Research in Developmental Disabilities 35 (2014) 3131–3138

Contents lists available at ScienceDirect

Research in Developmental Disabilities

Deficient motor timing in children with neurofibromatosis type 1

Julie Debrabant [a,*], Ellen Plasschaert [b], Karen Caeyenberghs [a,c], Guy Vingerhoets [d], Eric Legius [b], Sandra Janssens [e], Hilde Van Waelvelde [a]

[a] Department of Rehabilitation Sciences and Physiotherapy, Ghent University, Campus Heymans, Ghent University Hospital, 2B3, De Pintelaan 185, B-9000 Ghent, Belgium
[b] Centre of Human Genetics, University Hospitals Leuven, & Department of Human Genetics, KU Leuven, Campus Gasthuisberg, Herestraat 49, B-3000 Leuven, Belgium
[c] Department of Movement and Sports Sciences, Ghent University, Watersportlaan 2, B-9000 Ghent, Belgium
[d] Department of Experimental Psychology, Ghent University, Henri Dunantlaan 2, B-9000 Ghent, Belgium
[e] Center for Medical Genetics, Ghent University Hospital, De Pintelaan 185, B-9000 Ghent, Belgium

ARTICLE INFO

Article history:
Received 14 April 2014
Received in revised form 29 July 2014
Accepted 29 July 2014
Available online

Keywords:
Neurofibromatosis type 1
Reaction time
Motor timing
Motor development
Children

ABSTRACT

Neurofibromatosis type 1 (NF1) is one of the most common single-gene disorders affecting fine and visual-motor skills. This case–control study investigated motor timing as a possible related performance deficit in children with NF1. A visual-motor reaction time (VRT) test was administered in 20 NF1 children (mean age 9 years 7 months) and 20 age- and gender-matched typically developing (TD) children. Copying and tracing performance were evaluated using the Beery-Buktenica Developmental Test of Visual-Motor Integration (Beery VMI). Children with NF1 responded with an increased reaction time (RT) to temporally predictive stimuli compared to TD children, whereas RT at unpredictive stimuli did not differ between groups. Motor timing indexed by the RT decrease at predictive stimuli significantly associated with the Beery VMI copy and tracing outcomes. Deficient motor timing as an actual symptom may add to further research on the pathogenesis of NF1-associated motor impairment and the development of more effective treatment.

© 2014 Elsevier Ltd. All rights reserved.

1. Introduction

Neurofibromatosis type 1 (NF1) is one of the most common single-gene disorders with an estimated incidence rate of 1:2700, caused by a mutation in the *NF1* gene coding for neurofibromin on chromosome 17q11.2 (Evans et al., 2010). NF1 patients exhibit multisystem clinical symptoms, including café-au-lait spots, freckling, Lisch nodules, optic pathways gliomas, neurofibromas, and specific bone abnormalities (Williams et al., 2009). These neurocutaneous symptoms are initiated by a hyperactive Ras-MAPK pathway due to insufficient neurofibromin-mediated inhibition of the Ras-signaling molecule (Krab, Goorden, & Elgersma, 2008). Other NF1 symptoms involve cognitive, visual-spatial and motor deficits (Williams et al., 2009). Visual-spatial memory and attentional dysfunctions emerge from increased GABA-mediated

* Corresponding author. Tel.: +32 09 332 69 23; fax: +32 09 332 38 11.
E-mail addresses: Julie.debrabant@ugent.be, julie.debrabant@gmail.com (J. Debrabant).

http://dx.doi.org/10.1016/j.ridd.2014.07.059
0891-4222/© 2014 Elsevier Ltd. All rights reserved.

inhibition and significantly reduced long-term potentiation because of the hyperactive Ras-MAPK signaling cascade (Costa et al., 2002). Ras-MAPK pathway dysregulation is also implicated in autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD), of which augmented prevalence rates occur in NF1 populations (Garg et al., 2013; Walsh et al., 2013). Co-occurring gross and/or fine motor problems are common in NF1 (Soucy, Gao, Gutmann, & Dunn, 2012) as well as in ADHD (McLeod, Langevin, Goodyear, & Dewey, 2014) and ASD (Gustafsson et al., 2014). Fine motor problems in children with NF1, such as writing difficulties may lead to significant difficulties in daily life functioning and academic achievement (Krab et al., 2011) and are found to significantly coincide with impaired visual-motor performance as measured with the copy subtest of the Beery Buktenica developmental test of visual motor integration (Beery VMI) (Gilboa, Josman, Fattal-Valevski, Toledano-Alhadef, & Rosenblum, 2010; Krab et al., 2011). According to parental reports, 53% of children with NF1 displayed poor handwriting (Hyman, Shores, & North, 2005). NF1-related fine motor deficits have been hypothesized to associate with cerebellar anomalies, i.e., hyperintensities visible on T2-weighted MR images or UBOs (unidentified bright objects) (Feldmann, Denecke, Grenzebach, Schuierer, & Weglage, 2003). Besides, NF1 specifically affects GABAergic neurons, and the cerebellar GABAergic Purkinje neurons are among the highest neurofibromin expressing neurons in the brain (Costa et al., 2002). However, extended research is required to clarify the pathogenesis of NF1 motor symptoms.

This study focussed on NF1-related fine motor deficits in children. Specifically, deficient motor timing has been suggested to contribute to NF1-related fine and visual-motor limitations. In support of this, behavioral findings in children with NF1 denote poorer steadiness and speed during fine motor manipulations and finger tapping as compared with typically developing controls (Feldmann et al., 2003). Motor timing is also subserved by a distributed network of cortico-cerebellar motor-related brain areas (Pecenka, Engel, & Keller, 2013) favoring the aforementioned cerebellar hypothesis.

Predictive timing allows to pre-select motor programs based on temporal predictions of upcoming events that facilitate motor performance. Adequate motor timing hence enables fine-tuned and anticipatory reactions at temporally predictive (i.e., regularly paced) sensory stimuli relative to unpredictive (i.e., irregularly paced) ones. Anticipatory reactions refer to fast responses initiated in omission of external sensory guidance (Karatekin, Marcus, & White, 2007). The RT advantage at sequences of predictive visual stimuli was found a significant predictor of fine motor tracing abilities in typically developing children (Debrabant, Gheysen, Vingerhoets, & Van Waelvelde, 2012). Poor drawing and writing performance in children with NF1 is therefore likely to result from erroneous "starting and stopping" (e.g., overshoot errors) rather than improper rotation, integration, or distortion. This kind of visual-motor impairment is recurrently assessed by means of the Beery VMI, which is a valid clinical test battery (Beery & Beery, 2004). Two Beery VMI subtests encompass copying (*VMI copy*) and tracing (*VMI tracing*) of geometric figures using a pencil on paper forms. A third Beery VMI subtests evaluates visual discrimination abilities of those geometric figures (*VMI visual discrimination*). NF1 also frequently implies attentional difficulties which may in turn affect fine motor outcomes. Attentional functioning strongly depends on processing speed as captured by RT performance conform previous studies (Hillman, Castelli, & Buck, 2005; Tamnes, Fjell, Westlye, Ostby, & Walhovd, 2012). Intellectual and general motor impairment may also affect the evaluation of motor timing as a NF1-associated motor symptom. These possible confounding effects need to be accounted for by standardized testing of the individual child with NF1.

The purpose of this study is to investigate motor timing abilities in association with fine and visual-motor impairment in children with NF1. An improved understanding of these deficits can contribute to identifying their neural underpinnings as well as the development of effective therapeutic interventions.

2. Methods

2.1. Study design, standard protocol approvals and consents

This was an age- and sex-matched, case–control study of RT performance and fine motor skills in 8- to 12-year-old children with NF1 and typically developing control children. The study was approved by the ethics commission of Ghent University. Written informed consent from legal guardians and child assent were obtained before testing.

2.2. Subject selection and criteria

Children with NF1 between 8 and 12 years of age were referred from two multidisciplinary outpatient clinics. All participants with NF1 fulfilled the diagnostic criteria specified by the National Institutes of Health (Gutmann et al., 1997) as confirmed by a clinical interview. Exclusion criteria were segmental NF1, deafness, uncorrected impaired vision, orthopedic deformities inhibiting motor performance, and an IQ below 85. Typically developing (TD) children were recruited from mainstream schools and were included for participation if their IQ score was above 85 and total Movement Assessment Battery for children – second edition (MABC-2) (Henderson, Sugden, & Barnett, 2007) score above the 16th percentile (no indications of motor problems).

The short form of the Wechsler Intelligence Scale for Children-third edition-Dutch Version (WISC-III-NL) was used to estimate the child's IQ based on two verbal tests (word similarities and comprehension) and two performance tests (picture arrangement and block design) (Grégoire, 2000). This abbreviated form of the WISC-III is a valid and reliable instrument to assess full scale IQ (reliability coefficient of .92) (Grégoire, 2000).

Download English Version:

https://daneshyari.com/en/article/10317340

Download Persian Version:

https://daneshyari.com/article/10317340

Daneshyari.com