Published in final edited form as:
Adv Neurodev Disord. 2018 March ; 2(1): 49–61. doi:10.1007/s41252-017-0051-3.

Early Vocal Development in Autism Spectrum Disorder, Rett Syndrome, and Fragile X Syndrome: Insights from Studies using Retrospective Video Analysis

Laura Roche[1], **Dajie Zhang**[2], **Katrin D Bartl-Pokorny**[2], **Florian B Pokorny**[2,3], **Björn W Schuller**[4,5], **Gianluca Esposito**[6,7], **Sven Bölte**[8,9], **Herbert Roeyers**[10], **Luise Poustka**[11], **Markus Gugatschka**[12], **Hannah Waddington**[1], **Ralf Vollmann**[13], **Christa Einspieler**[2], and **Peter B Marschik**[2,8]

[1]School of Education, Victoria University of Wellington, Wellington, New Zealand [2]iDN – interdisciplinary Developmental Neuroscience, Department of Phoniatrics, Medical University of Graz, Graz, Austria [3]Machine Intelligence & Signal Processing group, MMK, Technical University of Munich, Munich, Germany [4]Chair of Embedded Intelligence for Health Care and Wellbeing, Augsburg University, Augsburg, Germany [5]GLAM – Group on Language, Audio & Music, Imperial College London, London, UK [6]Social & Affective Neuroscience Lab, Division of Psychology – HSS, Nanyang Technological University, Singapore, Singapore [7]Affiliative Behaviour and Physiology Lab, Department of Psychology and Cognitive Science, University of Trento, Trento, Italy [8]Center of Neurodevelopmental Disorders (KIND), Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden [9]Child and Adolescent Psychiatry, Center of Psychiatry Research, Stockholm County Council, Stockholm, Sweden [10]Department of Experimental Clinical and Health Psychology, Ghent University, Ghent, Belgium [11]Department of Child and Adolescent Psychiatry and Psychotherapy, University Medical Center Göttingen, Göttingen, Germany [12]Department of Phoniatrics, Medical University of Graz, Graz, Austria [13]Department of Linguistics, University of Graz, Graz, Austria

Abstract

This article provides an overview of studies assessing the early vocalisations of children with autism spectrum disorder (ASD), Rett syndrome (RTT), and fragile X syndrome (FXS) using retrospective video analysis (RVA) during the first two years of life. Electronic databases were systematically searched and a total of 23 studies were selected. These studies were then

Author contributions

LR was the primary author of the manuscript; she implemented the original literature search, and collated and analysed the data from all of the included studies. DZ provided edits and insight into the formation of the draft and final manuscript. KBP and FP provided edits on the draft of manuscript, and reliability checks on all of the included articles. BWS provided expertise in the field of early vocalisation analysis and speech processing as well as edits on the draft of manuscript. GE provided expertise on early vocal development in autism spectrum disorders and edits on the manuscript draft. SB provided edits on the definitions, diagnoses and features of the included neurodevelopmental disorders. HR provided expertise on neurodevelopmental disorders in general and edits on the draft of manuscript. LP provided expertise in the field of autism spectrum disorders and final edits on the manuscript. MG provided expertise from a phoniatric point of view and edits on the draft of manuscript, and HW conducted reliability checks on features of chosen articles for inclusion. RV provided expertise from a linguistic point of view and edits on the draft. CE provided expertise in the field of Rett syndrome and edits on the draft manuscript, and PBM provided insight into the formation of the draft and edits on the final manuscript.

Europe PMC Funders Author Manuscripts

categorised according to whether children were later diagnosed with ASD (13 studies), RTT (8 studies), or FXS (2 studies), and then described in terms of (a) participant characteristics, (b) control group characteristics, (c) video footage, (d) behaviours analysed, and (e) main findings. This overview supports the use of RVA in analysing the early development of vocalisations in children later diagnosed with ASD, RTT or FXS, and provides an in-depth analysis of vocalisation presentation, complex vocalisation production, and the rate and/or frequency of vocalisation production across the three disorders. Implications are discussed in terms of extending crude vocal analyses to more precise methods that might provide more powerful means by which to discriminate between disorders during early development. A greater understanding of the early manifestation of these disorders may then lead to improvements in earlier detection.

Keywords

Vocalisation analysis; autism spectrum disorder; Rett syndrome; fragile X syndrome; retrospective video analysis; babbling; speech-language; early detection

Introduction

A critical achievement in the early stages of neurotypical development is the emergence of pre-linguistic vocalisations which form the basis for functional human communication. Atypicalities in these early vocalisations are indicators of altered development, which can be analysed to detect neurodevelopmental disabilities (e.g., Marschik et al., 2017; Oller, Eilers, Neal, & Schwartz, 1999; Zwaigenbaum, Bryson & Garon, 2013). In typical infants, pre-linguistic vocalisations emerge during the first months of life, and continually progress and change in appearance, frequency, complexity, and variability. Milestones during the first year of life include the transition from cooing to babbling, and proto-words to first conventional words (Karmiloff & Karmiloff-Smith, 2009; Locke, 1995; Marschik, Einspieler, Garzarolli, & Prechtl, 2007; McCune & Vihman, 2001; Stark, 1980; Tager-Flusberg & Caronna, 2007). The age at which early pre-linguistic vocalisations appear is considered significant to the development of typical speech-language functions, and has been extensively studied (e.g., McCune & Vihman, 2001; Oller, 1980; Stark, 1980), whereas the quality of early vocal development has received less attention thus far (Marschik et al., 2017). Particular features of vocal development across neurodevelopmental and genetic disorders with a clinical onset at or beyond toddlerhood, might offer valuable insight into the manifestation of these disorders during infancy. A greater understanding might then enable earlier detection, differentiation, and treatment of these disorders (Marschik et al., 2017).

The vocal behaviour of infants during the second half of the first year of life (6 to 12 months) involves the rapid expansion in the articulation of vocal sounds. From approximately 6 to 10 months of age, vocalisations like cooing (which typically emerge prior to 6 months) gradually disappear and early marginal-babbling sets in, followed by additional and more complex canonical syllable and babbling sounds (McCune & Vihman, 2001; Oller et al., 1999; Paul et al., 2011; Stark, 1980). Canonical syllables can be defined as supra-glottal consonant- (C) vowel- (V) combinations with adult-speech-like timing (Oller, 1980; Oller et al., 1999; Stark, 1980). For example; /ba/, /da/, or /ka/, as CV realizations.

Europe PMC Funders Author Manuscripts

Canonical or reduplicated babbling is the repetition of CV syllables to form a dialogue or string of early word-like approximations, for example; /baba/, /dada/, /mama/ (Fagan, 2009; Oller et al., 1999; Stark, 1980). As expressive language is composed of canonical syllables, it is critical that one obtains control over using and producing canonical syllables to later acquire proficiency in verbal language (Oller et al., 1999; Paul et al., 2011; Patten et al., 2014). From approximately 10 to 12 months of age, infants' vocal behaviour evolves from canonical and variegated babbling (e.g., /dagubab/), to the emergence of proto-words; defined as having a consistent phonetical structure, but not necessarily the target language's convention yet (Karmiloff & Karmiloff-Smith, 2009; Locke, 1995; McCune & Vihman, 2001; Oller et al., 1999; Tager-Flusberg & Caronna, 2007). Thus the emergence of specific syllable production and more complex babbling displays are considered significant milestones in speech-language acquisition in the first year of life, and provide further insight into both typical and atypical developmental traits (Chericoni et al., 2016; Oller et al., 1999; Patten et al., 2014; Paul et al., 2011; Stark, 1980; Tager-Flusberg & Caronna, 2007).

Particular neurodevelopmental and genetic conditions, such as autism spectrum disorder (ASD), Rett syndrome (RTT), and fragile X syndrome (FXS), share deviances in early vocalisation and speech-language development. These conditions are often formally diagnosed late in toddlerhood, during the preschool years, or older in milder or atypical cases. There is emerging evidence suggesting that identification of developmental biomarkers is in reach, enabling detection of these conditions earlier in development, particularly within the first two years.

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterised by persistent impairment in social communication skills and the presence of restricted and repetitive behaviours (DSM-5: Diagnostic Statistical Manual 5th edition, American Psychiatric Association, 2013), with a currently estimated prevalence of 1.5% (CDC: Centers for Disease Control and Prevention, 2016). The specific causes driving the atypical neurodevelopment of ASD remain poorly understood. Genome sequencing data suggest the existence of numerous ASD-related and risk genes, both rare and common, interacting with environmental risks (Vorstman et al., 2017). Currently ASD is formally diagnosed around 3 to 4 years old (CDC, 2016; Dawson & Bernier, 2013). To accurately identify ASD, and other neurodevelopmental disorders earlier, developmental trajectories have been studied using several paradigms. First, retrospectively during the first two years of life (i.e., during the prediagnostic period) by analysing early vocalisations, early motor development, sensory-motor processing, and interactive behaviours (Baranek, 1999; Chericoni et al., 2016; Einspieler et al., 2014; Oller et al., 1999; Ozonoff et al., 2011; Paul et al., 2011; Zwaigenbaum et al., 2013). Secondly, and more recently, prospective studies have been adopted to assess the development of younger siblings of children diagnosed with ASD over time. These cases are informative in that younger siblings have an increased likelihood of receiving a diagnosis of ASD due to shared genetic risks (e.g., Bölte et al., 2013; Charman et al., 2017; Loth et al., 2017; Ozonoff et al., 2011; Paul et al., 2011; Zwaigenbaum et al., 2009). Prospective studies have identified several early behavioural signs of ASD during the first year of life including atypical visual fixation and engagement, and delays in the complexity of early vocalisations (Chericoni et al., 2016; Patten et al., 2014). Reliably identifying these early signs prior to the current typical age of diagnosis, which is still often

after early childhood (Costanzo et al., 2015), might enable earlier detection and provide opportunities for targeted intervention to improve developmental outcomes for these children (Bölte et al., 2016; Green et al., 2017; Spreckley & Boyd, 2009).

Atypicalities in the emergence of early vocalisations are not specific to ASD, they are also characteristic of a number of other neurodevelopmental disabilities. In particular, impairments in the quality and delays in the progression of early vocalisations and communication skills are among the earliest indicators to raise suspicion of RTT and FXS (e.g., Baranek et al., 2005; Belardi et al., 2017; Marschik & Einspieler, 2011; Marschik et al., 2009; Zhang et al., 2017). There is a growing consensus that assessing the prodromal period of these other disorders may lead not only to a better understanding of how these disorders manifest during infancy, and therefore increase opportunities for earlier detection, but also their differentiation from ASD (Jones et al., 2014; Marschik et al., 2017).

Rett syndrome (RTT) is a neurodevelopmental disorder that primarily results from a genetic mutation in the *MECP2* gene, estimated to affect 1/10,000 live female births (Amir et al., 1999; Neul et al., 2010). It has long been believed that RTT manifests in infants following an initial period of supposed typical development. The growing body of knowledge regarding the early development of RTT however suggests that atypicalities are already present within the first months of life (e.g., Einspieler, Freilinger, & Marschik, 2016; Einspieler, Kerr, & Prechtl, 2005a, 2005b; Leonard & Bower, 1998; Marschik et al., 2013b; Marschik et al., 2013a). With increasing age, children with RTT experience a regression period resulting in the loss of purposeful hand use, severe intellectual disability, severe physical deficits, atypical breathing patterns, and a significant loss of functional communication skills. A plateau stage is then reached where no further skill loss is observed (Hagberg & Anvret, 1993; Hagberg & Witt-Engerström, 1987; Neul et al., 2010). Variants of RTT exist where children share many of the diagnostic features of RTT, such as regression, yet do not share all of the features associated with a diagnosis of classic RTT (Neul et al., 2010). For example, children who re-gain some spoken communication skills following regression, and demonstrate a wider range of non-verbal and verbal skills in comparison to those with classic RTT, are categorised as having the preserved speech variant (PSV) of RTT (Neul et al., 2010; Renieri et al., 2009). Current literature demonstrates that early expressive communication, such as pre-linguistic vocalisations, have been identified as atypical or severely delayed already during the pre-regression period encompassing the first year or sometimes the first two years of life (Bartl-Pokorny et al., 2013; Marschik et al., 2013b; Marschik et al., 2013a). Evidence of these atypicalities further supports the argument that development in these children does not progress in a typical nature during the pre-regressional stage (e.g., Marschik et al., 2009; Marschik et al., 2013a). Accurate and reliable methods of identifying atypicalities in early vocalisations may provide opportunities for earlier detection and further delineate the early progression of this syndrome (Marschik et al., 2017; Pokorny, Marschik, Einspieler, & Schuller, 2016).

Fragile X syndrome (FXS) is a genetic disorder that often results from the excessive repeat of a trinucleotide CGG at the Xq 27.3 site on the fragile X mental retardation gene 1 (*FMR1*) (Crawford, Acuña, & Sherman, 2001; Hagerman, 2002). FXS is the leading cause of inherited intellectual disability in males and the full mutation, where there are over 200

repeats of the trinucleotide CGG, is estimated to affect approximately 1/4000 males and 1/8000 females (Bailey, Hatton & Skinner, 1998; Bailey, Raspa, Bishop, & Holiday, 2009). The result of this genetic mutation leads to a deficiency, or total absence, of the FMR1 protein which is critical for typical brain development and function (Crawford et al., 2001; Hagerman, 2002). The reduction or total loss of this protein causes severe deficits in motor skills, cognitive capabilities, and communication development (Bailey et al., 1998). Consistent with ASD and RTT, individuals with FXS display atypicalities in the development of vocalisations and later profound communication deficits, in that functional or meaningful verbal language is often unobtainable (Bailey et al., 1998; Baranek et al., 2005; Hagerman, 2002; Hinton et al., 2013).

Various analysis approaches, particularly the above mentioned prospective high-risk sibling approach, have advantages in identifying markers of atypicalities in early development in comparison to retrospective analysis (see Marschik et al., 2017; Zwaigenbaum et al., 2013). However, prospective analysis is limited in its application to rare disorders that are usually detected late, such as RTT or FXS (e.g., Bailey et al., 2009; Tarquinio et al., 2015). In girls with RTT for example, a prospective analysis and cohort is almost impossible to obtain (Marschik et al., 2017) due to the main cause of RTT by *de novo* mutations in the *MECP2* gene. Disorders, such as RTT and FXS are also less prevalent than ASD, and are diagnosed similarly in late toddlerhood or during the pre-school years. The parents of children with neurodevelopmental disorders however often report concerns in early deficits or delays in their child's speech as one initial indication that something was unusual during their child's early development. These concerns are generally recognised at an earlier age than that of formal diagnosis (Bailey et al., 2009; Zhang et al., 2017). Despite this, parents are less accurate in identifying specific forms of pre-linguistic vocalizations (Paul et al., 2011). Thus the search for effective tools to reliably screen for these early atypical behaviours and communication deficits is warranted, to provide detailed and precise indicators so that children with these neurodevelopmental disorders are detected at an earlier age (Costanzo et al., 2015; Marschik et al., 2017; Paul et al., 2011; Zhang et al., 2017; Zwaigenbaum et al., 2013).

Retrospective Video Analysis (RVA) has proved a valuable tool in the process of reliably documenting specific behaviours and deviances or atypicalities presented by infants in the early years of life (Costanzo et al., 2015; Palomo, Belinchón, & Ozonoff, 2006; Zwaigenbaum et al., 2013). In particular, the early vocalisations of infants who were later diagnosed with ASD or RTT have been analysed to evaluate early canonical babbling frequency and the rate of total vocalising behaviours (Chericoni et al., 2016; Marschik et al., 2012a; Patten et al., 2014; Pokorny et al., 2016; Werner & Dawson, 2005). Studies adopting RVA have employed the use of home video tapes to annotate and evaluate various settings and interactive situations involving the infant and additional contextual variables. For example, many studies have analysed audio-video material during familiar home routines like bathing, feeding, and during special events such as birthdays (e.g., Chericoni et al., 2016; Patten et al., 2014; Werner & Dawson, 2005).

This overview of current literature attempts to highlight the appropriateness of RVA as a research tool to map the vocal development of infants during the first two years of life, who

Europe PMC Funders Author Manuscripts

are later diagnosed with ASD, RTT, or FXS. Specifically, this article summarises the findings of selected studies into participant characteristics, control group characteristics, video footage used, behaviours analysed, and the general findings. The general findings are segmented into three categories: (a) vocalisations that includes the presence of pre-linguistic behaviours for communicative functions, vocal imitation, person directed vocalisations, semantically meaningful vocalisations, contingent vocalisations during an interaction, and the presence of vocalisations that are unspecified or unmodulated, (b) the complexity of vocalisations including canonical syllable production, canonical babbling, variegated babbling, proto-words, first words, and word combinations, and (c) the rate or frequency of vocalisations (volubility), and the specific report of complex babble, first words, and word combinations. The overall findings and comparable aspects of vocal development across the three conditions are then discussed.

Method

Search Terms

In December 2016, the following terms were searched by the first author in online, open access search engines: ERIC, ProQuest, google scholar, and PubMed. The search terms included: *home video analysis* AND *retrospective analysis* with each of the following: *ASD* AND *early vocalisations, Rett syndrome* AND *early vocalisations, fragile X syndrome* AND *early vocalisations*. From these results, the identified titles of the articles and abstracts were initially screened against the inclusion criteria presented below. Additionally, the authors and co-authors of accepted studies were searched using the above mentioned search engines to further identify any remaining studies that may have been missed. Twenty one articles were initially included. Three studies were removed from the original sample as these studies were identified as: (a) lacking a specific focus on vocal behaviours, and (b) containing video data with poor audio quality (as stated in the paper, only half of the videos had audio able to be analysed). A second search run, identical to that performed earlier by the first author, was conducted in July 2017 to further identify any additional studies. Five papers were included following the second search cycle, thus 23 studies were included within the final review.

Inclusion criteria

Studies which retrospectively analysed the home videos of the early spontaneous or communicative (e.g., cooing, babbling) vocalisations of children with either ASD, RTT, or FXS during the first two years of life, with or without a typically developing control group, were included in this overview. More specifically, studies were screened for: (a) the inclusion of retrospective video analysis, (b) a focus on the early vocal behaviour of infants during the first two years of life, (c) infants that were later diagnosed with ASD, RTT, or FXS, (d) published within peer reviewed academic journals or were published as peer reviewed conference proceedings, (e) were written after 1990 to ensure videos were of an adequate quality for precise analysis, and (f) were written in English.

Analysis

The three conditions targeted in this overview are separated into three tables describing the selected studies focusing on the early vocalisations of children with ASD (Table 1), RTT

(Table 2), and FXS (Table 3). Thirteen studies were included for ASD, 8 focused on RTT, and 2 studies analysed the vocal behaviours of infants later diagnosed with FXS. Studies are organised according to year of publication and tables include information regarding the target and control participant characteristics, the age range analysed, the specific types of vocal behaviours which were coded, and the main findings in terms of vocalisation presentation, the complexity of vocalisations, the rate/frequency of vocal production, and the inter-rater reliability scores.

Results

Tables 1, 2, and 3 provide summaries of the studies adopting RVA to assess the vocalisations of children later diagnosed with ASD, RTT, or FXS respectively.

Participant characteristics

Of the 13 studies which analysed infants who later received a diagnosis of ASD, a total of 290 participants' early vocal behaviours were investigated using RVA. Not all of the studies provided details regarding the gender of the participants or the control group members (Mars, Mauk, & Dowrick, 1998; Werner, Dawson, Osterling, & Dinno, 2000). Thus of the 11 studies noting the genders, 161 were male and 34 were female in the ASD groups, and 103 male and 37 females were included in the comparison groups. In all but two of the studies (Osterling, Dawson, & Munson, 2002; Zappella et al., 2015) typically developing children served as comparison groups to the ASD participants (see Table 1). The majority of these studies recorded the participants later received a diagnosis of ASD, however several studies highlighted participants who received an early onset diagnosis of ASD or displayed regressive symptoms (Werner & Dawson, 2005), or distinguished between a diagnosis of ASD and PDD-NOS (Mars et al., 1998; Maestro et al., 2002). Vocalisations during the first year of life was analysed in six studies (Brisson et al., 2014; Maestro et al., 2002; Maestro et al., 2005; Osterling et al., 2002; Werner et al., 2000; Zappella et al., 2015). Receveur et al. (2005) analysed children from 10-12 months, and then 16-18 months old. Two studies analysed vocalisations during the second year of life (Mars et al., 1998; Werner & Dawson, 2005) with the remaining four studies analysing vocalisations across the whole 24 months (Chericoni et al., 2016; Eriksson & de Chateau, 1992; Maestro et al., 2001; Patten et al., 2014). Of the eight studies which analysed infants who later received a diagnosis of RTT, a total of 40 participants' early vocal behaviours were investigated using RVA (see Table 2). Comparative typically developing females were used in two of the studies (Marschik et al., 2013b; Pokorny et al., 2016). Analyses focused on the first year of life (Marschik et al., 2009), from 6 to 12 months (Pokorny et al., 2016), from 9 to 12 months (Bartl-Pokorny et al., 2013), 9 to 24 months (Marschik et al., 2013b), the second year of life (Marschik et al., 2012b), and the first two years of life (Marschik et al., 2012a; 2013a; Marschik et al., 2014a). Of the two studies which analysed infants who later received a diagnosis of FXS, a total of 17 participants' early vocal behaviours were investigated using RVA (see Table 3). Three females and 14 males with FXS were included in these studies with one study adopting nine males and three females as typically developing comparisons (Belardi et al., 2017). Both studies focused on the time period from 9 to 12 months of age (Marschik et al., 2014b; Belardi et al., 2017).

Europe PMC Funders Author Manuscripts

Video footage

All studies included within this overview adopted a retrospective analysis of home videos provided by the families of the children involved. These criteria ensured that no participant had received a diagnosis prior to the recording of the video footage, thus all videos captured a time in the infant's life during which the parents were unaware of a formally assigned developmental atypicality. In the ASD studies, footage ranged from three minutes to 314 minutes in total. In one study, a total of 714 infants' vocalisations, 209 of which were from infants with ASD, were analysed (Brisson et al., 2014). More footage was available for coding in the RTT studies where the total ranged from 170 minutes to 40.5 hours. This range does not include one study which provided no detail on the amount of footage used for coding (Marschik et al., 2009). In the two studies focussing on FXS, a total of 224 minutes was available in the analysis conducted by Marschik et al. (2014b), and a total of 240 minutes of video clips (10 min clips for each of the 24 participants) were coded by Belardi et al. (2017).

Method of Vocal Analysis

Within all of the 23 studies, targeted vocalisations (as indicated by each study) were analysed for the duration of the video data provided. As described above, this resulted in varying amounts and types of vocal behaviours available for analysis as the duration of video data, and the age ranges assessed, varied across the studies. For example, all pre-linguistic vocalisations such as cooing, crying, and fussing were analysed in Zappella et al. (2015). Other studies adopted more specific sampling procedures to isolate particular vocalisations for analysis. For example, vocalisations that were reported as contingent upon adult interaction were specifically analysed in two studies (Brisson et al., 2014; Maestro et al., 2001), and (pre-)linguistic vocalisations that matched the forms and functions outlined in the Inventory of Potential Communicative Acts (IPCA: Sigafoos et al., 2000) were analysed in four studies (Bartl-Pokorny et al., 2013; Marschik et al., 2012b; Marschik et al., 2013b; Marschik et al., 2014b). In the remaining studies, the observation of complex vocalisations such as canonical syllables, canonical babbling, proto words, and first and second word production was assessed (Belardi et al., 2017; Chericoni et al., 2016; Eriksson & de Chateau, 1992; Maestro et al., 2002; Mars et al., 1998; Marschik et al., 2009; Marschik 2012a; Marschik 2013a; Marschik et al., 2014a; Osterling et al., 2002; Patten et al., 2014; Pokorny et al., 2016; Werner & Dawson, 2005; Werner et al., 2000).

Vocalisations in children later diagnosed with ASD, RTT, or FXS

ASD: Within the 13 ASD studies, a large range of vocal behaviours were analysed (see Table 1). Specifically; vocalising explicitly labelled as intentional was assessed in three studies (Chericoni et al., 2016; Mars et al., 1998; Werner & Dawson, 2005), all present pre-linguistic vocalisations were coded in the study conducted by Zappella et al. (2015), and vocal imitation was coded for in three studies (Mars et al., 1998; Maestro et al., 2001; Receveur et al., 2005). Vocal complexity was assessed in terms of either simple or complex babbling in Werner & Dawson (2005), and was distinguished between either non-reduplicated babbling or two-syllable babbling in Chericoni et al. (2016). Canonical syllables and babbling were specifically analysed in Patten et al. (2014) with only singular

canonical syllables and vowel sounds analysed in one study (Werner et al., 2000). Word production was analysed in five studies where two studies specifically isolated the occurrence of one-word utterances and word combinations (Mars et al., 1998; Werner & Dawson, 2005), and one study analysed the occurrence of first words only (Chericoni et al., 2016). One study (Brisson et al., 2014) analysed the prosodic production of infants during a vocal interaction with their mothers. Results could be categorised across specific age ranges, for example:

0-6 months: Evidence of atypical vocalisations became apparent during this time frame, particularly for spontaneous vocalising including unspecific vocalisations, atypical cooing sounds (Zappella et al., 2015), the dominant use of simple vocal inflection contours (Brisson et al., 2014), and lower instances of person directed vocalisations (Maestro et al., 2002; Maestro et al., 2005). Additionally, lower frequencies of overall vocalisations in comparison to controls were observed (Chericoni et al., 2016).

6-12 months: Significant differences were documented, in comparison to controls, in intentional vocalising including: person directed vocalising (Maestro et al., 2005), and contingent vocalisations (Werner et al., 2000), as well as decreases in total vocalisations from 6 to 12 months old, as reported in one study (Chericoni et al., 2016). Frequencies of vowel sounds and simple and complex babbling were observed less often in the ASD children compared to the control participants in Werner and Dawson (2005), and children with ASD also demonstrated significantly lower frequencies of canonical syllables, babbling, and volubility in comparison to control participants (Patten et al., 2014; Werner et al., 2000).

12-24 months: A salient feature of this age range was the significant differences in the complexity of vocalisations produced in comparison to the control participants. Specifically, the presence of first words (Chericoni et al., 2016; Mars et al., 1998; Werner & Dawson, 2005), and word combinations (Mars et al., 1998; Werner & Dawson, 2005) were significantly lacking in the ASD group by 24 months. Additionally, deficits were present in vocal imitation (Mars et al., 1998), ‘semantically meaningful’ vocalisations (Maestro et al., 2001), and the frequency of complex babble (Werner & Dawson, 2005). Several studies identified the decrease in frequency, or regression of, vocalising and complex babble or babbling with re-duplicated syllables from approximately the end of the first year until the end of the second year of life in children with ASD (Chericoni et al. 2016; Eriksson & de Chateau, 1992).

RTT: A broad range of vocal behaviours was also analysed in the RTT studies (see Table 2). These studies focused on communication and emotional vocalisations during the period prior to 24 months old. Vocalisations were divided into atypical, (pre-)linguistic and non-linguistic vocal behaviours. For example, in Marschik et al. (2012a) atypical vocalisations were categorised as inspiratory vocalisations, pressed or strained vocalisations, and high-pitched crying-like vocalisations. (Pre-)linguistic vocalisations included vowel sounds, consonant-vowel (CV) combinations, canonical syllables, canonical babbling, proto-words and complex CVC+ babbling. Non-linguistic vocalisations included laughter, fussing, or crying (Bartl-Pokorny et al., 2013; Marschik et al., 2013b; Marschik et al., 2012a). Across

all of the eight RTT studies, atypicalities in vocalisations were observed during the pre-regression period. Specifically, high frequencies of atypical and non-linguistic vocalisations with reduced demonstrations of (pre-)linguistic behaviours were identified (Bartl-Pokorny et al., 2013; Marschik et al., 2012b; Marschik et al., 2013b), and the presence of atypical vocalisations interspersed with typical babbling and vocalising was observed (Marschik et al., 2009; Marschik et al., 2012a; Marschik et al., 2014a). Although the milestone of babbling was reached by some of the girls with RTT (Marschik et al., 2012b; Marschik et al., 2012a; Marschik et al., 2013a), frequent abnormalities in the quality of the vocalisations were often reported (Marschik et al., 2012a; Marschik et al., 2013a). Proto-words and first words were analysed in five studies (Marschik et al., 2009; Marschik et al., 2012b; Marschik et al., 2012a; Marschik et al., 2013a; Marschik et al., 2014a). Proto-words were demonstrated by fewer girls with classic RTT compared with PSV-RTT. Three girls with PSV-RTT demonstrated first words, all at around 12 months of age (Marschik et al., 2009; Marschik et al., 2014a; Marschik et al., 2013a).

The IPCA (Sigafoos et al., 2000) was used to code for the repertoire of verbal and non-verbal behaviours for communicative purposes in three studies (Bartl-Pokorny et al., 2013; Marschik et al., 2012b; Marschik et al., 2013b). Particular results from these studies reported that complex forms of vocalising, such as canonical babbling, were limited in participants later diagnosed with PSV-RTT, and very rarely observed in girls with classic RTT (Bartl-Pokorny et al., 2013; Marschik et al., 2012b; Marschik et al., 2013b). Three studies reported restricted communicative repertoires (Bartl-Pokorny et al., 2013; Marschik et al., 2012b; Marschik et al., 2013b) and shared the common feature of the total lack of behaviours indicating a request for information or to make a choice (Bartl-Pokorny et al., 2013; Marschik et al., 2012b).

Females who were later diagnosed with PSV-RTT demonstrated some differences in comparison to those later diagnosed with classic RTT, for example: (a) vocalisation development in girls with PSV more closely resembled that observed in the typically developing controls (Marschik et al., 2013b), (b) girls with PSV demonstrated a wider range of communicative forms and functions on the IPCA than girls with classic RTT (Bartl-Pokorny et al., 2013; Marschik et al., 2013b), and (c) girls with PSV were more likely than girls with classic RTT to reach the canonical babbling and/or produce first words during the second year of life (Bartl-Pokorny et al., 2013; Marschik et al., 2013b).

FXS: Results from the two studies analysing infants later diagnosed with FXS demonstrated atypicalities in early vocalisations, similar to those observed in the ASD and RTT groups (see Table 3). Specifically, from 9-12 months old, these individuals engaged in high frequencies of un-specified (not transcribed in detail) babbling (Marschik et al., 2014b), were less likely than controls to reach the canonical babbling stage by 12 months old, and produced significantly lower canonical babbling ratios and lower volubility than controls (Belardi et al., 2017; Marschik et al., 2014b). Similarly to the females later diagnosed with RTT and PSV-RTT, infants in the FXS group displayed limited repertoires of communicative functions and relied upon non-linguistic forms of communication, as identified by the IPCA (Marschik et al., 2014b). Word production was not observed in either of the FXS studies.

Discussion

The aim of this overview was to evaluate early vocal behaviours present in the first two years of life for individuals later diagnosed with ASD, RTT, or FXS. This overview sought to answer two questions. The first, regarding whether RVA is an appropriate tool to map the developmental progression, or regression, of vocal development in children with ASD, RTT, or FXS, and secondly whether the vocal development of children later diagnosed with these disorders are able to be compared when using RVA as an analysis tool. In regards to the first question, this overview adds to the growing opinion that atypicalities are apparent in the early development of children with ASD, RTT, and FXS and that differences can be (at least partly) identified early in life using RVA (e.g., Dawson & Bernier, 2013; Marschik et al., 2017; Zwaigenbaum et al., 2013).

It remains difficult, however to extract direct comparisons from the literature regarding vocal development for these children as: (a) there were more studies with a larger overall sample size of children later diagnosed with ASD, compared with RTT and FXS, (b) the studies included a wide variation in the age ranges assessed and types of vocalisations analysed, and (c) the focus of each study was variable, leading to different analyses and particular data reported for specific vocal behaviours. However, across all three groups overall, children demonstrated reduced frequencies or rates of vocal production compared with typically developing controls, and those who were later diagnosed with ASD, RTT, or FXS were less likely to progress to more complex forms of vocalisations, such as canonical babbling and variegated babbling, compared to typically developing controls (Belardi et al., 2017; Brisson et al., 2014; Chericoni et al., 2016; Marschik et al., 2014a; Patten et al., 2014).

Specifically, the results of this paper were segmented in terms of vocalisation presentation, the development of more complex vocalisations, and the frequency/rate of vocalisations. Apparent similarities in the production of more complex vocalisations across the three disorders include: (a) the reduced likelihood that infants with either ASD, RTT, or FXS would reach the canonical babbling stage, (b) if infants did reach the canonical babbling stage, there was a delay in canonical syllable production (compared to controls – as identified in several of the ASD studies and one of the FXS studies), and (c) participants included in the ASD studies were significantly less likely to produce first words or word combinations as compared to typically developing controls. Whereas participants in the RTT studies rarely demonstrated first words with almost no participants producing word combinations (Marschik et al. 2013a). Similarities in the frequency of vocal production were identified for those in the ASD and FXS groups which reported significantly lower volubility in comparison to typically developing controls (Belardi et al., 2017; Patten et al., 2014).

From the literature it appears difficult to detect reliable and significant differences in the pre-linguistic vocalisations of very young children (Zappella et al., 2015) due to the nature and limited array of vocal behaviours able to be assessed. However consistent and detectable atypicalities become more apparent during the second year of life (Chericoni et al., 2016; Patten et al., 2014; Werner & Dawson, 2005) where a greater sample of vocalisations are available for analysis due to the increased variability, frequency, and complexity of vocal

behaviours. This trend was reported in the ASD studies as well as in the RTT studies, however the age ranges included in the FXS studies were from 9-12 months, thus only a limited timeframe for analysis was available. Still in Belardi et al. (2017), canonical babbling and volubility distinguished the children with FXS from typically developing controls. All three disorders, ASD, RTT, and FXS, exhibit the autistic phenotype of socio-communicative deficits, where early vocal production is infrequent, and lacks complexity. Reaching the canonical babbling stage, for example, is considered critical in acquiring subsequent verbal communication proficiency (Oller et al., 1999; Stark, 1980), and considering that canonical babbling typically emerges in the infant from 6-10 months old, the lack of, and/or the significant delays in, canonical syllable production in these children later diagnosed with ASD, RTT, or FXS is one distinctive behavioural marker than can be identified during the first year of life. Early atypicalities and/or delays in vocal development appear to be critical and informative behavioural markers for identifying children with atypical development or, at the very least, who might develop some disorder that shares similarities with the autistic phenotype.

Although this manuscript includes a relatively small sample of 23 studies, it is clear from the available literature that atypicalities in the development of early vocalisations can be detected in children diagnosed with ASD, RTT, or FXS. However, this overview is limited in the ability to extract direct comparisons of the vocal development between participants within the three groups due to several reasons. Firstly, not all of the studies included control groups for comparison. As discussed in the review by Palomo et al. (2006), control groups are crucial components in analyses such as these to gain an appreciation of the typical progression of development, and to form a basis from which to draw conclusions and analyse deviances. Nonetheless, a benchmark level of what is considered ‘typical presentation of development’ can be considered for descriptive analyses and the delineation of behavioural phenomena. Secondly, a wide distribution of age ranges across the first two years of life was analysed in the ASD and RTT studies, with a more restricted age range analysed in the studies focusing on FXS. This led to a wider range of more complex vocal behaviours being available for analysis in those later diagnosed with ASD or RTT, such as first words, and word combinations; which are typically observed from 12 months and into the second year. Within the studies, limitations in the quality of footage obtained for analysis, the duration of usable footage, and the particular contexts in which the footage was captured, all limit the external validity of the data collected using RVA (Marschik & Einspieler, 2011; Palomo et al., 2006). Further this overview focused on studies that specifically analysed the vocal development of infants later diagnosed with ASD, RTT, and FXS, and did not include additional studies that focused on, for example: the effect of context on behaviour (e.g., Thorsen, Goldberg, Osann & Spence, 2008), validating parental reports of development (e.g., Goldberg, Thorsen, Osann & Spence, 2008), or acoustic features of crying (e.g., Esposito & Venuti, 2009). This was to ensure that vocal presentation, complex vocalisations, and the rate/frequency of vocal production was the focus, or a significant component, of the overall analysis. Lastly, a lack of homogeneity across contexts and situations means that precise and consistent conclusions are difficult to draw from the RVA literature (Palomo et al., 2006; Zwaigenbaum et al., 2013).

In spite of these limitations, this overview adds to the literature demonstrating that RVA is an appropriate tool in detecting early vocal atypicalities, be it in form or function, present in those later diagnosed with ASD, RTT, or FXS. This overview also lends further support to the argument that early detection and the potential for early diagnosis are feasible options during the first two years of life for children with one of these neurodevelopmental disorders (Palomo et al., 2006; Oller et al., 1999; Zwaigenbaum et al., 2013). However, further research into the detailed analysis of vocal characteristics, i.e. objective (rater independent) analysis on signal level (Marschik et al., 2017), and a more precise understanding of vocal developmental trajectories is required. Still, the results from these studies taken together with additional behavioural studies (Baranek, 1999), social-communication skills (Clifford & Dissanayake, 2008) and prospective studies (e.g., Charman et al., 2017; Loth et al., 2017; Ozonoff et al., 2011; Paul et al., 2011) strengthens the argument that early identification of RTT, FXS, and for ASD in particular, is robust. It must be said that RVA as a tool for analysing particular behavioural markers is indispensable for a range of neurodevelopmental disorders, especially in those with rarer cases or non-hereditary pathways where prospective studies are not always able to be implemented.

Future prospects for the earlier detection of disorders, which are currently recognised during late into toddlerhood, might adopt more advanced measures by which to reliably and accurately compare and contrast the development of early vocalisations. The use of intelligent audio analysis circumvents some of the major limitations impacting the reliability of RVA (Marschik et al., 2017; Pokorny et al., 2016), providing an audio-only analysis on an acoustic signal level where small fragments of audio data (vocalisations or parts of vocalisations) can be automatically analysed. The application of this method could help to reliably differentiate between typical development and various conditions, or developmental disorders, based on specific bio-behavioural parameters.

Acknowledgements

This overview was supported by the Austrian Science Fund (FWF; P25241 and TCS 24), the Austrian National Bank (OeNB; 16430), the Brain, Ears & Eyes – Pattern Recognition Initiative (BEE-PRI; BioTechMed-Graz), and LR was supported by the Ernst Mach grant (OeAD).

References

*Studies included within the overview

American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5®). American Psychiatric Publishing; 2013.

Amir RE, Van den Veyver IB, Wan M, Tran CQ, Francke U, Zoghbi HY. Rett syndrome is caused by mutations in X-linked MECP2, encoding methyl- CpG-binding protein 2. Nature Genetics. 1999; 23:185–188. [PubMed: 10508514]

Bailey DB Jr, Hatton DD, Skinner M. Early developmental trajectories of males with fragile X syndrome. American Journal on Mental Retardation. 1998; 103:29–39. [PubMed: 9678228]

Bailey DB Jr, Raspa M, Bishop E, Holiday D. No change in the age of diagnosis for fragile X syndrome: Findings from a national parent survey. Pediatrics. 2009; 124:527–533. [PubMed: 19581269]

Baranek GT. Autism during infancy: A retrospective video analysis of sensory- motor and social behaviors at 9–12 months of age. Journal of Autism and Developmental Disorders. 1999; 29:213–224. [PubMed: 10425584]

Baranek GT, Danko CD, Skinner ML, Donald B Jr, Hatton DD, Roberts JE, Mirrett PL. Video analysis of sensory-motor features in infants with fragile X syndrome at 9–12 months of age. Journal of Autism and Developmental Disorders. 2005; 35:645–656. [PubMed: 16172809]

*. Bartl-Pokorny KD, Marschik PB, Sigafoos J, Tager-Flusberg H, Kaufmann WE, Grossmann T, Einspieler C. Early socio-communicative forms and functions in typical Rett syndrome. Research in Developmental Disabilities. 2013; 34:3133–3138. [PubMed: 23891731]

*. Belardi K, Watson LR, Faldowski RA, Hazlett H, Crais E, Baranek GT, et al. Oller DK. A retrospective video analysis of canonical babbling and volubility in infants with fragile X syndrome at 9–12 months of age. Journal of Autism and Developmental Disorders. 2017; 47:1193–1206. [PubMed: 28247019]

Bölte S, Bartl-Pokorny KD, Jonsson U, Berggren S, Zhang D, Kostrzewa E, Falck-Ytter T, Einspieler C, Pokorny FB, Jones E, Roeyers H, et al. How can clinicians detect and treat autism early? Methodological trends of technology use in research. Acta Paediatrica. 2016; 105:137–144. [PubMed: 26479859]

Bölte S, Marschik PB, Falck-Ytter T, Charman T, Roeyers H, Elsabbagh M. Infants at risk for autism: A European perspective on current status, challenges and opportunities. European Child & Adolescent Psychiatry. 2013; 22:341–348. [PubMed: 23536211]

*. Brisson J, Martel K, Serres J, Sirois S, Adrien JL. Acoustic analysis of oral productions of infants later diagnosed with autism and their mother. Infant Mental Health. 2014; 35:285–295.

Charman T, Loth E, Tillmann J, Crawley D, Wooldridge C, Goyard D, et al. Buitelaar JK. The EU-AIMS Longitudinal European Autism Project (LEAP): Clinical characterisation. Molecular Autism. 2017; 8:27. [PubMed: 28649313]

Centers for Disease Control and Prevention. [Accessed August 2017] National Center on Birth Defects and Developmental Disabilities. Autism and Developmental Disabilities Monitoring Network. 2016. http://www.cdc.gov/ncbddd/dd/aic/states/default.htm#addm

*. Chericoni N, De Brito Wanderley D, Costanzo V, Diniz-Gonçalves A, Gille ML, Parlato E, et al. Muratori F. Pre-linguistic vocal trajectories at 6–18 months of age as early markers of autism. Frontiers in Psychology. 2016; 7:1595. [PubMed: 27807424]

Clifford SM, Dissanayake C. The early development of joint attention in infants with autistic disorder using home video observations and parental interview. Journal of Autism and Developmental Disorders. 2008; 38:791–805. [PubMed: 17917803]

Costanzo V, Chericoni N, Amendola FA, Casula L, Muratori F, Scattoni ML, Apicella F. Early detection of autism spectrum disorders: From retrospective home video studies to prospective 'high risk'sibling studies. Neuroscience & Biobehavioral Reviews. 2015; 55:627–635. [PubMed: 26092266]

Crawford DC, Acuña JM, Sherman SL. FMR1 and the fragile X syndrome: Human genome epidemiology review. Genetics in Medicine: Official Journal of the American College of Medical Genetics. 2001; 3:359–371. Dawson, G, & Bernier, R. (2013). A quarter century of progress on the early detection and treatment of autism spectrum disorder. *Development and Psychopathology, 25,* 1455–1472. [PubMed: 11545690]

Dawson G, Bernier R. A quarter century of progress on the early detection and treatment of autism spectrum disorder. Development and Psychopathology. 2013; 25:1455–1472. [PubMed: 24342850]

Einspieler C, Freilinger M, Marschik PB. Behavioural biomarkers of typical Rett syndrome: moving towards early identification. Wiener Medizinische Wochenschrift. 2016; 166:333–337. [PubMed: 27514944]

Einspieler C, Kerr AM, Prechtl HF. Is the early development of girls with Rett disorder really normal? Paediatric Research. 2005a; 57(5 Pt 1):696–700.

Einspieler C, Kerr AM, Prechtl HF. Abnormal general movements in girls with Rett disorder: the first four months of life. Brain Development. 2005b; 27:S8–S13. [PubMed: 16182501]

Einspieler C, Sigafoos J, Bartl-Pokorny KD, Landa R, Marschik PB, Bölte S. Highlighting the first 5 months of life: General movements in infants later diagnosed with autism spectrum disorder or Rett syndrome. Research in Autism Spectrum Disorders. 2014; 8:286–291.

*. Eriksson AS, de Chateau P. Brief report: A girl aged 2 years and seven months with autistic disorder videotaped from birth. Journal of Autism and Developmental Disorders. 1992; 22:127–129. [PubMed: 1592762]

Esposito G, Venuti P. Comparative analysis of crying in children with autism, developmental delays, and typical development. Focus on Autism and Other Developmental Disabilities. 2009; 24:240–247.

Fagan MK. Mean Length of Utterance before words and grammar: Longitudinal trends and developmental implications of infant vocalizations. Journal of Child Language. 2009; 36:495–527. [PubMed: 18922207]

Goldberg WA, Thorsen KL, Osann K, Spence MA. Use of home videotapes to confirm parental reports of regression in autism. Journal of Autism and Developmental Disorders. 2008; 6:1136–1146.

Green J, Pickles A, Pasco G, Bedford R, Wan MW, Elsabbagh M, et al. Johnson MH. Randomised trial of a parent-mediated intervention for infants at high risk for autism: Longitudinal outcomes to age 3 years. Journal of Child Psychology and Psychiatry. 2017; 58:1330–1340. [PubMed: 28393350]

Hagberg, B., Anvret, M. Rett syndrome - Clinical and biological aspects: Studies on 130 Swedish females. Cambridge University Press; 1993. (No. 127)

Hagberg B, Witt-Engerström I. Rett syndrome: Epidemiology and nosology -- Progress in knowledge 1986 -- A conference communication. Brain and Development. 1987; 9:451–457. [PubMed: 3324795]

Hagerman, RJ. The physical and behavioral phenotype. Fragile X syndrome: Diagnosis, treatment, and research. 3rd edition. Hagerman, RJ., Hagerman, PJ., editors. Baltimore: Johns Hopkins University Press; 2002. p. 206-248.

Hinton R, Budimirovic DB, Marschik PB, Talisa VB, Einspieler C, Gipson T, Johnston MV. Parental reports on early language and motor milestones in fragile X syndrome with and without autism spectrum disorders. Developmental Neurorehabilitation. 2013; 16:58–66. [PubMed: 23249372]

Jones EJ, Gliga T, Bedford R, Charman T, Johnson MH. Developmental pathways to autism: A review of prospective studies of infants at risk. Neuroscience & Biobehavioral Reviews. 2014; 39:1–33. [PubMed: 24361967]

Karmiloff, K., Karmiloff-Smith, A. Pathways to language from fetus to adolescent: The developing child series. USA: Harvard University Press; 2009.

Leonard H, Bower CB. Is the girl with Rett syndrome normal at birth? Developmental Medicine & Child Neurology. 1998; 40:115–121. [PubMed: 9489500]

Locke, JL. The child's pathway to spoken language. (2nd Edition). USA: Harvard University Press; 1995.

Loth E, Charman T, Mason L, Tillmann J, Jones EJ, Wooldridge C, et al. Buitelaar JK. The EU-AIMS Longitudinal European Autism Project (LEAP): Design and methodologies to identify and validate stratification biomarkers for autism spectrum disorders. Molecular autism. 2017; 8:24. [PubMed: 28649312]

*. Maestro S, Muratori F, Barbieri F, Casella C, Cattaneo V, Cavallaro MC, et al. Stern DD. Early behavioral development in autistic children: The first 2 years of life through home movies. Psychopathology. 2001; 34:147–152. [PubMed: 11316961]

*. Maestro S, Muratori F, Cavallaro MC, Pecini C, Cesari A, Paziente A, et al. Palacio-Espasa F. How young children treat objects and people: An empirical study of the first year of life in autism. Child Psychiatry and Human Development. 2005; 35:383–396. [PubMed: 15886871]

*. Maestro S, Muratori F, Cavallaro MC, Pei F, Stern D, Golse B, Palacio-Espasa F. Attentional skills during the first 6 months of age in autism spectrum disorder. Journal of the American Academy of Child & Adolescent Psychiatry. 2002; 41:1239–1245. [PubMed: 12364846]

*. Mars AE, Mauk JE, Dowrick PW. Symptoms of pervasive developmental disorders as observed in prediagnostic home videos of infants and toddlers. The Journal of Pediatrics. 1998; 132:500–504. [PubMed: 9544908]

*. Marschik PB, Bartl-Pokorny KD, Sigafoos J, Urlesberger L, Pokorny F, Didden R, et al. Kaufmann WE. Development of socio-communicative skills in 9-to 12-month-old individuals with fragile X syndrome. Research in Developmental Disabilities. 2014b; 35:597–602. [PubMed: 24480609]

*. Marschik PB, Bartl-Pokorny KD, Tager-Flusberg H, Kaufmann WE, Pokorny F, Grossman T, Windpassinger C, Petek E, Einspieler C. Three different profiles: Early socio-communicative capacities in typical Rett syndrome, the preserved speech variant, and normal development. Developmental Neurorehabilitation. 2013b; 17:34–38. [PubMed: 24088025]

Marschik PB, Einspieler C. Methodological note: Video analysis of the early development of Rett syndrome -- One method for many disciplines. Developmental Neurorehabilitation. 2011; 14:355–357. [PubMed: 22136120]

Marschik PB, Einspieler C, Garzarolli B, Prechtl HF. Events at early development: Are they associated with early word production and neurodevelopmental abilities at the preschool age? Early Human Development. 2007; 83:107–114. [PubMed: 16876340]

*. Marschik PB, Einspieler C, Oberle A, Laccone F, Prechtl HF. Case report: Retracing atypical development: A preserved speech variant of Rett syndrome. Journal of Autism and Developmental Disorders. 2009; 39:958–961. [PubMed: 19224352]

*. Marschik PB, Kaufmann WE, Einspieler C, Bartl-Pokorny KD, Wolin T, Pini G, et al. Sigafoos J. Profiling early socio-communicative development in five young girls with the preserved speech variant of Rett syndrome. Research in Developmental Disabilities. 2012b; 33:1749–1756. [PubMed: 22699249]

*. Marschik PB, Kaufmann WE, Sigafoos J, Wolin T, Zhang D, Bartl-Pokorny KD, et al. Johnston MV. Changing the perspective on early development of Rett syndrome. Research in Developmental Disabilities. 2013a; 34:1236–1239. [PubMed: 23400005]

*. Marschik PB, Pini G, Bartl-Pokorny KD, Duckworth M, Gugatschka M, Vollmann R, et al. Einspieler C. Early speech–language development in females with Rett syndrome: focusing on the preserved speech variant. Developmental Medicine & Child Neurology. 2012a; 54:451–456. [PubMed: 22348320]

Marschik PB, Pokorny FB, Peharz R, Zhang D, O'Muircheartaigh J, Roeyers H, et al. Kaufmann WE. A novel way to measure and predict development: A heuristic approach to facilitate the early detection of neurodevelopmental disorders. Current Neurology and Neuroscience Reports. 2017; 17:43. [PubMed: 28390033]

*. Marschik PB, Vollmann R, Bartl-Pokorny KD, Green VA, van der Meer L, Wolin T, Einspieler C. Developmental profile of speech-language and communicative functions in an individual with the Preserved Speech Variant of Rett syndrome. Developmental Neurorehabilitation. 2014a; 17:284–290. [PubMed: 23870013]

McCune L, Vihman MM. Early phonetic and lexical development: A productivity approach. Journal of Speech, Language, and Hearing Research. 2001; 44:670–684.

Neul JL, Kaufmann WE, Glaze DG, Christodoulou J, Clarke AJ, Bahi-Buisson N, et al. Percy AK. Rett syndrome: Revised diagnostic criteria and nomenclature. Annals of Neurology. 2010; 68:944–950. [PubMed: 21154482]

Oller, DK. The emergence of the sounds of speech in infancy. Child Phonology. Yeni-Komshian, G.Kavanagh, J., Ferguson, CA., editors. Vol. 1. NY: Academic Press; 1980. p. 93-112.

Oller DK, Eilers RE, Neal AR, Schwartz HK. Precursors to speech in infancy: The prediction of speech and language disorders. Journal of Communication Disorders. 1999; 32:223–245. [PubMed: 10466095]

*. Osterling JA, Dawson G, Munson JA. Early recognition of 1 year old infants with autism spectrum disorder versus mental retardation. Journal of Developmental Psychopathology. 2002; 14:239–251.

Ozonoff S, Young GS, Carter A, Messinger D, Yirmiya N, Zwaigenbaum L, et al. Hutman T. Recurrence risk for autism spectrum disorders: A Baby Siblings Research Consortium study. Pediatrics. 2011; 128:488–495.

Palomo R, Belinchón M, Ozonoff S. Autism and family home movies: A comprehensive review. Journal of Developmental & Behavioral Pediatrics. 2006; 27:S59–S68. [PubMed: 16685187]

*. Patten E, Belardi K, Baranek GT, Watson LR, Labban JD, Oller DK. Vocal patterns in infants with autism spectrum disorder: Canonical babbling status and vocalization frequency. Journal of Autism and Developmental Disorders. 2014; 44:2413–2428. [PubMed: 24482292]

Paul R, Fuerst Y, Ramsay G, Chawarska K, Klin A. Out of the mouths of babes: Vocal production in infant siblings of children with ASD. Journal of Child Psychology and Psychiatry. 2011; 52:588–598. [PubMed: 21039489]

*. Pokorny FB, Marschik PB, Einspieler C, Schuller BW. Does she speak RTT? Towards an earlier identification of Rett Syndrome through intelligent pre-linguistic vocalisation analysis. Proceedings Interspeech 2016. 2016:1953–1957.

*. Receveur C, Lenoir P, Desombre H, Roux S, Malvy J. Interaction and imitation deficits from infancy to 4 years of age in children with autism: A pilot study based on videotapes. Autism. 2005; 9:69–82. [PubMed: 15618263]

Renieri A, Mari F, Mencarelli MA, Scala E, Ariani F, Longo I, et al. Zappella M. Diagnostic criteria for the Zappella variant of Rett syndrome (the preserved speech variant). Brain and Development. 2009; 31:208–216. [PubMed: 18562141]

Sigafoos J, Woodyatt G, Keen D, Tait K, Tucker M, Roberts-Pennell D, Pittendreigh N. Identifying potential communicative acts in children with developmental and physical disabilities. Communication Disorders Quarterly. 2000; 21:77–86.

Spreckley M, Boyd R. Efficacy of applied behavioral intervention in preschool children with autism for improving cognitive, language, and adaptive behavior: A systematic review and meta-analysis. The Journal of Pediatrics. 2009; 154:338–344. [PubMed: 18950798]

Stark, RE. Stages of speech development in the first year of life. Child Phonology: Production. Yeni-Komshian, G.Kavanagh, JF., Ferguson, CA., editors. Vol. 1. New York: Academic Press; 1980. p. 73-95.

Tager-Flusberg H, Caronna E. Language disorders: Autism and other pervasive developmental disorders. Pediatric Clinics of North America. 2007; 54:469–481. [PubMed: 17543905]

Tarquinio DC, Hou W, Neul JL, Lane JB, Barnes KV, O'Leary HM, et al. Skinner SA. Age of diagnosis in Rett syndrome: Patterns of recognition among diagnosticians and risk factors for late diagnosis. Pediatric Neurology. 2015; 52:585–591. [PubMed: 25801175]

Thorsen KL, Goldberg WA, Osann K, Spence MA. Birthday and non-birthday videotapes: The importance of context for the behaviour of young children with autism. The Journal of Autism and Developmental Disorders. 2008; 6:1047–1058.

Vorstman JA, Parr JR, Moreno-De-Luca D, Anney RJ, Nurnberger JI Jr, Hallmayer JF. Autism genetics: Opportunities and challenges for clinical translation. Nature Reviews Genetics. 2017; 18:362–376.

*. Werner E, Dawson G. Validation of the phenomenon of autistic regression using home videotapes. Archives of General Psychiatry. 2005; 62:889–895. [PubMed: 16061766]

*. Werner E, Dawson G, Osterling J, Dinno N. Brief report: Recognition of autism spectrum disorder before one year of age: A retrospective study based on home videotapes. Journal of Autism and Developmental Disorders. 2000; 30:157–162. [PubMed: 10832780]

*. Zappella M, Einspieler C, Bartl-Pokorny KD, Krieber M, Coleman M, Bölte S, Marschik PB. What do home videos tell us about early motor and socio-communicative behaviours in children with autistic features during the second year of life - An exploratory study. Early Human Development. 2015; 91:569–575. [PubMed: 26246137]

Zhang D, Kaufmann WE, Sigafoos J, Bartl-Pokorny KD, Krieber M, Marschik PB, Einspieler C. Parents' initial concerns about the development of their children later diagnosed with fragile X syndrome. Journal of Intellectual & Developmental Disability. 2017; 42:114–122.

Zwaigenbaum L, Bryson S, Garon N. Early identification of autism spectrum disorders. Behavioural Brain Research. 2013; 251:133–146. [PubMed: 23588272]

Zwaigenbaum L, Bryson S, Lord C, Rogers S, Carter A, Carver L, et al. Fein D. Clinical assessment and management of toddlers with suspected autism spectrum disorder: Insights from studies of high-risk infants. Pediatrics. 2009; 123:1383–1391. [PubMed: 19403506]

Europe PMC Funders Author Manuscripts

Table 1

An overview of studies analysing the early vocal behaviours of infants later diagnosed with Autism Spectrum Disorder

Authors	Participants (M/F)	Control group (M/F)	Age range (in months)	Behaviours analysed	Results
Eriksson & de Chateau (1992)	1 (0/1)	-	0-24	Simple and complex babbling Words.	• From birth to 13 months, high frequencies of babbling. From 13 months onwards, loss of babbling, no word production. • All videos were double coded, IRR not reported.
Mars et al. (1998)	ASD: 10 (-/-) PDD-NOS: 15 (-/-)	25 (-/-)	12-30	Vocalisations One or more words Vocal imitation.	• Imitating vocalisations was significantly observed less frequently in children with ASD compared to controls • The expression of one or more words was significantly observed less frequently in children with ASD compared to controls. • IRR was reported as 88%.
Werner et al. (2000)	ASD: 8 (-/-) PDD-NOS: 7 (-/-)	15 (-/-)	8-10	Vowel sounds Canonical syllables.	• The production of vowel sounds per minute was observed less frequently in ASD group compared to controls, canonical syllables was higher in frequency per minute for ASD group than controls (although not statistically different). • All videos were double coded, k= 0.68-0.91.
Maestro et al. (2001)	15 (10/5)	15 (11/4)	T1: 0-6 T2: 6-12 T3: 12-18 T4: 18-24	Social behaviour (vocalise towards another person) Inter-subjectivity (vocal imitation) Symbolic (semantically meaningful vocalisations).	• During T4 significant difference in semantically meaningful vocalisations compared to controls. • The presence/absence of vocalisations was discussed.
Maestro et al. (2002)	15 (10/5) ASD: 7 PPD-NOS: 8	15(9/6)	0-6	Vocalisations towards object/person Sounds towards object/person Babbling towards object/person.	• Vocalising to people (but not objects) was observed significantly less in ASD group compared to controls. • Observers were trained to reach 80% agreement on vocal behaviour analysis.
Osterling et al. (2002)	20 (18/2)	ID- 14 TD- 20	12	Vocalisations Babbling.	• Could distinguish between infants with ASD from those of the TD and ID groups based on differences in frequency of babbling. • ICC reported as >0.75.
Maestro et al. (2005)	15 (11/4)	13 (5/8)	T1: 0-6 T2: 6-12	Vocalisations towards object/person Sounds towards object/person Babbling towards object/person.	• Vocalising to people was observed significantly less for the ASD group compared to controls at T1, but not at T2.

Europe PMC Funders Author Manuscripts

Authors	Participants (M/F)	Control group (M/F)	Age range (in months)	Behaviours analysed	Results
					• Observers were trained to reach 80% agreement on vocal behaviour analysis.
Receveur et al. (2005)	18 (13/5)	-	10-12 16-18	Imitation of sounds, words, and sentences Echolalia.	• No significant differences found according to group membership. • The weighted k (Kw) across the two time periods ranged from 0.82-0.87.
Werner & Dawson (2005)	36 (33/3) ASD regression: 15 Early-onset ASD: 21	20 (16/4)	T1: 12 T2: 24	T1: frequency of simple and complex babbling, and frequency of words T2: frequency of complex babbling, frequency of single words, or word combinations.	• At T1 significant differences observed for ASD group in the frequency of complex babbling and words compared to controls. At T2 significantly lower frequency for ASD group in complex babbling, single words, and word combinations compared to controls. • All videos were double coded. ICC for frequency codes: at 12 months (0.81-091), at 24 months (0.76-0.87). Kappa-coefficient scores for duration codes: at 12 months (0.71-97), at 24 months (0.69-0.90).
Brisson et al. (2014)	13 (11/2)	13 (9/4)	0-6	Vocalisations produced during an interaction with mother: Modulated vocal productions (inflection contours) Vocal duration Vocal pitch.	• Infants later diagnosed with ASD produced significantly fewer complex contours (with fewer than two melodic modulations) than controls, and more frequently produced simple vocalisations (simple inflection contours). • No significant differences were observed in other prosodic elements, such as pitch or utterance duration. • All videos were double coded, ICC for: pitch= 0.69, pitch contour= 0.94, and duration= 0.99.
Patten et al. (2014)	23 (19/4)	14 (11/3)	T1: 9-12 T2:15-18	Canonical syllables/babbling Volubility Canonical babbling ratio.	• ASD children (during both age ranges) produced significantly lower canonical babbling ratios compared with TD children • ASD infants (during both age ranges) displayed significantly lower volubility compared to the TD children. • ICC reported as >0.75.
Zappella et al. (2015)	10 (10/0)	–	T1: 1-2 T2: 3-4 T3: 5-6	Crying Fussing Unspecified vocalisations Cooing Pleasure vocalisations/laughter.	• 7 children displayed age-specific vocalisations, especially cooing and pleasure vocalisations, 3/10 did not demonstrate cooing and had unspecified hardly modulated vocalisations. • All videos independently scored, k=0.69.
Chericoni et al. (2016)	10 (9/1)	10 (8/2)	T1: 0-6 T2: 6-12 T3: 12-18	Vocalisations Long reduplicated babbling Two-syllable babbling First words.	• At T2, significantly fewer vocalisations observed in ASD group vs TD group, significant decrease in vocalising from T1-T2 in ASD group

Europe PMC Funders Author Manuscripts

Authors	Participants (M/F)	Control group (M/F)	Age range (in months)	Behaviours analysed	Results
					• No significant differences in the rates per minute of babbling, significantly fewer first words produced in ASD participants than controls at T3. • All variables double coded, k reported as >0.70.

ICC: Intra-class coefficients, k: Kappa coefficient.

Europe PMC Funders Author Manuscripts

Table 2

An overview of studies analysing the early vocal behaviours of infants later diagnosed with Rett Syndrome

Authors	Participants (M/F)	Control group (M/F)	Age range (in months)	Behaviours analysed	Results
Marschik et al. (2009)	PSV-RTT: 1 (0/1)	–	0-24	Vocalisations Vocalisation atypicalities Babbling Word production.	• At 6 months old, repetitive un-modulated vocalisations were present. Inspiratory vocalisations were observed. First words occurred around the first birthday; word combinations were not observed before regression • Instances of normal babbling were observed interspersed with atypical babbling. • All vocalisations were double coded, k=0.91.
Marschik et al. (2012a)	PSV-RTT: 6 (0/6)	–	T1: 7-8 T2: 9-10 T3: 11-12 T4: 13-24	Canonical babbling Volubility Vocalisation atypicalities Proto-word combinations Lexical diversity.	• Presence of atypical vocalisations in all participants from 13-24 months old • 4/6 females demonstrated canonical syllables and produced proto-words, one participant developed proto-word combinations, complex consonant-vowel clusters were rarely seen • Volubility (total) increased from 7-12 months, then decreased from 13-24 months. • Vocalisations scored by three observers, Fleiss' coefficient= 0.92.
Marschik et al. (2012b)	PSV-RTT: 5 (0/5)	–	12-24	Non-linguistic and (pre-)linguistic vocalisations used for communicative purposes *.	• Non-verbal behaviours dominated over verbal behaviours for most communicative purposes. • All vocalisations double coded, k=0.86.
Marschik et al. (2013a)	Typical RTT: 10 (0/10) PSV-RTT: 5 (0/5)	–	0-24	Cooing Babbling (Proto-)words Word combinations Vocalisation atypicalities.	• 12/15 participants demonstrated cooing, 9 participants demonstrated canonical babbling, Proto-words were observed in 3 of the typical RTT group and 3 of the PSV group, 1 PSV-RTT participant demonstrated word combinations. The more complex the vocalisation, the fewer participants presented it. • Cooing and babbling was frequently observed to be atypical. • Vocalisations scored by four observers, agreement reported as 0.97.
Marschik et al. (2013b)	Typical RTT: 1 (0/1) PSV-RTT: 1 (0/1)	1 (0/1)	T1: 9-12 T2: 13-18 T3: 19-24	Non-linguistic and (pre-)linguistic vocalisations used for communicative purposes *.	• Repertoire of pre-linguistic vocalisations greater in TD child> female with PSV> female with typical RTT (where no pre-linguistic vocalisations were observed). • All vocalisations double coded, disagreements (7%) discussed.

Europe PMC Funders Author Manuscripts

Authors	Participants (M/F)	Control group (M/F)	Age range (in months)	Behaviours analysed	Results
Bartl-Pokorny et al. (2013)	Typical RTT: 6 (0/6)	–	9-12	Non-linguistic and (pre-)linguistic vocalisations used for communicative purposes *.	• Non-linguistic vocalisations were used to gain attention and answer, also to request an object, reject, and to respond in the social convention; pre-linguistic vocalisations for communicative purposes were not observed. • All vocalisations double coded, disagreements (13%) discussed.
Marschik et al. (2014a)	PSV-RTT: 1 (0/1)	–	0-24	Babbling Volubility Vocalisation atypicalities (Proto-)words Word combinations.	• Typical babbling (appeared at 7 months) was interspersed with atypical vocalisations • First words produced around 12 months; mental lexicon of 12 proto-words; word combinations produced around 21 months. Echolalia was also observed • Quantitative and qualitative analysis demonstrated reduced volubility and complexity of vocalisations. • All vocalisations double coded, disagreements discussed.
Pokorny et al. (2016)	4 (0/4)	4 (0/4)	6-12	Acoustic (signal level) characteristics of pre-linguistic vocalisations.	• An unweighted average recall of 76.5% was achieved for automatically identifying the RTT group vs. the TD group. • Disagreements discussed.

* i.e. unspecified vocalisations, pleasure vocalisations, laughing, crying, fussing, canonical and variegated babbling, onomatopoetics, (proto-)words, word combinations. ICC: Intra-class coefficients, k: Kappa coefficient.

Europe PMC Funders Author Manuscripts

Table 3

An overview of studies analysing the early vocal behaviours of infants later diagnosed with Fragile X Syndrome

Authors	Participants (M/F)	Control group (M/F)	Age range (in months)	Behaviours analysed	Results
Marschik et al. (2014b)	7 (5/2)	–	9-12	Non-linguistic and (pre-)linguistic vocalisations used for communicative purposes *.	• 5 participants engaged in unspecified vocalisations; 2 participants used babbling for communicative purposes; non-verbal behaviours dominated over pre-linguistic forms of communication. (Proto-)words were not observed. • Disagreements discussed.
Belardi et al. (2017)	10 (9/1)	14 (11/3)	9-12	Canonical syllables Canonical babbling Canonical babbling ratio Volubility.	• FXS participants were significantly less likely to reach canonical babbling stage by 9-12 months than TD group, participants with FXS produced significantly lower canonical babbling ratios • Infants with FXS demonstrated significantly lower volubility than TD infants. • 20% of all data double coded, ICC ranged from 0.89-0.94.

* i.e. unspecified vocalisations, pleasure vocalisations, laughing, crying, fussing, canonical and variegated babbling, onomatopoetics, (proto-)words, word combinations. ICC: Intra-class coefficients, k: Kappa coefficient.