

Alzheimer's disease in adults with Down syndrome: a challenge

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The Committee for Science & Society of the Trisomy 21 Research Society (T21RS) regularly addresses issues raised by parents and Down syndrome associations through summarizing the state-of-the-art knowledge from a scientific perspective. The Committee for Science & Society* is strongly committed to introducing scientific research and explaining recent findings in an understandable way. Today, the second edition of the T21RS Science & Society Bulletin: key issues on Alzheimer's disease in Down syndrome.

- Are changes in memory part of normal aging?
- Are the age-related memory problems the same as those associated with Alzheimer's disease?
- How do memory problems associated with Alzheimer's disease manifest in adults with Down syndrome? Are they different from the general population?
- How do I know when to seek help?
- What needs to be ruled out when assessing memory problems?
- What therapeutic options are there?



**Frequently Asked Questions on
memory problems associated with
Alzheimer's disease in Down syndrome**

Life expectancy of people with Down syndrome has increased dramatically in the last 50 years due to improved health care. It is now common for adults with Down syndrome to reach old age and to live beyond 50, 60 and 70 years of age. Although there are many exciting events that accompany getting older, old age can also pose unforeseen challenges, such as "new" medical problems [1]. Adults with Down syndrome, their families and their caregivers are often unaware or do not feel adequately prepared to cope with this new scenario.

The main health problems associated with aging in adults with Down syndrome are neurological diseases, in particular Alzheimer's disease and epilepsy. Approximately 50-70% of adults with Down syndrome will develop Alzheimer's disease, reaching a prevalence greater than 80% in those above 60 years of age [2].

This is an extremely high percentage when compared to dementia in the general population: 2.9% (65-74 years of age), 10.9% (75-84 years) and 30.2% in non-Down syndrome people of 85 years and older [3].

Therefore, Alzheimer's disease in adults with Down syndrome is the biggest challenge for both the medical profession and society. Health professionals, however, do not feel sufficiently prepared to face the problem [4]. The diagnosis of cognitive deterioration in a population with intellectual disabilities requires specific training as well as adapted tests and instruments. From a social point of view, Alzheimer's disease strikes this population in an age range (40-70 years of age) in which the main carers, their parents (or siblings) in many cases, are themselves in a situation of vulnerability due to advanced age. Moreover, institutions are not prepared to cope with this problem either. This is another challenge of which everyone (family, caregivers, doctors, politicians...) should be aware.

Aging in DS

Although it is not easy to define, it is generally considered that aging is a progressive deterioration of the physiological mechanisms necessary to keep the "internal environment" constant. In other words, aging is a physiological process of decline, which encompasses the changes that occur over time in the body leading to functional disturbances and, ultimately, death. These changes in the physical appearance, psychological, functional and biochemical order are characterized by a progressive loss over time of the adaptability and of the reserve capacity of the organism. All these changes produce a progressive increase vulnerability to stress and eventually death. Adults with Down syndrome suffer from "accelerated aging", which means that they have the same problems and physical characteristics of aging as the general population, but that these changes occur faster [1]. The reasons for this accelerated aging are not clear, but several genes on chromosome 21 have been associated with the aging process.



Diagnostic of Alzheimer's disease in Down syndrome

The diagnosis of cognitive impairment in Down syndrome is more complex than in the general population and requires the assessment of deterioration in a population with pre-existing intellectual disabilities. Moreover, the cognitive presentation of Alzheimer's disease in Down syndrome is controversial as different presentations (amnesic, executive dysfunction, behavioural) have been described [5].

Cognitive complaints are seldom the referral symptom; in contrast, neuropsychiatric disturbances and/or deterioration in their activities of daily living constitute the main reason for consultation. However, some frequent neuropsychiatric disturbances in Alzheimer's disease, such as apathy and depression, are also common in Down syndrome without dementia (5,6).

Furthermore, there is great variability among Down syndrome subjects in everyday performance (particularly at older ages). Cognitive functioning not only depends on the genetic background, but also depends on environmental factors. Education, learning, cognitive stimulation, social engagement and, ultimately, the life experience of each individual can play a role on the structure, organization and functioning of the brain, and in consequence in the intensity of cognitive disorders.

In the medical evaluation of Down syndrome subjects, it is therefore essential to consider both the basal functioning of the person, but also to perform longitudinal evaluations. Diagnostic procedures and follow-up assessments differ greatly between different regions and countries, referral is often late, and specialized centers with knowledge about aging in intellectual disabilities are scarce. Diagnostic and referral operating procedures are not yet standardized in many cases, and local Down syndrome associations often need to re-invent the wheel. Therefore, the T21RS Committee for Science & Society selected a successful example of a comprehensive medical evaluation programme in Spain, which is described below.

A novel and comprehensive health plan for adults with Down syndrome in Catalonia



In Catalonia, a collaboration between the Catalan Down Syndrome Foundation and the Hospital of Santa Creu i Sant Pau has enabled the development of a pioneering plan to address the medical comorbidities associated with aging in Down syndrome with a specific emphasis on Alzheimer's disease and neurological diseases.

The Down Medical Centre (DMC) is a service provided by the Catalan Down Syndrome Foundation. The DMC, located in Barcelona (Catalonia), was created almost 30 years ago and offers medical care specifically for people with Down syndrome. The DMC is divided into a pediatric and an adult

outpatient clinic, and works in collaboration with the public Health Services provided by the Catalan Government (Generalitat de Catalunya). Its main objective is the design and implementation of health plan to diagnose those medical comorbidities associated with Down syndrome. Currently, it is formed by 15 different medical specialists and 5 psychologists and has over 2500 medical histories from Down syndrome individuals (more than 1800 adults with Down syndrome, 30% of them over 40 years old). The DMC acts as the referral center for Down syndrome in Catalonia and attends approximately 50% of the Down syndrome population.

To enjoy all the wonderful aspects of a longer life it is important to take the initiative and meet the problems that may arise. In 2011, the Catalan Down Syndrome Foundation, aware of the magnitude of the new challenge represented by the cognitive impairment in Down syndrome adults, introduced a renewed health plan in adults to address this problem.

The renewed health plan in adults involves two phases. The first one (primary medicine) is a "screening" of medical illnesses and evaluation of cognitive status. The core team performing this first phase of health plan is composed of neurologists, (neuro)psychologists and social workers. This screening consists of a standardized medical, neurological and comprehensive neuropsychological evaluation. An electroencephalogram and a blood test are also performed. These evaluations are performed every three years between 18 and 30 years of age; every 2 years between 30 and 40 years of age, and annually thereafter.

The second phase of this health plan (tertiary medicine) starts whenever any neurological or other medical disturbance is suspected. In those cases, adults with Down syndrome are referred to a tertiary hospital (Hospital de la Santa Creu i Sant Pau, located in Barcelona) which centralizes the specialized care in order to confirm the diagnosis with any necessary ancillary evaluation and to apply the corresponding treatment. This health plan is active from May 2014, and is freely offered to any individual with Down syndrome who is a resident in Catalonia.

Clinical research associated with the health plan

The Alzheimer's disease natural history in Down syndrome subjects is poorly understood. Therefore, the diagnosis of Alzheimer's disease in Down syndrome is difficult and often arrives late. Consequently, there is an urgent need for longitudinal observational studies to better understand the disease and enable future therapeutic approaches. Biomarkers are measurable "indicators" of the severity or presence of a disease state. Alzheimer's disease biomarkers have been extensively developed and are now part of the new diagnostic criteria in the general population. Unfortunately, few studies have been reported in Down syndrome.

For these reasons, a clinical research study has been implemented: the "Down Alzheimer Barcelona Neuroimaging Initiative" Project (DABNI). This clinical research study is offered to all adults with Down syndrome included in the aforementioned health plan and consists of the following periodic evaluations (carried out at the same time as the screening visits of the health plan): biomarker analysis, brain imaging, and a sleep study with a polysomnogram. The results, embedded in different international collaborations, will allow us to better understand the evolution of cognitive impairment in Alzheimer's disease, and therefore, to enhance an earlier detection in order to improve the health and the quality of life of adults with Down syndrome.

** The Committee for Science & Society consists of prof. dr. Peter Paul De Deyn (chairman, Belgium), Juan Fortea (Spain), Sebastián Videla (Spain), Hannah Wishnek (USA) and Alain Dekker (The Netherlands).*



T21RS is the first, and only, non-profit scientific organization of researchers studying Down syndrome, founded to promote research, apply new scientific knowledge to develop improved treatments and cures, and to explain (recent) findings to the general public. More information? Visit www.T21RS.org or send a mail: info@T21RS.org (in English, Francais, Nederlands).

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