UNIVERSITÀ DEGLI STUDI DI UDINE
DIPARTIMENTO DI SCIENZE UMANE
**CORSO DI DOTTORATO DI RICERCA IN COMUNICAZIONE MULTIMEDIALE**
CICLO XXIV

TESI DI DOTTORATO DI RICERCA

# Virtual and behavioral habilitation techniques in children with Autism

DOTTORANDO:
Dott.ssa **Livia FORNASARI**

RELATORE:
Prof. **Lucio COTTINI**

CORRELATORE:
Dott. **Paolo BRAMBILLA**

ANNO ACCADEMICO
2011/2012

1. Reviewer: Professor **Filippo Muratori**

2. Reviewer: Doctor **Leonardo Zoccante**

Day of the defense: April 23, 2012

Head of PhD committee: Professor **Leopoldina Fortunati**

# Abstract

The purpose of this study was to examine two different habilitation techniques in children with autism. Indeed autism is a severe disorder and it is important to implement targeted interventions designed on the strengths and needs of affected children to improve their daily life.

In the first two chapters there is a review of the literature on autistic disorder and habilitation techniques.

Two studies are then presented.

The first is a longitudinal study to evaluate the best age to start a low-intensive TEACCH (Treatment and Education of Autistic and Communication handicap CHildren normal development)-oriented intervention. In this study twenty-eight children with autism were treated two times per week following the guidelines inspired by the TEACCH intervention. Developmental abilities were rated at baseline and after six and 12 months with the Psychoeducational Profile - Revised (PEP-R) scale. Developmental abilities significantly improved during the first 6 months with progressive amelioration throughout the 12-month follow-up period, particularly for children under 40 months of age. Specifically perception, motricity and cognition improved only in patients who begun the program before 60 months of age. This study shows that early low-intensive TEACCH habilitation is effective in improving developmental abilities in autism even after 6 months, particularly in patients that start it at the very early stages of the disease. It is therefore crucial to begin the habilitation program in autism at the very early stages of the illness in order to maximize the effectiveness of the treatment.

**Abstract**

The second study analyzed navigation and exploration of an urban Virtual Environment by children with autism compared to children with typical development to focus specifically on understanding navigation and exploration in children with autism. Sixteen children with autism and 16 controls 1:1 matched for age, sex, race, language, education and IQ participated. After an initial training phase, children carried out two tasks: the first one was navigation in an unknown urban environment that children could freely explore; the second was navigation in the same environment but with the goal of finding specific target objects as in a treasure hunt. In the first task, children with autism spent significantly less time in active exploration and explored fewer zones than controls. No differences were found between the two groups when children had to find objects. Our data suggests that children with autism poorly explore raw unfamiliar environments, while they tend to be more motivated and active when they are stimulated by a task organized as a game.

*To my family*

# Acknowledgments

My greates thanks go to Doctor Paolo Brambilla. It is a privilege to work with you. Thank you for your guidance and expertise, not only for the present thesis, but also for all the research projects I worked with you.

I especially thank my tutor, Professor Lucio Cottini, for giving me the opportunity to explore this interesting research area.

I sincerly thank Professor Luca Chittaro, who developed the virtual environments used in this thesis, and Professor Franco Fabbro, for valuable suggestions.

I would like to thank Professor Leopoldina Fortunati, PhD Director, for her expertise in the field of multimedia communications and for the interesting lessons that she has organized.

I would also like to thank my external reviewers, Prof. Filippo Muratori and Dott. Leonardo Zoccante.

Thank you to all children and their families, who participated in these studies and to operators of “La Nostra Famiglia”, Scientific Institute IRCCS “E. Medea”, Udine and of Child Neuropsychiatric Unit of the National Health Service of Udine, for their kindness and helpfulness.

I would like to thank all my wonderful colleagues: Marco, Gioia, Carolina, Anna and Sara.

I sincerly thank my amazing parents, Maurizio e Isabella, and my beloved brother, Lorenzo. I am forever indebted to you.

Thank you Davide, I love you.

# Index

# 1

# Autism

## 1.1 Autistic Disorder

Autism (Autistic Disorder) is classified within a clinical spectrum known as Pervasive Developmental Disorders (American Psychiatric Association, 2000) or Autism Spectrum Disorders (ASDs) that includes various conditions such as Autistic Disorder, Asperger's syndrome, Atypical Autism, and Pervasive Developmental Disorder Not Otherwise Specified (NOS). According to the DSM-IV-TR, autism is a severe disorder characterized by the presence of at least 6 out of 12 symptoms concerning communication, reciprocal social interaction, behaviour, and activities that are present from the age of three years.

In the present work we will focus on the Autistic Disorder, while other types of Pervasive disorders will be only briefly mentioned.

### 1.1.1 History of Autism

The word "autism" comes from the Greek word "autos",that means "self". The term "autism" was first used in 1911 by Eugen Bleuler, a Swiss psychiatrist, to refer to one group of schizophrenic symptoms. In 1943 Dr. Leo Kanner of the John

Hopkins Hospital studied a group of eleven children with emotional or social problems and used the term “autism” to refer to these children, whose behaviour was characterized by social withdrawal and routines, as well as by language production problems.

In the same period the German scientist Hans Asperger described Asperger’s syndrome in group of children, and defined it as a disorder whose main features were: a lack of empathy, little ability to form friendships, circumscribed interests and awkward movements.

Autism and schizophrenia were considered as associated disorders until the 1960s.

A popular theory by Bettelheim (Bettelheirn, 1967) put the causes of autism down to a too cold mothering style that had traumatic effect on the infants. From the 1960s through the 1970s treatments for autism were focused on medications such as LSD, electric shock, and behavior change techniques.

During the 1980s and 1990s autism was considered a behavioral syndrome, and Behavior Therapy, using controlled learning environments, became the main therapeutic approach to many forms of autism and related conditions.

### 1.1.2 Epidemiology

Autism occurred more often in boys than girls (4:1) (Fombonne, 2005) and there was a significant increase of diagnosis over the past decades, with an incidence of approximately 4 per 10 000 to 6 per 1000 children (Faras et al., 2010; Lasalvia and Tansella, 2009).

Recent reviews tend to estimate a prevalence of 1–2 per 1,000 for autism and close to 6 per 1,000 for ASDs. Pervasive Developmental Disorders-NOS's prevalence has been estimated at 3.7 per 1,000, Asperger syndrome at 0.6 per 1,000, and Childhood Disintegrative Disorder at 0.02 per 1,000 (Fombonne, 2009). The recent increase of these disorders is largely attributable to changes in diagnostic practices, referral patterns, availability of services, age at diagnosis, and public awareness (Fombonne, 2009; Wing and Potter, 2002).

### 1.1.3 Diagnostic features and diagnostic criteria

The conditions for a diagnosis of Autistic Disorder are: the presence of abnormal or impaired development in social interaction and communication and a markedly restricted repertoire of activity and interests.

Manifestations of the disorder vary greatly depending on the developmental level and chronological age of the individual.

The DSM-IV-TR (pages 70-71) (American Psychiatric Association, 2000) describes the diagnostic features of Autistic Disorders as follows:

> "The impairment in reciprocal social interaction is gross and sustained. There may be marked impairment in the use of multiple nonverbal behaviors (e.g., eye-to-eye gaze, facial expression, body postures and gestures) to regulate social interaction and communication (Criterion A1a). There may be failure to develop peer relationships appropriate to developmental level (Criterion A1b) that may take different forms at different ages. Younger individuals may have little or no interest in establishing friendships. Older individuals may have an interest in friendship but lack understanding of the conventions of social interaction. There may be a lack of spontaneous seeking to share enjoyment, interests, or achievements with other people (e.g., not showing, bringing, or pointing out objects they find interesting) (Criterion A1c). Lack of social or emotional reciprocity may be present (e.g., not actively participating in simple social play or games, preferring solitary activities, or involving others in activities only as tools or "mechanical" aids) (Criterion A1d). Often an individual's awareness of others is markedly impaired. Individuals with this disorder may be oblivious to other children (including siblings), may have not concept of the needs of others, or may not notice another person's distress.
>
> The impairment in communication is also marked and sustained and affects both verbal and nonverbal skills. There may be delay in, or total lack of, the development of spoken language (Criterion A2a). In individuals who do speak, there may be marked impairment in the ability to initiate or sustain a conversation with others (Criterion A2b), or a stereotyped

and repetitive use of language or idiosyncratic language (Criterion A2c). There may also be a lack of varied, spontaneous make-believe play or social imitative play appropriate to developmental level (Criterion A2d). When speech does develop, the pitch, intonation, rate, rhythm, or stress may be abnormal (e.g., tone of voice may be monotonous or inappropriate to context or may contain questionlike rises at ends of statements). Grammatical structures are often immature and include stereotyped and repetitive use of language (e.g. repetition of words or phrases regardless of meaning; repeating jingles or commercials) or idiosyncratic language (i.e., language that has meaning only to those familiar with the individual's communication style). Language comprehension is often very delayed, and the individual may be unable to understand simple questions or directions. A disturbance in the pragmatic (social use) of language is often evidenced by an inability to integrate words with gestures or understanding humor or nonliteral aspects of speech such as irony or implied meaning. Imaginative play is often absent or markedly impaired. These individuals also tend not to engage in the simple imitation games or routines of infancy or early childhood or do so only out of context or in a mechanical way.

Individuals with Autistic Disorder, have restricted, repetitive, and stereotyped patterns of behavior, interests, and activities. There may be an encompassing preoccupation with one of more stereotyped and restricted patterns of interest that is abnormal either in intensity or focus (Criterion A3a); an apparently inflexible adherence to specific, nonfunctional routines or rituals (Criterion A3b); stereotyped and repetitive motor mannerisms (Criterion A3c); or a persistent preoccupation with parts of objects (Criterion A3d). Individuals with Autistic Disorder display a markedly restricted range of interests and are often preoccupied with one narrow interest (e.g. dates, phone numbers, radio station call letters). They may line up an exact number of play things in the same manner over and over again or repetitively mimic the actions of a television actor. They may insist on sameness and show resistance to or distress over trivial changes (e.g. a younger child may have a catastrophic reaction to a minor change in the environment such as rearrangement of the furniture or use of a new set of utensils at the dinner table). There is often an interest in nonfunctional routines or rituals or an unreasonable insistence on following routines (e.g. taking exactly the same route to school every day). Stereotyped body movements include the hands (clapping, finger flicking) or whole body (rocking, dipping, and swaying). Abnormalities of posture (e.g. walking on tiptoe, odd hand movements and body postures) may be present. These individuals show a persistent preoccupation with parts of objects (buttons, parts of the body). There may also be a fascination with movement (e.g. the spinning wheels of toys, the opening and closing of doors, an electric fan or other rapidly revolving object). The person may be highly attached to some inanimate object (e.g. a piece of string of a rubber band).

The disturbance must be manifest by delays or abnormal functioning in at least one (and often several) of the following areas prior to age 3 years: social interaction, language as used in social communication, or symbolic or imaginative play (Criterion B). In most cases, there is no period of unequivocally normal development, although in perhaps 20% of cases parents report relatively normal development for 1 or 2 years. In such cases, parents may report that the child acquired a few words and lost these or seemed to stagnate developmentally.

By definition, if there is a period of normal development, it cannot extend past age 3 years. The disturbance must not be better accounted for by Rett's Disorder or Childhood Disintegrative Disorder (Criterion C) ".

A summary of the diagnostic criteria for Autistic Disorder, as reported in the DSM-IV-TR, is listed below.

A) Six (or more) items from (1), (2), and (3), with at least two from (1), and one each from (2) and (3) must be present:

(1) qualitative impairment in social interaction, as manifested by at least two of the following: i) marked impairment in the use of multiple nonverbal behaviors such as eye-to-eye gaze, facial expression, body postures, and gestures; ii) a deficit in regulating social interactions and a failure to develop peer relationships appropriate to developmental level, iii) a lack of spontaneous seeking to share enjoyment, interests, or achievements with other people (e.g., by a lack of showing, bringing, or pointing out objects of interest)

lack of social or emotional reciprocity

(2) qualitative impairments in communication as manifested by at least one of the following: i) absence or a delay in the development of spoken language (not compensated by alternative methods of communication such as gesture or mime);

ii) in individuals with adequate speech, marked impairment in the ability to initiate or sustain a conversation with others, stereotyped and repetitive use of language or idiosyncratic language; iii) lack of varied, spontaneous make-believe play or social imitative play appropriate to developmental level
(3) restricted, repetitive and stereotyped patterns of behavior, interests, and activities, as manifested by at least one of the following: i) preoccupation with one or more stereotyped and restricted patterns of interest that is abnormal either in intensity or focus; ii) apparently inflexible adherence to specific, nonfunctional routines or rituals; iii) stereotyped and repetitive motor mannerisms (e.g., hand or finger flapping or twisting, or complex whole-body movements); iv) persistent preoccupation with parts of objects.

B. Delays or abnormal functioning in at least one of the following areas, with onset before 3 years of age: i) social interaction; ii) verbal social communication; iii) symbolic or imaginative play.

C. The disturbance is not better accounted for by Rett's Disorder or Childhood Disintegrative Disorder.

### 1.1.4 Associated features and disorders

Anxiety, depression, sleeping and eating disorders, attention difficulties and aggression problems are also present (World Health, 2006). Mental retardation and epilepsy are often comorbid with autism (Parmeggiani et al., 2007) in the 70% and 25% of autism cases respectively (Canitano, 2007; Chakrabarti and Fombonne, 2001). Other areas of co-morbidity related to behavioural symptoms include: a) hyperactive-inattentive cluster symptoms; b) tics, Tourette syndrome, and movement disorder symptoms; c) compulsive repetitions, explosive/self-injury symptoms and mood disorder symptoms (Bailey et al., 1986).

Finally, individuals with Autistic Disorder may show a range of behavioral symptoms including hyperactivity, short attention span, impulsivity, aggressiveness, self-injurious behaviors, odd responses to sensory stimuli, and eating or sleeping habits.
Disturbs in mood or affect may also be present, as well as a lack of fear in response to real dangers, and excessive fearfulness in response to harmless objects. A variety of self-injurious behaviors may be reported.

### 1.1.5 Prognosis

The degree of impairment among individuals suffering with autism may vary greatly and, although treatments are reported to be beneficial in many cases, the impact of this syndrome is generally life-changing for the affected persons and their families (Newschaffer et al., 2007).
The 15% of people with autism can acquire a certain level of autonomy in old age adulthood, with outcomes being better for early intervention (Howlin, 1998).
Factors predicting outcome include the presence of communicative speech by around the age of 5 and overall cognitive ability. Furthermore, it is crucial to early promote the development of the functional potentials in children with autism (Schreibman, 2000).
In order to help people with autism, their carers and educators more studies on intervention and rehabilitation are needed (Goodwin, 2008).
To date, there are not available specific psychopharmacological treatments for autism.

## 1.2 Causes

It is agreed that autism does not relate to parenting style, social economic status, race or ethnicity. The causes of this disorder are still largely unknown (Brambilla et al., 2003; Brambilla et al., 2004), but it has been suggested that genetic,

developmental, and environmental factors are involved, alone or combined, as possible causal or predisposing factors toward development of autism (Bolton et al., 1994; Mengotti et al., 2010; Minshew and Payton, 1988; Pensiero et al., 2009; Stevens et al., 2000).
Several explanations of the possible causes of Autistic Disorder had been proposed. The main theoretical approaches are reported below.

### 1.2.1 The psychological models

Deficit in executive function (Ozonoff, 1997; Pennington and Ozonoff, 1996): this model explained the causes of autism in term of poor abilities to maintain a problem solving mind set forward planning, and organization skills, and assumed a neural localization (*i.e.* prefrontal cortex) of these difficulties, and thus a genetic basis. However, the mentioned deficits are not specific to autism and are not strongly related to the degree of social difficulty.
Weak central coherence (Happe and Frith, 1996):
this model referred to difficulties in integrating information into meaningful wholes. Many individuals with autism have a fragmented learning style and difficulties in this area. Also this theory had limitations and lacks support from empirical data. Developmental features of theory are weak as well.
Teory of mind (Baron-Cohen et al., 2000):
this model explained autism as a difficulty in intersubjectivity (ability to put oneself in another person's place), leading to problems in understanding mental states and in using such knowledge in everyday life. Children with autism are presumed to be unable to think about other people's intentions, desires, feelings, and beliefs, thus showing problems in social interaction. Some studies on neural basis have been undertaken. The main limitation of this model is the strong relation of theory-of-mind abilities to language, with many high-functioning individuals

with autism being able to complete usual theory of mind tasks despite having striking social difficulties.

### 1.2.2 Neurobiology

In addition to these theories, many studies have been conducted to study the brain processes involved in autism. Post-mortem investigations have shown abnormalities with reduction in the number of neurons and reduced dendritic arborization in amygdala, hippocampus, septum and anterior cingulate areas (Kemper and Bauman, 1998; Minshew et al., 1997).

Finally, brain mechanisms in autism have been studied in vivo and non-invasively using MRI techniques revealing a higher brain volume (from 2 to 10%) (Piven and Arndt, 1995) and an over-grown white matter (WM) in children with autism as compared to healthy controls, with abnormal WM growth patterns in the frontal lobes and temporal and limbic structures (e.g. the amygdala) (Pardo and Eberhart, 2007), brain regions that are thought to be crucial in social development, communication and motor skills deficits. Also a study recently demonstrated a role of left parietal gray matter volumes in delayed language development in children with autism (Zoccante et al., 2010). Structural abnormalities in the total brain volume, the cerebellum and, recently, the corpus callosum have been consistently reported. The available evidence suggests the existence of a disturbed neural network involving cortical and subcortical areas, including temporo-parietal cortex, limbic system, cerebellar, and prefrontal regions (Brambilla et al., 2003). Functional neuroimaging (fMRI) studies involving autistic patients explored face recognition, theory of mind and executive functions. The existing literature indicate the presence of abnormal functional mechanisms in face recognition, mentalization and executive functions in adults with high-functioning autism or Asperger's syndrome, possibly due to brain maturation abnormalities, resulting in dysfunctional reciprocal cortico-subcortical connections (Brambilla et al., 2004).

### 1.2.3 Genetics and environmental

There is evidence that autism spectrum disorders have a strong genetic basis. Indeed, the risk to have another child who will be diagnosed with autism is proved to be 20-50 times higher among the closest relatives of individuals with autism, if compared to the population base rate. Also, parents and siblings of children with autism often exhibit manifestations similar to the symptoms of autism (e.g. delayed language, difficulties with social aspects of language (pragmatics), delayed social development, absence of close friendships, and a perfectionist or rigid personality style (Losh et al., 2008).

Autism spectrum disorders are associated with known genetic causes in 10–15% of cases and studies on twins (O'Roak, 2008) suggest that 60–90% of monozygotic twins are concordant for autism spectrum disorder, compared with about 10% for dizygotic twins (Bailey et al., 1995). Moreover studies on twins indicate that heritability is 0.7 for autism and as high as 0.9 for ASD, and siblings of those with autism are about 25 times more likely to be autistic than the general population (Geschwind, 2009). Causes of autism include also fragile X syndrome (about 3%), tuberous sclerosis (about 2%), and others cytogenetic anomalies. None of these causes are specific to the disorder, but generalize to a range of phenotypes, including intellectual disability. Also environmental factors can contribute to develop ASD, such as certain foods, solvents, diesel exhaust, substances used in plastic products, pesticides, brominated flame retardants, alcohol, smoking, illicit drugs, vaccines and prenatal stress (Kinney et al., 2008; Newschaffer et al., 2007).

## 1.3 Diagnostic tools

Diagnosis of Autism is based on behavioral parameters. For this reason it is essential to refer to standard conditions of observation and use appropriate rating scales developed to detect the typical Autistic Disorder's behavioral manifestations. The instruments most commonly used for the diagnosis of autism are listed below.

### 1.3.1 Childhood Autism Rating Scale (CARS) (Schopler et al., 1986).

This scale assesses behaviors in 14 domains that are typically affected in autism, plus one concerning a general impression on the children conduct, with the aim to identify children with autism. The scale is composed by the following items: i) Relating to people; ii) Imitative behavior; iii) Emotional response; iv) Body use; v) Object use; vi) Adaptation to change; vii) Visual response; viii) Listening response; ix) Perceptive response; x) Fear or anxiety; xi) Verbal communication; xii) Non-verbal communication; xiii) Activity level; xiv) Level and consistency of intellective relations; xv) General impressions.
Scores range from 1, indicating an appropriate behavior, to a score of 4, pointing out a severe deviance, with respect to the person's age level. The scores obtained at each item are summed up into a total score, which classifies the child as not autistic (below 30), mild or moderately autistic (30–36.5) or severely autistic (above 36.5).

### 1.3.2 Autism Diagnostic Observation Schedule (ADOS) (Lord et al., 2000).

This is a semi-structured assessment used to evaluate autism from children with no speech to verbally fluent adults. The assessment involves activities that allow the examiner to detect behaviors that are considered core symptoms of autistic disorder. The ADOS considers five main domains: Language and Communication; Reciprocal Social Interaction; Play; Stereotyped Behaviors and Restricted Interests; Other abnormal behaviors. Scores range from 0 (not abnormal behavior), through 2 or 3 (most abnormal). The ADOS includes four modules, each requiring about 35 to 40 minutes to administer. The instructions provided in the manual guides, the choice of the appropriate module for each person, according to verbal skills and age. Module 1 is used for children who do not consistently use phrase speech, Module 2 is addressed to children who can use phrase speech but are not verbally fluent, Module 3 is for fluent children, and Module 4 is for fluent adolescents and adults.

The ADOS provides cutoff scores for diagnosis of PDD/atypical autism/autism spectrum, following diagnostic criteria of DSM-IV and ICD-10,

### 1.3.3 Autism Diagnostic Inteview-Revised (ADI-R) (Lord et al., 1994).

This interview is designed to be used in combination with the Autism Diagnostic Observation Schedule (ADOS). The interview is aimed at parents or teachers to individuals from infancy to adulthood, with a mental age above 2 years. The ADI-R is focused on the observation of systematic and standardized behaviors given as diagnostic criteria according to ICD-10 and DSM-IV: Language and communication, Reciprocal social interaction, Stereotyped behaviors and restricted interests.

### 1.3.4 Autism Behavior Checklist (ABC) (Krug et al., 1979)

This scale assesses the presence of typical autistic behaviors and consists of 57 items, each corresponding to a single score for any single symptomatological area. Five areas are considered: sensory, relating, stereotypes and object use, language, and self-help and social. The total score is obtained by summing up the scores for each area. Scores range from 1 to 4 and the 57 items are divided as follows: 9 items for sensory area, 12 for relating, 12 for stereotypes and object use, 13 for language, 11 for self-help and social.

### 1.3.5 Gillian Autism rating Scale (GARS) (Gilliam, 1995).

This is a behavioral checklist filled out by the parents that corresponds to the DSM-IV (APA, 1994) and provides an Autism Quotient, a standard score representing the likelihood for an individual to be classified as ASD, that is derived from four subscales (three behavioral subscales paralleling DSM-IV categorie: Stereotyped behaviors, Communication, Social interaction and a subscale addressing early developmental history: Developmental Disturbances). It was intended to be used in both research and clinical settings.

### 1.3.6 Evaluation tools

In addition to the tools mentioned above, which have a "diagnostic" purpose, other two scales are used as "Evaluation Tools”: i.e. i) the Psycho Educational Profile (PEP-R) (Schopler et al., 1990) and ii) the Vineland-Adaptive Behavior Scales (VABS) (Sparrow et al., 1984).

The PEP-R provides a profile of development and allows to plan a specific individualized intervention program in children with mental age raging from 6 months to 7 years. It takes 45-90 minutes for administration. It is composed by 131 items and it can be divided into seven sub-scales concerning: i) Imitation; ii) Perception; iii) Fine Motor; iv) Gross Motor; v) Eye-hand Coordination; vi) Cognitive Performances; vii) Verbal Performances. The seven domains together provide a cumulative Developmental Score. The scores can be divided into two categories: “passing”, when the item is achieved, and “emerging”, when the item is partially achieved.

The VABS is a semi-structured interview assessing the adaptive level in individuals from 9 to 18 years of age, investigating those behaviors that allow a person to be sufficiently independent and responsive to environmental demands and expectations. The scale is divided into 4 items: communication (receptive and expressive language, reading and writing), socialization (interpersonal relationships, play and leisure, social rules), daily living skills (personal skills, home and community), motor skills (fine and gross).

# 2

# Habilitation techniques

## 2.1 Treatment

Autism is currently considered a behavioral syndrome. The diagnosis is based on the observation of a series of manifestations representing the expression of a functional impairment in three areas: social interaction; communication; interests and activities. It follows that the treatment includes the activation of actions to improve the social interaction and communication, as well as to encourage the broadening of interests and beahviour flexibility.

The majority of the studies on autism focused on epidemiology, genetics and neurobiology, but more intervention research is needed to help children with autism, their caregivers and educators. In this context, it is crucial to develop tools for neurocognitive intervention enabling children with autism to improve their ability to carry on everyday activities.

The chances of success increase dramatically if the intervention is started at an early age.

Crucial factors are:

♦ identify autistic children and intervene as soon as possible, as this may improve the speed of the child's general development, with a reduction of inappropriate behaviors, and better long-term functional outcomes;
♦ tailor the interventions on the basis of the specific strengths and needs of the child and family;
♦ constantly monitoring the child's progress.

Parents must be actively involved, to the extent of their resources, in all aspects of the child's assessment and intervention.

Evidence (Rogers, 1996) shows that the most effective treatments are starting between 2 and 4 years of age. Also, the establishment of appropriate management strategies in the early years seems to minimize, or even avoid, many subsequent behavioral problems and to gain cognitive and adaptive functioning, with respect to children who do not receive services (Harris and Handleman, 2000; Remington et al., 2007).

No a unique strategy of intervention is ever likely to be effective for all children and all families and it should be adapted to individual needs (Howlin, 1998).

Nonetheless, the strategies commonly recommended and adopted, may be categorised into behavioral and evolutionary approaches.

The following section briefly discusses the main models of intervention and then two types of intervention for children with autism will be described: *i.e.* TEACCH and Virtual Reality.

### 2.1.1 Behavioral and evolutionary approaches

Applied Behavior Analysis (ABA) consists in the study of behavior, behavior changes and the factors that determine these changes based on the following 4 elements:

1. the antecedents preceding the observed behavior;
2. the observable and measurable actual behavior;

3. the consequences deriving from the observed specific conduct;
4. the context (*i.e.* place, people, materials, activities or time of day) in which the behavior occurs.

The techniques used by behavior therapy to promote changes in the person's conduct typically are: the prompting, the modeling, the shaping and the reinforcement.

ABA has been used since 1960 to teach specific skills to improve socialization, communication and adaptive behavior. In the early 80's Lovaas developed the Discrete Trial Training (Lovaas et al., 1981), a treatment protocol including a series of sessions, for a total of 40 hours weekly. The theoretical assumption is that the whole behavior can be resolved into its cause (antecedent) and consequence which can be controlled through a careful analysis of the behavior and training. The positive reinforcement is a key point of the method to change and shape the behavior. According to Lovaas et al., the task will continue if positively reinforced, while it will stop when ignored or punished. This model has two basic assumption:

- the need for a highly structured teaching, with a 1:1 ratio, in a environment specifically organized;
- the inability of the autistic child to learn in a "natural" environment that often acts only as a "distraction".

On these assumptions the model "The University of California at Los Angeles (UCLA) Young Autism Project" has been developing. Designed by Lovaas (Lovaas, 1979; Lovaas et al., 1981) and based on Applied Behavior Analysis (ABA), the model requires a large involvement of the children's families and a variable amount of hours per week (up to 40 hours per week).

However, learning in an artificial environment may lead to problems of generalization of the acquired skills. Also, it was recently recognized that ASDs children with autism can learn in "natural" environments, such as family or school, with the involvement of parents, brothers, teachers and peers, if they receive an appropriate training to implement the programs on the child.

On these grounds, several models was developed:

- "Walden Early Childhood programs at the Emery University School of Medicine", using incidental teaching (incidental Learning ) in integrated classes (children with autism and normal children);
- "Learning Experiences, an Alternative Program for Preschoolers (LEAP) at the University of Colorado - School of Education," which is based on teaching to peers how to provided the treatment to the children with autism (National Research Council . Committee on Educational Interventions for Children with, 2001).

Further models are based on evolutionary approaches: e.g. "Denver Model at the University of Colorado" (Rogers et al., 2000); "Developmental Intervention Model Heath Sciences Center at The George Washington University School of Medicine" (Greenspan and Wieder, 1999); "Thérapie d'Echange et de Développement (TED) de l'Université François Rabelais, CHU de Tours" (Barthelemy et al., 1995), and are characterized by a "child-centered" intervention to promote free expression, initiative and participation. Emotional and relational dimensions are key points of this approach, as the environment is no more considered a mere physical space in which doing exercises, but a space in which the relation between the child and the operators is central.

## 2.2 TEACCH

TEACCH (Treatment and Education of Autistic and Communication Handicap Children normal development) is a psycho-educational habilitation intervention, based on a close collaboration between parents and professionals and on the integration of all interventions attended by the affected persons. It was created in the 60s by Eric

Schopler (Cox and Schopler, 1993) and aim to modify the environment to meet the needs of people with Autistic Disorder (Schopler, 1994). Key features include: an early assessments and continuous monitoring after the first diagnosis, promoting active collaboration with other family members, teaching new adaptive skills, planning of specific interventions, using of cognitive-behavioral strategies. The TEACCH program is addressed to act on those aspects which represent the major difficulties for autistic children, as the comprehension of abstract concepts, the meaning of imitation, the interpersonal relationships and the characteristics of events in space and in time. It was defined by Eric Schopler as a global approach based on a close collaboration between parents and professionals. The program was specifically designed for children with autism and the parents are given the role of co-therapists. The purpose of TEACCH is to minimize the child's difficulties using structured and continuous intervention, environmental adaptation (modify the environment in order to meet the needs of autistic children) and augmentative communication.
The TEACCH approach is called "structured teaching" because it is based on "Culture of autism" (Mesibov and Shea, 2010) that highlights deficits and strengths of individuals with autism such as:

- Preference for visual information
- Attention to details but difficulties with sequencing, integrating tasks
- Variability in attention and difficulties shifting attention
- Communication problems
- Problems with the time( for example in recognizing the beginning and the end of an activity
- Difficulties to generalize from the original learning situation
- Interest in favorite activities but also difficulties disengaging once engaged.

The principles of TEACCH's structured teaching include:
(a) Understanding the culture of autism;

(b) Developing a tailored person and family centered plan, rather than using a standard curriculum;
(c) Structuring the physical environment so that it will facilitate the understanding in the autistic students;
(d) Using visual supports to plan the sequence of the eveyday activities, so to make them predictable and understandable;
(e) Using visual supports to make individual tasks understandable.
The foundation for structured teaching is the principle of modifying the environment to accommodate the needs of autistic students(Schopler et al., 1995), which involves four connected components:

1. *Physical organization*. The physical layout of the classroom or the area for teaching should help to adequately promote a student's independent functioning together with his recognition of and compliance with rules and limits. Visual information is provided as important element to direct the student's activities in a predictable manner.
2. *Scheduling*. Due to autistic student's problems with sequential memory and organization of time, they need schedules. Visual schedules provide a clear timing of the activities that will take place and of their sequence (Schopler et al., 1995). Schedules also assist them in predicting events, lessening their anxiety.
3. *Work systems*. Work systems visually specify to the students which activity should be completed in specific independent areas, the amount of work that must be done and when that work session or task is complete. (Schopler et al., 1995).
4. *Task organization*. Task organization determines which work students do independently, which needs to be done within a task, how many items must be completed, and expected outcomes (Schopler et al., 1995).

### 2.2.1 TEACCH and autism

To date, there are no available psychopharmacological treatments specific to autism. Nonetheless, it is crucial to early promote the functional potentials of children with autism (Schreibman, 2000).

Children with autism show a range of difficulties concerning organization, attention, sequencing and generalization that can vary in number and severity from one individual to another. This makes important to use targeted interventions, designed on the strengths and needs of each affected children (Schopler and Reichler, 1971) as, for instance, the TEACCH program (Treatment and Education of Autistic and Communication handicap CHildren normal development).

According with Schopler (Schopler and Reichler, 1971), children with autism responded more favorably to structured than unstructured settings. TEACCH program demonstrated to be effective in improving the individual skills displayed during work sessions (Panerai et al., 1997; Panerai et al., 1998; Panerai et al., 2002) and in reducing self injurious behaviors (Norgate, 1998). Furthermore other studies found that TAECCH program was effective to ameliorate developmental abilities in children with autism even when started at different ages: 4.06 (±0.529; range: 3-5) years (Tsang et al., 2007), 9.09 (±2.07; range: 6-14) years (Panerai et al., 2009), 4.42 (±1.025; range: 3.6-5,8) years (Ozonoff and Cathcart, 1998); mean ages are reported.

## 2.3 Virtual environments[1]

Cybertherapy is the use of advanced technologies (such as Internet, virtual reality) to improve traditional forms of therapy (Wiederhold et al., 2004). Virtual Reality (VR) is a simulation of the real world, using computer graphics in which individual becomes

[1] Part of 2.3 section is modified by the paper published by Bellani M., Fornasari L., Chittaro L., Brambilla P. (2011) "Virtual reality in autism: state of the art", *Epidemiology and Psychiatric Sciences*, Vol. 20, no. 3, pp 235-238.

participant in the environment represented on the screen. The goal, in using VR is to promote behavioural responses in the virtual environments that are similar to real world (Bohil et al., 2011) and can be generalized to the real world. Virtual environments (VEs) makes a representation of the real world as we know it or it creates entirely new worlds, and provide experiences which could help the patients to understand some concepts and at the same time could help them to learn how to do some specific tasks, which can be repeated as many times as necessary (Chittaro and Ranon, 2007).

“Presence” is a very important concept when we use VR which means to feel more a part of the virtual environment. Two factors are important if we want to experience presence: the involvement, which can be defined as the state that people experience when they pay attention to some stimuli and which depends on the motivation level, and the immersion which is the perception to be involved in the environment. We also need to consider that VEs are more adequate for learning than for real environments because they (1) eliminate competing and confusing stimuli from the social and environmental context, (2) manipulate time using short pauses to explain to the participants the variables involved in the processes of interaction and (3) allow subjects to learn at the same time that they play (Vera et al., 2007).

Until not so long ago, head-mounted displays (HMDs) were generally used in VR to increase the sensation of immersion in the VE. Unfortunately, this solution was not only more expensive and less comfortable regarding normal and traditional computer screens, HMDs could also provoke ‘cyber-sickness’ (Parsons et al., 2004), the most frequent symptoms for them could be nausea, vomiting, headache, drowsiness, loss of balance and altered eye–hand coordination. However, VEs can also be visualized and explored by using a normal computer screen attached to a normal personal computer (desktop VEs).

The realism of the simulated environment permits the child to learn some important skills, making higher the probability to transfer them into the actions they do everyday (Strickland, 1997). In the desktop VE the user can move using simple input devices, such as a keyboard, a mouse, a joystick or a touchscreen, and interactions between child and therapist are also supported (Holden, 2005; Standen et al., 2002). Desktop VEs are less expensive and they are more accessible for educational use, and less susceptible to provoke symptoms of cyber-sickness.

### 2.3.1 Therapeutic Application

In two recent reviews (Bohil et al., 2011; Carvalho et al., 2010) were described therapeutic applications of VR.

VR has successfully been applied in three domains: psychiatric disorders, pain management and neurorehabilitation. The VR was used as an alternative to the techniques of cognitive-behavioural theory, such as exposure therapy (the pateint is exposed in vivo to anxiogenic stimuli in order to cause habituation and extinction of phobic responses) and imaginal therapy (the patient have to elaborate mental images that contein the stimuli that he consider anxiogenic). The VEs allowed therapist to adapt the level of exposure, based on the characteristics and needs of the patient. Several studies, using exposure in virtual environments, found good results for acrophobia, arachnophobia, aviophobia, agoraphobia, claustrophobia, fear of public speaking, fear of flyng, binge eating disorders, body image disturbance and post-traumatic stress disorders. Also in pain remediation there are VR applications, such as for analgesia and for patients with burns. Finally, the Bohil's review underlined the usefulness of the VR in neurorehabilitation. Using VEs allowed repetitive practice that can be useful in several areas such as balance disorders, postural and gait disorders, and recovery of function after stroke.

### 2.3.2 Virtual reality in Autism

VR can be a valid tool to habilitate children with autism improving quality of life of children with autism and their families. Using VR with children with autism is useful because (Strickland, 1997):

- Virtual environments can be simplified to the level of input stimuli tolerable by individual.
- Minimal modification across similar scenes may allow generalization and decreased rigidity.
- A virtual learning world provides a safer environment for developing skills associated with activities of daily living.
- Mistakes are less catastrophic and overall stimuli can be reduced or increased.
- Environments can be made progressively more complex until realistic scenes similar to the real world.
- VR used visual and auditory responses, rather than other senses such as touch, and many studies show a preference for visual stimuli, particularly those deliverd by computer screen (Mineo et al., 2009).
- Individuals with autistic disorders vary widely in their strengths and weaknesses. Using VR is possible create individualized treatment.

Thus it is important to develop tools in order to improve abilities in performing daily-life abilities in children with autism, because autism changes life of children with autism and their families (Newschaffer et al., 2007).

In this context, several studies have demonstrated potential benefits of VR for habilitation of children with autism (Bellani et al., 2011; Bölte et al., 2010; Mineo et al., 2009; Parsons et al., 2009; Wang and Reid, 2010) and in supporting the learning process (Ehrlich and Miller, 2009; Goodwin, 2008; Parsons and Mitchell, 2002; Strickland, 1997; Strickland et al., 1996).

The simulated environment, which does not seem to be experienced by children with autism in a different way from the controls (Wallace et al., 2010), allows the child to learn important skills, increasing the probability to transfer them into their everyday lives (McComas et al., 1998; Strickland, 1997).

Research has analyzed the ability of autistic children in using VEs and different studies showed that they acquire with great success new pieces of information from VEs. In particular, participants with ASD learned how to use the device very fast and demonstrated some very important improvements in required tasks (for example, to identify some objects or walk through some specific spaces in virtual scenes) after a few tests in the VE (Parsons et al., 2004; Strickland et al., 1996). Some more studies using VEs had the result that social skills (i.e. abilities to recognize and manifest emotions) improved after the VE intervention (Cheng and Ye, 2010; Mitchell et al., 2007; Moore, 2005) and that the competences acquired in VEs were transferred to the real word (Herrera et al., 2008). Two different studies, using desktop VEs as a tool for habilitation, have recently been done to teach children how to behave in social domains and how to interpret some social conventions (Herrera et al., 2008; Mitchell et al., 2007). The first study showed that by using a VE which reproduces a 'virtual cafe' to teach social skills, the speed of putting into practice the social task in the VE improved after the repetition of the task. The same study showed also an improvement of understanding social skills after the VE session. The second study used a VE that reproduces a 'virtual supermarket' with different exercises about use of objects. It was found that the actions carried out by the participants, as they were established from the result of some specific tests, increased after the VE intervention.

Some other studies were done by using collaborative virtual environments (CVEs) which support multiple simultaneous users, in particular the patient and the therapist. They can interact and communicate with each other through their avatars. CVEs have been used to examine and investigate the ability to recognize some emotions (Moore, 2005) as well as to improve social interaction, teaching students how to manifest and express their emotions and understand the emotions of other people (Cheng and Ye, 2010). Both these studies, after intervention, found a good performance in the task to identify emotions and an improvement in social performance. Table 2.1 summarized also other behavioural studies that used VR in individuals with autism.

In these reported studies, VEs were used as diagnostic and rehabilitation tools, but no studies on individuals with autism have yet focused specifically on understanding navigation and exploration, which are fundamental activities in using VEs.

Studies about exploratory behavior in children with autism in the real-world found a reduced environmental exploration, in terms of time spent in active exploration (Pierce and Courchesne, 2001) and atypical object exploration (Ozonoff et al., 2008). Further another study, carried out in a real experimental room found that with increasing visual complexity of the environment the time spent in exploration decreased (Kawa and Pisula, 2010).

Table 2.1: In this table are described behavioural studies investigating Virtual Reality in individuals with Autism. This table is modified by that published by Bellani M., Fornasari L., Chittaro L., Brambilla P. (2011) "Virtual reality in autism: state of the art", *Epidemiology and Psychiatric Sciences*, Vol. 20, no. 3, pp 235-238.

| **Study** | **Subjects (N)** | **Measures** | **Results** |
|---|---|---|---|
| Strickland *et al.,* (1996) | 2 patients, 7.5-9 years | Level of acceptance of head mounted display equipment, ability to fulfil task and concentrate on the VE (i.e: ability to identify cars and colors, when asked, in three different street scenes). | Children put on the helmets without any problem and completed the tasks properly (i.e they identified car colors correctly even when they were presented different street scenes). |
| Strickland, (1997) | 2 patients, 7.5-9 years | Level of acceptance of head mounted display equipment, ability to recognize a virtual object (i.e cars in street scene) and ability to look for and eventually find an object in a VE. | Children had no difficulty in using the VR equipment and their ability to carry out the task means that VR is useful as a learning tool (i.e both children identified car colors and found the hidden object). |
| Parsons *et al.,* (2004) | 36 subjects, 13-18 years : 12 (VIQ:68.9-PIQ:91.9), 12 (VIQ : 70.3), 12 (PIQ : 92.1) | Use and understand desktop VE (performance: time and errors made) in training trials and in a "Virtual Cafè". | Participants with ASDs learned how to use the equipment quickly and showed very important improvements in performance after some trials in the VE. |
| Parsons *et al.*, (2005) | 34 subjects, 13-18 years : 12 (VIQ:67.3-PIQ:88.4) 11 (VIQ : 68.5) 11 (PIQ : 89.9) | Determine if the participants apply some social rules like for example not walking on the grass in gardens and public places, or not walking between two people (performance, participant explanation of the routes they decide to take) during exploration desktop VEs. | Not many patients applied the social norms; others showed a considerable "off-task" behaviour and little understanding of the VE. |
| Moore *et al.,* (2005) | 34 patients, 7.8-16 years | Utility of Collaborative Virtual Environment for autistic children with and ability to recognize emotions (using tasks like for example recognizing the emotions expressed by the avatar, identifying the appropriate emotion which corresponds to the context or identifying the context in which to express a given emotion). | Most participants (30 of 34) were capable of using the avatars and to understand and recognize emotions in the correct way. |
| Mitchell *et al.*, (2007) | 7 patients, 14-16 years | To understand some social skills during sessions which represented on desktop a place like a "Virtual café", | Improved ability and quicker completion of different successive tasks' session during intervention. Improved ability in minimum |

| | | | |
|---|---|---|---|
| | | using tasks like for example "look for and find a place where to sit down". Video Measures: participants saw videos, Café or Bus, before and after intervention and they provided oral explanations of what they would have done if they were in a situation like the one proposed by the video. | 1 video in thinking and taking a decision about where to sit and choosing where to sit specifically after intervention. |
| Herrera *et al.,* (2008) | 2 patients, 8-15 years | Ability, using touchscreen, to understand the meaning of symbols and to use imagination (Virtual supermarket tool with tasks like for example "*I'm going to act as if…*" using specific tests to determine the increase in performance after intervention). | Performance is significantly improved after treatment for both children in functional, symbolic, imagination understanding. For one child, according to what parents have reported as well as professionals, the skills acquired were generalized to the external environment. |
| Cheng *et al.,* (2010) | 3 patients, 7-8 years | Social competence (recognition and expression of feelings; recognition of non-verbal behaviors; eye contact; proper manners, being able to listen to others) using a desktop VE which reproduces a "Virtual Classroom and Outdoor situation". | After the intervention, participant's performance in social competence improved, and for the two children this improvement persisted into follow-up (10 days after). |

VE: Virtual Environment, VR: Virtual Reality;
VIQ: Verbal Intelligent Quotient; PIQ: Performance Intelligent Quotient

# 3

# Research Design and Methodology

## 3.1 TEACCH and Virtual Environments for children with Autism[2]

In the previous chapter was thorough the literature about TEACCH and virtual environments. Two studies, on these two topics, have been conducted for this thesis.

The first was longitudinal study to evaluate the effectiveness of an oriented low-intensive TEACCH intervention, conducted in Italy.

The second study, using Virtual Environments (VEs), i.e. simulations of the real world based on 3D computer graphics, was made to analyzed navigation and exploration of an urban VE by children with autism compared to children with typical development.

---

[2] Based on these two studies, two papers "Twelve months of TEACCH oriented habilitation on an italian population of children with autism" by L. Fornasari, M. Garzitto, F. Fabbro, D. Londero, D. Zago, C. Desinano, S. Rigo, M. Molteni, P. Brambilla and "Navigation and exploration of a urban virtual environmen by children with autism" by L. Fornasari, L. Chittaro, L. Ieronutti, Lucio Cottini, Sebastiano Dassi, Massimo Molteni, Franco Fabbro, Paolo Brambilla have been prepared and are currently submitted and under review in international journals.

## 3.2 Objectives of the studies

In the first study we explored the effectiveness of our TEACCH inspired habilitation intervention in ameliorating developmental abilities in a sample of children with autism. Particularly we were interested in obtaining data about the best ages to start TEACCH intervention.

In the second, given the above mentioned promising results in the use of VEs (chapter 2), and the little knowledge available on environmental exploration and space preference in children with autism, the purpose of this paper was to analyze navigation of VEs in children suffering from autism compared to children with typical development. To date no studies on persons with autism have yet focused specifically on understanding navigation and exploration (which are fundamental activities in using VEs).

## 3.3 Study 1: Methods

### 3.3.1 Participants

Twenty-eight children with autism (age at baseline=50.25±18.18 months; range age=23-97 months; 23 males and 5 females) were treated with a psychoeducational treatment inspired by the TEACCH philosophy. Diagnoses were made according to the DSM-IV criteria and were confirmed by consensus meeting including a child psychiatrist and a child psychologist. Illness severity was determined by the Childhood Autism Rating Scale (CARS) (Schopler et al., 1986): four children showed moderate autism (CARS=35.75±1.66) and 24 severe autism (CARS=44.44±4.35). Non-Verbal Intelligence Quotient (nv-IQ) was determined using the Leiter-R (Roid et al., 1997) (nv-IQ=68.71±16.61, ranges=49-95) or the WISC-R scales (Wechsler, 1974) (nv-IQ=82.14±18.07, ranges=50-126). Only the Performance Scale was taken into account since the Verbal Scale score appeared not to be reliable for all subjects (Tsatsanis et al., 2003). None of the patients had comorbid ADHD, seizure disturbance or any other associated disorder known to support autistic features.

Children were recruited at “La Nostra Famiglia”, Scientific Institute IRCCS “E. Medea”, Pasian di Prato, Udine, which is a non-profit organization of social utility whose purpose is to promote and safeguard health care, education and services for people with special needs, in particular children and adolescents. There are 35 centers in Italy and abroad with about 2,000 health professionals and about 870,000 services per year, representing a unique national network for the diagnosis, treatment and rehabilitation of developmental disorders. In this context, the Scientific Institute IRCCS “E. Medea” was founded in 1985 by the “Associazione La Nostra Famiglia” to develop clinical research particularly in the field of child neuropsychiatry. To date the IRCCS "E. Medea" is the only Scientific Institute in Italy recognized for research and rehabilitation in childhood and adolescence (see http://www.emedea.it/).

In Italy children with disabilities are commonly integrated in regular schools with support teachers: all children who participated in the study attended public schools and lived with their own family.

The procedures were approved by the Ethics Committee of the Scientific Institute (IRCCS) Eugenio Medea.

### 3.3.2 Procedures and Materials

The approach used at the IRCCS “E. Medea” is a psychoeducational treatment inspired by the TEACCH philosophy. It was planned as follows: the daily program was clearly and easily communicated to children by means of pictures or drawings; space and environment were organized with concrete and visual references; activities and tasks were proposed with simple instructions. In particular, it consisted in a close collaboration between the Institute, the family and the school in order to provide specific indications for structuring the environment and organizing the work strategies at home and at school. In particular a psychologist administered five sessions of training for parents and met the teachers at least every 6 months to formally provide

operational guidance. Furthermore, the psycho-educationist and psychologist, met families and teachers several times during the treatment period to provide operational advices, according to the expressed needs. Furthermore, children attended individual TEACCH sessions, lasting 45 minutes each, at our Institute two times per week. The trained psycho-educationists individually treated each child mainly focusing on developmental skills. Cognitive-behavioural techniques were used, such as positive/negative reinforcement, physical/verbal prompts, task-analysis, physical block, token economy, auto-instruction, time out and hyper correction.
Our TEACCH habilitation intervention was evaluated with the developmental scale of the Psychoeducational Profile-Revised (PEP-R), at baseline and after six and 12 months, wich was administered by an educator who did not treat the child. It consists of a series of games and fun activities performed by the child with an examiner, who also records subject's responses. The PEP-R is composed by 131 items and can be divided in seven sub-scales related to the developmental abilities, i.e. Imitation, Perception, Fine Motor, Gross Motor, Eye-hand Coordination, Cognitive Performances and Verbal Performances. These subsacales provide together a cumulative Developmental Score. Also, a standardized Developmental Age is obtained by Developmental Score, using the appropriate conversion tables.
Scores can be divided into two categories: "passing", when the item is achieved, and "emerging", when the item is partially achieved. Emerging scores were used by educators to identify the targets developmental skills.

### 3.3.3 Statistical analysis

All statistical analyses were conducted using the SPSS for Windows software, version 15.0 (SPSS Inc., Chicago). A two-tailed significance level of $p<0.05$ was adopted. Raw scores and percentages of changes in PEP-R were analyzed.
To examine the effects of TEACCH on the PEP-R after six and 12 months, one way repeated measure analyses of variance and Sheffé's post hoc test were applied.

The changes of the PEP-R scores over time, considering the chronological age, were detected with a one way repeated measures analysis of variance and with a paired sample t-test for percentage improvements; Scheffé's post-hoc test was also applied.

## 3.4 Study 2: Methods

### 3.4.1 Participants

Sixteen children with autism were enrolled and diagnoses were made according to the DSM-IV-TR criteria, confirmed by consensus meeting including a child psychiatrist and a child psychologist. Children were recruited at "La Nostra Famiglia", Scientific Institute IRCCS "E. Medea", Pasian di Prato, Udine, and at the Child Neuropsychiatric Unit of the National Health Service of Udine, which are social service organizations that promote and protect health care, education and services for people with special needs, in particular children and adolescents. None of the patients had comorbid ADHD, seizure disturbance or any other associated disorder known to cause autism. Participants in control group were 1:1 matched to patients for age, sex, race, language, education and IQ as evaluated by means of the Raven Standard Progressive Matrices test (Raven, 1954). Exclusion criteria for controls included no significant medical or neuropsychiatric history and no major developmental disabilities. The two groups did not differ for age, educational level, IQ, parental education and occupational status as evaluated with the Hollingshead Scale of Socio-Economical Status (Barrat, 2006) (Table 3.1).

The procedures were approved by the Ethics Committee of the Scientific Institute (IRCCS) Eugenio Medea. Written informed consensus was obtained from parents.

### 3.4.2 Materials

To characterize the patients' disorder as compared to the controls several neuropsychological and clinical scales were administered (Table 3.2).

All participants completed the three selected subtest of the visuospatial domain of the NEPSY-II (Korkman et al., 1998; Korkman et al., 2007). The subtests selected were: Block Construction, to evaluate the visuospatial and visuomotor ability to reproduce three-dimensional constructions from models; Picture Puzzles, to assess visual discrimination, spatial localization, visual scanning and the ability to recognize part of a whole picture; Route Finding, to evaluate knowledge of visual spatial relations.
The Rey-Osterrieth Complex Figure Test (Osterrieth, 1944) was administered. This test asks to reproduce a complicated line drawing, first by copying it and then by recalling it in memory after a 3-minutes interval (the test provided two different scores for copy and memory, based on centiles scores). Two different versions of the age-appropriate test were used (figure Rey A for children aged nine years or above, figure Rey B for younger children). This test allow to evaluate different functions, such as visuospatial abilities, memory, attention, planning, and working memory (executive functions).
The Gillian Autism Rating Scale (GARS) (Gilliam, 1995) filled out by the parents, is a behavioral checklist. Items on the GARS are based on the definitions of autism adopted by the Autism Society of American and the *Diagnostic and Statistical Manual of Mental Disorders: Fourth Edition* (DSM-IV) (American Psychiatric Association. Task Force on, 1994). This scale provides an Autism Quotient, a standard score (M= 100, SD= 15), obtained from the sum of four subscales: Stereotyped behaviors, Communication, Social interaction e Developmental Disturbance. These scales measures the possibility that a child has autism.
Achenbach's Child Behavior Checklist for ages 6-18 (CBCL) (Achenbach et al., 2001) is a checklist used to evaluate a wide variety of behavioral problems, that are resumed by eight scales with T-scores ( M= 50, SD= 10). In our study it was compiled by the mothers of patients and controls.

The desktop VEs used in this research were built by the Human-Computer Interaction Laboratory (HCI Lab) of the University of Udine. VEs were run on a laptop computer and a mouse was employed to navigate them. Children, holding down the left mouse button, could move inside the VE and the movements of mouse –forward, side or back- allowed participants to orient themeselves in the VE.

There were two VEs; the first was a training environment that realistically reproduced the courtyard of a villa. Children entered through a gate in the garden that was surrounded by walls and in front there was a villa. Children could move in the garden, pass under the arcades and go up the stairs (see Figure 3.1 top). The second VE reproduced a small town; there were roads, surrounded by buildings, along which children could move to explore different zones, containing landmarks such as a fountain, buildings with arcades, a church, a baptistery. Two tasks were carried with this VE: the first ("free exploration") required to navigate and freely explore this unfamiliar urban environment (see Figure 3.1, bottom); the second ("treasure hunt") required to navigate the VE to find specific objects (parrots) (see Figure 3.2).

### 3.4.3 Procedure

Tasks were administered in a single experimental session, lasting 45 minutes. Clinical and neuropsychological scales were performed in a second session carried out within one week.

Before participants used the equipment, an experimenter explained and demonstrated how to use the training VE. The experimenter showed how to navigate the VE and then left children to freely explore it for a maximum of two minutes in order to make sure that children had understood the task and how to use the mouse.

After this period of familiarization, participants completed the "free exploration" and the "treasure hunt" experimental tasks, in the same order for all participants.

The instructions given by the experimenter were the same in the two tasks for all children. In "free exploration" task, the child was told to freely explore the environment, moving through the streets of the city, until he thought he had seen it entirely. In "treasure hunt" the experimenter, before beginning the task, showed the image of an object (parrot) on the computer screen and explained that there were 5 parrots to search for in the VE. The experimenter also explained how to select them when found: children had to click the object with the mouse and the object disappeared with a sound. Further for each objects found, the computer screen displayed a sign indicating how many items were left to search or if the task was completed. Every time these messages were read aloud by the experimenter to the child. The navigation in each VE could last up to 8 minutes, so as not to allow behavior persevering and cause strain on the children. The navigation was interrupted before the end of the 8 minutes if the child had found all the parrots.

### 3.4.4 Dependent Measures of VEs

The measures, listed below, were obtained using VU-Flow (Chittaro et al., 2006) a tool able to record users' movements in a VE and provide experimenters with visual abstract representations such as navigation paths followed by participants on the map of the VE or heat maps that indicate where in the VE participants walked most.

The VE reproduces an urban area whose size is 140x275.5 meters. To record positions and movements of subjects in the area, we have divided it in square cells, and the side of each cell is 0.444 meters long. As a result, the plane on which subjects walk is made of 315x620 cells that can detect his/her position.

Seven main measures were used in the present study:

- Number of Zones: Number of zones visited. The VE was divided into 11 areas (as shown in Figure 3.3).This measure was obtained by counting manually areas crossed at least once by the navigation path of each child.
- Walked-1: Number of cells of the map on which the child virtually walked at least once.
- Walked-2: Number of cells of the map on which the child virtually walked at least two times. This indicates on how many already visited cells the child went back at least one time.
- Stationary: time in seconds during which the child was standing still
- Moving: time in seconds during which the child was moving

- Length: total length of the walked path.
- Number of objects found: number of parrots found by children

### 3.4.5 Statistical analysis

All statistical analyses were conducted using SPSS for Windows, version 15.0 (SPSS Inc., Chicago). A two-tailed significance level of $p < 0.05$ was adopted. Raw scores and percentages of changes for each group were analyzed. One-way ANOVA was employed to compare the neuropsychological and clinical data of patients and controls, and to compare the seven navigation variables between the two groups, for “free exploration” and for “treasure hunt” tasks. Mann-Whitney test was employed to compare number of visited zones and number of objects found between the two groups. Paired sample t-tests were performed to compare each group between the two tasks. Furthermore, separate Pearson tests were performed to study possible correlations between performance in the two tasks, “free exploration” and “treasure hunt”, with NEPSY-II subtests and CBCL-ASD profile (correlations were adjusted by Bonferroni correction).

**Table 3.1** In this table are presented demographic information of patients and age matched controls.

| | Autistic Group | Control Group | | |
|---|---|---|---|---|
| | Mean | Mean | F | p |
| Age (years) | 9.56 | 9.69 | 0.03 | 0.86 |
| SES education | 11.72 | 11.88 | 0.02 | 0.90 |
| SES occupation | 21.72 | 23.12 | 0.16 | 0.69 |
| SES total | 33.44 | 35.13 | 0.17 | 0.68 |
| IQ (centile) SPM or PM47 Raven | 51.56 | 70.25 | 3.32 | 0.08 |

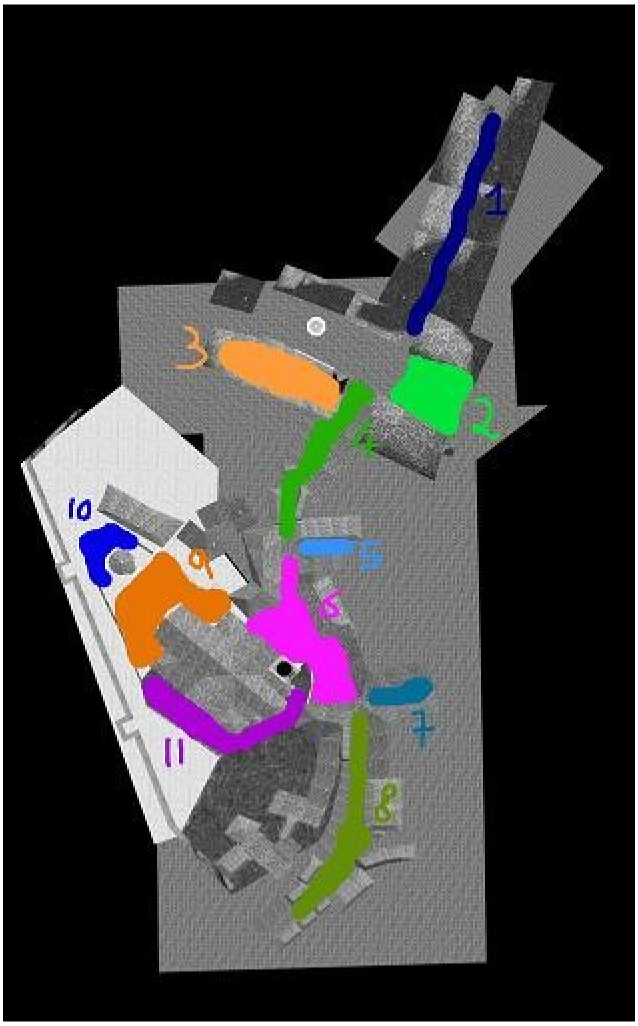
**Table 3.2** Clinical and neuropsychological information of patients and age matched controls. One-Way analysis of variance was performed (df=1,30)

| | Autistic Group | Control Group | | |
|---|---|---|---|---|
| | Mean | mean | F | p |
| Nepsy II (total) | 29.25 | 42.50 | 15.91 | **<0.001** |
| Nepsy II: Pictures Puzzles | 9.58 | 15.06 | 16.02 | **<0.001** |
| Nepsy II: Building Blocks | 13.07 | 18.19 | 8.22 | **0.007** |
| Nepsy II: Route Finding | 7.08 | 9.25 | 10.92 | **0.002** |
| Fig. Rey A or B Copy | 37.63 | 59.94 | 4.65 | **0.039** |
| Fig. Rey A or B memory | 25.19 | 48.38 | 3.92 | 0.06 |
| GARS Autism Quotient | 75.81 | 46.00 | 56.04 | **<0.001** |
| CBCL mother: Internalizing | 60.81 | 52.63 | 12.84 | **0.001** |
| CBCL mother: Externalizing | 51.69 | 48.16 | 0.92 | 0.35 |
| CBCL mother: Total Score | 61.31 | 49.09 | 17.06 | **<0.001** |
| CBCL mother:Anxious/Depressed | 58.25 | 55.16 | 1.72 | 0.20 |
| CBCL mother: Withdrawn/Depressed | 62.19 | 54.46 | 18.35 | **<0.001** |
| CBCL mother: Somatic Scales | 56.25 | 54.56 | 0.76 | 0.39 |
| CBCL mother: Social Problems | 63.31 | 53.27 | 38.80 | **<0.001** |
| CBCL mother: Thought Problems | 63.75 | 53.76 | 16.13 | **<0.001** |
| CBCL mother: Attention Problems | 64.19 | 56.06 | 8.63 | **0.006** |
| CBCL mother: Rule- Breaking Behavior | 54.69 | 52.95 | 0.64 | 0.43 |
| CBCL mother:Aggressive Behavior | 55.63 | 53.66 | 0.61 | 0.44 |
| CBCL-ASD Profile | 189.25 | 161.44 | 33.85 | **<0.001** |

**Figure 3.1** The VEs used in this study: map and pictures of VEs used in training VE (top) and in "free exploration" task (bottom).

**Figure 3.2** Pictures, taken from "treasure hunt" task, with parrots to find.

**Figure 3.3** Areas in which the virtual environment was divided.



# 4

# Results

## 4.1 Study 1: TEACCH Results

### 4.1.1 Effects of TEACCH on the PEP-R after 6 and 12 months

During the 12 month exposure to TEACCH training, children with autism showed gradual and significant improvement for all the developmental subscales at the PEP-R (all with $p<0.001$) as seen in table 4.1.
The specific changes over time of the PEP-R after the TEACCH intervention were also explored, with significant improvement for the Developmental Score and all the developmental subscales after six months and consistent progressive amelioration after 12 months (post-hoc: $p<0.05$), with the exception for the Perception subscale between six and 12 months ($p=0.210$). The emerging scores did not decreased significantly over time during the TEACCH habilitation both at six- and 12-month evaluation points (respectively $p=0.658$ and $p=0.252$).

### 4.1.2 Role of age on the TEACCH intervention over time

Three groups were created based on chronological age, Group-1: children under 40 months (N=9); Group-2: children between 40 months and 60 months (N=12); Group-3:

children over 60 months (N=7). There was no significant statistical difference between groups for illness severity, determined by the CARS ($F_{2,27}$=0.309, p=0.737) and for Non-Verbal Intelligence Quotient, determined with Leither-R or WISC-R ($F_{2,27}$=2.731, p=0.085). In order to compare developmental levels of subjects, Developmental Quotients were obtained, dividing PEP-R Developmental Ages by chronological ages (Delmolino, 2006); no significant differences between groups were found in Developmental Quotient at the baseline ($F_{2,27}$=1.192, p=0.320).
Repeated measures analysis of variance with time as the within subjects repeated factor and age as between-subjects factor was performed to explore the changes of the PEP-R over time in the three groups.

Total Developmental Score

Significant main effects of time ($F_{2,50}$=190.6, p<0.001) and of age ($F_{2,25}$=21.23, p<0.001) on the total Developmental Score were shown, with significant time by age interaction effect ($F_{4,50}$=4.29, p=0.005), as seen in figure 4.1.
Performance of the three groups increased with time and age (post hoc: p<0.05). In particular, time by age interaction effect showed that all groups had significant amelioration after 6 months and that Group-1 (<40 months) and Group-3 (>60 months) had significant better performance after six months (Group-1: p<0.001, Group-2: p<0.001, Group-3: p=0.003) while Group-2 (between 40 and 60 months) improved, also, between six and 12 months (p<0.001), as seen in table 4.2.
After 12 months, the increase of average values in Group-1, in comparison to the baseline values, showed a percentage increase of 180.11% on the Developmental Score (from a mean of 21.22 to a mean of 59.44; $t_8$=-7.12, p<0.001), in Group-2 of 118.30% (from 41.17 to 90.5; $t_{11}$=-15.85, p<0.001) and in Group-3 of 36.04% (from 80.86 to 110.00; $t_7$=-7.12, p<0.001) (paired sample t-test). Accordingly, the three groups significantly differed for the percentage changes of the Developmental Score after 12 months of habilitation treatment ($F_{2,25}$=5.15, p=0.013)

<u>Developmental subscales</u>

For all the PEP-R developmental subscales there was a significant main effect of time (Imitation: $F_{2,50}$=99.21, p<0.001; Perception: $F_{2,50}$=52.52, p<0.001; Fine Motor: $F_{2,50}$=119.8, p<0.001; Gross Motor: $F_{2,50}$=57.46, p<0.001; Eye-Hand Coordination: $F_{2,50}$=104.1, p<0.001; Cognitive Performances: $F_{2,50}$=116.78, p<0.001; Verbal Performance: $F_{2,50}$=39.23, p<0.001) and age (Imitation: $F_{2,25}$=2.24, p<0.001; Perception: $F_{2,25}$=26.35, p<0.001; Fine Motor: $F_{2,25}$=18.17, p<0.001; Gross Motor: $F_{2,25}$=19.57, p<0.001; Eye-Hand Coordination: $F_{2,25}$=27.13, p<0.001; Cognitive Performances: $F_{2,25}$=22.14, p<0.001; Verbal Performance: $F_{2,25}$=10.17, p<0.001). Performance of these dimensions improved significantly with time and age (Group-1 vs Group-2; Group-2 vs Group-3, Group-1 vs Group-3) (p<0.05, Scheffé's post-hoc test), with the exception of Perception (no significant differences after 6 months and 12 months, p=0.12), Gross Motor (no significant differences between Group-2 and Group-3, p=0.15) and Cognitive Verbal subscales (no significant differences between Group-1 and Group-2, p=0.41).

There was a significant time by age group interaction for three subscales, i.e. Perception ($F_{4,50}$=5.30, p=0.001), Gross Motor ($F_{4,50}$=3.08, p=0.024) and Cognitive Performance ($F_{4,50}$=3.76, p=0.009). Indeed, at the Scheffé's post-hoc test Group-1 and Group-2 (p<0.05), but not Group-3, significantly improved in all these three dimensions from baseline to 12 months. In contrast, Group-3 ameliorated only for Cognitive Performance from baseline to 6 month (p<0.05).

## 4.2 Study 2: navigation and exploration of a virtual environment

### 4.2.1 Neuropsychological and Clinical scales

The clinical and neuropsychological data of patients and controls are reported in Table 3.2. Average scores for autistic participants were lower than controls on all selected subtests of NEPSY-II. From a neuropsychological point of view, autism is very similar to the negative symptoms of schizophrenia (deficit of executive functions, language, movement and memory) (Cheung et al., 2010; King and Lord, 2011). Also in the copy in the Rey-Osterrieth Complex Figure Test average scores for autistic participants were lower than controls, while the difference for memory in this test was only close to significance. Children with autism had higher scores than controls in the GARS and in the Internalizing Scales and Total scales of the CBCL. The analysis of the CBCL subscales showed that patients had higher scores than controls on the Withdrawn/Depressed, Social Problems, Thought Problems and Attention Problems. The CBCL-ASD profile (Biederman et al., 2010) composed by the sum of the CBCL-Withdrawn, Social and Thought Problems scales was significantly higher in children with autism than controls.

### 4.2.2 Navigation in the "free exploration and "treasure hunt" tasks

The analysis of "free exploration" revealed significant differences between the two groups in Number of Zones ($F_{1,30}$=6.3, p=0.02, $\eta^2_p$=0.17) and in Moving ($F_{1,30}$=6.0, p=0.02, $\eta^2_p$=0.16), i.e. the children with autism visited fewer zones and spent less time moving in the VE than controls when the assigned task was to freely explore the environment. The Mann-Whitney test, carried out in each Zone, showed significant differences between the two groups in Zone 1 (U=80, Z=-2.41, p=0.02, r=-0.43). No other significant differences between the two groups were found for the other variables considered in "free exploration" task (Table 4.3). Interestingly, the difference between groups in the averages of Number of Zones and Moving decreased and was not statistically significant when the assigned goal was to find the parrots. More generally, no significant differences for any variable between patients and healthy subjects (Table 4.3) were found for the "treasure hunt" task. Lack of significant differences included also the number of items found by the two groups which was analyzed with a Mann-Withney test (U=97, Z=-1.36, p=0.19, r=-0.24).

Paired sample t-tests revealed no significant differences in children with autism between the two tasks ($-1.71 < t_{15} < 1.54$, p>0.10), whereas control subjects significantly differed for Moving ($t_{15}$=2.30, p=0.03) and Length ($t_{15}$=2.18, p=0.04) (Table 4.4).

### 4.2.3 Correlations

In “free exploration” positive correlations, which survived Bonferroni correction, were found in children with autism between the CBCL-ASD profile and Walked-2 (r=0.59, p=0.01) and Length values (r=0.612, p=0.01). The other scales did not correlate with performance variables in “free exploration” task ($-0.48 < r < 0.53$, $p > 0.03$).

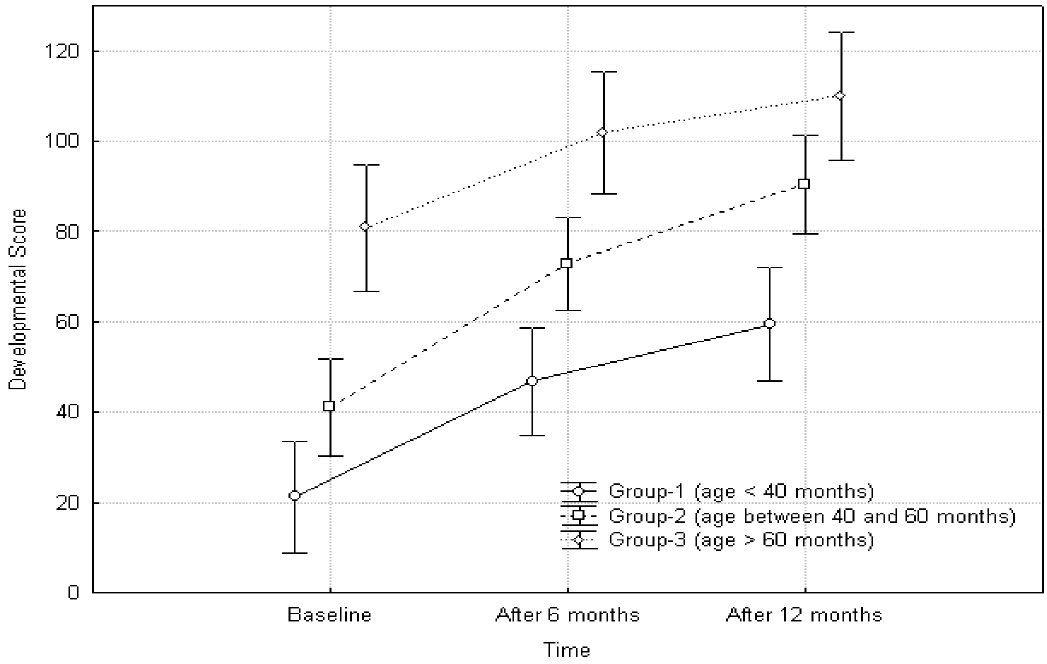
In “treasure hunt” a significant negative correlation between Route Finding of NEPSY-II and Stationary (r=-0.65, p=0.003) was found for children with autism. The other scales were not correlated with performance in “treasure hunt” task.

In “free exploration” as well as in “treasure hunt” tasks, no significant correlations were instead found between the controls’ seven VE measures and their individual scores in the NEPSY-II subtest and in the CBCL-ASD profile.

**Table 4.1** PEP-R scores over time after TEACCH intervention. Repeated measure analysis of variance was performed (df=2,54).

| PEP-R Scales | Baseline | 6-months | 12-months | F | p |
|---|---|---|---|---|---|
| N=28 | mean | Mean | mean | | |
| Imitation | 4.93 | 9.39 | 10.90 | 103.51 | **<0.001** |
| Perception | 7.96 | 11.01 | 11.73 | 49.76 | **<0.001** |
| Fine Motor | 6.96 | 10.42 | 11.94 | 119.73 | **<0.001** |
| Gross Motor | 9.89 | 13.89 | 15.45 | 58.59 | **<0.001** |
| Eye-Hand Coordination | 5.64 | 8.01 | 9.73 | 110.90 | **<0.001** |
| Cognitive Performance | 5.93 | 12.11 | 15.52 | 109.93 | **<0.001** |
| Verbal Performance | 3.39 | 5.92 | 9.56 | 42.15 | **<0.001** |
| Developmental Score | 44.68 | 71.75 | 85.39 | 175.71 | **<0.001** |
| Emerging Score | 13.36 | 12.29 | 10.32 | 3.48 | **0.038** |

**Figure 4.1** Developmental Score during the 12-month of TEACCH treatment for the three groups.




Vertical bars indicate 0,95 confidence intervals.

Group-1: children below 40 months of age; Group-2: children between 40 months and 60 months of age; Group-3: children over 60 months of age

**Table 4.2** Developmental Score changes in children below 40 months (Group-1), between 40 months and 60 months (Group-2) and over 60 months of age (Group-3). The Sheffé post-hoc test on time by age interaction was performed (df=31,622).

| Age | | Group-1 | | | Group-2 | | | Group-3 | | |
|---|---|---|---|---|---|---|---|---|---|---|
| N | | 9 | | | 12 | | | 7 | | |
| Time | | Base line | 6 month | 12 month | Base line | 6 month | 12 month | Base line | 6 month | 12 month |
| Mean | | 21.22 | 46.78 | 59.44 | 41.17 | 72.92 | 90.50 | 80.86 | 101.86 | 110.00 |
| Group-1 | Baseline | | <0.001 | <0.001 | 0.605 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| | 6 month | | | 0.137 | 0.999 | 0.243 | 0.003 | 0.115 | 0.001 | <0.001 |
| | 12 month | | | | 0.710 | 0.931 | 0.087 | 0.682 | 0.019 | 0.002 |
| Group-2 | Baseline | | | | | <0.001 | <0.001 | 0.021 | <0.001 | <0.001 |
| | 6 month | | | | | | 0.001 | 0.999 | 0.214 | 0.039 |
| | 12 month | | | | | | | 0.995 | 0.984 | 0.722 |
| Group-3 | Baseline | | | | | | | | 0.003 | <0.001 |
| | 6 month | | | | | | | | | 0.830 |
| | 12 month | | | | | | | | | |

**Table 4.3** Results of patients and controls on "free exploration" and "treasure hunt" One-Way analysis of variance was performed (df= 1,30)

| | Free exploration | | | | Treasure hunt | | | |
|---|---|---|---|---|---|---|---|---|
| | Autistic Group | Control Group | | | Autistic Group | Control Group | | |
| | Mean | mean | F | p | Mean | mean | F | p |
| Number Zones | 6.50 | 8.31 | 6.29 | **0.018** | 7.56 | 8.44 | 1.80 | 0.189 |
| Walked-1 | 11191.63 | 13563.19 | 3.61 | 0.067 | 10533.13 | 10593.94 | 0.00 | 0.963 |
| Walked-2 | 1422.63 | 1564.56 | 0.13 | 0.722 | 978.19 | 1087.88 | 0.05 | 0.821 |
| Stationary | 70.18 | 62.43 | 0.15 | 0.698 | 68.28 | 64.96 | 0.03 | 0.857 |
| Moving | 255.82 | 324.68 | 6.00 | **0.020** | 216.75 | 248.77 | 0.69 | 0.412 |
| Lenght | 1477.68 | 1711.92 | 1.28 | 0.267 | 1238.39 | 1277.19 | 0.03 | 0.87 |

**Table 4.4** Changes within each group from “free exploration” to “treasure hunt”. Paired sample t-test were performed (df= 15)

| | | Autistic Group | | | Control Group | | |
|---|---|---|---|---|---|---|---|
| | | Mean | t | p | Mean | t | p |
| Pair1 | N. Zones | 6.50 | -1.71 | 0.108 | 8.31 | -0.18 | 0.858 |
| | N. Zones | 7.56 | | | 8.44 | | |
| Pair2 | Walked-1 | 11191.63 | 0.61 | 0.553 | 13563.19 | | |
| | Walked-1 | 10533.12 | | | 10593.94 | 2.03 | 0.061 |
| Pair3 | Walked-2 | 1422.63 | 1.49 | 0.157 | 1564.56 | 1.64 | 0.122 |
| | Walked-2 | 978.19 | | | 1087.88 | | |
| Pair4 | Stationary | 70.18 | 0.29 | 0.774 | 62.43 | -0.34 | 0.735 |
| | Stationary | 68.28 | | | 64.96 | | |
| Pair5 | Moving | 255.82 | 1.54 | 0.144 | 324.68 | 2.30 | **0.030** |
| | Moving | 216.75 | | | 248.77 | | |
| Pair6 | Length | 1477.68 | 1.43 | 0.172 | 1711.92 | 2.18 | **0.040** |
| | Length | 1238.39 | | | 1277.19 | | |

# 5

# Discussion

## 5.1 Study 1: Discussion

This study shows that that early structured habilitation intervention (e.g. TEACCH) is effective in ameliorating developmental skills in autism, even when low intensively applied, with consistent and progressive improvements after six and 12 months. Our results are consistent with other studies, which reported that a 12-month TEACCH program is effective even when applied at home or school or when implemented with different operational criteria (number of meetings and duration of sessions per week) (Ozonoff and Cathcart, 1998; Panerai et al., 2002; Panerai et al., 2009). The literature provides some evidence that also treatment with low-intensive schedule can be effective for young children with autism in ameliorating adaptive skills (Peters-Scheffer et al., 2010). Another study that used an intensive 7-hours of TEACCH habilitation per day (Tsang et al., 2007) found that children with autism (N=18) aged between three and five years improved in all the PEP-R subscales after 12 months.

Moreover, our study found that children under 40 months of age had a better percentage improvement of the general developmental abilities compared to children who started the intervention later, as shown by significant increase of the

Developmental Score after 12 months. Furthermore, our study found a specific and progressive amelioration for perception, motricity and cognition in children undergoing the treatment before 60 months of age. In this regard, one prior study (Tsang et al., 2007) also showed that, in comparison to children with autism treated as usually, those treated by TEACCH significantly improved in Perception, Fine Motor and Gross Motor subscales. This is in line with our findings, suggesting that perception and motricity are the developmental abilities for which the TEACCH is particularly effective. Interestingly, other habilitation programs (i.e. ABA or Lovaas) are reported to be more effective when children with autism begin the interventions between 24-48 months of age (Howlin, 1998; Rogers, 1996; Sheinkopf and Siegel, 1998).

Therefore early identified children with autism will have better outcomes after habilitation interventions, as previously reported (Baird et al., 2001; Iverson and Wozniak, 2007; Zwaigenbaum et al., 2005). It is then mandatory to begin the habilitation training in autism as early as possible in order to maximize the effectiveness of the program.

Some limitations should be kept in mind when considering this study. First, it should be noted that children of present research were not randomized and thus the lack of a control group composed by children with autism not treated with TEACCH might be a limitation. However, this could not be performed for ethical reasons, indeed all the children with autism referring to our Centre attend the TEACCH habilitation intervention. Second, it could not completely be ruled out the role of neurodevelopment in improving abilities in our patient population, although it is clear that early intervention lead to better efficacy. Third, relatively small sample size may have limited the generalizability of the results. Future studies should involve larger numbers of children with autism on TEACCH program at different ages and assess the longitudinal behavioral changes with the PEP-R. Some strength should also be kept in mind. First, this study was longitudinally designed based on a two step evaluation at six and 12 months. Second, the PEP-R scale was independently administered and scored by an independent psycho-educationist who did not treat the child.

In conclusion, our study found that developmental abilities in autism improved over a 12-month period of TEACCH habilitation, particularly for children under 40 months of age. In particular, a better outcome for perception, motricity and cognition was shown for children undergoing the program before 60 months of age. Future imaging studies should investigate the structural and functional neural substrates related to the amelioration of these dimensions resulting after treatment

## 5.2 Study 2: Discussion

The aim of this study was to make an analysis of how children with autism navigated and explored virtual environments in comparison to children with typical development. Differences in Number of Zones and in Moving were found in the "free exploration" task that were both lower in children with autism than in the control group. Moreover, the two groups differed in the number of visits to Zone 1, which was lower for children with autism. An aspect that distinguishes Zone 1 from other areas of the VE is that it has a single entrance which is not clearly visible, and therefore it requires a more accurate visual analysis of the VE by the participants in order to detect it.

It is worth of noting that the results stated above, which were obtained by free exploration of a virtual environment, are compatible with some studies (Kawa and Pisula, 2010; Pierce and Courchesne, 2001), conducted on children with autism, that analyzed real-world environment exploration. Especially, using respectively one or three rooms with objects distributed throughout the room, these studies found that children with autism spent significantly less time in active exploration and explored fewer objects than a control group. Moreover, Kawa found that the time spent in exploration diminished when there was a greater visual complexity of the environment (Kawa and Pisula, 2010).

In our study, the CBCL-Autism Spectrum Disorders (ASD) profile, obtained by adding Withdrawn, Social and Thought Problems scales, showed a positive significant correlation with Walked-2 and Length measures. Thus, children with higher CBCL-ASD profile traveled for longer distances (Length) and the number of cells of the map on which they repeatedly walked (at least two times) was higher. Interestingly, the correlation between CBCL-ASD profile and Walked-2 confirmed that the main symptoms of autism, such as restricted patterns of interest and repetitive and stereotyped movements, affected the exploration of the unknown urban VE.

Therefore, our results in the "free exploration" task and their similarity with the results found in real environments by other authors, could suggest that free exploration of an unfamiliar environment by children with autism has similar characteristics in virtual and real environments. Reduced exploration of children with autism in "free exploration", furthermore, could be associated with clinical aspects, as seen by the correlations with CBCL subscales.

During the "treasure hunt" task, which was done after "free exploration", no significant differences in VE measures between the two groups were found. There were no significant differences in the number of objects found by the two groups either. This result was different from the one that Vernazza-Martin had obtained (Vernazza-Martin et al., 2005) who had explored goal-directed locomotion in children with autism, by using an environment which was real (a psychometric room) and had found that children with autism were impaired, in comparison to the children in the control group, in achieving the experimenter-imposed goal. In particular, the study came to the conclusion that children with autism were impaired in planning their movements and this problem was caused by typical executive dysfunction in autism, e.g. attention, planning and inhibition. (e.g. attention, planning and inhibition) in autism.

Our results suggest that "treasure hunt" was explored in a more targeted and strategic way by both groups. In our study, significant differences were found between the two tasks in control groups, with a reduction in time during which the child moved (Moving) and in total length of the walked path (Length). Also, children with autism showed a reduction for these two measures in "treasure hunt", although lower than the control group (8.04% vs 21.57% for Moving; 2.95% vs 20,51% for Length, respectively).

The improvement found in "treasure hunt" task in both groups can be explained by two factors.

The first one is that we could make a hypothesis that exploring a virtual environment which has already been visited could have helped also autistic children in reducing their differences in performance in regards to control group. This hypothesis is also backed by the fact that other authors have found that performance of children with autism got better after repetition using VEs (Mitchell et al., 2007; Parsons et al., 2004). Moreover, in "treasure hunt" task, a negative correlation was found between Route Finding of NEPSY-II and Stationary. Route Finding subtest of visual spatial domain was designed to determine the knowledge of visual spatial relations and directionality, as well as the ability to use this knowledge to transfer a route from a simple schematic map to a more complex one. Thus, children with autism, who were more capable in this subtest, spent lower time standing still in the VE.

The second factor concerns the formulation of the exploration goal as a game in the "treasure hunt" task which could have increased the motivation of autistic children.

Several studies reported that in persons with autism there are visual strenghts, also in visual search tasks (Joseph et al., 2009; Samson et al., 2011); preference for visual stimuli, especially if proposed by VR applications, has been noted (Mineo et al., 2009). The ability to think visually are reported in autism (Grandin, 2009) supporting the ability to search parrots in our task. Especially, a study which is based on the fact that volition is the most important aspect in getting people to enroll in tasks, showed that, in children with cerebral palsy, VR created this type of volition and therefore it enhanced motivation (Harris and Reid, 2005). Moreover, that research underlined some elements such as variation in the game, level of engagement required by the task and competition during VR that may increase the volition. In our task, stating the goal as a game, could have also contribute to increase the level of engagement required because children had to use a strategy.

Two limitations should be taken into consideration in this study. The first one is that future studies should involve larger numbers of subjects because the relatively small sample size in this study may have reduced the generalizability of the data obteined .
The second is that although the navigation in "treasure hunt" was more strategic and targeted, it cannot be completely ruled out whether the repetition of the navigation or the formulation of the exploration goal as a game was more efficient.

# 6

# Final Conclusions

## 6.1 Autistic Disorder

As stated before, the degree of impairment in autism can vary greatly among individuals. Nonetheless Autistic Disorder is universally life-altering for both the affected person and their family (Newschaffer et al., 2007).

Despite this, more intervention research is still needed in order to improve autistic's treatment protocols, as well as to give more helpful indications to caregivers and educators who deal with children with autism in their everyday life. Autism is a permanent disability (Cottini, 2010) that follows a person throughout their lifetime, even though the characteristic social deficits may vary as time passes by. The majority of the current researches focused on epidemiology, genetics, and neuroscience providing critical data for understanding the cause and course of this syndrome, but very little of this information translates into practice for individuals who currently have a diagnosis of autism (Goodwin, 2008).

Now, it is important to integrate the previous knowledge with investigations aimed to implement interventions designed on the strengths and needs of affected children, allowing to improve effectively their daily life.

### 6.1.1 Autism and early intervention

Despite the heterogeneity of autism spectrum, there is spreading consent that rehabilitation is much more effective if it starts at an early age. In fact, it was proved that the prognosis for children with autism is more favorable in case of an early rehabilitative intervention. The importance of early identification is increasingly stressed and many studies showed that children with autism receiving services prior to 48 months of age improve more than those who enter programs later (Corsello, 2005; Sheinkopf and Siegel, 1998). Therefore making an early diagnosis is essential in order to start rehabilitation as soon as possible.
Clear indicators can allow therapist to make an early diagnosis, even before a child is 2-3 years old and, in this direction, tools for early diagnosis, e.g. the M-CHAT, (Robins et al., 2001) are increasingly developing.

### 6.1.2 Autism and computers

Computers are becoming largely used in treatment of ASD, as they generally catch the interest and are highly motivating in many people with autism. Therefore emerging technologies carry great potential for providing innovative and individualized interventions. Using computers for learning has many advantages with ASD children (Murray, 1997).
Despite the increased popularity of structured learning programs aimed at ASD individuals, many of the skills acquired during those trainings fail to generalize to novel environments. However, differently from other computer tasks, virtual reality may lead to learning that is generalized to novel real situations, in virtue of some similarities that it shares with the real external world.

## 6.2 Our studies

The purpose of the present work was to examine two different habilitation techniques in ASD children.

Two studies had been carried out.

In the first longitudinal study we evaluated the efficacy and the age at which it was more effective to start a low-intensive TEACCH- oriented intervention.

Twenty-eight children with autism were treated two times per week following a procedure inspired by the TEACCH intervention guidelines. Developmental abilities were assessed at baseline and after six and twelve months using the PEP-R scale. A significant improvement during the first 6 months and a progressive amelioration throughout the 12-month follow-up period were obtained. This was particularly evident in children below 40 months of age. Also, perception, motricity and cognition improved only in those children with autism who begun the program earlier than 60 months of age.

These results showed that early low-intensive TEACCH habilitation had an effective positive impact on autism' developmental abilities, especially if it was started at the very first stages of the disease. This suggests the importance to administer the habilitation program when the first autistic manifestation appears in order to maximize its effectiveness.

The second study compared children with autism to a control sample of children with typical development in a task implying navigation and exploration of an urban Virtual Environment, and specifically focused on understanding of navigation and exploration in children with autism.

Sixteen children with autism and 16 controls matched for age, sex, race, language, education and IQ took part in the study. After an initial training phase, children carried out two tasks: 1) navigation in an unfamiliar urban environment that children could freely explore; 2) navigation in the same environment with the goal to find specific target objects as in a treasure hunt.

In the first task children with autism spent significantly less time in active exploration, also exploring fewer zones than controls. However no differences emerged between the two groups in the second task, when children had to find objects.
Results suggest that children with autism poorly explore raw unfamiliar environments, while they tend to be more motivated and active when stimulated by a task that is structured as a game.

## 6.3 Future developments

The TEACCH habilitation method is comonly adopted in many Italian clinical structures and services and, as described in previous sections of the present work, many studies published in literature support the effectiveness of this technique.
Our study raised the hypothesis that this education model has a more favourable impact on autistic developmental abilities if started at the first stages of the disorder onset, as suggested by the PEP-R assessment.
Despite its increasingly diffusion as a diagnostic and rehabilitation device, at the best of our knowledge, in Italy the potential applications of virtual reality in Autistic Disorder has been poorly studied and was not adopted in clinical practice. The second our study indeed investigated the navigation pattern in virtual reality environment in children with autism and pointed out that the task repetition, a reduction in visual complexity and proposing the task as a game can be useful to improve their performance in virtual environments. The present work could be further developed in the next future, e.g. building virtual environments tailored on the children with autism need, to promote competences that can be generalized to everyday life, as social interaction skills.

As pointed out earlier, autism implies a change in lifestyle for the affected children and their families. For this reason it becomes very important to investigate new habilitation techniques that have immediate therapeutic applications.

Introducing new technologies do not represent the ultimate alternative to psychotherapeutic and rehabilitation methods, but an approach integrating new and traditional strategies can facilitate the habilitation process (Riva et al., 2002).

Currently, VR is used as an alternative to cognitive-behavioural thechniques (exposure therapy and imaginal therapy) in treating several disorders in adult patient (phobia, eating disorders, body image disturbance, post-traumatic stress disorders) (Carvalho et al., 2010) but also in children with autism, attention deficit hyperactivity disorder and cerebral palsy were performed (Wang and Reid, 2010).

In our work TEACCH and VEs were used separately but it will be useful to create navigation programs in the context of a TEACCH model in autism, where intact or superior visuospatial abilities have been found (Caron et al., 2006; Manjaly et al., 2007). In addition, persons with autism have some other neuropsychological features, such as attention to detail, communication problems, concrete thinking and difficulties in organizing, sequencing and generalizing. In this regard, TEACCH takes into account all of this, which can be called "Culture of Autism" (Mesibov and Shea, 2010). Also VR, provides an environment with low complexity of stimulation and a safe, which is ideal for autism since it helps in controlling the external stimuli and in promoting the generalization of aquired skills.

The TEACCH core characteristic is that any intervention is modulated according to the specific needs of each autistic child, and virtual reality navigation programs allows a similar modulation.

The aim of our future research will be teaching social skills modalities using interactive situations, displayed using virtual reality or video modeling intervention, with the aim to create a model of integrate intervention for children with autism.

# References

Achenbach, TM, Rescorla, LA, Achenbach System of Empirically Based, A (2001) *Manual for the ASEBA School-Age: Forms & Profiles.* ASEBA.

American Psychiatric Association (2000) *Diagnostic and statistical manual of mental disorders: DSM-IV-TR.* Washington: APA Publishing.

American Psychiatric Association. Task Force on, D-I (1994) Diagnostic and Statistical Manual of mental Disosrder (4th ed.) Washington, DC: American Psychiatric association Press.

Bailey, A, Le Couteur, A, Gottesman, I, Bolton, P, Simonoff, E, Yuzda, E, Rutter, M (1995) Autism as a strongly genetic disorder: evidence from a British twin study. *Psychological medicine,* 25(1): 63-78.

Bailey, DB, Simeonsson, RJ, Winton, PJ, Huntington, GS, Comfort, M, Isbell, P, O'Donnell, KJ, Helm, JM (1986) Family-focused intervention: A functional model for planning, implementing, and evaluating individualized family services in early intervention. *Journal of Early Intervention,* 10(2): 156-171.

Baird, G, Charman, T, Cox, A, Baron-Cohen, S, Swettenham, J, Wheelwright, S, Drew, A (2001) Screening and surveillance for autism and pervasive developmental disorders. *Archives of Disease in Childhood,* 84(6): 468-475.

Baron-Cohen, SE, Tager-Flusberg, HE, Cohen, DJ (2000) *Understanding other minds: Perspectives from developmental cognitive neuroscience.* Oxford University Press.

Barrat, W (2006) The Barrat Simplified Measure os Scoial Status (BSMSS) measuring SES. *Unpublished manuscrit. Indiana State Univesity, available at http://wbarratt.indstate.edu/socialclass/Barratt_Simplified_Measure_of_Social_Status.pdf.*

Barthelemy, C, Hameury, L, Lelord, G (1995) *L'autisme de l'enfant. La Thérapie d'Echange et de développment.*: Elsevier Masson.

Bellani, M, Fornasari, L, Chittaro, L, Brambilla, P (2011) Virtual reality in autism: state of the art. *Epidemiology and Psychiatric Sciences,* 20(03): 235-238.

Bettelheirn, B (1967) The empty fortress. New York: Free Press.

Biederman, J, Petty, CR, Fried, R, Wozniak, J, Micco, JA, Henin, A, Doyle, R, Joshi, G, Galdo, M, Kotarski, M (2010) Child Behavior Checklist Clinical Scales Discriminate Referred Youth With Autism Spectrum Disorder: A Preliminary Study. *Journal of Developmental & Behavioral Pediatrics,* 31(6): 485-490.

Bohil, CJ, Alicea, B, Biocca, FA (2011) Virtual reality in neuroscience research and therapy. *Nature Reviews Neuroscience,* Published online(doi:10.1038/nrn3122).

Bölte, S, Golan, O, Goodwin, M, Zwaigenbaum, L (2010) What can innovative technologies do for Autism Spectrum Disorders? *Autism : the international journal of research and practice,* 14(3): 155-159.

Bolton, P, Macdonald, H, Pickles, A, Rios, P, Goode, S, Crowson, M, Bailey, A, Rutter, M (1994) A case control family history study of autism. *Journal of Child Psychology and Psychiatry,* 35(5): 877-900.

Brambilla, P, Hardan, A, di Nemi, SU, Perez, J, Soares, JC, Barale, F (2003) Brain anatomy and development in autism: review of structural MRI studies. *Brain Research Bulletin,* 61(6): 557-569.

Brambilla, P, Hardan, AY, di Nemi, SU, Caverzasi, E, Soares, JC, Perez, J, Barale, F (2004) The functional neuroanatomy of autism. *Functional neurology,* 19(1): 9-17.

Canitano, R (2007) Epilepsy in autism spectrum disorders. *European child & adolescent psychiatry,* 16(1): 61-66.

Caron, MJ, Mottron, L, Berthiaume, C, Dawson, M (2006) Cognitive mechanisms, specificity and neural underpinnings of visuospatial peaks in autism. *Brain,* 129(7): 1789-1802.

Carvalho, MRD, Freire, RC, Nardi, AE (2010) Virtual reality as a mechanism for exposure therapy. *World Journal of Biological Psychiatry,* 11(2_2): 220-230.

Chakrabarti, S, Fombonne, E (2001) Pervasive developmental disorders in preschool children. *JAMA: the journal of the American Medical Association,* 285(24): 3093-3099.

Cheng, Y, Ye, J (2010) Exploring the social competence of students with autism spectrum conditions in a collaborative virtual learning environment-The pilot study. *Computers & Education,* 54(4): 1068-1077.

Cheung, C, Yu, K, Fung, G, Leung, M, Wong, C, Li, Q, Sham, P, Chua, S, McAlonan, G (2010) Autistic disorders and schizophrenia: related or remote? An anatomical likelihood estimation. *PloS one,* 5(8): e12233.

Chittaro, L, Ranon, R (2007) Web3D technologies in learning, education and training: Motivations, issues, opportunities. *Computers & Education,* 49(1): 3-18.

Chittaro, L, Ranon, R, Ieronutti, L (2006) VU-Flow: a visualization tool for analyzing navigation in virtual environments. *IEEE Transactions on Visualization and Computer Graphics,* 12(6): 1475-1485.

Corsello, CM (2005) Early intervention in autism. *Infants & Young Children,* 18(2): 74-85.

Cottini, L (2010) L'autismo non è solo infantile. *Autismo e Disturbi dello Sviluppo,* 8(1): 65-99.

Cox, RD, Schopler, E (1993) Aggression and self-injurious behaviors in persons with autism: The TEACCH approach. *Acta Paedopsychiatrica: International Journal of Child & Adolescent Psychiatry,* 56(2): 85-90.

Delmolino, LM (2006) Brief Report: Use of DQ for estimating cognitive ability in young children with autism. *Journal of Autism and Developmental Disorders,* 36(7): 959-963.

Ehrlich, JA, Miller, JR (2009) A virtual environment for teaching social skills: AViSSS. *IEEE computer graphics and applications,* 29(4): 10-16.
Faras, H, Al Ateeqi, N, Tidmarsh, L (2010) Autism spectrum disorders. *Annals of Saudi medicine,* 30(4): 295-300.
Fombonne, E (2005) Epidemiology of autistic disorder and other pervasive developmental disorders. *The Journal of clinical psychiatry,* 66: 3-8.
Fombonne, E (2009) Epidemiology of pervasive developmental disorders. *Pediatric research,* 65(6): 591-598.
Geschwind, DH (2009) Advances in autism. *Annual review of medicine,* 60: 367-380.
Gilliam, JE (1995) *Gilliam Autism Rating Scale.*: TX: Pro-ed.
Goodwin, MS (2008) Enhancing and Accelerating the Pace of Autism Research and Treatment. *Focus on Autism and Other Developmental Disabilities,* 23(2): 125-128.
Grandin, T (2009) How does visual thinking work in the mind of a person with autism? A personal account. *Philosophical Transactions of the Royal Society B: Biological Sciences,* 364(1522): 1437-1442.
Greenspan, SI, Wieder, S (1999) A functional developmental approach to autism spectrum disorders. *Research and Practice for Persons with Severe Disabilities,* 24(3): 147-161.
Happe, F, Frith, U (1996) The neuropsychology of autism. *Brain,* 119: 1377-1400.
Harris, K, Reid, D (2005) The influence of virtual reality play on children's motivation. *Canadian Journal of Occupational Therapy,* 72(1): 21-29.
Harris, SL, Handleman, JS (2000) Age and IQ at intake as predictors of placement for young children with autism: A four-to six-year follow-up. *Journal of Autism and Developmental Disorders,* 30(2): 137-142.
Herrera, G, Alcantud, F, Jordan, R, Blanquer, A, Labajo, G, De Pablo, C (2008) Development of symbolic play through the use of virtual reality tools in children with autistic spectrum disorders. *Autism,* 12(2): 143-157.
Holden, MK (2005) Virtual environments for motor rehabilitation: review. *Cyberpsychology & behavior,* 8(3): 187-211.
Howlin, P (1998) Practitioner review: psychological and educational treatments for autism. *Journal of Child Psychology and Psychiatry,* 39(3): 307-322.
Iverson, JM, Wozniak, RH (2007) Variation in vocal-motor development in infant siblings of children with autism. *Journal of Autism and Developmental Disorders,* 37(1): 158-170.
Joseph, RM, Keehn, B, Connolly, C, Wolfe, JM, Horowitz, TS (2009) Why is visual search superior in autism spectrum disorder? *Developmental science,* 12(6): 1083-1096.
Kawa, R, Pisula, E (2010) Locomotor activity, object exploration and space preference in children with autism and Down syndrome. *Acta neurobiologiae experimentalis,* 70(2): 131-140.
Kemper, TL, Bauman, M (1998) Neuropathology of infantile autism. *Journal of neuropathology and experimental neurology,* 57(7): 645-652.
King, BH, Lord, C (2011) Is schizophrenia on the autism spectrum? *Brain research,* 1380: 34-41.
Kinney, DK, Munir, KM, Crowley, DJ, Miller, AM (2008) Prenatal stress and risk for autism. *Neuroscience & Biobehavioral Reviews,* 32(8): 1519-1532.

Korkman, M, Kirk, U, Kemp, S (1998) *NEPSY : A Developmental Neuropsychological Assessment.* Psychological Corporation.
Korkman, M, Kirk, U, Kemp, S (2007) NEPSY-II: Clinical and interpretive manual. *San Antonio, TX: The Psychological Corporation*.
Krug, DA, Arick, JR, Almond, PJ (1979) Autism screening instrument for educational planning: Background and development. *Autism: Diagnosis, Instruction, Management and Research. University of Texas: Austin*.
Lasalvia, A, Tansella, M (2009) Childhood trauma and psychotic disorders: evidence, theoretical perspectives, and implication for interventions. *Epidemiologia e psichiatria sociale,* 18(4): 277-283.
Lord, C, Risi, S, Lambrecht, L, Cook, EH, Leventhal, BL, DiLavore, PC, Pickles, A, Rutter, M (2000) The Autism Diagnostic Observation Scheduleâ€"Generic: A standard measure of social and communication deficits associated with the spectrum of autism. *Journal of Autism and Developmental Disorders,* 30(3): 205-223.
Lord, C, Rutter, M, Couteur, A (1994) Autism Diagnostic Interview-Revised: a revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *Journal of Autism and Developmental Disorders,* 24(5): 659-685.
Losh, M, Childress, D, Lam, K, Piven, J (2008) Defining key features of the broad autism phenotype: A comparison across parents of multiple-and single-incidence autism families. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics,* 147(4): 424-433.
Lovaas, OI (1979) Contrasting illness and behavioral models for the treatment of autistic children: A historical perspective. *Journal of Autism and Developmental Disorders,* 9(4): 315-323.
Lovaas, OI, Ackerman, A, Alexander, D, Firestone, P, Perkins, J, Young, D (1981) *Teaching developmentally disabled children: The me book.* Pro-ed Austin^ eTX TX.
Manjaly, ZM, Bruning, N, Neufang, S, Stephan, KE, Brieber, S, Marshall, JC, Kamp-Becker, I, Remschmidt, H, Herpertz-Dahlmann, B, Konrad, K (2007) Neurophysiological correlates of relatively enhanced local visual search in autistic adolescents. *Neuroimage,* 35(1): 283-291.
McComas, J, Pivik, P, Laflamme, M (1998) Current uses of virtual reality for children with disabilities. *Studies in health technology and informatics,* 58: 161-169.
Mengotti, P, D'Agostini, S, Terlevic, R, De Colle, C, Biasizzo, E, Londero, D, Ferro, A, Rambaldelli, G, Balestrieri, M, Zanini, S (2010) Altered white matter integrity and development in children with autism: a combined voxel-based morphometry and diffusion imaging study. *Brain Research Bulletin,* 84(2): 189-195.
Mesibov, GB, Shea, V (2010) The TEACCH program in the era of evidence-based practice. *Journal of Autism and Developmental Disorders,* 40(5): 570-579.
Mineo, BA, Ziegler, W, Gill, S, Salkin, D (2009) Engagement with electronic screen media among students with autism spectrum disorders. *Journal of Autism and Developmental Disorders,* 39(1): 172-187.
Minshew, NJ, Payton, JB (1988) New perspectives in autism, Part I: The clinical spectrum of autism. *Current problems in pediatrics,* 18(10): 561-610.

Minshew, NJ, Sweeney, JA, Bauman, ML (1997) Neurological aspects of autism. *Handbook of autism and pervasive developmental disorders,* 2: 344-369.

Mitchell, P, Parsons, S, Leonard, A (2007) Using virtual environments for teaching social understanding to 6 adolescents with autistic spectrum disorders. *Journal of Autism and Developmental Disorders,* 37(3): 589-600.

Moore, D (2005) Collaborative virtual environment technology for people with autism. *Focus on Autism and Other Developmental Disabilities,* 20(4): 231-243.

Murray, D (1997) Autism and information technology: therapy with computers. *Autism and learning: a guide to good practice*: 100-117.

National Research Council . Committee on Educational Interventions for Children with, A (2001) *Educating children with autism.* National Academies Press.

Newschaffer, CJ, Croen, LA, Daniels, J, Giarelli, E, Grether, JK, Levy, SE, Mandell, DS, Miller, LA, Pinto-Martin, J, Reaven, J (2007) The epidemiology of autism spectrum disorders*. *Annu. Rev. Public Health,* 28: 235-258.

Norgate, R (1998) Reducing Self Injurious Behaviour in a Child with Severe Learning Difficulties. *Educational Psychology in Practice,* 14(3): 176-182.

O'Roak, BJ (2008) Autism genetics: strategies, challenges, and opportunities. *Autism Research,* 1(1): 4-17.

Osterrieth, PA (1944) Le test de copie d'une figure complexe. *Archives de psychologie,* 30: 206-356.

Ozonoff, S (1997) Components of executive function in autism and other disorders. *Autism as an executive disorder*: 179-211.

Ozonoff, S, Cathcart, K (1998) Effectiveness of a home program intervention for young children with autism. *Journal of Autism and Developmental Disorders,* 28(1): 25-32.

Ozonoff, S, Macari, S, Young, GS, Goldring, S, Thompson, M, Rogers, SJ (2008) Atypical object exploration at 12 months of age is associated with autism in a prospective sample. *Autism,* 12(5): 457.

Panerai, S, Ferrante, L, Caputo, V (1997) The TEACCH strategy in mentally retarded children with autism: a multidimensional assessment. Pilot study. Treatment and Education of Autistic and Communication Handicapped children. *Journal of Autism and Developmental Disorders,* 27(3): 345-347.

Panerai, S, Ferrante, L, Caputo, V, Impellizzeri, C (1998) Use of Structured Teaching for Treatment of Children with Autism and Severe and Profound Mental Retardation. *Education and Training in Mental Retardation and Developmental Disabilities,* 33(4): 367-374.

Panerai, S, Ferrante, L, Zingale, M (2002) Benefits of the Treatment and Education of Autistic and Communication Handicapped Children (TEACCH) programme as compared with a non specific approach. *Journal of Intellectual Disability Research,* 46(4): 318-327.

Panerai, S, Zingale, M, Trubia, G, Finocchiaro, M, Zuccarello, R, Ferri, R, Elia, M (2009) Special education versus inclusive education: the role of the TEACCH program. *Journal of Autism and Developmental Disorders,* 39(6): 874-882.

Pardo, CA, Eberhart, CG (2007) The neurobiology of autism. *Brain Pathology,* 17(4): 434-447.

Parmeggiani, A, Posar, A, Antolini, C, Scaduto, MC, Santucci, M, Giovanardi-Rossi, P (2007) Epilepsy in patients with pervasive developmental disorder not otherwise specified. *Journal of child neurology,* 22(10): 1198-1203.

Parsons, S, Mitchell, P (2002) The potential of virtual reality in social skills training for people with autistic spectrum disorders. *Journal of Intellectual Disability Research,* 46(5): 430-443.

Parsons, S, Mitchell, P, Leonard, A (2004) The use and understanding of virtual environments by adolescents with autistic spectrum disorders. *Journal of Autism and Developmental Disorders,* 34(4): 449-466.

Parsons, TD, Rizzo, AA, Rogers, S, York, P (2009) Virtual reality in paediatric rehabilitation: A review. *Developmental Neurorehabilitation,* 12(4): 224-238.

Pennington, BF, Ozonoff, S (1996) Executive functions and developmental psychopathology. *Journal of Child Psychology and Psychiatry,* 37(1): 51-87.

Pensiero, S, Fabbro, F, Michieletto, P, Accardo, A, Brambilla, P (2009) Saccadic characteristics in autistic children. *Functional neurology,* 24(3): 153-158.

Peters-Scheffer, N, Didden, R, Mulders, M, Korzilius, H (2010) Low intensity behavioral treatment supplementing preschool services for young children with autism spectrum disorders and severe to mild intellectual disability. *Research in developmental disabilities,* 31(6): 1678-1684.

Pierce, K, Courchesne, E (2001) Evidence for a cerebellar role in reduced exploration and stereotyped behavior in autism. *Biological psychiatry,* 49(8): 655-664.

Piven, J, Arndt, S (1995) The cerebellum and autism. *Neurology,* 45(2): 398-399.

Raven, JC (1954) Progressive matrices (1938). *Firenze: Organizzazioni Speciali*.

Remington, B, Hastings, RP, Kovshoff, H, degli Espinosa, F, Jahr, E, Brown, T, Alsford, P, Lemaic, M, Ward, N, MacLean, JWE (2007) Early intensive behavioral intervention: outcomes for children with autism and their parents after two years. *American Journal on Mental Retardation,* 112(6): 418-438.

Riva, G, Bacchetta, M, Baruffi, M, Molinari, E (2002) Virtual-reality-based multidimensional therapy for the treatment of body image disturbances in binge eating disorders: a preliminary controlled study. *Information Technology in Biomedicine, IEEE Transactions on,* 6(3): 224-234.

Robins, DL, Fein, D, Barton, ML, Green, JA (2001) The Modified Checklist for Autism in Toddlers: An initial study investigating the early detection of autism and pervasive developmental disorders. *Journal of Autism and Developmental Disorders,* 31(2): 131-144.

Rogers, SJ (1996) Brief report: Early intervention in autism. *Journal of Autism and Developmental Disorders,* 26(2): 243-246.

Rogers, SJ, Hall, T, Osaki, D, Reaven, J, Herbison, J (2000) The Denver model: A comprehensive, integrated educational approach to young children with autism and their families. *Preschool education programs for children with autism. 2nd ed. Austin (TX): Pro-Ed*: 95-113.

Roid, G, Miller, L, Lieter, RG (1997) Leiter International Performance Scale-Revised: Examiner's manual. *Stoelting: Wood Dale, IL (620 Wheat Ln., Wood Dale 60191).*

Samson, F, Mottron, L, Soulières, I, Zeffiro, TA (2011) Enhanced visual functioning in autism: An ALE meta-analysis. *Human Brain Mapping,* doi: 10.1002/hbm.21307. [Epub ahead of print].

Schopler, E (1994) A statewide program for the treatment and education of autistic and related communication handicapped children (TEACCH). *Psychoses and Pervasive Developmental Disorders,* 3(7): 91-103.

Schopler, E, Mesibov, GB, Hearsey, K (1995) Structured teaching in the TEACCH system. *Learning and cognition in autism*: 243-268.

Schopler, E, Reichler, RJ (1971) Parents as cotherapists in the treatment of psychotic children. *Journal of Autism and Developmental Disorders,* 1(1): 87-102.

Schopler, E, Reichler, RJ, Bashford, A, Lansing, MD, Marcus, LM (1990) The Psychoeducational Profile Revised (PEP-R) Austin. *TX: Pro-Ed*.

Schopler, E, Reichler, RJ, Renner, BR (1986) *The Childhood Autism Rating Scale (CARS): For diagnostic screening and classification of autism.* Irvington New York.

Schreibman, L (2000) Intensive behavioral/psychoeducational treatments for autism: Research needs and future directions. *Journal of Autism and Developmental Disorders,* 30(5): 373-378.

Sheinkopf, SJ, Siegel, B (1998) Home-based behavioral treatment of young children with autism. *Journal of Autism and Developmental Disorders,* 28(1): 15-23.

Sparrow, SS, Balla, DA, Cicchetti, DV, Doll, EA (1984) *Vineland adaptive behavior scales: Interview edition, expanded form manual.* American Guidance Service Circle Pines, MN.

Standen, PJ, Brown, D, Horan, M, Proctor, T (2002) How tutors assist adults with learning disabilities to use virtual environments. *Disability & Rehabilitation,* 24(11): 570-577.

Stevens, MC, Fein, DA, Dunn, M, Allen, D, Waterhouse, LH, Feinstein, C, Rapin, I (2000) Subgroups of children with autism by cluster analysis: a longitudinal examination. *Journal of the American Academy of Child & Adolescent Psychiatry,* 39(3): 346-352.

Strickland, D (1997) Virtual reality for the treatment of autism. *Studies in health technology and informatics,* 44: 81-86.

Strickland, D, Marcus, LM, Mesibov, GB, Hogan, K (1996) Brief report: Two case studies using virtual reality as a learning tool for autistic children. *Journal of Autism and Developmental Disorders,* 26(6): 651-659.

Tsang, SKM, Shek, DTL, Lam, LL, Tang, FLY, Cheung, PMP (2007) Brief Report: Application of the TEACCH Program on Chinese Pre-School Children with Autism—Does Culture Make a Difference? *Journal of Autism and Developmental Disorders,* 37(2): 390-396.

Tsatsanis, KD, Dartnall, N, Cicchetti, D, Sparrow, SS, Klin, A, Volkmar, FR (2003) Concurrent validity and classification accuracy of the Leiter and Leiter-R in low-functioning children with autism. *Journal of Autism and Developmental Disorders,* 33(1): 23-30.

Vera, L, Campos, R, Herrera, G, Romero, C (2007) Computer graphics applications in the education process of people with learning difficulties. *Computers & Graphics,* 31(4): 649-658.

Vernazza-Martin, S, Martin, N, Vernazza, A, Lepellec-Muller, A, Rufo, M, Massion, J, Assaiante, C (2005) Goal directed locomotion and balance control in autistic children. *Journal of Autism and Developmental Disorders,* 35(1): 91-102.

Wallace, S, Parsons, S, Westbury, A, White, K, Bailey, A (2010) Sense of presence and atypical social judgments in immersive virtual environments. *Autism,* 14(3): 199-213.

Wang, M, Reid, D (2010) Virtual Reality in Pediatric Neurorehabilitation: Attention Deficit Hyperactivity Disorder, Autism and Cerebral Palsy. *Neuroepidemiology,* 36(1): 2-18.

Wechsler, D (1974) Wechsler intelligence scale for children-revised.

Wiederhold, BK, Mba, B, Wiederhold, MD (2004) 14 The future of Cyb ertherapy: Improved options with advanced technologies.

Wing, L, Potter, D (2002) The epidemiology of autistic spectrum disorders: is the prevalence rising? *Mental retardation and developmental disabilities research reviews,* 8(3): 151-161.

World Health, O (2006) *International Statistical Classification of Diseases and Related Health Problems: Tabular List of Inclusions and Four-character Subcategories.* World Health Organization.

Zoccante, L, Viviani, A, Ferro, A, Cerini, R, Cerruti, S, Rambaldelli, G, Bellani, M, Dusi, N, Perlini, C, Boscaini, F (2010) Increased left parietal volumes relate to delayed language development in autism: a structural mri study. *Functional neurology,* 25(4): 217-221.

Zwaigenbaum, L, Bryson, S, Rogers, T, Roberts, W, Brian, J, Szatmari, P (2005) Behavioral manifestations of autism in the first year of life. *International Journal of Developmental Neuroscience,* 23(2-3): 143-152.