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Differences in speech and language abilities between children with 22q11.2 deletion syndrome and children with phenotypic features of 22q11.2 deletion syndrome but without microdeletion

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ABSTRACT

Background: 22q11.2DS is the most common microdeletion syndrome in humans, usually associated with speech and language delay (SLD). Approximately 75% of children with 22q11.2 microdeletion have congenital heart malformations (CHM) which after infant open-heart surgery might lead to SLD.
Aims: The purpose of this study was to determine whether factors associated with microdeletion contribute to SLD in children with 22q11.2DS.
Methods and procedures: We compared speech and language abilities of two groups of school-aged children: those with 22q11.2 microdeletion (E1) and those with the phenotype resembling 22q11.2DS but without the microdeletion (E2). An age-matched group of typically developing children was also tested.
Outcomes and results: The obtained results revealed that children from group E1 have lower level of speech and language abilities compared to children from group E2 and control group. Additionally, mild to moderate SLD was detected in children from group E2 compared to children from the control group.
Conclusions and implications: The obtained results imply that both CHM after infant open-heart surgery and other factors associated with 22q11.2 microdeletion, contribute to SLD in patients with 22q11.2 microdeletion. Based on this, we could postulate that there is/are some potential candidate gene(s), located in the 22q11.2 region, whose function could be important for speech and language development.

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What this paper adds?

To the best of our knowledge, no published studies have yet compared the speech and language abilities of school-aged children (5–10 years old) with 22q11.2 microdeletion and school-aged children with the phenotype resembling 22q11.2DS but without microdeletion. The aim of this study was to compare both groups of children for a) the age at which their first functional word appeared, b) oral praxis, c) articulation skills and d) the level of speech and language development. The results indicated that children with 22q11.2DS had more severe SLD compared to children with phenotype resembling 22q11.2DS but without microdeletion.

1. Introduction

22q11.2 deletion syndrome (22q11.2DS) is the most common microdeletion syndrome in humans with an estimated incidence of approximately 1/4000 per live births (Fernandez et al., 2005; Kobrynski & Sullivan, 2007). This syndrome, encompassing DiGeorge syndrome, velocardiofacial syndrome (VCFS) and conotruncal anomaly face syndrome, is a contiguous gene deletion syndrome. The mode of inheritance of 22q11.2DS is autosomal dominant. About 7% of patients have 22q11.2 microdeletion inherited from parents, while in approximately 93% of the cases the deletion has occurred *de novo* (McDonald-McGinn, Emanuel, & Zackai, 2013).

22q11.2DS is among the most clinically variable syndromes, with more than 180 features related with the deletion, but commonly it includes congenital heart malformations (CHM), facial dysmorphism, thymic hypoplasia, cleft palate/velopharyngeal insufficiency (VPI), hypoparathyroidism with hypocalcaemia, feeding difficulties, speech and language delay (SLD) and developmental delay (Firth, Hurst, & Hall, 2005; Hennekam, Allanson, Krantz, & Gorlin, 2010; McDonald-McGinn et al., 1999; Squarcione, Torti, Di Fabio, & Biondi, 2013).

22q11.2DS is the second most common genetic syndrome associated with CHM after Down syndrome (Bassett & Chow, 1999; Wiehahn et al., 2004). CHM has been reported in 75% of patients with 22q11.2 microdeletion (Kobrynski & Sullivan, 2007; McDonald-McGinn et al., 1999, 2001). It has been revealed that infants with CHM are at risk for neurodevelopmental disorders, including cognitive, motor, social and language impairments (Homsy et al., 2015). The literature suggests that children with non-syndromic CHM may also exhibit a range of developmental difficulties following open-heart surgery in infancy, including delays in communication and language (Majnemer et al., 2008). Additionally, the literature indicates that the most children who had infant cardiac surgery have developed an appropriate level of receptive language, but their skills in the expressive domain have often been impaired (Bellinger et al., 2003; Hovels-Gurich et al., 2002; Hovels-Gurich, Seghaye, Dabritz, Messmer, & von Bernuth, 1997; Mahle et al., 2000; Majnemer et al., 2008). Also, there are reports which emphasise that fine motor skills (articulation skills), visuospatial skills, cognition (including memory, attention, and higher-order language skills) and psychosocial abilities are affected in children with isolated CHM (Bellinger et al., 2003; Hovels-Gurich et al., 2002, 2008; Marino et al., 2012). Considering that both our examined groups of children (the groups with and without microdeletion) have CHM and open-heart surgery which could lead to speech and language delay (Majnemer et al., 2008; Marino et al., 2012), the aim of this study was to determine whether factors associated with microdeletion (certain genetic disturbances arising from microdeletion) contribute to SLD in children with 22q11.2DS.

2. Material and methods

2.1. Participants

We examined the speech and language abilities of three groups of children (5–10 years old):

a) an experimental group 1 (group E1) consisting of 11 children with 22q11.2 microdeletion,
b) an experimental group 2 (group E2) consisting of 11 children with the phenotypic features of 22q11.2DS but without the microdeletion 22q11.2 and c) a control group (group C) comprising 11 typically developing participants.

Children from experimental groups E1 and E2 have had at least two out of five major clinical characteristics of 22q11.2DS (congenital heart malformations (CHM), characteristic facial appearance, thymic hypoplasia, cleft palate/VPI and hypocalcaemia) (Table 1). Children were consecutive patients at University Children's Hospital, Belgrade, Serbia. Specifically, all children with phenotypic features of 22q11.2 deletion syndrome aged 5–10 years who visited the hospital between 2012 and 2015 were recruited to the study. Children who had hearing loss (conductive or sensorineural), any form of cleft palate/VPI and physical deformity of speech organs, were excluded. All children from experimental groups E1 and E2 had open-heart surgery in infancy.

All children were evaluated by a medical team (clinical geneticist and pediatric cardiologist) from University Children's Hospital and by speech – language specialists from the Institute for Experimental Phonetics and Speech Pathology (IEPSP). The control group were recruited from a nursery and public primary school in Belgrade. None had, or had in the past, any neurodevelopmental disorders, CHM, recurrent hearing disorders, SLD or other learning disabilities. They were age and gender matched to children in the E1 and E2 groups. The socio-economic status was comparable to that of the E1 and E2 groups. Parental interviews were used to obtain information about the families' socio-economic status. Parents were asked