Levels of cognitive and linguistic development in Angelman syndrome: a study of 20 children

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Angelman syndrome (AS) is a genetic disorder associated with severe developmental delay. The purpose of this study was to investigate cognitive and linguistic development in AS. Piaget's developmental model was used to evaluate the test results. The participants comprised 20 children (14 boys and 6 girls) aged 2–14 years (median age 7.4 years). AS was diagnosed either according to typical clinical criteria or confirmatory genetic testing. Cognitive functioning was evaluated with Griffiths' Mental Development Scale. Language development was also evaluated with Receptive–Expressive Emergent Language Scale 2 (REEL-2). Cognitive functioning, based on results on the Performance Scale, never exceeded Piaget's sensorimotor stage, 0–2 years. The median mental age for language development was 9 months. Expressive verbal vocabulary consisted of less than 2 words ($n = 11$), 2–3 words ($n = 7$) and 4–5 words ($n = 2$). Analyses according to REEL-2 did not indicate a consistent discrepancy between impressive and expressive language.

Key words: Angelman syndrome, cognitive development, receptive language, expressive language.

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INTRODUCTION

A specific new syndrome was first described in three mentally retarded children by the English paediatrician Harry Angelman in 1965. He commented on their ataxic, jerky gait and pronounced tendency for outbursts of laughter and called them ''happy puppet children''. This unscientific term has later been replaced by Angelman syndrome (AS). The prevalence of AS has been estimated at 1:12 000 (12) to 1:15000 (19). The genetic mechanisms involved in the aetiology of AS are not fully understood. In the majority of cases, it is caused by a small deletion of maternally inherited material on the long arm of chromosome 15 at 15q11-13 (18). Alternatively, although rarer, AS may be caused by inheriting both pairs of 15q from the father, a mechanism known as uniparental disomy (13). However, in approximately one-third of the cases of AS, a genetic defect cannot be demonstrated and the diagnosis has therefore also been founded on clinical criteria (17). The clinical findings do not differ according to the underlying genetic defect, although uniparental disomy has been reported to be associated with a slightly less severe phenotype (4). The clinical features include neurological, craniofacial, behavioural and electroencephalographic (EEG) abnormalities. Neurological functioning is characterised by profound mental retardation, cerebellar ataxia and epilepsy. Developmental delay is usually detectable from the first months of life, although the syndrome may not be diagnosed before 2–5 years of age. Craniofacial dysmorphism, which may be mild in young infants, includes a small head, flat occiput, prominent lower jaw, large mouth and wide spaced teeth. The ''happy'' disposition is present from an early age, but is frequently overlooked as a feature of clinical significance. The behaviour is stereotyped with severe hyperkinesia and obsessions, playing with running water, for example. Other features are jerky movements of the extremities and trunk, tongue thrusting, hypersalivation and teeth grinding. Sleep is usually disturbed from an early age and, in the majority of cases, there is a tendency for vomiting or regurgitation. The EEG is nearly always abnormal and, apart from epileptic activity, shows runs of high-voltage discharges not associated with drowsiness. (5).

Several studies have been conducted focusing on different aspects of the cognitive development in AS, including that of Clayton-Smith (6) who described a detailed clinical history of 82 individuals. Jollef and Ryan (9) observed that these children have developed

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Table 1. *The correspondence between the individuals' scores according to Griffiths' Performance Scale and the stages according to Piaget's sensorimotor period*

Sensorimotor stages	Stage duration in months	Stage characteristics	No. of individuals at each stage
Stage 1	0–1	Behaviour characterised by inborn reflexes	0
Stage 2	1–4	Schemes of behaviour occurs	0
Stage 3	4–8	Beginning intentionality in activity	5
Stage 4	8–12	Increasing will directedness	10
Stage 5	12–18	Experimental behaviour	2
Stage 6	18–24	Simple cause–effect relations	3

very few words and have difficulties in using gestures and sign systems. Penner *et al*. (15) concluded that all individuals in their study were functioning within Piaget's sensorimotor cognitive period (16), that is, within the range of 0–2 years.

The purpose of this study was to investigate levels of cognitive and linguistic development in the AS group.

Piaget's developmental model (10, 16) has been used to evaluate the results. This model describes cognitive development in different stages; sensorimotor stage (0–2 years), pre-operational stage (2–7 years), concrete-operational stage (7–12 years) and formal-operational stage (12–18 years). Each period is divided into levels. This study concentrates on the six levels within the sensorimotor period. Characteristics of these levels are described in Table 1.

MATERIALS AND METHODS

Participants and procedures

Children with AS were ascertained via several channels, including all cases diagnosed at the Section for Child Neurology, Department of Paediatrics, National Hospital, Oslo. All regional paediatric and habilitation departments in Norway were contacted and requested to refer cases to us for further assessment. All university departments of genetics in Norway (Oslo, Bergen and Tromsø) were asked to report AS cases diagnosed in their laboratories. These cases were kept anonymous to us, except for date of birth and gender, and were matched against other participants in order to avoid double registration. Altogether, 36 AS cases born between 1982 and 1996 (24 boys and 12 girls) were reported to us. Due to limited resources, our study population was chosen as the first 20 participants (14 boys and 6 girls) in a consecutive row for whom consent was obtained. No other criteria were used to select this study population. The median age was 7.4 years (range 2–14 years). Neurological functioning was assessed in a semistructured manner (PS) with one or both parents present. The parents were interviewed about their child's developmental milestones, behavioural characteristics and possible seizures. All medical notes from previous investigations were obtained. On examination, the typical features of AS previously described were carefully looked for. Confirmatory genetic testing was positive in 13 participants (deletion 11, uniparental disomy 2), while the diagnosis was based on typical clinical and EEG features in 7.

Cognitive and language development

Griffiths' Mental Development Scale, Swedish standardisation 1991, was used for cognitive evaluation (1). The testing was conducted by one of the educational pscychologists (WHA) with one or both parents present. The test is divided into five scales of development: Locomotor Scale, Personal and Social Mastering Scale, Hearing and Speech Scale, Eye and Hand Co-ordination Scale and Performance Scale. The results of all five scales in Griffiths' Mental Development Scale are presented to make possible a comparison between the sub-scales. Ruth Griffiths (7) emphasises the Hearing and Speech Scale and the Performance Scale as essential regarding cognitive development. In the article, the main focus has been on these two sub-scales, seeing the Performance Scale as testing non-verbal cognition. The Performance Scale requires motor responses like placing objects in boxes or frames. The ataxia of the AS persons could make responses on the Performance Scale difficult, thus invalidating the Performance Scale as an instrument for testing non-verbal cognition. Clinical experience with AS persons indicated that the ataxia was not a hindrance for scoring if credits were given when there was a clear intention of placing the object in the right box or frame. Griffiths' Mental Development Scale is also used for testing persons with different handicaps (1). In testing handicapped children, the manual recommends the tester to adapt the manual to the child's handicap, to obtain its potentials. We

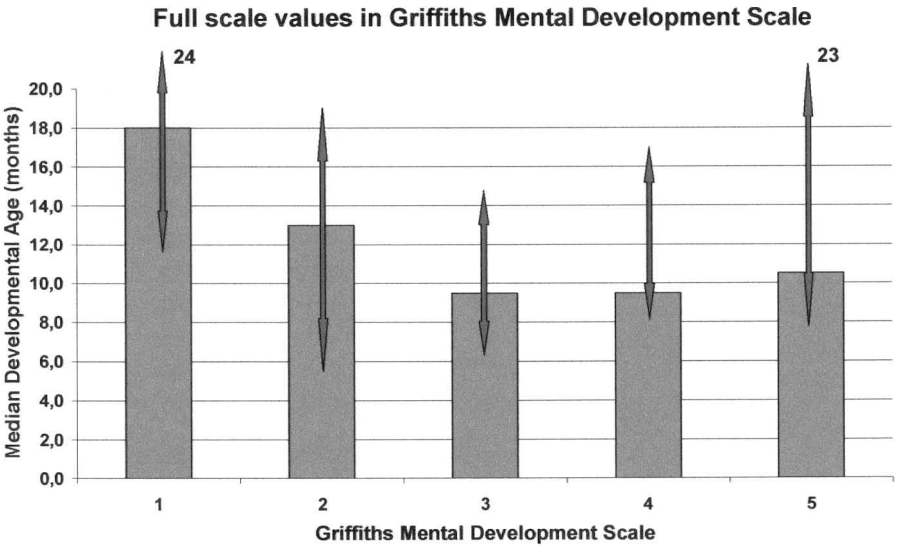

Fig. 1. Full scale values in Griffiths' Mental Development Scale. 1, Locomotor Scale. 2, Personal and Social Mastering Scale. 3, Hearing and Speech Scale. 4, Eye/Hand Co-ordination Scale. 5, Performance Scale. Arrows indicate max/min developmental age of the different scales.

see the scoring adaptation on the Performance Scale in line with the recommendation given in the manual.

The strength of Griffiths' Mental Development Scale is that it scores the same functions at different ages, reusing the same tasks and material, but with increasing degrees of difficulty. This has been an advantage to the group studied, where the span in cognitive function was less than the age span. The use of a standardised developmental scale gave an opportunity to observe developmental deviation within the group of AS. All participants were also observed in spontaneous play and activity.

Language development was also assessed by Receptive–Expressive Emergent Language Scale 2 (REEL-2) (20), administered by an educational psychologist (RKR). REEL-2 is a 132-item screening checklist using observational information reported by parents or teachers on receptive and expressive language-interactive behaviours from birth to 3 years of age. The items on the checklist are grouped by age intervals and the informant is asked to react to statements like: "Gives some attention to music or singing" (receptive scale, age level 6–7 months) and "Uses some word-like vocal expressions" (expressive scale, age level 6–7 months).

RESULTS

Full scale values at Griffiths' Mental Development Scale are shown in Fig. 1. The diagram shows the median developmental age within the different scales. The arrows are indicating minimum and maximum developmental age at each scale. The median values at the Locomotor Scale and the Personal and Social Scale reach stage 5 in Piaget's sensorimotor period, while the median values at Hearing and Speech Scale, Eye–Hand Co-ordination Scale and Performance Scale only reach stage 4 (ref. Table 1). The mastering profile indicates better results on tasks measuring motor skills and practical daily life skills than tasks with higher cognitive loading.

Cognitive development

Cognitive development, based on results at the Performance Scale at Griffiths' Mental Development Scale, corresponded to median mental age of 10 months with an age span of 7–23 months. The lowest and highest mental ages were found in two participants (individuals 10 and 12 in Fig. 2), with chronological ages of 7 years and 3 months and 7 years and 9 months, respectively. Fig. 2 also demonstrates a lack of correspondence between chronological age and mental age in our participants.

Sub-tasks at the Performance Scale require different cognitive functioning and competence. Sub-tasks requiring general understanding of complex activities and abilities of abstract thinking showed reduced mastering. This is shown in Table 1, where 15 of the participants reached a cognitive level at stages 3 and 4, two participants reached level 5, and only 3 participants satisfied the requirements in stage 6 of the sensorimotor period. This can also be seen in Table 2 where no participant managed to build a train of three bricks and drive with it, even if it was demonstrated.

We found beginnings of intentional activities in all participants. Intentional activities were defined as eye pointing, leading by hand, and using signs. These activities became apparent when the participants wanted special toys or play. Constructive play was observed in six participants, for example, playing

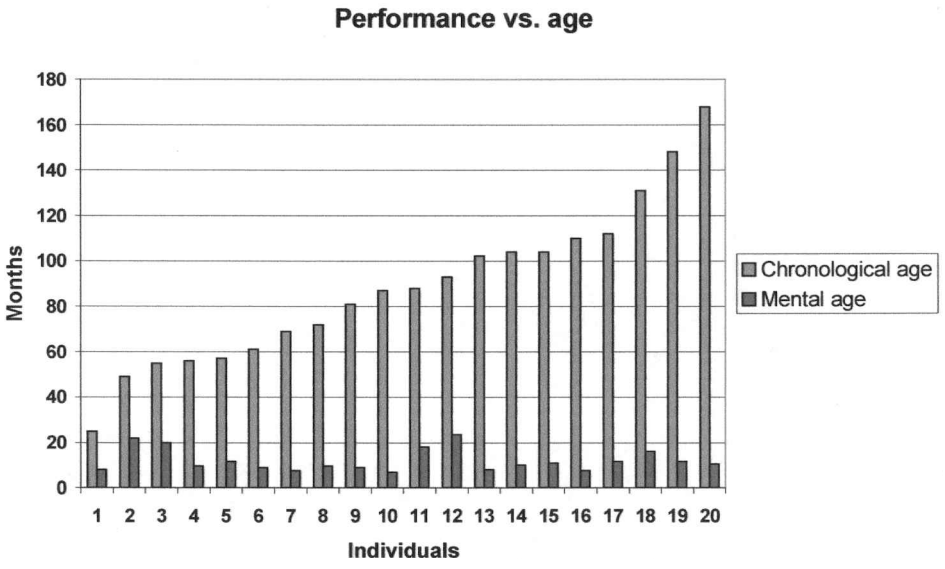

Fig. 2. Scores in Griffiths' Performance Scale versus chronological age.

with a ball or a toy car. Constructive playing with test materials such as wooden bricks, plastic boxes and small figures was observed in only two participants, and included the putting of bricks into boxes and building of brick towers of up to three bricks. No participant mastered symbolic play, for example, building a train of bricks and driving around with it. Only in one participant did we see attempts at symbolic play as the child let a puppet do some jumps over the table. Four participants mastered all form puzzles belonging to the test. Their main use of the toys was to knock, hit, wave, throw, or chew on the play items. Table 2 shows the participants' mastering of different play activities.

Language development

Fig. 3 shows the correspondence between chronological age and language abilities. Median mental age for language development, according to Griffiths' Mental Development Scale 3, Hearing and Speech, was 9 months (age span 6–15 months). The lowest developmental age, 6 months, was observed in 3 participants aged 4, 7 and 9 years. The highest developmental age, 15 months, was observed in 2 participants aged 7 and 13 years. One participant at 4 years of age had language abilities corresponding to those of 14 months. Expressive language consisting of 0–1 words was found in 11 participants. A maximum of 2–3 words was found in seven participants, and two participants had 4–5 words. Six participants could use certain signs or pictograms. Table 3 shows that nearly all participants belonged to the sensorimotor stages 3 and 4 (17/20). Only three participants reached stage 5 and none stage 6. According to REEL-2, our participants' receptive language was in the age range 5–24 months and expressive language 3–14 months (Table 4). The highest age score on the Receptive Scale was 24 months, the lowest age score 5 months. The highest age score on the Expressive Scale was 14 months, the lowest score was 3 months. The highest difference between the two scales was 10 months, the lowest 0 months. All REEL-2 scores were within the sensorimotor period as seen on the sub-scale Hearing and Speech on the Griffiths' Mental Development Scale test.

Abnormal babbling pattern and reduced sound production are reported by almost all parents.

Table 2. *Frequency of manifestations of play activities based on Griffiths' Mental Development Scale 1*

Cognitive abilities	No.
Two words expressive	5/20
Five words expressive	1/20
Appreciates picture book, looks and turns pages	5/20
Identifies four toys	4/20
Names one picture	1/20
Points out one body part	6/20
Points out three body parts	5/20
Symbolic play with doll	1/20
Builds train of three bricks and drive	0/20
Puts bricks back in box on command	5/20
Constructive play with toys	6/20
Draws a circle after demonstration	0/20
Imitates simple play	7/20
Rolls ball co-operatively	9/20
Puzzles small and large circle	4/20
Puzzles circle, square and triangle	4/20

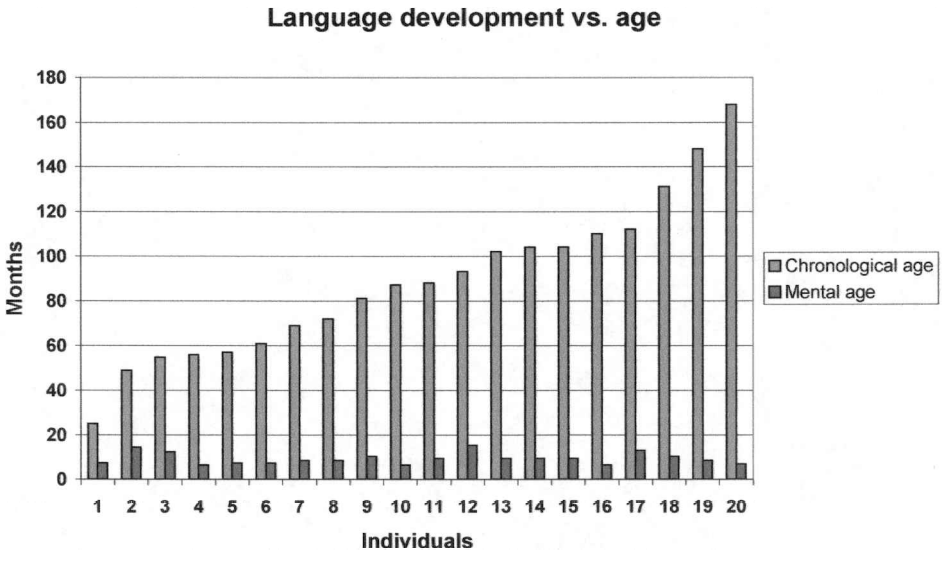

Fig. 3. Scores in Griffiths' Hearing and Speech Scale versus chronological age.

DISCUSSION

A study design including the possibility for inter-observer reliability would have been preferable in order to avoid bias in the assessment of developmental deviation. However, the risk of not having such data available was partially compensated by the fact that the observers had long clinical experience in assessing development in mentally retarded children. Furthermore, our results showed that the developmental abnormalities were severe and relatively homogeneous and therefore readily appreciated by the observer. Also, to secure a proper interpretation, all results were discussed with the investigators, as well as with the children's parents.

Our results showed that cognitive development, based on the results on Griffiths' Mental Development Scale, Performance Scale, was within the sensorimotor period of 0–2 years for all the participants in the study. Certain cognitive characteristics were observed. Median developmental age on the Performance Scale was 10 months, varying from 7 to 23 months. These results are in accordance with the findings of Penner *et al.* (15). In the AS group, there was a variation on the Performance Scale among participants at the same chronological level. Highest and lowest cognitive functioning was registered in two children, both 7 years of age. In some of the oldest children we saw a wider field of interests and interests of a different character than is usually found in persons at the same developmental level. This stresses the importance of analysing activities and problem solving in terms of the cognitive burden they represent. Field of interest may easily be mistaken for a higher level of cognitive function. According to Piaget, the sensorimotor period is characterised by six levels where the child learns through motor activity stimulated by its perceptions. Behaviour is controlled by categories of actions and not by concept categories.

A developmental age of 10 months in cognitive development corresponds to level 4 in Piaget's model. At this developmental level, the child is gradually getting more intentional, and toys are handled more according to their functions. The characteristics of the level were seen in the child's eye pointing, leading by hand and use of gestures and some signs. Based on the results on the Performance Scale, we found that the cognitive level varied from level 3 to 6 according to Piaget's model, implying a difference in handling toys from a simple banging, hitting, and mouthing to mastering of simple puzzles. The repetitive banging and hitting of toys are sometimes described as "perseveration" of activities or "stereotypic" handling. However, according to the developmental levels 3–4 in the sensorimotor period, it is more likely normal activity and representative of a secondary circular reaction expected to emerge at this developmental level. Activities at level 6 are characterised by some constructive research of toys and the beginning of understanding of sensorimotor cause and effect relations. Even though three AS persons met the level 6 criteria in the test situation, little of the flexible cognitive handling of situations and objects was observed. Piaget describes a difference between operational and figurative knowledge (8). Operational knowledge has been assimilated and internalised and used in flexible handling of different situations. The person starts getting an inner symbolic concept which gives a possibility for generalisa-

Table 3. *The correspondence between the individuals' scores according to Griffiths' Hearing and Speech Scale and the stages according to Piaget's sensorimotor period*

Sensorimotor period	Duration in months	Stage characteristics	No. of individuals at each stage
Stage 1	0–1	Reacts to sound, Produces sound and cry	0
Stage 2	1–4	First vocalisation, babbling	0
Stage 3	4–8	Recognises words, begins to understand symbols	10
Stage 4	8–12	First expressive word	7
Stage 5	12–18	Increasing no. of words (vocabulary)	3
Stage 6	18–24	Syntactical expressive language	0

tion. Figurative knowledge, however, is connected to the execution of a skill rather than to the understanding of a concept. We interpret the level 6 scores as figurative knowledge, more mechanically learned skill, rather than operative knowledge. This interpretation is supported by the lack of symbolic play in the group and absence of generalisation skills.

Level of language development on the REEL-2 Receptive Scale is somewhat higher than on the Griffiths' Mental Development Scale, but is within Piaget's sensorimotor period. The REEL-2 registration is an interview with one of the parents, thus representing familiar activities in familiar settings and in the company of familiar persons. In this setting, understanding language is less dependent on conceptual categories and more dependent of contextual understanding. Griffiths' Mental Development Scale, on the other hand, was administered by an unknown person in an unknown situation, and showing more of operational, conceptual knowledge. The REEL-2 registration is based on parents' reports and open to a more subjective and positive interpretation of a child's language-behaviour than the interpretation done by a professional tester. This may also count for some of the discrepancies between the Griffiths' Mental Development Scale and REEL-2 results. The registration on REEL-2 showed some discrepancy between receptive and expressive language, but the difference was not consistent throughout the group. These findings are in accordance with Jollef and Ryan. (9). Median developmental age for language was 9 months on the Griffiths' Mental Development Scale. This corresponds to stage 4 in Piaget's model. Penner *et al.* (15) refer to stage 5 and Kahn (11) to stage 6 as a prerequisite for language and speech development. At stage 5 and 6, cognitive structures necessary for concept formation develop. Behaviour is not primarily guided by sensorimotor stimulation, but by concepts and mental representations (3). Oller *et al.* (14) have investigated deficiencies in babbling in mentally re-

Table 4. *Scores on the Bzoch-League REEL-2 scale*

Child no.	Chronological age (years)	Comprehension (months)	Expression (months)
1	2; 2	7	3
2	4; 1	20	14
3	4; 7	16	14
4	4; 8	11	7
5	4; 10	11	6
6	5; 1	12	12
7	5; 9	12	10
8	6; 0	11	9
9	6; 10	11	7
10	7; 4	11	6
11	7; 4	7	5
12	7; 9	24	14
13	8; 8	12	6
14	8; 8	12	4
15	8; 8	11	5
16	9; 2	5	4
17	9; 4	16	14
18	10; 11	22	12
19	12; 4	14	10
20	14; 0	12	10

tarded children. The ability to produce well-formed syllabic vocalisations is one of the prerequisites for later development of speech. Only 2 out of 20 AS persons had a near normal babbling pattern. Ataxia, divergent orofacial structure, severe problems with imitation of movements, and short attention span (as observed although not systematically evaluated in this study) together with severe mental retardation contribute to the speech and linguistic production deficits in AS.

Our study focused on cognitive and linguistic developmental levels in a group of persons with AS. Even though all participants fell within Piaget's sensorimotor period, we observed a relatively wide variation in cognitive development, receptive and expressive language within the group. This variation shows the necessity of a thorough evaluation of the cognitive and linguistic capacity of each individual. Systematic studies on how to stimulate communicative abilities in the AS group are needed to secure good educational programs for persons with AS.

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SAMMANFATTNING

Kognitiv och lingvistisk utveckling vid Angelmans syndrom: en studie av 20 barn

Angelman syndrom (AS) er en genetisk lidelse som er karakterisert ved alvorlige utviklingsforstyrrelser. Hensikten med studien var å beskrive kognitiv og språklig utvikling hos 20 personer med AS (2–14 år). Griffiths utviklingsskala 1, med hovedvekt på Utføringskalaen og Språkskalaen ble brukt i vurderingen. Videre informasjon om språkutvikling ble innhentet gjennom et systematisk foreldreintervju (REEL-2). Piagets modell av kognitiv utvikling ble brukt til analyse av resultatene. Resultatene viser at kognitiv utvikling, som målt med Utføringsskalaen, ikke forekom utover Piagets senso-motoriske periode 0–2 år. Median utviklingsalder på Utføringsskalaen var 10 måneder (trinn 4 hos Piaget). Karakteristisk aktivitet med leker var å slå, banke vifte eller kaste objektene. Kunnskaper og ferdigheter bar preg av å være figurativ kunnskap mer enn operativ kunnskap. Median utviklingsalder for språklige ferdigheter var 9 måneder (trinn 4). Ekspressivt verbalspråk bestod av 0–1 ord (11), 2–3 ord (7) og 4–5 ord (2). Seks barn brukte noen tegn eller piktogrammer. Analyse av REEL resultatene indikerte at det ikke er systematisk diskrepans mellom impressivt og ekspressivt språk i gruppen AS.

YHTEENVETO

Kognitiivisen ja kielellisen tason kehittyminen Angelmanin syndroomassa: 20 *lapsen tutkimus*

Angelmanin syngrooma (AS) on geneettinen häiriö, joka aiheuttaa vakavan kehityshäiriön. Syndroomaan liittyvistä kommunikaatio-ongelmista tarvitaan enemmän tietoa. Tämän tutkimuksen tarkoitus oli sen vuoksi tutkia kognitiivisia ja kielellisiä puutteita AS-lapsilta varsinkin opetuksen näkökulmasta katsottuna. Tutkimukseen osallistui 20 lasta (14 poikaa ja 6 tyttöä), joiden ikä oli 2–14 vuotta (keskimäärin 7.4 vuotta). AS diagnosoitiin joko syndroomalle tyypillisten kliinisten kriteerioiden perusteella tai geneettisen testin perusteella. Kognitiivista tasoa mitattiin Griffithsin mentaalisella kehitysasteikolla (Griffith's Mental Development Scale). Kielikykyä tutkittiin REEL-2:lla (Receptive-Emergent Scale 2). Tuloksena oli, ettei kognitiivinen taso ylittänyt Piagetin sensomotorista tasoa, 0–2 vuotta. Keskimääräinen mentaalinen kielen kehityksen taso oli 9 kuukautta. Ekspressiivinen verbisanasto sisälsi vähemmän kuin 2 sanaa (N = 11), 2–3 sanaa (N = 7) ja 4–5 sanaa (N = 2). REEL-2 analyysin mukaan myös impressiivinen kielikyky oli suurin piirtein samalla tasolla ekspressiivisen kanssa.