Aristotle's illusion reveals interdigit functional somatosensory alterations in focal hand dystonia

Michele Tinazzi,1 Angela Marotta,1 Alfonso Fasano,2 Francesco Bove,2 Anna Rita Bentivoglio,2 Giovanna Squintani,3,4 Lara Pozzer1 and Mirta Fiorio1

In focal hand dystonia, the cortical somatosensory representation of the fingers is abnormal, with overlapping receptive fields and reduced interdigit separation. These abnormalities are associated with deficits in sensory perception, as previously demonstrated by applying tactile stimuli to one finger at a time. What is still unknown is whether the sensory deficits can be observed when tactile perception involves more than one finger. To address this issue, we applied ‘Aristotle’s illusion’ to 15 patients with focal hand dystonia, 15 patients with dystonia not affecting the hand (blepharospasm and cervical dystonia) and 15 healthy control subjects. In this illusion, one object touching the contact point of two crossed fingertips is perceived as two objects by a blindfolded subject. The same object placed between two parallel fingertips is correctly perceived as one. The illusory doubling sensation is because of the fact that the contact point between the crossed fingers consists of non-adjacent and functionally unrelated skin regions, which usually send sensory signals to separate spots in the somatosensory cortex. In our study, participants were touched by one sphere between the second–third digits, the second–fourth digits and the fourth–fifth digits of both hands, either in crossed or in parallel position, and had to refer whether they felt one or two stimuli. The percentage of ‘two stimuli’ responses was an index of the illusory doubling. Both healthy control subjects and dystonic patients presented Aristotle’s illusion when the fingers were crossed. However, patients with focal hand dystonia presented a significant reduction of the illusion when the sphere was placed between the crossed fourth and fifth digits of the affected hand. This reduction correlated with the severity of motor disease at the fingers. Similar findings were not observed in non-hand dystonia and control groups. The reduction of Aristotle’s illusion in non-affected fingers and its preservation in affected fingers suggests dissociation between the abnormal processing of sensory signals and the motor impairment. Based on previous evidence showing that the sensory signals coming from the fourth digit determine lower activation in the somatosensory cortex than those coming from the fifth digit, we suggest that in the crossed position, the tactile information conveyed by the fifth digit prevailed over the fourth digit, thus resulting in the perception of one stimulus. The reduction of the illusory doubling perception, therefore, may represent the functional correlate of the different level of activation between the fourth and the fifth digit in the somatosensory cortex.

Keywords: focal hand dystonia; diplesthesia; somatosensory processing; tactile illusion
Introduction

Focal hand dystonia is a movement disorder characterized by involuntary and prolonged contractions of the forearm and hand muscles that cause abnormal movements and postures at the elbow, wrist and fingers (Sitburana and Jankovic, 2008). In recent decades, research has demonstrated that the somatosensory system plays an important role in the pathophysiology of focal hand dystonia. More precisely, neuroimaging studies have revealed abnormal somatotopy of the digits represented in the somatosensory cortex, mainly consisting of reduced interdigit separation with enlarged and overlapped digit maps of activation (Bara-Jimenez et al., 1998; Elbert et al., 1998; Butterworth et al., 2003; Nelson et al., 2009). These alterations might underpin changes in somatosensory perception, as demonstrated by studies on spatial discrimination, in which patients with focal hand dystonia showed reduced capability to detect close tactile stimuli as being separate (Bara-Jimenez et al., 2000; Sanger et al., 2001; Molloy et al., 2003). All the studies on spatial discrimination were performed by applying the tactile stimuli to one finger. Tactile perception, however, can also derive from the integration of the sensory information arising from more than one finger. In this regard, we are able to perceive the unity of one object even when it exercises pressure on two different fingers (Gibson, 1962). This property of somatosensory perception might be associated with the pre-determined anatomical configuration of the hand, in which the position of the fingers and the contact regions between the fingertips is stable. Despite the evidence showing that in focal hand dystonia, the somatotopic representation of the fingers is altered, it is still unknown whether this alteration is associated with changes in sensory perception when the detection of one stimulus derives from more than one finger, or in other words, when tactile perception depends on the functional relation between fingers.

One simple, but cogent, way to investigate this issue is the so-called ‘Aristotle’s illusion’. Aristotle (in Metaphysica IV, 6) first noticed that by crossing the fingers, one gets the illusion of doubling a single stimulus positioned in the contact point of the fingertips (McKeon, 1941). As noticed here by Aristotle, an unusual configuration of the body (i.e. crossed fingers) causes a distortion in the perception of a physical stimulus. This type of tactile illusion has been experimentally investigated in a series of behavioural studies by Benedetti (1986a, b, 1991), who introduced the term ‘diplophasia’ to refer to the illusory doubling of one tactile object, as a tactile counterpart of the visual doubling called ‘diplopia’ (Benedetti, 1986a). The diplophasic sensation is explained by the functional correlation between adjacent and non-adjacent skin regions of the fingers. More precisely, two fingers or skin regions can be defined as functionally correlated if, when simultaneously touched, they produce the perception of one object. In this condition, the signals coming from the tactile receptors located on each fingertip are combined in a unitary representation of the stimulus. On the other hand, two fingers or skin regions cannot be defined as functionally correlated if, when simultaneously stimulated, they evoke a perceptual disjunction of one stimulus (as in the case of Aristotle’s illusion or diplophasia) (Benedetti, 1986a).

In our study, we applied, for the first time, Aristotle’s illusion paradigm to investigate the impairment of somatosensory processing in patients with focal hand dystonia. We particularly focused on the relationship between the strength of the tactile illusion with respect to the distance between fingers (adjacent and non-adjacent fingers) and to the presence of motor symptoms (affected and non-affected fingers). Furthermore, based on the current evidence of sensory alterations in several forms of focal dystonia (Molloy et al., 2003; Scontrini et al., 2009; Tinazzi et al., 2009), we investigated whether any change in the illusory perception could be recognized in other types of focal dystonia, such as blepharospasm and cervical dystonia, or whether it can be considered as an exclusive trait of focal hand dystonia.

Materials and methods

Participants

We recruited 30 patients with primary focal dystonia divided into two groups, depending on the localization of the motor symptoms: involving or not involving the hand (see later in the text for detailed description). Biochemical, CT and MRI examinations were normal, thus suggesting that dystonia was primary. Biochemical tests included urinary copper excretion, urinary organic acids and urinary amino acids, blood count, film for acanthocytes, plasmatic copper and caeruloplasmin levels, immunoglobulins, blood amino acids, creatine kinase level, α-fetoprotein, calcium, liver function indices, lactate and pyruvate. Patients did not present a family history of dystonia. The exclusion criteria for patients included the occurrence of other neurological diseases or sensory deficits localized to the hands. The patients were recruited at the Department of Neurology, University of Verona and at the Department of Neurology, University Hospital ‘Agostino Gemelli’ of Rome. The local ethical committee approved the study. Demographic and clinical information is shown in Table 1.

Focal hand dystonia

This group consisted of 15 patients (nine male; mean age ± standard deviation 45 ± 10.8) with dystonia localized to the dominant hand (14 right-handed, 1 left-handed), without involvement of the non-dominant hand. Eleven patients were affected by writer’s cramp and four patients were affected by musician’s cramp.

To assess the severity of dystonia at the arm, patients were evaluated with the Burke–Fahn–Marsden Movement Scale (Burke et al., 1985). The mean score was 3.78 ± 2.94 (range: 1–12, indicating slight to severe degree of motor symptoms). We also used the Writer’s Cramp Rating Scale (Wissel et al., 1996) to obtain a more detailed evaluation of the severity of disease. Among other parameters, this scale allows for the assessment of the severity of motor impairment during writing, by attributing severity scores to the fingers mostly involved in writing (the first, second and third digits). The fingers score depends on the level of pathological flexion or extension of the fingers during writing (0 = none, 1 = moderate, 2 = marked). This scoring method was also used to evaluate the severity of motor symptoms in the fingers of patients with musician’s cramp. In this case, we evaluated the amount of pathological flexion or extension of the fingers when patients played their instrument. The total finger score in focal hand dystonia group was 3.13 ± 1.46 (range: 0–6, indicating absent to severe motor symptoms at the fingers). Disease
duration (starting from the onset of motor symptoms) ranged from 1 to 40 years (11.9 ± 11.0 on average). Eleven patients were untreated. Four patients were treated with botulinum toxin no later than 4 months before the experiment.

### Control group

We recruited 15 healthy subjects as the control group (five male; mean age, 50.5 ± 15.8). All the participants were right-handed.

### Procedure

We applied a specifically designed Aristotle’s illusion paradigm to explore tactile perception in dystonic patients. Tactile stimuli consisted of one plastic sphere of 8-mm diameter and two plastic spheres of 4-mm diameter each (Benedetti, 1991). All the spheres were attached to a von-Frey filament, to ensure the same pressure (~35 g) during the task.

Participants sat comfortably on a chair with one hand palm-up on a table. The experimenter was seated near the participant, on the side of

<p>| Table 1 Demographic and clinical data for patients |
|---------------------------------|----------------|----------------|----------------|-----------------|----------------|----------------|</p>
<table>
<thead>
<tr>
<th>Group</th>
<th>Patient/gender</th>
<th>Age (years)</th>
<th>Type of dystonia</th>
<th>Disease duration (years)</th>
<th>Severity of diseasea</th>
<th>WCRS: FS (total)</th>
<th>Affected fingers</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>FHD 1/F</td>
<td>46 WC</td>
<td>15</td>
<td>4</td>
<td>6</td>
<td>D1, D2, D3</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FHD 2/F</td>
<td>51 WC</td>
<td>3</td>
<td>6</td>
<td>5</td>
<td>D1, D2, D3</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FHD 3/M</td>
<td>39 WC</td>
<td>8</td>
<td>3</td>
<td>2</td>
<td>D1, D2, D3</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FHD 4/M</td>
<td>40 WC</td>
<td>6</td>
<td>6</td>
<td>3</td>
<td>D1, D2, D3</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FHD 5/F</td>
<td>40 WC</td>
<td>11</td>
<td>4</td>
<td>3</td>
<td>D1, D2, D3</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FHD 6/M</td>
<td>60 WC</td>
<td>30</td>
<td>12</td>
<td>3</td>
<td>D1, D2, D3</td>
<td>BoNT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FHD 7/M</td>
<td>37 WC</td>
<td>2</td>
<td>4</td>
<td>3</td>
<td>D1, D2</td>
<td>BoNT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FHD 8/F</td>
<td>31 WC</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>D1, D2</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FHD 9/M</td>
<td>56 WC</td>
<td>12</td>
<td>1</td>
<td>0b</td>
<td>No</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FHD 10/M</td>
<td>40 MC</td>
<td>10</td>
<td>1</td>
<td>2c</td>
<td>D2</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FHD 11/M</td>
<td>51 MC</td>
<td>12</td>
<td>2</td>
<td>3c</td>
<td>D1, D2</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FHD 12/F</td>
<td>57 WC</td>
<td>40</td>
<td>4</td>
<td>5</td>
<td>D1, D2, D3</td>
<td>BoNT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FHD 13/M</td>
<td>24 MC</td>
<td>1</td>
<td>1</td>
<td>3c</td>
<td>D1, D2, D3, D4, D5</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FHD 14/F</td>
<td>42 WC</td>
<td>15</td>
<td>4</td>
<td>4</td>
<td>D1, D2, D3</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FHD 15/M</td>
<td>61 MC</td>
<td>10</td>
<td>6</td>
<td>2c</td>
<td>D2, D3</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHD 1/F</td>
<td>74 BS</td>
<td>18</td>
<td>0.5</td>
<td>NA</td>
<td>BoNT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHD 2/F</td>
<td>78 BS</td>
<td>1</td>
<td>0.5</td>
<td>NA</td>
<td>BoNT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHD 3/F</td>
<td>63 BS</td>
<td>10</td>
<td>2</td>
<td>NA</td>
<td>BoNT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHD 4/F</td>
<td>50 BS</td>
<td>34</td>
<td>1</td>
<td>NA</td>
<td>BoNT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHD 5/F</td>
<td>66 BS</td>
<td>2</td>
<td>1</td>
<td>NA</td>
<td>BoNT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHD 6/F</td>
<td>79 BS</td>
<td>15</td>
<td>2</td>
<td>NA</td>
<td>BoNT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHD 7/M</td>
<td>78 BS</td>
<td>5</td>
<td>2</td>
<td>NA</td>
<td>BoNT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHD 8/F</td>
<td>77 BS</td>
<td>20</td>
<td>2</td>
<td>NA</td>
<td>BoNT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHD 9/M</td>
<td>74 BS</td>
<td>8</td>
<td>4</td>
<td>NA</td>
<td>BoNT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHD 10/M</td>
<td>59 BS</td>
<td>3</td>
<td>4</td>
<td>NA</td>
<td>BoNT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHD 11/M</td>
<td>65 BS</td>
<td>4</td>
<td>6</td>
<td>NA</td>
<td>BoNT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHD 12/F</td>
<td>55 CD</td>
<td>1</td>
<td>3</td>
<td>NA</td>
<td>BoNT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHD 13/F</td>
<td>46 CD</td>
<td>4</td>
<td>12</td>
<td>NA</td>
<td>BoNT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHD 14/F</td>
<td>79 CD</td>
<td>7</td>
<td>13</td>
<td>NA</td>
<td>BoNT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHD 15/M</td>
<td>62 CD</td>
<td>10</td>
<td>14</td>
<td>NA</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*aBurke–Fahn–Marsden movement scale score.*

*bThis patient presents wrist extension dystonic movements during the writing task, whereas fingers do not show dystonic postures or movements, the severity of ‘Wrist score’ (subscale of Writer’s cramp rating scale) is 2 (marked pathological extension of wrist).*

*cWe provided to the assessment of motor symptoms fingers in musician’s cramp patients by using the same parameters of the ‘Finger score’ subscale (one of the subscale of Writers’ cramp rating scale).*

BS = blepharospasm; BoNT = botulinum toxin; CD = cervical dystonia; D1 = first digit (thumb); D2 = second digit (index); D3 = third digit (middle); FHD = focal hand dystonia; FS = finger score; MC = musician’s cramp; NA = not administrable; NHD = non-hand dystonia; WC = writer’s cramp; WCRS = Writer’s Cramp Rating Scale.
the hand to be tested. The participants were informed that one or two spheres could be applied to one or two fingertips or to the contact point between two fingertips. To allow subjects to familiarize themselves with the tactile sensation associated with the stimuli, a short training session was carried out in which two fingers were touched by one or two stimuli. The stimuli were not shown to the participants. After the instructions, participants were asked to keep their eyes closed throughout the experiment. The experimenter applied the stimuli to the subject’s fingertips, by randomly varying the type of the stimulus (one or two spheres), the stimulated pair of fingers (second–third digit, second–fourth digit or fourth–fifth digit) and the finger position (crossed or parallel) (Fig. 1A). The random order was standardized across subjects. In all the trials, the fingers were passively moved by the experimenter in parallel or crossed position and maintained in contact for the duration of the trial, until the participant’s response. In the ‘crossed’ condition, the subject’s fingers were crossed by the experimenter and touched by the 8-mm sphere in the contact point between the two fingertips (Fig. 1A). The stimulus was removed after 5 s, and the participants were asked whether they have been touched by one or two stimuli. This condition evokes, in healthy subjects, the illusion of doubling sensation and typically the subject’s answer is ‘two stimuli’ (Benedetti, 1985). In the ‘parallel’ condition, the fingers were positioned in parallel by the experimenter and again touched with the 8-mm sphere at the contact point between the fingertips for 5 s (Fig. 1A). Usually, the ‘parallel’ condition does not produce doubling sensation and the subject perceives the touch of one object (Benedetti, 1985). To prevent the possibility that a cutaneous displacement could cause the tactile illusion even in the parallel condition (Benedetti, 1986a), the experimenter carefully avoided exerting excessive pressure while maintaining contact with the fingertips.

To avoid any response bias because of a mere association between the finger positions and the type of answer (i.e. crossed position—answer ‘two stimuli’; parallel position—answer ‘one stimulus’), we introduced two additional control conditions (Fig. 1B): one consisted of touching only one fingertip with the 8-mm sphere while keeping the fingers in a crossed position. This condition does not evoke the illusory doubling perception, and the subject’s answer should be ‘one stimulus’, although the fingers are in a crossed position. Another control condition consisted of touching the two fingertips with the two 4-mm spheres by keeping the fingers in a parallel position. There is no illusory perception, and the subject’s answer should be ‘two stimuli’.

To test the functional relationships between adjacent and non-adjacent fingers, each condition was tested with three pairs of digits: second–third digit (D2–D3), second–fourth digit (D2–D4) and fourth–fifth digit (D4–D5). Furthermore, this protocol allowed assessing digits more or less usually affected in focal hand dystonia (D2–D3 and D4–D5, respectively) (Elbert et al., 1998; Nelson et al., 2009).

There were 90 trials: 30 in the crossed condition (10 for each digit pair), 30 in the parallel condition (10 for each digit pair) and 30 in the additional control conditions (10 for each digit pair). We tested both the dominant (affected in patients with focal hand dystonia) and non-dominant hand, with a counterbalanced order across participants.

To control the degree of overlap of the digits, the experimenter preliminarily marked precise reference points on the fingertips and, subsequently, moved the subject’s fingers to position them into contact exactly where the points were marked. More precisely, the skin area to bring into contact was marked on the distal phalanx by drawing two longitudinal segments on the sides of the phalanx and perpendicular to interphalangeal joint (Fig. 1C). The distance between the two segments was 4 mm. Starting from D2, the experimenter marked a point 1 cm from the interphalangeal joint. This point served as reference to define the contact point of all the other fingers, both in the parallel and in the crossed condition. Through this procedure, the degree of overlap was the same in all the digit pairs, in all the participants and on both hands.

**Data analyses**

The preliminary analyses to ensure that the two patient groups and the control group did not differ in demographic characteristics revealed no
difference in age between patients with focal hand dystonia and control subjects \( t(28) = -1.12, P > 0.050 \), whereas significant age differences emerged between non-hand dystonia and focal hand dystonia \( t(28) = 5.50, P < 0.001 \), as well as between non-hand dystonia and control subjects \( t(28) = 3.30, P = 0.003 \). Therefore, age was included as a covariate in the main analysis.

To rule out differences because of peripheral somatosensory impairment, we compared the response with the additional control conditions in patients and control subjects by means of t-test for independent samples. These preliminary analyses showed that the number of correct responses in the two control conditions (i.e. touching one fingertip by keeping the fingers in a crossed position and touching two fingertips by keeping the fingers in a parallel position) was high on both hands and comparable between both groups of patients and control subjects (for all comparisons, \( P > 0.050 \)), thus suggesting that all the subjects were able to perceive the stimuli applied to the fingertips.

For each condition (crossed and parallel), we computed the degree of the illusion as a percentage of ‘two stimuli’ responses. This percentage was analysed in each pair of fingers separately by means of repeated measures analyses of covariance with age as covariate. ‘Group’ (focal hand dystonia versus non-hand dystonia versus control subjects) was the between-subject factor, whereas ‘Finger Position’ (crossed versus parallel) and ‘Hand’ (dominant versus non-dominant) were the within-subject factors. Bonferroni correction for multiple comparisons was applied when post hoc analyses were necessary. Finally, Spearman’s correlation was carried out to assess whether the severity of motor symptoms in the dominant hand of patients with focal hand dystonia correlated with the percentage of illusion. As an index of severity, we used the total finger score, computed as the sum of the severity scores of the affected fingers in patients with focal hand dystonia. \( P \)-values of \( < 0.050 \) were considered significant.

### Results

The main analysis on the percentage of illusion showed that the factor ‘Finger Position’ was significant for all the pairs of digits \( D2–D3: F(1,41) = 185.80, P < 0.001; D2–D4: F(1,41) = 46.74, P < 0.001; D4–D5: F(1,41) = 85.50, P < 0.001 \) because of a higher percentage of ‘two stimuli’ response in the crossed (mean-standard error of the mean, \( D2–D3: 96 \pm 1\%; D2–D4: 96 \pm 1\%; D4–D5: 91 \pm 2\% \)) than in the parallel position (\( D2–D3: 1 \pm 0.4\%; D2–D4: 23 \pm 3\%; D4–D5: 2 \pm 1\% \)).

In the \( D4–D5 \) pair, the interaction ‘Group’ \( \times ‘Finger Position’ \) was also significant \( F(2,41) = 4.87, P = 0.012 \). Post hoc comparisons showed that in the crossed position, patients with focal hand dystonia had a lower percentage of the ‘two stimuli’ response than control subjects (focal hand dystonia: \( 92 \pm 3\% \), control subjects: \( 96 \pm 3\%; P = 0.024 \)). Interestingly, the triple interaction ‘Hand’ \( \times ‘Finger Position’ \times ‘Group’ \) was also significant \( F(2,41) = 3.76, P = 0.031 \). Post hoc comparisons showed that patients with focal hand dystonia reported a lower percentage of ‘two stimuli’ response (\( 73 \pm 5\% \)) compared with control subjects (\( 96 \pm 5\%, P = 0.010 \)) and patients with non-hand dystonia (\( 97 \pm 6\%, P = 0.033 \)) in the crossed position of the dominant hand (affected in focal hand dystonia) (Fig. 2A). No significant difference between groups has been found in the parallel position (\( P > 0.050 \)) (Fig. 2B). Furthermore, patients with focal hand dystonia presented a lower percentage of ‘two stimuli’ responses in the dominant hand (\( 73 \pm 5\% \)) compared with the non-dominant hand (\( 92 \pm 4\% \)) in the crossed position (\( P = 0.005 \)). No significant difference between the two hands was found in the other two groups (\( P > 0.050 \)).

With the digit pairs \( D2–D3 \) and \( D2–D4 \), the factors ‘Group’, ‘Hand’ and the interactions were not significant (for all factors, \( P > 0.050 \)). No correlation was found between the percentage of illusion in \( D2–D3 \) and \( D2–D4 \) and the disease severity at the total finger score (Spearman’s \( \rho = -0.28, P > 0.050 \)). By contrast, an inverse correlation was found between the percentage of illusion in \( D4–D5 \) and the total finger score (Spearman’s \( \rho = -0.61, P = 0.016 \)) (Fig. 3).

### Discussion

In keeping with previous studies (Benedetti, 1985, 1986a), we found that the illusory perception of a double stimulus occurs...
more frequently when the fingers are in the crossed than in the parallel position, thus confirming the validity of the applied paradigm. Our study reveals for the first time that the same finding is detectable for all the tested digit pairs in patients with focal hand dystonia. Notably, a reduction of the illusory doubling perception was found in the digit pair D4–D5 of the affected hand. As will be discussed later in the text, the illusory decrease on the least dystonic fingers D4–D5, but not on the other digits, and the fact that this failure occurred only on the affected hand, may have important implications for understanding the nature of sensory alterations in focal hand dystonia.

The illusory doubling perception arises from the simultaneous stimulation of skin areas usually separated during tactile exploration, thus resulting in the activation of two distant spots in the primary somatosensory cortex (Benedetti, 1986a, b). By testing different pairs of fingers located more or less laterally or medially in respect to the hand map, Benedetti (1986b) demonstrated that the stimulation of adjacent fingers in a parallel position results in higher percentage of ‘one stimulus’ response compared with the stimulation of non-adjacent fingers. Hence, the diplophesthetic illusion can be more strongly evoked in non-adjacent than in adjacent finger pairs, independent of their position on the hand map. This notion is in line with the findings by Chen et al. (2003) on the ‘funnelling illusion’, which occurs when multiple brief stimuli are simultaneously applied to different skin sites. Particularly, these authors highlighted the role of the distance between digits in evoking the illusion: if the digits were adjacent, the multiple sensory inputs conveyed to the primary somatosensory cortex were elaborated in an integrated manner, resulting in the sensation of a unique object; on the other hand, if the digits were non-adjacent, their simultaneous stimulation produced the activation of two spots in the primary somatosensory cortex, resulting in a sensation of multiple sites of stimulation (Chen et al., 2003).

In this study, we examined adjacent (D2–D3 and D4–D5) and non-adjacent (D2–D4) fingers. The digit pair D2–D4 consisted of two functionally less correlated fingers, compared with D2–D3 and D4–D5 (Benedetti, 1986a). This might explain the apparent high percentage of ‘two stimuli’ response even in the parallel position of this fingers pair (Fig. 2). Nonetheless, in all the examined digit pairs, the stimulated skin regions were more functionally correlated in the parallel than in the crossed position (Benedetti, 1985, 1986a). Hence, in the crossed condition, we could assist the illusory doubling perception when one stimulus touched the contact point between the fingers (Benedetti, 1985, 1986a).

In our sample, 14 of the 15 patients with focal hand dystonia (93.3% of the group) were affected at D2, and 9 of the 15 patients (60% of the group) showed motor symptoms localized to both D2 and D3 (Table 1). This is in keeping with the notion that in writer’s cramp, the second and the third digits of the dominant hand are consistently (the former) and commonly (the latter) affected (Nelson et al., 2009), whereas in musician’s cramp, the third digit is often affected, but the second digit can also be affected (Elbert et al., 1998). Only one patient had the involvement of D4 and D5 (Case 13, Table 1); therefore, we consistently used Writer’s Cramp Rating Scale, which only rates the occurrence and severity of symptoms at D1, D2 and D3. The fact that patients with focal hand dystonia presented on both hands with a high percentage of ‘two stimuli’ response in the crossed D2–D3 and D2–D4, comparable with non-hand dystonia and control subjects, suggests that the presence of motor symptoms does not influence the establishment of the illusory perception. This conclusion is further supported by the lack of correlation between the degree of illusory doubling at D2–D3 and the fingers severity score.

The most interesting finding of our study regards the reduction of the illusory doubling perception in the crossed position of D4–D5 on the dominant affected hand in focal hand dystonia. Namely, although patients with focal hand dystonia presented the illusory doubling sensation in the crossed compared with the parallel position, the percentage of illusion in this digit pair was significantly reduced relative to the other two groups. This finding is surprising because it involves two adjacent digits, which are usually not affected by motor symptoms in dystonia (Nelson et al., 2009).

A possible explanation derives from a recent study of patients with focal hand dystonia (Nelson et al., 2009). In particular, the study revealed a reduction in the activation of the primary somatosensory cortex for the sensory inputs coming from D2, D3 and D4 and a level of activation similar to healthy control subjects in response to sensory inputs from D1 and D5 (Nelson et al., 2009). We could hypothesize that the imbalance of sensory signals coming from D5 (i.e. stronger than the ones coming from D4) has contributed to the reduction of the percentage of ‘two stimuli’ responses when placing one object on the contact point between D4 and D5 in a crossed position. In other words, we suggest that touching the contact point of the crossed D4–D5 determined a sort of competition in which the sensory signals from D5 often prevailed over the sensory signals from D4, thus resulting in the perception of one stimulus. Accordingly, Aristotle’s illusion was preserved in the other digit pairs, as the same level of activation likely characterizes the primary somatosensory area in which D2, D3 and D4 are represented (Nelson et al., 2009). Hence, following the same line of reasoning, the sensory signals derived from these three digits did not prevail over each other, thus allowing the
illusive doubling perception when the crossed fingers were touched at the contact point.

The reduction of Aristotle’s illusion in non-affected fingers and its preservation in affected fingers could be interpreted as dissociation between the abnormal processing of sensory signals and the motor impairment. This apparent dissociation could be related to the methodological choice of positioning the fingers in an artificial, passive way, while subjects were relaxed. Namely, as it is not possible to voluntarily cross all the digits, and particularly D2–D4 and D4–D5, the fingers had to be manually positioned by the experimenter. It is reasonable that in patients with focal hand dystonia, the absence of voluntary movements could have reduced the impact of the motor symptoms on the illusory perception. This is in line with a neurophysiological study in focal hand dystonia demonstrating that, at rest, motor abnormalities are absent, whereas somatosensory alterations are present (Weise et al., 2012). Hence, we could conclude that with our paradigm, we were able to disentangle the mere contribution of the sensory alterations (i.e. the different level of activation between digits) in determining the reduction of illusion in D4–D5.

The reduction of the illusion found in D4–D5 correlated with the severity score evaluated at the first three fingers. Interestingly, a qualitative inspection of the data showed that six of the nine patients with focal hand dystonia who presented motor symptoms both at D2 and at D3 had a reduced illusion at D4–D5 (<100%), whereas only two of the five patients with focal hand dystonia who were affected at D2, but not at D3, had a reduced illusion at D4–D5. These findings might be explained by a diffusion of sensory abnormalities (Byl et al., 1996, 1997; Blake et al., 2002a, b) from the most affected fingers (i.e. D2 and D3) to the non-affected adjacent finger (i.e. D4), thus probably amplifying at the cortical level the activation gap between D4 (reduced) and D5 (normal) and, therefore, further hindering the illusion. This hypothesis suggests a link between the altered illusory perception and the spread of motor symptoms in focal hand dystonia.

Another interesting finding is that the reduction of the illusion was only detectable in the dominant (affected) hand of patients with focal hand dystonia. This result is different from previous psychophysical studies, in which the occurrence of sensory deficits in both the affected and non-affected hand of patients with focal hand dystonia supported that these abnormalities were not exclusively linked to the presence of motor symptoms (Bara-Jimenez et al., 2000; Fiorio et al., 2003). Our findings support an altered activation of the primary somatosensory cortex specifically for the hemisphere controlling the affected hand. In other words, if the reduction of the illusion in D4–D5 is the expression of a different level of activation between digits in the somatosensory cortex, the fact that this reduction is present only on the affected hand could suggest that the decreased activation for D2, D3 and D4, found by Nelson et al. (2009), is a specific trait of the affected hemisphere. Consequently, the unbalanced activation of the sensory signals from D4 and D5 would be present in only one somatosensory cortex. As Nelson et al. (2009) did not investigate the level of cortical activation of the non-dominant unaffected hand, this interpretation is based on our behavioural findings and deserves further study to be confirmed. Support for this notion, however, derives from animal models with dystonia, in which the changes of the somatosensory cortex after repetitive movements were also associated with the manifestation of motor symptoms in the dominant hand (Byl et al., 1996).

On the other hand, repetitive movements per se might induce cortical plastic changes, as revealed by a study in blind multi-finger Braille readers, demonstrating that repetitively performing the same movements result in de-differentiation of cortical representations of the hands’ skin areas and in overlapping of the digits’ receptive fields in the contralateral hemisphere (Sterr et al., 1998). Given these well-known features of somatosensory plasticity, we could hypothesize that the discriminating factor associated with the reduction of the illusion in patients with focal hand dystonia is the excessive and abnormal use of the dominant (affected) hand (Pascual-Leone et al., 1995; Elbert et al., 1998; Sterr et al., 1998; Candia et al., 2005).

To summarize, applying the stimuli to the relaxed fingers allowed us to disentangle the selective contribution of the somatosensory system on the illusory perception. This procedure revealed an altered functional relation between two digits (D4–D5), resulting in a reduced illusion. Although from a clinical point of view, both D4 and D5 are spared by motor symptoms, at a subclinical level, the activation of D4 in the somatosensory cortex could be reduced in respect to D5, thus explaining our results. Reasonably, the reduced activation of D4 is because of a spread of sensory abnormalities deriving from the most affected digits D2 and D3, as suggested by Nelson et al. (2009). This would explain why the reduction of the illusion in D4–D5 is to be observed only on the affected hand.

Moreover, in contrast with previous findings of sensory alterations in different forms of focal dystonia (Bara-Jimenez et al., 2000; Fiorio et al., 2003, 2008; Molloy et al., 2003; Tinazzi et al., 2004), the reduction of Aristotle’s illusion seems to be as a specific feature of focal hand dystonia. Namely, patients with non-hand dystonia showed a performance comparable with healthy control subjects.

The neural underpinnings of this illusory tactile perception still remain unknown. Until now, the neural correlates of two different tactile illusions have been investigated: the rabbit illusion—in which a sequence of rapid stimuli is delivered first to the wrist and then to the elbow creating the sensation of stimuli moving from the wrist to the elbow—has been investigated in humans by functional MRI (Blankenburg et al., 2006), and the funnelling illusion has been investigated in monkeys with optical imaging (Chen et al., 2003) and high-field functional MRI (Chen et al., 2007). To date, there is no study on the brain circuits involved in Aristotle’s illusion. Further investigations applying neuroimaging or neurophysiological techniques that combine both high temporal resolution (to randomize the conditions trial by trial) and spatial resolution (to study adjacent fingertips) might allow for the detection of fine neuronal changes that could explain the mechanisms associated with Aristotle’s illusion.

In conclusion, Aristotle’s illusion allowed us to increase the current knowledge of the somatosensory alterations in focal hand dystonia. In particular, through this simple paradigm, we highlighted for the first time the perceptual correlate of the inter-digit somatosensory abnormality in focal hand dystonia. Our findings revealed that the reduction of illusory perception (i) may...
represent the functional correlate of the different level of activation between fingers; (ii) is present only in the affected hand; and (iii) is a specific feature of focal hand dystonia. Further studies should be developed to explore the clinical and pathophysiological underpinnings of this specific feature.

**Funding**


**References**


