European Down's Syndrome Association

NewsLetter

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EDSA Newsletter: present and future

Starting from the year 1999, EDSA will have its own official journal: it will be "Down Syndrome, Research and Practice", published in the U.K. by the Down Syndrome Educational Trust. In the same time, EDSA Newsletter will cease its activity changing into a part of that journal.

This event is very important for the European Down's Syndrome Association, because it will enhance its image in the international scientific world and will give it more room for expressing its ideas and designs.

As the first editor of the Newsletter, I want here to recall what this paper has meant for EDSA. During the eight years of its life, the constant efforts of the editorial staff have been directed to obtain a strong connection between the Advisory Board and the local Associations throughout Europe.

Informations on the main topics related to the development of persons with Down Syndrome, i.e. physical rehabilitation, schooling, language development, social insertion, specific diseases, were given through papers of distinguished authors. The most important congresses on DS were highlighted, as well as communications on any subjects that could be of interest for the families.

Undoubtably our path has been bristling with difficulties and sometimes we were not up to our task, but the Newsletter has grown up step by step, along with the associative movement in Europe. EDSA is also increasing its influence in Central and Eastern Europe: new Associations from these countries are joining it with new and different questions. The Newsletter should be the means to offer answers to these new needs.

Moreover, in the last few years EDSA has strongly advocated the creation of a World Federation on Down Syndrome. This has now become a reality. The field of information is also much wider for the Newsletter. The challenge for the future is to be able to afford new situations and try to maintain a cohesion among all the Associations linking up to EDSA.

Finally, I thank here all the people that helped me in the publication of EDSA Newsletter with their contributions, suggestions and advices.

To the incoming editorial staff my sincere wishes of good work.

Prof. Dr. Alberto Rasore-Quartino
General Editor

Neurophysiology of sleep in Down Syndrome

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The possibility that mentally retarded subjects might show an association between cognitive deficits and alterations of sleep mechanisms was postulated for the first time in the early thirties. Since then, several studies have been carried out focusing attention on sleep patterns of patients with mental retardation of different etiology. The main findings of such studies pointed out to the peculiar modifications of two basic sleep parameters in these subjects: 1) reduction in percentage of rapid eye movement (REM) sleep, and 2) prolonged latency of the first REM period.

It is well known that within human sleep two main separate states are defined based on a number of specific physiological parameters: the already mentioned "rapid eye movement" (REM) sleep and the "non-rapid eye movement" (NREM) sleep, which is conventionally subdivided into four stages (stages 1, 2, 3, and 4). The EEG pattern of NREM sleep is generally described as "synchronous", with typical waveforms known as sleep spindles, K complexes and high voltage slow waves; whereas the EEG pattern of REM sleep is defined as "activated", with the association of muscle atonia and episodic bursts of rapid eye movements (REMs).

Studies based on experimental evidence in animals revealed that REM sleep percentage increases after intensive learning sessions, thus confirming the hypothesis that REM stage is specifically involved in cognitive processes in mammals. In fact, REM sleep has been considered as an index of the so-called brain "plasticity", i.e. the ability of the human brain of selecting, processing and retaining information. In these last years, new observations on the possible role of REMs in humans showed that high-frequency REMs - that is REMs separated by short time intervals (<1 s) - tend to increase significantly with age and after learning trials. Therefore, high frequency REMs have been indicated as a functional index of the "organizational" abilities of the human brain, i.e. its capability to rearrange information from a random pool of outer or inner inputs into meaningful elements of the long-term memory. Interestingly, recent evidence has been reached on a significant reduction of the number of REMs separated by brief intervals in mentally retarded patients.

Sleep pattern

Similarly to other groups of mentally retarded subjects, sleep pattern of Down syndrome (DS) patients has been found to be characterized by three peculiar modifications as compared to normal subjects: 1) significant reduction in the percentage of REM sleep, more evident in the most severely retarded subjects; 2) marked delay in first REM latency; 3) statistically significant decrease in high-frequency REMs during REM sleep. In order to explain the reduction in REM sleep percentage in these subjects, studies evaluated the effects of a particular drug called butoctamide hydrogen succinate (BAHS) on sleep of DS patients, since it was known that this substance is able to increase the amount of REM sleep in normal controls and in animals. The administration of BAHS in DS patients was seen to cause a significant increase in REM sleep, although high-frequency REMs resulted unmodified in these subjects. On the other hand, experimental protocols based on intensive learning sessions were able to increase in these patients the ratio between high-frequency and low-frequency REMs but did not affect REM sleep percentage. These data seem to confirm the basic hypothesis that the percentage of REM sleep in humans, as previously mentioned, can be viewed as a physiological index of brain "plasticity" and that the number of high-frequency REMs can express and measure the brain ability to organize information. Moreover, such studies gave further neurophysiological basis to a psychopedagogical approach aimed at improving learning and memory disabilities in DS subjects.

Growth hormone production during sleep

Growth hormone (GH), also known as somatotropin, is produced and secreted by the anterior lobe (adenohypophysis) of a small rounded, bilobate endocrine gland (hypophysis or pituitary gland) which lies in the *sella turcica* of the sphenoid bone in the skull. Its primary function is to promote growth, but it has also direct influence on the metabolism of carbohydrates, fats and proteins.

Recent studies have shown that during slow wave sleep (stages 3 and 4 of NREM sleep), in normal subjects, growth hormone is released in the vascular flow following a rhythmic, periodical, "pulsatile" modality. The physiological mechanism of this phenomenon seems to be mediated by a neuronal pool located in a particular cerebral structure called hypothalamus, to which the hypophysis is connected by a stalk called *infundibulum*.. Since the mean height of DS adults, both in males and females, is usually below the average found in normal subjects, a possible dysfunction of GH production during sleep has been recently hypothesized in these subjects. Some findings obtained in a group of DS children on a possible relationship between sleep structure and GH production showed a clearly decreased peak

amplitude of nocturnal GH secretion. Although in these patients a certain pulsatility in the modality of GH production was still evident, the synchrony with slow wave sleep stages was poor. It should additionally be considered that GH release is known to be reduced in children with sleep disorders, probably because of the consequent sleep fragmentation. In particular, children with sleep apnea show a short stature which can be corrected by a specific treatment.

Also, many subjects with DS have been reported to present obstructive apnea during sleep.

Sleep apnea in Down syndrome

Sleep apnea is defined as a cessation of airflow trough nose or mouth during sleep lasting 10 seconds or more. If no respiratory effort is present, the event is termed "central". When the respiratory effort persists despite cessation of airflow, the apnea is "obstructive" (OSA). The so-called "obstructive sleep apnea syndrome" (OSAS) is the consequence of repetitive partial (hypopnea) or complete (apnea) obstruction of the upper airway during sleep, that is a succession of OSAs and/or hypopneas during night sleep

Recent polysomnographic studies on obstructive sleep apnea episodes occurring in DS patients showed that the presence of OSAS in DS subjects varies from 30 to 60%, whereas hypoventilation and blood oxygen desaturation were found in about 80% and 50% of cases, respectively.

Very recently, in order to evaluate the eventual effects of CNS impairment on respiration in DS, the respiratory patterns during sleep were studied in a group of DS children and young adults without relevant upper airway pathology, that is without obvious risk factors for OSA. The possible effects of sleep structure and mental retardation on the results obtained were controlled by comparing data from DS with those obtained from a group formed by subjects with fragile X syndrome, which is another genetically determined type of mental retardation. Although sleep structure appeared to be similar in both groups, DS subjects showed significantly higher values of central sleep apnea and of blood oxygen desaturation than fragile X patients. This significant preponderance of central, as opposed to obstructive, sleep apneas found in DS patients showed also a significant age-related increase. Central apneas were mostly preceded by sighs, occurred more frequently during NREM sleep stage 1 and REM, and were often organized in long sequences of periodic-like breathing. Sleep structure was not significantly modified by apneas and blood oxygen desaturation. In this study, it was hypothesized that the increase in central sleep apneas is related to a dysfunction of the central respiratory control at a brainstem level in DS. The brainstem is suspected to be the probable site of a specific dysfunction in DS patients also because a deficit in brainstem inhibitory mechanisms has been suggested in order to explain the shortening of the central conduction time of brainstem auditory evoked potentials usually observed in these subjects. Moreover, also this peculiar feature becomes more evident with age in DS patients.

Heart Rate Variability during Sleep in Down Syndrome

In order to confirm a brainstem dysfunction causing central sleep apnea, heart rate variability during sleep in a group of 7 DS subjects was recently evaluated and compared with the results obtained in a group of 6 normal controls. Heart rate is under the physiological control of efferent sympathetic and vagal activities directed to the sinus node, which are modulated by central brainstem (vasomotor and respiratory centers) and peripheral (oscillation in arterial pressure and respiratory movements) oscillators. Spectral analysis of heart rate variability is a quantitative reliable method for analyzing the modulatory effects of neural mechanisms on the sinus node and two main components are currently considered: the vagal activity is the major contributor to the high-frequency component, while the low-frequency component is considered by some authors as a marker of sympathetic modulation and by others as a parameter including both vagal and sympathetic influences.

The spectral analysis of heart rate variability during the different stages of sleep and during epochs with or without episodes of central sleep apnea was recently also performed. The comparison between DS patients and normal controls carried out only on epochs without apnea showed a significant alteration of the ratio between the low-frequency and high-frequency components in DS in all sleep stages, with a statistical significance for sleep stage 1 and slow-wave sleep. The sympathetic-correlated low-frequency component was always higher in DS; on the contrary, the vagal-controlled high-frequency component was always lower in the same group. Also in this study, a low frequency of obstructive sleep apnea was found because subjects were selected with the same criteria of the previously mentioned investigation on central sleep apnea. The presence of this type of apnea, in DS patients, induced a further significant increase in low-frequency and very-low-frequency components of heart rate variability, similarly to the effects of the presence of OSAs already described in the literature .

This final study allowed us to confirm the existence of an impaired brainstem function in DS which is demonstrated by abnormalities in brainstem auditory evoked potentials, abnormal presence of central sleep apnea and impaired balance between sympathetic and vagal control of heart rate variability during sleep.

Finally, the altered balance between the simpathetic and vagal systems can be viewed also in psychophysiological terms, following the ideas of the so-called "Polyvagal Theory", which states that the vagal system does not represent a unitary dimension and is formed by two distinct motor systems. The first one is the vegetative status originating in the dorsal motor nucleus, associated with passive automatic regulation of visceral subdiaphragmatic functions; the second is the smart vagus, originating in the *nucleus ambiguus* (NA), associated with the active processes of attention, motion, emotion, and communication, with supradiaphragmatic target organs. Thus, the changes reported in the autonomic function of DS subjects, together with the already reported changes in central control of respiration, might be physiopathologically connected with the basic mechanisms of their developmental psychomotor problems. In this respect, there is a need of further research.

Review of the controversial medical therapies in Down's Syndrome

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The innumerable drug therapies established in people affected by Down's syndrome (DS) testify the complexity of the topic.
The hypothesis of panhypopituitarism as a contributing factor in DS suggested the use of pituitary extract to Goldstein (1956) and Benda (1960). However, Berg et al. (1961), Diamond and Moon (1961), and Freeman (1970), found it unuseful in increasing intellectual and social development.
Histopathologic studies of Benda (1969) on thyroids of people with DS showed a lot of microscopic structural abnormalies and prompted the use of thyroid hormone. Thyroid hormone hes been used in persons with DS since the past century by Smith (1896), Koch et al. (1965) published a six-year double blind longitudinal study on 73 home-reared children with DS. The sample was separated in three random-made groups; the first was given sodium lyothyronine, the second a placebo, the third nothing. No statistical difference appeared among the three groups with regard to the intellectual development.
Dimethyl Sulfoxide (DMSO) is an industrial solvent made from coal, oil and lignin (similar to turpentine) that is a by-product of paper manufacturing. When administered to humans it produces a garlic-like taste and odor on the breadth and skin that can last as long as three days. One of the properties of DMSO is that it is absorbed very rapidly through the skin and cell membranes, carrying along almost anything else (particularly low molecular weight molecules) dissolved in it that would not otherwise be able to cross those barriers. DMSO was used by Aspillaga et al. (1975), who published a study, subsequently heavily criticized, reporting improvements in children with DS treated with this drug. These authors gave DMSO and γ-aminobutyric acid (GABA), γ-amino-β-hydroxybutyric acid (GABOB), acetylglutamine and arginine by intramuscular injections, alternated with rest periods, when they gave capsules containing only GABA, GABOB, acetylglutamine and arginine. They noticed "a greater receptiveness to ouiside stimuli, greater activity and improved muscular tonus". Gabourie et al. (1975) compared two groups, paired for age, functioning level and diagnosis, from a sample of 67 persons with mental retardation, including children with DS. The first was submitted to a high-dose trial, and the second to a low-dose trial, ever orally. A third group of 23 children was not treated. No significant difference was observed among the three groups regarding behaviour and learning. The only use of DMSO approved by the U.S. Food and Drug Administration (FDA) is that of bladder instillations of a 50% solution (sold under the trade name "Rimso-50") to relieve symptoms of interstitial cystitis, a painful chronic bladder disorder.
Cellular treatment refers to a group of related procedures that may be referred to as "live cell therapy", "cellular therapy", "cellular suspensions", "glandular therapy", or "fresh cell therapy". In general, cellular treatment involves injections of freeze-dried cells coming from various organs obtained from animal embryos or fetuses. It was developed in Switzerland in the early 1930's by Paul Niehans, MD, and became widely known when various public figures received the treatment and claimed it restored their youth or extended their lives. Cell therapy was used in the 1950's for the treatment of people with mental retardation. Schmid (1976) reached an increase of the height and head circumference of people with DS treated. Schmid maintained that the cell therapy, started early, would normalize the brain volume index and increase significantly the intelligence quotient of children with DS. These sentences and the results of the study have been heavily criticized for the lack of a correct explanation of materials and methods. Bardon (1964) studied 10 children with DS, paired for age, sex, physical development and intelligence. Each pair was separated according to the injections of cell therapy (yes or not). Both one year and two years afterwards the increase of intellective function did not show any statistical difference between the two groups. Such last results have been confirmed by Black et al. (1966) and Van Dyke et al. (1990).
Nutritional supplementations with several mixtures of vitamins, minerals, hormones and enzymes have been used in people with DS. Any comment on these treatments is made difficult by the huge number of substances. One should comment on the use of each single substance and then analyse the effect of all the ingredients in the whole. I would say that the main components of these formulas are Aminoacids, Antioxidants, Minerals, Vitamins and the recently added Digestive enzymes and Fat supplements.
The theory behind the supplementation of aminoacids is firmly linked to a study on people (children and adults) with DS published by Lejeune et al. (1992), where they found a decrease in the plasm concentrations of serine and an increase of cysteine and lisine. A recent study (1996) of Heggarty et al. on children with DS found only hyperlysinemia.
Hyperlysinemia is known as a benign condition, not leading to a treatment. This result rules out a supposed aminoacid profile in DS, which warrants a specific supplementation. Glutamic acid (glutamate) is simply converted to glutamine and is synthesized from arginine, ornithine, and proline. It is abundant in both animal and vegetable proteins and is found in high concentrations in the human brain. Glutamic acid, which is important to brain function, is the only aminoacid metabolized in the brain. The corversion of glutamic acid to glutamine helps clear potentially toxic ammonia. Glutamic acid, with the help of vitamin B6 and manganese, is also a precursor of GABA, an important neurotransmitter in the central nervous system. Glutamic acid helps transport potassium into the spinal fluid and is itself an excitatory neurotransmitter (GABA, however, is inhibitory). Glutamic acid thus has been used in the treatment of fatigue, parkinsonism, schizophrenia, mental retardation, muscular dystrophy and alcoholism. Glutamic acid and its derivates gave good results

in children with DS accordining to Gadson (1951) and Goldstein (1956), but not significant according to Lombard et al. (1955) and Astin and Ross (1960). Low levels of serotonine found in people with DS by Tu and Zellweger (1965) induced the use of 5-hydroxytryptophan, a serotonin precursor. Bazelon et al. (1967) were the first to use it and found an improvement in muscle tone, a reduction of tongue protrusion and an increased activity level. Partington et al. (1971) didn't find any improvement in the motor, behavioural or neurological functions in children with DS treated with 5-hydroxytryptophan during a controlled clinical trial. Subsequently Coleman (1973) compared two groups of children, one taking the 5-hydroxytryptophan and the other a placebo, not finding any statistically significant difference in the cognitive development. These results have been afterwards confirmed by Weise et al. (1974). Pueschel et al. (1980) treated with 5-hydroxytryptophan and pyridoxine, both singly and in combination, 89 children with DS during the first three years of life without any significant improvement in the motor, mental or social development. The report of sporadic vitamin deficiences (Harrell et al., 1981; Colombo et al., 1989) is counterbalanced by plenty of studies denyng it (Metcalfe et al., 1989; Pueschel et al., 1990, del Arco et al., 1992).

Furthermore, the supplementation of megadoses of vitamins may have adverse effects: Vitamin A in excess can cause dermatologic and neurologic abnormalities, Vitamin C in excess can lead to urinary tract irritations. The main minerals supposedly decreased in people with DS are zinc and selenium.

Zinc therapy has been used in persons with DS for the treatment of the following conditions: 1) growth delay, 2) immunological derangement, 3) hypothyroidism. The rationale of the use of zinc in subjects with DS lies on the key role played for the efficiency of the nervous, neuroendocrine, and immune systems (Fabris et al., 1988, 1991). Napolitano et al. (1990) have conducted a therapeutic trial with zinc sulphate on 22 persons, with DS for a period ranging from six to nine months, at the dosage of lmg/Kg/day in three daily doses. Fifteen out of 22 subjects reached an higher centile on their growth charts. Mean velocity of height increase moved from 23.84±7,98mm/6months to 40.80±7.68mm/6months. GH and serum somatomedines increased too. Main shadow of this study is the lack of information regarding zinc serum levels before and after the treatment. Stabile et al. (1991) used zinc sulphate at the dosage of 20mg/Kg/day for two months in 38 home-reared children with DS, 24 with low zinc serum levels (LZSL) and 14 with normal zinc serum levels (NZSL). No correlation was found between LZSL and the recurrence and/or the intensity of infections. The subjects with LZSL showed a response of the peripheral mononucleated blood cells to the phytohemagglutinine significantly lower than those with NZSL. A significant increase in DNA synthesis was achieved after the oral administration of zinc sulphate. The lymphocyte response to the phytohemagglutinin was normal in all subjects up to six months from the end of zinc therapy and returned low in half the subjects 22 months after the end of the therapy. Napolitano et al. (1990) found a decrease of fT3 in 17 subjects with DS and subclinical hypothyroidism treated with zinc sulphate and reported an improvement of the thyroid function in 9 subjects with DS and LZST, treated with zinc sulphate. Licastro et al. (1992) reported 25 children with DS, LZSL, low rT3, and high levls of TSH, treated them for four months with zinc sulphate, and reached a normalization of plasmatic zinc, thymulin, TSH and a significant increase of the plasmatic levels of rT3. After zinc therapy no difference was found between children with DS and the 14 control children, but a decreased incidence of infectious diseases and an increased school attendance. Licastro et al. (1993, 1994) confirmed such data in two subsequent publications. On the contrary, Brigino et al. (1996) reported that low levels of thymulin in 4 children with DS remained low despite the normalization of cellular zinc levels. Lockitch et al. (1989) supplemented with zinc 64 children (1-19 years) with DS in a double-blinded controlled 1-year study. The serum immunoglobulins, complement, and lymphocyte function were unchanged, but the sick days decreased. Further studies are needed to reach a conclusion about the usefulness of zinc therapy in DS. Selenium is a cofactor in the enzyme glutathione reductase, which plays a role in the scavenging of free radicals, turning hydrogen peroxide into oxygen and water. Annerén et al. (1989) reported increased plasma and erythrocyte selenium concentrations with decreased erythrocyte glutathione peroxidase activity after selenium supplementation in children with DS. Surprisingly, the infections were referred to be decreased by the parents. An increase in serum concentrations of IgG2 and IgG4 after selenium supplementation was reported subsequently by the same authors (Annerén et al., 1990). These preliminary results deserve further research. No information about possible side effects of chronic supplementation of zinc and selenium is available. The supposed lack of certain digestive enzymes in DS is not substantiated by the facts. Docosahexaenoic acid (DHA) is an omega-3 fatty acid, part of the cell membranes, particularly important in the retina and brain, synthesized from other fatty acids in the diet. Only prematures can have an incomplete capability to do so, and then infant formulas for prematures must be added with DHA. The effect of the DHA supplementation is limited to the first two months of life (Carlson and Werkman, 1996). Consequently, the claimed use of DHA or other fatty acids in older children with DS for the improved eye and brain development has no scientific basis. Moreover, DHA in excess can suppress the immune system, usually impaired in DS. Choline is a precursor of the neurotransmitter acetylcholine, which is produced by neurons progressively gone lost with the process of aging in DS. No study has proven that choline can increase the myelination of neurons and the levels of acetylcholine. Cantor et al. (1986) treated with phosphatidylcholine a child with DS, reporting some improvement of the language. A similar study has not been repeated so far. Piracetam is a cyclic derivative of GABA, commonly known as a "nootropic" drug, used for several condidons, like dyslexia, senile dementia, myoclonus, aphasia, stroke and blood disorders. Its use, in truth, is not approved by FDA. Fialho (1977) treated 26 children with DS with Piracetam and a mixture of pyriglutine and 5-hydroxytryptophan called Dromia, reporting an improvement in muscle tone, motor and mental development, speech, affective-social development, scholastic achievement and EEG trace. This paper must be heavily criticized, because there is no control group, you cannot know if the study is blinded, and the methodology is not explained in a clear way. Vampirelli (1978) treated for three months with Piracetam at the dosage of 50 mg/kg/die four children with Down's syndrome aged 4 to 8 years. The only reported effect of treatment was a relative stir with psychomotor instability. These two studies cannot lead to a scientific use of piracetam in DS. Haubold (1955, 1967) reported positive effects with a

cocktail of vitamines, hormones and minerals. Since 1975 Turkel (1975) started treatments with the so-called U series (cocktail of 50 pharmacological substances like thyroid hormone, vitamins, minerals, enzymes, aminophylline and clorpheniramine maleate) in children with DS, achieving, he said, physical and intellective improvements. Seven controlled studies (White and Kaplitz, 1964; Bumbalo et al., 1964; Bremer, 1975; Hitzig 1975; Coburn et al., 1983; Ellman et al., 1984; Smith et al., 1984; Menolascino et al., 1989; Bidder et al., 1989) did not find any differences between the groups. Furthermore Bidder et al. (1989) reported a decrease in the development and various side effects of these substances. Harrell et al. (1981) published a paper reporting on the improved IQ scores and "physical changes toward normal" due to its supplementation of vitamins, minerals, and thyroid hormone. These mixture is the basis of the Haps Caps, which is now promoted during traveling clinics by Jack Warner, M.D. In 1995 Dixie Lawrence Tafoya presented, during an interview aired by ABC News, her own formula, based on the original Turkel's U-series, but increased in number of substances and with the presence of the drug piracetam. The supplementation was produced by Nutri-Chem Labs and named MSB Plus, under her supervision. Mrs. Lawrence withdrew this agreement in 1996 and started promoting the formula under the name of NuTriVene-D, marketed by International Nutrition. With regard to a general comment on the nutritional supplementation in children and adults with DS, my opinion is exactly that of Mary Coleman (1997): "Careful examination of any child can indicate evidence of vitamin or mineral deficiencies; such deficiencies have clinical symptoms to alert the examining physician. In addition, there are routine checks that are made periodically in any child with DS. When deficiencies are found in a child, such as thyroid, vitamin A or zinc, then, and only then, would supplements be indicated for the child."

Facial plastic surgery has been used for the first time in 1977 (Hóler). It has been accomplished removing epicanthal folds, straightening slanted palpebral fissures, inserting silicone or cartilage implants in the nasal bridge, cheeks and chin, reducing lower lip, wedge resecting the tongue (Lemperle and Radu, 1980), (Olbrisch, 1982, 1983), (Lemperle, 1985). Supporters of these operations asserted that the result should be an improvement of the speech, a better acceptance in the society, a decreased salivation, an improved chewing and swallowing and a reduction of respiratory infections. A questionnaire administered by Olbrisch (1982) to the parents of children with DS operated by plastic surgery gave the following results: 85% hadn't open mouth behaviour, 78% reduced the number of respiratory infections, 83% showed an improved speech and feeding, 78% were satisfied for the new facial look of their children and only 28% highlighted the improved acceptance of the children by the society. Arndt et al. (1986) observed 24 children with DS operated by plastic surgery and reported that their parents were happy for the different look of their children, whereas independent observers preferred the old look. Parsons et al. (1987) studied the articulation of speech in 18 children with DS before and after tongue resection surgery, finding no statistically significant difference. Margar-Bacal et al. (1987) studied the intelligibility of speech in 23 children with DS before and after tongue resection surgery without any statistically significant difference.

Another hot spot in the medical treatment of people wilh DS is the possible therapy of the subclinical or compensated hypothyroidism, e. g. increased TSH with T3 and T4 within the normal range. Crinò et al. (1996) studied 160 children with DS, 73 of whom showed high values of TSH. Height growth velocity was reduced in 31% of them vs. 30% of those with normal TSH values. Pueschel and Sustrova (1996), reporting on 25 children with DS, positive antithyroid autoantibodies, but normal levels of T3, T4 and TSH, observed an height growth comparable to that of the other children with DS. A significantly delayed height growth was shown by 3 children with DS and uncompensated hypothyroidism (TSH >3SD and T4 >2 SD). A lesser delay of the height growth was present in 8 children with DS and compensated hypothyroidism (TSH >3 SD and normal T4). Rubello et al. (1995) evaluated 344 subjects with DS and compared them with 257 control subjects and 120 parents of persons with DS. The prevalence of subclinical hypothyroidism was 32.5% in the first group, 1.1 % in the controls and 0% in the parents. The prevalence of antithyroid antibodies was 18% in subjects with DS, 5.8% in controls, and 6.6% in parents of subjects with DS. However, no correlation has been found among subjects with DS between prevalences of antithyroid antibodies and subclinical hypothyroidism: antithyroid antibodies were present in 18.7% of those with subclinical hypothyroidism and in 15.8% of those euthyroid. No statistically significant difference have been found between such two groups with regard to T3, T4, fT4. A follow-up of 201 subjects with DS was set up for a mean period of 3.1 years: 35.7% of subjects with DS, subclinical hypothyroidism and positive antithyroid antibodies developod a thyroid disease clinically evident (frank hypothyroidism or hypertyroidism), whereas none of subjects with DS, subclinical hypothyroidism and negative antityroid antibodies shifted towards a clear thyroid disease.

With regard to the use of growth hormone in children with DS, Annerén et al. (1996) observed an increased linear height growth, but motor and mental development were unchanged. Castells et al. (1996) observed an increased height standard deviation score in prepuberal children with DS and growth delay with a normalization of predicted adult height in 91% of children treated. Ragusa et al. (1996) observed 21/40 subjects with DS showing a subnormal growth hormone (GH) secretion. Nine of them were treated with GH, and seven of them increased their height centile. The usefulness of GH seems, then, limited t height increase, but further studies are needed to understand if the increase of adult height be ever present. A fault of these studies lies in the current problems of GH evaluation (Rosenfeld et al., 1995): it is ever needed to join auxological and laboratory examination.

All I've written here allows a personal opinion of the reported data. The final message I would like to give is that a person with DS must be followed up with a clinical schedule which encompasses the early diagnosis of the most frequently prone conditions (congenital heart defects, gastrointestinal malformations, respiratory infections, celiac disease, hypothyroidism, atlanto-axial dislocation, psychiatric disturbances). It's ever the common sense which must lead the medical follow-up of a person with DS. An early rehabilitation in the areas of swallowing, chewing, speech (speech therapy) and motor skills (psychomotility and physical therapy), without overload the child, remains essential in order to achieve the best quality of life. Experimental treatments may be suggested only within specific research projects.

References will be sent on request.

A word processing course for young people with Down Syndrome

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INTRODUCTION

The Word Processing Course intended for young people with Down Syndrome which was carried out jointly by the Italian Association for People with Down Syndrome and Finsiel in Rome, gave rise to the following observations.

The description of this 600 hour-long training course demonstrates how the acquisition of the skills instrumental in using a PC and Word for Windows can influence the overall cognitive development and metacognitive skills of people with Down Syndrome.

This educational experience is the result of a concerted effort between two very different kinds of institutions: on the one hand, n entrepreneurial firm, Finsiel, and on the other, the Italian Association for People with Down Syndrome (AIPD). Their collaboration began earlier with a brief experimental course, An Approach to Computer Science for 10 young people with Down Syndrome. Together they confirmed that this route was not only feasible, but in fact, a compelling opportunity for further cognitive development of these youth.

Furthermore, providing these young people with the basic Word Processing skills meant equipping them with qualifications useful in the work place. This brought about the planning of a more extensive and structured course which was held from March 1995 to September 1995 for a total of 600 hours. This course was carried out with eight young people with secondary school diplomas, between the ages of 18 and 25.

THE STUDENTS

Eight young people were chosen through an evaluation process which controlled the following areas:

- The level of psycho-social development through:
  - Vineland Adaptive Behavior Scale (Sparrow 1984, relative to communication, daily life, socialization, motor skills) which was administered to the youths' parents.
  - observation in real-life situations of the level of personal and social autonomy and skills in relationships.
- General cognitive abilities through the administration of the following tests:
  - Wechsler Adult Intelligence Scale (WAIS-R), from which we can draw a qualitative analysis of the youths' cognitive profiles through an analysis and comparison of verbal and performance I.Qs.
  - Raven's Colored Progressive Matrices (1949) to evaluate the ability to reason by analogy, to conceptualize and to elaborate a systematic reasoning method, independently of language and the level of schooling.
  - battery of neuropsychological and perceptive tests. The purpose of administering this battery of tests was to identify the various cognitive skills through stimuli and critical situations. The tests are: Verbal Fluency Test, Category Access, Verbal Memory Test, Visual Memory Test, Developmental Test of Visual Motor Integration (V.M.I), Boston Naming Test, Token Test.
- Level of passive and active linguistic skills through:
  - a reading test
  - a writing test

All the young people that were chosen demonstrate:

an excellent level of personal independence
- self-sufficiency in personal grooming
- ability to get organized in order to carry out an assigned task

- an excellent level of social independence
  - ability to orient oneself in a given location
  - ability to ask for help
- good relationship skills
  - initiative in spontaneous communication
  - fairly good semantic-verbal understanding of concrete situations
  - ability to follow simple instructions
  - general cognitive skills. In this regard, examine the following chart:

Student	age	Verbal I.Q.	Performance I.Q.	Total I.Q.
B.D.	20	63	68	65
C.L.	19	70	62	65
D.A.	18	54	58	56
M.M.	19	70	65	66
M.D.	22	59	62	60
S.C.	24	70	51	60
S.A.	19	73	57	65
V.R.	18	67	62	64

As seen, three cases have an Intelligence Quotient between 56 and 60 and five cases between 64 and 66: according to the classification of the World Health Organization, this is within the range of slight mental insufficiency.

Some of the young people achieved better results in verbal testing while others did well on the performance test; this conforms to individual variations typical to the Syndrome. This is due not only to a genetic factor but also to the evolutionary development which is strongly conditioned by past experiences and the social-educational context of school and family where the person has been brought up.

A normal, rather homogeneous trait is a good visual memory both short and long term. It was beneficial to inform the teachers of the course about this aspect so that it could be advantageously used in their teaching and be taken into consideration regarding verbal memory tasks.

- linguistic and verbal communication skills:
  - in two cases articulation problems were encountered during verbal expression which did not constitute an obstacle to the calm determination to communicate (however, it did require the ability to wait and the same calm determination on the part of the interlocutor); their simple sentence structure was complete.
  - in two cases communication was made easier because they exhibited no problems in articulating and simple sentence structure was complete.
  - in four cases there was an excellent level of verbal fluency, rich vocabulary and complex sentence structure.

- Linguistic skills in reading and writing:
  - six young people demonstrated a good mastery of reading
  - two young people also adequately understood what they were reading
  - one boy wrote only by copying or by dictation
  - seven young people independently wrote sentences about everyday experiences and personal thoughts, with very few spelling errors.
- In short, the group was selected from the higher range of young people with Down Syndrome; in fact, the professional goals of the course necessitate a certain level of cognitive abilities.

GOALS OF THE COURSE

The ultimate educational goals included;

- knowledge concerning:
  - the general operation of the Personal Computer and how its components work
  - the difference between the operative system DOS and the application software, Windows
  - how databases work and how they are organized
  - how basic office equipment works
- operative and process/methodological skills in:
  - turning the Personal Computer and its accessories on and off following the correct sequence
  - navigating in Windows
  - making Words for Windows work
  - saving files on the hard disk and on floppies
  - making the printer work
  - using the telephone, fax and photocopier correctly
- professional conduct:
  - understanding the expectations in all vertical and horizontal transactions
  - knowing how to plan out one's own work
  - paying attention to the correct application of procedures
  - aiming for the maximum precision possible
  - completing assigned tasks
  - controlling the results of one's own work
- relationship skills, social and personal independence:
  - managing individual and group interpersonal relationship
  - communicating one's own needs
  - asking for and accepting help
  - giving assistance and collaborating
  - behaving responsibly and accepting the consequences of one's own conduct

Other miscellaneous goals included:

- an increase in overall cognitive development and metacognitive skills
- an extended attention span through the mastery of an "object" - the Personal Computer. Some of its components (especially the monitor and the keyboard) exert a considerable "halo effect".

TOOLS AND METHODOLOGY

The course was divided into two phases:

- the first educational phase lasted for about three months, for a total of 300 hours
- the second training/practical application phase was held at Finsiel offices and also lasted for three months

During the first phase each student had his/her own Personal Computer. Various teaching methods were employed: brief theoretical lessons (supported by a maxi screen connected to the PC), interactive reviews with continuous prompting of individual students, numerous practical often personalized exercises mainly regarding copying/saving/printing of texts with special characteristiecs and pre-set formats. Since these were young people with mental retardation, as the classroom lessons grew gradually more abstract, problems of theoretical comprehension arose; however, this did not hinder the mastery of using the tool itself. Two educational aids were prepared:

- the manual, "A Computer as a Friend", which contains a section intended for the students (simple notes about computer science and word processing) and a section intended for teachers (basic elements of computer science and word processing, explanation of the exercises on the software)
- the interactive software "A Computer as a Friend" which offers in five sections (the Personal Computer, general information about Windows, word processing, getting to know Word, a typical work day) a "serious game" approach to function keys, alpha-numerics, arrows, objects in Windows such as icons, windows, buttons, bars for scrolling, for menus and titles, etc.

The exercises were set up by the computer technicians at Finsiel and later supervised by staff members of the Italian Association for People with Down Syndrome (AIPD) to ensure that they were calibrated to the level of the students' cognitive development. From the outset, the young people taking the course were highly motivated, and they demonstrated an increasingly prolonged attention span. Exercises for strengthening linguistic skills and stimulating logical-deductive skills were prepared; in addition grids for systematic observation, multiple choice questionnaires, index cards for recording learning progress were provided, Programming provided for periodic meetings to monitor the teaching/learning process and to identify personalized learning strategies. We believe that the multimedia educational packet is a valid tool for normally endowed younger students and/or students at lower grade levels that tackle the PC and word processing for the first time.

LEARNING RESULTS

At the end of the educational phase, all of the young people had acquired the following skills:

- use of the mouse
- keyboard: recognition of the characters and gradual increase in typing speed
- navigating in Windows
- recognition of the icons in Word
- saving files
- opening files
- reproduction of text according to a pre-set format

Five of them were also able to:

- copy a complete text without typing errors
- reproduce a text with a special format (newspaper, etc.)
- independently set up a page for text (font, alignment, tabs, etc.)
- use charts
- number paragraphs and pages
- independently use copy and paste commands
- substitute parts of the text
- independently make use all the tools up to and including printing.

OFFICE TRAINING

These five young people attended training sessions over a three month period at the offices of Finsiel. Simultaneously, the other three students continued their lessons in the classroom. During this longer time period the three students were able to approach these skills although they did not entirely master them due mainly

to difficulty or unwillingness in conforming to the rules.
The five young people put their acquired skills to use during the training sessions: they did various data entry jobs (data regarding employees who attended training courses, data relative to employee invoicing, etc.), they typed and printed out letters and documents according to the standards indicated, they filed papers in alphabetical and/or chronological order, they answered the telephone and left written messages, they faxed documents, they opened and arranged the mail ready to receive reference numbers, they delivered interoffice mail, they photocopied and collated documents, they prepared signature-books for directors.
At the end of the training period, they underwent and successfully passed an examination before a commission of the Lazio Region.

CONCLUSIONS

Aware from the outset that this experience in computer science called for particular aptitudes, it was clearly not suitable for all young people with Down Syndrome; furthermore, it was evident that these aptitudes should be developed from the standpoint of professional training and inclusion in the work force. Among the young people selected, only a few would actually be able to independently hold down the job of a Word Processor. However, thanks to daily practice, all of them have developed diverse and interesting skills that can be used in office jobs where Personal Computers are being utilized.
The objective of increasing cognitive independence was fully achieved: a series of indicators point to the fact that all the students had longer concentration and attention spans, ability to self-organize and plan out his/her own work, processes of self-regulation and monitoring, problem solving and transfer skills. Learning to use the PC and word processing created circumstances that prompted the students to reflect on what they were doing and to actively choose the rhythms, ways, and skills useful in dealing with new situations. Having to solve problems at the level of operative thinking (which definitely is within the grasp of subjects with mental retardation) signifies using the tool in a non-mechanical way. To independently word process a text means to know how to analyze it. For example, if a series of tools such as character formatting (bold, italics, etc..) are used in reproducing a text, it is necessary to choose the keywords to be modified. This implies a more than trivial understanding of the text itself. In short, learning procedures for the PC (an "object" that requires reflective thinking but that also fosters contemplation) brings into play processes of selfregulation and monitoring such as identifying the problem, foreseeing and choosing the general procedure and the specific strategy, planning, evaluating through feedback. On the job, all of this produces operative independence and skills in problem solving, in transferring the strategies learned, in generalization.
In conclusion we wish to point out, that in our opinion, this experience could be repeated not only with people with Down Syndrome, but also with other types of disabilities in the realm of psychology and mental retardation.

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Down Syndrome Society in the Slovak Republic

Dr. M. Šustrová, Bratislava, Slovak Republic

Down Syndrome Society in the Slovak Republic (DSS) was established in 1993 as an independent, non governmental civic association with the aim to support people with Down Syndrome (DS) and their families.
The goal of the society is to protect the interests and needs of individuals with Down Syndrome and their families, enforce improvement of health care quality, and defend the right to appropriate education and integration of DS individuals into the society.
In 1997 the society started cooperation with The Down Syndrome Department at the Institute of Preventive and Clinical Medicine (IPCM) in Bratislava. It was an impulse for the creation of a Center for children and adults with Down Syndrome, their parents, professionals and volunteers.

Research

In the area of research the Center is oriented to follow up biochemical and immune changes in persons with Down Syndrome. The following projects are explored in the cooperation with other professionals of the IPCM and the Comenius University College of Medicine:

- the changes in immune system in persons with Down Syndrome and the prevention of infections and autoimmune diseases,
- the antioxidant status in persons with Down Syndrome,
- the changes in lipid metabolism,
- the role of vitamins and trace elements,
- DNA damage.

Besides this original research activities, DSS organizes professional meetings, seminars, and conferences in the Slovak Republic or some of them bilaterally with the Czech DS society. Three Slovak lecturers operate in Prague (M. Šustrová, M.D., Ph.D., Dr. Papánková - psychologist, and Mrs. Matejíčková - physioterapeutist).
Dr. Mária Šustrová presents the result s of her work by active participation in international events, her research colleagues Ass. Prof. Z. Ďuračková, Dr. Jana Muchová, Y. Garaiová, Ph.D. and Dr.

M. Papánková also participated in Madrid in the VI World Congress on Down Syndrome. Unconventional poster "The Life Tree - or the Family Album" captured attention with its unusual orientation. In 1994 we organized the first international conference, with 300 domestic and 50 foreign participants. Professor Alberto Rasore-Quartino represented EDSA and Professor S. M. Pueschel from the USA took part as the honorary president.

The care of persons with Down Syndrome

Families with DS children visit the Center at least once a year. More than 2000 people with DS are registered, but there are estimated to be additional 2000 persons with DS in the Institutions of Social Care and Psychiatric Departments in the Slovak Republic. According to the program "Optimal Health Care of Persons with Down Syndrome" the Early Developmental Stimulation, the development of DS children is monitored, appropriate procedures for prevention of additional diseases are proposed and a proper drug and surgical treatment is designed. A group of professionals keeps contacts with other specialists and professional health workers from hospitals. A balanced diet and a fitting physiotherapy from the early childhood is accented. The program of care of adolescent and adult DS persons is gradually growing. Cooperative partners still have not been found in the areas of general medicine as well as geriatric and psychiatric treatment.

Except for specific health care we cooperate with other professionals, mostly with psychologists, special educationists and physioterapeutists. Parent advisory service utilizes interviews with professionals, video presentations, available literature and parental meetings and their mutual help and support. The parents can get qualified answers for all their questions.

Particularly helpful have been seminars for parents of a particular age group of children, for example seminar for 1 to 3 years children with practical presentations of physiotherapy methods (Bobath, Castillio - Morales). We provided psychological interviews for parents of children up to 3 years; for parents of children between 3 and 6 years we concentrate on specific educational approach and preparation of children to enter kinder-gardens (logopedical preparation, psychological intervention), lectures on integration to the main educational system for children between 6 and 15 years, speech and language therapy preparation, psychological specifics of the DS children school age, nutrition, stomatological care and others. Programs for the parents of adolescent and adult DS persons are being prepared.

One-day seminars take place in the IPCM for the parents coming from all parts of the Slovak Republic. There is a surprising interest from distant places, for example from East Slovakia, often a whole day journey (500-600 kilometers) away.

Recently we are concentrating on publications, which are insufficient in the area of DS. We published two illustrative materials on the Down Syndrome Center in the Slovak Republic and an information for parents after a birth of a DS child, translated Sue Buckley's monograph "Development of reading and speaking abilities in children with Down Syndrome", and monograph "Barborka" by parents of a two-year Barborka. We are preparing translations of "A Parents Guide to Down Syndrome. Toward A Brighter Future" by S.M. Pueschel and "Adolescents with Down syndrome" by Prof. Pueschel and Dr. Šustrová.

Activities of the Society

The DSS forms one large family. With the help of professionals and volunteers we contact new families with DS children, who become members of our society. The society organizes a number of cultural, sport and recreational activities within Slovakia.

A week stay for complete families with DS children is organized annually. We fund the costs for the DS child and one companion, other family members can participate on their own expenses. These stays are organized in recreational localities, mostly spas, where we utilize the physiotherapy in swimming pool with healing water. The spas are located in the beautiful environment of Slovak mountains, where except bathing we can hike or take a walk. The children have an exact schedule, except for physiotherapy in the water; they learn to swim, use sauna, play table-tennis, tennis, team games or cycling. The afternoon programs include art-therapy - painting, music therapy, disco evenings, carnival and preparation of scenic plays. The programs are adjusted to the age of the children, a condition for acceptance is one year. The advantages of these events are parents meetings, exchange of experiences, mutual help, new friendships between the parents and children as well. The physicians, educationists and students participate voluntarily. An important asset is cooperation with respected artists who work with the DS children in utilizing their free time and enlarging their inner world and aesthetical feelings (Mrs. and Mr. Cipar, Mrs. Bartova).

In addition to the week stays, the DSS organizes one-day recreational events. In the spring it is the welcoming of the spring with all the corresponding activities, there is a sporting day in the beginning of May when there is a Children Day, in the fall a music evening and disco and a meeting with Santa-Claus in December.

Senec group of parents organized a concert. Two our representatives Juraj Šuster and Zuzka Dvoráková exhibited on the Madrid congress in October 1997 in the gala program with exhibits of Slovak folk dances and songs.

Since the fall 1997 we quarterly publish our own magazine "SLNEČNICA".

In 1997 the television addressed the DS problem and the DSS twice, one of which was a 30 minute program. There were two broadcasts of the Slovak Radio on these themes, three times in country-wide newspapers (twice in "Nedel'ná Pravda" magazine, once in "Katolícke noviny" newspaper) and several times in local periodicals.

The DSS activities are rich and versatile. Despite the help of volunteers and sponsors we still face deficiencies as is ignoranc of the whole society, insufficient public funds, low integration of the DS children. Several negatives are outweighed by the effort of some society members as well as the personal leadership from the IPCM in Bratislava (director Prof. Dr. Trnovec) by enabling not only research in DS but also by providing space for the examination of persons with Down Syndrome (specific treatment and counseling), as well as for meetings with parents, organization of seminars and other activities of the society.

To overcome some of the difficulties we took part in international activities, which resulted in bilateral projects:

- bilateral project with the Rhode Island Hospital - Prof. Pueschel in the area of antioxidant status in persons with Down Syndrome,
- bilateral project with the nongovernmental organization from Toulouse to help the Down Syndrome Society and to improve the conditions of families with DS children (project PHARE - LIEN),
- participation of Slovak physicians on the PHARE project with the Czech DS club,
- preparation of a bilateral cooperation with the University of Iowa.

Fourth European Down Syndrome Conference
Malta - 10-13 March, 1999

CONFERENCE PROGRAMME

WEDNESDAY 10th March

14.00 - 17.00	Registration at the Main Conference Hotel Opening Ceremony at the hotel Oracle Conference Centre
17.30 - 17.40	MERHBA by a person with Down Syndrome Welcome address by Mr. John L. Peel, Chairman, Down Syndrome Association (Malta)
17.40 - 17.50	Address to delegates by Prof. Jean A. Rondal, President European Down Syndrome Associatio
17.50 - 18.00	The Fourth Time by Dr. Mark G. Borg, Chairman, Scientific Committee
18.00 - 18.15	Opening & Address by HE The President of the Republic of Malta, Patron Down Syndrome Association (Malta)
18.15 - 18.30	Address to delegates by Hon Dr. Louis Galea, Minister for Education
18.30 - 19.00	A Showcase of Maltese Culture and History

THURSDAY 11th March

09.00 - 10.00	Keynote Speech - 'Breaking the News' Mr. Kenn Jupp (U.S.A.)
10.30 - 13.00	Symposia: 1. 'Early Intervention' Dr. Renè Eminyan (Malta) 2. 'Genetics, Health & Medical Issues' Prof. Alfred Cuschieri (Malta)
15.00 - 16.00	Keynote Speech - 'Congenital heart diseases in persons with Down Syndrome - Dr. Victor Grech (Malta)
16.00 - 17.00	Individual Papers Sessions 1

FRIDAY 12th March

09.00 - 10.00	Keynote Speech - Language Prof. Sue Buckley (United Kingdom)
10.30 - 13.00	Symposia: 3. 'School and Community: Parental Experiences and Aspirations' - Mr. Erik de Graaf (Netherlands) 4. 'ICT in Education' Mr. Dave Kisly (Canada)
15.00 - 16.00	Keynote Speech - 'Sexuality in Down Syndrome' Prof. Ben Sachs (United Kingdom)
16.00 - 17.00	Individual Papers Sessions 2

SATURDAY 13th March

09.00 - 10.00	Keynote Speech - 'Independent Living' Dr. S.M. Pueschel (U.S.A.)
10.30 - 13.00	Symposia: 5. 'Building Relationships' Dr. Monica Cuskelly (Australia) 6. 'Community and Home based Services'
15.00 - 16.00	Keynote Speech - 'The rights of Persons with Down Syndrome' Ms. Leena Matikka (Finland)
16.00 - 17.00	Individual Papers Sessions 3
17.30 - 18.15	Presentation by persons with Down Syndrome
18.15 - 18.30	Address to delegates by Dr. Lawrence Gonzi, Minister for Social Policy
18.30 - 18.45	Good Bye and Safe Journey by Mr. John L. Peel, Chairman, Down Syndrome Association (Malta)

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Sponsored by YATED, the Israel Down Syndrome Society

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