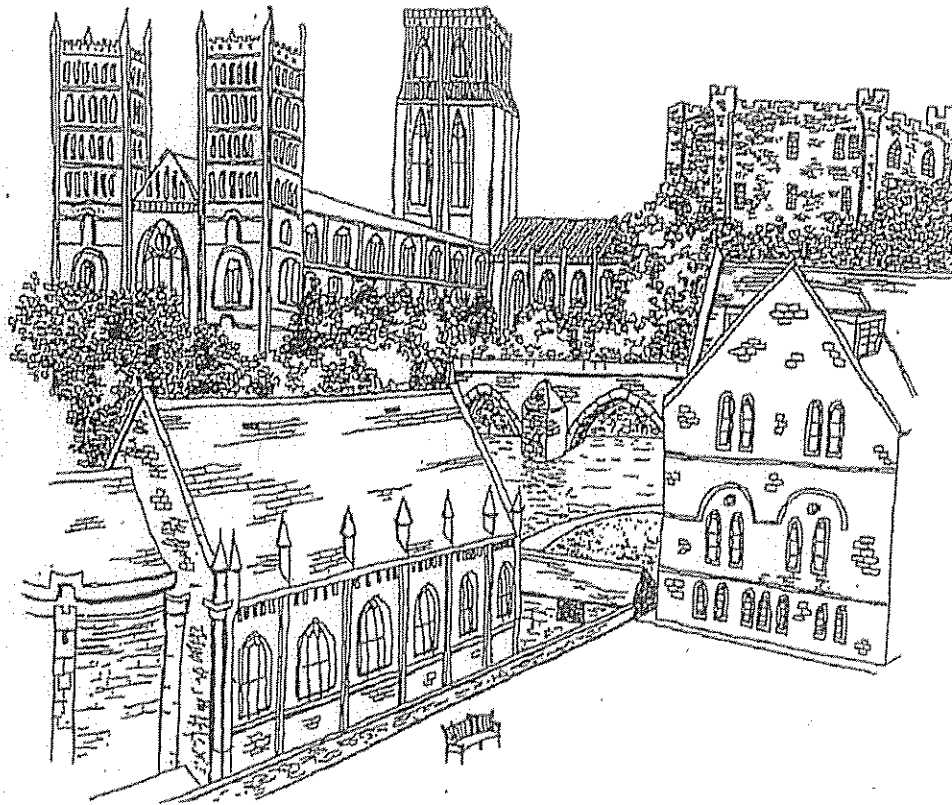


25th Anniversary

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Identification of Very Early Signs of Autism: implications of clinical and treatment evidence

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Introduction

This paper is divided into two parts: the first part describes very early signs associated with autism identified in a study of 110 infants during their first 15 months of life. The second part discusses the implications of these findings in short term treatments, comparing the results of treatment in two different age groups.

Part 1: A Clinical Retrospective Study 1997 - 2007

A retrospective study conducted at the Mifne Centre in Israel, from 1997 until 2007, examined 110 infants, 84 boys and 26 girls who had been diagnosed with autism between the ages of 2-3 years, using retrospective analysis of video-recordings filmed by their parents during their first 15 months of life, before any suspicion concerning the infant's development arose. In addition to the video data, questionnaires were distributed to the parents, after completing the diagnosis between the ages of 2-3 years.

The investigated variables were developmental characteristics, associated with the autism spectrum:

1. *Lack of Eye Contact*

In their research, Elsabbagh and colleagues (2012) found that particular characteristics of eye gaze shifts during infancy were associated with autism diagnosed at 36 months. Lack of eye contact is one of the obvious characteristics of autism. The question is whether this deficient eye contact is the result of a deficiency in making contact or an inherent inability to form eye contact restricts making contact... since from the beginning of the baby's development it creates a different perception.

The question then is why do babies who do not form eye contact with others, create eye contact with an object? In other words it seems that focus is not the main difficulty in these cases, but that the baby prefers an inanimate object.

In our study, we examined the baby's eye contact with their parents or other caregivers. Measures of their tendency to follow objects with their eyes included: in which direction did the baby look; for how long; did the baby ignore the object; eye contact during closeness; during feeding, and during play.

Lack of eye contact or very low eye contact evaluated as 10-20% of the time, was found in 77.3% of the infants. Fifteen babies exhibited some reasonable but inconsistent eye contact.

2. *Lack of Reaction to the Presence/Voice of Parents*

Lack of reaction was defined by Alonim (2007) as: no turning of the head; there is no deflection of the baby's gaze; no smile or babbling; no reaction when their name is called; there is no attempt to divert attention; there is no reaction to the parents' departure.

Most of the research concerning the development of social and affective behaviour has concentrated on cortical-related activity, mostly the amygdala–limbic system and the medial prefrontal and fronto-parietal systems (Amodio and Frith, 2006). Geva and colleagues (2011) claim that early brainstem dysfunction detected during its major maturational spurt in the late prenatal period will directly affect the modulation of gaze as a function of arousal to social stimuli, thereby compromising social engagement (Geva, et al., 2011).

It was evident from the video analysis of this study that the babies who did not react to voices also did not react to presence, and vice-versa. There were no babies amongst those examined who reacted to presence but did not react to voices, which characterizes babies with hearing loss.

Lack of reaction to parents' voices and presence, was observed in 44.5% of the infants.

3. *Excessive-passivity*

Excessive-passivity was defined by Greenspan (1992) in cases of: lack of crying, lack of movement, lack of interest in what is happening in the surroundings, do not track people with their gaze, lack of effort to attain an object, babies are "easy to take care of".

According to Jiang (2009) this period is a critical one for major developmental changes in the equilibrium and the auditory pathways in the brainstem, including myelination. This is supported by Doesburg (2011) who claims that disruptions in myelination may disrupt white matter maturation and the integrity of neural connectivity and synchronization of neural oscillations. These in turn may bear implications for the establishment of emotional and attentional functions. Karlsson and others (2005) found that brainstem injury to disrupted physiological regulation and homeostasis. These disruptions impact the autonomic nervous system. According to (Batterhamet, 2007) they also affect circadian arousal regulation, as well as visceral homeostasis modulation of

internal states, such as hunger and thirst All of these systems are interrelated and moderate emotional and attentional regulation in infants during the neonatal phase (Geva et al., 1999). Analytic observation of these developmental components indicated a lack of regulation. Jiang (2009) suggested that brainstem systems play an integral role in these higher level capacities like self-regulation.

Over-passivity was found in 44.5% of the infants.

There was a gap between girls and boys: 57.75% in girls and 40.5% in boys.

4. *Delayed Motor Development*

Movement disturbances play an intrinsic part in the phenomenon of autism and can be used to diagnose the presence of autism in the first few months of life (Teitelbaum et al., 1998).

In his research on movement in first days old mice, Horev (2012) claims that in typical motor development the mice spread out four limbs to form a stable support base, while mice with inappropriate development who lacked Chromosome P16, a lack that according to research is found in 1% of children with autism, were observed as having a different motor phenotype, whereby they contracted their arms and lay on an unstable base of support.

In this study, we checked the base of support; when the baby rolled over; crawled; stood up; or walked at the appropriate development times; and whether the baby was hypotonic.

Delay of motor development appeared in 33.6% of the infants. Hypotonia was found in 67% of them. 42% of these infants started to walk after the age of 18 months (Girls 50.5% and boys 28%).

5. *Excessive Activity*

Excessive activity was defined by Alonim (2007) as consistent restless movement, consistent crying, obsessive occupation with an object.

Analytic observation of all the components of the babies' development pointed to a lack of regulation, which was expressed in many cases by over-activity, these components were all measured according to parameters of time and frequency of the phenomenon.

As mentioned above and supported also by Trevarthen (2000), brainstem systems such as self-regulation play an integral role in these higher level capacities.

Excessive -activity and repetitive behaviours appeared in 28.2% of the infants (boys 31% and girls 19.2%)

6. *Refusal to Eat*

Abnormalities in eating habits were pointed out by Wing (1987) as associated features of the autism *disorder*, but did not attract much attention at that time.

This category was divided into a main element of 'refusal to eat' and three sub-categories: 'refusal to move on to fruits or vegetables', 'refusal to move on to solid foods', and 'fixation on food'. Food refusal is defined by Riordan (1989), as the consumption of fewer than the number of necessary calories as an outcome of rejection of food. Food over-selectivity is defined by Luiselli (1994) as consistently eating only a limited variety of food.

In a long-term study, Alonim (1999-2007) followed 60 toddlers from various countries, who suffered from eating disorders, and found that most of the eating problems in children with autism are included in the category of behavioural and sensory disturbances, which is again linked to lack of self-regulation. This finding is supported by the findings of Schwartz (2003).

The eating disorders seen in toddlers with autism are described in the DSM-5 autistic traits.

"Avoidant restrictive food intake disorder is a fairly frequent presenting feature of autism spectrum disorder, and extreme and narrow food preferences may persist" (DSM-5, 2013)

Refusal to eat was found in 20.9% of the babies

7. Accelerated Growth of Head Circumference

In his studies, Courchesne (2011) highlights neurobiological findings during the first years of life, and emphasizes early brain overgrowth as a key factor in the pathobiology of autism. He claims that head circumference overgrowth in males with autism involved an abnormal excess number of neurons in the Frontal Cortex which is also responsible for emotional and behavioural processing. This is supported by findings from his recent study (2014), claiming that neural damage may appear during pregnancy.

In this study, accelerated growth of head circumference was found in 12.7% of the infants, but contrary to Courchesne's findings, this phenomenon appeared more in females (girls 23.1%, boys 9.5%).

8. Aversion to Touch

Physical touch is defined by Carvill (2001) as the amount of mass and physical proximity that the baby allows.

The definition of recoil relates to contraction or arching back, an expression of dissatisfaction, when the baby is held, cuddled or kissed. The difficulty in allowing contact usually stems from a tactile overload that makes the baby feel uncomfortable or even pain.

Difficulties in sensory processing characterize autism. Although for decades, relevant literature reported a lack of responsiveness as a sensory deficiency; in the last two decades it has become clear that this is actually over-sensitivity in the tactile, visual, audial and oral systems. Since this

involves a lack of integration between the systems, there is no sensory modulation (Dunn & Westman, 1995)

According to Alonim (2011), a lack of sensory modulation may create confusion and anxiety, and in order to overcome this state the infant holds on to fixated habits that may help them to decrease their anxiety.

Aversion to parent's touch was found in 10.0% of the infants (girls 15.4%, boys 8.3%).

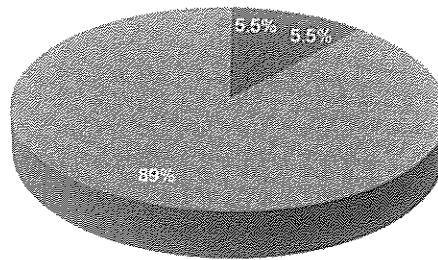
Findings of the 110 babies:

Six babies were diagnosed with pathologies; 3 neurological; 1 Angleman; 1 Rett's; 1 metabolic disease.

Six babies showed no signs of a developmental disorder of any kind during their first year of life, and according to their parents' reports, regression set in between the age of 12-18 months.

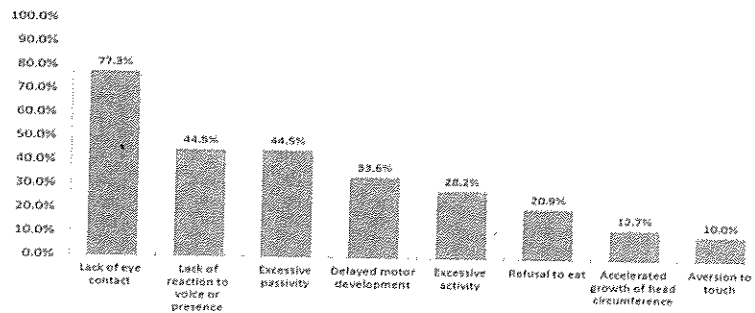
Ninety eight of the babies (89%) showed early signs associated with autism between 4 to 15 months old.

Diagram no. 1:
 ■ Pathological findings
 ■ No symptoms visible
 ■ Symptoms visible



Variables associated with autism found in 98 infants:

Graph no. 1:



The study's findings also suggested that since each infant displayed at least 2 different signs; early diagnosis of autism depends on the ability to identify various combinations of indicative pre-autism symptoms.

Table no. 1:
Percentage of variables combination findings

Delayed motor development	Aversion to touch	Refusal to eat	Lack of reaction to voice or presence	Lack of eye contact	Excessive activity	Excessive passivity	
						0.0%	Excessive activity
					21.8%	35.5%	Lack of eye contact
				37.3%	7.3%	29.1%	Lack of reaction to voice or presence
			11.8%	14.5%	2.7%	6.2%	Refusal to eat
		3.6%	6.4%	7.3%	5.5%	2.7%	Aversion to touch
	1.8%	10.0%	16.4%	25.5%	0.9%	20.0%	Delayed motor development
7.3%	1.8%	2.7%	4.5%	11.8%	2.7%	7.3%	Accelerated growth of head circumference

Secondary Findings

Analysis of the parents' reports revealed four categories:

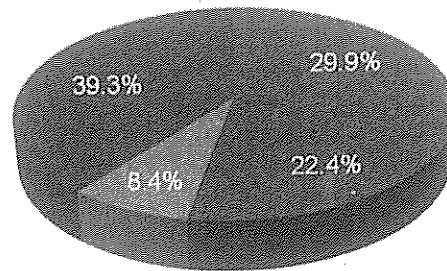
Group A: In 29.9% of the cases the parents (especially mothers) had suspected that something was inappropriate in the babies' development but were reassured that all was well.

Group B: In 22.4% of the cases, extended family members said that they felt something was wrong but did not tell the parents.

Group C: In 8.4% of the cases family members had suggested that it would be worthwhile testing the baby, but this suggestion was rejected by the parents.

Group D: In 39.3% of the cases parents claimed they had not noticed any unusual signs.

Diagram no. 2:
 ■ Parents' suspicions
 ■ Extended family
 ■ Grandparents
 ■ No suspicion arose



Outcomes

Although, the videos filmed by the families were recorded at different stages of the babies' first year of life and it was impossible to clearly point out in which phase exactly the specific sign first appeared, findings of this study indicate that it was possible to identify early symptoms relating to the autistic disorder already during the first year of 98 (out of 110) infants' lives.

As an outcome of this earlier study, analysis of results led to: a. the development of the Evaluation Scale for Pre-Autism Signs in Infants (ESPASI). b. the establishment of a pilot unit for early detection in the Sourasky Tel Aviv Medical Centre, to which parents, who have suspicions regarding the contact and communication development of their infants can apply for a battery of tests at a very early stage. Infants considered being at high risk after these tests are referred to the Mifne Centre.

The Mifne (meaning Turning Point in Hebrew) Centre for treatment, training and research is a non-profit organization, and was established in 1987. The Centre specializes in the detection of infants at risk, and in treatment of infants up to the age of two, who are diagnosed on the autism spectrum, from across Israel and overseas.

The Treatment Programme focuses on the entire range of the infant's developmental components: physical - sensory - motor - emotional and cognitive aspects, through the use of Reciprocal Play Therapy, a method which was developed at the Centre, to motivate the infant's abilities to engage with parents and caregivers out of curiosity and pleasure, and which is specially designed for each infant individually, taking into clinical consideration the early signs which were pointed up earlier.

Family Therapy - Adopting the perception that autism affects each member of the family, and that parents are actually the main resource of their children, the programme encompasses the entire nuclear family. The therapeutic approach combines bio-psycho-social and environmental aspects. Parents are fully involved and trained according to the therapeutic processes that their children undergo, in order to sustain and implement them in their daily life.

The three-stage treatment framework includes:

1. Intensive, residential family therapy for three weeks, 7 days a week, at least 8 hours per day, at the Centre
2. Aftercare treatment in the family home supported by Mifne trained therapists
3. Integration in kindergarten with follow-up supervision

Part 2: A follow-up study of infants and toddlers treated at the Mifne Centre between the years 2007-2012, (2013)

The current study followed the progress of two groups:

- a. 39 toddlers aged 2-3 years, who were treated between the years 2007-2009.
- b. 45 infants aged 1-2 years, who were treated between the years 2010-2012.

The infants were referred to the Centre by the Sourasky Medical Centre, and by other various medical clinics in Israel, and in the United States. Since the participant infants were first diagnosed in different locations, and there was no standardization of diagnostic tools, all of them were re-evaluated; the older group by ADOS, the younger group by the Evaluation Scale of Pre Autism Signs in Infants (ESPASI), and by the M-Chat.

Daily Evaluation Scale analysis, data from video-records, parents' responses to questionnaires and therapists' daily reports, produced 20 variables divided into 4 categories (engagement, communication, play and functioning), which were investigated in this study. Evaluation was measured weekly during the first intensive treatment stage and after 6 months of the aftercare programme.

The differences in results between infants who were treated between the ages of two and three and those treated under the age of two are seen in the following t-test paired performed between the 'pre-treatment' mean and the 'post-treatment' mean for each of the variables in each age group separately:

Table 2: n=84 (45 ages 1-2; 39 ages 2-3)
 t test for independent groups

Engagement components		Ages 1-2		Ages 2-3		t
		M	S.D	M	S.D	
Pre-treatment	Eye contact	2.00	1.07	2.00	.95	0.00
	Physical contact	4.00	1.41	3.00	1.52	3.12
	Obsessions	8.00	1.09	9.00	.97	-4.41
	Detachment	7.00	1.51	8.00	1.00	-3.52
Post-treatment	Eye contact	8.00	1.13	6.00	1.32	7.49
	Physical contact	9.00	1.52	6.00	1.24	9.82
	Obsessions	2.00	1.04	6.00	1.54	-14.09
	Detachment	2.00	1.19	4.00	1.41	-7.05
Difference	Eye contact	6.00	1.58	4.00	1.67	5.63
	Physical contact	5.00	1.89	3.00	1.78	4.96
	Obsessions	-6.00	1.65	-3.00	1.84	-7.88
	Detachment	-5.00	1.46	-4.00	1.78	-2.83

Eye contact; Physical contact; Obsessions; Detachment
 Graph no. 2:

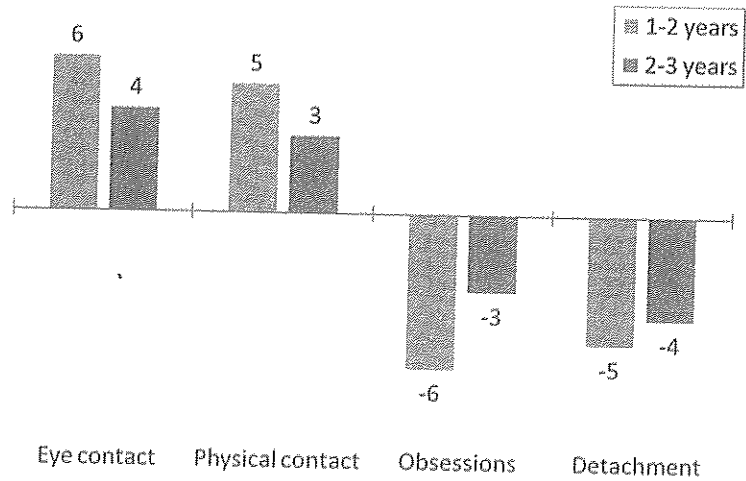


Table 3: n=84

Communication components	Age 1-2		Age 2-3		t	
	M	S.D	M	S.D		
Pro-treatment	Pointing	1.00	.95	.00	.00	6.54
	Vocals	2.00	1.26	3.00	1.21	-3.69
	Speech	1.00	.98	2.00	1.12	-4.36
	Situation comprehension	2.00	1.13	3.00	1.30	-3.78
	Language comprehension	2.00	1.04	3.00	.95	-4.57
	Hand pulling	6.00	1.45	7.00	1.47	-3.14
Post-treatment	Screaming	9.00	1.31	9.00	1.52	.00
	Pointing	6.00	1.43	3.00	1.17	10.42
	Vocals	8.00	1.17	6.00	1.50	6.95
	Speech	5.00	1.41	4.00	1.36	3.29
	Situation comprehension	7.00	1.48	6.00	1.61	2.97
	Language comprehension	8.00	1.35	6.00	1.69	6.04
Difference	Hand pulling	1.00	.98	3.00	1.03	-9.14
	Screaming	3.00	1.33	5.00	1.41	-6.67
	Pointing	5.00	1.64	3.00	1.17	6.35
	Vocals	6.00	1.57	3.00	2.00	7.70
	Speech	4.00	1.76	2.00	1.88	5.04
	Situation comprehension	5.00	2.11	3.00	1.79	4.64
	Language comprehension	6.00	1.71	3.00	1.92	7.59
	Hand pulling	-5.00	1.88	-4.00	1.69	-2.62
	Screaming	-6.00	1.71	-4.00	1.95	-5.02

Pointing; Vocals; Speech; Situation Comprehension; Hand Pulling; Screaming
Graph no. 3:

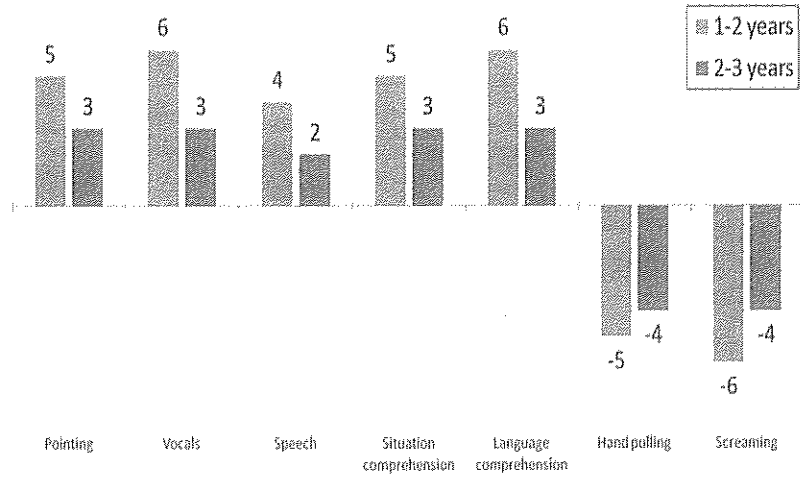


Table 4: n=84

Play components		Ages 1-2		Ages 2-3		t
		M	S.D	M	S.D	
Pre- treatment	Curiosity	2.00	1.02	2.00	1.05	.00
	Concentration	1.00	.93	2.00	1.21	-4.27
	Creativity	1.00	.90	2.00	1.28	-4.18
	Structured/Ritualistic	7.00	1.19	9.00	1.65	-6.43
Post-treatment	Curiosity	7.00	1.21	5.00	1.24	7.49
	Concentration	6.00	1.40	5.00	1.05	3.66
	Creativity	6.00	1.48	4.00	1.50	6.14
	Structured/Ritualistic	2.00	1.17	5.00	1.32	-11.06
Difference	Curiosity	5.00	1.55	3.00	1.67	5.69
	Concentration	5.00	1.73	3.00	1.47	5.66
	Creativity	5.00	1.91	2.00	1.79	7.39
	Structured/Ritualistic	-5.00	1.72	-4.00	2.04	-2.44

Curiosity; Concentration; Creativity; Ritualistic
Graph no. 4:

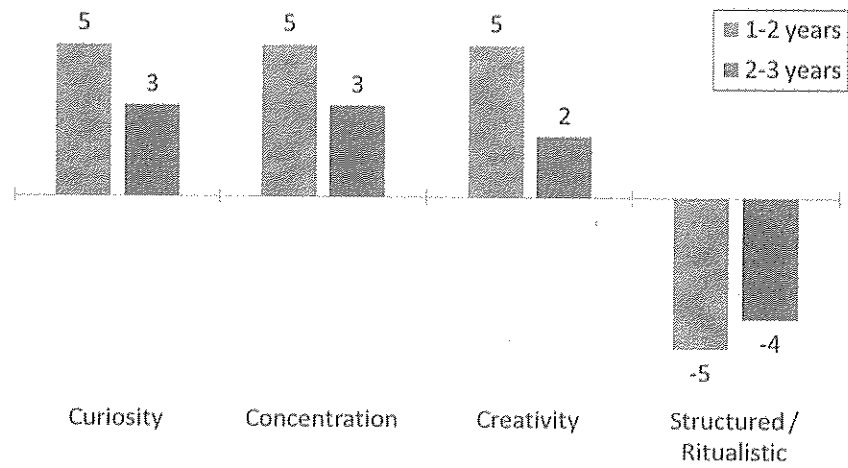
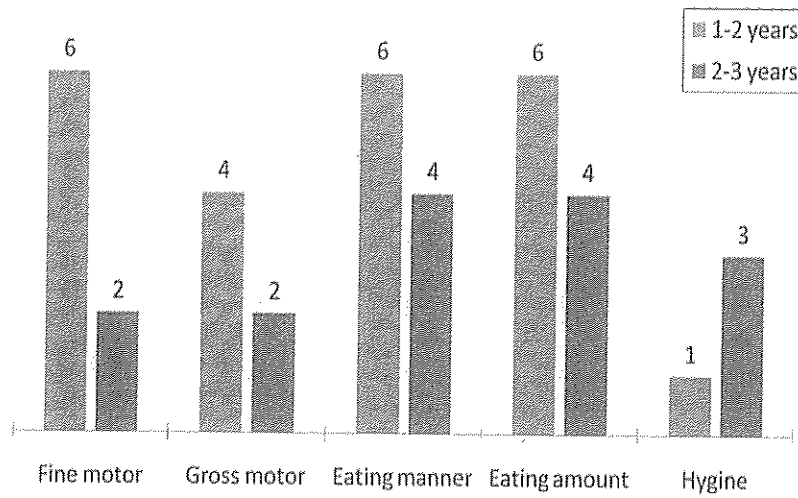


Table 5: n=84

Functioning components	Ages 1-2		Ages 2-3		t	
	M	S.D	M	S.D		
Pre-treatment	Fine motor	1.00	.98	3.00	1.26	-6.20
	Gross motor	3.00	1.19	5.00	1.28	-7.43
	Eating manner	1.00	1.04	1.00	.95	.00
	Eating amount	2.00	1.30	2.00	1.15	.00
	Hygiene	.00	.000*	.00	.000*	
Post-treatment	Fine motor	7.00	1.24	5.00	1.03	7.97
	Gross motor	7.00	1.24	7.00	1.10	.00
	Eating manner	7.00	1.37	5.00	1.17	7.15
	Eating amount	8.00	1.28	6.00	1.00	7.09
	Hygiene	1.00	.90	3.00	.97	-9.76
Difference	Fine motor	6.00	1.69	2.00	1.41	11.65
	Gross motor	4.00	1.77	2.00	1.75	5.19
	Eating manner	6.00	1.89	4.00	1.75	5.00
	Eating amount	6.00	1.93	4.00	1.65	5.06
	Hygiene	1.00	.90	3.00	.97	-9.76

Fine motor; Gross motor; Eating Manner; Eating amount; Hygiene
Graph no. 5:



Each of the graphs displays grades for the two groups before the treatment commenced, after treatment and the difference between 'pre-treatment' and 'post-treatment' status in the measured dimension. As can be seen in both graphs, before the treatment commenced both groups had a relatively low status with an improvement for the more mature babies. In contrast to this 'pre-treatment' situation, the values in the columns representing 'post-treatment' status are higher for both groups but the trend has reversed so that the younger babies are now in a better status than the more mature babies. This trend is most evident in the grades for the difference; firstly in both groups an improvement process has taken place since the grades for difference are positive; secondly for the younger babies the grades for difference were significantly higher than the grades for difference for the older babies. This trend is repeated in all the measured dimensions.

Findings

The analysis displayed in the above tables show that at the 'pre-treatment' measurement point the older toddlers had slightly better behaviour or at least had identical behaviour to the younger ones.

For most of the variables, the difference between the older and the younger toddlers was significant (in favour of the older ones). In contrast, the 'post-treatment' measurement points to a significant difference for almost all the variables contrarily indicating a difference in favour of the younger toddlers.

The Delta shows that with regard to the differences in post-treatment status in all the variables, both for the older and the younger toddlers, there was significant improvement, but for the group of 1-2 years the difference was far larger.

This analysis found that in both age groups there was a significant difference at a very good level ($p < .001$) between the 'pre-treatment' and 'post-treatment' measurements.

Nevertheless, the difference in the younger group was far greater and far more significant for all studied variables.

Conclusions

The initial retrospective study findings affirmed the assumption that symptoms of ASD frequently appear in the first year of life, which is now supported by DSM-5

Symptoms are typically recognized during the second year of life (12-24 months of age) but may be seen earlier than 12 months if developmental delays are severe, or noted later than 24 months if symptoms are more subtle (DSM-5, 2013)

The current follow-up study findings, suggest that:

1. Early detection can and should in many cases take place around the age of one year to be followed by early treatment
2. Intervention already at the age of one can potentially positively alter the predicament and future of many children and their families (Alonim, et al., 2011).

Despite the evidence from all recent studies, there is still a debate about age diagnosis. Autism is more than the sum of its parts. Therefore, I would like to suggest that: although diagnosis is essential in order to map the infant's needs and to provide a focal treatment, the bottom line is that treatment is ultimately given to the infant and not to the diagnosis.

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