Published in final edited form as:

Schizophr Res. 2019 April ; 206: 27–36. doi:10.1016/j.schres.2018.10.010.

Clarifying the Overlap Between Motivation and Negative Symptom Measures in Schizophrenia Research: A Meta-Analysis

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Abstract

Motivation and negative symptom research has recently been hampered by a series of inconsistent findings, leading to calls for a greater consensus on the type of measures used across studies. To inform this issue, we conducted a meta-analysis that quantified the association between motivation measures (self-report, performance-based) and clinician-rated negative symptom measures as well as a series of moderator analyses to develop a greater understanding of the measurement factors impacting this relationship. Forty-seven eligible studies with people with schizophrenia-spectrum disorders were included. Using a random-effects meta-analytic model, a small but significant overall effect size emerged between motivation and clinician-rated negative symptoms ($r = -.18$). Several significant moderators were identified, including the generation of negative symptom measures such that there was a significantly stronger relationship between motivation and second-generation ($r = -.38$) than first-generation negative symptom measures ($r = -.17$). Further, the type of performance-based measure used moderated the relationship, with effort discounting tasks most strongly related to negative symptoms ($r = -.44$). The domain of motivation assessed (intrinsic, extrinsic, amotivation) also moderated the relationship. These findings help to identify sources of inconsistencies observed in prior studies and point to both second-generation and effort discounting tasks as the most promising types of measures, particularly for those interested in validating motivation measures or assessing the effectiveness of motivation treatments. Although additional research is needed, our results suggest that using these measures may help to reduce inconsistencies across studies and move the field forward.

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Contributors: Ms. Luther conducted the literature search, coded the studies, performed the data analysis, and lead manuscript draft writing. Ms. Fischer, Dr. Firmin, and Dr. Salyers, provided conceptual input and assisted with the manuscript drafting and editing.

Conflicts of Interest: The authors declare that they have no conflicts of interest.

Keywords

Avolition; apathy; psychosis; effort; measurement; effort-based decision-making

1. Introduction

Motivation—an internal state that directs and sustains goal-directed behavior (Kleinginna and Kleinginna, 1981)—is often impaired among those with schizophrenia (Cooper et al., 2015; Fervaha, Foussias, et al., 2015). These reductions contribute to reduced quality of life, social relationships, and occupational attainment (Fervaha, Foussias, et al., 2014; Foussias et al., 2011; Thomas et al., 2017; Vancampfort et al., 2013). While motivation deficits have recently been categorized as a core subdomain of negative symptoms, there is still debate about the role that motivation deficits play in negative symptoms. For example, the National Institute of Mental Health's Measurement and Treatment Research to Improve Cognition in Schizophrenia (NIMH-MATRICS; Kirkpatrick et al., 2006) Consensus Development Conference on Negative Symptoms indicated that amotivation was one of the five principal negative symptom domains alongside anhedonia, asociality, restricted affect, and alogia. However, some researchers posit that amotivation is actually the primary overarching negative symptom (Foussias and Remington, 2008) or one of two overarching negative symptom factors (Sarkar et al., 2015). Further, the degree to which these conceptualizations align with widely used negative symptom measures varies, with several commonly used negative symptom measures differing in the extent to which motivation deficits are assessed (Foussias and Remington, 2008). These differences have contributed to the inconsistent findings plaguing much of motivation research (Hartmann-Riemer et al., 2018; Kremen et al., 2016), making interpretation of findings across studies difficult and hindering the field from moving forward. For example, depending on the negative symptom measure used, associations with similar motivation measures have ranged from nonsignificant to large (Hartmann et al., 2015; Tobe et al., 2016; Wolf et al., 2014). Given the functional significance of motivation and the common use of negative symptom measures as a main outcome in motivation treatment trials (Green et al., 2015; Kirkpatrick et al., 2006), ascertaining which negative symptom measures are best assessing reduced motivation is critical. Indeed, if negative symptom measures do not adequately assess motivation deficits, then using them to assess the efficacy of interventions targeting motivation may lead to an inaccurate evaluation of these interventions. Thus, in an effort to understand the inconsistencies and to help researchers identify the best negative symptom measures for clinical trials targeting motivation, this study aimed to synthesize the associations between motivation and negative symptom measures.

Clinician-rated measures have long been the gold-standard for assessing negative symptoms. Although developed over thirty years ago, two commonly-used clinician-rated measures are the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1982) and the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987). However, these older measures (referred to here as first-generation) may be problematic for assessing newer treatments and measures as the conceptualization of negative symptoms in schizophrenia research has changed. Indeed, first-generation measures often include items such as attention

or abstract thinking that are now considered a separate domain related to cognition (Harvey et al., 2006) or contain individual items that conflate seperable symptoms or processes (Horan et al., 2006). Further, first-generation scales can emphasize behavioral indicators at the expense of understanding internal experiences linked to negative symptoms (Blanchard et al., 2011). However, internal experiences are particularly important for motivation, given that one's drive or interest in a particular activity even in the absence of behavior indicates that motivation at some level is present.

Partially as a result of these limitations, the NIMH-MATRICS negative symptoms consensus statement (Kirkpatrick et al., 2006) recommended creating new negative symptom measures ("second-generation") to address these limitations. This resulted in the development of the Clinical Assessment Interview for Negative Symptoms (CAINS; Horan et al., 2011; Kring et al., 2013) and the Brief Negative Symptom Scale (BNSS; Kirkpatrick et al., 2010; Strauss et al., 2012). Although these second-generation scales have demonstrated promising psychometric findings, including strong convergent validity with first-generation negative symptom assessments (Kring et al., 2013), limited empirical evidence suggests that second-generation measures are indeed better capturing individual negative symptom domains such as motivation deficits than first-generation scales. Further, first-generation scales are still widely used. If we are to create greater consensus in measurement and reduce inconsistencies across studies examining motivation so that we can better help people struggling with these deficits, we need more research focused on identifying whether second-generation scales are truly better at assessing different symptom domains than first-generation measures.

Consistent with the range of conceptual approaches for negative symptoms, schizophrenia researchers have also approached measuring and conceptualizing motivation in several ways. Many schizophrenia researchers have looked to arguably the most prominent theory of motivation, Self-Determination Theory (SDT; Deci and Ryan, 1985; Ryan and Deci, 2000, 2017) to elucidate the multidimensional nature of motivation (Choi et al., 2010; Medalia and Brekke, 2010; Silverstein, 2010). Briefly, SDT explicates that there are different types of motivation that can be distinguished by the sources or reasons for the behavior. Specifically, SDT posits that motivation has three domains: 1) intrinsic motivation—behaviors or activities that are performed because they are inherently interesting and the primary "reward" is the associated feelings of enjoyment or satisfaction, 2) extrinsic motivation—behaviors that are completed in order to attain a separable outcome from the activity such as an external financial reward, social praise, evasion of punishment, or an esteemed outcome, and 3) amotivation—lack of behaviors or intentions to engage in or complete an activity (Ryan and Deci, 2000, 2017; Deci, Olafsen, et al., 2017). Further, these motivation domains can also be impacted by one's environment and fulfillment of the three basic psychological needs of competence, relatedness or belongingness, and autonomy or self-regulation (See Deci and Ryan, 2000; Ryan and Deci, 2017 for more information). Given SDT's prominent role in schizophrenia motivation research, several frequently used motivation self-report measures are SDT-derived measures, including the Intrinsic Motivation Inventory for Schizophrenia Research (IMI-SR; Choi et al., 2014), which assesses intrinsic motivation for a specific task. Other commonly used self-report motivation measures also align with the SDT-derived domains, including the self-report Apathy Scale (AES-S; Marin et al., 1991) or

Self-Evaluation of Negative Symptoms (SNS; Dollfus et al., 2015), which both assess amotivation.

More objective, performance-based motivation measures have also recently been developed to measure how willing participants are to work for external rewards. These measures, generally referred to as effort-based decision-making tasks, overcome some limitations associated with self-report and clinician-rated measures (e.g., reliance on ability to recall information, extensive training needed to reliably administer/score measures) and can elucidate compromised subprocesses or mechanisms that might underlie motivation deficits (Green et al., 2015). Indeed, many of the performance-based measures have been translated from animal paradigms that have been linked to specific neural mechanisms related to reduced motivation (e.g., Anterior cingulate cortex dysfunction; ventral striatal dopamine depletion (Fervaha, Foussias, et al., 2013)), which can help to pinpoint whether these regions are also implicated in motivation deficits in humans with schizophrenia. Despite these promising benefits, this avenue of research has been hampered by inconsistent findings in the magnitude and even direction of the relationship between performance-based motivation measures and negative symptoms (McCarthy et al., 2016; Reddy et al., in press), leading to questions about the utility and validity of these measures.

A main source of the inconsistencies observed in prior studies likely stems from the type of performance-based or clinician-rated negative symptom measures used. Indeed, there are three broad types of performance-based motivation measures currently used. The first type, forced-choice non-adaptive reward tasks, are the most-widely used and involve tasks where participants complete a number of forced-choice trials where they select to complete either a low effort task that provides low monetary reward (usually fixed at for example $1.00) or a task involving relatively greater effort that offers larger rewards (usually variable, e.g., ranges between $1.24 - $4.30). Importantly, the reward values are not modified over time based on participant responses, and the most commonly used indicator of motivation is the number of hard choices chosen across trials. In contrast, effort discounting tasks use reward manipulation to identify the indifference point, which is the amount of reward when a person becomes indifferent to completing the low effort and high effort task options. The third type of task, progressive ratio tasks, generally involve single choice trials where the level of effort needed to attain a reward increases over time and motivation is indicated by the greatest effort amount a person is willing to expend (breakpoint score). Notably, across all three types of tasks, effort can be physical (e.g., button presses, handgripping) or cognitive (e.g., identifying whether numbers are greater than or equal to a specified number). Further, extant studies examining the association between these tasks and clinician-rated negative symptoms have yielded mixed results. For example, some studies using forced-choice non-adaptive reward tasks have found small but significant inverse associations (Barch et al., 2014; Horan et al., 2015), while others have failed to find significant associations (Fervaha, Duncan, et al., 2015; Moran et al., 2017), found a trend level association (Treadway et al., 2015), or even an unexpected positive association with clinician-rated negative symptoms (McCarthy et al., 2016). On the other hand, compared to forced-choice non-adaptive reward tasks, some studies examining the magnitude of the relationship between both effort discounting and progressive ratio tasks and clinician-rated negative symptoms have found relatively stronger associations with negative symptoms (i.e., medium to large (Culbreth et al., 2016; Strauss et

al., 2016; Wolf et al., 2014); but also see Bismark et al., 2018 & Docx et al., 2015). A synthesis of these prior studies, which were often based on small samples, can help to clarify the degree to which each type of task is capturing a process related to negative symptoms and can help to realign our efforts towards the most promising and beneficial assessment approaches. Further, identifying which type of performance-based measure is most strongly aligned to negative symptoms can help to more precisely elucidate behavioral and neural mechanisms underlying negative symptoms, which can help to inform novel treatment development.

The present study aimed to inform conceptual and measurement issues surrounding motivation and negative symptoms in people with schizophrenia by first conducting a metaanalysis that quantified the relationship among motivation measures and clinician-rated negative symptom measures. Although prior literature examining this association has been mixed (Barch et al., 2014; Fervaha, Duncan, et al., 2015), based on the conceptual link, we hypothesized that that there would be a significant, small overall effect size between these measures. To develop a more precise understanding of the different measurement and conceptualization factors as well as participant characteristics that may affect this relationship, we then examined a series of potential moderators:

1. Type of motivation measure (i.e., self-report versus performance-based). Given both self-report motivation and clinician-rated negative symptom assessments incorporate self-report participant information, we hypothesized that self-report motivation measures would have a stronger relationship with negative symptoms than performance-based measures.
2. Negative symptom measure type (i.e., first-generation versus second-generation). Because second-generation measures were developed to more comprehensively assess negative symptom domains, we hypothesized that motivation would demonstrate a stronger relationship with second-generation rather than first-generation negative symptom measures.
3. Motivation domain (i.e., intrinsic, extrinsic, or amotivation). We hypothesized that the relationship would be strongest between amotivation and negative symptoms given their stronger conceptual overlap.
4. Participant characteristics that might impact the magnitude of the relationship, including factors previously associated with motivation such as illness length (Luther et al., 2015) and antipsychotic medication dose (Kirsch et al., 2007; Luther et al., 2016). These moderator analyses were exploratory.

2. Methods

2.1. Literature Search

Guidelines from the evidence-based Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA; Moher et al., 2009) were followed. Once we discussed our search strategy with a science-focused librarian, we identified eligible studies in three steps. First, keywords including derivatives of motivation, schizophrenia, and a comprehensive combination of measurement terms (e.g. self-report, performance-based) were searched in

Embase, Medline, PsychINFO, PsychARTICLES, Pubmed, and *Web of Science Core Collection* in September 2017. We selected relevant filters (i.e., English, human-based studies) when possible. Conference presentations and dissertations were included to reduce publication bias (Borenstein et al., 2009; Lipsey and Wilson, 2001). We next examined the references of reviews focused on motivation in schizophrenia (i.e., Green and Horan, 2015; Green et al., 2015; Kremen et al., 2016; Markou et al., 2013; Medalia and Brekke, 2010; Reddy, Horan & Green, 2015; Strauss et al., 2014). Lastly, because studies were required to use either a self-report or performance-based assessment of motivation, forward searches of the corresponding seminal measure articles were conducted.

2.2. Study Eligibility Criteria

Eligible studies were those that 1) were obtainable in English; 2) used an empirical self-report and/or performance-based motivation assessment and a global (i.e., measured multiple domains) clinician-rated negative symptom measure. We aimed to look at global negative symptoms and not negative symptom factors (e.g., experiential and expressive negative symptoms (Llerena et al., 2018)) based on the conceptual issues mentioned above (e.g., some individual negative symptom items conflate different symptoms) and differing empirical evidence supporting the presence of and included negative symptom domains (e.g., anhedonia) in experiential and expressive negative symptom factors across negative symptom measures, particularly between first-generation and second-generation negative symptom measures (Ahmed et al., in press; Blanchard and Cohen, 2006; Liemburg et al., 2013). For the motivation assessments, we also did not include clinician-rated motivation scales for analytic purposes (e.g., in order to avoid shared method variance that would likely conflate the strength of the associations found) and feasibility reasons (e.g., clinician-rated motivation is largely assessed via subscales of negative symptom measures); 3) had a motivation measure that aligned with intrinsic motivation, extrinsic motivation, or amotivation; choosing measures that align with these domains helps to decrease the difficulties operationalizing motivation, lessens construct validity concerns, and is consistent with the widely used and theoretically driven SDT-based conceptualizations of motivation in schizophrenia research; 4) the self-report and clinician-rated assessments used aligned with reviews of motivation and negative symptoms by Kremen et al. (2016) and Lincoln et al. (2017), and the performance-based tasks used were consistent with those described in the review from Markou et al. (2013). We chose these reviews because they detail the most widely used and validated motivation and negative symptom measures, which is important for reducing content validity issues; 5) used these measures with a schizophrenia-spectrum sample; and 6) contained a univariate association among motivation and overall negative symptoms; if these variables were assessed with eligible measures, but the univariate association was not reported, we emailed the study authors. In treatment or experimental studies, we only included baseline relationships. Studies were omitted when samples overlapped with another included study or univariate associations were unable to be collected after emailing study authors.

2.3. Coding

Studies were coded following published strategies (Card, 2012; Lipsey and Wilson (2001). Sample characteristics included age, gender, illness length, chlorpromazine equivalent doses,

and diagnoses. We coded measure name and score used, measurement type, motivation domain assessed (based on Kremen et al. (2016), Lincoln et al. (2017), and Markou et al. (2013)) and generation of negative symptom measure (i.e., second-generation measures were those created based on the NIMH-MATRICS negative symptoms consensus statement (Kirkpatrick et al., 2006)).

2.3.1. Effect Size Coding—We extracted effect size information (e.g., correlation coefficient) that represented the univariate relationship between motivation and negative symptoms for each study. Effect sizes were first changed into Pearson's correlations and coded so higher motivation measure values represented greater motivation, and higher negative symptom levels represented more negative symptoms. Correlations were then transformed using Fisher's Z-transformation and weighted based on sample size. Following the recommendation of Card (2012) and Lipsey and Wilson (2001), if a study contained more than one effect size, we averaged the effect sizes to reduce bias and maintain statistical independence (Card, 2012). Meta-analytic calculations were conducted in Comprehensive Meta-Analysis, V. 3 (CMA; Borenstein et al., 2015).

2.4. Analyses

To quantify the overall association between motivation and negative symptoms, we calculated the mean overall effect size based on a random-effects model. Cohen (1992)'s recommendations for correlations (.10 = small, .30 = medium, .50 = large) were used to interpret the effect size magnitude.

For moderation analyses, we used the Q-statistic to identify whether significant ($p < .05$) heterogeneity was present (Card, 2012), and the I^2 index was used to identify the percentage of variation resulting from between-study variability (Higgins and Thompson, 2002; Huedo-Medina et al., 2006). Moderation analyses were completed if the Q-statistic was significant and the I^2 index ≥ 25%, as this I^2 value suggests greater variability than expected by chance (Huedo-Medina et al., 2006). We used an Analysis of Variance analog to test categorical moderators and meta-regressions to test continuous moderators. Continuous moderators were significant when the significance of the beta weight was $p < .05$; categorical moderators were significant when (Qbetween was significant ($p < .05$).

To determine that no individual study disproportionately impacted the overall effect size, we utilized a one-study removed sensitivity analysis (Borenstein et al., 2009). Studies that looked like outliers on forest plots as well as greatly changed the effect size if excluded were considered for removal. We examined publication bias by examining the funnel plot and conducting Egger's regression approach (Egger et al., 1997) to assess for asymmetry. Bias is likely present when the funnel plot has an asymmetrical distribution (Card, 2012) and the Egger's test intercept is significant ($p < .05$) (Egger et al., 1997).

3. Results

3.1. Study Characteristics

Our search yielded 47 eligible studies (Figure 1 contains the Study Retrieval Flow Diagram). Included study summary characteristics are reported in Table 1; study characteristics,

measure information, and effect sizes for each study are reported in Table 1 in the online supplemental material. Across all studies, 2,908 people diagnosed with a schizophrenia-spectrum disorder were included. Thirty-three studies included a self-report motivation measure (most commonly a version of the Intrinsic Motivation Inventory (IMI; Ryan, 1982)), 12 included a performance-based motivation measure (predominantly the Effort Expenditure for Rewards Task (Treadway et al., 2009)), and two included both motivation measurement types. The majority of studies used self-report measures that assessed amotivation (k= 24); fewer studies used self-report measures of intrinsic (k= 14) and extrinsic motivation (k = 3). For negative symptoms, thirty-four studies used a first-generation negative symptom measure (most commonly the PANSS), three used a second-generation measure, and ten used both generations of negative symptom measures. Table 1 of the online supplemental material details included measures.

3.2. Sensitivity Analysis

The one-study removed forest plot suggested there was variation among effect sizes; however, McCarthy et al. (2016)'s study appeared to be overly impacting the overall effect size based on the effect size point estimates. Since McCarthy et al. (2016) also had divergent demographics (e.g., was older), this study was excluded from the remaining analyses. All other studies were retained.

3.3. Main Analyses

3.3.1. Overall motivation—negative symptoms meta-analysis—The remaining 46 studies were used in the meta-analysis evaluating the overall association between motivation and negative symptoms (see Figure 2). In accord with our hypothesis, we observed a small, negative, significant effect size (r = −.18, p <.001, 95% Cl [−.24, −. 12]), such that greater motivation was associated with lower negative symptoms. Individual study correlations were between r = −.55 to r= .15. In regards to heterogeneity, the Q- statistic was significant (Q = 104.13, P <001), and the I^2 index was 56.78%; thus, moderator analyses were conducted.

3.4. Moderator Analyses

3.4.1. Motivation measurement type—Contrary to hypotheses, categorical moderator analyses indicated that the motivation measurement type did not moderate the relationship between motivation and negative symptom measures (Qbetween = 1.39, p = .24; see Table 2). Both measurement types demonstrated significant but small inverse relationships with negative symptoms (self-report: r = −.19, p < .001; performance-based: r = −.14, p= .003).

To further identify whether a specific performance-based measure might be best capturing negative symptoms, we explored whether the type of performance-based measure used moderated the relationship. Significant moderation was observed (Qbetween = 6.53, p = . 04); effort discounting tasks demonstrated the strongest—and only significant—relationship with negative symptoms (r = −44, p = .001), followed by progressive ratio (r = −.12, p = .23) and the forced-choice non-adaptive reward tasks (r = −.09, p = .09). However, these analyses were based on few studies and were likely underpowered.

3.4.2. Negative symptom measurement—As hypothesized, the generation of negative symptom measure moderated the motivation and negative symptoms association (Qbetween = 23,35, $p < .001$), such that there was a significantly stronger inverse relationship between motivation measures and second-generation ($r = -.38$, $p < .001$) rather than first-generation negative symptom measures ($r = -.17$, $p < .001$). In exploratory analyses, we separately examined whether motivation measurement subtypes (self-report, performance-based) were also more strongly associated with second-generation negative symptom assessments. Similar to our overall analyses, generation of negative symptom measure significantly moderated the self-report motivation and negative symptoms association (Qbetween = 25.38, $p < .001$). Self-report motivation measures demonstrated a significantly stronger relationship with second-generation ($r = -.45$, $p < .001$) rather than first-generation ($r = -.18$, $p < .001$) negative symptom measures. For performance-based motivation measures, we also observed that the generation of negative symptom measure was a significant moderator (Qbetween = 4.02, $p = .045$); performance-based motivation measures had a significantly stronger relationship with second-generation ($r = -.26$, $p < .001$) as opposed to first-generation ($r = -.10$, $p = .04$) negative symptom measures.

We also explored whether the specific negative symptom measure affected the magnitude of the relationship with motivation. Significant moderation was observed (Qbetween = 24.54, $p < .001$), with the BNSS ($r = -.39$, $p < .001$) and CAINS ($r = -.36$, $p < .001$) demonstrating the strongest associations with overall motivation. Of the first-generation measures, the negative symptom factors from the PANSS ($r = -.21$, $p < .001$) and Brief Psychiatric Rating Scale (Overall and Gorham, 1962) ($r = -.22$, $p < .001$) demonstrated relatively stronger associations than the SANS ($r = -.12$, $p < .001$) and Negative Symptom Assessment (NSA; Alphs et al., 1989) ($r = -.11$, $p = .28$). However, given that the NSA was only used in one study, these results should be interpreted cautiously.

3.4.3. Motivation domain—The motivation domain assessed also significantly moderated the association between self-report motivation and negative symptoms (Qbetween = 6.86, $p = .03$). As hypothesized, the strongest relationship was between self-report amotivation and negative symptoms ($r = -.22$, $p < .001$); of note, this relationship suggests that higher amotivation is associated with higher negative symptoms (correlations were all coded such that higher scores = greater motivation). The self-report intrinsic motivation and negative symptoms association was weaker but still significant ($r = -.12$ $p = .005$), whereas the association with self-report extrinsic motivation was even weaker and non-significant ($r = -.06$, $p = .47$).

3.4.4. Participant Characteristics—Five characteristics were examined as moderators of the overall association between motivation and negative symptoms: average age, illness length, and chlorpromazine equivalent doses and percent female and percent of the sample with a schizophrenia diagnosis; none were significant moderators.

3.5. Publication Bias

The funnel plot of the effect sizes for the overall motivation and negative symptoms association was relatively symmetrical and triangular, and Egger's test was not significant (p = .89), indicating that publication bias was likely not present.

4. Discussion

Motivation and negative symptom research has recently been hampered by a series of inconsistent findings, leading to calls for a greater consensus on the type of negative symptom and motivation measures used (Hartmann-Riemer et al., 2018). To inform this issue, we first conducted a meta-analysis that quantified the relationship between motivation measures (self-report, performance-based) and clinician-rated negative symptom measures to develop a greater understanding of the consistency of the relationship and the role motivation deficits play in negative symptoms. Consistent with our hypothesis, we observed a small but significant negative association between overall motivation and clinician-rated negative symptoms (r = −.18), with motivation explaining 3.24% of the variance in clinician-rated negative symptom measures. These results build on prior findings by including a substantial amount of unpublished data, with only 11 of the 47 (23.4%) studies previously publishing these univariate associations between motivation and negative symptom measures. In addition, this study overcomes the shortcomings of many prior studies that included small samples by pooling together data from 2,908 people with schizophrenia-spectrum disorders. Moreover, we were able to systematically assess potential sources of variability in the relationship between motivation and negative symptom measures through moderator analyses, and our findings point to generation of negative symptom measure, type of performance-based measure, and domain of self-report motivation measure used as primary candidates that might explain some of the inconsistencies observed in the literature.

Notably, the amount of variance explained by motivation measures in negative symptoms was small (i.e., 3.24%). Indeed, the NIMH-MATRICS negative symptoms consensus statement (Kirkpatrick et al., 2006) and recent empirical findings indicate that motivation is one of five key negative symptoms (Ahmed et al., in press). Further, others have posited that amotivation is actually the primary overarching negative symptom (Foussias & Remington, 2008) or one of two key negative symptom factors (Sakar et al., 2015). Although these conceptualizations differ in the extent that motivation deficits play in negative symptoms, they all indicate that motivation deficits should explain more than 3.24% of the variance in negative symptoms. If measures do not give enough weight to negative symptoms domains that are critical to improved functioning and quality of life, such as motivation deficits, using these tools to evaluate the effectiveness of negative symptom interventions may fail to capture clinically significant or meaningful change. Indeed, consistent with recommendations for clinical trials targeting negative symptoms (Marder et al., 2013), global or total negative symptom scores are often used as endpoints in clinical trials; however, our results suggest that using a clinician-rated negative symptom total score alone may lead to an underrepresentation of improvements on motivation deficits. Thus, although more work is needed to clarify the role of reduced motivation in negative symptom

conceptualizations, these findings suggest that negative symptom measures by themselves may not adequately capture motivation deficits.

Regarding the generation of negative symptom measure, there was a significantly stronger overlap between overall motivation and second-generation (medium effect) than first-generation (small effect) negative symptom measures. Further, both self-report and performance-based measures of motivation were more strongly related to second-generation as opposed to first-generation measures. Similarly, our exploratory analyses with specific negative symptom measures showed that the two second-generation negative symptom assessments, the BNSS and CAINS, demonstrated the strongest relationships with motivation measures. Although prior theoretical articles have suggested that second-generation negative symptom measures are better at capturing negative symptom domains such as reduced motivation (Blanchard et al., 2011), our findings provide much needed empirical evidence for this supposition. Further, they suggest, that we should not expect large correlations between motivation measures and the first-generation negative symptom measures included in these analyses. Indeed, these findings are consistent with one of the goals of the second-generation negative symptom measures, which is to assess motivation deficits in terms of both intentions and behaviors (i.e., desire and actual engagement) in order to overcome the concern that first-generation measures primarily focus on behaviors. Capturing internal processes related to motivation may help to not only yield a more comprehensive picture of motivation deficits, especially when environmental restrictions may limit behaviors, but also help to improve the consistency of the relationship between motivation and negative symptom measures. Thus, these findings suggest that it may be time, particularly for those interested in validating motivation measures or assessing the efficacy of motivation treatments, for a more comprehensive shift towards using second-generation measures as a means to reduce inconsistencies resulting from measurement issues across studies.

Exploratory analyses found that the type of performance-based motivation measure significantly moderated the motivation and negative symptoms association. Specifically, the strongest and only significant relationship was with effort discounting tasks, followed in magnitude by the progressive ratio tasks, with the forced-choice non-adaptive reward task showing the weakest relationship with negative symptoms. Although our results should be interpreted cautiously given that some tasks were used in few studies, these findings suggest that effort discounting tasks may be the most promising tasks for elucidating key behavioral or neural mechanisms related to negative symptoms in people with schizophrenia. Alternatively, the forced-choice non-adaptive reward tasks demonstrated little overlap with negative symptoms, suggesting that these measures, or at least the score commonly used to represent motivation (i.e., % hardest tasks chosen), may not be a sensitive enough measure for negative symptomology or that other factors such as defeatist performance beliefs may more strongly influence the relationship between this type of task and negative symptoms (Reddy et al., in press). While additional research assessing the relationships between these tasks and negative symptoms is needed, our results provide preliminary evidence indicating that our resources may be best focused on effort discounting tasks to further refine and develop our conceptualization of motivation and negative symptoms in people with schizophrenia.

An additional source of variability in the motivation and negative symptoms association was the motivation domain assessed among self-report measures. Consistent with our hypothesis, we observed the strongest relationship, albeit still small in magnitude, between amotivation and negative symptoms. Intrinsic motivation and negative symptoms also demonstrated a small, significant relationship, while the extrinsic motivation and negative symptoms association was negligible and non-significant. These findings align with amotivation being a key negative symptom domain according to the NIMH-MATRICS negative symptom consensus statement (Kirkpatrick et al., 2006) as well as the notion that targeting intrinsic motivation with psychosocial treatments may lead to negative symptom reductions (Kremen et al., 2016). However, our observed associations between both intrinsic and extrinsic motivation and negative symptoms indicate that there may be less overlap between these domains—when self-reported—and negative symptoms than previously thought. Although these constructs are often categorized under the broader umbrella of motivation deficits or negative symptoms, our findings indicate we should not always expect to observe large correlations between the motivation domains of intrinsic and extrinsic motivation and negative symptoms despite their theoretical overlap. Further, in addition to negative symptom scales, these results support the use of multi-domain assessments of motivation to provide a more complete assessment, particularly in validation and treatment studies targeting these motivation domains.

There were also several factors that did not influence the strength of the relationship between motivation and negative symptoms. First, none of the participant characteristics examined moderated the relationship, suggesting that the measurement factors noted above may be greater contributors to the inconsistent relationships across studies. There was also no significant difference in the magnitude of the relationship between type of motivation measure (self-report, performance-based) and negative symptoms—both motivation measurement types evidenced small but significant relationships with negative symptoms. Taken together with studies finding limited overlap among motivation self-report and performance-based assessments (Luther et al., 2018), this may indicate that these forms of motivation assessments are capturing divergent—although similar overall amounts—of underlying processes related to negative symptoms. Further, the smaller than expected relationship between self-reported motivation and negative symptom measures may also suggest that intentions or perceptions of behavior captured by self-report measures do not always lead to or map on to behaviors, particularly in the time-frames that are assessed by clinician-rated negative symptom measures.

As with all meta-analyses, this study is impacted by the limitations of the included studies, including the use of convenience sampling. One potential limitation specific to this study was that not all measures purported to measure motivation were included; however, we chose to narrow our focus, guided by SDT and prior literature, to increase construct validity. Similarly, for the analytic and feasibility methods previously mentioned, we did not examine the association between clinician-rated motivation and negative symptoms. However, this likely resulted in a less biased (i.e., reduced shared method influence) estimate of the motivation and negative symptoms association. Relatedly, not all existing negative symptom measures were used in the eligible studies; thus, these results can only be applied to the negative symptom measures that were included in our analyses. Some of our analyses with

performance-based motivation measures or individual negative symptom scales (i.e., NSA) were also based on few studies and were likely underpowered; these results should be interpreted with caution. Indeed, given that the NSA was only used in one eligible study, additional research clarifying the association between motivation measures and the NSA is needed. Further, although the majority of the studies included used similar scoring methods for measures like the PANSS and SANS, differing scoring methods or negative symptom factors were used across studies or exist in the literature; additional work is needed to create a greater consensus on the scoring methods that best capture motivation deficits or negative symptoms. Further, partly due to motivation's functional significance, we focused on this negative symptom domain, but additional work is needed to evaluate associations between measures of the remaining negative symptom domains (e.g., anhedonia, blunted affect) and first-generation and second-generation negative symptom measures. Similarly, future research could clarify the associations between individual negative symptom domains and negative symptom factors (e.g., experiential and expressive negative symptoms), particularly by using second-generation negative symptom scales that may have more distinguishable factors than some of the first-generation negative symptom scales. Finally, we were limited by the state of the motivation and negative symptom schizophrenia research, and as these results highlight, there is still much to improve and understand about measuring and ultimately treating these domains.

Despite these limitations, our findings have important implications for motivation and negative symptom measurement, research, and treatment. In order to truly help those with motivation deficits, we need greater consistency in the types of motivation and negative symptom measures used in this line of research. Our findings offer insights into some measurement factors that might reconcile some of the inconsistency and point to the most promising measures to assess these symptoms. First, our results suggest that second-generation negative symptom assessments (i.e., BNSS, CAINS) are more strongly aligned with self-report and performance-based assessments of motivation than first-generation measures. Thus, for those interested in validating motivation measures or assessing the effectiveness of motivation treatments, second-generation measures may best capture the motivational subdomain of negative symptoms. From the motivation side of assessment, our results point towards effort discounting tasks as explaining the largest quantity of variance in negative symptoms. These results also provide preliminary evidence indicating that of the three types of performance-based assessments, effort discounting tasks may be the most promising for elucidating subprocesses and neural regions linked to negative symptomology. Finally, despite their theoretical similarities, our results suggest that motivational subdomains such as intrinsic motivation may not always be strongly correlated with negative symptoms; this limited overlap may be particularly important when choosing measures for validation and treatment studies focused on these domains. Taken together, although additional research and discussion are needed to further develop consensus around gold standard motivation and negative symptom measures, our results offer preliminary suggestions for the most promising measures in these domains for motivation research.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements:

The authors are incredibly grateful for the researchers who provided additional data for this meta-analysis. This work was supported by a Predoctoral Award from the Indiana Clinical and Translational Sciences Institute (to L.L.), which is funded in part by a National Institutes of Health (NIH), National Center for Advancing Translational Sciences, Clinical and Translational Sciences Award (# UL1TR001108) and by a NIH training grant (to R.L.F.) (# 5T32MH096682).

Role of the funding source: The funding sources had no role in the study design, statistical analysis, interpretation of findings, writing of the manuscript, or in the decision to submit for publication.

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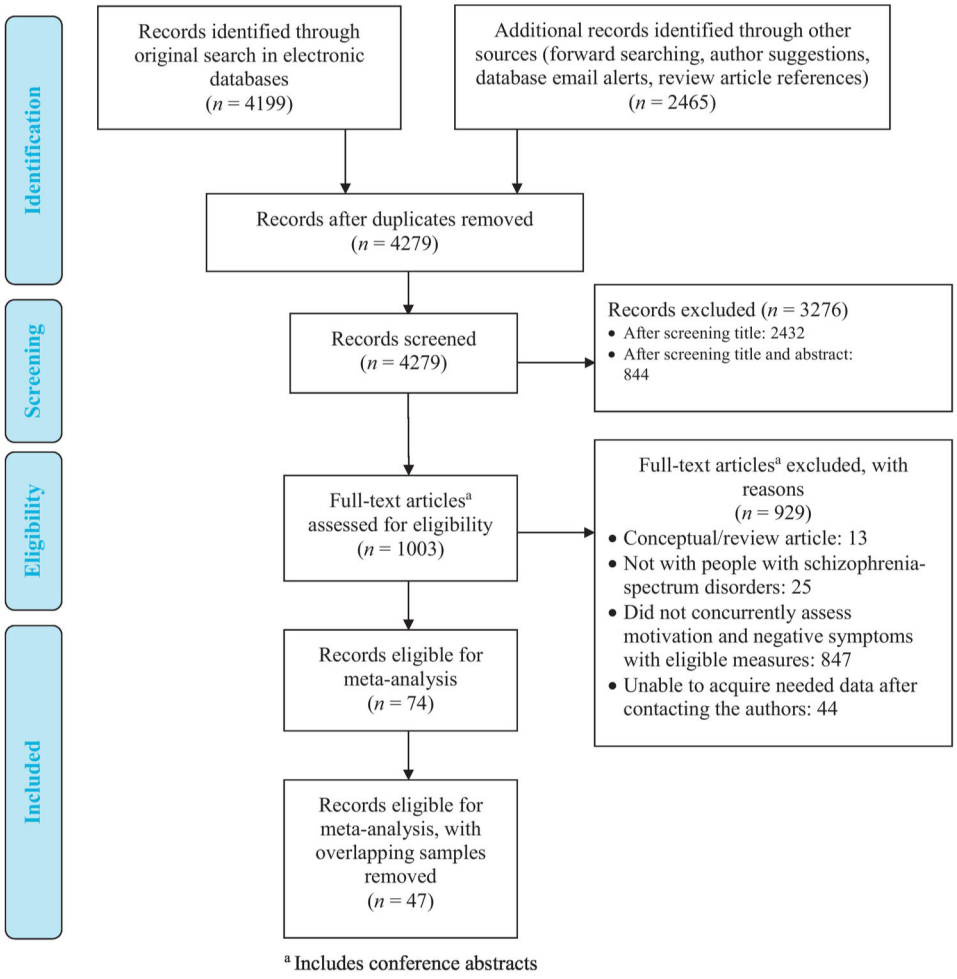

Fig. 1.
PRISMA study retrieval flow diagram.

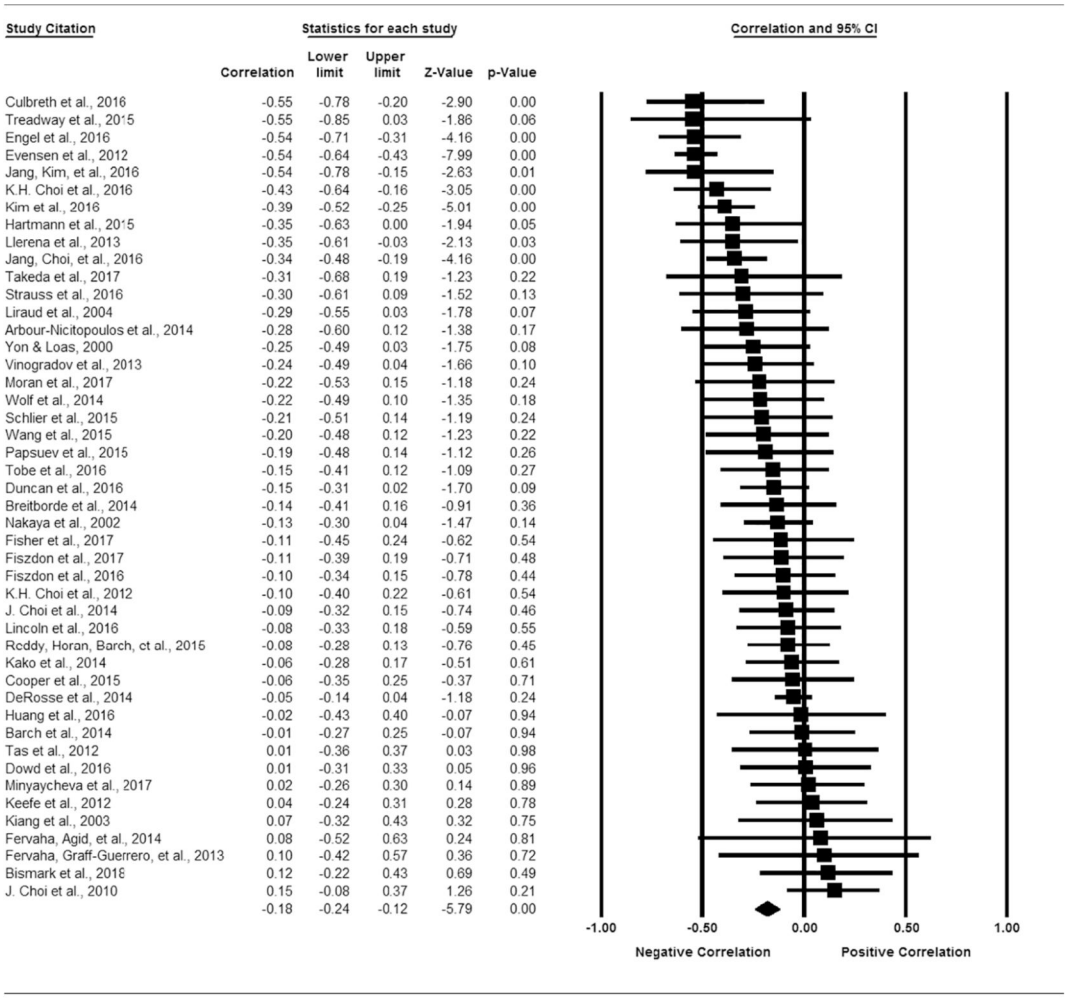

Fig. 2.

Forest plot of studies in the meta-analysis between motivation and clinician-rated negative symptom measures (k = 46) (Arbour-Nicitopoulos et al., 2014; Breitborde et al., 2014; Choi et al., 2012; Choi et al., 2016; DeRosse et al., 2014; Dowd et al., 2016; Duncan et al., 2016; Engel and Lincoln, 2016; Evensen et al., 2012; Fervaha et al., 2013b; Fervaha et al., 2014a; Fisher et al., 2017; Fiszdon et al., 2016; Fiszdon et al., 2017; Gard et al., 2014; Huang et al., 2016; Jang et al., 2016a; Jang et al., 2016b; Kako et al., 2014; Keefe et al., 2012; Kiang et al., 2003; Kim et al., 2016; Lincoln et al., 2016; Liraud et al., 2004; Llerena et al., 2013; Minyaycheva et al., 2017; Nakaya et al., 2002; Papsuev et al., 2015; Reddy et al., 2015a; Schlier et al., 2015; Takeda et al., 2017; Tas et al., 2012; Vinogradov et al., 2013; Wang et al., 2015; Yon and Loas, 2000).

Table 1

Overall characteristics across independent samples (k = 47)

Sample Characteristics	Mean (SD)	K
Age	38.4 (6.3)	47
Percent Female	39.0 (10.2)	47
Percent Diagnosis[a]		42
Schizophrenia	83.9 (17.1)	-
Schizoaffective	13.2 (14.5)	-
Other Psychosis	2.8 (8.8)	-
Length of illness	14.5 (6.4)	23
Chlorpromazine equivalent doses	513.3 (323.3)	20
Sample Characteristics	**Mean (SD)**	**K**
Data source (k, %)		47
Published Article[b]	44 (93.6)	-
Conference Abstract	3 (6.4)	-
Median Year (range)	2015 (2000-2018)	47
Mean Sample size (range)	61.9 (12-482)	47
Study Location (k, %)		47
Asia	11 (23.4)	-
Europe	9 (19.1)	-
North America	27 (57.4)	-

[a] All included samples had schizophrenia-spectrum disorder diagnoses.

[b] Includes studies that were published as both a conference abstract and article.

Table 2

Moderator Analyses of the Relationship Between Motivation and Negative Symptoms

Moderator	***k***	***r***	**95% CI**	Q_b	I^2
Categorical Moderators					
Motivation measurement type				1.39	
Self-reported	35	−19***	[−.23, −.15]		62.15
Performance-based	13	−.14**	[−.22, −.05]		16.88
Performance-based measurement type				6.53*	
Forced-choice non-adaptive reward tasks	8	−.09	[−.19, .01]		0.00
Effort discounting tasks	2	−.44**	[−.64, −.20]		0.00
Progressive Ratio tasks	3	−.12	[−.31, .08]		36.28
Negative symptom measure generation – overall motivation				23.35***	
First-generation	43	−17***	[−.21, −13]		51.92
Second-generation	11	−38***	[−.45, −31]		66.19
Negative symptom measure generation – self-report motivation				25.38***	
First-generation	34	−18***	[−.22, −.14]		58.37
Second-generati on	6	−.45***	[−.54, −.36]		68.33
Negative symptom measure generation – performance-based motivation				4.02*	
First-generation – performance-based motivation	10	−.10*	[−.20, −.004]		0.00
Second-generation – performance-based motivation	6	−.26***	[−.38, −.14]		45.51
Negative symptom individual measures – overall motivation				24.54***	
Brief Psychiatric Rating Scale – Negative symptom factor	7	− 22***	[−.31, −13]		69.80
Scale for the Assessment of Negative Symptoms	12	−12***	[−.18, −.05]		30.82
Positive and Negative Syndrome Scale – Negative symptom factor	27	−.21***	[−.26, −.16]		54.32
Negative Symptom Assessment	1	−.11	[−.31, .09]		0.00
Brief Negative Symptom Scale	5	−39***	[−.52, −.23]		67.64
Clinical Assessment Interview for Negative Symptoms	6	−.36***	[−.44, −.27]		71.51
Motivation domain				6.86*	

Moderator	*k*	*r*	95% CI	Q_b	I^2
Amotivation	24	−22***	[−.26, −.17]		70.90
Intrinsic motivation	14	−.12**	[−.20, −.04]		5.94
Extrinsic motivation	3	−.06	[−.23, .11]		33.05
Continuous moderators	***k***	***B***	**95% CI**	***z***	I^2
Mean age	46	.00	[−.01, .01]	.46	54.37
Mean illness length	23	.00	[−.01, .01]	−.04	37.59
Mean CPZ equivalent doses	20	.00	[.00, .00]	−.03	0.00[a]
% female	46	−.01	[−.01, .00]	−1.60	51.17
% schizophrenia diagnosis	41	.00	[.00, .00]	−.82	33.41

Note. *k* = number of studies; *r* = correlation, 95% CI = 95% confidence interval; Q_b = *Q*-statistic statistically comparing effect sizes between groups; I^2 = extent of the heterogeneity; *B* = regression coefficient; z = test for statistical significance of regression coefficient; CPZ = chlorpromazine equivalent doses.

[a]The subset of studies that reported CPZ equivalent doses has an $I^2 = 0.00$.

*$p < .05$.

**$p < .01$

***$p < .001$