Appendix 1. Research priorities identified by workshop participants through the on-line survey (Step 1/Group A)

Measurement	**Neurobiology**	**Treatment**
Validate existing standardized anxiety measures to address the overlap between ASD and anxiety symptoms.	Understand the unique physiological and neurological expression of anxiety in ASD (e.g., amygdala function, amygdala/prefrontal cortex connectivity, valid and reliable peripheral nervous system biomarkers)	Understand whether psychological mechanisms that underpin anxiety (e.g., cognitive rigidity, intolerance of uncertainty, emotion dysregulation) will respond to treatment
Develop valid measures for non-verbal individuals and individuals with intellectual disability	Identify biological targets that can be incorporated into intervention studies to accompany behavioral measures of change (e.g., is abnormal connectivity amenable to psychological treatment)	Develop treatments to target specific populations (e.g., minimally verbal children, adults, those with ASD/ID, preschoolers)
Define "atypical" anxiety and validate measures to assess for it	Include well-characterized samples of individuals with ASD and clinical control groups such as those with anxiety disorders	Identify how ASD symptoms affect treatment response
Develop objective measures of anxiety (e.g., behavioral paradigms, physiological tools)	Examine whether increased anxiety is a problem of enhanced fear acquisition or delayed fear extinction	Implement evidence-based practice to real world contexts
Examine the role of emotional dysregulation in the development and maintenance of anxiety.	Link ASD and anxiety research with RDoC and broader transdiagnostic initiatives	Explore transdiagnostic approaches to treatment (e.g., mindfulness based interventions)
Develop measures that more accurately reflect the nature of worries, e.g., perfectionism and intolerance of		Examine whether the same treatments are effective in reducing DSM anxiety disorders as well as “atypical" anxiety

uncertainty.		
Measure comorbidity and suicide rates associated with anxiety		Examine whether changing the educational environment reduces anxiety rather than treatments that target the child
A better understanding of self-report and parent report anxiety questionnaires (e.g., test-retest reliability and reliability between parent and child reports).		Conduct treatment trials that examine the efficacy of meds vs. combination treatments (e.g., medications + CBT)

ASD: autism spectrum disorder, ID: intellectual disability; RDoC: research domain criteria; CBT: cognitive behavioral therapy; DSM: Diagnostic and Statistical Manual

Appendix 2. Questions for each research priority

Measurement Research Priority #1: To validate existing standardized anxiety measures to address the overlap between autism spectrum disorder (ASD) and anxiety symptoms

1. What is the factor structure of anxiety measures in ASD and how are they similar to people with anxiety disorders without ASD?
2. Do existing measures of ASD or anxiety show measurement invariance in typically-developing (TD) vs. ASD populations?
3. What is the relationship between observational measures, clinician interview, and physiological measures for anxiety in ASD?
4. What are the differences of existing standardized anxiety measures between well-characterized samples of ASD + anxiety, ASD-anxiety, and TD + anxiety groups?
5. Examine self vs. other (e.g., parent) report of anxiety to determine discrepancies in ASD
6. What factors are distinct when comparing measures of ASD and of anxiety?
7. Do existing measures for anxiety in ASD capture the full range of anxiety symptoms in ASD (e.g., atypical anxiety)?

Measurement Research Priority #2: To develop objective measures of anxiety (e.g., behavioral paradigms, physiological tools)

1. Can cognitive measures (e.g., dot probe, emotional stroop test) identify what processes not only correlate with clinical anxiety, but predict anxiety longitudinally?
2. Can anxiety be assessed using a structured behavioral observation measures (i.e., similar to the Autism Diagnostic Observation Schedule)?
3. Are there differences in biophysiological measures between different anxiety triggers (e.g., social, phobia, sensory)? Do these responses correlate with standardized assessment tools?
4. Is there a behavioral or psychological mechanism that is an early indicator of anxiety in TD youth and does it map onto anxiety in ASD?
5. Can we use physiological measures to capture anxiety during an in vivo anxiety triggering experiences (e.g., playing with peer on playground)?
6. Is anxiety reflected in the same biophysiological mechanisms in ASD and TD populations?
7. To what degree do physiological measures of anxiety converge?
8. Do fear conditioning paradigms capture anxiety in ASD?

Measurement Research Priority #3: To examine the role of emotional dysregulation in the development and maintenance of anxiety

1. What are the risk factors that moderate the relationship between emotion dysregulation (ED) and anxiety?
2. Is there a relationship between parental ED and child anxiety levels in the ASD population?
3. Are there early dispositional traits or biomarkers that predict the emergence of ED and anxiety?

4. How do measures of emotional dysregulation relate to a failure to habituate to uncertainty in individuals with ASD and anxiety?
5. Does targeting ED in treatment decrease anxiety?
6. Does difficulty identifying one's own emotions cause uncertainty and anxiety in individuals with ASD?
7. Do attention regulation difficulties mediate the association between ER and anxiety in ASD?
8. Does the level of ED impact anxiety severity?
9. Are there certain subgroups in the ASD population that are of particular risk for heightened ED and heightened anxiety? Does cognitive functioning level play a role in this relationship?
10. How do potentially age-appropriate emotion regulation strategies (e.g., escape) actually maintain anxiety in later ages?
11. Is emotional dysregulation a vulnerability marker for anxiety?

<u>Neurobiology Research Priority #1: To understand the unique physiological and neurobiological expressions of anxiety</u>

1. Are there distinct neurobiological correlates of different subtypes of anxiety (typical/atypical) in ASD?
2. Are changes in reward circuitry and social motivation in ASD associated with a reduction in anxiety symptoms?
3. Is there an identifiable peripheral nervous system biomarker of anxiety and ASD and if so which measure or combination of measures captures it most reliably?
4. Can we test the hypothesis that the high prevalence of anxiety in ASD is due to delayed habituation and develop behavioral and neural paradigms to pursue this investigation?
5. Are there validated behavioral paradigms to look at the role of various stresses response systems (e.g., HPA axis versus sympathetic activity) in ASD/anxiety versus TD/anxiety groups?
6. Can we identify early biomarkers that reflect early atypical arousal responses that will later predict anxiety in ASD?
7. What differences exist in terms of frontal-limbic connectivity in ASD and TD individuals with anxiety (both structural and functional connectivity and developmental differences)?
8. How are patterns of insula activity related to anxiety in individuals with ASD? Could there be a greater role for insula activity in youth with anxiety and ASD given its role in interoceptive processing, awareness, and disgust?
9. Are different physiological markers related to different factors (e.g., intolerance of uncertainty) that contribute to anxiety in ASD and TD youth?
10. Is biology/physiology differentially responsive to exposure (habituation) in ASD? How long does it take those with ASD to return to baseline after being startled?
11. Do differences in prefrontal cortex function map onto changes in effortful control and emotion regulation symptoms in anxiety? Do differences in amygdala function map onto task-based avoidance/fear and physiological symptomatology?

Neurobiology Research Priority #2: To identify physiological/neurobiological targets related to treatment response

1. Are there shared and ASD-unique attentional biases in response to threat in ASD and how do they compare with attention bias in other disorders (i.e., repetition related), TD individuals with and without anxiety disorders?
2. Are differences in physiological and neurobiological correlates of anxiety (e.g., amygdala-prefrontal connectivity, heart rate variability. cortisol, startle, attention bias) susceptible to change in response to treatment? If so, are these changes enduring? How do they relate to other measures of anxiety (e.g., self-report)?
3. Are there changes in the prefrontal cortex as result of utilizing cognitive and emotional strategies?
4. Do acute stress responses related to anxiety triggers respond to treatment (e.g. cortisol stress response)?
5. Does a more pronounced baseline startle response predict less favorable treatment outcome?
6. Could we use physiological markers (e.g., skin conductance) to examine avoidance and escape responses during behavioral paradigms?
7. Can the use of galvanic skin response or heart rate be used to predict responders are nonresponders to treatment?
8. Are biofeedback treatment methods effective in ASD populations?
9. Is an abnormal habituation response amenable to change via cognitive behavioral therapy (CBT) protocols with heavy emphasis on exposure?

Neurobiology Research Priority #3: To examine transdiagnostic constructs related to anxiety in ASD

1. Do repetitive behaviors serve a similar function in ASD versus obsessive-compulsive disorder (OCD) - what are the distinctive and differentiating features between repetitive behaviors differentiating ASD and OCD?
2. Are there differences in amygdala function for children with ASD and typical anxiety in comparison to atypical anxiety?
3. In large samples, do we see consistent versus heterogeneous findings in amygdala function (in one direction or another) in those with ASD versus those with ASD and anxiety versus those with anxiety only (assuming we can differentiate these groups).
4. Is the expression of anxiety (behaviorally/physiologically) different across the ASD spectrum and across clinical conditions (ASD versus schizophrenia versus specific anxiety disorders, etc.)?
5. Are underlying neurophysiological processes similar or different in people with ASD and anxiety/versus depression/versus those with externalizing difficulties?
6. Can there be subtypes of anxiety that map on to research domain criteria (RDoC) criteria as identified by neurobiological responses to a given paradigm?

7. How do transdiagnostic constructs (e.g., rigidity, alexithymia) relate to ASD + anxiety and ASD - anxiety?
8. How do physiological measures differ in different ASD subgroups? For instance, does a physiological measure index anxiety differently and mean something qualitative different in those with ASD + anxiety versus those with ASD + anxiety + attention-deficit hyperactivity disorder (ADHD) for example?

Treatment Research #1: To understand whether psychological mechanisms that underpin anxiety (e.g., cognitive rigidity, intolerance of uncertainty, emotion dysregulation) respond to treatment

1. Does CBT ameliorate alexithymia in anxiety?
2. Does the relationship between fear of negative evaluation and anxiety change over the course of treatment?
3. What is the role of awareness of social skills deficits in treatment?
4. How does intolerance of uncertainty affect response to treatment?
5. Can we effectively treat anxiety maintaining cognitions in ASD?
6. Do relaxation techniques influence emotional regulation?
7. Does early intervention improve cognitive flexibility and emotional regulation?
8. Are specific treatment modalities more effective in treating specific psychological mechanisms (e.g. 3rd wave therapies target emotional regulation)?

Treatment Research Priority #2: To identify how ASD symptoms affect treatment response

1. What ASD symptoms (e.g., presence of sensory deficits, attention bias, higher order repetitive behaviors, low social motivation, cognitive inflexibility, alexithymia) correlate with treatment outcomes?
2. Do atypical anxiety features make CBT less effective?
3. How do sensory sensitivities impact on the ability of individuals with ASD to utilize mindfulness strategies?
4. How do rigidity and impaired self-awareness impact treatment response?
5. Are some treatment modalities (e.g., CBT vs acceptance and commitment treatment or ACT) more acceptable to ASD youth?
6. What is the role of executive functioning in treatment response? Does is affect patient motivation/treatment acceptability?
7. Does family history of ASD (e.g., simplex versus multiplex) affect treatment response?
8. Are certain ASD symptoms more or less responsive to treatment?
9. Do children with ASD develop therapeutic rapport and does this affect treatment outcome?

Treatment Research Priority #3: To implement evidence-based practice to real world contexts

1. Can CBT be utilized as a prevention strategy in school-age children with anxiety and ASD?
2. Can small clinical programs implement group CBT? What are the barriers?

3. Can individuals with ASD benefit from non-ASD specific, non-manualized mental health treatments?
4. What is the feasibility and sustainability of current CBT models for implementation in schools?
5. What is the optimal level of training and supervision needed to implement CBT effectively?
6. How do treatments for anxiety in ASD need to be adapted across cultures?
7. How long do clinicians continue to meet fidelity after training in a specific intervention?
8. Can self-help programs be effective for treating anxiety the ASD population?
9. Can computer based approaches yield treatment benefits as a standalone or augmentative treatment for anxiety in the ASD population?
10. What are the differences in efficacy between individual vs. group and telehealth vs. in-person treatment for anxiety in ASD?
11. How much can therapy fidelity deviate from manualized interventions without reducing outcomes for anxiety in ASD?
12. How does varying the length of manualized treatments affect outcomes for treating anxiety in ASD?

Appendix 3. Research priorities offered by participants in the expert group (n=7)

Measurement	
	Measurement of anxiety in young children
	Measurement of anxiety in children with intellectual disability
	Subjective perceptions of anxiety in youth with ASD
Treatment	
	School-based interventions to decrease impact of anxiety in ASD [a]
	Family based interventions to treating anxiety and mood problems in ASD
	Interventions to prevent the development of anxiety and trauma related symptoms
	Treatment of anxiety for ASD levels 2 and particularly level 3 [a]
	Interventions for individuals with intellectual impairment and ASD [a]
Other	
	Role of adverse life events and trauma in the development of anxiety
	Identification of risk factors for development of anxiety
	Links between anxiety and depression
	Long term outcomes of anxiety

[a]These priorities were part of the initial list of priorities by Group A in the 'research priorities' survey. The remaining nine priorities are new.
ASD: autism spectrum disorder