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Intellectual and adaptive behaviour functioning in pantothenate kinase-associated neurodegeneration

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Abstract

Background—Pantothenate kinase-associated neurodegeneration (PKAN), an extremely rare autosomal recessive disorder resulting in iron accumulation in the brain, has a diverse phenotypic expression. Based on limited case studies of one or two patients, intellectual impairment is considered part of PKAN. Investigations of cognitive functioning have utilized specific neuropsychological tests, without attention to general intellectual skills or adaptive behaviour.

Methods—Sixteen individuals with PKAN completed measures of global intellectual functioning, and participants or care providers completed measures of adaptive behaviour skills and day-to-day functional limitations. Clinicians provided global ratings of condition severity.

Results—Testing with standardized measures documented varied phenotypic expression, with general cognitive skills and adaptive behaviour ranging from high average to well below average. Age of disease onset correlated with measures of intellectual functioning, adaptive functioning and disease severity.

Conclusions—Findings support previously described clinical impressions of varied cognitive impairment and the association between age of onset and impairment. Further, they add important information regarding the natural history of the disease and suggest assessment strategies for use in treatment trials.

Keywords

brain iron accumulation; cognitive functioning; functional skills; pantothenate kinase-associated neurodegeneration

Introduction

Neurodegeneration with brain iron accumulation (NBIA, formerly Hallervorden–Spatz syndrome) is a heterogeneous group of disorders that affects children and adults. Approximately one-half of patients with NBIA have pantothenate kinase-associated neurodegeneration (PKAN). PKAN is caused by mutations in the *PANK2* gene, located on chromosome 20p13 (Zhou *et al.* 2001). The phenotypic spectrum of PKAN is broad (Hayflick *et al.* 2003), ranging from severe, early onset dystonia and pigmentary retinopathy to adult-onset dystonia, dysarthria and rigidity. All patients have abnormal iron deposition in the basal ganglia with a specific radiographic finding on T2-weighted magnetic resonance imaging (MRI; Sethi *et al.* 1988). There is an absolute correlation between this finding and mutations in the *PANK2* gene (Hayflick *et al.* 2003). A prevalence rate of one to three in 1 000 000 has been proposed (Hayflick 2002).

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Neurodegeneration with brain iron accumulation has been associated with intellectual impairment (Dooling *et al.* 1974; Swaiman 1991), although there has been question as to whether this is an essential feature of PKAN (Hayflick 2002). Existing research focuses on specific neuropsychological function, utilizing idiosyncratic tests limited in focus. Problems with executive functioning, attention, spatial and verbal learning, memory, judgment, and persistence have been reported in PKAN (Cossu *et al.* 2002; Molinuevo *et al.* 2003; Marelli *et al.* 2005). Because the *PANK2* gene was discovered in 2001 (Zhou *et al.* 2001), reports prior to that time do not specify whether patients had PKAN, although retrospective review of MRI images aids with this distinction. Loring *et al.* (1990) demonstrated slowed processing speed, motor sequencing difficulties, constructional dyspraxia, impaired recent memory functioning, poor language functioning and visual-spatial deficits in two African American females aged 20 and 38 years. Clinical descriptions and MRI results suggest that the younger patient likely had PKAN and the elder had a different form of NBIA.

Although extant research suggests unique neuropsychological deficits in PKAN, published findings are quite limited. First, there are only four published studies investigating cognitive functioning in PKAN, all of which were one- or two-patient case reports. Evaluations of larger numbers of individuals are needed to provide better information about common phenotypic expression. Second, investigators have selected narrowly focused tests that involve tasks associated with the basal ganglia (e.g. selective attention, perseveration), overlooking measures of general intellectual functioning. Attention to general intelligence is important, as post-mortem examinations of individuals with NBIA reveal cerebral atrophy (Suri 2001).

Given these limitations, additional research on the intellectual and functional capacities of patients with PKAN is needed. While neurological symptoms of PKAN result in limitations in functional/adaptive capacities, no systematic investigation of this issue using standardized, norm-referenced assessment strategies has been conducted. Using such measures allows for a better description of impairment and assists in measuring disease progression. Similar justification exists for investigating cognitive impairment. Further, evaluation of intellectual abilities is warranted because neurological symptoms such as dysarthria and dystonia may interfere with demonstration of cognitive skills in unstructured, interpersonal interactions.

The primary goal of the current investigation was to conduct an extensive assessment of the intellectual and adaptive functioning of a large number of individuals with PKAN. Doing so provides descriptions of clinical presentation that may be more representative of a spectrum of condition presentation, as well as serving as a marker against which others may compare findings. The secondary goal was to gather information regarding the utility of intelligence and functional capacity assessment strategies with individuals with this condition, an issue raised in previous research on NBIA (Loring *et al.* 1990). Although exploratory in nature, this investigation is considered important, given the dearth of rigorous studies of the functional aspects of PKAN.

Method

Oregon Health and Science University's Institutional Review Board approved all procedures used. The participants or their legal guardians documented informed consent in writing.

Participants and setting

Sixteen individuals (six male, 10 female; age range 7–69 years) diagnosed with PKAN by molecular testing and MRI participated (see Table 1). The spectrum of symptoms was broad. Six patients were no longer ambulatory and three others were still able to walk but used wheelchairs regularly. Three required feeding gastrostomy tubes, one who also had a

tracheostomy. Some adult participants were still able to work or were taking college courses, and most of the children and young adults participated in school or day programmes.

Measures

Assessment of intellectual skills

Wechsler Abbreviated Scale of Intelligence (WASI; The Psychological Corporation 1999) The WASI is an abbreviated scale of intelligence used with individuals ages 6 through 89. It includes four sub-scales, two measuring verbal reasoning (i.e. vocabulary, similarities) and two measuring non-verbal reasoning (i.e. block design, matrix reasoning). Estimates of verbal, performance, and full-scale intelligence quotients (IQ) are yielded.

Leiter International Performance Scale – Revised (Leiter-R; Roid & Miller 1997) The Leiter-R is a test of non-verbal reasoning and visualization skills. The Visualization and Reasoning Battery, used in this investigation, consists of seven subtests and results in a total quotient, fluid reasoning quotient and spatial visualization quotient. This battery is completed non-verbally; respondents simply rearrange picture cards into a particular order or point from picture cards to corresponding areas on a larger stimulus picture presented. If rearranging cards is too difficult, the individual can simply point to indicate preferred card arrangement. Administration typically takes 30–40 min, although testing length occasionally lasted 45–60 min with this cohort.

Peabody Picture Vocabulary Test, Third Edition (PPVT-III; Dunn & Dunn 1997) The PPVT-III is considered a test of receptive vocabulary and a screening test of verbal ability. No speech or movement from the examinee is necessary for administration. The examinee is shown cards each of which contains four drawings. After the examiner states a test word, the examinee indicates which of the four drawings best depicts that word, either by pointing at the drawing or by giving an affirmative sign as the examiner points to each of the four options. Administration time is approximately 15–20 min.

Assessment of adaptive behaviour

Vineland Adaptive Behavior Scales, Interview Edition (VABS; Sparrow et al. 1984) The VABS is a semi-structured interview completed with an individual and/or care providers to assess one's personal and social sufficiency from birth to adulthood, providing an overall adaptive behaviour composite and composite scores in four main areas (i.e. socialization, daily living skills, communication and motor Skills). The interview typically takes 20–30 min.

Adaptive Behavior Assessment Scale (ABAS; Harrison & Oakland 2000) The ABAS consists of two versions, a parent and an adult questionnaire. The appropriate version was administered based on the participant's age. A total composite score and 10 domain scores are provided (i.e. communication, community use, functional academics, home living, health and safety, leisure, self-care, self-direction, social and work). Completing the questionnaire typically takes 10–15 min.

Care and Comfort Hypertonicity Questionnaire (CCHQ; McCoy et al. 2006) The CCHQ is an interview questionnaire consisting of 27 questions divided into four scales: personal care, positioning/transferring, comfort and interaction/communication. Questions are answered using a 7-point Likert scale; mean scale score is calculated. The interview takes approximately 10 min to administer. It provides a measure of functional limitation and has some quality-of-life elements with questions relating to pain and self-esteem. It indicates disease severity in terms of degree of disability.

Global rating of disease severity

A medical geneticist and neurologist completed a global rating of disease severity (RDS; Guy 1976). Ratings were based on the histories and physical examinations completed at the time of the visit and represent a subjective estimate of neurological and adaptive impairment. Each participant was assigned a rating on a 7-point scale; lower scores represent less impairment.

Procedures

Study participants and their caregivers were inpatients for 3 days in our General Clinical Research Center. During the visit each patient completed a series of medical and non-medical evaluations, including those described in this study.

Intellectual testing and functional assessment occurred in the patient's private room. When possible, only the examiner and participant were present when completing tests of cognitive functioning. Because some patients had limited speech or were difficult to understand, having a caregiver present to interpret responses was sometimes necessary. Each participant was initially tested with the WASI. If he or she was unable to complete all four sections because of physical limitations, the Leiter-R was then administered. Given the progressive nature of PKAN, participants and/or their caregivers were told to consider the participants' functioning during the preceding 3 months when completing the VABS and ABAS. When completing the CCHQ, participants and their caregivers were instructed to consider how easy or difficult it is for oneself or one's caregiver to perform particular tasks within the last 2 weeks. Global RDS were completed at the end of the admission and were based on observations from standardized clinical and neurological examinations, including the Burke–Fahn–Marsden rating scale for dystonia (Burke *et al.* 1985).

Results

Descriptive summary

During standardized testing, participants demonstrated diverse symptom expressions. Motor skills ranged from no apparent problems to severe dystonia. The spectrum included unilateral or bilateral mild hand tremors, spastic facial and limb movements, and rigidity of limbs. Speech production also varied, with some participants demonstrating clear and fluid speech, others displaying mild to moderate dysarthria and others being completely unable to speak in an intelligible manner because of dysarthria.

Intelligence testing results were obtained on 15 participants (see Table 2). Ten successfully completed the WASI. Five were unable to complete all portions of the WASI and were subsequently assessed using the Leiter-R. One European participant, who spoke English as a second language, was tested with the WASI with some assistance from an interpreter and was also tested with the Leiter-R. One participant who was legally blind secondary to PKAN-associated retinitis pigmentosa was unable to be tested with either instrument. PPVT-III results were obtained on 11 participants (see Table 2). One participant was not testable with the PPVT-III because of vision-related constraints, and three additional individuals were not testable because of the inability to establish a basal set.

Significant variability in intellectual abilities was observed. Although the mean general IQ was 90.1 on the WASI and 52.7 on the Leiter-R, wide range distributions (WASI = 67–114, Leiter-R = 32–98) and large standard deviations (WASI = 17.08, Leiter-R = 27.93) were evident. Less variability was observed in scores on the PPVT-III (M = 94.6, range = 82–127, SD = 13.1). However, given that four participants were unable to complete the PPVT-III, greater variability in skills assessed by this measure likely exists in PKAN than was captured.

Adaptive behaviour functioning was successfully measured by the VABS for all participants (Table 3), ABAS for 14 of the participants (Table 4) and the RDS and CCHQ for all participants (Table 5). On the VABS, the observed means, range of scores and standard deviations demonstrate significant variability across participants (composite: M = 62.3, range = 20–117, SD = 37.9; communication: M = 66.7, range = 20–109, SD = 33.5; daily living skills: M = 60.4, range = 20–119, SD = 40.04; socialization: M = 70.8, range = 20–117, SD = 30.4; motor skills: M = 57.4, range = 20–113; SD = 33.4). Similar results are shown on the ABAS (general adaptive composite: M = 79.0, range = 40–120, SD = 27.6).

The CCHQ showed similar variability (composite: M = 2.5, range = 1.2–4.5, SD = 1.1; personal care: M = 2.4, range = 1.0–5.6, SD = 1.4; positioning/transferring: M = 2.7, range = 1.0–6.3, SD = 1.6; comfort: M = 2.1, range = 1.0–5.3, SD = 1.4; interaction/communication: M = 2.7, range = 1.5–3.7, SD = 0.7), as did the RDS (composite: M = 3.38, range = 1.0–5.0, SD = 1.5; see Table 5).

The association between age of disease onset and outcome variables was assessed, given that early onset of PKAN is typically related to greater impairment (Hayflick *et al.* 2003). One-sided Pearson product-moment correlations revealed that age of disease onset was significantly correlated with intelligence (using a variable comprising either the WASI general IQ or Leiter-R general IQ; $r = 0.47$, $P < 0.05$), RDS ($r = -0.53$, $P < 0.05$), and with VABS and ABAS total composite scores ($r = 0.69$ and 0.68, respectively, both $P < 0.01$); all other correlations were non-significant.

Assessment of relative strengths and weaknesses

Ten participants completed all subtests of the WASI, allowing for a comparison of verbal and non-verbal reasoning abilities. No statistically significant difference in these abilities, as estimated by the WASI verbal (M = 86.6, SD = 14.68) and performance (M = 93.2, SD = 23.88) IQs, were observed ($t = -1.396$, $P > 0.05$). The WASI matrix reasoning (M = 47.82, SD = 10.91) sub-scale scores differed significantly from vocabulary (M = 38.18, SD = 12.88) and similarities (M = 41.36, SD = 6.07) sub-scale scores ($t = -3.95$, $P = 0.03$ and $t = -2.27$, $P = 0.047$, respectively). No other sub-scale scores differed significantly.

To investigate whether relative weaknesses in functional capacities were evident, obtained mean scores on composites of the VABS and scales of the ABAS were compared using a paired-sample *t*-test. Mean scores on the VABS socialization (M = 70.81) and daily living skills (M = 60.44) composites differed significantly ($t = -2.630$, $P = 0.019$). Further, scores on the socialization composite were significantly higher than on the estimated motor skills composite (M = 57.38; $t = 3.284$, $P = 0.005$). Comparisons of ABAS sub-scales also revealed differences in specific areas of functional capacities. Specifically, scores were higher on the leisure scale (M = 7.79) as compared with the community use (M = 6.29) and self-direction (M = 5.93) scales ($t = -2.242$, $P = 0.043$ and $t = 2.879$, $P = 0.013$, respectively). Within the CCHQ, the positioning/transferring scale correlated closely with the personal care and interaction/communication scales ($P = 0.006$, $P = 0.000$, respectively). The highest (worst) scores were positioning/transferring and interaction/communication (M = 2.7, M = 2.7, respectively).

Comparison of methods to assess skills

The secondary goal of this investigation was to gather information about the utility of various assessment strategies. One method of accomplishing this is to evaluate whether measures of similar constructs provide similar scores. Thus, scores on the general composite score of each of the three measures of functional capacities (i.e. VABS, ABAS, CCHQ) were compared to see if similar results were obtained. As would be expected, the correlation between the general

composite scores of the VABS and ABAS was high ($r = 0.854$, $P < 0.001$), and both correlated negatively with the CCHQ summary score although not as strongly (VABS $r = -0.672$; ABAS $r = -0.721$, both $P < 0.01$). However, mean total composite scores on the ABAS were significantly higher than those obtained on the VABS ($t = -2.264$, $P = 0.041$).

Further, we compared scores obtained on intelligence measures with those obtained on the PPVT-III. To do so, we created a variable consisting of either the WASI general IQ score or Leiter-R general IQ score and compared that against obtained PPVT-III scores. Again, although scores on intelligence tests and the test of vocabulary were correlated ($r = 0.686$, $P = 0.02$), PPVT-III scores (M = 94.64) were significantly higher than the combined mean IQ variable (M = 80.09; $t = -2.371$, $P = 0.039$). A similar outcome was obtained when comparing PPVT-III scores (M = 96.67) with WASI verbal IQ scores (M = 87.00) for nine subjects ($t = -3.07$, $P = 0.015$). However, scores on the PPVT-III did not differ significantly from the WASI performance IQ mean score (M = 85.5; $t = -1.637$, $P = 0.136$).

Although clinical observation is often used to describe impairment of NBIA and PKAN, methods used in the current study allow for an analysis of whether clinical impressions correspond to performance on standardized measures of intellectual and functioning in PKAN. A strong negative association was observed between RDS scores and Leiter-R total scores ($r = -0.948$, $P = 0.004$), as would be expected because the Leiter was employed only with the most impaired subjects. In contrast, no significant correlation was identified between RDS and WASI total scores ($r = -0.485$, $P > 0.05$). However, when RDS scores were correlated with IQ test scores (either the WASI or Leiter-R), a significant negative correlation emerged ($r = -0.824$, $P < 0.001$). RDS scores and the total scores of both the VABS and ABAS were strongly negatively correlated ($r = -0.848$, $P < 0.000$ and $r = -0.709$, $P = 0.005$, respectively). The CCHQ composite score correlated significantly with the RDS ($r = 0.644$, $P = 0.007$). The CCHQ had consistently lower (less severe) summary scores than the RDS (M = 2.5 vs. M = 3.38, true in 13 out of 16 patients). This finding is perhaps related to the quality-of-life elements of this scale, which could be quite independent of actual physical disease severity or progression.

Discussion

The current study shows varied cognitive phenotypic expression in PKAN as measured by standardized, norm-referenced evaluation tools. Estimates of general cognitive functioning indicate general intellectual skills ranging from high average to markedly below average. Similar variability in adaptive behaviour functioning was found. Age of disease onset was associated with measures of intellectual functioning, adaptive behaviour and disease severity.

Results offer important information about general intellectual functioning in PKAN. Marked differences in non-verbal and verbal abilities may not exist, given the absence of statistically significant difference between verbal and performance IQ scores on the WASI. However, non-verbal methods of assessing cognitive functioning may be necessary with more severely affected individuals. Participants demonstrated significantly higher scores on the PPVT than on tests of intelligence (i.e. WASI or Leiter-R). The PPVT may well provide a better estimate of verbal cognitive abilities in PKAN patients with significant physical limitations.

The data show a relative strength in visual-spatial reasoning as compared to general fund of knowledge (i.e. significantly better scores on the matrix reasoning sub-scale than on the vocabulary sub-scale of the WASI). Additional evaluation of cognitive functioning and change over time for individuals with PKAN is warranted to determine whether specific areas of functioning are more affected than others and whether decline is global or idiosyncratic. Given that iron is largely deposited in the basal ganglia, specifically the globus pallidus and substantia

nigra, one would expect most significant changes in cognitive abilities to be related to those directly or indirectly influenced by these nuclei. However, post-mortem findings of cerebral atrophy in NBIA (Suri 2001) highlight the importance of attention to cognitive skills influenced by cortical functions (such as general reasoning abilities).

Measurement of adaptive behaviour skills suggests differential impact of PKAN on functional limitations, as socialization and leisure skills were rated as more intact than other adaptive skills. Such results are not surprising, as the neuromotor consequences of PKAN (e.g. dystonia) impair articulation and movement but would not necessarily impact to the same degree a person's ability to interact with others or engage in preferred activities, as these types of activities may be more adaptable.

The current findings are also informative regarding assessment strategies for individuals with PKAN. Results confirm that existing standardized measures of intellectual abilities are appropriate for many individuals with PKAN. While physical limitations necessitated a flexible testing protocol for certain participants, most were able to complete the WASI, Leiter-R or PPVT. Certainly, physical limitations must be considered when selecting assessment instruments (Sattler 2001). Further, the purpose of the assessment must be clearly defined. Dynamic, non-standardized assessment processes may ultimately prove more useful for planning purposes, whereas adherence to standardized procedures may be most important when documenting condition status, progression or response to intervention.

Measures of adaptive behaviour functioning (i.e. VABS, ABAS, CCHQ) correlated with measures of intellectual functioning and with clinician-rated symptom severity. Thus, these measures appear to capture functional capacities of individuals with PKAN. However, scores obtained with each measure were discrepant. Which measure is most representative of functioning remains unclear, as no independent measure of adaptive behaviour functioning was obtained. Our sense of the study population was that there was a wide variability in adaptive function, and each measure had utility in different ways. The VABS and ABAS are interchangeable in terms of the global construct assessed, but we preferred the ABAS because it relies more heavily on the perspective of the respondent, who theoretically knows the individual better than the examiner. Perception of quality-of-life issues resides mainly in the CCHQ comfort domain, which yielded the lowest (best) mean score of the four. The ABAS, VABS and CCHQ directly reflect a patient's and/or caregiver's perspective on the individual's functioning/abilities, whereas the RDS is essentially the physician's interpretation of the disease impact for the patient. Which perspective most accurately reflects impairment is unanswered and should be empirically investigated. A separate unanswered question remains which measure(s) will capture change over time best. This has particular relevance to treatment studies.

The current findings should be viewed within the context of the study limitations. Although this paper represents largest number of patients with PKAN studied to date, the absolute number of participants with this rare disorder is still quite small. This limits statistical power. Further, extrapolating from the present findings to other individuals with PKAN is difficult, particularly given our findings of diverse phenotypic expression. Additionally, the same assessment protocol was not administered to each patient, because of individual impairment, introducing another potentially confounding variable into our analyses. Finally, serial assessment was not undertaken, preventing analysis of the association between disease progression and functioning over time.

These limitations notwithstanding, the findings are a significant contribution to research on PKAN and suggest directions for future research. Serial assessment is needed to further investigate the natural history of cognitive decline secondary to PKAN. Such analyses should

examine both global functioning, as was done in the current investigation, as well as specific neuropsychological functions to determine which are more or less affected with disease progression. While such an analysis has been carried out with patients with NBIA (Cooper *et al.* 2000), it has not been completed with individuals with PKAN specifically. Precedence for serial assessment has been established with other degenerative conditions (Comi *et al.* 1998), both to investigate natural progression and as part of clinical trials. The availability of natural history is crucial to evaluating intervention on cognitive functioning. While there is no cure for PKAN, supplemental pantothenate (vitamin B5) has been suggested as an intervention to compensate for enzymatic deficiency, specifically in individuals with later-onset or atypical PKAN (Hayflick *et al.* 2003). Evaluations of such intervention on cognitive and adaptive functioning and on care and comfort characteristics will be important to objectively document benefits of treatment. Finally, investigation of similarities and differences in cognitive skills between individuals with early vs. late-onset PKAN, as well as between PKAN and the other two disorders of brain iron accumulation, neuroferritinopathy and aceruloplasminemia, will help further differentiate the behavioural phenotype of these conditions.

Pantothenate kinase-associated neurodegeneration is a neurodegenerative condition with a broad phenotypic spectrum, supported by current findings using standardized assessment measures. Given that the genetic defect of PKAN was discovered only recently (Zhou *et al.* 2001), as well as the rarity of the disorder (Hayflick 2002), additional work is needed to better understand the impairments of the condition and how interventions alter those impairments.

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Table 1

Summary of participant variables

Patient	Sex	Age at diagnosis (year)	Age at testing (year)
HS185-201	Female	3	7
HS235-201	Male	10	11
HS136-201	Female	1	15
HS197-201	Male	14	16
HS116-201	Female	13	16
HS34-201	Female	1	18
HS197-202	Female	17	19
HS199-201	Female	18	20
HS232-201	Male	Unknown	20
HS65-302	Female	10	21
HS65-301	Female	8	23
HS230-201	Male	14	29
HS234-201	Male	7	33
HS38-201	Male	13	34
HS146-201	Female	17	43
HS65-102	Female	23	69

Table 2

Results of intelligence and vocabulary testing

	Wechsler Abbreviated Scale of Intelligence							Leiter – Revised			
Patient (age, sex)	**Full-4**	**Ver**	**Per**	**Voc**	**BD**	**Sim**	**MR**	**Total**	**SV**	**PPVT**	**FR**
HS185-201 (7, F)	67	68	72	20	33	31	31	*	*	*	+
HS235-201 (11, M)	85	87	87	38	30	45	53	*	*	*	98
HS136-201 (15, F)	+	71	+	23	+	35	40	77	92	76	96
HS197-201 (16, M)	75	80	72	35	20	39	43	*	*	*	84
HS116-201 (16, F)	+	+	+	+	+	+	+	40	52	63	*
HS34-201 (18, F)	+	+	+	+	+	+	20	32	48	55	+
HS197-202 (19, F)	106	90	121	47	72	41	53	*	*	*	96
HS199-201 (20, F)	99	86	114	41	60	40	57	98	104	90	+
HS232-201 (20, M)	81	77	89	30	37	39	49	*	*	*	84
HS65-302 (21, F)	+	+	54	+	21	+	20	33	48	55	89
HS65-301 (23, F)	+	+	55	+	22	+	20	36	52	57	82
HS230-201 (29, M)	107	91	104	47	63	42	64	*	*	*	107
HS234-201 (33, M)	+	55	+	20	+	20	+	+	+	+	+
HS38-201 (34, M)	114	109	116	63	61	49	58	*	*	*	127
HS146-201 (43, F)	68	77	62	27	20	41	30	*	*	*	85
HS65-102 (69, F)	99	101	95	49	46	53	48	*	*	*	93

Asterisk (*) indicates subject not tested; plus symbol (+) indicates subject could not complete the test.

Full-4, Ver, Per, Total, FR, SV, and PPVT Mean = 100, Standard Deviation = 15; Voc, BD, Sim, MR Mean = 50 Standard Deviation = 10. Ver, verbal; Per, performance; Voc, vocabulary; BD, block design; Sim, similarities; MR, matrix reasoning; FR, fluid reasoning; SV, spatial visualization; PPVT, Peabody Picture Vocabulary Test.

Table 3

Vineland adaptive behaviour scales results

Patient (age, sex)	Composite	Communication	Daily living skills	Socialization	Motor skills
HS185-201 (7, F)	39	50	31	46	24
HS235-201 (11, M)	75	92	69	79	97
HS136-201 (15, F)	40	90	20	66	22
HS197-201 (16, M)	106	92	105	117	81
HS116-201 (16, F)	29	34	20	43	20
HS34-201 (18, F)	20	20	20	20	20
HS197-202 (19, F)	108	109	100	109	102
HS199-201 (20, F)	108	109	106	104	113
HS232-201 (20, M)	23	21	34	47	47
HS65-302 (21, F)	25	44	20	48	33
HS65-301 (23, F)	42	53	33	51	37
HS230-201 (29, M)	113	109	119	102	81
HS234-201 (33, M)	25	20	20	44	27
HS38-201 (34, M)	86	92	92	85	87
HS146-201 (43, F)	40	51	59	61	43
HS65-102 (69, F)	117	81	119	111	84

Composite and factor scales Mean = 100, Standard Deviation = 15.

Table 4

Adaptive behaviour assessment system results

Patient (age, sex)	Total	C	CU	FA	HL	HS	L	SC	SD	S	W
HS185-201 (7, F)	52	1	1	1	6	1	4	1	1	5	NA
HS235-201 (11, M)	90	9	9	10	9	6	11	2	8	10	NA
HS136-201 (15, F)	54	1	1	3	1	1	6	1	1	8	NA
HS197-201 (16, M)	120	11	10	11	13	12	13	12	13	11	11
HS116-201 (16, F)	40	1	1	1	1	1	1	1	1	1	NA
HS34-201 (18, F)	40	1	1	1	1	1	1	1	1	1	NA
HS197-202 (19, F)	120	14	14	15	14	14	14	12	12	12	11
HS199-201 (20, F)	89	12	7	9	6	8	12	10	5	5	10
HS232-201 (20, M)	63	8	1	5	4	3	4	6	4	6	4
HS65-302 (21, F)											NA
HS65-301 (23, F)											NA
HS230-201 (29, M)	96	11	12	13	13	13	8	8	9	4	8
HS234-201 (33, M)	56	7	1	1	1	1	5	1	2	6	NA
HS38-201 (34, M)	95	7	7	8	12	12	9	12	10	11	NA
HS146-201 (43, F)	93	7	11	10	4	10	11	9	12		NA
HS65-102 (69, F)	98	6	11	9	12	11	10	12	9	12	NA

Total Mean = 100, Standard Deviation = 15; individual scales Mean = 10, Standard Deviation = 3.

C, communication; CU, community use; FA, functional academics; HL, home living; HS, health and safety; L, leisure; SC, self-care; SD, self-direction; S, socialization; W, work; NA, not applicable.

Table 5

Results of the ratings of disease severity (RDS) and Care and Comfort Hypertonicity Questionnaire (CCHQ)

Patient (age, sex)	RDS	CCHQ				
		PC	P/T	C	I/C	SuSc
HS185-201 (7, F)	3	2.7	3.7	4.6	2.7	3.4
HS235-201 (11, M)	1	1.3	1.0	1.0	2.0	1.3
HS136-201 (15, F)	4	4.9	4.0	4.0	2.6	3.9
HS197-201 (16, M)	3	1.3	1.2	1.0	2.0	1.4
HS116-201 (16, F)	5	2.9	4.3	5.3	2.9	3.9
HS34-201 (18, F)	5	5.6	6.3	2.2	3.7	4.5
HS197-202 (19, F)	2	1.0	1.0	1.3	1.5	1.2
HS199-201 (20, F)	2	1.6	1.5	1.0	3.2	1.8
HS232-201 (20, M)	4	1.0	1.0	2.3	2.0	1.6
HS65-302 (21, F)	5	2.7	3.0	1.0	3.6	2.6
HS65-301 (23, F)	5	2.9	3.2	1.0	3.3	2.6
HS230-201 (29, M)	2	1.8	2.0	1.0	2.0	1.7
HS234-201 (33, M)	5	1.9	2.2	1.3	2.8	2.1
HS38-201 (34, M)	3	1.5	3.3	1.8	2.4	2.4
HS146-201 (43, F)	4	3.7	4.8	3.3	3.4	3.8
HS65-102 (69, F)	1	1.0	1.0	1.5	3.0	1.6

RDS range 1–7; CCHQ range 1–7.

PC, personal care; P/T, positioning/transferring; C, comfort; I/C, interaction/communication; SuSc, summary score.