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Evidence for two distinct domains of negative symptoms: Confirming the factorial structure of the CAINS

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A B S T R A C T

Negative symptoms are an important predictor of course of illness as well as social and occupational functioning. Clinically effective interventions are scarce. For negative symptoms to become a reliable primary endpoint in treatment studies, clear operationalization and construct validation is needed. Recent factor analyses mostly find two main factors for negative symptoms: diminished expression und amotivation/anhedonia. The Clinical Assessment Interview for Negative Symptoms (CAINS) consists of the subscales “motivation and pleasure” and “expression”. We assessed three samples of subjects with schizophrenia (n = 105) for different aspects of the scale's reliability and validity. A confirmatory factor analysis (CFA) of the CAINS confirmed its two-factorial structure. The subscales had distinct correlational profiles: "Motivation and pleasure" was strongly associated with functional outcome and depression and further with neurocognition, positive symptoms and social cognition. "Expression" seems independent of sources of secondary negative symptoms and neurocognition. We found good internal consistency and interrater agreement. Test-retest reliability (two-week interval) was moderate for the CAINS and its “expression” subscale and low for the “motivation and pleasure” subscale. Our findings indicate that the CAINS differentiates reliably between the two main domains of negative symptoms with some questions remaining concerning the validity of the “motivation and pleasure” subscale.

1. Introduction

Psychotic disorders are characterized by cognitive dysfunctions as well as positive and negative symptoms (e.g. Owen et al., 2016). Positive symptoms have been relatively well defined for quite some time, whereas the construct „negative symptoms“ wasn't theoretically refined and empirically tested until the 1980s by—amongst others—Andreasen (1982). The scientific discussion intensified with the development of interventions to treat negative symptoms, since they are an important predictor of e.g. course of illness as well as social and occupational functioning (e.g. Kaiser et al., 2017; Marder and Galderisi, 2017). A meta-analysis on treatments for negative symptoms found no clinically effective (even if statistically significant) interventions so far (Fusar-Poli et al., 2015). The authors called for the development of new, specific treatments. According to Lutgens et al. (2017)’s meta-analysis on nonbiological interventions, cognitive-behavioral therapy, skills-based training (and particularly social skills training (see also Kurtz and Mueser, 2008; Turner et al., 2018)), exercise, and music treatments are promising. For negative symptoms to become a reliable primary endpoint in treatment studies, clear operationalization and construct validation is needed (e.g. Marder and Galderisi, 2017).

1.1. Subdomains of negative symptoms

The National Institute of Mental Health consensus document (Kirkpatrick et al., 2006) has reviewed the concept “negative symptoms” that refers to Andreasen (1982).They identified five dimensions of negative symptoms: emotional blunting (lower intensity and range of verbal and nonverbal emotional expression), alogia (lack of speech, latency, poverty of speech content), avolition (lack of drive and motivation), anhedonia (inability to experience pleasure) and social withdrawal (reduced interest in, motivation for and enjoyment of social interaction and close relationships). Concerning anhedonia, there are findings indicating that patients with schizophrenia mainly show a deficit in anticipatory pleasure whereas consummatory pleasure is largely unaffected (Gard et al., 2007; Lambert et al., 2018; Wu et al., 2017). As there are different pathways leading to negative symptoms, the term secondary negative symptoms has been introduced and

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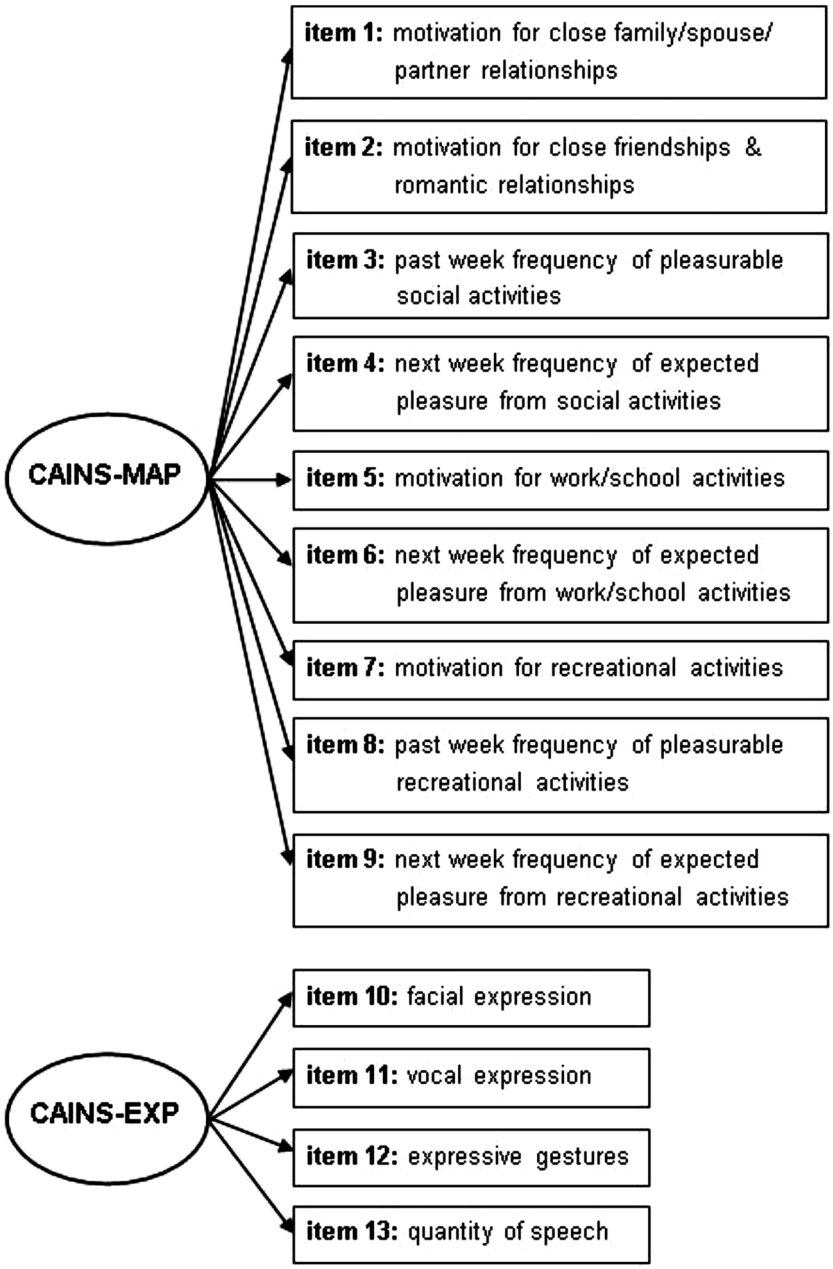

Fig. 1. CAINS subscales with items and item content.
Notes. CAINS-MAP = "motivation and pleasure" subscale (sum of items 1–9); CAINS-EXP = "expression" subscale (sum of items 10–13).

explored (Carpenter et al., 1988; Kirschner et al., 2017). Kirschner et al. (2017) argue that increased scores on negative symptom scales can be caused by depression (e.g. anhedonia (e.g. Lako et al., 2012)), positive symptoms (e.g. social withdrawal (e.g. Kelley et al., 1999; Tandon et al., 2000)), side effects of medication (e.g. emotional blunting (Kelley et al., 1999; Prosser et al., 1987)), substance use (e.g. amotivation (e.g. Rovai et al., 2013), and environmental conditions like social deprivation (e.g. avolition, social withdrawal (Kasanova et al., 2018; Oshima et al., 2005)). In contrast, primary negative symptoms are thought to be directly linked to schizophrenia.

1.2. Relationships with other symptom domains

When taking into account the phase of illness, positive symptoms and depressive symptoms don't seem to systematically correlate with negative symptoms. For positive symptoms, Peralta et al. (2000) report a nonsignificant correlation of 0.23 on admission but a significant and strong correlation of 0.57 on hospital discharge. Others found no significant correlations with negative symptoms (Schrank et al., 2014; Wallwork et al., 2012). Regarding depression, Peralta et al. (2000) found no relationship with negative symptoms on admission (0.01) and a large correlation (0.51) on discharge. Others found no significant (Kim et al., 2006; Wallwork et al., 2012) or a significant moderate relationship (Schrank et al., 2014) of negative and depressive symptoms. For cognitive dysfunction, there are small to moderate correlations with negative symptoms (0.07–0.29; Dominguez et al., 2009; Ventura et al., 2009).

1.3. Two-factorial structure of negative symptoms

Blanchard and Cohen (2006) present an overview of analyses of the factorial structure of negative symptoms. They found evidence for two

replicable factors encompassing the above mentioned subdomains in factorial analyses of the Scale for the Assessment of Negative Symptoms (SANS), the Schedule for the Deficit Syndrome (SDS), the Positive and Negative Syndrome Scale (PANSS; two-factorial structure also found by Liemburg et al. (2013)) and the Brief Psychiatric Rating Scale (BPRS). The first factor entails "diminished expression" covering emotional blunting and alogia, the second "amotivation" which contains avolition, anhedonia and social withdrawal. When evaluated, inappropriate affect, poverty of speech content, and reduced attention load on a third factor representing cognitive deficits/disorganization, which are at this point not thought of as part of the negative symptom domain (e.g. Marder and Galderisi, 2017). The two main factors "diminished expression" and "amotivation" correlate moderately (0.47–0.57) indicating a common underlying process (Blanchard and Cohen, 2006; Foussias and Remington, 2010; Kirkpatrick, 2014).

In a review, Kaiser et al. (2017) summarized that models of amotivation are currently converging on reward system dysfunction and aspects of goal directed behavior, while models of expressive deficits are still in an early phase of development. They find behavioral and neuroimaging studies to support distinct underlying mechanisms. Expressive deficits seem to be more persistent (Kelley et al., 2008) while amotivation correlates stronger with functional outcome (e.g. Fervaha et al., 2014). There is preliminary evidence for different outcomes for the two symptom domains concerning psychotherapeutic and pharmacological treatments as well as relapse (e.g. Kaiser et al., 2017; Riehle et al., 2017; Sayers et al., 1996).

1.4. The Clinical Assessment Interview for Negative Symptoms (CAINS)

Until recently, the SANS and the PANSS Negative Scale were most commonly used to assess negative symptoms. Both scales have been criticized for including items which presumably are not part of the negative syndrome and for featuring items that are not clearly defined. Also, the scales mostly assess behavior and rarely specifically inquire the patients' subjective experience. Overall, they don't seem to reflect the current state of the art in research anymore (Blanchard et al., 2010; Marder and Galderisi, 2017; Millan et al., 2014). The Marder Negative Symptom Factor Score (Marder Negative; sum of PANSS items N1–N4 and N6) aims to remediate some of the problems of the PANSS Negative Scale (Marder et al., 1997). Both the Brief Negative Symptom Scale (BNSS, Strauss et al. (2012)) and the measure under review here, the Clinical Assessment Interview for Negative Symptoms (CAINS, Kring et al. (2013)), are more recent instruments that refer to the above-mentioned two factors and confirmed those in exploratory analyses (Kring et al., 2013; Strauss et al., 2012). Both instruments facilitate differentiating amotivation and expression and thus advance the evaluation of new treatment options (Strauss and Gold, 2016).

The CAINS encompasses the five subdomains blunted affect, poverty of speech, avolition, anhedonia and social withdrawal. When assessing the "avolition/amotivation" factor, it focuses on the patients' inner experience. This is considered pivotal for emotional, social and motivational deficits and seen as different from behavior or functional outcome (e.g. Kring et al., 2013). The CAINS' structure can be seen in Fig. 1 and consists of a "motivation and pleasure" subscale (CAINS-MAP) and an "expression" subscale (CAINS-EXP). CAINS-MAP taps attitudes, intrinsic motivation as well as subjective experience and expectation of pleasure with nine items. CAINS-EXP rater-assesses expressive deficits straightforwardly with four items.

When validating the CAINS, Kring et al. (2013) found a two-factorial structure using exploratory principal-axis factorial analysis and hierarchical cluster analysis. They reported a correlation of 0.24 between the subscales, good internal consistency (CAINS: Cronbach's $\alpha = 0.76$, CAINS-EXP: $\alpha = 0.88$, CAINS-MAP: $\alpha = 0.74$), test-retest reliability (0.69 for both scales) and interrater-reliability (CAINS-MAP: 0.93, CAINS-EXP: 0.77). Good convergent validity was established with regard to other rater assessments of negative symptoms (BPRS, SANS), self-reports tapping pleasure, motivation and sociability and measures concerning the assessment of facial emotion expressions. Functional capacity (skills/capability) was not, but functional outcome (actual behavior) was linked to the measure. The authors found adequate discriminant validity regarding depression, medication side effects and cognitive functioning. However, positive symptoms and agitation were correlated with the "motivation and pleasure" subscale.

Engel et al. (2014) evaluated a German translation of the CAINS. Their exploratory principal-axis factor analysis also found the two-factor structure. Here, the two subscales were moderately correlated (0.44). The CAINS' overall internal consistency and the CAINS-MAP's were good (0.87, respectively), the CAINS-EXP's was acceptable (0.80). Inter-rater agreement was high for all CAINS items (≥ 0.73). Concerning convergent validity, there were high correlations between both CAINS scales and the PANSS Negative Scale. The subscales were significantly negatively related to self-rated consummatory pleasure but not to anticipatory pleasure. Discriminant validity was good with no significant correlations with positive symptoms, depression and general psychopathology. CAINS-MAP was significantly correlated with the Global Assessment of Functioning (GAF).

1.5. Objectives

This validation of the German CAINS's psychometric properties aims to confirm and expand on Engel et al. (2014). We analyze a larger sample and—to our knowledge—this is the second confirmatory factorial analysis (CFA; the first being a Chinese sample (Xie et al., 2018)) of the CAINS' two-factorial structure. This is complemented by a comprehensive multitrait-multimethod approach to assess convergent and discriminant validity of the two subscales. Test-retest reliability has not been reported for the German version as of yet; we assessed this, as well as interrater reliability.

2. Methods

2.1. Participants

Three independently collected samples were used: a "convergent and discriminant validity" sample (sample V), a "test-retest and interrater reliability" sample (sample R) and an additional sample to increase the sample size of the pooled "confirmatory factor analysis" sample (CFA sample). Inclusion criteria across all samples were diagnosis of a psychotic disorder according to DSM-IV, age 18–65 years, sufficient German language skills, normal or corrected to normal vision and hearing as well as capability to give consent. Exclusion criteria were substance dependence as the leading clinical problem and intellectual disability (IQ < 70, approximated by level of education). In addition to these common inclusion and exclusion criteria, there were sample-specific differences.

Sample V was used to assess the CAINS' convergent and discriminant validity and included 70 outpatients in a stable phase. Since sample V was the baseline examination of a study that aimed to improve negative symptoms using individual- and group-CBT, the participants had to have relevant negative symptoms (sum of PANSS items N1–4, N6, G7 and G16 ≥ 10) and to be in outpatient treatment to be included. Sample V's additional exclusion criteria were severe depressive symptoms (PANSS, G5 > 4), structural brain lesions, severe extrapyramidal side effects (Modified Simpson–Angus Rating Scale (MSAS) > 11), and current psychotherapeutic treatment. The diagnosis of a psychotic disorder according to DSM-IV was established using the Structured Clinical Interview for DSM-IV (SCID-I) for sample V. Sample V's participants received a monetary compensation for their assessment, the other samples did not.

Sample R was primarily used to assess the scale's interrater- and test-retest reliability and comprised 25 in-patients; 19 of whom were still available for the second assessment. In sample R, the assessment

Table 1
Demography of sample V, sample R and CFA-sample.

	Sample V (n=70)	Sample R (n=25)	CFA-Sample (n=105)
Age (yrs)	39.92 (11.06)	38.16 (10.68)	39.11 (10.94)
Male (%)	71.4	60	69.5
Age at 1st Hospitalization (yrs)	25.82 (8.64)	24.04 (8.10)	25.47 (8.13)
Univ. Entrance Qualification (%)	58.6	44.0	60.0
Diagnosis (%)			
Schizophrenia	85.7	76	85
Schizoaffective disorder	14.3	24	15
PANSS Total Score	62.16 (12.35)	66.80 (20.87)	63.87 (14.83) (n=93)
PANSS Positive Score	12.79 (4.67)	13.36 (5.31)	13.00 (4.86) (n=93)
PANSS Marder Negative Score	20.27 (4.75)	14.20 (7.65)	16.21 (4.86)
CDSS Total Score	4.23 (4.30)		
PSP	48.40 (13.00)		

Note. Univ. = University; PANSS = Positive and Negative Syndrome Scale; CDSS = Calgary Depression Scale for Schizophrenia; PSP = Personal and Social Performance Scale.

was videotaped, so the participants had to agree to this.

The additional sample comprised 12 inpatients and outpatients used to increase the overall sample size for the CFA. Sample R and the additional sample were diagnosed with the German Brief Diagnostic Interview of Mental Disorders (Mini-DIPS).

Both sample V and R as well as the additional sample (n = 105 because of overlap between the samples) were used for factorial analysis and to assess the internal consistency of the measure. Demographic and clinical characteristics of the samples can be found in Table 1.

2.2. Procedures and measures

The study protocol was approved by the ethics committee of the University of Tuebingen's medical faculty. After giving informed consent, all screened participants that met inclusion criteria were interviewed using the following measures: (1) a structured interview to obtain basic demographic data, (2) the PANSS (30-item clinician-rated measure of psychosis symptoms scored on a 7-point Likert scale ranging from 1 (absent) to 7 (extreme)) as well as (3) the CAINS (13-item semi-structured interview scored on a 5-point Likert scale ranging from 0 (no impairment) to 4 (severe deficit)). All raters were trained by observing experienced raters conduct the CAINS, applying the CAINS themselves using the manual and discussing the assessment amongst each other.

Sample V was assessed by two raters (MCE, KK); this took approximately four hours and included the following additional measures: (1) the Time Budget Measure (TBM) whose structured retrospective assessment of the past week is intended to reflect the actual level of activity, (2) the Calgary Depression Scale for Schizophrenia (CDSS), (3) the Personal and Social Performance Scale (PSP) as a rating of psychosocial functioning as well as (3) the Modified Simpson–Angus Scale (MSAS) assessing extrapyramidal side effects. Additionally, there was a performance assessment of social skills using role play, the Social Skills Performance Assessment (SSPA), which was audio recorded. Furthermore, we assessed cognitive functioning employing (1) the Trail Making Test A and B (TMT-A, TMT-B), (2) the German version of the auditory verbal learning test (VLMT), (3) the Tower of London (ToL) as well as (4) the Wechsler Adult Intelligence Scale‘s Digit Span task (WAIS-IV-DS). Lastly, the participants were asked to fill in additional questionnaires: (1) the Frankfurt Self-Concept Scales (FSKN), assessing components of self-concept including the subscale “appreciation by others” as a measure of social cognition (FSWA; tapping feelings of insufficiency and rejection in social situations) and (2) the Temporal Experience of Pleasure Scale (TEPS), assessing anticipatory und consummatory pleasure.

Sample R's initial assessment lasted approximately one hour during which the CAINS interview was videotaped. The raters CB and LS conducted one half of the interviews, respectively and assessed the videos of the other half. 14 (+/−5) days after the first assessment, participants were evaluated again, which took about 25 minutes.

The additional sample's assessment was done by the raters LH and SR, included further measures and took approximately 1.5 hours.

The German versions of the CAINS and TEPS were kindly made available to us by the research group led by Tania Lincoln, Department of Clinical Psychology and Psychotherapy, University of Hamburg. The German manual and rating sheet of the CAINS can be found in our supplementary data as well as downloaded free of charge under the creative commons license here: http://dx.doi.org/10.23668/psycharchives.775. The English versions of the TBM and SSPA were translated into German by our research group and retranslated by an English native speaker. Differences to the original English versions were discussed among the translators and a consensus was agreed on.

2.3. Data analysis

For demographic data a rate of missing items ≤10% was not reported. When calculating the scale composites, a rate of 5% and 10% of missing values for assessments and self-ratings respectively were tolerated and replaced by the scale's mean. Data points with more missing items were excluded from the respective analysis. The data quality of the CAINS, its subscales and items was high with no missing data.

Using SPSS v24 and AMOS v21, we assessed (1) the CAINS’ and its two subscales’ internal consistency, test-retest reliability and interrater reliability, (2) the CAINS’ latent structure using confirmatory factor analysis (CFA) and (3) the scales’ and its subscales’ convergent and discriminant validity.

We tested for normal distribution and homoscedasticity. Pearson or Spearman correlations respectively were used to evaluate test-retest reliability as well as convergent and discriminant validity. There, Holm–Bonferroni sequential correction was used to deal with the multiple comparisons problem. For interrater reliability the average Intraclass Correlation Coefficient (ICC) estimate and 95% confidence intervals were calculated based on a mean-rating (k = 2), absolute-agreement, two-way random model.

Concerning confirmatory factor analysis, we follow the

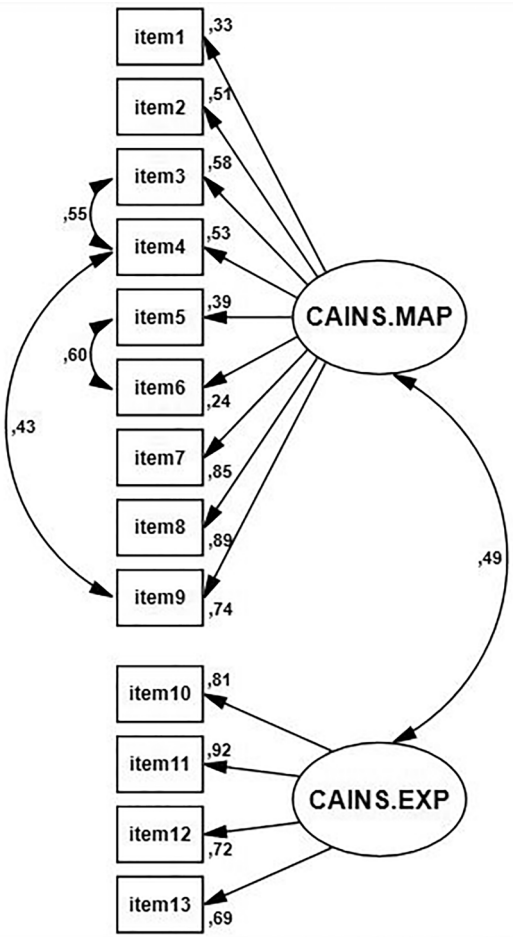

Fig. 2. Plot of the two-factor-CFA (final model) with covariances and standardized regression weights.
Notes. CAINS.MAP = "motivation and pleasure" subscale (sum of items 1–9); CAINS.EXP = "expression" subscale (sum of items 10–13); item 1–item 13 = CAINS items.

recommendations of Jackson et al. (2009). With regards to sample size, Jackson et al. (2013) propose to take p/f ratios (number of measured variables loading on each factor), number of latent variables and loading size into account. Their results suggest that for our two factors, a p/f of 4 and 9 and expected loading sizes between 0.4 and 0.9, a sample size of 50–100 could be sufficient. Curve estimation for all relationships in our model found them to be sufficiently linear. We then assessed univariate and multivariate normality. Skewness and kurtosis values for the items were all $<|2|$ and <7 respectively, suggesting adequately normal distribution. Mardia's coefficient, however, was 9.21 with a critical ratio of 2.39 (cut-off <1.96) which suggests significan—but not excessive—multivariate nonnormality (Byrne, 2009). There were no multivariate outliers identified via Mahalanobis distance at $\alpha = 0.001$ and nine at $\alpha = 0.05$ (Tabachnick and Fidell, 2007); there was no justification for the exclusion of any outliers (Byrne, 2009).

For the CFA, the analysis was performed on the observed covariance matrix. We used maximum likelihood estimation which is thought to be robust to minor deviations from normality (e.g. Chou and Bentler, 1995). To account for the multivariate nonnormality we used Bollen–Stine bootstrapping to adjust *p*-values for the χ^2 goodness-of-fit test of our model (Byrne, 2009). We report goodness-of-fit statistics CMIN, Comparative Fit Index (CFI; >0.9 indicating adequate and >0.95 good model fit), Root Mean Square Error of Approximation (RMSEA; <0.08 is considered adequate (Browne and Cudeck, 1992), <0.05 good (Steiger, 1990)), and Akaike Information Criterion (AIC; with smaller numbers indicating better fit). Fan et al. (1999) consider RMSEA and CFI to be less sensitive to sample size compared to other indices. We used the bias-corrected percentile method to calculate confidence intervals for the standardized regression weights and covariances (Byrne, 2009).

3. Results

3.1. Internal consistency (CFA sample)

The internal consistency of the scale was good: Cronbach's $\alpha = 0.87$, with no "α if item deleted" >0.87. For the subscales, we found good internal consistency as well: CAINS-MAP's Cronbach's $\alpha = 0.83$, CAINS-EXP's Cronbach's $\alpha = 0.86$.

3.2. Interrater reliability (sample R)

The single measure ICC was 0.81 (CI 0.61–0.91; ($F(24) = 9.17$, $p < 0.001$) indicating good reliability. For the subscales, interrater reliability was 0.81 for CAINS-MAP (CI 0.61–0.91; ($F(24) = 9.23$, $p < 0.001$) and 0.80 (CI 0.60–0.91; ($F(24) = 8.70$, $p < 0.001$) for CAINS-EXP.

3.3. Test-retest reliability (sample R)

For the CAINS we found a test-retest reliability of 0.71, $p = 0.001$, which is considered acceptable. CAINS-EXP had good test-retest reliability ($r = 0.82$, $p < 0.001$); CAINS-MAP's was poor to moderate ($r_S = 0.57$, $p = 0.011$).

3.4. Confirmatory factor analysis (CFA sample)

The CFA of a two-factorial structure of the CAINS with items 1–9 loading on the "motivation and pleasure" factor and items 10–13 loading on the "expression" factor had no cross-loadings but proved to be no good fit for the data ($\chi^2(64) = 197.57$, Bollen-Stine $p < 0.001$; CFI = 0.79, RMSEA = 0.14 (90%-CI 0.12–0.16), AIC = 251.57). Inspection of modification indices showed high covariances between some error terms of the "motivation and pleasure" scale. We iteratively included them in post hoc model fitting to account for the relevant item overlaps in the "motivation and pleasure" scale (e.g. Jöreskog and Long, 1993). The final model still had items 1–9 loading on the "motivation and pleasure" factor and items 10–13 loading on the "expression" factor and included overlap of items 3 and 4, 5 and 6, as well as 4 and 9: $\chi^2(61) = 93.28$, Bollen–Stine bootstrap $p < 0.98$; CFI = 0.95, RMSEA = 0.07 (90%-CI 0.04–0.10), and AIC = 153.28. Its structure, standardized regression weights and covariances can be found in Fig. 2. We compared the two nested models and found a significantly worse fit for the original model: $\Delta\chi^2(3) = 104.29$, $p < 0.001$. Table 2 shows estimates and confidence intervals for its standardized regression weights as well as covariances of the subscales.

3.5. Convergent and discriminant validity (sample V)

Table 3 shows correlations of the CAINS and its subscales CAINS-MAP and -EXP with supposed related and unrelated domains. The CAINS-MAP was found to be strongly associated with functional outcome and depression and further with neurocognition, positive symptoms and social cognition. CAINS-EXP was independent from positive and extrapyramidal symptoms, depression and neurocognition.

4. Discussion

To further establish the two factors of negative symptoms, firstly the instruments that try to measure them have to have adequate reliability. Secondly, distinct profiles should be found and replicated for structure

Table 2
Estimate and confidence intervals for the final model's standardized regression weights and covariances.

Estimates&Confidence Intervals for the Final Model's Standardized Regression Weights&Covariances

Parameters		Estimates (CIs)	p
Standardized Regression Weights			
CAINS-MAP	item 1	0.33 (0.08 - 0.55)	0.011
	item 2	0.52 (0.30 - 0.67)	0.002
	item 3	0.58 (0.37 - 0.72)	0.002
	item 4	0.53 (0.30 - 0.68)	0.001
	item 5	0.39 (0.18 - 0.55)	0.001
	item 6	0.24 (-0.03 - 0.45)	0.082
	item 7	0.85 (0.77 - 0.91)	0.001
	item 8	0.89 (0.80 - 0.95)	0.002
	item 9	0.74 (0.59 - 0.84)	0.001
CAINS-EXP	item 10	0.81 (0.71 - 0.88)	0.001
	item 11	0.92 (0.83 - 0.98)	0.001
	item 12	0.72 (0.58 - 0.83)	0.001
	item 13	0.69 (0.55 - 0.80)	0.001
Covariances			
CAINS-MAP - CAINS-EXP		0.37 (0.19 - 0.56)	0.001
item 5 - item 6		0.74 (0.47 - 1.07)	<0.001
item 3 - item 4		0.35 (0.23 - 0.53)	<0.001
item 4 - item 9		0.23 (0.14 - 0.33)	0.001

Note. CIs = confidence intervals; CAINS-MAP = "motivation and pleasure" subscale; CAINS-EXP = "expression" subscale, item 1–item 13 = CAINS items.

as well as content. Summarizing the results, we found good internal consistency for the CAINS and its subscales. Interrater agreement was good for all scales. We confirmed the CAINS' two-factorial structure with minor adjustments for the "motivation and pleasure" subscale. The two subscales showed distinct patterns of association with related symptoms and domains.

4.1. Test-retest reliability

This is the first evaluation of the test-retest reliability of the German translation of the CAINS, which was in a medium range for the CAINS ($r = 0.71$) and its "expression" subscale ($r = 0.74$) and low for the "motivation and pleasure" subscale ($r = 0.57$). The CAINS' and CAINS-EXP's stability is in line with the original validation study (Kring et al. (2013), $n = 162$, two-week interval, $r = 0.69$, for CAINS-EXP and CAINS-MAP), and two further studies (Blanchard et al. (2017), $n = 447$, three-month interval, CAINS-EXP: $r = 0.75$, CAINS-MAP: $r = 0.80$; Xie et al. (2018), $n = 23$, two-week interval, $r = 0.68$ for CAINS, 0.63 for CAINS-EXP and 0.68 for CAINS-MAP). We expected higher test-retest reliability for the CAINS-MAP considering the short period of time between the assessments and the widely reported (moderate) stability of negative symptoms (e.g. Ventura et al., 2015). We found no blatant differences between the other studies' and our samples that could explain the differences in the CAINS-MAP's test-retest reliability. However, our test-retest reliability sample R is small and mainly consists of in-patients (although most were in the stabilization phase). Thus, we might have measured a nonnegligible amount of possibly less stable secondary negative symptoms. Consistent with our results, both Galderisi et al. (2013) and Kelley et al. (2008) found diminished expression to be more persistent across time; amotivation seems to be more sensitive to changes. The CAINS-MAP's focus on inner experience as opposed to observable behavior could entail a higher variability of answers when retesting. We think for the CAINS, further evaluation of mainly the "motivation and pleasure" subscale's stability is needed; overall, the stability of all different aspects of negative symptoms (deficit syndrome, persistent negative syndrome, primary and secondary negative symptoms as well as the two (possibly five) factors of negative symptoms) seems to be worth looking into.

4.2. Confirmatory factor analysis

Since this is a smaller sample, we did not compare different factorial models. There is a recent comprehensive factor-analysis on the Brief Negative Symptom Scale (BNSS, Strauss et al. (2012)) that found the best fit for a hierarchical 5-factor model with two second-order factors reflecting "expression" and "amotivation" as well as 5 first-order factors reflecting blunted affect, alogia, anhedonia, avolition, and asociality which seems worth exploring in further studies (Ahmed et al., 2018). However, we confirmed previous exploratory analyses of the CAINS

Table 3
Correlation of the CAINS,its 'motivation and pleasure' subscales, and relavant domains.

Correlations of the CAINS, its 'Motivation and Pleasure' and 'Expression' Subscales, and Relevant Domains

Domain	Measuring Instrument	CAINS		CAINS-MAP		CAINS-EXP	
Negative Symptoms	PANSS Marder Negative	r = 0.53***,	p<0.001	r = 0.40**,	p=0.008	r_S= 0.49***,	p<0.001
	Anticipatory Pleasure (TEPS-ANT)	r = -0.28,	p=0.080	r = -0.30*,	p=0.040	r_S= -0.11,	p=1
Functional Outcome	Psychosocial Functioning (PSP)	r_S= -0.56***,	p<0.001	r_S= -0.57***,	p<0.001	r_S= -0.26,	p=0.256
	Level of Activity (Time Budget Measure)	r_S= -0.27,	p=0.080	r_S= -0.30*,	p=0.040	r_S= -0.06,	p=1
	Social Competence (SSPA)	r_S= -0.61***,	p<0.001	r_S= -0.58***,	p<0.001	r_S= -0.40**,	p=0.009
Social Cognition	Appreciation by Others (FSKN-WA)	r = -0.25,	p=0.080	r = -0.32*,	p=0.036	r_S= 0.00,	p=1
Neurocognition	Index of VLMT, Digit Span, TMT, Tower of London	r = -0.34*,	p=0.042	r = -0.32*,	p=0.040	r_S= -0.20,	p=0.763
Positive Symptoms	PANSS Positive Symptom Scale	r_S= 0.29,	p=0.070	r_S= 0.33*,	p=0.036	r_S= 0.10,	p=1
Depression	Calgary Depression Scale for Schizophrenia (CDSS)	r = 0.38**,	p=0.007	r_S= 0.40**,	p=0.008	r_S= 0.19,	p=0.763
EPS	Modified Simpson Angus Rating Scale (MSAS)	r_S= 0.12,	p=0.312	r_S= 0.10,	p=0.400	r_S= 0.05,	p=1

Note. EPS = extrapyramidal symptoms; r = Pearson correlation; r_S = Spearman correlation; p-values Holm–Bonferroni-adjusted for each scale/subscale (hence $p = 1$ in some cases); * = $p < 0.05$, ** = $p < 0.01$, *** = $p < 0.001$.

that overwhelmingly yielded two factors. We consider the CFA's final model an overall well fitting and parsimonious model that confirms the two-factorial structure of the CAINS. There were no cross-loadings of CAINS-MAP items to the CAINS-EXP subscale and vice versa. Hence, the individual items are specific for their respective scales. The loadings of items 10–13 on the "expression" subscale are both high and reliable. However, there is some concern with some items of the "motivation and pleasure" subscale. The lower bound of the item loadings' confidence intervals is below 0.3 for items 1, 5 and 6. These items tap motivation for family relationships as well as motivation for and expectation of pleasure at work and/or school, respectively. The original validation study's exploratory factor analysis found factor loadings of 0.33 for item 1 (there: 1. social: family relationships), of 0.24 for item 5 (there: 6. vocational: motivation) and of 0.39 for item 6 (there 8. vocational: expected pleasure). Those three items were in the bottom four of factor loadings (Kring et al., 2013). Substantial conceptual overlap between some CAINS-MAP items was not unexpected. Relevant overlap was found for items 5 and 6 which inquire motivation for and expectation of pleasure at work and/or school, for items 3 and 4 which appraise past-week and expected pleasure concerning social activities as well as for items 4 and 9 which assess expected pleasure in regard to social and leisure activities, respectively. We consider all CAINS item contents important, however, to further establish the relevance and validity of the specific items of the "amotivation" factor, further analysis of a larger sample would be interesting. A first step could be exploratory factor analysis to determine, whether Ahmed et al. (2018)'s hierarchical 5-factorial model of the BNSS also holds true for the CAINS. It should be noted, however, that partly the two-factorial solution could be explained by common-method variance: CAINS-MAP mainly assesses verbal report of experience; CAINS-EXP is a rating of within-interview behavior.

4.3. Validity assessment

With the two-factorial structure of the CAINS adequately established, a nuanced discussion of the validity assessment is warranted. Overall, there seem to be distinct correlational profiles for the two subscales; this further substantiates them measuring different aspects of negative symptoms. The "expression" subscale might be less impacted by secondary negative symptoms (Farreny et al., 2018). The "motivation and pleasure" scale has more positive associations with related domains than the "expression" subscale. This mirrors the more advanced theoretical models for the "amotivation" subdomain (Kaiser et al., 2017). Both subscales correlate well with the PANSS Marder Negative score and moderately (CAINS-EXP) to strongly (CAINS-MAP) with social competence. For the "expression" domain, Marder and Galderisi (2017) suggested that abnormal functioning of the mirror neuron system could explain deficits of (1) social perception and (2) motor activity which might affect social competence. Fittingly, Riehle et al. (2018) found significantly fewer positive facial expressions in subjects with schizophrenia with predominantly expressive deficits than in those without as well as in controls; the former were also rated significantly lower on social performance skills assessed by role-play. Furthermore, it is highly likely for assessments derived from behavioral observation—i.e. both in interview and role-play—to overlap. For the "motivation and pleasure" domain, poor social cognition seems linked to asociality/social withdrawal, although the direction of that link is unclear up to now (e.g. Marder and Galderisi, 2017). Blanchard et al. (2015) also found strong associations for CAINS-MAP symptoms with performance-based affiliative skills (i.e. responding to a video) as well as role-play; this could point to an influence of social amotivation. We think those aspects could partially explain the observed association of social competence and both CAINS-MAP and CAINS-EXP. The self assessed anticipatory anhedonia (TEPS-ANT) correlates moderately with the CAINS-MAP. Anticipatory anhedonia was consistently found to be associated with motivational processes specific to the "amotivation" domain of negative symptoms (Gard et al., 2007). Functional outcome consistently is linked more strongly to amotivation than expressive deficits (Marder and Galderisi, 2017); we also found this in our data. The CAINS' "motivation and pleasure" subscale has a significant but smaller than expected correlation with the very meticulously measured level of activity (Time Budget Measure). This probably is due to the CAINS-MAP focusing on inner experience as opposed to mainly assessing behavior. Experience sampling depends on the symptoms being accessible, identifiable and reportable for the patient. When using more behavior-based assessments, however, confounding symptoms and outcome is a significant issue. Correctly identifying the origin of symptoms (primary, secondary) is difficult for assessments based on self-report as well as performance-based measures. Assessing "true amotivation" will probably remain difficult and will need assessment from more than one perspective (i.e. to rule out confounding aspects). Maybe a compound score of performance assessment, experience sampling, and self-report could achieve this aim.

In qualification it should be noted, that the validity sample V consisted of outpatients with relevant negative symptoms, whereas depressive symptoms had to be below "severe". Also, our sample showed a very low rate of extrapyramidal symptoms. The subjects often were assessed shortly after hospital discharge; this is a phase of illness associated with less positive and more depressive symptoms (Peralta et al., 2000). Overall, there are high comorbidity rates for schizophrenia and unipolar depression across stage and state of illness (Upthegrove et al., 2017). Even though we excluded severely depressed patients, the "motivation and pleasure" subscale is weakly linked to positive and depressive symptoms. The latter could be due to conceptual overlap of depressive and negative symptoms. Mainly the "avolition" factor entails symptoms that are also main symptoms of depression: loss of interest, anhedonia, and reduced energy. For schizophrenia patients and the CAINS or its "motivation and pleasure" subscale's self rating MAP-SR, some researchers found no significant associations with measures of depression (Engel et al., 2014; Kring et al., 2013; Llerena et al., 2013) while others found a weak to moderate correlations (Engel and Lincoln, 2016; Park et al., 2012). Shared method variance could also play a part in the overlap of mainly "amotivation" and positive and depressive symptoms.

We found no significant association of our global index of neurocognition and CAINS-EXP and a moderate correlation for the CAINS-MAP. Marder's 2017 review reports amotivation to be linked to deficits in abstraction/flexibility and executive functioning—deficits in executive functions probably impair action planning and lead to apathy. Strauss et al. (2015) found low cognitive effort to be associated with severe negative symptoms; both predicted global neurocognitive impairment. However, diminished expression usually correlates with impaired overall cognitive performance (Hartmann-Riemer et al., 2015). Cohen et al. (2014) proposed a cognitive resources limitation model with speech reduction as reaction to cognitive overload, hence a specific relationship of alogia and verbal fluency. Overall, our neurocognitive index seems too global to clarify the complex association between cognitive dysfunction and the two factors of negative symptoms.

4.4. Conclusion

To relevantly improve negative symptoms, we need to (1) increase our understanding of the symptom complex, (2) develop specific treatment strategies aiming at different aspects of negative symptoms, and (3) precisely assess these interventions. We consider the CAINS to be overall well suited to promote these purposes. We would recommend against solely using the composite CAINS score, but to take into account both CAINS subscales separately. Researchers interested in utilizing the results of our CFA more specifically could use the following formulas to compute the CAINS subscales: CAINS-MAP = (0.33 × item 1 + 0.51 × item 2 + 0.58 × item 3 + 0.53 × item 4 + 0.39 × item 5 + 0 0.24 × item 6 + 0.85 × item 7 + 0.89 × item 8 + 0.74 × item

9) ÷ 9; CAINS-EXP = (0.81 × item 10 + 0.92 × item 11 + 0.72 × item 12 + 0.69 × item 13) ÷ 4. Since there are only four CAINS-EXP items to nine CAINS-MAP items, the motivation aspect is over-represented in the total score. Moreover, we think the CAINS-MAP subscale might benefit from more research clarifying the individual items' specific subdomains, importance for the subscale, and stability as well as discriminant validity with depression. Overall, the two subscales clearly and mostly reliably measure distinct aspects of negative symptoms; we think the research on negative symptoms could benefit from consistently taking note of both.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2018.12.043.

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