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Association between enterovirus infection and speech and language impairments: A nationwide population-based study



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ABSTRACT

Background and aims: Delay and impairment in Speech and language are common developmental problems in younger populations. Hitherto, there has been minimal study of the association between common childhood infections (e.g. enterovirus [EV]) and speech and language. The impetus for evaluating this association is provided by evidence linking inflammation to neurodevelopmental disorders. Herein we sought to determine whether an association exists between EV infection and subsequent diagnoses of speech and language impairments in a nationwide population-based sample in Taiwan.

Methods: Our study acquired data from the Taiwan National Health Insurance Research Database. The sample was comprised of individuals under 18 years of age with newly diagnosed EV infection during the period from January 1998 to December 2011. 39669 eligible cases were compared to matched controls and assessed during the study period for incident cases of speech and language impairments. Cox regression analyses were applied, adjusting for sex, age and other physical and mental problems.

Results: In the fully adjusted Cox regression model for hazard ratios, EV infection as positively associated with speech and language impairments (HR = 1.14, 95% CI: 1.06–1.22) after adjusting for age, sex and other confounds. Compared to the control group, the hazard ratio for speech and language impairments was 1.12 (95% CI: 1.03–1.21) amongst the group of EV infection without hospitalization, and 1.26 (95% CI: 1.10–1.45) amongst the group of EV infection with hospitalization.

Conclusions: EV infection is temporally associated with incident speech and language

Abbreviations: ICD-9-CM, International Classification of Disease; Revision 9, Clinical Modification; DSM-5, The American Psychiatric Association's Diagnostic and Statistical Manual Fifth Edition; EV, enterovirus or enteroviruses; NHIRD, National Health Insurance Research Database; CNS, central nervous system; HR, hazard ratio; CI, confidence intervals

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impairments. Our findings herein provide rationale for educating families that EV infection may be associated with subsequent speech and language problems in susceptible individuals and that monitoring for such a presentation would be warranted.

What this paper adds?: Speech and language impairments associated with central nervous system infections have been reported in the literature. EV are medically important human pathogens and associated with select neuropsychiatric diseases. Notwithstanding, relatively few reports have mentioned the effects of EV infection on speech and language problems. Our study used a nationwide longitudinal dataset and identified that children with EV infection have a greater risk for speech and language impairments as compared with control group. Infected children combined other comorbidities or risk factors might have greater possibility to develop speech problems. Clinicians should be vigilant for the onset of language developmental abnormalities of preschool children with EV infection.

1. Introduction

Speech and language impairments are common developmental problems in general pediatrics (Schum, 2007). Studies have indicated that speech and language delays occur at prevalence rates between 10% and 20% (Horwitz et al., 2003; Nelson, Nygren, Walker, & Panoscha, 2006; Rescorla, 1989; Zubrick, Taylor, Rice, & Slegers, 2007), and these problems have direct impacts on a child's social interactions, social relationships, and academic attainment (Simms, 2007). Speech and language impairments among childhood are variously described as children who do not talk, have difficulty in speaking, unable to understand others' speech, or have stutter problem (American Psychiatric Association, 2013). The International Classification of Disease, Revision 9, Clinical Modification (ICD-9-CM) differentiates several types of speech and language problems, including stuttering, developmental speech or language disorder, aphasia, voice disturbance, and other speech disturbance (ICD-9Data, 2015). The American Psychiatric Association's Diagnostic and Statistical Manual Fifth Edition (DSM-5) classifies communication disorder into five categories resembling the diagnoses of ICD-9-CM (American Psychiatric Association, 2013).

The etiology and pathogenesis of speech and language impairments are complex and varied. Poor speech and language developments are often associated with physical health problems (e.g., cerebral palsy, epilepsy, traumatic brain injury, hearing disorders), and mental disorders (e.g., mental retardation, autism spectrum disorders, attention deficit hyperactivity disorder) (Simms, 2007). Multiple risk factors for speech and language impairments have also been discussed in the literature, including family history, sex, preterm, perinatal factors, temperament, birth orders, socioeconomic status, and other environmental factors (Chaimay, Thinkhamrop, & Thinkhamrop, 2006; Harrison & McLeod, 2010; Prathanee, Thinkhamrop, & Dechongkit, 2007). Primary care professionals should identify and provide support for children who are at-risk.

Infection-related neurocognitive and mental health problems have continuously raised attention in global researches (John et al., 2015). Speech and language impairments associated with virus infections have been reported in the literature. Among the survivors of Japanese encephalitis patients in one prospective study, 79% of patients had various types of speech disturbances initially. 98% of patients with all types of speech disturbances got rapid or gradual improvement within 5 years (Sarkari et al., 2012). A considerable number of survivors of herpes simplex encephalitis suffer from pronounced long-term cognitive deficits, including memory, naming, semantic knowledge, executive functions or emotional regulation (McGrath, Anderson, Croxson, & Powell, 1997; Utley, Ogden, Gibb, McGrath, & Anderson, 1997). The neuropsychological data analysis revealed language disturbances in herpes simplex encephalitis were associated with gray matter loss in lateral temporal lobe, thalamus and left insula (Baratelli, Laiacona, & Capitani, 2015; Frisch et al., 2015).

Enteroviruses (EV), a group of single-stranded sense RNA viruses (Rhoades, Tabor-Godwin, Tsueng, & Feuer, 2011), are among the most common and medically important human pathogens. They are highly infectious and cause 10–15 million symptomatic infections each year in the United States (Sawyer, 2002). In our literature review, just few studies reported EV infection related speech problems. Freund reported a 4-year-old girl with a prolonged upper respiratory tract infection developed indistinct speech and other neurological symptoms within a few days (Freund, Zass, Kurlmann, Schuierer, & Ullrich, 1998). A rise in echovirus type 21 neutralization titer gave evidence of an acute echoviral infection. At follow-up after 3 months clinical symptoms had fully resolved. Another 32-month-old girl was reported by Marques to have enteroviral encephalitis confirmed by polymerase chain reaction in cerebrospinal fluid (Marques, Brito, Conde, Pinto, & Moreira, 2014). She experienced unfavorable clinical course with marked developmental regression, autistic features, persistent stereotypes and aphasia. She presented with slow clinical improvement and received early interventions with speech and language therapy. Both case reports suggest that an association between EV with the onset of speech and language problems exists and such an association is linked to alterations in MRI (Magnetic Resonance Imaging) measure brain structural/functional changes.

To our best knowledge, there was no large scale study exploring the temporal association between EV infection and speech and language impairments. Our study aimed to investigate the association between EV infection and subsequent diagnoses of speech and language impairments in a nationwide population-based sample. Furthermore, our study also examined other potential factors associated with speech and language impairments in the same sample.

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