

# Variability of the Aging Process in Dementia-Free Adults With Down Syndrome

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## Abstract

The aim of this cross-sectional study was to analyze the typical aging process in adults with Down syndrome, focusing on its variability. The sample comprised 120 adults with Down syndrome who were free of dementia. Ages ranged from 20 to 69 years. Each participant was assessed on cognitive functioning and social adaptation, and was checked for the presence of psychopathological disorders. Results revealed an age-related deterioration in both cognitive and social adaptation skills, the extent of this decline depending on the dimension under scrutiny, and interindividual variability in aging profiles.

**Key Words:** *Down syndrome; aging; social adaptation; cognitive functioning*

The aim of the present study was to explore age-related cognitive changes in *healthy* (i.e., free of dementia) adults with Down syndrome (DS). Given the prevalence of this syndrome, plus improvements in the life expectancy of people with DS, the time seemed right to look at how social and cognitive abilities change across the lifespan, focusing on variability in the aging process. We set out to answer two questions. First, is there a general, across-the-board decline, or do some psychological functions or domains deteriorate faster than others? Second, and above all, does the entire population of older adults with DS exhibit the same pattern of decline, or is there a degree of interindividual variability?

## Demographic Data: Incidence, Prevalence, and Life Expectancy

Although the incidence of DS remains relatively stable (1 birth in 650–1,000; Bittles, Bower, Hussain, & Glasson, 2006), the prevalence of DS has been on the increase, mainly resulting from improved life expectancy. At the present time, there are estimated to be 350,000 people with DS in the United States, 30,000 in the United Kingdom, and 32,000 in Spain (Rondal, 2009). Over the past 50 years, the survival rate at 1 year

for babies with DS has risen from 50% (Record & Smith, 1955) to more than 90% to 95% (Bittles et al., 2006; Leonard, Bower, Petterson, & Leonard, 2000). In their study, Weijerman et al. (2008) reported a neonatal mortality rate of 1.65% for babies with DS, compared with 0.36% in the general population, and an under-1-year mortality rate of 4% versus 0.48%. When Quanhe, Rasmussen, and Friedman (2002) looked at mortality and morbidity among people with DS living in the United States, they found that the median age at death was 25 years in 1983 and 49 years in 1997, but stressed that there were major disparities between different ethnic groups. According to Rasore-Quartino (1999), life expectancy improved consistently across the previous century, rising from 9 years in 1929 to 12 years in 1947, and 52 years in 1970. It has now reached 61.1 years for men and 57.8 years for women (Bittles et al., 2006; Glasson et al., 2003), although we should point out that not all studies have found a sex difference in life expectancy (Coppus et al., 2008; Torr, Strydom, Patti, & Jokinen, 2010). The study conducted by Bittles et al. (2006), based on data from 298 death certificates, found that 29.9% of the adults in their sample died after the age of 50 years, with a quarter of these dying between the ages of 57 and 62 years. Many factors have been

put forward to explain this trend, including the move away from institutionalized care that began in the 1970s, improved healthcare, and educational provision. Despite their longer life expectancy, people with DS still have higher mortality rates than the general population in every age group (Coppus et al., 2008; Quanhe et al., 2002). In early life, mortality risks are often associated with heart defects and leukemia, whereas in adulthood, the risks are associated with Alzheimer's disease and accelerated aging (Quanhe et al., 2002). Coppus et al. (2008) underscore the sheer number of different mortality risk factors for adults with DS, the main ones being age, the presence of dementia, and mobility restriction. Western societies are therefore seeing a steady rise in the number of adults with DS age 40 years or above. Projective studies suggest that the size of this group will increase by 100% between now and 2045 (Larsen & Kirkevold, 2008). As recently as the early 1980s, Alzheimer's disease was considered an inevitable result of growing old with DS. Epidemiological studies clearly show that not all members of this at-risk population go on to show symptoms of Alzheimer's-type dementia (Zigman, 2013; Zigman & Lott, 2007). Despite these data, normative aging in DS is an understudied area of investigation. More research is therefore needed to explore age-related cognitive changes in cognitive and adaptive skills, focusing on variability aging process. Interindividual variability analyses may well improve our knowledge of the typical aging process in adults with DS and help us to design targeted interventions to assist this population.

### **Normative Aging and Alzheimer's Disease**

There is a relative consensus among studies of aging in adults with DS that cognitive functions and social adaptation skills gradually deteriorate with age. It should be stressed at this point that the premature aging observed in DS is quite different from the negative changes that occur as a result of Alzheimer's disease, a degenerative disorder that affects 30% of adults with DS over the age of 55 years (Coppus et al., 2006). At the cognitive level, research has highlighted a decline in cognitive functioning (Carr, 2003, 2005; Coppus et al., 2008; Iacono, Torr, & Wong, 2010) that is particularly rapid among adults with DS exhibiting Alzheimer's-type dementia (Devenny, Krinsky-McHale, Sersen, & Silverman,

2000; Silverman, Zigman, Krinsky-McHale, & Schupf, 2011). Beciani, Vetro, Barisnikov, De-traux, and Van der Linden (2011)'s study of 115 dementia-free adults with DS age 25–56 years found a negative correlation between age and executive functions (memory, selective attention, and planning). Meanwhile, in their longitudinal study of 58 dementia-free adults with DS age 31–56 years, Hawkins, Eklund, James, and Foose (2003) observed a similar aging process to that seen in the general population, but occurring earlier in life. In adults with DS, abilities reflecting crystallized intelligence continue to increase until 50 years, but there is an early decline in the abilities involved in fluid intelligence (Hawkins et al., 2003). Given that the decline in cognitive functions is less rapid in high functioning adults with DS (Oliver, Crayton, Holland, Hall, & Bradbury, 1998; Temple, Jozsvai, Konstantareas, & Hewitt, 2001), a high intellectual quotient may help to protect against aging and the risk of Alzheimer's-type dementia (Zigman & Lott, 2007). Concerning language, several cross-sectional studies have highlighted differences in linguistic performances between older individuals with DS (40–70 years) and their younger counterparts (Moss, Tomoeda, & Bayles, 2000; Prasher, 1996). The greatest differences concern language comprehension, articulatory precision, and speech rhythm. It should be noted that other studies have failed to find any effect of age on lexical and morphosyntactic aspects (Das, Divis, Alexander, Parrila, & Naglieri, 1995; Rondal, 2009), and Rondal (2009) goes as far as to say that there are insufficient data to confirm the hypothesis of a linguistic decline setting in dementia-free adults with DS before the age of 50. Although there has been less research on changes in the social adaptive behaviors of older adults with DS than on changes in their cognitive functioning, it is nonetheless crucial to find out more about the impact of age and the advent of Alzheimer's-type dementia on these behaviors. Both longitudinal and cross-sectional studies have reported a decline in adaptive behaviors from 45 to 50 years onwards (Collacott, 1992; Collacott & Cooper, 1997; Hawkins et al., 2003; Prasher & Chung, 1996). For example, Hawkins et al. (2003)'s longitudinal investigation, based on dementia-free adults with DS, found that adaptive behaviors were relatively stable up to the age of approximately 45 years, but beyond that point there was a deterioration in performances. The rate of decline accelerates with

age, especially among adults with DS exhibiting Alzheimer's-type dementia (Burt et al., 1995; Prasher, Chung, & Haque 1998). Intersyndrome comparisons have shown that adults with DS are more exposed to premature aging than other populations with intellectual disabilities (Prasher, 1999; Rasmussen & Sobsey, 1994; Zigman, Schupf, Lubin, & Silverman, 1987). As for possible differences in the extent to which each adaptive domain is affected, the data are rather divergent. In their study, Zigman et al. (1987) found that this decline was more marked in the daily living domain, but other researchers have reported deterioration in communication, especially the receptive aspect of language (Collacott & Cooper 1997; Rasmussen & Sobsey, 1994). No variability of any sort was observed by Hawkins et al. (2003), who reported a uniform decline. These divergent results can probably be attributed to the diversity of methods used, be it in terms of measurement tools, approach (longitudinal vs. cross-sectional) or the participants' age range. The decline in cognitive functioning and social adaptation that occurs in the normative aging in DS does not appear to be accompanied by a worsening of mental health. Several studies have looked for and failed to find an age-related increase in the prevalence of psychiatric disorders (Beciani et al., 2011; Mantry et al, 2008), including the investigation conducted by Patti and Tsiouris (2006) among 206 adults with DS age 20–71 years. These authors found that anxiety and mood disorders were more frequent than psychotic ones, regardless of age group. For their part, Urv, Zigman, Silverman, and MacLean (2008) concluded that the number and severity of maladaptive behaviors are indicators of the progression of Alzheimer's disease. As the disease worsens, these behaviors become increasingly severe. In theory, adults with DS should develop Alzheimer's-type dementia from 35 to 40 years onwards. Although the presence of the characteristic lesions is typical of aging in DS, however, epidemiological studies clearly show that not all members of this at-risk population go on to show symptoms of Alzheimer's-type dementia (Bittles et al., 2006; Coppus et al., 2008; Quanhe et al., 2002; Torr et al., 2010). The risk of developing this disease therefore parallels the risk within the general population, but 20–25 years earlier for adults with DS, highlighting the interval between the appearance of the neuropathological signs and the disease's clinical onset (Zigman, 2013; Zigman & Lott, 2007). The

case report by Krinsky-McHale et al. (2008) is a good illustration of the variations in aging that can occur in DS. Mr. C, a 70-year-old with free trisomy 21, displayed none of the cognitive and functional deterioration that typifies the disease, let alone dementia, and the authors even titled their article "Successful aging." To gain a clearer understanding of normal aging in DS, we conducted a cross-sectional study of a large sample of adults with DS aged 20–69 years, in which we assessed their cognitive functioning, social adaptation skills, and the possible presence of psychopathological disorders. We set out to answer two questions. First, is there a general, across-the-board decline, or do some psychological functions or domains deteriorate faster than others? Second, and above all, does the entire population of older adults with DS exhibit the same pattern of decline, or is there a degree of interindividual variability? To meet our objectives, we used two types of statistical analysis. The first one was an analysis of variance (ANOVA) designed to reveal differences between participants along several dimensions. The second one, based on the hierarchical clustering procedure, was intended to highlight interindividual variability in the aging profiles.

## Method

### Participants

The sample comprised 120 adults with DS (57 men and 63 women), age 20–69 years, who were free of dementia. All the participants were assessed on the Dementia Scale for Down Syndrome (Geydye, 1995), and none of them were found to display any signs of dementia. The sample was divided into four age groups: Group 1 (20–29 years), Group 2 (30–39 years), Group 3 (40–49 years), and Group 4 (50 years and above). The characteristics of the sample are set out in Table 1, which also includes sociodemographic variables.

### Procedure

The participants were assessed as part of their regular medical and psychological follow-up at the genetics department of St. Etienne University Hospital (France). Before this assessment, a letter of consent stating the purpose of the study and describing its procedures was sent to all the adults with DS, as well as to their legal guardians, in accordance with the code of conduct of the

Table 1  
*Sample Characteristics (N = 120)*

	Group 1 (20–29 yrs)	Group 2 (30–39 yrs)	Group 3 (40–49 yrs)	Group 4 (50+ yrs)
Mean age ( <i>SD</i> )	24.4 yrs (3.1)	34.5 yrs (3.1)	44.2 yrs (2.8)	55.2 yrs (5.4)
Sex	18 men 18 women	16 men 23 women	14 men 14 women	9 men 8 women
Living arrangements:	11%	2.5%	0%	12%
<i>Own home</i>	78%	61.5%	21.5%	12%
<i>Parental home</i>	11%	36%	78.5%	76%
<i>Institution</i>				
In employment	64%	77%	67%	47%
<i>N</i>	36	39	28	17

American Psychological Association (2012). This letter of consent, together with the research project, was approved by the hospital’s institutional review board. Only those adults who had given their written informed consent took part in the study. The entire sample was assessed on cognitive functioning, social adaptation, and possible behavioral disorders. The participants were tested individually in a quiet, isolated room in the hospital’s genetics department.

**Cognitive functioning.** Cognitive functioning was assessed by means of Raven’s matrices, a set of nonverbal intelligence tests eliciting analogical and inductive-logic reasoning. We chose to use Raven’s Colored Progressive Matrices (CPM; Raven, Court, & Raven, 1998) because they are more suitable for adults with intellectual disabilities, in terms of material, test duration, and level of difficulty. Participants are shown series of cards featuring increasingly complex problems. Each problem comprises a colored, abstract pattern (or set of patterns) that participants have to complete by selecting the correct part from a number of options. There are three series: *A* (sameness and difference in continuous patterns); *Ab* (discrete patterns belonging to a spatially organized whole); and *B* (analogical modifications of logically and spatially organized drawings).

**Social adaptation.** Adaptive behavior was assessed by means of the Vineland Adaptive Behavior Scales (VABS; Sparrow, Balla, & Cicchetti, 1984). This assessment took the form of a semistructured interview between the experimenter and an adult (parent/primary carer) who knew the participant well. We focused on four domains

of adaptive behavior: (a) Communication (receptive, expressive and written); (b) Daily living skills: personal (eating, dressing, practicing personal hygiene), domestic (which household tasks the person performs), and community (how the person uses his or her time, money, telephone, occupational skills); (c) Socialization: interpersonal relationships (whether the individual interacts properly with others), play and leisure time, and coping skills (demonstrates responsibility within the group and sensitivity toward others); and (d) Motor skills: gross motor skills (how the participants moves their arms and legs and coordinates their movements), and fine motor skills (using fingers and hands to manipulate objects). Each behavioral item was rated on the basis of regularity and performance, on a scale of zero (*No, never*), 1 (*Sometimes or partly*), and 2 (*Yes, habitually*). *Not applicable* and *Don’t know* responses could also be given, but were not taken into account in the scoring. A raw score was calculated for each domain, by summing the scores for all the relevant items. The Communication domain comprised 67 items (maximum raw score = 134), Daily Living 92 items (maximum raw score = 184), Socialization 66 items (maximum raw score = 132), and Motor skills 36 items (maximum raw score = 72).

**Psychopathological disorders.** The presence of behavioral disorders was assessed by means of the Reiss Screen for Maladaptive Behavior (RSMB; Reiss, 1988). This measurement instrument is designed to screen for psychiatric problems in people above the age of 12 years with intellectual disabilities, and contains 38 items describing the



symptoms of one or more mental health problems, based on *DSM-III-R* criteria (American Psychiatric Association, 1987). For each of these items, a respondent who knows the person well has to state whether the behavior is *not a problem* (zero), *a problem* (1) or *a major problem* (2) in that person's life. Based on these ratings, an overall score is calculated (maximum = 76).

The data analyses (cluster analyses and ANOVA) were performed on the raw scores on all these different assessments.

## Results

### Effect of Age

**Effect of age on CPM scores.** To investigate the effect of age on the participants' cognitive functioning, we ran a repeated-measures ANOVA comparing the raw scores of the four age groups on the three CPM series. The first part of Table 2 sets out the mean (standard deviation) overall scores and series scores for each of the four age groups.

We found a medium main effect of Age,  $F(3, 116) = 4.28, p = .007, \eta = .32$ . Results showed that scores declined noticeably with age, especially after 40 years. Thus, while the scores of the two older groups (Groups 3 and 4) did not differ significantly from each other, they were significantly lower than those of the two younger groups (Groups 1 and 2) (Scheffé's post hoc test,  $p < .05$ ). There was also a large main effect of Series, with better performances on Series A than on Series Ab which, in turn, yielded higher scores than Series B,  $F(2, 232) = 200.17, p = .0001, \eta = .89$ . There was a medium effect of the Age x Series interaction,  $F(6, 232) = 4.02, p = .0001, \eta = .31$ . This effect showed that differences in scores between the different age groups depended on the series. Thus, while there were very considerable differences for Series A and Ab, the only significant difference for Series B was between Group 1 (20–29 years) and the other three groups (Scheffé's post hoc test,  $p < .05$ ).

**Effect of age on VABS scores.** We ran a repeated-measures ANOVA to compare the VABS scores of the four age groups. To render the domain scores comparable, we calculated the participants' success rates (expressed as percentages), by dividing their raw scores by the maximum possible scores, then multiplying them by 100. The second part of Table 2 sets out the mean (standard deviation) success rates subjected to the ANOVA.

Results revealed a main effect of Age, with the youngest participants achieving the highest scores,  $F(3, 116) = 7.22, p = .0001, \eta = .40$ . There was also a large main effect of Domain,  $F(3, 116) = 168.10, p = .0001, \eta = .98$ , in that communication scores were lower than scores on daily living and socialization, which did not differ from each other but were both lower than motor skill scores. There was a small Age x Domain interaction effect,  $F(9, 348) = 2.41, p = .01, \eta = .24$ . Scores on communication did not differ significantly between groups, but between-group differences were found on motor skills, socialization, and daily living. Regarding the latter, there was a sharp decline after 40 years. Thus, though the scores of the two older groups (Groups 3 and 4) did not differ significantly from each other, they were lower than those of the two younger groups (Groups 1 and 2) (Scheffé's post hoc test,  $p < .05$ ).

**Effect of age on RSMB scores.** To verify that psychopathological disorders were independent of age, we ran a single-factor multivariate analysis of variance (MANOVA) to compare the overall scores on the RSMB and the subscale scores for each of the four age groups (shown in the last part of Table 2). No significant difference emerged between the four groups, underlining the absence of an effect of age on the onset or worsening of psychopathological problems.

### Cluster Identification

**Data analysis strategy.** The purpose of the cluster analysis was to identify different types of psychological functioning within our sample of adults with DS ( $N = 120$ ), in order to show that interindividual variability was not restricted to differences in the overall scores between high and low performing individuals. The clustering procedure brings distinctive profiles to light and provides a means of exploring the variables associated with these distinctive profiles. A cluster is an entity containing individuals who share a similar profile across a set of variables. Because this is an exploratory type of analysis, in that the number of potential clusters is not known beforehand, it requires two separate steps. In the first step, which serves to determine the minimum number of clusters required for a psychologically relevant grouping, the dataset is sorted in ascending order (Johnson, 1967). In the second step, the individuals are reliably classified. We used *K*-means clustering, one of the most widely

**Table 2**  
*Mean Scores (Standard Deviation) on Raven’s Colored Progressive Matrices (RCPM), the Vineland Adaptive Behavior Scales (VABS), and Psychopathological Disorders (RSMB) for the Four Age Groups of Adults With DS*

		20–29 yrs	30–39 yrs	40–49 yrs	50+ yrs
RCPM (Raven)	Overall score	21.77 (6.29)	21.46 (6.26)	17.39 (6.62)	17.06 (6.78)
	Series A	8.72 (2.31)	9.49 (2.20)	7.29 (2.58)	7.65 (2.78)
	Series Ab	8.03 (2.86)	7.90 (2.85)	5.96 (3.19)	6.00 (3.43)
	Series B	5.03 (2.10)	4.15 (1.89)	4.14 (1.73)	3.41 (2.27)
VABS (Vineland)	Overall score	211.42 (55.64)	195.82 (49.56)	157.86 (48.79)	170.82 (64.80)
	Communication	23.04 (13.66)	21.64 (11.90)	18.07 (9.11)	22.40 (14.47)
	Daily living	30.07 (11.95)	28.37 (11.27)	19.80 (9.09)	23.24 (13.35)
	Socialization	44.26 (14.26)	38.27 (113.64)	31.30 (13.51)	32.26 (12.93)
	Motor skills	92.13 (8.00)	89.07 (9.95)	77.63 (14.33)	78.84 (13.76)
RSMB (Reiss)	Overall score	4.69 (5.54)	6.82 (5.88)	7.68 (7.18)	7.00 (7.09)
	Agressive B.	0.47 (1.30)	0.31 (0.77)	0.25 (0.80)	0.65 (1.27)
	Psychosis	0.06 (0.23)	0.49 (0.94)	0.68 (1.28)	0.53 (0.87)
	Paranoia	0.42 (0.81)	0.62 (1.07)	0.71 (1.05)	0.76 (0.83)
	Depression (B.)	1.00 (1.35)	1.28 (1.41)	1.47 (1.53)	1.29 (1.49)
	Depression (P.)	0.97 (1.42)	1.18 (1.43)	1.43 (1.50)	1.64 (2.15)
	Dependant	0.89 (1.09)	0.92 (0.90)	1.18 (1.40)	0.76 (1.09)
	Avoidant	0.67 (1.31)	1.32 (1.96)	1.32 (1.52)	1.06 (1.39)
	Autism	0.22 (0.54)	0.60 (0.88)	0.64 (0.99)	0.29 (0.77)

*Note.* RSMB = Reiss Screen for Maladaptive Behavior; DS = Down syndrome; B. = Behavior; P. = Physic. The mean score in the adaptive behavior (VABS) are expressed in success rates.

used methods in psychometrics, and one that is relatively robust (Lattin, Carroll, & Green, 2003; Saita, Raphael, & Smith, 2008). Adopting the same approach as that of Tsao and Kindelberger (2009), we focused on the adaptive and cognitive performance dimensions. We therefore positioned the individuals according to their raw scores for each VABS domain (communication, daily living, socialization, and motor skills) and their level of cognitive functioning (CPM). To achieve reasonable cluster sizes, we opted to analyze the whole sample, collapsing the four age groups. We then looked at whether the clusters we had identified differed on age, sex, or psychopathological disorders.

**Cluster analysis results.** After normalizing the scores, we sorted the data in ascending order, using Ward’s algorithm (1963). The final tree diagram clearly pointed to the existence of five clusters. *K*-means clustering is sensitive to outliers (Saita et al, 2008); but because the dataset contained few extreme values (4 out of 210), we believe that the clustering results were reliable. Moreover, we repeated the procedure several times

to check that the classification was not affected by the randomness of the initial cluster centers—a potential drawback with this procedure (Jain & Dubes, 1988). Figure 1 shows the five different profiles we established for our sample of adults with DS, based on their VABS and CPM scores. There was a between-clusters effect for each of the five dimensions we considered: communication,  $F(4, 115) = 226.03, p = .0001$ ; daily living,  $F(4, 115) = 105.63, p = .0001$ ; socialization,  $F(4, 115) = 70.75, p = .0001$ ; motor skills,  $F(4, 115) = 45.12, p = .0001$ ; and cognitive functioning,  $F(4, 115) = 42.68, p = .0001$ . The clusters differed on the participants’ overall levels of performance. Thus, Clusters 2 and 4 contained adults with DS who performed significantly better than those in the other three clusters. Conversely, Clusters 1 and 3 contained adults with DS who performed more poorly than those in the other three clusters. The adults in Cluster 5 achieved average scores on all five dimensions.

Two clusters (Clusters 1 and 2) had atypical profiles. Cluster 2 differed significantly from Cluster 4 on three dimensions. It was characterized by better performances on communication,

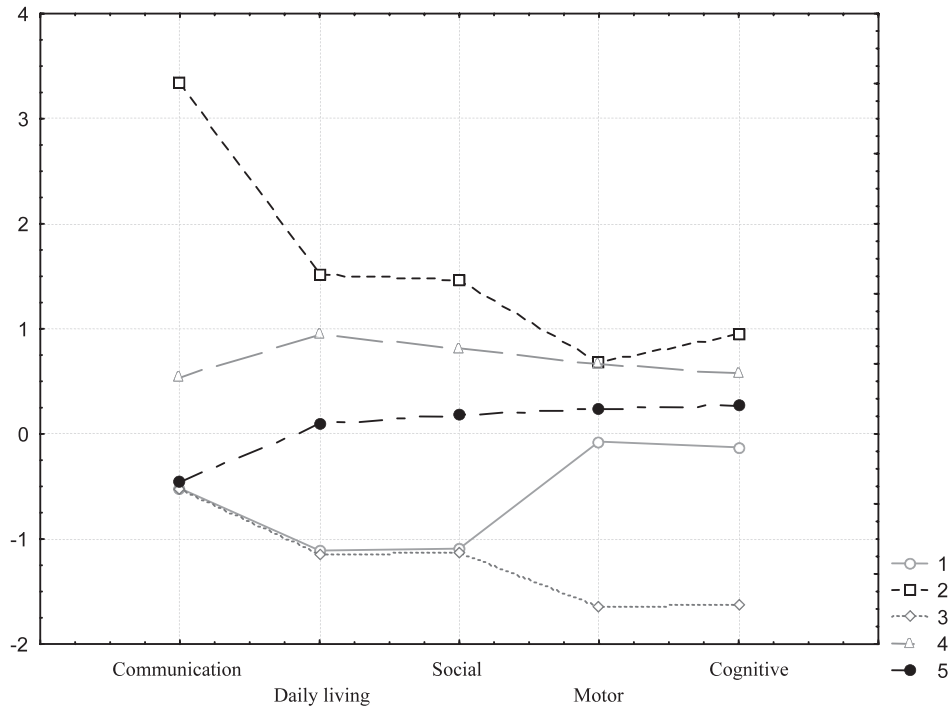


Figure 1. Profiles of the five clusters.

$t(49) = 12.16, p = .0001$ , daily living,  $t(49) = 2.29, p = .02$ , and socialization,  $t(49) = 2.24, p = .03$ . Similarly, although the adults in Cluster 1 generally performed poorly, they fared slightly better on motor skills and cognitive functioning (CPM), especially compared with Cluster 3,  $t(36) = 6.37, p = .0001$  and  $t(36) = 6.37, p = .0001$ .

**Clusters, age, and sex.** Chi-square analyses showed that each cluster contained the same number of men as women,  $\chi^2(4) = 2.38, p = .67$ , indicating that the profiles were independent of sex. To study the relationship between age and cluster membership, we collapsed the original four age groups to form a *younger adults* group, comprising Groups 1 (20–29 years) and 2 (30–39 years), and an *older adults* group, comprising Groups 3 (40–49 years) and 4 (50+ years). This new grouping gave us a sufficient number of participants in each new group to run the chi-square tests and was coherent with our initial results. Analyses revealed that cluster membership was not independent of age,  $\chi^2(4) = 19.04, p = .0008$ . Cluster membership distribution by age (Table 3) showed that the two clusters with atypical profiles (Clusters 1 and 2) contained equal numbers of younger and older adults, whereas the clusters characterized by a generally uniform level of performance had an asymmetrical distribution, in

that younger adults were over-represented in Clusters 4 and 5, and older adults in Cluster 3.

We can conclude that all five profiles were unrelated to sex and that the two atypical profiles were also independent of age, unlike the three others.

**Profiles and psychopathological disorders.** Our initial results had shown that psychopathological disorders were not age-related. We therefore used the clustering procedure to explore whether these disorders were related to distinctive cognitive and adaptive profiles, running a MANOVA to compare the five clusters on their mean level of psychopathological disorders (RSMB). This revealed a main effect of Cluster,  $F(32, 400) = 2.70, p = .0001$ . All the results are set out in Table 4.

Although psychopathological disorders were not related to age, as revealed in the initial results, they were significantly related to some of the profiles. The overall scores on psychopathological disorders were higher for Clusters 1, 2, and 3, than for Clusters 4 and 5. It should be recalled that Clusters 1 and 3 contained adults with DS who scored poorly on all five dimensions, whereas Cluster 2 contained adults with DS who had consistently high levels of performance. Clusters 1 and 3 appeared to be characterized by psychosis,

**Table 3**  
*Distribution of Younger and Older Adults Across the Clusters*

Age group	Cluster				
	1	2	3	4	5
Younger	4	9	5	29	28
Older	3	10	14	6	12
Total	7	19	21	35	40

autism, avoidant disorder and depression (physical signs), whereas participants in Cluster 2 only scored higher on depression. These results clearly showed that poor performers and those with atypical profiles were more affected by psychopathological disorders.

### Discussion

The aim of this article was to explore age-related changes in cognitive functioning and adaptive behaviors among dementia-free adults with DS age 20–69 years. Data analyses revealed a decline in both social and cognitive skills with age. Further, results (a) showed that the extent of the age-related changes varied according to the dimension under scrutiny, and (b) highlighted interindividual variability in the aging profiles.

### Age and Dimension

As far as cognitive functioning is concerned, the ANOVAs on the raw CPM series scores revealed a general decline in performances. It also highlighted an interaction effect of Age and Series, with Age having a greater effect on Series A and Ab than on Series B. The relative stability of the Series B scores can probably be attributed to the fact that all the age groups, including the youngest ones, scored poorly on these items, because of the complex processes they elicited (analogical modifications in spatially and logically organized drawings). Facon and Nuchadee (2010) found that a similar pattern of performance on the 36 items (Series A, Ab, and B) of the CPM was displayed by three different groups (DS, intellectual disability, unselected), although other studies have identified distinctive patterns of errors made by people with DS (Gunn & Jarrold, 2004; Vakil & Lifshitz-Zehavi, 2012). Results also showed that the decline observed in fluid intelligence, as measured by the CPM, is far from linear between 20 and 69 years. A significant drop in scores was observed at around 40 years, marking the start of accelerated aging. Further studies are needed, however, to undertake more finely tuned analyses of the aging process in different areas of cognitive development using a neuropsychological battery. Regarding adaptive behaviors, our data once again showed that, though

**Table 4**  
*Mean Scores (Standard Deviation) of the Five Clusters for Each Type of Psychopathological Disorder (RSMB)*

	Cluster					F	p
	1	2	3	4	5		
Overall score	10.26 (6.50)	7.29 (7.18)	10.05 (9.30)	4.66 (5.53)	4.46 (4.14)	5.39	.0006
Aggressive behavior	0.74 (1.69)	0.71 (1.25)	0.90 (1.55)	0.22 (0.75)	0.16 (0.48)	2.48	.05
Psychosis	0.47 (0.51)	0.00 (0.00)	1.43 (1.69)	0.31 (0.74)	0.09 (0.36)	9.56	.0001
Paranoia	0.84 (0.83)	0.71 (1.11)	0.76 (1.22)	0.66 (1.18)	0.40 (0.66)	0.95	.44
Depression (behavioral signs)	1.63 (1.30)	1.86 (2.04)	1.24 (1.61)	1.13 (1.43)	1.12 (1.38)	0.77	.55
Depression (physical signs)	2.32 (1.89)	1.71 (2.42)	1.86 (1.80)	0.63 (1.18)	0.91 (1.09)	5.50	.0005
Dependent personality disorder	1.11 (1.20)	1.57 (1.51)	1.24 (1.37)	0.81 (1.00)	0.79 (0.99)	1.29	.28
Avoidant disorder	2.37 (2.17)	0.71 (1.11)	1.81 (1.91)	0.75 (1.46)	0.58 (0.76)	6.59	.0001
Autism	0.79 (1.08)	0.00 (0.00)	0.81 (0.93)	0.16 (0.45)	0.42 (0.79)	3.76	.007

*Note.* RSMB = Reiss Screen for Maladaptive Behavior.



the general level of abilities deteriorated with age, the extent of the age-related changes varied according to the domain. Although the scores on motor skills, socialization, and daily living all declined, they remained stable for communication. Several studies have shown that in some areas of language, such as vocabulary reception and production, there are no age-related changes (Das et al., 1995; Rondal, 2009). As with Series B of the CPM, the relative stability of communication skills can probably be explained by the fact that all the age groups, including the youngest ones, scored poorly. These data are probably closer to the well-known phenotype of DS. Though this behavioral phenotype includes strengths in some aspects of visuospatial processing and social functioning, language has been described as a major area of deficit, with particular difficulties in expressive language, grammar, and articulation (Dykens, Hodapp, & Finucane, 2005; Fidler, Philofsky, & Hepburn, 2007). Further, although performances on motor skills and socialization underwent a steady deterioration, daily living skills declined sharply from 40 years onwards. These data are in line with the results reported by Zigman et al. (1987), who showed that skills in this domain are extremely sensitive to age in adults with DS. It appears that the most sensitive manifestations of regression in DS population are found in behavioral domains related to activities of daily living. This observation can be explained by initial low levels of competence in cognitive skills or language.

Concerning behavioral disorders, our analyses of RSMB scores failed to reveal any age-related increase in the prevalence of psychiatric disorders within our sample of adults with DS but free of dementia. These data confirm the results of previous studies (Beciani et al., 2011; Mantry et al., 2008; Patti & Tsiouris, 2006) and show that typical aging in adults with DS is not characterized by the onset of psychiatric problems, but rather a decline in the level of cognitive functioning and social adaptation skills.

### **Profile Variability**

To look for aging profiles, we implemented a clustering procedure that yielded five clusters, or homogeneous categories of individuals, each corresponding to a different profile. These profiles could be differentiated on the basis of their overall levels of cognitive and social skills, with the adults with DS in Clusters 2 and 4 performing

significantly better than those in the other three clusters. Although Cluster 4 represented relatively homogeneous skills, however, Cluster 2 was characterized by particularly good communication performances. Clusters 1 and 3 contained adults with DS who scored below average on all five dimensions. Once again, there was one homogeneous profile (Cluster 3) and one (Cluster 1) that was characterized by higher scores on motor skills and cognitive functioning. Cluster 5 contained adults with average performances across the board. Though psychopathological disorders were not age related (as shown by the initial results), the clustering procedure revealed that they were significantly related to three of the cognitive and adaptive profiles (Clusters 1, 2, and 3). These results clearly showed that poor performers and individuals with atypical profiles are more affected by psychopathological disorders. It is important to note that the variability we observed in the profiles was not linked solely to age. Although younger adults (20–39 years) dominated the consistently high- or average-performance clusters (Clusters 4 and 5) and their older counterparts the consistently low-performance cluster (Cluster 3), they were evenly distributed within the two atypical clusters (Clusters 1 and 2), where performances were heterogeneous. The fact that these two clusters contained equal numbers of older and younger adults leads us to conclude that membership of these particular clusters was not dependent on age. This finding can be explained by the educational opportunities afforded to people with DS. As in several previous studies (Coppus et al., 2008; Temple et al., 2001; Zigman & Lott, 2007), we can postulate that environmental factors play a key role in aging and were responsible for the some of the interindividual differences reported here. A number of studies have highlighted the importance of education and medical care in the development of people with DS (Buckley, Bird, Sacks, & Archer, 2006; Couzens, Haynes, & Cuskelly, 2012; Hanson, 2003). Although comprehensive health assessment programs have improved health outcomes among people with intellectual disability (Cooper et al., 2006), many adults with DS still do not have access to regular health care, despite the high frequency of medical complications (Henderson, Lynch, Wilkinson, & Hunter, 2007; Määttä et al., 2011). The variability we found can also be attributed to epigenetic factors, such as allelic variation and genomic imbalance (Lott & Dierssen, 2010); and we can

surmise that the complexity and variability of gene-environment interactions play a decisive role in cognitive changes. These potential explanations must be followed up by future research before conclusions can be drawn.

### Limitations and Prospects

Although cluster analyses allow data to be examined from a different angle, they are largely dependent on the nature of the data and, accordingly, on the individuals selected for study. Their findings cannot, therefore, be generalized; and the profiles they yield will not necessarily be identified in the parent population. A limitation of the present data is the unknown general developmental level of the various age groups and clusters. More research based on mental age level is therefore required to establish consistent profiles. In addition, results from cross-sectional research designs, which are subject to confounds associated with cohort effects, are especially difficult to interpret. Cohort effects arise from the different life experiences of people who reach specific ages at different historical points in time, characterized by different societal attitudes, treatment practices, and policies. It may be that the diversity we found in aging profiles can be accounted for simply by the diversity of the participants' life events. The variability of the aging profiles suggests that additional research is needed to probe the relationship between aging and genetic and environmental factors. Instead of studying isolated individuals, we need to explore a system in which interdependent factors help to define individual trajectories of change, and by so doing, identify the ecology of aging. To gain a clearer understanding of aging in DS and the diversity of the variables involved, we conducted a cross-sectional study of the same sample, in which we investigated the relationship between these measures and various sociodemographic variables linked to the adults' life-event history. A focus on medical and educational information (medical history, educational support, schooling, employment, and living arrangements) would help us to gain a more accurate picture of the many variables involved in aging. Given the recent increases in life expectancy among adults with DS and the related rise in the number of older people who are free of dementia, it is vital that we understand normative aging in DS. Nevertheless, a number of general recommendations can be made on the

basis of our findings. The different profiles we were able to detect underline the need to take variability in the expression of intellectual disabilities into account in order to develop targeted interventions for adults. This information will be particularly useful for identifying needs for age-appropriate services, as well as for helping to slow losses or prevent premature decline.

### References

- American Psychiatric Association. (1987). *Diagnostic and statistical manual of mental disorders, third edition revised (DSM-III-R)*. Washington, DC: Author.
- American Psychological Association. (2012). Ethical principles of psychologists and code of conduct. Retrieved from <http://www.apa.org/ethics/code/index.aspx>
- Beciani, S., Vetro, E., Barisnikov, K., Detraux, J. J., & Van der Linden, M. (2011). Elaboration d'une batterie d'évaluation des signes du vieillissement dans la trisomie 21. *Revue Francophone de la Déficience Intellectuelle*, 22, 129–140.
- Bittles, A. H., Bower, C., Hussain, R., & Glasson, E. J. (2006). The four ages of Down syndrome. *European Journal of Public Health*, 17(2), 221–225. <http://dx.doi.org/10.1093/eurpub/ckl103>
- Buckley, S., Bird, G., Sacks B., & Archer, T. (2006). A comparison of mainstream and special education for teenagers with Down syndrome: Implications for parents and teachers. *Down Syndrome Research and Practice*, 9, 54–67. <http://dx.doi.org/10.3104/reports.295>
- Burt, D. B., Loveland, K. A., Chen, Y. W. C., Chuang, A., Lewis, K. R., & Cherry, L. (1995). Aging in adults with Down syndrome: Report from a longitudinal study. *Journal on Mental Retardation*, 100, 262–270.
- Carr, J. (2003). Patterns of ageing in 30–35 year olds with Down's syndrome. *Journal of Applied Research in Intellectual Disabilities*, 16, 29–40. <http://dx.doi.org/10.1046/j.1468-3148.2003.00129.x>
- Carr, J. (2005). Stability and change in cognitive ability over the life span: A comparison of populations with and without Down's syndrome. *Journal of Intellectual Disability Research*, 49, 915–928. <http://dx.doi.org/10.1111/j.1365-2788.2005.00735.x>

- Collacott, R. A. (1992). The effect of age and residential placement on adaptive behavior of adults with Down's syndrome. *British Journal of Psychiatry*, *161*, 675–679. <http://dx.doi.org/10.1192/bjp.161.5.675>
- Collacott, R. A., & Cooper, S. A. (1997). A five year follow up study of adaptive behaviour in adults with Down's syndrome. *Journal of Intellectual and Developmental Disability*, *22*(3), 187–197. <http://dx.doi.org/10.1080/13668259700033401>
- Cooper, S. A., Morrison, J., Melville, C., Finlayson, J., Allan, L., Martin, G. & Robinson, N. (2006). Improving the health of people with intellectual disabilities: outcomes of a health screening programme after 1 year. *Journal of Intellectual Disability Research*, *50*, 667–677. <http://dx.doi.org/10.1111/j.1365-2788.2006.00824.x>
- Coppus, A., Evenhuis, H., Verbene, G. J., Visser, F., Oostra, B. A., Eikelenboom, P., ... Van Duijn, C. (2008). Survival in elderly persons with Down syndrome. *Journal of the American Geriatrics Society*, *56*, 2311–2316. <http://dx.doi.org/10.1111/j.1532-5415.2008.01999.x>
- Coppus, A., Evenhuis, H., Verberne, G. J., Visser, F., van Gool, P., Eikelenboom, P., & van Duijn, C. (2006). Dementia and mortality in persons with Down's syndrome. *Journal of Intellectual Disability Research*, *50*, 768–777. <http://dx.doi.org/10.1111/j.1365-2788.2006.00842.x>
- Couzens, D., Haynes, M., & Cuskelly, M. (2012). Individual and environmental characteristics associated with cognitive development in Down syndrome: A longitudinal study. *Journal of Applied Research in Intellectual Disabilities*, *25*, 396–413. <http://dx.doi.org/10.1111/j.1468-3148.2011.00673.x>
- Das, J. P., Divis, B., Alexander, J., Parrila, R., & Naglieri, J. (1995). Cognitive decline due to aging among persons with Down syndrome. *Research in Developmental Disabilities*, *16*, 461–478. [http://dx.doi.org/10.1016/0891-4222\(95\)00030-5](http://dx.doi.org/10.1016/0891-4222(95)00030-5)
- Devenny, D. A., Krinsky-McHale, S. J., Sersen, G., & Silverman, W. P. (2000). Sequence of cognitive decline in dementia in adults with Down's syndrome. *Journal of Intellectual Disability Research*, *44*(6), 654–666. <http://dx.doi.org/10.1046/j.1365-2788.2000.00305.x>
- Dykens, E. M., Hodapp, R. M., & Finucane, B. (2005). *Genetics and mental retardation syndromes: A new look at behavior and interventions*. Baltimore, MD: Paul H. Brookes.
- Facon, B., & Nuchadee, M. L. (2010). An item analysis of Raven's Colored Progressive Matrices among participants with Down syndrome. *Research in Developmental Disabilities*, *31*, 243–249. <http://dx.doi.org/10.1016/j.ridd.2009.09.011>
- Fidler, D. J., Philofsky, A., & Hepburn, S. L. (2007). Language phenotypes and intervention planning: Bridging research and practice. *Mental Retardation and Developmental Disabilities Research Reviews*, *13*(1), 47–57. <http://dx.doi.org/10.1002/mrdd.20132>
- Gedye, A. (1995). *Dementia scale in Down's syndrome*. Vancouver, BC: Gedye Research & Consulting.
- Glasson, E. J., Sullivan, S. G., Hussain, R., Petterson, B. A., Montgomery, P. D., & Bittles, A. H. (2003). Comparative survival advantage of males with Down syndrome. *American Journal of Human Biology*, *15*, 192–225. <http://dx.doi.org/10.1002/ajhb.10132>
- Gunn, D. M., & Jarrold, C. (2004). Raven's matrices performance in Down syndrome: Evidence of unusual errors. *Research in Developmental Disabilities*, *25*, 443–457. <http://dx.doi.org/10.1016/j.ridd.2003.07.004>
- Hanson, M. J. (2003). Twenty-five years after early intervention: A follow-up of children with Down syndrome and their families. *Infants and Young Children*, *16*, 354–365. <http://dx.doi.org/10.1097/00001163-200310000-00008>
- Hawkins, B. A., Eklund, S. J., James, D. R., & Foose, A. K. (2003). Adaptive behavior and cognitive function of adults with Down syndrome: Modeling change with age. *Mental Retardation*, *41*(1), 7–28. [http://dx.doi.org/10.1352/0047-6765\(2003\)041<0007:ABACFO>2.0.CO;2](http://dx.doi.org/10.1352/0047-6765(2003)041<0007:ABACFO>2.0.CO;2)
- Henderson, A., Lynch, S. A., Wilkinson, S., & Hunter, M. (2007). Adults with Down's syndrome: The prevalence of complications and health care in the community. *British Journal of General Practice*, *57*, 50–55.
- Iacono, T., Torr, J., & Wong, H. Y. (2010). Relationships amongst age, language and related skills in adults with Down syndrome. *Research in Developmental Disabilities*, *31*, 568–576. <http://dx.doi.org/10.1016/j.ridd.2009.12.009>
- Jain, A. K., & Dubes, R. C. (1988). *Algorithms for clustering data*. Englewood Cliffs, NJ: Prentice Hall.
- Johnson, S. C. (1967). Hierarchical clustering schemes. *Psychometrika*, *32*, 241–253. <http://dx.doi.org/10.1007/BF02289588>
- Krinsky-McHale, S. J., Devenny, D. A., Gu, H., Jenkins, E. C., Kittler, P., Murty, V. V., ...



- Silverman, W. (2008). Successful aging in a 70-year-old man with Down syndrome: A case study. *Intellectual and Developmental Disabilities, 46*, 215–228. <http://dx.doi.org/10.1352/2008.46:215-228>
- Larsen, F., & Kirkeveld, O. (2008). The aging population with Down syndrome in Norway, 1969–2045. *Journal of Intellectual Disability Research, 52*, 644.
- Lattin, J. J., Carroll, J. D., & Green, P. E. (2003). *Analyzing multivariate data*. Belmont, CA: Duxbury Press.
- Leonard, S., Bower, C., Petterson, B., & Leonard, H. (2000). Survival of infants born with Down's syndrome: 1980–96. *Paediatric Perinatal Epidemiology, 14*, 163–171. <http://dx.doi.org/10.1046/j.1365-3016.2000.00252.x>
- Lott, I. T., & Dierssen, M. (2010). Cognitive deficits and associated neurological complications in individuals with Down's syndrome. *The Lancet Neurology, 9*, 623–633. [http://dx.doi.org/10.1016/S1474-4422\(10\)70112-5](http://dx.doi.org/10.1016/S1474-4422(10)70112-5)
- Määttä, T., Määttä, J., Tervo-Määttä, T., Taanila, A., Kaski, M., & Iivanainen, M. (2011). Healthcare and guidelines: A population-based survey of recorded medical problems and health surveillance for people with Down syndrome. *Journal of Intellectual and Developmental Disability, 36*, 118–126. <http://dx.doi.org/10.1080/13668250.2011.570253>
- Mantry, D., Cooper, S. A., Smiley, E., Morrison, J., Allan, L., Williamson, A., ... Jackson, A. (2008). The prevalence and incidence of mental ill-health in adults with Down syndrome. *Journal of Intellectual Disability Research, 52*, 141–155.
- Moss, S., Tomoeda, C., & Bayles, K. (2000). Comparison of the cognitive linguistic profiles of Down syndrome adults with and without dementia to individuals with Alzheimer's disease. *Journal of Medical Speech Language Pathology, 8*, 69–81.
- Oliver, C., Crayton, L., Holland, A., Hall, S., & Bradbury, J. (1998). A four year prospective study of age-related cognitive change in adults with Down's syndrome. *Psychological Medicine, 28*, 1365–1377. <http://dx.doi.org/10.1017/S0033291798007417>
- Patti, P. J., & Tsiouris, J. A. (2006). Psychopathology in adults with Down syndrome: Clinical findings from an outpatient clinic. *International Journal on Disability and Human Development, 5*, 357–364. <http://dx.doi.org/10.1515/IJDHD.2006.5.4.357>
- Prasher, V. P. (1996). Age-associated functional decline in adults with Down's syndrome. *European Journal of Psychiatry, 10*, 129–135.
- Prasher, V. P. (1999). Adaptive behavior. In M. P. Janicki & A. J. Dalton (Eds.), *Dementia, aging and intellectual disabilities: A handbook* (pp. 157–182). Philadelphia, PA: Taylor & Francis.
- Prasher, V. P., & Chung, M. C. (1996). Causes of age-related decline in adaptive behavior of adults with Down syndrome: Differential diagnosis of dementia. *American Journal on Mental Retardation, 101*, 175–183.
- Prasher, V. P., Chung, M. C., & Haque, M. S. (1998). Longitudinal changes in adaptive behavior in adults with Down's syndrome: Interim findings from a longitudinal study. *American Journal on Mental Retardation, 103*, 175–183. [http://dx.doi.org/10.1352/0895-8017\(1998\)103<0040:LCIABI>2.0.CO;2](http://dx.doi.org/10.1352/0895-8017(1998)103<0040:LCIABI>2.0.CO;2)
- Quanhe, Y., Rasmussen, S. A., & Friedman, J. M. (2002). Mortality associated with Down's syndrome in the USA from 1983 to 1997: A population-based study. *Lancet, 359*, 1019–1026. [http://dx.doi.org/10.1016/S0140-6736\(02\)08092-3](http://dx.doi.org/10.1016/S0140-6736(02)08092-3)
- Rasmussen, D. E., & Sobsey, D. (1994). Age, adaptive behavior, and Alzheimer disease in Down syndrome: Cross-sectional and longitudinal analyses. *American Journal of Mental Retardation, 99*, 151–165.
- Rasore-Quartino, A. (1999). The present state of medical knowledge in Down syndrome. In J. Rondal, J. Perrera, & L. Nadel (Eds.), *Down syndrome: A review of current knowledge* (pp. 153–162). London, UK: Whurr.
- Raven, J. C., Court, J. H., & Raven, J. (1998). *Progressive Matrices Couleur/Colored Progressive Matrices*. Paris, France: Editions du Centre de Psychologie Appliquée.
- Record, R. G., & Smith, A. (1955). Incidence, mortality, and sex distribution of mongoloid defectives. *British Journal of Preventive and Social Medicine, 9*, 10–15.
- Reiss, S. (1988). *The Reiss Screen for Maladaptive Behavior test manual*. Worthington, OH: International Diagnostic Systems.
- Rondal, J. A. (2009). *Psycholinguistique du handicap mental*. Marseilles, France: Solal.
- Saitta, S., Raphael, B., & Smith, I. F. C. (2008). A comprehensive validity index for clustering. *Intelligent Data Analysis, 12*, 529–548.



- Silverman, W., Zigman, W., Krinsky-McHale, S., & Schupf, N. (2011). Diagnosis of dementia for adults with Down syndrome. *Journal of Applied Research in Intellectual Disabilities, 23*, 408–418.
- Sparrow, S., Balla, D., & Cicchetti, D. (1984). *Vineland Adaptive Behavior Scales*. Circle Pines, MN: American Guidance Service.
- Temple, V., Jozsvai, E., Konstantareas, M. M., & Hewitt, T. A. (2001). Alzheimer dementia in Down's syndrome: The relevance of cognitive ability. *Journal of Intellectual Disability Research, 45*, 47–55. <http://dx.doi.org/10.1046/j.1365-2788.2001.00299.x>
- Torr, J., Strydom, A., Patti, P., & Jokinen, N. (2010). Aging in Down syndrome: Morbidity and mortality. *Journal of Policy and Practice in Intellectual Disabilities, 7*, 70–81.
- Tsao, R., & Kindelberger, C. (2009). Variability of cognitive development in children with Down syndrome: Relevance of good reasons for using the cluster procedure. *Research in Developmental Disabilities, 30*, 426–432. <http://dx.doi.org/10.1016/j.ridd.2008.10.009>
- Urv, T. K., Zigman, W. B., Silverman, W., & MacLean, W. E., Jr., (2008). Maladaptive behaviors related to dementia status in adults with Down syndrome. *American Journal on Mental Retardation, 113*, 73–86. [http://dx.doi.org/10.1352/0895-8017\(2008\)113\[73:MBRTDS\]2.0.CO;2](http://dx.doi.org/10.1352/0895-8017(2008)113[73:MBRTDS]2.0.CO;2)
- Vakil, E., & Lifshitz-Zehavi, H. (2012). Solving the Raven Progressive Matrices by adults with intellectual disability with/without Down syndrome: Different cognitive patterns as indicated by eye-movements. *Research in Developmental Disabilities, 33*, 645–654. <http://dx.doi.org/10.1016/j.ridd.2011.11.009>
- Ward, J. H. (1963). Hierarchical grouping to optimize an objective function. *Journal of the American Statistical Association, 58*, 236–244. <http://dx.doi.org/10.1080/01621459.1963.10500845>
- Weijerman, M., Van Furth, M., Vonk Noordegraaf, A., Van Wouwe, J., Broers, C., & Gemke, R. (2008). Prevalence, neonatal characteristics and mortality rate during the first year in Down syndrome. *Journal of Pediatrics, 152*, 15–19. <http://dx.doi.org/10.1016/j.jpeds.2007.09.045>
- Zigman, W. B. (2013). Atypical aging in Down syndrome. *Developmental Disabilities Research Reviews, 18*, 51–67. <http://dx.doi.org/10.1002/ddrr.1128>
- Zigman, W. B., & Lott, I. T. (2007). Alzheimer's disease in Down syndrome: Neurobiology and risk. *Mental Retardation and Developmental Disabilities Research Review, 13*, 237–246. <http://dx.doi.org/10.1002/mrdd.20163>
- Zigman, W. B., Schupf, N., Lubin, R. A., & Silverman, W. P. (1987). Premature regression of adults with Down's syndrome. *American Journal of Mental Deficiency, 92*, 161–168.

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Received 6/30/2013, accepted 5/6/2014.

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We would like to thank the patients and their families.

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