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The identification and measurement of autistic features in children with septo-optic dysplasia, optic nerve hypoplasia and isolated hypopituitarism

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ABSTRACT

This study aimed to highlight the occurrence of autism spectrum disorders (ASDs) in children with septo-optic dysplasia (SOD) and optic nerve hypoplasia (ONH). A cross-sectional study was designed, including 28 children with SOD and 14 children with ONH. Clinician diagnosis of ASD was reported in 14 children. The Social Communication Questionnaire (SCQ) reported that 23 children met the cut-off point for ASD, and 9 children met the cut-off point for autism. Greater levels of intellectual disability and visual loss were reported in children with ASD in comparison to those without ASD, but, of the two, intellectual disability was a better predictor for ASD. The SCQ lost its sensitivity and specificity in children who had greater visual loss which highlights a requirement for a measure that is sensitive to visual loss. It is also recommended that children with SOD/ONH would benefit from routine screening for ASDs.

1. Introduction

1.1. Background

The diagnosis of autistic spectrum disorders (ASDs) can be the crucial gateway for acquiring appropriate levels of support for a child at risk of social and communicative impairment. However, when diagnosing autism in a child with visual loss, misunderstandings between 'autistic-like' behaviours or 'blindisms' and ASDs can often lead to a missed diagnosis of autism by clinicians. These issues were highlighted during outpatient paediatric clinics at the Birmingham Children's Hospital (UK) with an Endocrinologist and Clinical Psychologist, where ASDs were frequently observed in children with septo-optic dysplasia (SOD) and optic nerve hypoplasia (ONH). For these reasons, this study aimed to highlight the occurrence of ASDs in children with SOD and ONH, and the importance of screening for ASDs in these children. In addition, this study sought to identify which of the syndrome characteristics (visual impairment and intellectual disability) best predicted autistic phenomenology in children with SOD and ONH.

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1.1.1. The conditions of SOD and ONH

Septo-optic dysplasia (SOD) is a rare congenital condition which is diagnosed by a variable combination of: (1) dysgenesis of midline forebrain structures (absence, or hypoplasia, of septum pellucidum and/or corpus collosum); (2) hypothalamic-pituitary dysfunction (hypopituitarism, ranging from isolated to multiple hormone deficiencies); and (3) optic nerve hypoplasia (ONH; underdevelopment of the optic nerve) (Polizzi, Pavone, Iannettu, Manfre, & Ruggieri, 2006). To make the diagnosis of SOD, a child must exhibit at least two of the three features of the triad (McNay et al., 2007). The reported prevalence of SOD and ONH is 13.8 per 100,000 live births (Atapattu et al., 2012), and the phenotype is variable in its severity and symptom manifestation.

Children with SOD and ONH demonstrate a wide spectrum of visual function, ranging from good visual acuity to no light perception. A high percentage of children with ONH have nystagmus (involuntary movements of eyes), mild light intolerance, and varying degrees of impairment to their depth perception (Lambert, Hoyt, & Narahara, 1987; Zeki, 1990). Historically, research studies have used the terms SOD and ONH synonymously, due to the similarities in their pathologies and symptom manifestation (Borchert & Garcia-Filion, 2008).

The common expression of these three features has been attributed to the early development of the forebrain during the first trimester of pregnancy (Lubinsky, 1997). For example, if trauma occurred and affected this particular region at a critical time in development, then this could explain the particular expression of the combination of symptoms which are reported in SOD patients. We have recently demonstrated environmental features, including reduced maternal age and primagravida births, plus increased 1st trimester bleeding, which support this hypothesis (Atapattu et al., 2012). Risk-taking behaviours such as maternal engagement in antenatal smoking, alcohol use and recreational drug taking, have also been identified in a number of studies (Patel, McNally, Harrison, Lloyd, & Clayton, 2006; Tornqvist, Ericsson, & Källén, 2002). In addition, two UK studies reported that living in high-density populations and inner cities was associated in some cases of SOD and ONH (Atapattu et al., 2012; Patel et al., 2006).

Homozygous mutations of the homeobox gene HESX1 have been reported in patients with SOD (Dattani et al., 1999; Webb & Dattani, 2010), although this mutation accounts for approximately 1% of cases (McNay et al., 2007). Genetic mutations in SOX2, SOX3 and OTX2 have also been identified in cases of SOD (McCabe, Alatzoglou, & Dattani, 2011). For these reasons, the aetiology of SOD and ONH to date is considered multi-factorial (Atapattu et al., 2012; McCabe et al., 2011).

1.1.2. ASDs in children with SOD and ONH

The behavioural phenotype of children with SOD and ONH is also highly variable. For instance, Margalith, Jan, McCormick, Tze, and Lapointe (1984) first reported a correlation with neuropsychiatric disorders in nearly three-quarters of cases of ONH. In study of 115 children with SOD and ONH, 98 children displayed additional impairments, with the most common being a combination of intellectual disability and motor impairments (Tornqvist et al., 2002). Similarly, developmental delays were reported in 52 out of 73 children with ONH, with the corpus callosum being highly implicated in impairments in the domains of personal, adaptive, communication, and cognitive functioning (Garcia-Filion et al., 2008). However, research has reported that some of the developmental delays observed in children with SOD and ONH are not typically observed in other groups of blind children, with different aetiologies for their visual impairment (Bahar & Brody, 2003). These researchers observed that children with SOD and ONH showed impairments within the 'triad of impairments' (Wing & Gould, 1979), which included avoiding social interaction, engaging in atypical language development, and a rigid adherence to routines (Bahar & Brody, 2003). These traits at present encompass the broad spectrum of autism spectrum disorders (ASDs) (DSM-IV-TR; American Psychiatric Association, 2000) which includes autistic disorder, Asperger's disorder, and pervasive developmental disorder not otherwise specified (PDD-NOS). All can be characterised by severities in three symptom domains, namely, deficits in social interaction, deficits in verbal and nonverbal communication, and stereotypies and rigid patterns of behaviour. Autism is now understood to be a neurodevelopmental disorder with a strong genetic component (Bailey et al., 1995; Folstein & Rutter, 1977; Santangelo & Tsatsanis, 2005) (genetic abnormalities which are associated with SOD and ONH have not been identified in cases of ASD). The greatest risk factor for ASD is being both male (Werling & Geschwind, 2013) and having an intellectual disability (Vivanti, Barbaro, Hudry, Dissanayake, & Prior, 2013). Epidemiological studies have indicated that the prevalence of ASDs is 10 cases in every 10,000 (Fombonne, 2003).

A small-scale study reported ASDs in six of thirteen children with SOD and ONH, and an autistic-like condition in another three children. Eight of the children had cognitive capacities within the normal or near-normal range, and five children had varying degrees of intellectual disability (Ek, Fernell, & Jacobson, 2005). The largest and most recent study to date of ASDs in children with SOD and ONH used retrospective case studies dating from 1977 to 2009. Researchers reported that 48 out of 83 children had difficulties in one domain of ASD and 31 of these children had difficulties in all three domains, of whom 26 out of the 31 received a clinical diagnosis of ASD. Children with profound visual impairment were more likely to experienced impaired social communication and show repetitive behaviours than those with severe visual impairment. Children were also most likely be diagnosed with ASD between the ages of 2 years 4 months and 4 years 6 months. Therefore, the overall prevalence of ASD was one-third in children with SOD and ONH, a prevalence rate that is similar to that reported in children with diagnostically heterogeneous visual impairment (Parr, Dale, Shaffer, & Salt, 2010).

This over-representation of autistic behaviours in children with visual impairments, in comparison to the general population, has been noted over the decades (Chase, 1972; Chess, Korn, & Fernandez, 1971; Fazzi et al., 2007; Fraiberg, 1977; Gense & Gense, 2005; Hobson & Bishop, 2003; Hobson, Lee, & Brown, 1999; Keeler, 1958). However, it is not known whether ASDs in children with visual loss can be attributed to neurological impairments or their visual impairment. As a result,