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RESEARCH ARTICLE

Developmental topographical disorientation: a newly discovered cognitive disorder

Giuseppe Iaria · Jason J. S. Barton

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Abstract A variety of lesions in different cerebral regions may affect the human ability to orient in the environment, resulting in 'topographical disorientation'. In a recent study, we documented the first case of Developmental Topographical Disorientation (DTD), in a person with a life-long inability to orient despite otherwise well-preserved cognitive functions, and in the absence of a cerebral injury/malformation or other neurological condition. This selective topographical disorientation was due to her inability to form a 'cognitive map', a mental representation of the environment, which in turn impaired her ability to orient in both familiar and unfamiliar surroundings. Here, we describe 120 new cases of DTD recruited via the internet and assessed with an online battery testing their cognitive and orientation skills. We found that people with DTD differ from matched (age, gender and education) healthy controls only in those skills confined to the orientation/navigation domain, among which the ability to form a cognitive map was the most significant factor that distinguished a person affected by DTD from control subjects.

Keywords Cognitive map · Hippocampus · Landmark · Navigation · Orientation · Virtual environment

Introduction

Topographical orientation is the ability to orient and navigate in both familiar and unfamiliar surroundings (Berthoz 2001; Wang and Spelke 2002). Although it may appear effortless, this is a complex activity that relies on a variety of cognitive processes such as attention, memory, perception, and decision-making skills, all of which play important roles in spatial cognition (Berthoz and Viaud-Delmon 1999; Corbetta et al. 2002; Burgess 2006; Lepsien and Nobre 2006). Given this complexity, it is not surprising that a variety of acquired brain injuries can affect the ability to orient (Barrash 1998), resulting in what is termed as "topographical disorientation" (De Renzi 1982; Aguirre and D'Esposito 1999; Iaria et al. 2005). As suggested in a recent taxonomy of topographical orientation disorders (Aguirre and D'Esposito 1999), lesions of the posterior parietal cortex, the retrosplenial cortex, the fusiform and lingual gyrus, and the hippocampal complex all may affect one's ability to orient but in different ways, resulting in a variety of orientation defects, such as the ability to use egocentric (body-centered) co-ordinates to localize environmental landmarks (Stark et al. 1996), the ability to derive directional information from landmarks (Takahashi et al. 1997), or even the ability to recognize landmarks (Pallis 1955). Key support for this taxonomy has come from the growing ranks of patients with acquired damage to various cerebral structures (Nyffeler et al. 2005; Wilson et al. 2005; Burgess et al. 2006;

G. Iaria (✉)
Neurolab, Departments of Psychology and Clinical Neurosciences, and Hotchkiss Brain Institute,
University of Calgary, Administration Building A218,
2500 University Drive, NW, Calgary, AB T2N 1N4, Canada
e-mail: giaria@ucalgary.ca
URL: www.neurolab.ca; www.gettinglost.ca;
www.orientationtesting.com

J. J. S. Barton
Human Vision and Eye Movement Laboratory,
Departments of Medicine (Neurology) and Ophthalmology
and Visual Sciences, University of British Columbia,
Vancouver, BC, Canada

Greene et al. 2006; Brunsdon et al. 2007; Ino et al. 2007; Tamura et al. 2007).

In a recent study (Iaria et al. 2009), we documented a case of topographical disorientation that differed from those previously reported. The case concerned a woman who had never been able to orient within the environment despite otherwise intact cognitive skills. By performing a variety of behavioral tests as well as functional magnetic resonance imaging (fMRI), we found that the patient's topographical disorientation was due to a selective impairment in the ability to form a mental representation of the environment that is a cognitive map (Tolman 1948). A cognitive map is defined as a spatial representation of the individual's surrounding that contains information about the environment's layout, the objects (i.e. landmarks) available within it and, most importantly, the spatial relationships between these objects (O'Keefe and Nadel 1978). Cognitive maps are critical for flexible orientation since, after being formed, they allow individuals to reach any target location from anywhere within the environment. Without them (as is the case for healthy subjects in novel surroundings) individuals get lost easily. As the person described in our study has been unable to orient since childhood, and had no evidence of brain damage or any known neurological condition, we speculated that she had never developed that orientation skill and named this condition "Developmental Topographical Disorientation" (DTD).

After the publication of this first case, we were contacted by many people from all over the world who claimed to have life-long symptoms of DTD similar to those of the first patient. To study these subjects, we created a website, www.gettinglost.ca, and developed a battery of tests assessing different cognitive skills relevant to DTD, which we made suitable for online evaluation of this geographically widespread group. In this report, we describe the performance on this battery of the first 120 new cases of people affected by DTD.

Methods

Participants

The study included two groups of participants: the DTD group and the Control group. Each group included 120 subjects. Membership in the DTD group required the following four criteria: (1) getting lost daily or often (1 to 5 times a week) in the most familiar surroundings, such as their neighborhood and/or their own house, (2) reporting this difficulty since childhood, (3) no memory complaints or other cognitive difficulties that may affect daily life activities, and (4) no known brain injury, malformation, or condition affecting the central nervous system, with the exception of migraine. The Control group consisted of 120 subjects matched for gender, age and education to the participants in the DTD group. As with the DTD group, none of the participants in the Control group had a history of a central neurological condition or brain injury, and none reported memory complaints or other cognitive difficulties affecting their daily life. Participants in the Control group rarely (no more than 5 times per year) got lost and reported that these instances did not affect their daily life. Participants who reported that they never got lost were excluded. Participants in both DTD and Control groups reported normal or corrected-to-normal vision and, at the time of testing, were not taking any regular medication. Of note, 43 of the 120 DTD subjects claimed that at least one first-degree relative had a similar problem with orientation, with a similar frequency in both women (36%) and men (33%) respondents. Informed consent was obtained, and the protocol was approved by the institutional review boards of the University of British Columbia and Vancouver General Hospital in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) as printed in the British Medical Journal (18 July, 1964). Demographic data of all participants are reported in Table 1.

Procedure and tasks

Participants were recruited through the internet by a website (www.gettinglost.ca) designed to raise awareness of DTD. The website included a page dedicated to collecting demographic data and providing individuals with online assessments of cognitive skills relevant to orientation. Data were recorded in a password-protected database and analyzed offline. Participants' responses were collected individually for each trial included in each test. Written instructions were provided on the screen before performing each test. In total, participants performed nine tests, as follows.

Table 1 Demographic data (mean and SD) of participants in DTD and Control Group

	DTD	Control
N total	120	120
N females	102	102
N males	18	18
Age total (years)	43.7 (13.97)	42.3 (14.42)
Age females (years)	44.9 (13.79)	43.3 (14.34)
Age males (years)	36.9 (13.42)	37.4 (14.28)
Education total (years)	15.5 (4.39)	16.1 (3.97)
Education females (years)	15.6 (4.35)	16.1 (4.21)
Education males (years)	15.4 (4.78)	16.1 (2.32)
N Left-handed	3 M–6 F	3 M–7 F

The two groups were matched for age ($t(1,238) = 0.73$, $P = 0.47$) and education ($t(1,238) = -0.95$, $P = 0.34$)

Test 1: Object recognition

This test assessed the ability of the individuals to recognize common objects from different perspectives. The test consisted of 12 trials. In each trial, the participants were first shown a grayscale photograph displaying the target object, which was a common object (e.g. teacup, chair, shoe, etc.) sized to a width of 400 pixels for 2,000 ms. This was followed by a black screen lasting 2,000 ms, and then a second grayscale photograph displaying four different objects located in the four quadrants of the screen. Participants used the mouse to select the target object previously seen, which in the second photograph was rotated 45°, 90° or 135° from the first view. As soon as the participants responded, the four objects disappeared, a black screen appeared for 3,000 ms and a new trial began.

Test 2: Face identity recognition

This test assessed participants' ability to recognize faces, since in acquired topographical disorientation from inferior occipitotemporal lesions, prosopagnosia (i.e. the inability to recognize familiar faces) is a frequent association (Aguirre and D'Esposito 1999). Presentation format and timing were identical to that for Object recognition, but instead of objects, we used faces taken from the *Karolinska Database of Emotional Faces* (Lundqvist and Litton 1998). Participants viewed a grayscale photograph of a target face in frontal view and used a mouse to identify it among four choices presented in a second grayscale photograph, in which all faces were rotated 45° clockwise or counterclockwise from a frontal view.

Test 3: Face expression recognition

This test assessed the ability of the participants to recognize facial expressions, a skill that is distinct from face identity recognition. Presentation format was identical to the previous two tests. For stimuli we used four facial expressions (happiness, sadness, disgust, surprise), taken from the *Karolinska Database of Emotional Faces* (Lundqvist and Litton 1998). Participants first saw a grayscale photograph of a person showing one target expression, which was one of the four facial expressions. They were then shown a montage of four images of the different expressions, as expressed by the same person used for the target expression, and required to identify the target expression.

Test 4: Landmark recognition

This test assessed participants' ability to recognize landmarks encountered while navigating in an environment. The test consisted of 6 trials. In each trial, the participants were presented with a 30-s video clip showing a first-person perspective of movement through a virtual environment, during which they encountered three landmarks. Each landmark was a signpost displaying an abstract colored image. At the end of the video clip, the participants were shown 6 landmarks (signposts with abstract colored images) one at a time with unlimited duration. For each landmark, participants were asked whether or not that landmark was encountered during the journey in the video clip, and responded by selecting with the mouse "yes" or "no" buttons, which appeared next to the question that was placed below each landmark. The virtual environment was created by using the editor of a three-dimensional game software (Game Studio A6, La Mesa, CA, USA) and consisted of several buildings of the same texture and color, as well as the landmarks (see Fig. 1 for a snapshot of the virtual environment).

Test 5: Heading orientation

This test assessed participants' ability to recall directional information from landmarks. The test included 6 trials. The format and presentation was identical to Test 4 (Landmark recognition), and used the same virtual environment. In each trial, the participants saw a 30-s video clip from the first-person perspective of movement through a virtual environment, during which they encountered three landmarks, signposts displaying an abstract colored image (different from the ones in the Landmark Recognition test). At the end of the video clip, the participants were presented with the three landmarks, one at a time, which they encountered during the journey, and asked if the person in the video clip turned left or right at that landmark. As with

Fig. 1 The figure displays a snapshot of the virtual environment in which participants performed the navigational/orientation tests. The specific landmark depicted in this figure (i.e. the flower shop) was used to assess the formation and use of cognitive maps (Test 8 and Test 9). Buildings' texture and shapes, as well as sky and floor were common to all tests

the previous test, the question was presented below each landmark with “left” and “right” buttons provided for responses, which participants selected with the mouse.

Test 6: Left/right orientation (no landmarks)

This test assessed participants’ ability to learn a route based on a sequence of left/right turns made during locomotion. The test consisted of 6 trials. In each trial, participants were presented two consecutive video clips of 30 s from the first-person perspective of movement through a relatively featureless virtual environment of city blocks. In the first video clip, participants were shown a journey that included three (left/right randomized) turns. In the second video clip (presented soon after the end of the first video clip), participants were shown a journey that began from the same starting position in the first video clip and that included three turns as well. In one half of the trials, the journeys were the same, and in the other half, they were different, with the order of same and different trials randomized. Both clips had the same duration. At the end of the second video clip, participants were asked whether or not the two journeys in the two video clips were the same. Participants responded by selecting with the mouse one of two buttons, “Same” or “Different”, provided on the screen at the end of each trial. To solve this task, participants had to rely on the sequence of left/right turns since the virtual environment was composed of a grid of streets and buildings of the same size, shape and texture, without distinguishing features.

Test 7: Path reversed (no landmarks)

This test assessed participants’ ability to reverse a route to return from the final position back to the starting location. The test included 6 trials. In each trial, participants were presented with a 1-min video clip. The video clip showed a first-person perspective view of travel along a route for about 30 s, after which the virtual person stopped, turned around, and followed a route that in one half, the trials were the same route in reverse, and in other half, the trials were a route that were different from the first journey. At the end of the video clip, participants indicated with the mouse whether the second route was the same or different from the first. The virtual environment was identical to that used in the previous test, a grid of buildings of same size, shape and texture, which was designed to minimize landmark information to guide orientation.

Test 8: Formation of a cognitive map

A cognitive map is a mental representation of the environment that individuals create after becoming familiar with their surrounding and its landmarks. This test assessed the ability to form a cognitive map of a small virtual environment. The buildings included in the environment were not easily distinguishable from one another since they had similar shapes, sizes and textures. However, there were also four different, easily identifiable landmarks (a restaurant, flower shop, hotel, and cinema), in four different places. The test consisted of a number of trials: in each, they were shown a video clip depicting the first-person perspective of movement (randomly generated) through this environment, which visited a variable number of the landmarks that could vary from 1 to 3 (only in the first trial were all four landmarks visited in the same video clip). At the end of each video clip, the participants were shown an aerial-view map of the environment. Beside the map, there were four small icons depicting each of the four landmarks, each of which they were to drag with the mouse to place at the location on this map where they thought it was located. After all four icons were placed, the trial was considered completed and a new trial began. The test ended after participants situated all four landmarks correctly in two consecutive trials. To minimize the effects of guessing, participants received no feedback. Participants were given a maximum of 20 trials to form a cognitive map: thus, the theoretically minimum number of trials is 2 and the maximum is 20. The total duration of the video clips across all trials was 1,690 s. We measured the number of trials needed by the participants to solve the task, and therefore the time needed to form the cognitive map of the environment, which was our outcome variable.

Test 9: Use of a cognitive map

This last test assessed participants’ ability to use the cognitive map formed in Test 8. The test included 6 trials. In each trial, the participants were shown a short video clip from the first-person perspective of movement within the environment used in Test 8. Each video clip started with the virtual camera facing one of the four landmarks in the environment (i.e. the cinema) as well as a signpost instructing them to go to a specific target location (i.e. “go to the hotel”). After 5 s, the video clip showed the person navigating within the environment to reach the target location. At the end of the video clip, the participants were required to report whether or not the route followed in the video clip reached the target location by the shortest path. Participants used the mouse to select one of the two option buttons (“yes” or “no”) on the screen. Each trial had a different starting location and/or a different target location. In one half of the trials, the route was the shortest path, and in other half, it was not; the order of these trials was randomized.

Results

First, we performed *t-test* comparisons between groups (DTD, Control) for the nine tests that the participants performed (Fig. 2). Using Sidak's method to adjust for both multiple comparisons and inter-item correlation in controls, a P-value of 0.004 is required for an alpha level of 0.025. Both the DTD and Control groups performed equally well in the tests of Object Recognition ($t(1,237) = 1.21$, $P = 0.23$), Face Identity Recognition ($t(1,237) = 0.84$, $P = 0.40$) and Face Expression Recognition ($t(1,238) = 1.72$, $P = 0.09$). However, on the Landmark Recognition Test (Test 4), the DTD group performed worse than the Control group ($t(1,238) = 6.31$, $P < 0.00001$; Cohen's $d = 0.76$, effect-size $r = 0.38$). Similarly, the performance of the DTD group was poor when compared to the performance of the Control group in all remaining navigation/orientation tests, the Heading Orientation ($t(1,238) = 5.43$, $P < 0.00001$; Cohen's $d = 0.7$, effect-size $r = 0.33$), Left/Right Orientation ($t(1,238) = 3.98$, $P < 0.0001$; Cohen's $d = 0.52$, effect-size $r = 0.25$), Path Reversed ($t(1,237) = 5.08$, $P < 0.00001$; Cohen's $d = 0.65$, effect-size $r = 0.31$), as well as both Formation ($t(1,238) = 9.22$, $P < 0.00001$;

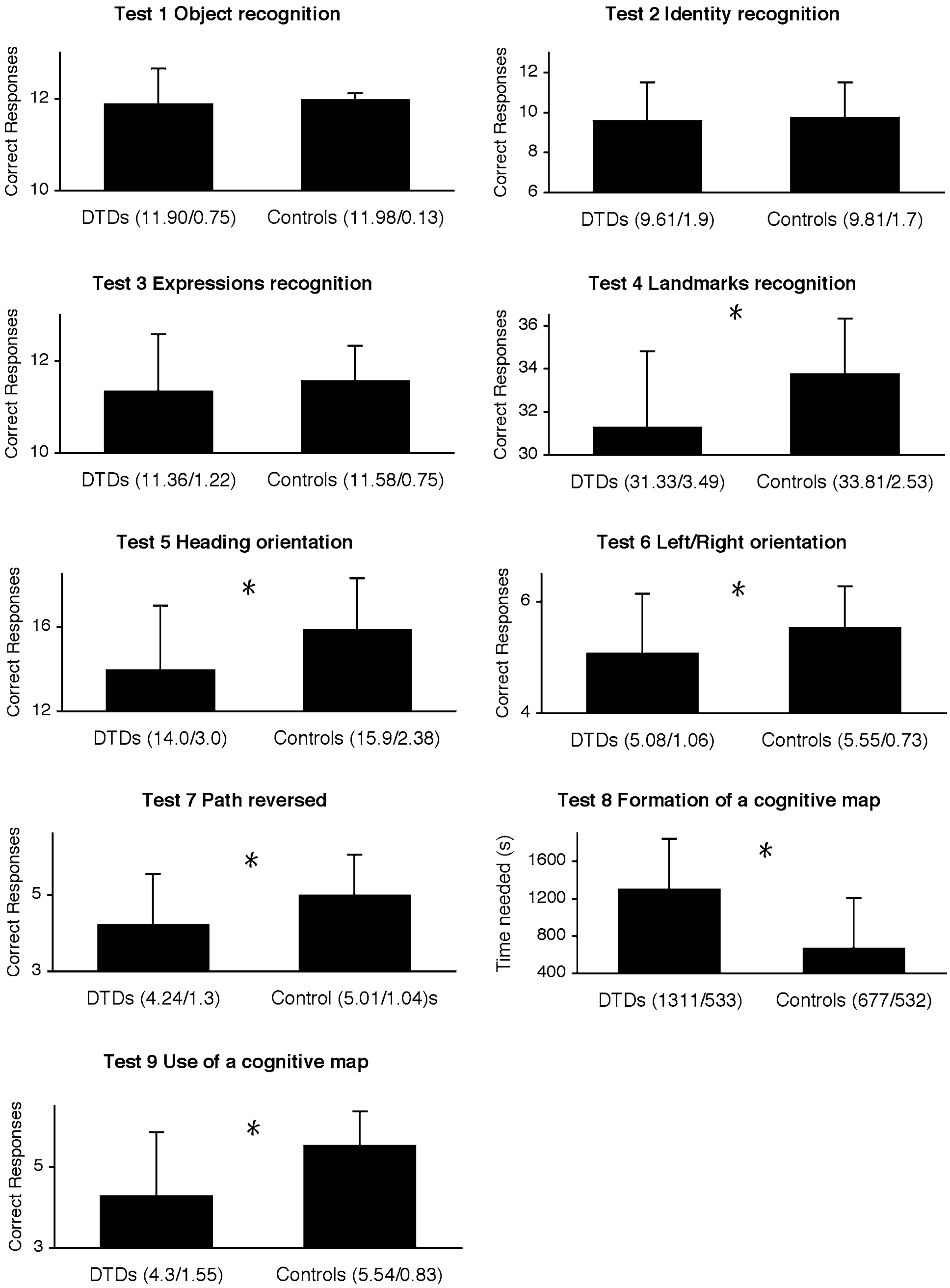

Fig. 2 The figure displays the performance (Mean/SD) of DTDs and Controls at the nine tests. *Asterisks* indicate statistically significant differences between groups

Cohen's $d = 1.19$, effect-size $r = 0.51$) and Use ($t(1{,}238) = 7.75$, $P < 0.00001$; Cohen's $d = 1.01$, effect-size $r = 0.45$) of a cognitive map (see Fig. 2).

Second, to assess which orientation tests were best at predicting the presence or absence of DTD, we performed a Two-Group Stepwise Discriminant Function Analysis in which we modeled as six variables the scores in the navigation/orientation tests (Test 4–9). Formation of a cognitive map (Test 8) was the most effective variable at discriminating between people with and without DTD ($F(1{,}238) = 85.07$, $P < 0.00001$), accounting for 72.92% correct of case-grouping (DTD, 70%; Control, 75.83%). The Landmark Recognition Test (Test 4) was the second most effective variable at discriminating between the two groups ($F(2{,}237) = 54.27$, $P < 0.00001$), accounting for 66.25% correct of case-grouping (DTD, 54.17%; Control, 78.33%). The Use of Cognitive Maps (Test 9) was the third most effective variable ($F(3{,}236) = 43.59$, $p < 0.00001$), accounting for 66.67% correct of case-grouping (DTD, 45.83%; Control, 87.5%). Finally, the Path Reversed Test (Test 7) was the fourth most effective variable ($F(4{,}235) = 33.19$, $p < 0.00001$) accounting for 64.58% correct of case-grouping (DTD, 55%; Control, 74.17%). Altogether these four variables accounted for 77.08% correct of case-grouping (DTD, 73.33%; Control, 80.83%). The Heading Orientation Test (Test 5) and Left/Right Orientation Test (Test 6) were variables excluded by the model as insignificant.

Discussion

We asked participants to perform a variety of tests assessing orientation and non-orientation skills. People affected by DTD did not differ from controls in the ability to recognize objects, face identity or facial expressions, despite the fact that impairments in face recognition and topographic orientation co-occur in some patients with acquired disorders (Aguirre and D'Esposito 1999). In contrast, they differ from controls in all other tests assessing skills critical for orientation and confined to the domain of spatial navigation. Despite this, the discriminant analysis indicated that the ability to form a cognitive map (Tolman 1948; O'Keefe and Nadel 1978) is the most significant factor in discriminating between people with or without DTD, just as it was the key deficit in the index DTD case that we reported (Iaria et al. 2009). However, given the poor performance on the other navigational tasks, caution is required before concluding that impaired cognitive map formation is the primary or sole deficit in DTD. It may be that a person with poor cognitive map formation from birth also fails secondarily to develop other navigation-related expertise with landmarks and route-finding, perhaps through lack of experience in development, which remains to be determined. Given the variety of cognitive skills and strategies that can be used in navigation, one possibility is that DTD encompasses a heterogeneous collection of functional disturbances, as is the case for acquired topographical disorientation (Aguirre and D'Esposito 1999). One of the challenges for the future will be to determine if DTD is a homogenous condition, with a primary deficit in cognitive map formation in all subjects, or a heterogenous one, in which deficits in one of several processes converge on the same end-result, navigational failure.

The ability to orient in an environment is a complex skill that, like all cognitive skills, varies among healthy individuals (Ohnishi et al. 2006). Hence, one important issue in diagnosing DTD is distinguishing these subjects from those healthy individuals with a 'poor sense of direction', who merely perform at the low end of the normal spectrum of navigational skills. In the absence of a genetic or structural marker at present, our inclusion criteria aimed at a behavioral distinction based upon three key observations. First, people with DTD get lost in their most familiar surroundings, such as the house or the neighborhood where they have lived for many years. Healthy people with a poor sense of direction do not get lost in highly familiar places, but instead may have difficulties in less-familiar surroundings, for example, with finding their car in an underground parking lot or getting lost in a new town. Second, people with DTD get lost in their most familiar surroundings almost daily, whereas people with a poor orientation skill experience problems much less frequently. Third, people with DTD report dramatic examples of their difficulties dating back to childhood. Although healthy people with a poor sense of direction presumably have this as a life-long trait too, it does not seem to cause childhood episodes of sufficient vividness to create enduring memories.

Our demographic data show that DTD affects a wide range of individuals. Of interest, 85% of our DTD subjects are women. This could reflect either a true gender bias in the prevalence of DTD, or a gender bias in the type of subjects likely to respond to and participate in a time-consuming internet assessment.

As it is the case for any newly discovered condition, at this stage, there are more questions than answers. Our online assessment was meant to determine whether our index patient was unique or if there were many others with similar symptoms and deficits. We confirmed that the latter was the case. Second, the online test battery was meant to provide a number of navigational tests, with the aim of (a) providing objective confirmation of subjective complaints of topographic disorientation and (b) a preliminary evaluation of different orientation skills as a first attempt at defining the key deficit in DTD. The online nature of the assessment allowed us to gather data worldwide from a sizeable sample, in a manner not previously possible. While this was a significant advantage, there are also limitations inherent to what can be learned from this electronic approach. First, although our tests show impairments on testing in a virtual environment, it remains to be seen how the orientation skills of DTD subjects differ in real-world tasks, as we did with our first case (Iaria et al. 2009). Second, although neither DTD nor control subjects admitted to memory or other cognitive defects, it would be important to confirm this with neuropsychological assessments of a DTD group tested in person. Third, although DTD subjects also denied neurological conditions or brain injury, this too should be verified in a DTD group with structural imaging (Iaria et al. 2008), which could also incorporate an investigation into the substrate of DTD with functional neuroimaging (Iaria et al. 2007; 2008). Fourth, a third of our subjects with DTD reported a living first-degree family member with similar orientation problems. Further investigations into this subset may help first to verify this purported hereditary tendency and second to determine if there is a genetic basis to DTD, similar to what has been speculated in at least some cases of developmental prosopagnosia (Grueter et al. 2007). Finally, moving from online to in-person testing will be important when it comes to investigating whether specific treatments can improve orientation in DTD, as has been shown in some other cases with congenital brain malformation (Incoccia et al. 2009). If so, it will also be imperative to develop diagnostic tools that can identify this condition in children to facilitate a more effective early intervention.

In summary, our online study establishes that DTD is a condition that affects a significant number of people, who show clear impairments in a number of orientation skills. Since our study was not designed to be a survey of the general population, we cannot as yet estimate the prevalence of DTD. The fact that this study found so many people affected by DTD in only a few months since the publication of our first case may reflect both extensive press coverage and also the power of the internet to recruit and discover individuals with unusual disorders. Nevertheless, we expect that many independent research laboratories will soon report other cases of DTD, as is already occurring (Bianchini et al. 2010). Further studies in our laboratory will aim at clarifying the structural, functional, and possibly even genetic aspects of this newly discovered condition, and ultimately provide appropriate rehabilitation to help these people find their way.

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