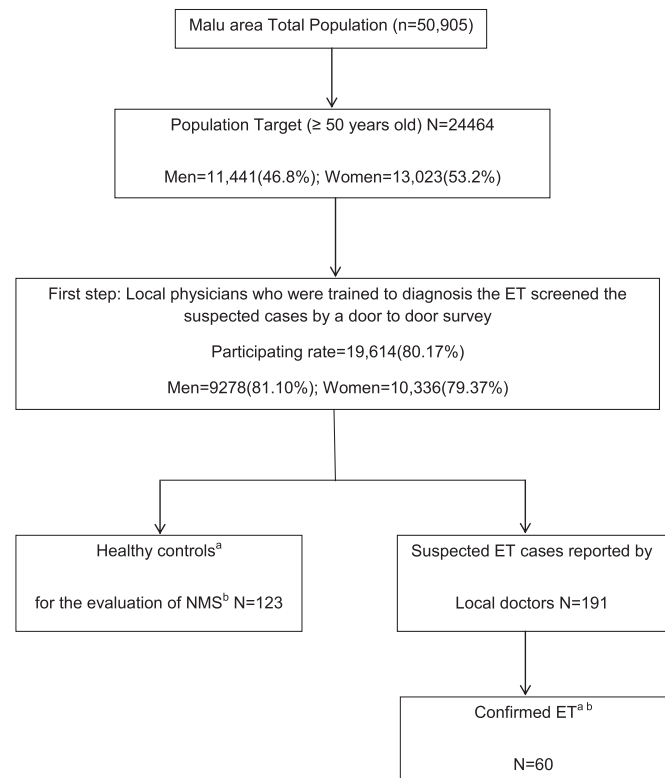
## 3. Study population

Malu town is located in northwestern Shanghai with an area of 57.16 km<sup>2</sup> and 50,905 inhabitants according to the population census. Only the residents aged 50 and above were recruited in our study. A resident was defined as an individual living in Malu area for at least 9 months each year. After excluding the non-residents and deceased individuals, the target population was 24,464. A cohort of randomly selected 123 aged and gender matched adults amongst the Malu residents who were free of neurological disorders were set up as healthy controls, for the evaluation of the NMS relative to ET patients.

## 4. Study design

The study employed a two-step design incorporating a population-based door-to-door screening and a face-to-face interview (Fig. 1). We initially held a 1-day workshop to train local doctors in Malu on the clinical diagnosis of ET. Two senior movement disorders specialists from the neurology department of Ruijin hospital were responsible for the whole training program. A combination of training materials were used for the 1-day program, including written instructions on clinical characters of ET, the use of screening questionnaire and videos of the tremor examination. Upon completion of the 1-day program, a local doctor was considered as qualified if he or she demonstrated competency in completing a standardized clinical examination for ET under the supervision by the movement disorder specialists. Only qualified local doctors were recruited for population screening in order to minimize inter-rater variability. These qualified local doctors subsequently visited residents  $\geq 50$  years in their dwellings and administered the screening questionnaire in a face-to-face interview and performed the ET examination on participants. The 9-question screening instrument included questioning regarding shaking limbs on was used to detect potential cases of ET [16]. The response options for the screening questionnaire were “yes” and “no”. Additionally, the participants were asked to perform three tasks to assess postural and kinetic tremors. These included 1) sustained bilateral arm extension, 2) bilateral finger-nose-finger maneuver and 3) drawing spirals with both the dominant and non-dominant arms. The presence of postural or kinetic tremor of upper limbs, or head tremor, were noted. Participants who responded positively to the screening questionnaire or were observed to have hands, forearms or head tremors were preliminarily diagnosed with suspected ET and progressed to step two.

In step two, suspected ET cases were further examined by movement disorder specialists to confirm their diagnosis. Two



**Fig. 1.** Flow of patients with ET through the study. a. Gender and age proportion between cases and controls was statistically matched. b. Assessments of NMS<sup>a</sup> including MMSE<sup>a</sup>, SS-16<sup>a</sup>, RBDSQ<sup>a</sup>, HAMD-17<sup>a</sup>, NMS-Quest<sup>a</sup>. <sup>a</sup>NMS: non-motor symptoms, MMSE: Mini-Mental State Examination, SS-16: the 16-item odor identification test from extended version of Sniffin'Sticks; RBDSQ: Rapid Eye Movement Sleep Behavior Disorder Screening Questionnaire; HAMD-17: Hamilton depression scale 17 items; NMS-Quest: Non-motor symptoms questionnaire.

movement disorder specialists independently examined the suspected ET cases using the standardized tremor examination described by Louis et al. [12,17], and a full neurological examination was also performed to exclude Parkinsonism and other movement disorders. A senior neurologist expert on movement disorders evaluated individuals when there was disagreement between the 2 movement disorder specialists and made the final diagnosis. The clinical diagnosis of ET was in accordance with the Consensus Statement of the Movement Disorders Society in 1998 [18]. Participants with parkinsonism, cerebellar (intention) tremor, drug induced tremors, dystonia and tremors with hyperthyroidism were all excluded from the study. Once the diagnosis of ET was confirmed, a detailed history documenting symptoms, treatment, medical and family history were collected along with a thorough physical examination. Tremor severity was assessed using the Fahn-Tolosa-Marin essential tremor rating scale (FTMRS).

To assess for non-motor symptoms, the following diagnostic tools were applied in both ET patients and the 123 healthy controls in simplified Chinese: (1) Mini-Mental State Examination (MMSE); (2) the 16-item odor identification test from extended version of Sniffin'Sticks (SS-16); (3) Rapid Eye Movement Sleep Behavior Disorder Screening Questionnaire (RBDSQ); (4) Hamilton depression scale 17 items (HAMD-17); (5) Non-motor symptoms questionnaire (NMS-Quest).

## 5. Data analysis

Data was analyzed using the Statistical Package for Social

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