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Developmental profile of speech-language and communicative functions in an individual with the Preserved Speech Variant of Rett syndrome

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Abstract

Objective—We assessed various aspects of speech-language and communicative functions of an individual with the preserved speech variant (PSV) of Rett syndrome (RTT) to describe her developmental profile over a period of 11 years.

Methods—For this study we incorporated the following data resources and methods to assess speech-language and communicative functions during pre-, peri- and post-regressional development: retrospective video analyses, medical history data, parental checklists and diaries, standardized tests on vocabulary and grammar, spontaneous speech samples, and picture stories to elicit narrative competences.

Results—Despite achieving speech-language milestones, atypical behaviours were present at all times. We observed a unique developmental speech-language trajectory (including the RTT typical regression) affecting all linguistic and socio-communicative sub-domains in the receptive as well as the expressive modality.

Conclusion—Future research should take into consideration a potentially considerable discordance between formal and functional language use by interpreting communicative acts on a more cautionary note.

Keywords

Rett syndrome; preserved speech variant; speech; language; communication

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Introduction

Rett syndrome (RTT, MIM 312750) is a severe progressive neurodevelopmental disorder affecting primarily females. It is associated with stereotyped hand movements (hand wringing, washing like movements) together with limited purposeful hand use, profound intellectual disability, severe communicative and speech-language deficiencies as well as autistic like behaviour [1–4]. Its prevalence lies between 1:5000 and 1.10.000 live female births [5]. Even almost 15 years after the discovery of its main aetiology, namely mutations in the MECP2 gene [6], the diagnosis remains primarily clinical. In particular, there are also patients with RTT without MECP2 mutations (and potentially mutations in the genes FOXG1 or CDKL5) or MECP2 mutation positive females without clinical symptomatology [4, 7]. The diagnostic criteria and nomenclature were recently revised for typical RTT and for its three variants (the early seizure variant, the congenital variant and the preserved speech variant, PSV [4, 7]). Besides the loss of purposeful hand movements, the appearance of hand stereotypies, a decrease in communicative and speech-language functions as well as the presence of a regression period followed by partial recovery or stabilization are among the required features [2–4, 8–10].

The pathogenesis of RTT follows a four-stage trajectory starting with the pre-regression period. This period and especially the first year of life was and partly still is considered to be “apparently normal” [11]. Based on an increasing body of knowledge about early motor and speech-language impairments, the idea of early abnormality - which has been speculated about for the last two decades [e.g., 12–15] - got however a recent boost towards changing this concept. Our own research on early abnormalities in RTT and its relatively milder preserved speech variant (PSV [16, 17]) contributed to this paradigm shift as well as a move toward re-labelling this variant [11, 18–25]. The main findings from our studies indicated early peculiarities in the developing linguo-cognitive domain beginning with the first vocalizations (vocalizations of inspiratory character were among the most salient early features of maldevelopment; [11, 24].

Whereas previously the majority of research on individuals with RTT mainly focused on post-diagnostic development more and more studies are nowadays carried out to delineate pre-regressional development. Initially these research approaches relied almost exclusively on medical histories or retrospective questionnaires, which are most obviously related to a number of restrictions such as memory bias of parents with affected children [26–28]. An alternative approach, also facing a body of limitations, is the retrospective analysis of family home videos, which has proven to be a valuable tool to document early development in children with developmental disabilities [e.g., 21, 29–33]. This method found broad application in the field of profiling early development of individuals with autism spectrum disorders or genetic disorders with a late clinical onset [e.g., 31–34]. This earlier work laid the foundation for the present study. That is, the detailed description and delineation of pre-, peri- and post-regressional development in a female with a high functioning form of RTT. We present a unique case report of a girl with PSV where we have profiled her speech-language and socio-communicative development over a period of 11 years.

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Methods

Participant

A girl, born in 1998 as singleton at 40 weeks of gestation with a birth weight of 2970 grams, body length of 53 cm, occipitofrontal head circumference of 34 cm, and Apgar scores 9 (1 min) and 10 (5 min) was clinically diagnosed with RTT at the age of three years. Genetic testing 9 months later revealed the following MECP2 mutation: a large intragenic deletion (c.378-43_964delinsGA) that most probably causes a complete loss of function of MeCP2. She was classified as PSV of RTT according to the revised diagnostic criteria for RTT and its variants [4]. The participant grew up in a monolingual German speaking family setting with a younger sister born in the year 2000. At the age of three she attended kindergarten and at the age of six she started school, first in an integrated school, then later in a school for children with special needs.

The participant's motor development and some aspects of her speech-language development during the pre-regressional stage (i.e. her first two years of life) are already reported elsewhere [11, 23, 24, 35]. To facilitate readability and provide the whole developmental profile over the period of 11 years at a glance a summary of her pre-regressional development is provided in the Results section of this case report.

Procedure

The focus of this study was to delineate age-specific speech-language and communicative abilities of our participant. She was longitudinally observed from birth to 11 years of age (i.e., from first vocalizations to expected complex linguistic and communicative abilities). With respect to the pathogenesis of RTT we applied different age-specific methods to assess different aspects of speech-language and communicative abilities. Before the onset of regression (referring to already published data), which set in at the age of two years as well as during regression until diagnosis was made (at the participant's age of three) we analyzed audio-video recordings of play situations and daily routines [29]. The female's parents made these videos unaware at that time that their daughter had RTT or PSV respectively. The footage of this period comprised a total of 282 minutes of family videos (first three years of life), including 170 minutes of (pre-)regressional development [11, 23, 24, 35]. A research assistant naive to the purpose of the study checked the recordings for sufficient length and quality standards. Relevant video recordings were then copied and prepared for analysis by unifying codecs and sampling the recordings across the age range.

Post-regressional and post-diagnostic development was documented and analyzed by the following methods and assessments: (A) audio-video recordings of spontaneous speech, picture book reading, story telling (5 stories) and daily routines (169 minutes; at the participant's age of nine, 10 and 11 years); (B) medical history data; (C) parental diaries and checklists: (i) the Austrian Rett survey; (ii) the Austrian adaptation of the Mac-Arthur-Bates Communicative Development Inventories [27], a checklist to assess early socio-communicative functions, early gestures, vocabulary and grammar; (iii) the Inventory of Potential Communicative Acts [36, 37], an inventory to define individual behaviours used for communicative purposes in 10 different communicative functions (i.e., social convention,

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attention to self, rejection/protest, request for an object, request for an action, request for information, comment, choice making, answer, imitation); and (D) standardized tests and assessments: (i) a German vocabulary Test (AWST-R [38]); (ii) TROG-D, test for the reception of grammar [39]; (iii) subtest 4 from the SET-K (a speech-language development test [40]) to elicit plural marking; and (iv) the Patholinguistic Assessment of Developmental Language Disorders (subtests 18 and 19 [41]).

All vocalizations, verbal utterances, and communicative behaviours were orthographically and phonologically transcribed in chronological order. The transcripts were rechecked by a second transcriber in order to ensure accuracy and consistency. In case of disagreement, video sequences were discussed within the team (PBM, RV, KDB, TW, CE) until agreement was achieved.

The analysis was partly carried out using the Noldus Observer XT (Noldus Information Technology, The Netherlands). The study was approved by the local research ethics committee. Consent for the analyses and publication of results were given by the parents.

Results

Pre-regression period

At the age of six months we observed repetitive and inspiratory vocalizations (i.e., modulated vocalizing while inhaling). Normal babbling, which appeared in time at seven months of age, was interspersed with atypical vocalizations often associated with grimaces of effort. At the same age the girl showed bursts of abnormal facial expressions consisting of several repetitions of the following sequence: head in midline with neutral facial expression (second 1); head turned sideward with a crying expression often combined with atypical inspiratory vocalization (second 2); head in midline with neutral facial expression (second 3); etc. The inspiratory vocalizations eventually disappeared at the end of the first year of age [24, 35]. Quantitative and qualitative assessments revealed a reduced volubility (i.e., utterances per minute) and complexity ratio of vocalizations [24]. The girl uttered her first words around her first birthday and was able to build a mental lexicon of 12 proto-words. At the age of 21 months we observed a few two-word utterances. We also observed verbal perseverations (echolalia), for example more than 20 consecutive unconventional vocalizations (without conventional meaning and no communicative intent) such as /tise/ or /oti/ that stopped with a high-pitched cry followed by the next stereotypic verbal event [24].

Potential Communicative Acts (PCAs [36, 37]) included body movements, facial expressions, eye movements and vocalizations used for the following presumed pragmatic functions in 8 out of 10 IPCA categories (PCAs [36, 37]): Social convention, attention to self, reject/protest, request object, request action, commenting, answering and imitating. None of the observed verbal and non-verbal behaviours were interpreted as requesting information or choice making behaviours [23]. Intentional gestures were limited and partly used in an inappropriate manner. She used gestures, mainly index finger pointing, to express needs. The total repertoire consisted of five gestures: waving, index finger pointing, extension of arms, shaking the head, and sending kisses [23].

Regression period

Around the girls second birthday her parents became seriously concerned about her development describing their first observations as peculiarities in language development. The previously acquired language abilities worsened affecting both the expressive and receptive modality in all levels of linguistic development (i.e., phonetic and phonological level, morphological level and syntactical capacities). Also, she withdrew from social contact, would run around aimlessly and in a disquieting manner, often screaming. The RTT typical trajectory of losing purposeful hand movements became more pronounced. Hand stereotypies (such as rubbing and washing like hand movements as well as hand-to-mouth and hand-to-tongue stereotypies) became more frequent. After clinical diagnosis of RTT at the age of three her gait had remained instable, her muscle tone was low and a reduced nociceptive sensitivity was confirmed. Autistic features became more prominent during this period and her behaviour was increasingly dominated by routines, obsessions and ritualistic actions. [35]

Post-regression period

Over the next years lost or fragmentarily preserved skills were partially and slowly regained. We observed a slow but steady improvement of gross and fine motor functions, a reduction of autistic like behaviours, and a recovery of speech-language and communicative functions. Her articulation abilities, the phonological and morphosyntactic capacities, and the size of her mental lexicon slowly increased, albeit frequently accompanied by idiosyncratic vocalizations and out of context speech [35]. The participant re-started to use gestures (mainly index finger pointing), pursued the index finger of communication partners, repeated familiar words, verbally refused instructions or requested objects and actions, reacted to name and started to imitate sounds.

The development of her mental lexicon showed the following pathway: After losing proto-conventional words during regression, she started to re-build a vocabulary. As documented by parental diaries and paediatric assessments the size of her mental lexicon remained stable over a period of three years; from age three to six. Whenever she learned a new word during this period, she lost one of the words of her vocabulary, so that the quantity remained 15 productive lexical items. During that time she also did not use multi-word utterances. After age six she started to acquire a larger lexicon and used two- and three-word utterances, although one-word utterances remained predominant.

Status between 9;5 and 11 years of age

General findings—At the participant's age of 11 autistic-like behaviours such as finding it hard to recognize borders of intimacy and obsessive behaviour were still observed. She appeared hyperkinetic and highly distractible, was hypersensitive to noise and, once excited, could hardly be calmed. Further typical signs of RTT were observed: distinct mood disturbances; unprovoked bursts of anger; hyperventilation; mild scoliosis; hypotonia; hypersalivation; moderate circulation problems; sleep disturbances; aerophagea. She regained the ability for purposeful hand use, although dyspraxia was noticeable; hand stereotypies, which were more frequent in her right hand, predominantly consisted of hand-to-mouth/tongue contacts; washing, rubbing, or clapping stereotypies were rare.

Speech-language and communication—In terms of language capacities she acquired a relatively complex system with a lexicon size comparable with that of a preschooler. The accuracy of articulation was, however, limited and we observed a significant phonological deficiency. There were also morpho-syntactic and socio-pragmatic limitations as well as dysfluency of speech, mostly caused by immediate echolalia or repetitive questioning [35]. In the SET-K subscale 4 she was able to correctly build seven out of 10 plural forms. Assessing her receptive grammatical abilities with the TROG-D at 10 years of age revealed a percentile rank below 1. The vocabulary assessed at 9;5 with the AWST (standardized up to age six) revealed a composite score of 61% correct naming of objects and actions (71% correct naming of actions and 57% correct naming of objects). Half a year later the same test revealed a composite score of 55% correct naming of objects and actions (46% correct naming of actions and 58% correct naming of objects).

Pragmatic competence—The participant was able to give and understand feedback (i.e., verbiage and repetitions were used) so that her behaviour appeared relatively inconspicuous in short conversations. She also replied appropriately both to yes/no questions and to wh-questions, but had difficulties continuing with the dialogue. She understood indirect speech acts such as “Now I have forgotten the name of your sister” (= “What is the name …?”) and replied to the given implicature. Only once was she able to keep up a topic over a longer stretch of time without the help of her communication partner. In all other situations, her interest in a topic comprised of only one sentence. She often initiated a conversation, especially after a pause when nobody addressed her for some time. Thereby, she was able to attract the attention of the people before going on with her sentence. But she did not keep up the topic any longer even with a cooperative partner.

In direct communication, she used deictic expressions and referred to the surroundings. However, her nonverbal behaviour, her facial expressions and gestures were not aligned to the content of what she was saying. Frequently, her utterances started with “Guck mal!” (‘Look!’) without showing anything to her conversation partner and without catching this person’s eyes. The participant rarely posed questions in order to inform herself about the knowledge of somebody else. A big part of her communication consisted of answers and short sentences whose relation to the context was not always obvious.

Textlinguistic competence—As for coherence, the child could create textual semantic connections, but her communicative acts were always very short, even with stories. As cohesive elements, she could maintain actant reference through the use of the appropriate personal pronouns. However, demonstrative pronouns in the same function were inconspicuously correct with respect to her dialectal variant of German. The developmentally early cohesive marker "und dann" ('and then') for the temporal progression of a story was used. Causal relations were not found; instead, "weil" ('because') was used only in its simplest function as discourse markers of main clauses (i.e., as a non-causal junctor, with verb-second- instead of subordinating verb-end-syntax). Tense was applied adequately to situations, with some morphological errors of irregular verbs. Most of her sentences were simple, unelaborated declarative sentences, with the addition of a few questions.

Narrative competence in free narratives—The participant could not interpret the pictures as being interconnected. The primary functions of her narratives were speaker-oriented self-expression/-portrayal as well as hearer-oriented information transfer. However, a few problems remain unsolved: evaluations could not be found, neither about what had happened in the story nor about the role of the story in the actual communication. Further narrative functions seemed to be missing as well, probably based on a fundamental lack of pragmatic-communicative abilities.

Narrative competence in picture stories—None of the five stories shown were recognized as a narrative by the child. The child's descriptions were vague, impersonal picture descriptions in short unrelated single declarative sentences. The chronological order of events was not recognized, contrary to normally developing preschool children. If asked about the aspects of the story, she replied only with one phrase, exactly as in spontaneous speech.

Discussion

We presented a unique case with high functioning PSV over a period of 11 years. The overall picture for the speech-language and communicative domains is comparable to the participant's previously reported motor functions. That is, despite achieving the gross motor milestones, she showed abnormal movements starting in her first months of life [35]. In addition to abnormal early motor behaviour (i.e. abnormal fidgety general movements [18, 42]), the appearance of hand stereotypies, asymmetric eye opening after a blink, and abnormal facial expressions are in accordance with previous findings on girls with typical Rett syndrome [19]. The same holds true for early vocalizations, gestural repertoire, and first words. With regard to the developmental milestones, all domains can be characterized by an interspersing character (typical and atypical behaviours during pre-regression period) or the predominance of peculiar-unexpected behaviours (during regression period) such as vocalizations of inspiratory character or a restricted use of the gestural repertoire [20, 24, 25]. We also observed morpho-syntactic and socio-pragmatic limitations as well as dysfluency of speech, caused by immediate echolalia or repetitive questioning. These findings add to the speculation in one of the first papers on PSV by Zappella, Gillberg and Ehlers [16], who suggested that mild abnormalities in social interaction might already occur during pre-regression period. Consequently, this study adds to the concept of early abnormalities in RTT and to the understanding that even this mild variant of RTT already manifests itself within the first months of life [11, 24, 35, 43].

Following the achievement of speech-language milestones during the first two years of life (cooing, babbling, first words and even word combinations), albeit atypical in quality of performance and characterized by reduced volubility, we observed the typical regression expected in RTT [3, 4, 44]. The regression was associated with the deterioration of speech-language and communicative abilities, withdrawal from social life and the loss of purposeful hand use [4, 7, 45]. In addition, while inspiratory vocalizations eventually disappeared, hand stereotypies and hand to mouth stereotypies became more prominent, which is in line with the diagnostic criteria for RTT and variants [4]. Regarding speech-language development it

is interesting to note, that both the expressive and receptive modality in all levels of linguistic development were affected from this profound regression.

Regression was followed by a slow but steady improvement of gross and fine motor functions, a reduction of autistic like behaviours, and a recovery of speech-language and communicative functions. The participant's articulation abilities, the phonological and morphosyntactic capacities, and the size of her mental lexicon slowly increased, albeit frequently accompanied by idiosyncratic vocalizations and out of context speech [35]. The participant re-started to use gestures (mainly index finger pointing), pursued the index finger of communication partners, repeated familiar words, verbally refused instructions or requested objects and actions, reacted to her name when called and started to imitate sounds. The development of her mental lexicon showed the following pathway. After losing proto-conventional words during regression, she started to slowly re-build a vocabulary. As documented by parental diaries and paediatric assessments the size of her mental lexicon remained stable over a period of three years; from age three to six. Whenever she learned a new word during this period, she lost one of the words of her vocabulary, so that the quantity remained at 15 productive lexical items. During that time she also did not use multi-word utterances. After age six she started to acquire a larger lexicon and used two- and three-word utterances, although one-word utterances remained predominant. Most of the (re-)acquired speech-language functions were related to imitating or mimicking her younger sister's behaviours. After the regression period we observed typical RTT features such as mood disturbances, hyperventilation, and physical problems such as mild scoliosis and cardio-vascular issues [4, 7]. Also, autistic like behaviours were persistent during post-regression as has been described by Kaufmann and colleagues [45]. The uniqueness of this comprehensive long-term case report also lies in the fact that individuals with verbal abilities constitute a distinct group (6%) of mutation positive RTT-patients [10, 46]. None of the known cases were reported to have distinguished linguistic and socio-communicative capacities in post-regression periods. The participant reported on here seemed not only to have recovered but also improved her speech-language abilities to reach a certain complexity of various linguistic functions that by far exceed those reported for typical RTT and PSV so far [4, 10, 16, 17]. On the other hand, deficiencies and idiosyncrasies on all linguistic levels (phonology, morphology, syntax, and pragmatics [47]) can easily be detected through detailed analyses. At the age of nine years, the mental lexicon, for example, reached the quantity of that of a late preschooler, albeit showing qualitative restrictions such as proto-characteristics of certain lexical entries (i.e., certain words were only used in certain contexts). To the best of our knowledge, there are no detailed descriptions of post-regression linguistic competences in girls with typical RTT or PSV (see also [8]). Our analysis revealed a broad set of syntactic and morphological competences: her sentences were syntactically correct, only irregular verbs resulted in some morphological errors.

Another linguistic level of interest is pragmatic abilities. It is based on premises such as joint attention, theory of mind, and comprises advanced competences such as the understanding of turn-taking and dialogic interaction, respect for conversational principles, or understanding of indirect speech acts, of implicatures and presuppositions, or making inferences from given information [48]. The participant's pragmatic skills in spontaneous dialogues were seemingly normal. For instance, she had no problems with understanding

feedback, implicatures, and indirect speech acts. She also gave feedback, initiated dialogues, and waited to get attention for what she had to say. When asked, her responses were inconspicuously correct. These faculties in combination with her formal linguistic knowledge and her lexicon enabled her to successfully take part in short interactions. On closer viewing, however, she lacked the competence to uphold a conversational topic or to respond to her dialogue partner. Communicative utterances such as "Look!" seemed to be rote-learned rather than spontaneously and socially motivated, since she did not conciliate her non-verbal behaviour and did not build up eye contact. In free narratives about her daily life, however, actant introduction and evaluation was lacking. In addition, the knowledge of the communication partners was not considered. In combination with her inability to follow a topic over a longer stretch of time this led to more evident peculiarities in narrations than could be seen in dialogic communication. For narrating picture stories, general pragmatic competence and dialogic competence are not relevant, since the telling of stories is carried out (almost) without caretaker intervention. Our participant did not tell "real" stories, cohesive elements and coherence were lacking. While reaction to picture stories can be compared to normally developing 3 year olds [49], the participant did not use personalizations, which 3 years olds usually do [50]. Narrative skills shed light on the communicative development, because they presuppose a whole number of functions which need to be readily developed first [51]. These are a minimum size of the mental lexicon, formal linguistic skills such as phonological, morphological, and syntactic competences, social skills, cognitive skills, and pragmatic skills [51–54]. Therefore, it is not only the narrative deficits which are important, but before all the causes for them as well as the underlying faculties.

Overall, it seems that our participant was able to successfully communicate in face-to-face dialogues, since her linguistic competence is based on learned strategies and syntactic knowledge, but not on socio-pragmatic functions and reference to the communication partner. This can be seen in the fact that her behaviour is not adapted to the linguistic content and that all social and personalized markers are missing in her text production. In a short communicative sequence, her strategies are relatively inconspicuous, but she fails when the setting is slightly changed. To sum up, she can skilfully apply her syntactic knowledge in order to appear an inconspicuous dialogue partner, although she seems to lack knowledge or insight into discourse functions and social relations.

This report incorporates many different methods of assessing behavioural phenomena of the speech-language and communicative domains that do have several limitations. Despite the methodological difficulties, it is nonetheless one of the few reports that cover the pre-, peri- and post-regressional development in an individual with PSV and might therefore be of interest to researchers as well as clinicians dealing with this genetic disorder. We are well aware of the fact that age-specific assessments using different methods have limited value for direct comparisons (e.g., vocabulary development as documented by means of checklists vs. spontaneous speech samples vs. parental diaries vs. standardized tests). Nonetheless, the conglomerate of these findings allows for a description of a general developmental trend that has never been described before. This study cannot be generalized for all individuals with PSV. Further research will have to show at what extent during early linguistic development,

the possible preservation of some communicative functions during the regression period, and post-regression-period development are intertwined.

Even though case reports are often considered to be of limited value to understand certain aspects of a developmental disorder, the presented case provides an important description of a very mild case of a mild variant of RTT. It is of importance for future research in the field, as her achieved level of complexity superficially appears higher than it really is. Her formal competence exceeded her abilities to use the formal language structures appropriately, be it in terms of pragmatic or semantic relations. Future research should take this into consideration by taking a cautionary approach when interpreting communicative acts given that in this case study there was a considerable discordance between the participant's formal and functional language use.

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