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Temporal discrimination threshold with healthy aging

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ABSTRACT

The temporal discrimination threshold (TDT) is the shortest interstimulus interval at which a subject can perceive successive stimuli as separate. To investigate the effects of aging on TDT, we studied tactile TDT using the method of limits with 120% of sensory threshold in each hand for each of 100 healthy volunteers, equally divided among men and women, across 10 age groups, from 18 to 79 years. Linear regression analysis showed that age was significantly related to left-hand mean, right-hand mean, and mean of 2 hands with R-square equal to 0.08, 0.164, and 0.132, respectively. Reliability analysis indicated that the 3 measures had fair-to-good reliability (intraclass correlation coefficient: 0.4–0.8). We conclude that TDT is affected by age and has fair-to-good reproducibility using our technique.

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1. Introduction

Aging is accompanied by changes in brain physiology. Age-related changes in brain physiology may make individuals more susceptible to disease, influence disease progression, or response to treatment. It would be important to study the effects of aging on any diagnostic tool probing brain physiology.

Fundamental to our sense of reality, both internal and external environments, is the experience of time. Temporal discrimination is the ability to detect elapsed time, specifically to perceive sequential stimuli. The temporal discrimination threshold (TDT) is the shortest interstimulus interval at which a subject can perceive successive stimuli as separate (Fig. 1). Stimuli can be tactile, visual, or auditory. Elevated values have been described in lesions in internal capsule, posterior parietal cortex lesions, caudate nucleus, putamen, medial thalamus, and lenticular nucleus (Lacruz et al., 1991), cerebellar atrophy (Manganelli et al., 2013), and in Parkinson disease, especially those with PINK1 mutations (Fiorio et al., 2008b), with a single dose of levodopa improving the TDT abnormality (Artieda et al., 1992; Conte et al., 2010; Di Biasio et al., 2015; Lee et al., 2005; Lyoo et al., 2012), while deep brain stimulation is associated with prolonged TDT (Conte et al., 2010). Even higher TDTs, sufficient to differentiate from Parkinson patients, were reported in multiple system atrophy (Rocchi et al., 2013). In dystonia, increased TDT (Bara-Jimenez et al., 2000; Bradley et al., 2012; Conte et al., 2014; Fiorio et al., 2003, 2008a; Sanger et al., 2001; Scontrini et al., 2009; Tinazzi et al., 1999) is not only prevalent but considered to be an endophenotype in autosomal-dominant primary torsion dystonia, seen even in unaffected carriers (Bradley et al., 2009; Fiorio et al., 2007; Kimmich et al., 2011). That TDT is highly associated with particular gene mutations has led to interest in developing TDT as a useful tool in performing genetic studies. TDT has been shown to differentiate between dystonic tremor (having elevated TDT) and essential tremor (Tinazzi et al., 2013). It has also been demonstrated to be elevated in isolated head and voice tremors (Conte et al., 2015), psychogenic dystonia (Morgante et al., 2011) and psychogenic tremor (Tinazzi et al., 2014).

Tactile TDT testing holds promise as a clinical probe in that it is easily performed, quick, and generally comfortable. Particularly in dystonia, it is useful because it has been shown to be unaffected by botulinum toxin (Scontrini et al., 2011) or pallidal stimulation (Sadnicka et al., 2013). However, there is great variety in technique as reported in the literature, there are no clear guidelines on normative values, and reproducibility data are scarce. Furthermore, age effects on tactile TDT are not known. Hoshiyama et al. (2004) studied 80 healthy volunteers from age 18 to 82 years and found that TDT increased with age only in subjects older than 65 years. Aging is associated with poorer auditory temporal discrimination (Fostick and Babkoff, 2013; Schneider et al., 2002; Snell and Frisina, 2000), which is believed to play a role in speech perception decline in the elderly.

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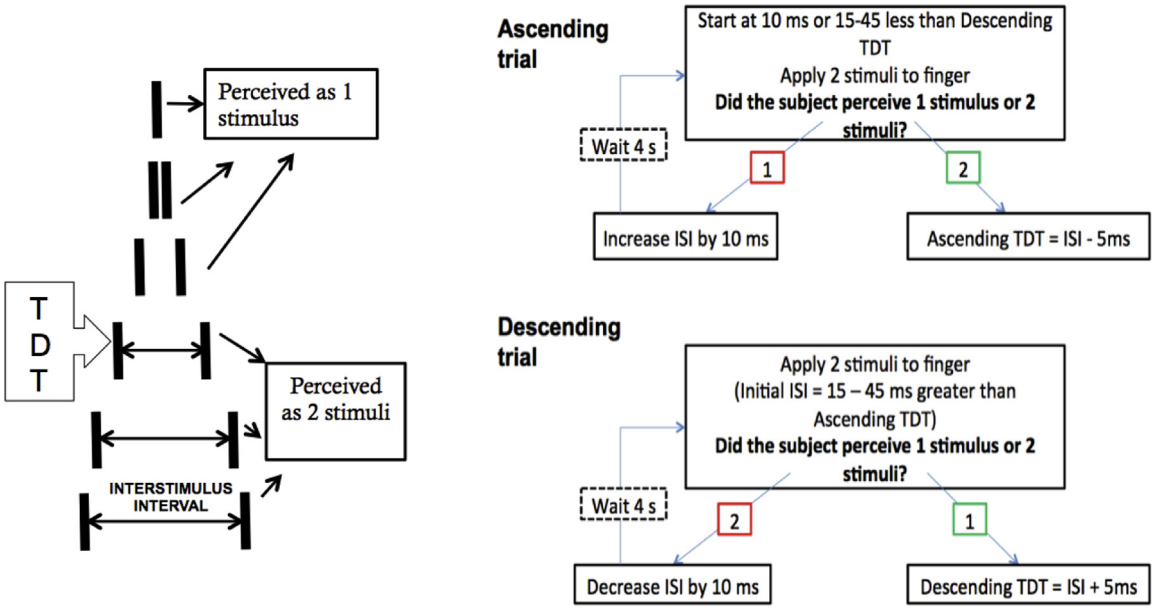

Fig. 1. The temporal discrimination threshold (TDT), the shortest interstimulus interval (ISI) that a subject can perceive successive stimuli, is tested using 6 trials of alternating ascending and descending limits.

To investigate the effects of aging on tactile TDT, we studied 100 healthy volunteers from age 18–79 years.

2. Materials and methods

2.1. Subjects

One hundred neurologically healthy subjects were recruited in 10 age groups of 5 men and 5 women each. Age grouping was 18–24, 25–30, 31–36, 37–42, 43–49, 50–55, 56–60, 61–66, 67–72, and 73–79 years old.

None of the subjects had history of any neurologic or psychiatric illness, including neuropathy, tremor, brain tumor, stroke, epilepsy or seizures, major depression or any major mental disorders (axis I disorders according to the Diagnostic and Statistical Manual of Mental Disorders, 4th ed.), had a head injury where there was a loss of consciousness, alcoholism, using illegal drugs, or CNS acting medications. Patients with peripheral sensory neuropathy, tremor, or focal neurologic findings documented on clinical examination were excluded. Patients with known or suspected family history of Parkinson disease or dystonia were excluded. Healthy volunteer status was based on interview and examination by neurologists. All subjects gave written informed consent consistent with the Declaration of Helsinki, which was approved by the CNS institutional review board of the National Institutes of Health, Bethesda, MD.

2.2. Temporal discrimination threshold procedure

Participants were seated in a comfortable chair with their testing hand on a table, palm facing up. All measurements were carried out in a quiet room at a temperature of 21–23 degrees centigrade. Each index finger was wiped clean with alcohol, then scrubbed with abrasive gel and wiped clean. The right index finger was tested before the left index finger for all participants. Prior to each index finger being tested, ring electrodes were placed in the distal and proximal interphalangeal creases with conductive gel, and tightened to a snug fit without causing any discomfort to the participants. The stimulation intensity for testing was set for each person individually at 120% of sensory threshold, defined as the minimum intensity where 10 out of 10 stimuli were perceived by the subject, determined by increasing the intensity of the stimulus from 2 mA in increments of 0.2 mA.

Two painless electrical stimuli with varying interstimulus intervals (ISIs) were used to determine the TDT of the index finger for each participant. Each stimulus consisted of a square wave pulse of 0.2-ms duration. Each participant was familiarized with the sensation of a single pulse (“one”) using ISI 0 ms, and the sensation of 2 pulses (“two”) using ISI 300 ms. Participants were informed that the ISI would be varied. Participants were asked to respond verbally by saying either “one” or “two” to indicate the number of pulses they perceived. Pairs of pulses were given at 4-second intervals to allow sufficient washout period. Each participant’s TDT was determined by the method of limits, with 3 ascending trials and 3 descending trials. Each ascending trial was followed by a descending trial for a total of 6 trials for each index finger. For ascending trials, ISI was increased from 0 ms in increments of 10 ms until 2 stimuli were perceived, and the ascending TDT was recorded as the smallest 10-ms increment that the subject was able to perceive 2 stimuli minus 5 ms. For descending trials, the ISI was increased 45 ms beyond the ascending TDT and the ISI was decreased by 10 ms until only 1 stimulus was perceived. The descending TDT was recorded as the highest 10-ms decrements plus 5 ms. The mean over the 6 trials was taken as the TDT. The TDT was considered valid when the participant consistently reported 2 stimuli with an ISI longer than the threshold for ascending trials, and consistently reported 1 stimulus with an ISI shorter than the threshold for descending trials. For each trial, at least 3 catch events consisting of an ISI 0 ms are included at random intervals to prevent perseverative responses and catch subject’s attention.

2.3. Reproducibility testing

Sixteen participants were retested following exactly the same protocol at least 1 week after the first test. No feedback was given from previous testing. Of these 16 participants, 10 were retested again at least 1 week after the second test.