

Short Report: Measuring the Behavioral Disturbance of Autism Spectrum Disorder by Cohen-Mansfield Agitation Inventory

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Abstract

Introduction: Cohen-Mansfield Agitation Inventory (CMAI) has originally been developed for the evaluation of agitation in Alzheimer's disease. Reliable tools for measuring behavioral symptoms in autism spectrum disorder (ASD) are missing.

Methods: The reproducibility of the CMAI was evaluated in 26 patients. The CMAI-questionnaire was filled for each participant by three different nurses. The measurement was repeated by the primary caregiver for 15 patients. Agreement between nurses was measured using Cohen's weighed kappa, intraclass correlation coefficient (ICC) was used to evaluate intra-rater reliability and Cronbach's alphas to quantify internal consistency.

Results: The inter-rater reliability was found to be substantial for all items ICC 0.64 (95%CI 0.43-0.80). Cronbach's alpha was good for the whole CMAI score ($\alpha=0.87$ with 95% CI 0.82-0.91). No statistically significant differences were seen in the CMAI-scores between repeated measurements.

Conclusions: The CMAI may be a reasonably reliable tool to follow-up changes in behavioral symptoms of ASD.

Introduction

Autism spectrum disorder is a cluster of disorders with neuropsychiatric comorbidities, the prevalence of which has steadily increased during the past decades affecting approximately 1 in 36 children [1]. Especially intellectually disabled autistic persons form one of the most difficult-to-treat patient group because of their limited verbal and social skills and severe, highly variable behavioral symptoms as well as diagnostic challenges [1,2]. Accordingly, evidence-based medical treatments are sparse. Furthermore, different tools used for the evaluation of efficacy in clinical trials complicate the comparisons between studies and, thus, the discovery of effective treatments [3].

There are several reasons why a Cohen-Mansfield Agitation Inventory (CMAI) might be useful in measuring behavioral symptoms in intellectually disabled, autistic persons as earlier has been shown through researching Alzheimer's disease [4]. This questionnaire was originally designed to measure the types

and frequencies of agitated behaviors exhibited by elderly nursing home residents [5]. The types of undesired behaviors between ASD and Alzheimer's disease are similar [5,6] and the CMAI has been suggested to be a useful evaluation tool especially for persons who are without a language [7] like autistic persons commonly lack. Furthermore, the CMAI is used commonly in clinical trials evaluating the efficacy of interventions for agitation in people with dementia [8] despite its methodological weaknesses [9].

The CMAI is a 29-item questionnaire, which is filled in by a primary caregiver based on the frequency with which the institutionalized older adults have manifested physical aggression and verbal agitation over the past two weeks [5]. The score for each question ranges from 1 (no symptoms) to 7 (the symptom occurring several times per hour). The purpose of this study was to examine whether the CMAI would be reliable in evaluation of agitation in intellectually disabled, autistic persons living in long-term institutionalized rehabilitation.

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Material and methods

Data for the CMAI was collected from 26 autistic, intellectually disabled persons, who live at Special Services for Developmentally Disabled, Tampere University Hospital (n=16) and at the Support and Expert Center for People with an Intellectual Disability, Southwest Finland (n=10).

Three nurses from the same unit (incl. a primary caregiver) filled independently the CMAI questionnaire for each of the 26 participants within 24 hours. In addition, for 16 of those participants, the primary caregiver repeated the CMAI collection after one and three months. During the data collection period the participants received ordinary rehabilitation including possibly some minor changes in medication. The measurements for all subjects were done within an eleven months' timeline (from October 2019 to September 2020) and the total score was recorded in the treatment chart for each participant.

Analyses were conducted using IBM SPSS Statistics (version 26.0; IBM SPSS, Chigaco, Illinois). The internal consistency of the items, subscales of behavior and entire questionnaire were studied using Cronbach's alphas with 95% confidence intervals (CI). Alpha values are assessed as follows: $0.7 \leq \alpha < 0.8$ as acceptable, $0.8 \leq \alpha < 0.9$ as good and $0.9 \leq \alpha$ as excellent [10].

The inter-rater reliability of agreements was calculated using intraclass correlation coefficients (ICC) for scales and Cohen's weighted kappa (K) for items with 95% CIs as following benchmark scales: <0.00 poor, 0.00-0.20 slight, 0.21-0.40 fair, 0.41-0.60 moderate, 0.61-0.80 substantial, 0.81-1.00 almost perfect degree of agreement [11]. Differences between each primary caregiver's three measurements were tested using repeated measures General Linear Models. All tests were two-sided and p-values <0.05 were considered statistically significant.

Permission to use registered CMAI data was obtained from the Research, Development and Innovation Center of Tampere University Hospital, Finland.

Results

A total of 26 autistic persons (18 males) with mean age of 27 (range 17 - 41) years participated the study.

Inter-rater reliability

The degree of accuracy was highest regarding Cohen's weighted kappa coefficient (p-value<0.001) for the items of hitting, hurting self or others, making physical sexual advances, trying to get to a different place, intentional falling, and repeating sentences or questions (Table 1). Additionally, statistically significant kappa (p<0.05) was found for all 3 nurse pairs with items of kicking, grabbing onto people, throwing things, tearing things or destroying property, paces, and aimless wandering, inappropriate dressing or disrobing, screaming, negativism and constant unwarranted request for attention or help. Intraclass correlation coefficient (ICC) with all the items was substantial 0.64 (95% CI 0.43-0.80) for all three nurses and, also for all three nurses separately (ranging from 0.60 - 0.69) as shown in Table 1.

Internal consistency

Cronbach's alpha was good 0.87 (95% CI 0.82-0.91) with all the 29 items for all three nurses, and at least acceptable for all nurses separately (Table 1). Alphas were better for psychical aggressive subscale $\alpha=0.78$ (95% CI 0.70-0.85) and psychical non-aggressive $\alpha=0.74$ (95% CI 0.64-0.82), but lower for verbal non-aggressive $\alpha=0.66$ (95% CI 0.52-0.77) and very low for verbal aggressive $\alpha=0.25$ (95% CI -0.18-0.52).

No statistically significant differences between nurses could be seen in any of the distributions of sums of items (Supplementary Table 1) between the measurements at three different time points measured from each of 15 participants by his/her own caregiver (grey markers in Figure 1). The third measurement for one participant was not available. Three nurses did the initial three measurements within 24 hours independently of each other. The CMAI scores of 15 participants varied from 44 to 133 at the first time point, from 39 to 93 in the second time point and from 37 to 113 at the third time point without notably change in medians (63, 66 and 66). The median of the minimum CMAI-value in any three measurement points was 55 (Interquartile Range, IQR 45-66, range 37-83). The median for maximum CMAI-values in any three measurements was 76 (IQR 64-109, range 49-133). Accordingly, the median for difference between maximum and minimum values was 21 (IQR 12-36,

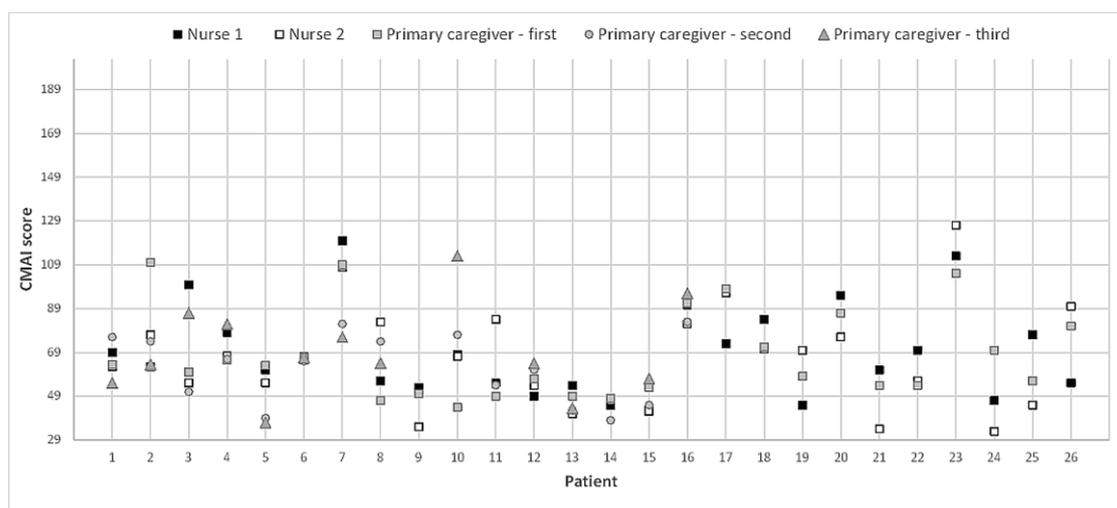


Figure 1. Comparison of the Cohen-Mansfield Agitation Inventory (CMAI) scores as collected by three different nurses (i.e., by each participant's primary caregiver and by two other nurses) within 24 hours from 26 autistic participants with intellectual disability (ID), are shown with boxes as a marker. Comparison of the CMAI scores measured by a primary caregiver on consequent three repeated measurements (at baseline, at one month and three month) are shown as grey markers.

Table 1. Comparison of Cohen-Mansfield Agitation Inventory (CMAI) as collected by three different nurses (i.e., by each participant's primary caregiver and two other nurses) within 24 hours from 26 autistic, intellectually disabled participants. Distributions of knowledge of behaviors were described using mean with standard deviation (Sd). Cohen's weighted kappa (K)1 was performed separately for all pairs of 3 nurses and 29 behaviors and shown with 95% asymptotic confidence intervals (CI). Intraclass correlation coefficients (ICC)2 and Cronbach's alphas (α)3 were calculated with 95% confidence intervals (CI). Highly statistically significant, $p < 0.001$, results are bolded.

Questions	Own nurse	Other nurse 1	Other nurse 2	Own nurse vs. another nurse 1		Own nurse vs. another nurse 2		Another nurse 1 vs. another nurse 2	
	Mean (Sd)	Mean (Sd)	Mean (Sd)	K	(95% CI)	K	(95% CI)	K	(95% CI)
Physical/Aggressive									
Hitting (including self)	2.12 (1.28)	2.58 (1.94)	2.46 (1.63)	0.56	(0.40-0.72)	0.53	(0.33-0.73)	0.49	(0.20-0.77)
Kicking	1.88 (1.31)	1.85 (1.26)	1.65 (1.06)	0.41	(0.14-0.67)	0.37	(0.08-0.66)	0.54	(0.25-0.84)
Grabbing onto people	2.42 (1.42)	2.46 (1.10)	2.65 (1.70)	0.3	(0.08-0.51)	0.45	(0.18-0.72)	0.33	(0.14-0.52)
Pushing	1.81 (1.30)	1.42 (0.86)	1.46 (0.90)	0.22	(-0.05-0.49)	0.18	(-0.04-0.40)	0.3	(0.05-0.55)
Throwing things	2.04 (1.08)	2.19 (1.47)	2.12 (1.42)	0.38	(0.14-0.62)	0.35	(0.08-0.62)	0.47	(0.30-0.64)
Biting	1.69 (1.16)	1.73 (1.40)	1.58 (1.36)	0.41	(0.08-0.74)	0.34	(0.04-0.64)	0.29	(-0.01-0.60)
Scratching	1.50 (0.86)	1.81 (1.06)	1.81 (1.44)	0.26	(0.01-0.51)	0.17	(-0.07-0.41)	0.65	(0.45-0.84)
Spitting	1.58 (1.33)	1.65 (1.55)	1.73 (1.56)	0.64	(0.35-0.93)	0.48	(0.16-0.80)	0.35	(-0.08-0.77)
Hurt self or others	2.92 (1.41)	2.92 (1.65)	2.92 (1.76)	0.55	(0.36-0.74)	0.47	(0.25-0.69)	0.47	(0.26-0.68)
Tearing things or destroying property	2.42 (1.60)	2.69 (2.00)	2.69 (1.67)	0.42	(0.22-0.62)	0.5	(0.32-0.68)	0.5	(0.34-0.65)
Making physical sexual advances	1.31 (1.19)	1.15 (0.61)	1.35 (1.06)	0.73	(0.49-0.97)	0.75	(0.56-0.93)	0.64	(0.37-0.92)
Physical/Non-Aggressive									
Paces, aimless wandering	3.77 (2.21)	3.42 (2.23)	3.27 (2.44)	0.3	(0.06-0.55)	0.31	(0.05-0.57)	0.43	(0.18-0.68)
Inappropriate dress or disrobing	2.46 (1.84)	2.73 (2.05)	2.62 (1.90)	0.49	(0.29-0.69)	0.45	(0.22-0.67)	0.42	(0.15-0.69)
Trying to get to a different place	2.38 (1.98)	2.54 (1.90)	2.38 (1.92)	0.53	(0.34-0.73)	0.6	(0.39-0.81)	0.56	(0.38-0.75)
Intentional falling	1.73 (1.48)	1.58 (1.42)	1.46 (1.21)	0.86	(0.64-1.07)	0.65	(0.34-0.95)	0.77	(0.52-1.02)
Eating/drinking inappropriately	1.77 (1.45)	2.19 (1.72)	1.62 (1.36)	0.41	(0.08-0.73)	0.39	(0.12-0.66)	0.28	(-0.06-0.62)
Handling things inappropriately	1.65 (1.41)	1.58 (1.36)	1.92 (1.38)	0.71	(0.40-1.01)	0.17	(-0.10-0.43)	0.21	(-0.03-0.44)
Hiding things	1.38 (0.85)	1.35 (0.98)	1.54 (1.24)	0.58	(0.28-0.88)	0.34	(-0.05-0.72)	0.36	(0.06-0.65)
Hoarding things	1.54 (1.33)	1.62 (1.50)	1.88 (1.56)	0.2	(-0.08-0.47)	0.38	(0.01-0.76)	0.41	(0.10-0.73)
Performing repetitious mannerisms	4.92 (1.94)	4.73 (2.05)	4.73 (2.09)	0.11	(-0.19-0.41)	0.05	(-0.23-0.32)	0.29	(0.04-0.54)
General restlessness	3.77 (1.48)	4.00 (1.60)	3.92 (1.85)	0.24	(-0.02-0.50)	0.43	(0.27-0.59)	0.17	(-0.06-0.39)
Verbal/Aggressive									
Screaming	3.15 (2.13)	3.73 (1.93)	3.38 (2.04)	0.32	(0.10-0.55)	0.57	(0.35-0.78)	0.36	(0.15-0.57)
Making verbal sexual advances	1 (0)	1 (0)	1 (0)						
Cursing or verbal aggression	1.35 (1.02)	1.12 (0.43)	1.15 (0.78)	0.29	(-0.16-0.74)	0.41	(-0.08-0.91)	0.65	(0.34-0.96)
Verbal/Non-Aggressive									
Repetitive sentences or questions	3.35 (2.67)	3.65 (2.40)	2.65 (2.42)	0.63	(0.41-0.85)	0.65	(0.45-0.86)	0.54	(0.29-0.78)
Strange noises (weird laughter or crying)	3.73 (2.32)	3.77 (1.92)	3.42 (1.88)	0.27	(0.01-0.53)	0.36	(0.13-0.58)	0.23	(-0.01-0.47)
Complaining	2.19 (1.72)	2.23 (1.80)	1.46 (1.36)	0.12	(-0.21-0.45)	0.15	(-0.04-0.35)	0.22	(-0.04-0.48)
Negativism	2.92 (1.67)	3.04 (1.80)	2.77 (1.80)	0.5	(0.27-0.73)	0.47	(0.24-0.71)	0.32	(0.05-0.59)
Constant unwarranted requests for attention or help	2.88 (1.70)	2.15 (1.64)	2.73 (2.20)	0.36	(0.10-0.62)	0.39	(0.12-0.65)	0.36	(0.08-0.64)
Total	67.6 (20.3)	68.9(20.9)	66.4(23.4)						
Total - ICC (random)				0.62	(0.32-0.81)	0.69	(0.42-0.85)	0.6	(0.29-0.80)
Cronbach's Alpha				0.77	(0.48-0.90)	0.82	(0.59-0.92)	0.75	(0.44-0.89)

¹Kappa (K): Measure of agreement of items for an inter-rater reliability between two raters with range of maximum (1=perfect agreement) to minimum (0=no agreement). ²Intraclass correlation coefficients (ICC) for intra-rater reliability of item ratings vary from minimum (0=poor reliability) to maximum (1=perfect reliability). For both Kappa and ICC, the minimum limit for acceptable agreement is 0.4. ³Cronbach's alphas (α), a measure of internal consistency is acceptable with values of alpha ≥ 0.7 and excellent with alpha values of 0.9 or more.

range 1-69). The median change was 5.5% between the first and third measurements (IQR from -30% to 36%, range from -49% to 157%) of 15 participants. Over 10% score reduction (range from -49% to -12%) was found in 6 (40%) participants.

Discussion

Based on this study both the inter-rater and intra-rater reliabilities as well as the internal consistency of CMAI in measuring the undesired behaviors was surprisingly good taken the highly variable symptoms of autistic, intellectually disabled persons. Internal consistency was good for the whole CMAI, and acceptable for psychical aggressive and psychical non-aggressive subscales. In our data of severely autistic persons verbal nonaggressive and aggressive subscales did not reach acceptable level, which is not surprising taken account the participants' deficient verbal skills. Consequently, the total score obtainable from CMAI questionnaire at different time points might be useful when measuring the change in autistic, intellectually disabled persons' undesired behaviors.

There are numerous individual factors affecting the behavior of these persons and, thus, affecting also the CMAI-scores as observed by repeated measurements in this study. The CMAI-values of all 15 persons ranged from the minimum of 37 - 83 to the maximum of 49 - 133 scores at three consequent time points. This means, that the CMAI-scores obtained at one point cannot be used to compare the undesired behavior between individuals. Instead, the change in an individual person's CMAI-scores over time can be expected to reflect the improvement or deterioration of his/her status provided that the individual baseline fluctuation of CMAI-scores is known.

For any reliable clinical conclusions, the follow-up times need to be sufficiently long both before and after the intended intervention or treatment, because of highly variable symptoms. In other words, one needs to find out what the individual baseline fluctuation of CMAI scores is before any experimental treatment is initiated. Based on our clinical experience the severity of symptoms is influenced by numerous factors, all of which cannot be controlled in clinical trials, and which may, thus, lead to biased results. For example, the natural course of symptoms can vary along time and autistic persons may behave differently in the company of different caregivers. The other person-dependent and individually appearing factors may include e.g. seasonal variation, special festivals or holidays or new roommates. Also, any unexpected change in a daily routine can influence remarkably the behavior of some autistic persons.

Taken the heterogeneity of this group and promising statistical analysis of the data collected for this study, the CMAI could provide a valuable tool for measuring the changes in the devastating behaviors experienced by autistic, intellectually disabled persons. In anecdotal cases, the clinical improvement is easy to recognize [12,13]. Unfortunately, the CMAI-evaluation was not used for the follow-up of these successful cases two of whom were treated with psychiatric electroconvulsive therapy [13] and one with gluten-casein free diet [12]. However, in those cases the CMAI-scores would have decreased to the minimum values. A decrement of $\geq 50\%$ or more from maximum CMAI-values can, be considered as proof of improvement in person's condition. Such score reduction was not seen in any of the 15 recorded persons under ordinary long-term rehabilitation.

Our sample size was too small for further modelling to ensure the construct validity. Yet, our results are promising. The Cohen's weighted kappa used in the study, made the clinically

expected differences between small and large disagreements clearly visible. The reliability of the scale chosen for this study could likely be increased by defining accurately the criteria for each symptom included in the CMAI questionnaire.

In clinical practice the multidisciplinary team has considered a systematic CMAI recording useful. We have continued recording the total CMAI scores in each person's treatment chart about once a month since 2020. Our electronic medical record can draw a graph from the treatment chart, thus, visualizing how an individual's condition has fluctuated over timeline.

Conclusions

The total score obtainable from the CMAI questionnaire at different time points might be useful for the long-term follow-up and for measuring the change in autistic, intellectually disabled persons' self-destructive and aggressive behavior. To obtain a much-needed evaluation tool for this group further development of CMAI appears justified based on our clinical data and statistical analyses.

Lay Summary

- Reliable tools for evaluating aggressive and self-destructive behavior related to intellectual disabilities and autism spectrum disorder (ASD) are missing.
- Heterogenous outcome measures used in clinical trials hamper the discovery of new effective treatments.
- Cohen-Mansfield Agitation Inventory (CMAI) was originally developed for the evaluation of agitation in Alzheimer's disease.
- The CMAI might be a reliable outcome measure for the follow-up of changes occurring on an individual basis in devastating symptoms of intellectually disabled patients with ASD.

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Conflict of interest statement

The authors declare no conflict of interest.

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