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The Relationship between Neurocognition and Social Cognition with Functional Outcomes in Schizophrenia: A Meta-Analysis

Anne-Kathrin J. Fett[a,c,d], Wolfgang Viechtbauer[b], Maria-de-Gracia Dominguez[a], David L. Penn[e], Jim van Os[a,d], Lydia Krabbendam[c,d]

[a]Department of Psychiatry and Neuropsychology, School of Mental Health and Neuroscience, Maastricht University, Maastricht, The Netherlands; [b]Department of Methodology and Statistics, School for Public Health and Primary Care, Maastricht University, Maastricht, The Netherlands; [c]Centre for Brain & Learning, Faculty of Psychology and Education, VU University Amsterdam, Amsterdam, The Netherlands; [d]Department of Psychosis Studies, Institute of Psychiatry, London, United Kingdom; [e]Department of Psychology, University of North Carolina Chapel Hill, United States.

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ABSTRACT

The current systematic review and meta-analysis provides an extended and comprehensive overview of the associations between neurocognitive and social cognitive functioning and different types of functional outcome. Literature searches were conducted in MEDLINE and PsycINFO and reference lists from identified articles to retrieve relevant studies on cross-sectional associations between neurocognition, social cognition and functional outcome in individuals with non-affective psychosis. Of 285 studies identified, 52 studies comprising 2692 subjects met all inclusion criteria. Pearson correlations between cognition and outcome, demographic data, sample sizes and potential moderator variables were extracted. Forty-eight independent meta-analyses, on associations between 12 a priori identified neurocognitive and social cognitive domains and 4 domains of functional outcome yielded a number of 25 significant mean correlations. Overall, social cognition was more strongly associated with community functioning than neurocognition, with the strongest associations being between theory of mind and functional outcomes. However, as three-quarters of variance in outcome were left unexplained, cognitive remediation approaches need to be combined with therapies targeting other factors impacting on outcome.

Keywords: Schizophrenia | Psychosis | Functional Outcome | Community Functioning | Quality of Life | Neurocognition | Social Cognition

INTRODUCTION

Eight separable domains of cognitive impairment have been identified for schizophrenia according to the NIMH-Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) consensus [1]. Seven of these (processing speed, attention/vigilance, working memory, verbal learning and memory, visual learning and memory, reasoning and problem solving and verbal comprehension) belong to the domain of neurocognitive (NC) functioning. Social cognition (SC), referred to as the mental operations underlying social behaviour, such as the interpretation of another person's intentions or emotions was identified as an additional domain. SC is a multi-dimensional construct that comprises functions such as: 1) emotional processing (EP); 2) social perception and knowledge (SP); 3) theory of mind (ToM) and 4) attributional bias (AS) [2-5]. Obviously, processing socially relevant information also relies on NC (e.g. attention or memory); yet research shows that NC and SC are largely distinct domains [6-9].

Besides cognitive impairment, schizophrenia patients also experience severe deficiencies in their everyday functioning that are manifest within various areas, such as independent living, the instantiation and maintenance of interpersonal relationships or vocational functioning and leisure [4-5, 10-12]. Finding potentially treatable determinants of functional outcome is one of the principal goals in schizophrenia research [13-16]. Being largely independent of other symptoms, present before the onset of illness and relatively stable over time, cognitive deficits fulfil the criteria of a potential treatment target [5, 13, 17-20]. Numerous studies corroborated that both SC and NC are related to everyday functioning in schizophrenia [11, 14, 21-23]. In fact, research has shown that NC may explain between 20% and 60% of variance in functional outcome and that it may be a better predictor than other characteristic symptoms of the illness [24-25]. Three reviews have been conducted to identify whether specific NC deficits restrict the functioning of schizophrenia patients. A review of 16 studies indicated that verbal memory, executive functioning, and vigilance may be separately associated with outcome in terms of community functioning/daily activities, instrumental skills, social problem solving and psychosocial skill acquisition [23]. This finding was confirmed by a systematic review of 37 studies that investigated associations between four cognitive domains and a pooled functional outcome measure. Specifically, mean correlations ranged from 0.20 for vigilance, 0.23 for executive functioning and 0.29 for secondary verbal memory, to 0.40 for immediate verbal memory [24]. A third review comprising 18 longitudinal studies showed that overall NC performance is

also related to functional outcome more than 6 months later [26]. This evidence established the potential of NC as treatment target.

Despite earlier evidence of being a determinant of daily functioning in schizophrenia [27-28] SC only came to the focus of attention more recently [3, 29]. A review of 22 studies on SC and functional outcome established associations between EP, SP and ToM and community functioning, social behaviour in the milieu, social problem solving and social skill [12]. Individual effect sizes ranged from zero to large. The overall magnitude of the associations, however, appeared small to modest. It has been suggested that SC functions as a mediator between NC and outcome [30-36]. Still, SC also appears to be a valid predictor by itself, since it explains additional variance in outcome that cannot be accounted for by NC [30, 37-40]. Other findings showed that SC may even exceed the value of NC and symptoms in explaining variance in outcome [41].

The issue of differential associations between SC and NC and functional outcome is important in order to identify specific cognitive domains as possible targets for treatment intervention [13]. The current systematic review and meta-analysis was conducted to provide an extended and comprehensive overview of the specific SC-outcome and NC-outcome associations in non-affective psychosis. We examined associations between 12 NC and SC domains and 4 domains of functional outcome and investigated differences between the associations of SC and NC and community functioning. To account for possible confounding illness chronicity, inpatient status, age and gender were taken into account in the analysis.

METHOD

Data Sources and Literature Search

Articles were identified through searches in the databases MEDLINE and PsychINFO that covered the period from January 1977 to August 2009. The keywords were *psychosis, schizophrenia, or schizoaffective disorder* combined with *functional outcome, independent living skills, skills of daily living, community functioning, social functioning, work functioning, occupational functioning, vocational functioning, social skill, quality of life, community behaviour, social behaviour, life satisfaction, social adjustment, social dysfunction or employment and neuropsych** or *neurocog** for NC and *SP, emotional perception, affect perception, emotional recognition, attribution, AS, ToM, mentalising/mentalizing, social cognition, prosody, social knowledge, mind reading, social cue, or social judgment* for SC. In addition, relevant articles were examined for

undetected references [12, 23-24, 26, 42-43]. The search yielded 285 potentially eligible articles that were inspected for inclusion.

Inclusion and Exclusion Criteria

The following criteria guided the inclusion of studies: a) the sample consisted of patients with a diagnosis of non-affective psychosis according to an established criterion-based diagnostic system, i.e. the *Diagnostic and Statistical Manual of Mental Disorder* [44-47], the research diagnostic criteria [48], the Schedule for Affective Disorders and Schizophrenia [49], and the *International Classification of Diseases* [50-51]. The study: b) included participants aged 18-66 years; c) used recognized cognitive tasks and outcome measures that could be classified into the current domains; d) (or authors) provided all correlations between cognitive performance and outcome; e) reported cross-sectional relationships. Studies that included patients with special characteristics that could affect cognitive performance (e.g. geriatric patients or patients with childhood psychosis) were excluded.

Neurocognitive Domains

The NC domains included the seven cognitive factors identified by the MATRICS committee: 1) reasoning & problem solving; 2) processing speed; 3) attention & vigilance; 4) working memory; 5) verbal learning & memory; 6) visual learning & memory; 7) verbal comprehension [16, 29]. Although verbal fluency most commonly loads on the factor processing speed it seems to be conceptually different from the other tasks that were used to measure processing speed. We therefore decided to include verbal fluency as an independent eighth factor [17, 29]. An often reported neurocognitive composite factor was incorporated as a ninth factor [52]. Accordingly, suitable NC tests were grouped into nine domains (Table 1).

Social Cognitive Domains

The classification of the SC domains was based on the recent MATRICS recommendations [4, 53]. Along these lines we grouped the tests into the most common cognitive domains in the field; 1) *theory of mind* (ToM), 2) *emotional perception & processing* (EP); and 3) *social perception & knowledge* (SP; Table 1). Only one study investigated the attributional style-outcome association [54]. Consequently, this domain could not be reviewed.

Domains of Functional Outcome

The included studies investigated multiple aspects of outcome. Some definitions, such as work functioning or living independently are rather direct indicators of real world functioning. Skill or competence based outcomes, such as role play performance, are more distal from how a person performs in reality but possibly more closely related to performance on NC and SC tests. To account for this variety we classified outcome into four previously described domains [12, 23-24, 26, 55].

1. C*ommunity functioning* encompasses a variety of behaviours and activities, such as independent living skills and social or work functioning that are direct indicators of everyday functioning. Most measures were rated by an interviewer.
2. *Social behaviour in the milieu* mostly refers to observed behaviour and comprises staff-ratings of the participants' behaviour in different treatment or (in)patient settings.
3. *Social problem solving* refers to the ability to recognize everyday social problems to generate respective solutions. The outcome is based on observed behaviour.
4. *Social skills* consists of behaviour based tests that assess interactional skills (e.g. eye contact, voice volume) in role-play tasks.

Social problem solving and social skills can be considered as intermediate variables rather than direct measures of functional outcome. Yet, research rarely reported intercorrelations with other outcome domains, which would have been required to test mediation or moderation. For that reason, we treated the two factors in line with the other outcome domains. The outcome domains, with their respective tests and parameters, are listed in Table 2.

Table 1 | Cognitive Domains, Tests and Parameters

Cognitive domain	Test	Parameters
1. Reasoning & problem solving (reported by 25 studies)	Block design [56]	Number of correctly chosen patterns
	COGLAB WCST [57]	Number of preservative errors
	Nelson's Modified Card Sorting Test [58]	Number of categories completed
	Penn Conditional Exclusion Test [59]	(pooled if both were reported)
	Wisconsin Card Sorting Test [60]	
	Standard Progressive Matrices [61]	Number of completed designs
	Tower of London (ToL), Tower of Hanoi	Number of steps to complete
	Behavioral assessment of the Dysexecutive Syndrome (BADS)[62]	Number of errors, time
	The Rule Shift Cards Test	Number of steps completed
	The Action Program Test	
	Key search test	Search strategy, time
	The Temporal Judgment Task	Number of correct time estimations
	Zoo map test	Number of errors/places visited, time
	Modified Six Elements Tests	Number of tasks attempted/rule breaks, time
2. Processing speed (reported by 14 studies)	COGLAB RT [57]	Reaction time
	Digit Symbol Substitution Test [63]	Number of symbols correctly copied
	Letter cancellation [64-65]	Number of correct cancellations
	Trail Making Test A and B [66]	Time to completion
3. Attention & vigilance (reported by 16 studies)	Continuous Performance Test (CPT)[67] and its variations	Number or percentage of omissions
	Degraded Stimulus-CPT [68]	Number or percentage of commissions
	Penn-CPT [69]	Efficiency (true positive responses/ average reaction time)
	Early visual processing masking procedure [70]	Correct target location/identification
	Span of apprehension [71]	Correct target identification and localization
	Test of Everyday Attention [72]	Number of correct counts
		Number of correct counts/found book entries
		Number of correct while doing both tasks
4. Working memory (reported by 11 studies)	Digit Span (DS) backward[63]	Number of digits recalled
	DS forward [63]	
	DS Distractibility Test [73]	
	Brief Assessment of Cognition in Schizophrenia (BACS) [74] digit sequencing	

Cognitive domain	Test	Parameters
5. Verbal learning & memory (reported by 26 studies)	California Verbal Learning Test [75]	Number of correct responses on either immediate or delayed recall
	Hopkins Verbal Learning Test [76]	
	Paired-Associate Learning subtest	
	Rey Auditory Verbal Learning Test [77]	
	Story recall	
	Logical Memory subtest Wechsler Memory Scale Revised [78]	
	Word List Learning Test (WLT) [79]	
6. Visual learning & memory (reported by 11 studies)	Benton Facial Recognition Test (BFRT)[80]	Number of items correct on either immediate or delayed recall
	Brief Visual Memory Test [81]	
	Rey–Osterrieth Complex Figure Test [82]	Number of figures correctly drawn
	WMS–R visual memory [78]	
7. Verbal comprehension (reported by 8 studies)	Multiple choice verbal comprehension test [83]	% correct words recognized
	Vocabulary/ information subtests of the WAIS [63]	Number of correct words
	Wide Range Achievement Test Reading Scale [84]	
8. Verbal fluency (reported by 9 studies)	BACS Category Instances Test	Either words from a certain category or words beginning with a certain letter
	Controlled Word Association Test (COWAT)[85]	
	Greek verbal fluency [86]	
	Letter and semantic fluency tests	
9. Overall cognition (reported by 11 studies)	COGTEST [87]	CPT, spatial WM, DS, Digit sequencing, nogo/go, set shifting, WLT, BFRT, DSST, target detection
	BACS [88]	WLT, DS, Token Motor Task, Category Instances Test, COWAT, ToL, DSST
	BADS [62]	Rule shift cards test, action program test, key search task, temporal judgment task, zoo map test, modified six elements test
	Groningen Intelligence Test [89]	Spatial abilities, arithmetic, verbal knowledge, verbal logical reasoning, and word fluency
	Shipley Institute of Living Scale [90]	Vocabulary and abstract pattern recognition
	More than two of the previously cognitive tests combined into one factor	

Cognitive domain	Test	Parameters
10. Theory of mind (reported by 5 studies)	Hinting task [91]	Number of correct identified hints
	Tom Picture Stories [92]	Number of correct sequenced cartoon story pictures, correct identified mental states
	Tom Vignettes [93]	Number of correct identified belief states
	Faux Pas Task [94]	Number of correct identified faux pas and empathy
	Eyes Test [95]	Number of correct chosen emotions fitting eye expression
	Implicit Mentalizing Task [96]	Number of mental and emotional state references/number speech phrases
11. Emotion perception & processing (reported by 14 studies)	Bell-Lysaker Emotion Recognition Test [97]	Number of correct identified emotion in faces
	Facial Affect Recognition [98-99]	% of correct identified emotion in faces
	Facial Emotion Identification Test [100]	
	Facial Expression of Emotion [101]	
	Penn Emotion Acuity Test [102]	
	Pictures of Facial Affect [99]	
	Videotape Affect Perception Test [103]	
	Emotional Differentiation Task [104]	Number of correct distinctions between emotions in faces/ voices
	Facial Emotion Discrimination Test	
	Voice Emotion Discrimination Test	
	Mayer-Salovey-Caruso Emotional Intelligence Test [105]	Number of correct identified emotions
		Number of correct evaluated usefulness of emotions in particular situations
		Number of correct identified emotions in a given social situation
		Number of correct identified effectiveness of a strategy to cope with emotions
	Prosody Task [106]	Number of correct identified emotions in voices
	Vocal Affect Recognition [107-108]	
	Voice Emotion Identification [100]	

Cognitive domain	Test	Parameters
12. Social perception & knowledge (reported by 8 studies)	Situational Feature Recognition Test [109]	Social cue sensitivity A' (hits/false alarms in determining features that fit certain situations)
		Number of correct identified situational features
	Schema Component Sequencing Task [110]	Number of correct juxtaposed/ordered cards that describe social situations
	Social Cue Recognition Task [111]	Number of correct identified intentions/goals of people in vignettes
	Social Cue Recognition Task-revised [112]	
	Social Stimuli Sequencing Task [113]	Number of errors
		Number of correct adjoining cards
	WAIS comprehension [78]	Number of correct answers on social problem solving and practical reasoning
	Half profile of Nonverbal Sensitivity [114]	% of scenes correctly labelled social cues in 110 videotaped scenes

Table 2 | Domains of Functional Outcome, Outcome Measures and Parameters

Domains of Functional Outcome	Outcome Measure	Parameters
Community functioning (reported by 33 studies)	Clinical Global Impression of Cognition in Schizophrenia [115]	Activities of daily living (ADL): Instrumental functioning: hygiene, hobbies, household chores. Social functioning: e.g. socializing with peers and family, community activities, dating.
	Community Adjustment form [116]	Living Situation, vocational, social functioning, activities of daily living, family involvement, medication usage.
	Disability assessment scale [117]	Personal care, family functioning, occupational functioning, and social functioning.
	Global assessment scale [118]	Based on CAF interview.
	Global assessment of functioning [44]	Global social functioning.
	Groningen Social Disability Scale [119]	Friendship, housekeeping, citizenship, self-care, leisure activities, occupation/study.
	Indian Disability Evaluation Scale [120]	Self care interpersonal activities, social relationships, communication, understanding, occupation.
	Independent Living Scales Inventory [121]	Personal management, hygiene, grooming, clothing, basic skills, interpersonal skills, home maintenance, money management, cooking, resource utilization, occupational skills, medication management.
	Multnomah Community Ability Scale [122]	Adjustment to living and social competence.
	Lehman work & productive activity scale [123]	Work, school, volunteer work, and care of living.
	Life Assessment for the Mentally Ill [124]	Daily living, interpersonal relations, work skills, endurance/stability, self-recognition.
	Life Skills Profile [125]	Communication, inter- and non-personal social behaviour, personal autonomy, self care.
	Performance Potential Inventory [126]	Functional disability.
	Physical, cognitive, affective, social, economic, ego functions [127]	Social activity, speech disturbance, self-care, community skills.
	Quality of Life Self Assessment Inventory [128]	Housing, environment, knowledge & education, contacts, dependence, inner experiences, mental & physical health, leisure, work, religion.
	Quality of Life Interview [129]	Performance & satisfaction with circumstances, resources, interpersonal relations.
	Role Functioning Scale [130]	Work, social functioning/ relationships, independent living/self care.
	Rehabilitation Evaluation Hall and Baker [131]	Social activity, speech disturbance, speech skills, self-care skills, community skills.
	Social Functioning Scale [132]	Social engagement, interpersonal communication, social activities, competence, frequency of activities of daily living, recreational activities, occupational activities.
	UCSD performance based skills assessment [133]	Household chores, communication, finance, transportation, planning recreational activities.

Domains of Functional Outcome	Outcome Measure	Parameters
Social behaviour in the milieu (reported by 9 studies)	Nurse's Observation Scale for Inpatient Evaluation [134]	Social competence, social interest, neatness, irritability, psychoticism, psychomotor retardation.
	Social Adjustment Scale [135]	Social behaviour: frequency of leisure, social, peer, romantic contact, activity in contacts.
	Social Dysfunction index [136]	Public self, independent living, occupational functioning, family relationships, important relationships other than family, community, leisure/recreation, acceptance/adherence to health regimes, communication, locus of control.
	Social Behavior Schedule [137]	Communication skills, social mixing, and hostile interactions.
	Work Personality Profile [138]	Work requirements: e.g. ability to relate to co-workers, personal presentation: e.g. how react to authority figures.
Social problem solving (reported by 7 studies)	Assessment of Interpersonal Problem Solving Skills test [139]	Interview & role play test, videotaped interpersonal scenes, problem identification (receiving), generation of solutions (processing), enacting solutions (sending).
	Response Evaluation Test [140]	Discriminate effective/ineffective social problem solving behaviour.
	Social Problem Solving Assessment [141]	Development of cognitive set, problem definition, generating alternatives, decision making, verification.
Social skills (reported by 9 studies)	Conversation Probe Role Play Test [142]	Rated: clarity, fluency, affect, gaze, involvement, asking questions. 3 min conversation with a stranger
	Role Play test [143]	Rated: eye contact, shaking, long pauses, rocking, fidgeting, restlessness, facial twitches, speed fluency. 3 minute interaction with stranger.
	Social Skills Performance Assessment [144]	Rated: fluency, clarity, focus, affect, grooming, social appropriateness, negotiation ability, persistence, overall conversation/argument. Role play.

Statistical Analysis

Results were quantified in terms of correlations. In some cases higher scores reflected worse cognitive performance or outcome, in other cases lower scores reflected worse cognitive performance or outcome. Therefore all correlations were recoded so that positive correlations indicated associations between better cognitive performance and better functional outcome. If a study reported several cognition-outcome correlations within the same domains correlations were pooled. All correlations were transformed with Fisher's r-to-z transformation before the meta-analytic methods were applied. Results from the meta-analysis were back-transformed into raw correlation metric whenever possible. Data extraction and calculations of effect sizes were performed independently by two authors (AKF & MdGD). All analyses were carried out with the 'metafor' package (version 0.5-7) in the statistical software R (version 2.10.0). First, we conducted 48 individual meta-analyses on the correlations between all cognitive and outcome domains pairs. Analyses based on three or more correlations were considered. We used a random-effects model to account for heterogeneity and to obtain unconditional inferences about the distribution of population correlations [145-146]. The amount of heterogeneity in the true correlations was estimated with restricted maximum-likelihood estimation. For each of these individual meta-analyses, we report *k* (number of studies), $\hat{\mu}_\rho$ (estimated average correlation in the population distribution), *CI* (95% confidence interval for μ_p); *p* (p-value for the test *H*0: $\mu_p = 0$), and the results from the Q-test for heterogeneity. Additional indices of the amount of variability in the correlations were $\hat{\tau}^2$ (estimated amount of heterogeneity in the true (transformed) correlations), H^2 (total variability in the observed (transformed) correlation coefficients/within-study variance due to sampling error), and I^2 (percentage of the total variability in the observed (transformed) correlation coefficients due to heterogeneity). A value of I^2 equal to 0 suggests the absence of heterogeneity, in which case the random-effects model simplifies to a fixed-effects model. In that case, $\hat{\mu}_\rho = \hat{\rho}$, where $\hat{\rho}$ denotes the estimated true (homogeneous) correlation. We examined all meta-analyses and the correlations between all cognitive domains and the four functional outcome domains for publication bias with funnel plots and regression tests for funnel plot asymmetry [147]. Some samples contributed multiple correlations and dependencies were present. We did not model dependencies, as this would have required information on all intercorrelations between the cognitive dimensions. Consequently, the results of the funnel plot asymmetry tests for the four outcome domains have to be treated with some caution. Second, illness chronicity, inpatient status, age, and male gender

were taken into the analysis as moderators, as they may influence cognition-outcome associations [148-152]. We used a mixed-effects meta-regression model to examine their influence. Again, restricted maximum-likelihood estimation was used to estimate the amount of residual heterogeneity [146, 153]. Due to incomplete information on moderator values within some studies, each moderator was examined individually. Results are expressed in terms of the estimated regression coefficients (i.e. $\hat{\beta}$'s) indicating by how much the average correlation (in the transformed units) is estimated to change with a 1-unit increase in the moderators. For age and illness chronicity one unit corresponds to one year, for male gender and inpatient status one unit corresponds to one percentage point. The corresponding 95%CI for the true regression coefficient is given. Because the *r*-to-*z* transformation is nonlinear, one cannot easily back-transform the slope of the regression coefficient into the raw correlation metric. Third, we examined differences in the average correlations between the SC-community functioning and NC- community functioning associations. Several of the 33 studies that investigated community functioning examined correlations for the neurocognitive and social cognitive dimension. In order to account for dependencies between these correlations the covariance between the values was calculated [154]. All studies that investigated associations between community functioning and both SC and NC reported the required inter-correlations.

RESULTS

In total 285 articles were considered for inclusion. Of these, 233 were excluded because the study: a) examined longitudinal associations (12%); b) did not report correlations or associations between cognition and functional outcome (42%); c) reported non-parametric correlations (5%); d) only reported significant correlations/non-significant correlations could not be obtained (5%); e) reported cognitive or outcome measures that could not be classified into one of the current domains (9%); f) sample completely overlapped with another included sample (3%); g) included participants below 18 or above 66 years of age (8%); h) did not meet our criteria for diagnosis or included specific samples (e.g. geriatric patients; 2%). i) Finally, thirty-three studies could not be obtained, even after contacting the authors (14%). Fifty-two studies fulfilled all inclusion criteria. NC-outcome correlations were investigated by 48 studies. SC-outcome correlations were investigated by 21 studies, 17 of which also investigated NC and outcome. Table 3 shows the included studies along with sample sizes and characteristics.

Overlapping Samples

Studies that fulfilled the inclusion criteria were examined for overlapping samples. Authors of studies performed at the same departments or catchment areas were asked for information on sample overlap. Overlap was dealt with in three ways:

(a) In case of overlapping samples and cognition-outcome associations within the same domains, the studies with the smaller sample size were excluded. This was the case for seven studies [34, 38, 155-159].

(b) Studies with overlapping samples were included if cognition-outcome correlations were reported for different domains. This was the case for ten studies [27, 30-31, 142, 160-165].

(c) In case of two studies [166-167] with overlapping samples of equal size and identical cognition-outcome associations that were assessed by means of the same instruments a mean correlation of both studies was included.

Descriptive Information

The included studies comprised at least 2692 individuals. To avoid counting a subject twice, the smaller studies of those with unknown degree of overlap were excluded from this calculation (total n = 3030). The mean age was 36.26 years (range 25.9 to 47.5; SD = 5.02) and 68.7% of the sample was male. The average education was 12.3 years (range 9.1 to 14.3; SD = 1.14). Overall, 87% were diagnosed with schizophrenia, 12% with schizoaffective disorder and 1% had other diagnoses in the non-affective psychosis spectrum. Five articles included samples of patients with schizophrenia or schizoaffective disorder but did not report exact numbers [28, 32, 164, 168-169]. The sample included 76.1% outpatients. The average illness duration was 12.78 years (range 3.4 to 22.5, SD = 5.1). Other variables such as illness severity, medication dosage or type or the number of psychotic episodes may be relevant for the association between cognition and outcome but were reported by too few studies to be taken into account.

Meta-analyses of Correlations between Cognitive Domains and Outcome Domains

Results for the meta-analyses are shown in Table 4. The analyses revealed a stable pattern of significant small to large mean correlations between both cognitive domains and functional outcome ($\hat{\mu}_\rho$ = 0.16 to 0.48, all *p's* < 0.001 to 0.016), with only one non-significant association between attention & vigilance and social

behaviour in the milieu ($\hat{\mu}_\rho$ = 0.19, *p* = 0.21). The mean correlations were somewhat higher for SC than for NC. The squared maximum correlation indicates that SC may explain slightly more variance in outcome than NC (23.3% vs. 15.2%). The moderators had little influence on NC-outcome associations and did not influence SC-outcome associations at all.

Neurocognition and Outcome. The largest effect size was present for the association between verbal fluency and community functioning ($\hat{\mu}_\rho$ = 0.32). Social behaviour in the milieu had the strongest associations with verbal learning & memory ($\hat{\mu}_\rho$ = 0.32) and visual learning & memory ($\hat{\mu}_\rho$ = 0.30). The association between attention & vigilance and social behaviour in the milieu, although into the expected direction, was not significant. Social problem solving had the strongest relationship with reasoning & problem solving ($\hat{\mu}_\rho$ = 0.29). Social skills was also associated with reasoning & problem solving ($\hat{\mu}_\rho$ = 0.34), but showed the strongest association with attention & vigilance ($\hat{\mu}_\rho$ = 0.39). The various NC-outcome associations differed in strength ($\hat{\mu}_\rho$ = 0.16 to 0.39) but largely overlapping confidence intervals indicate that these differences may not reach statistical significance.

Social Cognition and Outcome. The largest mean correlation was present for the relationship between ToM and community functioning ($\hat{\mu}_\rho$ = 0.48). The association between EP and social behaviour in the milieu was $\hat{\mu}_\rho$ = 0.22. The meta-analysis for social skills and SP yielded an effect size of $\hat{\mu}_\rho$ = 0.24. No meta-analyses could be performed on social problem solving and any SC domain due to lack of data. The various SC-outcome associations differed in strength. Again, the largely overlapping confidence intervals indicate that these differences may not reach statistical significance in most cases.

Table 3 | Included Studies and Descriptive Variables

	Study	N	Inpatients %	Men %	Illness Chronicity Yrs	Age yrs	Education yrs	Schizophrenia %	Schizoaffective %	Other Non-affective Psychoses %	Cognitive Domain	Functional Outcome Domain
1	Addington et al. [31]	103		70.4		30.2		82	1	17	9, 12	CF, SPS
2	Addington et al. [161]	103		70.4		30.2		82	1	17	9, 11	CF
3	Aksaray et al. [170]	57	0	66.7	14.5	38.8	11.3	100	0	0	1	CF
4	Bellack et al. [171]	27	100	55.5	8.4	30.3	12.04	100	0	0	7, 4, 5	SPS, SS
5	Bora et al. [172]	50	0	66.0	9.13	30.6	11.48	100	0	0	7, 2 , 6, 10	CF
6	Bowen et al. [173]	30	100	80.0		36.0	12.94	100	0	0	3, 4	SPS
7	Bozikas et al. [174]	40	0	62.5	11.9	36.3	10.93	100	0	0	1, 2, 5, 6	CF
8	Brekke et al. [160]	40	0	62.5	11.8	33.2	12.5	57.5	42.5	0	1	CF
9	Brekke et al. [30]	139	0	69.1	13.9	38.2	11.9	100	0	0	9, 11	CF, SBM
10	Bruene [40]	23	100	78.0	12.3	38.8		100	0	0	1, 7, 10, 11	SBM
11	Cohen et al. [175]	28	100	85.7		33.6	12.21	100	0	0	1, 3, 5, 6, 7, 11	SBM, SS
12	Corrigan and Toomey [28]	26	100	69.0	14.3	33.8	12.2				1, 3, 4, 5, 12	SPS
13	Eack and Keshavan [176]	58		69.0	3.4	25.9		66	34	0	9	CF
14	Fiszdon et al. [149]	151	0	78.0	20.2	42.8	13.19	69.5	30.6	0	1, 2, 4, 5	CF
15	Hatashita Wong et al. [162]	44	0	51.0	18	36.0		60	40	0	1, 2, 3, 4, 5, 7, 8	SPS
16	Hooker and Park [177]	20	100	75.0	18.8	39.3	12.7	100	0	0	6, 11	SBM
17	Horton and Silverstein [178]	31	35.48	71.0		47.0		77.4	22.6	0	3, 6, 5	CF
18	Ihnen et al. [179]	26	0	57.6		33.4	12.1	100	0	0	11, 12	SS
19	Kee et al. [163]	50	0	62.0	10.2	34.4	14.02	100	0	0	11	CF
20	Keefe et al. [180]	56	91.6	83.9		35.1	11.67	100	0	0	1, 2, 4, 5, 8	CF
21	Krishnadas et al. [181]	25	0	64.0	11.3	40.2	9.08	100	0	0	2, 4, 5, 6	CF
22	Laes and Sponheim [182]	39	0	74.4		43.9	14.1	100	0	0	1, 3, 5, 8, 9	CF
23	Lysaker and Davis [183]	65	0	100	22.5	47.5	12.2	41	24	0	1, 5, 7	CF
24	Meyer and Kurtz [32]	53	0	72.0	12.2	35.1	12.9			0	1, 3, 5, 11	SS
25	Mueser et al. [184]	55	100	45.5		33.2	11.5	61.8	38.2	0	5, 6	SS
26	Mueser et al. [185]	38			15.2	38.0	12.1	73.7	26.3	0	5, 6, 7, 8	SS
27	Mueser et al. [27]	28	100	47.0	9.5	44.8	11.02	71.4	28.6	0	6, 11	SBM, SS
28	Nakagami et al. [164]	120	0	62.9	13.7	38.3	12.16				1, 3, 4, 5, 8	CF
29	Nemoto et al. [186]	40	0	75.0	5.6	30.2	14	100	0	0	1, 2, 4, 5, 8	CF
30	Penn et al. [142]	38	100	55.3		36.2		92.1	7.9	0	1, 2, 3	SS
31	Penn et al. [165]	27	100	66.7		33.7		81.5	18.5	0	1, 2, 3, 11, 12	SBM
32	Pijnenborg et al. [41]	46	6.53	73.9	7	27.4		100	0	0	2, 5, 9, 10, 11	CF
33	Pinkham and Penn [39]	49	0	57.1	10.4	33.2	14.3	71.4	24.5	4.1	2, 5, 7, 10, 11, 12	SS

Study	N	Inpatients %	Men %	Illness Chronicity Yrs	Age yrs	Education yrs	Schizophrenia %	Schizoaffective %	Other Non-affective Psychoses %	Cognitive Domain	Functional Outcome Domain
34 Poole et al. [187]	26	0	54.0	15	40.0	14	100	0	0	9	CF
35 Poole et al. [188]	40	0	77.5		41.0	13	90	10	0	11	CF
36 Revheim and Medalia [189]	162	53.7	62.3	14.1	37.2	11.1	67.3	32.7	0	5, 12	CF
37 Revheim et al. [190]	38	63	74.0	18.6	39.2	11.5	76	24	0	1, 3, 5, 6, 8	CF
38 Savilla et al. [191]	57	0	75.4		36.1		100	0	0	1, 2, 4, 5, 8	CF
39 Sergi et al. [35]	75	0	92.0	21.2	46.7	13	100	0	0	3, 12	CF
40 Smith et al. [166]	46	0	63.0	21	39.0		57	43	0	1, 3, 4, 5, 6	CF, SBM
41 Smith et al. [167]	46	0	59.0	19	37.0		61	39	0	4, 5	SBM
42 Stewart et al. [96]	18		94.5	8.6	35.7	11.5	83.3	11.1	5.6	10	CF
43 Stratta et at. [192]	20	0	85.0		35.2	11	100	0	0	1	CF
44 Tyson et al. [193]	36	13.8	86.2	13	38.0		100	0	0	1, 3	CF
45 Van Beilen et al. [169]	52	46	75.0	3.8	27.6					1, 3, 5	CF
46 Vaskinn et al. [33]	26	100	65.4	6.7	32.2	13	100	0	0	9, 11	SPS
47 Vauth et al. [36]	133	100	64.7	6.6	28.8		100	0	0	1, 2, 3, 5, 12	SBM
48 Velligan et al. [168]	339	0	66.2		41.2	10.9				9	SBM
49 Ventura et al. [87]	33	0	66.0		38.5	13.6	82	3	15	9	CF
50 Villalta Gil et al. [194]	113	0	68.0	18.9	41.6		100	0	0	5, 9	CF
51 Woonings et al. [195]	44	0	86.4	8.7	30.7		100	0	0	1, 3, 5	CF
52 Zanello et al. [196]	20	0	50.0	8.3	32.6		80	20	0	1, 2, 5, 6, 8	SPS

Note: Data for age, education, and illness chronicity are in mean years. Schizophrenia, Schizoaffective and other diagnoses in the non-affective psychosis spectrum are in percentage. Cognitive domains: (1) Reasoning & problem solving; (2) processing speed; (3) attention & vigilance; (4) working memory; (5) verbal learning & memory; (6) visual learning & memory; (7) verbal comprehension; (8) verbal fluency; (9) overall neurocognition; (10) theory of mind; (11) emotion perception & processing; (12) social perception & knowledge. Domains of functional outcome: CF = community functioning; SBM= social behaviour in the milieu; SPS = social problem solving; SS = social skills.

Table 4 | Four x Twelve Meta-analyses of Correlation Coefficients between Functional Outcome and Cognitive Performance

		Cognitive Domain											
Outcome domain		Reasoning & problem solving	Processing speed	Attention & vigilance	Working memory	Verbal learning & memory	Visual learning & memory	Verbal compre-hension	Verbal fluency	Overall cognition	Theory of mind	Emotion perception & processing	Social perception & knowledge
CF	k	16	8	9	7	17	6	-	6	9	3	5	3
	$\hat{\mu}_\rho$	**0.19**	**0.25**	**0.16**	**0.22**	**0.26**	**0.20**		**0.32**	**0.25**	**0.48**	**0.31**	**0.41**
	Q	16.19	12.36	13.15	18.89**	69.54**	2.90		20.01**	4.58	0.81	1.67	16.85**
	$\hat{\tau}^2$	0.002	0.02	0.01	0.04	0.04	0		0.05	0	0	0	0.06
	I^2%	9.95	42.94	38.17	69.30	71.65	0.00		75.90	0	0	0	86.59
	H^2	1.11	1.75	1.62	3.26	3.53	1		4.15	1	1	1	7.46
	CI lb	0.12	0.13	0.04	0.05	0.15	0.07		0.10	0.18		0.21	0.14
	CI ub	0.26	0.37	0.27	0.38	0.37	0.33		0.51	0.31	0.32 0.61	0.40	0.63
	p	<0.001	<0.001	0.01	0.01	<0.001	0.003		0.004	<0.001	<0.001	<0.001	0.004
SBM	k	5	-	4	-	4	4	-	-	-	-	6	-
	$\hat{\mu}_\rho$	**0.23**		0.19		**0.32**	**0.30**					**0.22**	
	Q	2.06		14.95**		4.84	3.47					3.08	
	$\hat{\tau}^2$	0		0.07		0.01	0.01					0	
	I^2%	0		74.16		39.22	11.76					0	
	H^2	1		3.87		1.65	1.13					1	
	CI lb	0.11		-0.11		0.15	0.10					0.10	
	CI ub	0.35		0.45		0.47	0. 47					0.34	
	p	<0.001		0.21		<0.001	0.002					<0.001	
SPS	k	3	-	3	4	4		-	-	-	-	-	-
	$\hat{\mu}_\rho$	**0.29**		**0.25**	**0.25**	**0.26**							
	Q	0.73		1.45	0.29	0.44							
	$\hat{\tau}^2$	0		0	0	0							
	I^2%	0		0	0	0							
	H^2	1		1	1	1							
	CI lb	0.08		0.05	0.07	0.07							
	CI ub	0.47		0.43	0.41	0.43							
	p	0.008		0.02	0.007	0.003							

Outcome domain		Cognitive Domain											
		Reasoning & problem solving	Processing speed	Attention & vigilance	Working memory	Verbal learning & memory	Visual learning & memory	Verbal compre-hension	Verbal fluency	Overall cognition	Theory of mind	Emotion perception & processing	Social perception & knowledge
SS	k	3	-	3		7	5	5			-	-	5
	$\hat{\mu}_\rho$	**0.34**		**0.39**		**0.18**	**0.28**	**0.24**					**0.24**
	Q	1.04		0.22		8.54	5.22	3.81					0.72
	$\hat{\tau}^2$	0		0		0	0.02	0					0
	I^2 %	0		0		0	30.81	0					0
	H^2	1		1		1	1.45	1					1
	CI lb	0.17		0.22		0.06	0.07	0.07					0.10
	CI ub	0.50		0.53		0.31	0.46	0.40					0.38
	p	<0.001		<0.001		0.005	0.008	0.02					<0.001

Note. Bold values indicate associations between cognitive- and outcome domains that are statistically significant, *k* = number of studies, $\hat{\mu}_\rho$ = estimated average correlation in the population distribution, Q = Q-test for heterogeneity (degrees of freedom = k-1), $\hat{\tau}^2$ = estimated heterogeneity in true (transformed) correlations, I^2 = % of total variability in observed (transformed) correlations due to heterogeneity, H^2 = total variability in observed (transformed) correlations/within-study variance due to sampling error; CI= 95% confidence interval for μ_ρ, lb = lower bound, ub = upper bound, *p* = p-value for *H*0: $\mu_\rho = 0$, **significant at $\alpha = 0.01$.

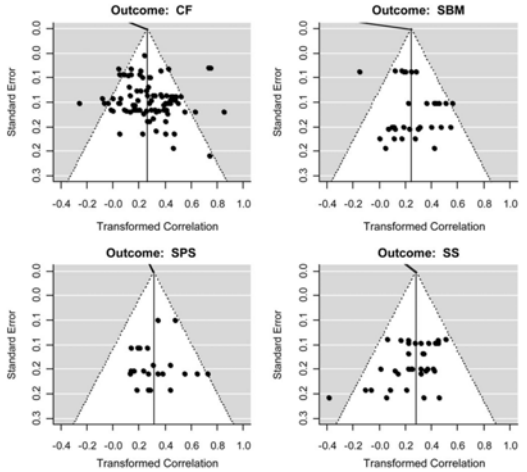

Figure 1 | Regression Tests for Funnel Plot Asymmetry for the Association between all Cognitive Domains within each Domain of Functional Outcome.

Regression Test for Funnel Plot Asymmetry

Most regression tests for funnel plot asymmetry were non-significant. One significant result was present for the association between community functioning and SP (p = 0.03). However, only three observations were included in this analysis, hence any interpretation about funnel plot asymmetry should be made with caution. The funnel plots for each outcome dimension and the combined cognitive domains are shown in Figure 1. The test for social skills was significant (p = 0.02). This finding was due to a single correlation of -0.37. After removing the correlation from the model the test was no longer significant, suggesting that publication bias should not be a reason of concern in the current analysis.

Effect of Moderator Variables

The moderators did not account for the heterogeneity in the correlations between cognition and functional outcome. The effect of male gender was not significant for most meta-analyses (all $\hat{\beta}$'s = -0.01/0.01, all *p's* = 0.10/0.99). An exception was the association between social skills and visual learning & memory ($\hat{\beta}$ = 0.01, p = 0.03, 95% CI = 0.00/0.01), which became stronger with increasing percentage of males. Also age did not influence the average correlations between most cognitive domains and outcome (all $\hat{\beta}$'s = -0.06/0.95, all *p's* = 0.09/0.95), except for social behaviour in the milieu and attention & vigilance ($\hat{\beta}$ = 0.06, p = 0.03, 95% CI = 0.03/0.10) and social skills and visual learning & memory ($\hat{\beta}$ = -0.04, p = 0.04, 95% CI = -0.08/-0.01). Whereas the association between attention & vigilance and social behaviour in the milieu became stronger with increasing age, the association between visual learning & memory and social skills became weaker with increasing age. There was no effect of inpatient status (all $\hat{\beta}$'s = -0.07/0.03, all *p's* = 0.06/0.96), except for community functioning and verbal learning & memory ($\hat{\beta}$ = 0.004, p = 0.02, 95% CI = 0.00/0.01) and verbal fluency ($\hat{\beta}$ = 0.01, p = 0.01, 95% CI = 0.00/0.01). Both associations became stronger with increasing number of inpatients. Illness chronicity had no effect on the average correlations (all $\hat{\beta}$'s = -0.07 to 0.04, all *p's* = 0.07/0.93).

Differential Correlations between Social - and Neurocognition and Community Functioning

Comparisons between all possible SC and NC community functioning combinations were computed. ToM was significantly stronger associated with community functioning than all NC domains (all *p's* < 0.05), except verbal fluency. EP was more strongly associated with community functioning than attention & vigilance (*p* <0.05). There were no significant differences between other NC and SC community functioning combinations. Exact test values of the comparisons are given in Table 5.

Table 5 | Comparisons between all neurocognitive and social cognitive domains and community functioning

Cognitive Domain				
Social Cognition	**Neurocognition**	**k**	**Estimated difference $\hat{\mu}_\rho$ Neuro vs. Social Cognition**	**p**
Theory of mind	Reasoning & problem solving	19	0.32	<0.001
	Processing speed	9	0.24	0.03
	Attention & vigilance	12	0.36	0.002
	Working memory	10	0.29	0.002
	Verbal learning & memory	19	0.24	0.03
	Visual learning & memory	8	0.31	0.005
	Verbal comprehension	4	0.31	0.01
	Verbal fluency	9	0.19	0.20
	Overall cognition	11	0.24	0.01
Emotion perception & processing	Reasoning & problem solving	21	0.12	0.06
	Processing speed	12	0.06	0.47
	Attention & vigilance	14	0.16	0.05
	Working memory	12	0.08	0.39
	Verbal learning & memory	21	0.04	0.55
	Visual learning & memory	7	0.11	0.30
	Verbal comprehension	11	-0.01	0.89
	Verbal fluency	11	0.11	0.20
	Overall cognition	11	0.06	0.25
Social perception & knowledge	Reasoning & problem solving	19	0.24	0.12
	Processing speed	11	0.18	0.28
	Attention & vigilance	11	0.28	0.08
	Working memory	10	0.21	0.23
	Verbal learning & memory	19	0.16	0.30
	Visual learning & memory	9	0.24	0.16
	Verbal comprehension	5	0.23	0.19
	Verbal fluency	9	0.10	0.57
	Overall cognition	12	0.18	0.25

Note. k = number of studies

DISCUSSION

Current Findings

NC and SC impairment were both substantially and consistently associated with functional outcome with small to medium range effect sizes. The strength of the associations between the 12 cognitive domains and the 4 outcome domains were largely independent of age, gender, illness chronicity and inpatient status. The magnitudes of the associations between NC and outcome were in line with what has been reported by the previous reviews [23-24, 26]. Community functioning was most strongly associated with verbal fluency, followed by verbal learning & memory and processing speed. Social behaviour in the milieu had the strongest associations with verbal learning & memory and visual learning & memory. Social problem solving was most strongly related to reasoning & problem solving and social skills had the strongest associations with attention & vigilance. The results indicate that different neurocognitive functions are somewhat differentially related to different domains of functional outcome with magnitudes ranging from $\hat{\mu}_\rho$ = 0.16 to 0.39. However, it is uncertain to what degree these differences have practical significance, given the often small differences in effect sizes and overlapping confidence intervals. The associations between SC and outcome were in the upper small to large range, with the largest effect size for ToM, followed by SP, and EP. An earlier descriptive review established associations between ToM, EP and SP and most outcome domains [12]. Our findings support and quantify the previous results and suggest small differences between mean effect sizes of the relations between the heterogeneous SC domains and outcome. Even though potentially meaningful, the statistical and practical significance of these differences is doubted by overlapping confidence intervals and the relatively small number of reviewed studies.

Are Social- and Neurocognition Differentially Related to Functional Outcome?

SC appeared to be more strongly related to community functioning than NC. The overall neurocognitive factor accounted for 6% of the variance in community functioning, while the amount of variance that could be explained by the average SC domains was 16%. Comparisons between all NC and SC domains and community functioning indicated that this difference was specifically due to stronger associations with ToM. This finding is in line with the suggestion that SC, despite likely having neurocognitive underpinnings, does explain unique variance in outcome [3, 9, 30]. Due to its proximity to community functioning (i.e. interpersonal relations, work functioning), SC functioning might be an even more important treatment target than

NC functioning. Fewer studies could be reviewed for the outcome domains social behaviour in the milieu, social problem solving and social skills. The associations between SC and the more performance based outcome domains, which at face value are expected to rely on SC abilities, did not appear different from their associations with the NC domains. However, this finding is based on a comparison with two mean correlations between SC and outcome (e.g. social behaviour in the milieu-EP and social skills-SP) only and warrants cautious interpretation. Within NC, verbal learning & memory, reasoning & problem solving, and attention & vigilance showed the strongest associations with social behaviour in the milieu, social problem solving and social skills, respectively. Yet again, the finding is based on few studies. Clearly, more research is needed to unravel whether specific cognitive functions are differentially related to functional outcome in the domains social behaviour in the milieu, social problem solving and social skills and whether the strength of the associations differs between the NC and SC domains.

The Importance of Distinguishing Different Domains of Functional Outcome

The strength of the association between the specific cognitive functions and functional outcome are clearly dependent on how one operationalizes functional outcome. Performance based assessments were thought to provide the theoretically most relevant link to SC and NC because they assess what an individual is capable of doing without being influenced by external factors [55]. Other aspects of outcome, such as work or managing relationships that are comprised in community functioning, might be confounded by factors as social support, finances or personal resources [12]. ToM had stronger associations with community functioning than the other cognitive domains, indicating that ToM may be a specific determinant of performance on broad based real world tasks. ToM and other SC abilities may also be important in achieving social support and personal resources, which both may influence real world outcome more than NC abilities. In this case one would also expect stronger associations between functional outcome in the domain social behaviour in the milieu and SC, as compared to NC. Conversely, deficits in both cognitive domains may limit understanding and performance on social problem solving and social skills tasks. Whereas problem analysis and decision making may rely heavily on executive functioning, interpreting a given situation and identifying the appropriate solution may rather require social knowledge.

Methodological Issues

Some methodological issues are important when considering the current findings. First, cognitive tests may vary in terms of sensitivity, which may be problematic in

view of the generalized cognitive deficit in schizophrenia [197-199]. That is, the difference between performance of patients with schizophrenia and healthy controls will be greater for tasks with higher sensitivity and variance, regardless of differences in true ability. Such variation may result in different likelihoods of correlating with other parameters, such as functional outcome. Second, several tests appear to tap functioning in various cognitive domains. We tried to overcome this problem by grouping tasks according to the results of factor analyses [29]. With regard to SC tasks, no such well-defined guidelines were available. The tasks are heterogeneous in nature and their psychometric properties are rarely investigated and warrant more research [20]. As for cognition, well-defined measures are also required for functional outcome [200]. Our results showed that associations with cognition are depending on the specific definitions of outcome, which also bring along their own limitations and advantages. More research is therefore needed to find reliable and less heterogeneous indices of real world functioning [201]. In addition, research should investigate which aspects of outcome are sensitive to changes in cognition. Crucial steps in doing so have recently been made, for example, with the VALERO expert survey [202]. Third, next to the included moderators, many other variables that are relevant to the cognition-outcome relationship (e.g. illness severity, pharmacological treatment, history of symptoms, genetic vulnerability or comorbidity) could not be examined due to underreporting. In addition, the necessary exclusion of a number of studies with incomplete information may have resulted in sample restriction. Fourth, it is important to note that the current cross sectional data do not allow for conclusions about causality. On theoretical grounds, it seems likely that cognitive performance influences outcome, but at the same time, outcome may also influence cognition. Negative social experiences, for instance, may drive the development of maladaptive social schemas or attribution styles. A deprived surrounding or an unhealthy lifestyle may influence NC.

Methodological Recommendations

Because of methodological inconsistencies and omission of important study details in potentially includable articles, the current meta-analysis could only include about one fifth of the possible total. This raises a number of issues that should be considered in future research. First, in order to be able to conduct good quality meta-analyses, future studies on cognition-outcome associations should always report the values of all non-significant and significant correlations. Second, future studies should also report the intercorrelations between the test scores on all utilized neurocognitive, social cognitive and functional outcome measures, as these inter-correlations are a

prerequisite for pooling of data. The availability of intercorrelations would allow for the comparison of cognition-outcome associations between the global factors, while accounting for conceptual overlap. Besides, intercorrelations are also required to test specific statistical models, such as mediation, which are of great interest because of the importance of SC functions as a possible key mediator between NC and functional outcome [31]. Third, a couple of studies had to be excluded from the current meta-analysis because they used cognitive or outcome measures that could not be classified into one of the current domains. In order to make research comparable, future studies should adhere to guidelines consistent with those that have been brought forward by the MATRICS committee and with those of the NIMH Initiative Cognitive Neuroscience Treatment Research to Improve Cognition in Schizophrenia (CNTRICS; [203]). Clearly, more guidelines and standardization are needed especially with regard to the social cognitive domain. Fourth, future studies on cognition-outcome associations should also make sure to always report standardized measures of psychotic symptoms, so that these can be taken into account as potential moderators of the cognition-outcome relationships. Fifth, it would be desirable if future studies reported correlations between specific cognitive sub-domains and functional outcome instead of correlations between aggregates thereof. Finally, a couple of longitudinal studies had to be excluded from the current meta-analysis because they did not report baseline correlations between cognition and outcome. Future longitudinal research on cognition-outcome associations should also consider reporting such information.

Conclusions

The current findings show that SC is related to functional outcomes, perhaps stronger than NC. However, to guide the development of specific interventions to improve functional outcome further knowledge is needed regarding NC and SC-outcome associations, especially for outcome categories other than community functioning. Several studies have demonstrated that the social cognitive deficits of schizophrenia are modifiable through brief experimental manipulations or psychosocial interventions [204-206]. Future clinical trials are challenged to further investigate whether improving individual cognitive domains, such as ToM can also improve functional outcome. Given their potential functional significance, the different SC domains and their assessment warrant specific attention (i.e. validation and standardization of the specific SC tasks and their sensitivity to change or the responsiveness of the different cognitive functions to specific interventions). Finally, it should be noted that both NC and SC leave the bulk of the variance in outcome unexplained. The data show that even the most comprehensive set of cognitive

factors can only explain a certain amount of variance in functional outcome of patients with schizophrenia. Accordingly, poor functional outcome must also be present in patients with little impaired cognitive functioning. Though possibly significant to a specific subgroup of patients, cognitive interventions may only be able to improve outcome to a small or medium extent [207]. There is support for the hypothesis that the relationship between cognition and functional outcome is partially mediated by negative symptoms. Negative symptoms are associated with both cognitive factors and appear to explain 17.6% of variance in outcome [208]. In addition, many other factors such as meta-cognition, motivation or social discomfort appear to influence the associations between cognition and functional outcome [209-211]. This highlights the multifactorial causation of poor functional outcome in psychosis and stresses the additional need to quest for other rate limiting factors that can account for the unexplained variance in functional outcome.

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