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## COMPUTERIZED NEUROCOGNITIVE ASSESSMENT IN RARE GENETIC DISORDERS WITH MODERATE TO PROFOUND INTELLECTUAL DISABILITIES: A PROOF OF PRINCIPLE STUDY

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### Abstract

**Objective:** Specific knowledge on neurocognitive functioning in (syndrome based) intellectual disability (ID) is important for the assessment, treatment and support of patients in whom this condition is present. The present study investigates the applicability of computerized neurocognitive testing in patients with rare monogenetic ID disorders by (1) determining the developmental age at which the use is contributive and (2) investigating the specificity of the tests for neurocognitive functions, independent of the ID.

**Method:** A total of 56 patients with monogenetic ID disorders, including Kleefstra Syndrome (KS; n=24), and a contrast group of various rare disorders (n= 32) participated. Assessments included (a) the Vineland Adaptive Behavior Scale (VABS) interview to calculate developmental age and (b) four simplified subtests of the Cambridge Neuropsychological Test Automated Battery (CANTAB). A cut-off in developmental age was estimated based on the ability to complete the CANTAB-tasks. A developmental age of 2,5 years and older allows practical application in our cohort.

**Results:** There was no significant correlation between developmental age and results on cognitive tests (range:  $-0,171 \leq \rho \leq 0,336$  with p-values  $> 0,07$ ). A between-group comparison shows a larger dropout in the KS sub cohort (based on cross tabulation) and longer latencies on the motor screening test.

**Conclusions:** Our results indicate that simplified CANTAB tasks are suitable for application in the ID population to unravel individual neurocognitive characteristics and, hence also, syndrome specific neurocognitive features. Furthermore, successful employment of computerized testing in this complex population may be the only way to avoid the restraints of standard classificatory clinical procedures that aim at categories of patients rather than at the individual patient with its unique cognitive neuropsychiatric complexion.

**Key words:** neurocognitive test, genetic disorder, intellectual disabilities

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### Introduction

Intellectual Disabilities (ID) comprise a heterogeneous disease category, characterized by deficits in adaptive as well as intellectual functioning that manifest at a young age, typically during the developmental period (APA 2013). Traditionally it is categorized by levels of adaptive functioning; in other words, the severity reflects the level of support that is required to function in daily life.

With recent advances in genetic techniques, people

with intellectual disabilities (ID) are more often diagnosed with a genetic syndrome underlying their ID (Willemsen and Kleefstra 2013, Gilissen et al. 2014, Vissers et al. 2016, DDD-study 2017). From a clinical perspective, in particular when challenging behaviors are present, it is not only important to have an estimate of a patient's level of intellectual functioning, but also to obtain full understanding of the neurocognitive functioning by including measures of attention, memory, executive functioning, and affective information processing. Since these various cognitive-

affective processes are essential for adequate daily functioning and can have a major impact on the quality of life, strengths and weaknesses thus identified are of utmost importance for the design and selection of targeted treatment - e.g., (Egger et al. 2007, Verhoeven and Egger 2014). As a matter of fact, with the advance of genetic testing and the rise of novel defined syndromes, it is increasingly noticed that such profiles of neurocognitive functioning are associated with specific genetic disorders (Roelofs et al. 2015, Egger et al. 2016). Results on neuropsychological tests in more established genetic syndromes, such as Down syndrome, 22q11.2 deletion syndrome, Williams syndrome, Prader-Willi syndrome, and Noonan syndrome, showed potential to optimize daily guidance as well as to obtain objective measures for follow-up studies and therapeutic interventions (Edgin et al. 2010, Rhodes et al. 2010, van Nieuwpoort et al. 2011, Wingbermhühle et al. 2012, Liogier d’Ardhuy et al. 2015, Roelofs et al. 2016).

While neurocognitive functioning has shown to be a well-established factor in the understanding of neurodevelopmental (genetic) disorders, there are specific complications that may arise when performing neurocognitive assessment in patients with ID. For instance, several tests rely on (verbal) instructions that require abilities in conceptual reasoning on average-and-above levels of intelligence. In addition, regarding the development of normative scores, patients with ID are not included and, consequently, differential performance in the low-IQ range may not reliably and validly detected. Furthermore, to address above issues, data are often obtained through indirect measurement, for example with proxy ratings via interviews or questionnaires. Although these are invaluable sources of information, they may be less reliable due to specific biases in particular when applied within the ID population (Havdahl et al. 2016, Vermeulen et al. 2017). All this often leaves the clinician relatively empty-handed, that is, with few possibilities to disentangle syndrome specific features from features caused by the level of ID and to build their interventions on the individual neurocognitive profile. Therefore, it is important to consider if and how neurocognitive

tests, which were originally developed for the general population, can be applied in the ID population.

In this study, we aim to determine the applicability of computerized neurocognitive testing for diagnostic assessment and phenotyping of genetic syndromes. Specifically, we are interested in what level of functioning is required to perform such neurocognitive tests and to what extent neurocognitive data are syndrome specific. Therefore, the use of four simplified tablet based neuropsychological tests from the widely used Cambridge Neuropsychological Test Automated Battery (CANTAB; (2017)) is investigated in patients with rare monogenetic disorders, with a main focus on Kleefstra Syndrome (KS, main clinical characteristics are listed in **table 1**) (Kleefstra et al. 2006, Willemsen et al. 2012). The specific group of KS patients has been chosen because we can build upon our expertise with this syndrome, already inventoried knowledge about the clinical picture, both adaptive as well as maladaptive (summary in **table 1**). Furthermore, for a rare neurodevelopmental disorder, this cohort is relatively large (n= 24) and comprises, at the time of inclusion, all known patients in the Netherlands and Belgium (Vermeulen et al. 2017).

In sum, the purpose of this study is fourfold, namely (1) to define at a group level (the “overall”-level) a cut-off value in developmental age for the meaningful application of these tests. In other words, we examine whether it is possible to disentangle the level of functioning from other cognitive characteristics (for example memory, cognitive flexibility and processing time) in a population with low general levels of functioning. Then, we want to establish at the inter-individual level (2) whether these tests provide additional information on neurocognitive functioning, incremental to the information already available from the lower general level of functioning. Consequently, (3) at this inter-individual level, we expect higher levels of dropout on these neuropsychological tests at lower levels of developmental age. And finally, we want to explore at the intra-individual level (4) if these tests provide additional information about the individual

**Table 1.** Background information on Kleefstra Syndrome

<i>Genetic defect</i>	
Kleefstra et al. (2006)	Chromosomal microdeletion or intragenic <i>EHMT1</i> mutation, both resulting in a similar clinical phenotype
<i>Clinical characteristics, somatic and psychiatric comorbidity</i>	
Kleefstra et al. (2006), Willemsen et al. (2012), Verhoeven et al. (2011), Vermeulen et al. (2017a), Vermeulen et al. (2017b)	<i>General:</i> Trias ID, childhood hypotonia and prominent facial features <i>Somatic:</i> Congenital heart abnormality, epilepsy, constipation <i>Psychiatric:</i> Autism spectrum disorder, psychosis, apathy, major depressive disorder
<i>Translational research in animal models</i>	
Kramer et al. (2011)	<i>Mutant EHMT1 Drosophila melanogaster:</i> Disturbed motor behavior, non-associative learning and courtship complex memory
Balemans et al. (2010)	<i>EHMT1 knock-out mice:</i> Problems with stimulus processing, high levels of anxiety, low levels of baseline activity, perseveration and deviation in social reactions to strangers

patient for personalized diagnosis and treatment and how this results in a personalized practice. Thus, across the overall, inter-individual, and intra-individual levels, four questions are examined to systematically map the additional value of these simplified computerized neuropsychological tests for application in the ID population with monogenetic disorders.

**Method**

For a detailed description of the recruitment of patients and the psychometric properties of the Vineland Adaptive Behavior Scale (VABS), we refer to our previous study (Vermeulen et al. 2017).

*Participants*

A total of 56 patients were included: 24 with Kleefstra Syndrome (*EHMT1* intragenic deletion or mutation) and 32 contrast participants with various monogenetic disorders. Patient characteristics and the monogenetic disorders are displayed in **table 2**.

Informed consent was obtained by legal representatives and included in the patient file. The medical research ethics committee CMO/METC Arnhem-Nijmegen, the Netherlands, approved the study (NL43187.091.13), which was performed in full accordance with the Declaration of Helsinki.

*Instruments*

**Vineland Adaptive Behavior Scale.** The Dutch adaptation of the Vineland Adaptive Behavior Scale (Sparrow 1984) is a widely used clinical interview, for determining the level of adaptive functioning (expressed in a developmental age) of people with an intellectual disability of three domains: communication skills, daily living skills, and social skills. Based on these, a total score is available.

**Cambridge Neuropsychological Test Automated Battery.** The Cambridge Neuropsychological Test Automated Battery (CANTAB, 2017) consists of a computer administrated set of (nonverbal)

neuropsychological tests developed to examine specific components of cognition. The CANTAB has been widely used in academic research and in clinical trials, and tests hold acceptable levels of concurrent validity and test-retest reliability (Lowe and Rabbitt 1998). Subtests are graded in difficulty, minimizing floor and ceiling effects, and allow for use in a wide variety of ages and conditions. Participants are given multiple training trials to learn the requirements of each task, and detailed recording of responses is made possible by using a touch-sensitive screen.

From earlier research with CANTAB tasks in Down syndrome (Edgin et al. 2010, Edward and Del Campo 2017) developed simplified versions of four CANTAB subtests that were applied in the present study. They are described below and were performed in the presented sequence:

1. The Motor Screening Test (MOT) is a training procedure designed to introduce the subject to the touch screen. In our cohort it also is an estimate to reactivity, which could not be tested with an official reaction time test, because of the complexity of the latter (pushing a button instead of the touchscreen during the task). The simplified version is comparable to the normal clinical mode, but uses a high visibility mode.
2. The Pattern Recognition Memory (PRM) is a test of visual pattern recognition memory in a 2-choice forced discrimination paradigm. These patterns are designed in a way that they can't easily be given verbal labels. The simplified version has the same amount of patterns (12). Stage 1 is exactly comparable to the normal clinical mode. Stage 2 in the simplified version includes direct testing of the displayed patterns, followed by delayed testing of these patterns. In the normal clinical mode, stage 2 only includes displaying the patterns without direct testing, so without repeat. The delayed recognition phase in our cohort is administered 10 to 20 minutes after the initial one, depending on the duration of the IED test performance.
3. The Intra-ExtraDimensional Test Shift (IED) is a test of rule acquisition and reversal. Visual

**Table 2.** Patient characteristics

Group	Genetic Defect	Male: female ratio (%)	Biological age: mean (SD; min-max) in years
<b>Total</b>		<b>26: 30</b>	<b>15,00 (± 10,248; 3-40)</b>
Kleefstra Syndrome, n= 24	<i>EHMT1</i> gene 16x Microdeletions 8x Mutations	9:15 (37,5% vs 62,5%)	15,42 (±10,421; 3-37)
Contrast Group, n= 32	<i>KANSL</i> gene microdeletions (12x) <i>KANSL</i> gene mutation (1x) 6x <i>GATAD2B</i> gene microdelition 3x <i>ANKRD11</i> gene mutation 3x <i>SIN3A</i> gene mutations 2x <i>PACSI</i> gene mutations 1x <i>FOXP2</i> gene mutation 1x <i>FBOX17</i> gene microdeletion (2p16.3) 1x <i>AUTS2</i> gene microdeletion (7q11.22) 1x <i>YWHAE</i> microduplication (17p13.3)	17:15 (53,1% vs 46,9%)	14,69 (± 10,272; 3-40)

discrimination, cognitive flexibility and sustained attention are tested. The structure is the simplified task is similar to the clinical mode, with exception of the termination criterium. In the simplified version the test terminates after 30 failing trials whereas the clinical mode terminates after 50 failing trials.

4. Paired Associate Learning (PAL) assesses visual memory and new learning. The simplified version is largely/ mainly comparable to the clinical mode. It also consists of 8 stages. The first 5 stages are similar between the simplified version and the clinical mode. In stage 6 the simplified version shows 4 patterns instead of 3 in the clinical mode. Stage 7 and 8 are comparable. (8 stages. Stage 1 → 1 pattern out of 6 boxes. Stage 2 → 1 pattern out of 6 boxes. Stage 3 → 2 patterns out of 6 boxes. Stage 4 → 2 patterns out of 6 boxes. Stage 5 → 3 patterns out of 6 boxes. Stage 6 → 3 patterns out of 6 boxes. Stage 7 → 6 patterns out of 6 boxes. Stage 8 → 8 patterns out of 8 boxes). Each stage is composed of several trials, consisting of the first presentation of the shape(s) and followed by representation when the subject makes an error. The simplified version terminates when 6 attempts are not successful, whereas the clinical mode terminates after 10 repeat presentations.

interview with the parents/ representatives to assess the followed by the simplified version of the CANTAB. All tests were performed in the vicinity of a proxy (parent, caregiver), who was completing questionnaires in the same or an adjacent (open) room. Further details on test procedures are described in detail in our previous report (Vermeulen et al. 2017). Questionnaires and an additional interview with the parents as well as the play observation with the patient were part of a larger study on genes and behavior (study NL43187.091.13).

### Analyses

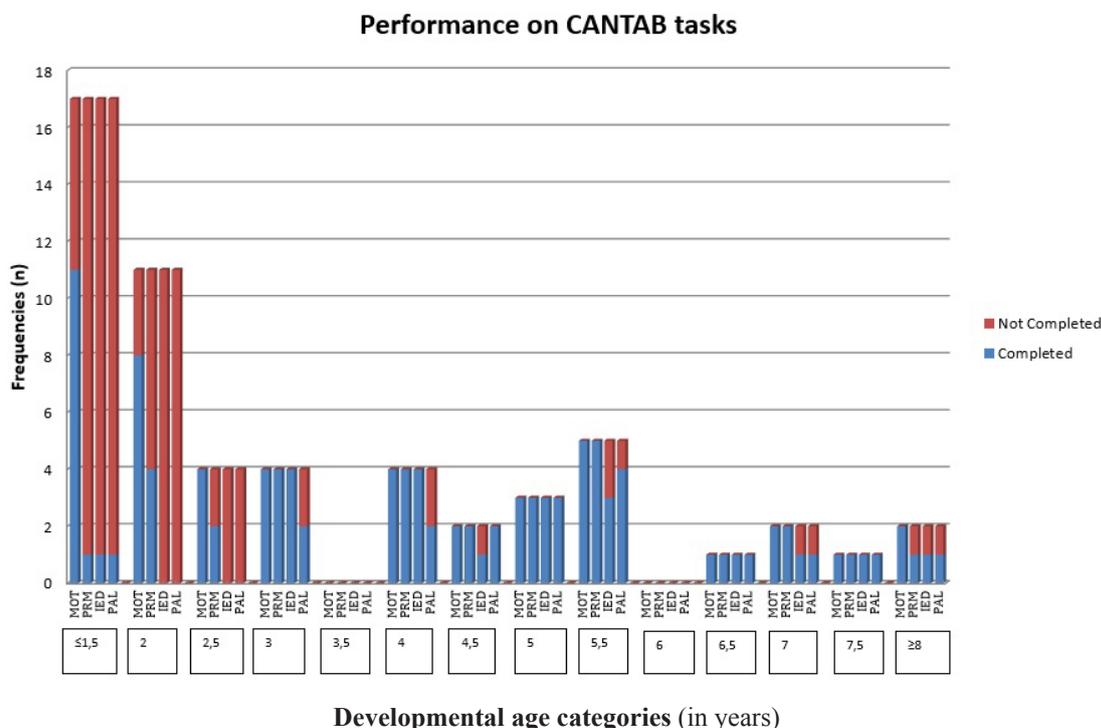
Statistical analyses were performed using IBM SPSS Statistics 22

Three different levels of measurement were examined when processing the results, (1) Overall level. The overall performance of all participants was assessed by using cross tabulations to answer the question at what developmental age testing is useful. Thereafter, the role of developmental age for the total group on results was assessed by using bivariate correlations for each of the CANTAB subtests and the developmental age. (2) Inter-individual level: results between groups were compared. Distribution of the variables under research did not meet the normality-criterion, hence Mann-Whitney U test was used to compare results of KS and contrast subjects. Finally, (3) at the intra-individual level, a profile of neurocognitive functioning was composed for each of the participants who were able to complete all tests. These profiles were inspected on strengths and weaknesses for the provision of clues for daily guidance and optimal functioning.

### Procedures

Patients were tested in a familiar place to reduce risk on sub-optimal results, e.g. distortion by fear of the unknown. The investigation started with a VABS

Figure 1. Performance on CANTAB tasks



Performance on the CANTAB. For the range of developmental age (displayed in categories on the X-axis) the number of participants who completed (blue) vs not completed (red) the tests are displayed on the Y-axis. The results for 4 simplified subtests of the CANTAB are displayed in each categorie on the X-axis: MOT= motor screening test. PRM= pattern recognition memory. IED= intra-extra dimensional test shift. PAL= paired associated learning.

## Results

Results are presented following the above-mentioned subdivision.

### Overall

The number of completed CANTAB-tests is displayed in **figure 1**. Some subjects were not able to complete any of the tests. As can be deduced from **figure 1**, in our cohort, MOT can be properly accomplished from a developmental age of 2 years (cut-off  $\geq 22$  months) while PRM can be completed from a developmental age of 2.5 years (cut-off  $\geq 31$  months). The results for IED and PAL are less clear: at a developmental age of 2.5 years and older, however, most subjects were able to complete the tests, with completing percentages of 79,2% for IED and 70,8% for PAL.

None of the subtests showed a significant correlation between developmental age and test performance. P-values for correlation of the several subtests between developmental age and test results are displayed in **table 3**.

### Inter-individual factors

Performance, expressed in completion rate, between KS and the contrast group was compared. Differences between the groups were calculated by cross tabulations for the several subtests of the CANTAB. The results are displayed in **table 4** and show a large drop-out in the KS group for all subtests. Interestingly, the KS patients with a younger biological age are more often able to complete the tests. After this, the results of the completed tests of KS subjects and subjects in the contrast group were compared. For the CANTAB subtests, only MOT was completed by enough subjects to compare results. Non-parametric testing on MOT latency (only in subjects who completed the test), using a Mann Whitney U test, shows a significant result between the groups on median latency ( $p < .05$ ). Patients with KS had longer latencies compared to the contrast group. The mean latency was not significant ( $p=0,74$ ) most probably due to the large variance in the contrast group (**figure 3**).

**Table 3.** *p-values for correlation between subtest results and developmental age*

Subtest	Pearson's correlation coefficient	P-value
MOT mean latency	-0,171	P= 0,268
PRM numbers correct	0,336	P=0,070
PRM scoring difference between direct and delayed recall	-0,17	P=0,932
IED stages completed	-0,052	P=0,829
PAL stages completed	0,256	P=0,306

**Table 4.** *Crosstabulations of simplified CANTAB tasks*

The crosstabulations show for all tests a significant (\*\*) higher drop-out than expected by chance.

<b>MOT</b>	KS	Contrast group
Completed	17	30
Expected	20,1	26,9

Pearson X<sup>2</sup>, Monte Carlo 2-zijdig= 0,048\*\*

<b>PRM 1<sup>st</sup> trial</b>	KS	Contrast group
Completed	8	24
Expected	13,7	18,3

Pearson X<sup>2</sup>, Monte Carlo 2-zijdig= 0,004\*\*

<b>PRM delayed</b>	KS	Contrast group
Completed	6	24
Expected	12,9	17,1

Pearson X<sup>2</sup>, Monte Carlo 2-zijdig=0,001\*\*

<b>IED</b>	KS	Contrast group
Completed	1	19
Expected	8,6	11,4

Pearson X<sup>2</sup>, Monte Carlo 2-zijdig= 0,00\*\*

<b>PAL</b>	KS	Contrast group
Completed	1	17
Expected	7,7	10,3

Pearson X<sup>2</sup>, Monte Carlo 2-zijdig= 0,001\*\*

### Intra-individual factors

Finally, we looked at Intra individual results. In Box 1, by means of three case examples, the relation between individual test results and treatment advice is described in detail. In a number of patients with KS, the slow latency time was not taken into account in daily living tasks (for example at school). Adjustments like giving a person more time to perform a task and stimulating activities, lead to a more optimal daily guidance. Other examples include the optimal benefit taking of the attention span (which could be measured exactly during test performance) for school tasks and the lowering the level of anxiety by providing more external structure and overview.

### Discussion

In this study, we set out to determine the applicability of computerized neurocognitive testing in patients with moderate to profound ID, using simplified test of the CANTAB. Also, we wanted to study whether neurocognitive data may have specific characteristics in different genetic syndromes. Firstly, our results indicate, on overall level of performance, that computerized

neurocognitive testing with the simplified subtests of the CANTAB can be successfully applied in subjects with a moderate to severe ID and some tests even in profound ID. Previously, some computerized neurocognitive tests were successfully applied in Down Syndrome (Edgin et al. 2010, Liogier d'Ardhuy et al. 2015) and Williams Syndrome (Rhodes et al. 2010), but in both groups, the level of ID is less pronounced with a main focus on borderline, mild and moderate ID. However, to the best of our knowledge, the current simplified versions of the four CANTAB subtests have never been tested before in the ID population. This may provide opportunities to collect data in different countries, since the tests are independent of language.

Secondly, on inter-individual level, our results indicate that there is no significant relation between subtest-performance and the level of functioning. In continuation of this, it turned out that the KS group had a lower performance rate and a longer median latency. This was consistent with our observations that subjects with KS needed much more time for action and reaction and were easily over stimulated. Because of high levels of unfocused attention, it was often not possible to complete IED and PAL for which sustained attention is needed. Their latency results on the MOT subtest, expressed in milliseconds, was even longer

#### Box 1. Case descriptions

Subject X is a 30 years old female, who completed all 4 simplified CANTAB tasks.

**Results:** She showed remarkable accuracy in her performance and reduced latency times for all tests, compared to her results. Direct recall was present for simple stimuli. However, direct recall of more complex stimuli and visual memory were impaired. Switching between paradigms was too complex for her. She was able to complete all tests, but with continuation of test administration, she showed problems with sustained attention and her latency time reduced even more.

**Advice:** The high level of accuracy in combination with her reduced latencies point out the importance of having enough time to complete tasks. In other words, based on her output, her environment will easily ask too much from her; leading to overstimulation. We advice to give her extra time to complete daily living tasks, like getting dressed in the morning.

Based on the problems with switching, her cognitive flexibility will be low. She needs help for this by making daily life more predictable. For example with a visualized (part-time) day programm. Tasks that are offered, should ask a maximum of 15 minutes effort from her, due to her limited attention span. Ideally, these are interspersed with moments of rest.

Subject Y is a 5,5 years old girl, diagnosed with a microdeletion at chromosome 17q21.31 resulting in KoolendeVries syndrome. She was able to complete all 4 subtests and was keen in managing the tablet. **Results:** This girl scored at the norm for biological age for speed of processing and accuracy at simple tasks. In the more complex tasks (after some patterns of the PRM and the complete IED and PAL) she showed a worse performance at learning ability, cognitive flexibility and memory. She took advantage of repeated practice.

**Advice:** It was advised to help this girl with external structure and overview as well as repetition of daily tasks. External help was also advised to practice skills in new situations. Her level of anxiety declined after the help was more focused on training and providing help rather than on taking things over. Her self esteem increased.

Subject Z is a 8 year old boy, diagnosed with a *ANKRD11* mutation (KBG Syndrome). He was able to complete all 4 tasks with some positive feedback ("wow, you already finished 3 tests, just one left!"). **Results:** He had normscores, adequate for biological age, on the visual memory tasks, but during the test performance, his attention span declined. For this reason the results on the last memory task (visuospatial memory) was poor. His speed of processing was high, but this was at the expense of his accuracy. The performance on task switching was at the lower end of the norm for his biological age.

**Advice:** It was advised to provide short, concrete/actual instruction before starting a new task and substantiate this with a visual clue. Independent taskperformance at school was adapted to his attention span and after 5-10 minutes another visual clue together with positive feedback was given ("well done!") to help him sustain attention. External help and extra tasks on accuracy were provided to practice and these were planned at the start of a school day, when his attention was best.

than had been estimated on the basis of observation and clinical impression. Translating this to daily guidance, the speed of talking, providing instructions and waiting for responses should be lowered significantly in this group of patients. Whether the prolonged MOT-latency time and the high drop-out on the other subtests may be associated with the clinical presence of ASD in subjects with KS (Edgin et al. 2010, Schmidt et al. 2016, Vermeulen et al. 2017) remains to be seen. Literature on ASD often mentions impairments in executive functioning (Hill 2004, de Vries and Geurts 2015, Van Eylen et al. 2015, Chen et al. 2016), which seems in agreement with the large dropout in our KS-cohort on the IED. Most literature regarding the use of CANTAB tests in neurodevelopmental disorders, however, do not mention the scores on the MOT, because this is only the first step to make participants familiar with the CANTAB. Nevertheless, the results of this subtest provide important information. Because of the large drop-out, it was not possible to compare our results to those of *EHMT* animal models (Benevento et al. 2017). Nor could we relate our results to previous research in Down Syndrome (Edgin et al. 2010, Liogier d'Arhuy et al. 2015) or Williams syndrome (Rhodes et al. 2010). The patients with a younger biological age showed plenty of practice operating the touchscreen compared to the older ones. This might be due to the spirit of the times, in which the younger ones grew up with regular exposure to touchscreens, e.g. of smartphones and tablets.

Finally, on intra-individual level, it was possible to point out strengths and weaknesses of the subject, based on test results and systematic observation associated with test administration. Based on these, specific targets can be formulated for individualized treatment and daily guidance. In our cohort, in several cases, this turned out to be useful in providing directions for stimulating the development and breaking through problem behaviors and/ or psychiatric symptoms. Although the advices were not new (slowing down speed of processing, providing external structure and overview), the CANTAB was helpful in the precise tailoring of the advices to the subject's needs and in particular, in matching the timing of help to the needs. This appeared to be specifically useful for (specialized) schools and day care centers but also for guidance at home.

A possible weakness of this study is the relatively small number of participants. This study nonetheless shows that with proper assessment tools, a more personalized treatment and guidance of people with moderate to severe ID is to some extent feasible. Previous work in Noonan Syndrome has also shown this to be the case (Roelofs et al. 2015, Roelofs et al. 2016). Those who work with people with moderate to severe ID should be aware of this and make efforts to provide adequate neurocognitive assessment for their patients. The focus is often on controlling disruptive behavior, rather than focusing on neurocognitive characteristics that could provide insight in capacities and limitations of a patient. Furthermore it provides opportunities to collect and combine data on genetic syndromes in different countries, since these tests are independent of language. This is an important aspect for future research and the field should build international networks for exchanging data of relatively rare genetic neuropsychiatric disorders and make an effort to develop standardized tests to achieve good standard scores. Ideally, for adequate neurocognitive testing, an observation schedule should be developed, to standardize observations during computerized

test performance. This is important because not only performance results, but also behavioral aspects during performance give clues about strengths and weaknesses of the subject.

In sum, the use of computerized neurocognitive assessment provides the opportunity to collect objective measures in a population where it is often difficult to get direct information of the subjects themselves. We suggest that a first step could be to enhance of the accessibility of the CANTAB-tests for the ID population. An advantage of the simplified versions is that verbal instruction is hardly necessary. The principle of Computerized Adaptive Testing (CAT), in which test administration can be specifically adjusted to the abilities of the subjects, should be applied in this population. The CAT method has its theoretical roots in multidimensional assessment of personality, and allows to leave fixed algorithms for test-items, adjust the items more specific to the test-subject (Segall 1996). According to Wang et al. 2012, the application of CAT in the neurocognitive domain holds the promise of more accurate measurement of intra-individual diagnostic factors. It therefore may be an important tool for tailored treatment and treatment monitoring. The latter may hold in particular for the objective observation of the natural course of genetic disorder, not only to establish cognitive decline, but also to monitor and clarify putative treatment effects in the ID population.

In summary, we recommend the use of the simplified CANTAB versions in neurocognitive assessments in the ID population. The results of these tests are helpful in diagnostic procedures, formulating personalized treatment and guidance as well as to enhance specific knowledge about genetic syndromes.

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