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Adaptive Behaviour Change and Health in Adults with Down Syndrome: A Prospective Clinical Follow-Up Study

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1. Introduction

People with Down syndrome are prone to early ageing and Alzheimer's disease (Zigman & Lott 2007). The functional decline in adults with Down syndrome starts decades earlier, compared to the mainstream population and other people with intellectual disabilities (Zigman *et al.* 1996; Strydom *et al.* 2007). The coping skills necessary for daily life, social interactions and work are gradually lost during the progression of dementia (Margallo-Lana *et al.* 2007).

Typical neuropathology of Alzheimer's disease is seen in virtually all people with Down syndrome by the age of 40 (Wisniewski *et al.* 1985). Depending on diagnostic criteria, 17-55% of them develop clinical dementia after that age (Holland *et al.* 2000; Janicki & Dalton 2000; Coppus *et al.* 2006). Genetic factors modifying the risk of dementia in adults with Down syndrome have been identified (Zigman & Lott 2007; Prasher *et al.* 2008; Patel *et al.* 2010). The rates of dementia in adults with intellectual disability without Down syndrome aged 60 years and older are greater than expected (Strydom *et al.* 2007).

The cognitive impairment in adults with Down syndrome has similarities to early cognitive changes in Alzheimer's disease (Brugge *et al.* 1994). Personality and behaviour changes (Ball *et al.* 2006), executive dysfunction (Ball *et al.* 2008) and selective attention deficits (Krinsky-McHale *et al.* 2008) are early signs of dementia in adults with Down syndrome. Frontal-like

dementia can be diagnosed in 33% in their thirties (Holland *et al.* 2000). Maladaptive behaviour is often seen and includes aggression, fearfulness, sadness, sleep problems, social inadequacy, stealing and general regressive behaviour (Urv *et al.* 2008). Increasing age associates with decreasing cognitive and language abilities; the deterioration with the age is largely explained by the presence of Alzheimer's disease (Iacono *et al.* 2010).

Identification of persons with risk of early dementia remains a challenge (Shulz *et al.* 2004). Direct assessments of cognitive functions of people with intellectual disabilities may be difficult (Pyo *et al.* 2007). Informant-based assessments are useful as complementary or alternative methods in clinical work (Ball *et al.* 2004; Prasher *et al.* 2004; Niuwenhuis-Mark 2009).

The Adaptive Behavior Scale - Residential and Community (Nihira *et al.* 1993) and its earlier versions have been widely used in research. Cross-sectional studies have demonstrated lower scores on people with Down syndrome older than 40 years compared to younger participants with Down syndrome (Collacott 1992). The age-related decline of adaptive behaviour associates to dementia (Prasher & Chung 1996). Prospective studies have confirmed changes in adaptive behaviour (Rasmussen & Sobsey 1994; Prasher *et al.* 1998). Zigman *et al.* (2002) described the incidence and temporal patterns of adaptive behaviour changes in adults with intellectual disabilities. Rasmussen and Sobsey (1994) found stability of adaptive behaviour in adults with Down syndrome in the age groups younger than 40 years and a pattern of decline in self-help and communication skills in several individuals with Down syndrome older than 40, including declines in dressing, receptive language, vocational and domestic behaviour.

Relative preservation of cognitive and functional ability in persons with Down syndrome older than 45 associates with better survival whereas clinically, the most important disorders that are related to mortality are dementia, mobility restrictions, visual impairment, and epilepsy (Coppus *et al.* 2008).

Health co-morbidities in ageing persons with Down syndrome and Alzheimer's dementia are common (McCarron *et al.* 2005). Depression often precedes the onset of dementia in people with Down syndrome (Burt *et al.* 1992). Visual impairment and hearing loss are very common in elderly people with Down syndrome (van Splunder *et al.* 2006; Meuwese-Jongejeugd *et al.* 2006; Meuwese-Jongejeugd *et al.* 2008). Epilepsy is often seen at the same age with dementia (Collacott 1993). Hypothyroidism may also affect adaptive behaviour (Bhaumik *et al.* 1991). The absence of a medical illness predicts a higher level of adaptive behaviour, while dementia is a predictive factor for increased maladaptive behaviour (Prasher & Chung 1996) and psychiatric symptoms (Urv *et al.* 2010).

Medication for Alzheimer's disease might benefit many people with Down syndrome by slowing the progression of the disease (Prasher *et al.* 2002). Accurate measures are important for the follow-up and evaluation of treatments. It is necessary to find and use valid, reliable and sensitive methods for assessments of adults and ageing people with Down syndrome and Alzheimer's disease.

The aim of the present study was to explore the clinical usefulness of repeated assessments of adaptive behaviour in people with Down syndrome and suspected or confirmed dementia. Repeated assessments of adaptive behaviour in people at risk of functional decline might help to confirm the change and lead to necessary additional evaluations of the underlying reasons and help in follow-up.

2. Methods

Study population

The participating adults with Down syndrome were recruited to the study at a specialized service centre for people with intellectual disabilities serving a population of 79 690 (December 2008), among them 723 people with identified intellectual disability. These include 84 people with Down syndrome; 19 of them were 0-19 years old, 65 were 20 years old or older. Forty of the 65 adults belonged to the age group 40 years old or older.

Assessments of adaptive behaviour were conducted to 42 persons with Down syndrome (Table 1). Twenty five persons had repeated assessments. These persons' proxies had noticed a change of mood, behaviour or performance. At the time of the first evaluation, their age range was 24-61 years, with a mean of 45.8 and SD of ± 8.4 ; at the time of the last evaluation, the corresponding figures were 25-65.5, 48.8, and ± 8.4 years, respectively. The mean time of follow-up was, thus, 3.0 years (range 0-8 years). Five participants died during the follow up. Twenty participants (80%) of the 25 were 40 years or older at the time of the first evaluation. Most participants (17/25, 68%) resided at the beginning of the follow-up in small group homes, seven (28%) at home with parents or siblings and one in institution. Fourteen participants (56%) had organized weekly activities outside the home and two participants had part time supported work.

Methods

Repeated informant evaluations regarding observed changes in behaviour were recorded prospectively. Evaluations of adults with Down syndrome were performed over ten years, beginning in 2001. Adaptive behaviour assessments were performed by the closest relatives or carers who lived or worked with the participants and knew the persons and their daily skills for a long time.

The current coping skills for daily living were assessed using the Adaptive Behavior Scale - Residential and Community, ABS-RC: 2 1993, Part I (Nihira *et al.* 1993). The Adaptive Behavior Scale (ABS) was chosen because the reliability and validity of this method are well established. Earlier research supports its feasibility in the use of scientific studies of ageing and dementia in people with intellectual disabilities (Rasmussen & Sobsey 1994; Prasher *et al.* 1998; Zigman *et al.* 2002).

The first part of ABS is focused on personal independence and includes ten domains or subscales: Independent Functioning, Physical Development, Economic Activity, Language

Development, Numbers and Time, Domestic Activity, Prevocational/Vocational Activity, Self-Direction, Responsibility and Socialization. The ABS Manual reports that factor analysis has found three Part One factors: Personal Self-Sufficiency, Community Self-Sufficiency, and Personal–Social Responsibility.

Clinical evaluations were done by the principal investigator. These included interviews of the proxies, referrals for differential diagnostics and specialist consultations, and prescriptions and assessments of medications. Additional clinical data was drawn from the case records of the health centres, central hospital and service centre regarding all persons with Down syndrome in the region. The data of medical treatments for Alzheimer's disease, depression, behavioural problems, epilepsy, and other major health concerns possibly affecting adaptive behaviour were analyzed. The age at the time of the first observation of functional decline was calculated.

Informant ratings by ABS were scored and analysed. Total scores, scores for the ten subscales and three factors of ABS and changes of scores from the first to the last evaluation were counted. The ABS score changes as percentages per three years were calculated for subgroups of participants with and without Alzheimer's disease, depression, epilepsy, hypothyroidism, and antipsychotic medication use for challenging behaviour.

The ethical committee of the Kainuu Central Hospital approved the study and permission for combining data from medical and social records was given by the Ministry of Social and Health Affairs.

3. Results

The number of people with Down syndrome living in the area is well known and their morbidity data was available for comparison. The participants with repeated ABS assessments were older than participants with single assessments. Dementia, medication use for challenging behaviour, depression and epilepsy were more common among participants than among adults with Down syndrome living in the region.

Alzheimer's disease

Alzheimer's disease with dementia was diagnosed in 15 out of the 25 participants assessed repeatedly. Four of them died during the survey. The diagnosis was confirmed in ten participants by a neurologist and in five participants by the first author with competence in intellectual disability medicine. Other causes of dementia were excluded. Computerized tomographies of the brain were performed in ten of these participants. Eleven persons received medication for Alzheimer's disease (donepezile, galantamine or rivastigmine, in three participants combined with memantine). Early dementia was suspected in an additional four participants; they had increasing difficulties following instructions and performing their usual domestic work.

The number of living people with diagnosed and suspected dementia (fifteen persons among the participants and two not participating in this study) among adults with Down syndrome

in the region gives prevalence's of dementia 38% (15 of 40 persons) in the age group 40 years and more, and 13% (two of 15 persons) in the age group 30-39 years. The prevalence estimate of dementia for the age group 30 years and more is thus 31% (17 of 55 persons).

Medical problems

Of the 25 participants eleven (44%) had experienced long periods of depression. Thirteen (52%) had received antipsychotic medication mainly for behavioural problems, six of them already during early adulthood and eight for behavioural problems with dementia. Eleven persons were treated for hypothyroidism. Varying degrees of visual impairment were common, and three had cataracts. Recurrent faints were seen in eight, with falls causing fractures in three persons. Epilepsy was diagnosed in eight persons.

Among participants with Alzheimer's disease (n=15), antipsychotic medication had been used for eleven (73%), depression had been diagnosed in ten (67%), thyroid disease in ten (67%), and epilepsy in seven (47%) participants. Among participants without Alzheimer's disease (n=10), antipsychotic medication had been used for two (20%), depression had been diagnosed in one (10%), thyroid disease in four (40%), and epilepsy in one participant (10%). Among eleven participants with depression (N=11), antipsychotic medication had been used for seven (64%), Alzheimer's disease had been diagnosed in ten (91%), thyroid disease in 6 (55%), and epilepsy in five (45%) participants.

Informant observations

A decline of daily functioning was observed by informants in regards to 19 of 25 persons, starting at the ages of 37-51 years with a mean of 44.9 and SD +/- 4 years in persons with full trisomy of chromosome 21. In addition, there was one participant with mosaic trisomy of chromosome 21 whose decline started only at the age of 60 (Figure 3, participant 2).

Adaptive Behavior Scale (ABS) scores

The mean ages, ABS total scores at first and last assessments and the calculated percentages of score changes per three years in subgroups of participants are presented in Table 1. The mean ABS total scores for the 25 participants with multiple assessments declined from 161 to 126 (21.8%) during the mean 3.0 years between the first and last assessments. The decline of ABS total scores associated very strongly to Alzheimer's disease: there was no decline in the mean ABS total scores in the group of participants with no suspected or confirmed Alzheimer's disease. The mean rates of ABS score change were higher in participant groups with Alzheimer's disease (33.6% in three years), and depression (32.0%) compared to participants without these conditions (0.6% and 13.9% respectively). The participants treated with medication for Alzheimer's disease had lower mean rates of score declines compared to untreated patients, 31% and 40% declines in three years respectively. The mean rates of change were almost similar in groups of persons with and without epilepsy, antipsychotic medication, and hypothyroidism. (Table 1)

Participants (number of persons)	Age of participants at first (last) assessment	ABS total scores, means at first (last) assessment	ABS score change percentage per three years, %
Participants with single assessments (17)	36.5 (36.5)	174 (174)	
males (10)	32.3 (32.3)	188 (188)	
females (7)	42.4 (42.4)	155 (155)	
Participants with repeated assessments (25)	45.8 (48.8)	161 (126)	-21.8
males (11)	43.8 (47.0)	135 (117)	-12.4
females (14)	48.4 (51.5)	193 (137)	-28.4
Alzheimer`s disease (AD, 15)	49.7 (52.9)	165 (106)	-33.6
AD, no medication (4)	47.8 (50.8)	155 (93)	-40.0
AD, medication (11)	50.6 (53.9)	170 (112)	-31.0
No AD (10)	40.0 (43.1)	154 (155)	+0.6
Depression (11)	47.6 (50.5)	159 (112)	-32.0
No depression (14)	44.4 (47.8)	162 (136)	-13.9
Epilepsy (8)	50.6 (54.5)	193 (141)	-23.0
No epilepsy (17)	43.5 (46.5)	145 (118)	-18.7
Antipsychotic medication (13)	49.0 (52.0)	168 (132)	-21.7
No antipsychotic medication (12)	42.3 (45.7)	152 (119)	-19.3
Hypothyroidism (11)	45.8 (48.7)	152 (125)	-19.4
No hypothyroidism (14)	45.8 (49.1)	166 (126)	-21.5

Table 1. Ages, ABS-RC:2 total scores and score changes in subgroups of participants with Down syndrome.

ABS-RC:2 subscale	Scores, first assessment Mean (SD)	Scores, last assessment Mean (SD)	Score change, %
Domestic Activity	9.6 (6.1)	5.8 (6.1)	-64.8
Responsibility	5.0 (3.0)	3.3 (3.1)	-51.2
Self-Direction	12.1 (5.9)	8.0 (6.9)	-50.3
Prevocational/Vocational Activity	5.8 (3.1)	4.0 (3.6)	-44.0
Numbers and Time	5.4 (3.4)	3.8 (3.8)	-41.1
Independent Functioning	64.8 (24.3)	52.3 (32.0)	-23.8
Language Development	21.0 (9.4)	17.2 (8.9)	-22.0
Economic Activity	3.6 (3.3)	3.2 (3.5)	-12.5
Physical Development	18.4 (3.5)	16.0 (5.5)	-15.0
Economic Activity	3.6 (3.3)	3.2 (3.5)	-12.5

Table 2. ABS-RC:2 subscale mean scores and their change during the prospective follow-up of 25 participants with Down syndrome.

The biggest mean declines were seen in the subscales Domestic Activity, Responsibility and Self-Direction, to 35.2, 48.8 and 49.7%, respectively. The slightest changes were seen in the domains of Economic Activity, Physical Development and Language Development (Table 2). The mean changes of scores for the ABS factors Personal Self-Sufficiency, Community Self-Sufficiency and Personal-Social Responsibility were 22.2, 27.9 and 36.8%, respectively.

Individual changes in ABS scores

The ABS scores remained stable in nine and improved in three persons. A progressive decline of ABS scores was seen in 13 of 25 (52%) participants after their early forties. The direction, amount and rate of change of ABS scores varied from an increase of 27% within a year in the youngest participant recovering from deep depression to 90% decline during seven years in an ageing participant.

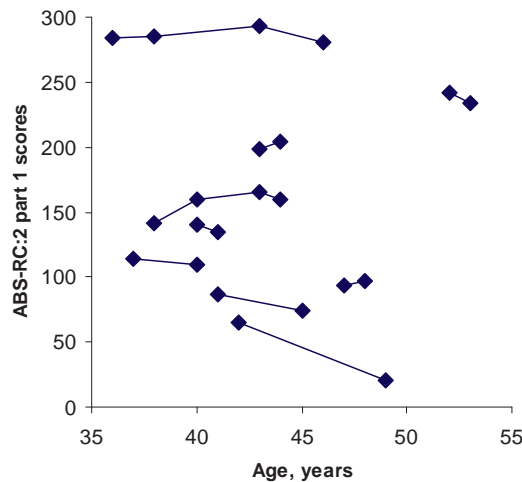


Figure 1. Adaptive behaviour in 9 participants without clinical Alzheimer's disease

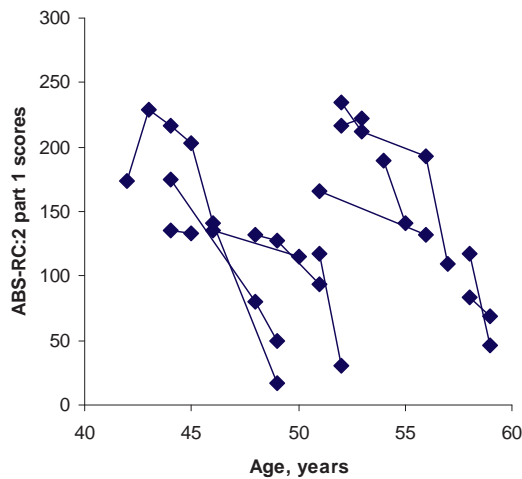


Figure 2. Adaptive behaviour in 12 participants with diagnosed Alzheimer's disease

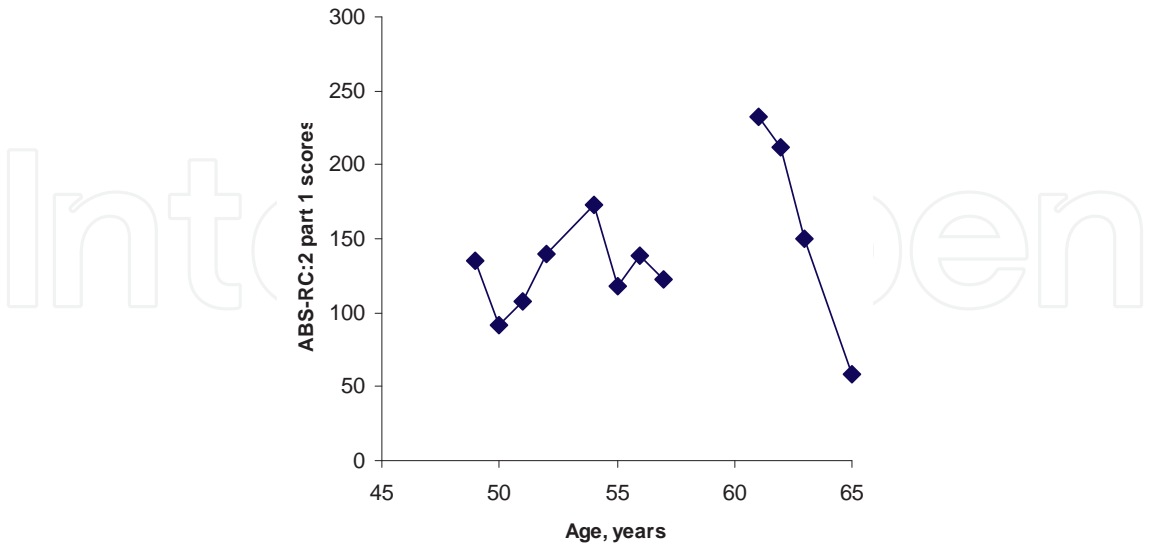


Figure 3. Adaptive behaviour in two participants with different clinical course of diagnosed Alzheimer’s disease: participant 1 with slow progression of dementia (clinical case data given in text), participant 2 with mosaic trisomy of chromosome 21 and late onset of dementia

4. Late onset of dementia with mosaic trisomy of chromosome 21

For most of the younger and many of older participants too, changes in ABS scores were minimal (Figure 1). Slight improvement in scores at ages 38-40 was seen in an participant after a change of residence, coupled with increasing exercise, weight loss and improved fitness. The highest scores with slight improvement at ages 38-43 were seen in a participant in spite of many treated health problems, including a slight permanent visual impairment, hypothyroidism, fractures associated with osteoporosis and bronchial asthma.

The ABS scores declined in most participants with Alzheimer’s disease (Figure 2). Improvements in ABS scores were seen in two elderly participants. In the first participant (Figure 2), the improvement at age 42 to 43 associated to the change of residence and medical treatment of Alzheimer’s disease with response for two years before advancing deterioration later. Epilepsy and loss of mobility after a fall resulting in a hip fracture, and poor visual acuity contributed to the loss of independent functioning.

The improvement of the other participant (Figure 3) during the treatment of confirmed Alzheimer’s disease, after a decline at age 48 to 49 lasted five years before further deterioration. Contributing factors to the functional improvement were the removal of cataracts resulting in improved visual acuity, active participation in activities with support of the carers, and

stabilization of mood and behaviour. This participant had a long history of hypothyroidism, depression and challenging behaviour and he had long-term antidepressant and antipsychotic medication, and successful treatment of late onset epilepsy.

5. Discussion

We report experiences of a long term prospective clinical follow-up of adults with Down syndrome. The participants in this study were adults with Down syndrome and behavioural changes as perceived by carers. Adults without behavioural or mood changes observed by their proxies were not actively recruited and thus this group is not represented in this survey. The participants represent adults with Down syndrome with observed change of mood, behaviour or performance causing concern in their proxies.

Depression and, among participants in their forties and older, Alzheimer's dementia were the most common underlying reasons for the behavioural change. The number of participants with diagnosed and suspected dementia gave estimates of prevalence comparable to published epidemiological studies. Most people with Down syndrome and diagnosed Alzheimer's dementia in this population participated in this study. A change of behaviour or adjustment had been noticed by their proxies before the diagnosis of Alzheimer's dementia.

The current coping skills of the participants were assessed repeatedly using Adaptive Behaviour Scale - Residential and Community, Part I (Nihira *et al.* 1993). Earlier research supports its feasibility in scientific studies of ageing and dementia in people with intellectual disabilities. The clinical use of ABS to monitor ageing and dementia from the early non-symptomatic phase to the advanced stages at various levels of abilities proved to be possible and helpful for the clinician. A decline in ABS scores was seen in most participants after their early forties. This supported the suspicion of Alzheimer's disease, led to differential diagnostic assessments and also helped in monitoring the progression of the disease.

Adaptive behaviour can be assessed by ABS in adults with intellectual disability at all phases of ageing and dementia. This informant-based method overcame many of the problems of cognitive based measures. For example, no cooperation or communication skills of the person to be evaluated were needed for this assessment. Direct evaluations of cognitive functions were not possible in this study due to the limited neuropsychological resources available. Stable scores in clinically stable participants between repeated evaluations supported the reliability of ABS, when used by proxy informants. The informants with a close and long familiarity to their proxies observed and reported subtle changes in daily life and completed adaptive behaviour questionnaires without obvious difficulty.

A careful evaluation of the life situation and comprehensive assessment of physical and mental health is necessary when carers describe a decline in everyday functioning - that is a difficulty in accomplishing daily tasks which the individual would normally complete with ease (Ball

et al. 2006). This is also needed in the elderly with established Alzheimer's disease because of common co-morbidities. In the case of a rapid deterioration of function, the underlying reasons should be assessed even when Alzheimer's disease has been diagnosed and treatment started. Visual acuity and hearing should be regularly monitored in all adults with Down syndrome because of high prevalence's of visual impairment and hearing loss. Alzheimer's disease does not protect from any other disease or disability. Other treatable conditions, including hypothyroidism, visual impairment and hearing loss, may be found.

The decline of the ABS total scores associated strongly to Alzheimer's disease; therefore the described declines in the ABS subscale scores probably reflect changes attributable to Alzheimer's disease. The relative rates of change among of the subscales of ABS differed. The scores of the domains Domestic Activity, Responsibility, Self-Direction and Vocational Activity declined more, as compared to other domains including Independent Functioning and Physical Activities. This may reflect the early impairment of frontal lobe functions among people with Down syndrome (Holland *et al.* 2000), including executive dysfunction in the development of Alzheimer's disease (Ball *et al.* 2008).

Individual differences of the functional skills assessed by ABS scores were considerable. Decline of skills with ageing started at very different ages among participants in this study. The improvements of adaptive behaviour seen in several participants highlight the need for careful assessment of treatable medical conditions and possibilities for supporting the maintenance of functional independence. Stabilization of ABS scores was seen during medication for Alzheimer's disease in one participant for up to five years. Studies using population based representative larger samples would be needed to further analyse factors that represent potential confounders affecting adaptive behaviour more vigorously.

A considerable proportion of people with Down syndrome do not develop clinical dementia at all (Coppus et al. 2006). People with Down syndrome differ in their individual biological and genetic risk of dementia (Zigman & Lott 2007; Prasher et al. 2008; Patel et al. 2008). Better understanding of genetic and environmental influences and medical conditions contributing to these differences is needed.

Repeated prospective assessments overcome memory errors compared to retrospective evaluations. Short questionnaires of adaptive behaviour change may be sufficient for screening purposes (Prasher *et al.* 2004). However, repeated assessments are needed for the confirmation of dementia and evaluation of interventions. The possibility of performing an assessment in various settings without special professional expertise is a benefit of this approach.

The informant-based assessments of coping skills for daily living may prove practical and useful for the follow up of ageing and dementia from the early non-symptomatic phase to the advanced stages at various levels of abilities. The authors suggest repeated assessments of adaptive behaviour and careful clinical evaluations to detect treatable medical conditions in adults with Down syndrome.

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