Motion perception deficit in Down Syndrome

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A B S T R A C T

It is a well established fact that Down Syndrome (DS) individuals have a tendency to develop Alzheimer’s disease (AD) (Lott, T., Head, E., 2005. Alzheimer disease and Down syndrome: factors in pathogenesis. Neurol. Aging 26, 383–389). They have therefore been proposed as a model to study the pre-dementia stage of Alzheimer’s (Mann, D.M., 1988). The pathological association between Down syndrome and Alzheimer disease. Mech. Ageing Dev. 43, 99–136). One of the specific deficits exhibited by AD patients is optic flow motion perception (Tetewsky, S.J., Duffy, C.J., 1999. Visual loss and getting lost in Alzheimer’s disease. Neurology 52, 958–965), but there are no corresponding systematic studies in DS individuals. We performed sensitivity measurements to optic flow with Visual Evoked Potentials (VEP) and psychophysical techniques in a group of young DS participants with mild mental retardation and without significant Alzheimer’s clinical symptoms. We found a significant reduction in direction discrimination sensitivity to optic flow (random dots moving in radial, rotational and translational trajectories) in DS participants compared to mental age-matched controls, while their sensitivity to direction of control moving stimuli (sinusoidal gratings) was similar to age-matched controls. Measurements of Visual Evoked Potentials (VEP) showed no response to optic flow, although the response to control stimuli (contrast-reversal checkerboard patterns) was significant. Overall, our results show a selective and substantial deficit in the perception of optic flow motion and a corresponding suppression of electroencephalographic activity in DS individuals, thus establishing a further common trait between Down Syndrome and Alzheimer’s disease.

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1. Introduction

Several studies have identified the cause underlying Down Syndrome (DS) (Berini and Kahn, 1987), its common physical features (Cunningham, 1982; Pueschel, 1988; Pueschel et al., 1987), associated medical problems (Evenhuis et al., 1992; Niva, 1988; Odell, 1988; Pueschel et al., 1987), and its developmental pattern, characterized by different levels of mental, physical and motor retardation (Gibson, 1978).

There is a well-established link between Down Syndrome and Alzheimer’s disease (AD) (Lott and Head, 2005). Neuropathological studies have provided the most consistent and convincing evidence of Alzheimer’s-like changes in the brain of DS individuals over 35 years old, including neuronal plaques, amyloidal deposits, and neurofibrillary tangles (Head et al., 2001; Wisniewski et al., 1985a, 1985b). The fact that the gene coding for the Beta amyloidal protein, responsible for neuronal plaques, is located on the chromosome involved in the DS (chromosome 21), and represents a genetic link between the two disorders (Lott et al., 2006; Rumble et al., 1989). Based on these observations, the Down Syndrome has been proposed as a model to study the pre-dementia stage of AD (Mann, 1988), although diagnosis of AD in the DS population is a difficult task (Nieuwenhuis-Mark, 2009).

A high incidence of defects of the visual function has been found among DS over 40 years of age, independently of an AD diagnosis (Castane et al., 2004). They comprise color vision deficits, such as abnormal chromatic transient Visual Evoked Potentials (VEPs) (Suttle and Lloyd, 2005) and color discrimination impairments (Rocco et al., 1997), associated with high stereo-acuity thresholds and reduced contrast sensitivity similar to those observed in AD Patients (Cronin-Golomb et al., 1991, 1993). Impairments in basic aspects of visual function, such as low visual acuity, reduced Vernier acuity, and increased contrast sensitivity thresholds, have also been found in young DS individuals (Cronin-Golomb et al., 1991, 1993). All these deficits have been primarily attributed to abnormal cortical activity or to the cognitive demand of the tasks rather than to either accommodative or ocular conditions – cataracts, high astigmatism, high hyperopia, high myopia, high ametropia, high strabismus, and other ocular anomalies.

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refractive errors, congenital glaucoma, strabismus – that are prevalent in this population (Woodhouse et al., 2000, 1996; Cregg et al., 2001; Stewart et al., 2007; Ahmad and Pruett, 1976; Catalano and Simon, 1990; Sherk and Williams, 1979).

No study yet has assessed the functionality of visual motion processing mechanisms in DS individuals. This investigation seems particularly worthwhile in view of the link between Down Syndrome and Alzheimer’s disease (AD) (Lott and Head, 2005) and the deficits in optic flow motion perception that have been described in AD patients, concerning, both the focus of expansion of optic flow stimuli (O’Brien et al., 2001; Tetewsky and Duffy, 1999), and the translational flow motion (Silverman et al. 1994), although this second aspect is still controversial (O’Brien et al., 2001).

The perception of optic flow, which is mediated by specific neural units (Britten and van Wezel, 1998; Morrone et al., 1995, 2000; Regan and Beverley, 1979; Tanaka et al., 1989), is used in the detection of self motion and motion of objects, which is crucial for accurate control of navigation and evaluation of time to collision with objects (Gibson, 1950). Impairments of its function may thus interfere with the use of visual information to guide self-movement, and may arguably be related to the spatial disorientation observed in AD (Fernandez et al., 2007; Kavicic and Duffy, 2003; Kavicic et al., 2006; Mapstone et al., 2006; Tetewsky and Duffy, 1999) – possibly linked to extra striate cortical motion processing disorders (Kavicic et al. 2006).

Given the genetic link between Down Syndrome and Alzheimer’s disease, we aim in this work to check for the existence of a similar impairment in the cortical processing of visual optic-flow motion. To this purpose, we evaluated the perception of optic flow in a sample of relatively young DS participants, not showing other Alzheimer’s symptoms, by means of psychophysical techniques. In a subset of these participants, we also performed measurements of Visual Evoked Potentials (VEP) for the same stimuli. The use of two independent tests, one of which requiring minimal active participation, helps ensuring the robustness of results, that have often turned out to be difficult to interpret in this kind of individuals.

2. Materials and Methods

2.1. Participants

Fifteen adult DS participants, of which 11 had full (non-mosaic) and four had mosaic trisomy 21, participated in the psychophysical tests. Seven of them also underwent VEP recordings. All DS participants received medical, neurological and psychiatric evaluations. The Dementia Scale for Down Syndrome (DDDS) (Gedye, 1995) was chosen as an informant-based measure of the degree of dementia. None of the 15 participants met the diagnostic criteria for dementia. To assess their intellectual level, Italian translations of the Wechsler Intelligence Scales for Children revised (WISC-R) (Rubini and Padovani, 1986) and Colored Progressive Matrices (CPM) were used (Belacchi et al., 2008). The WISC-R (Wechsler, 1974), testing knowledge and abilities of verbal (e.g. vocabulary, comprehension and verbal mathematical reasoning) and non-verbal nature (e.g. the arrangement of a series of pictures into a meaningful sequence, the assembly of an object given its parts), is currently used to test the intellectual level of DS (Devenny et al., 2000). The non-verbal CPM test (Raven et al., 1998) has been used as a help in assessing participants with speech impairment. The WISC-R and CPM scores were turned into a mental age (MA) evaluation, based on the chronological age at which an average individual reaches that same level of proficiency. Results of these tests show average IQ scores between 50 and 70, and a mental age of 8 years (Table 1), consistent with a mild cognitive deficit (American Psychiatric Association, 2013; Pfanner and Marcheschi, 2005). All participants were collaborative and able to participate in behavioral tasks.

Table 1

<table>
<thead>
<tr>
<th>Test</th>
<th>Mean</th>
<th>S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronological age (years)</td>
<td>25.7</td>
<td>4.0</td>
</tr>
<tr>
<td>WISC-R mental age (years)</td>
<td>7.5</td>
<td>1.2</td>
</tr>
<tr>
<td>WISC-R verbal mental age (years)</td>
<td>7.8</td>
<td>1.4</td>
</tr>
<tr>
<td>WISC-R non-verbal mental age (years)</td>
<td>7.2</td>
<td>1.3</td>
</tr>
<tr>
<td>CPM (IQ)</td>
<td>59.6</td>
<td>9.2</td>
</tr>
<tr>
<td>CPM (MA)</td>
<td>6.9</td>
<td>1.4</td>
</tr>
</tbody>
</table>

With respect to visual function, eight participants were hyperopes, four myopes, three emmetropes, and 12 had converging squint. All refractive deficits were corrected with appropriate lenses during all tests. Possible effects of poor visual acuity on global motion perception were assessed with preliminary behavioral tests (see Section 3); it has however been shown that blur does not affect perception of motion at these spatiotemporal stimulus parameters (Braddock et al., 2007). Six participants were affected by nystagmus, and separate statistical analyses were carried out on this sample to rule out possible effects on motion perception. There was no occurrence of cataract.

VEP recordings and psychophysical performances for the control stimulus (described further below) were compared to those of a group of seven chronological age-matched individuals. Psychophysical performances for optic flow were instead compared with those of a group of 16 mental age-matched children (M=6.5, S. D.=0.6), in consideration of the cognitive retard of DS participants and the fact that motion perception as been found to improve with cognitive level (Ellenberg et al., 2004; Gunn et al., 2002). These choices of patient matching, besides being well justifiable in themselves, are also conservative with respect to the effect we are looking for, of a possible stronger deficit in optic flow than in generic motion perception; that is, the effects we are searching for would appear stronger if evaluated by any other different matching criteria.

All participants or their legal guardians were aware of the purposes of the study and written consent forms were completed in accordance with the policy of the Stella Maris Scientific Institute and University of Florence review boards, that had approved this study. This work has been carried out in accordance with the Declaration of Helsinki.

2.2. Psychophysics

Random dots kinematograms were used (Julesz, 1971), consisting in arrays of 100 randomly placed dots, black and white on a mean gray background, moving coherently according optic flow trajectories. For radial motion stimuli, they were made to move either towards the center of screen (Fig. 1A, t1) or away from it (Fig. 2A, t3); for circular motion, they were made to move either clockwise (Fig. 1B, t1) or anticlockwise (Fig. 1B, t3); for translation they were moving either upward (Fig. 1C, t1) or downward (Fig. 1C, t3), to avoid a possible interference from horizontal ocular movements.

Stimulus duration was 300 ms, dot velocity was 10°/s, dot size was 0.4°, dot lifetime was 80 ms. In a limited-lifetime paradigm each dot, born at a certain location, follows a flow (or random) trajectory for a short time and finally disappears. This procedure minimizes activation of local motion areas and, consequently, enhances maximal response from global motion areas (Britten and van Wezel, 1998; Morrone et al., 2000; Tanaka et al., 1989). Background luminance was 20 cd/m². Stimuli were presented on a 60 Hz LCD display, driven by a laptop PC, and subtended 15° × 15°.
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