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Research paper

Examining anxious temperament in anorexia nervosa: Behavioural inhibition and intolerance of uncertainty and their contribution to trait anxiety in adolescents with anorexia nervosa

Lot C. Sternheim [a,*], Jojanneke M. Bijsterbosch [a], Mirjam C.M. Wever [b], Annemarie A. van Elburg [a], Guido K.W. Frank [c]

[a] Department of Clinical Psychology, Utrecht University, the Netherlands
[b] Department of Clinical Psychology, Leiden University, the Netherlands
[c] Department of Psychiatry, University of California San Diego, USA

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ABSTRACT

Background: Anorexia nervosa (AN) is a serious and complex psychiatric disorder yet treatment results are suboptimal. Insight into the etiology of this illness is much needed. Research highlights the implication of anxiety-related traits in the development and maintenance of AN. This study investigates firstly, behavioural inhibition and intolerance for uncertainty (IU) in adolescents with and without AN, and secondly relations between these traits.

Methods: In a cross-sectional study, 165 adolescent girls (AN = 94, HC = 71) completed questionnaires measuring behavioural inhibition, IU and trait anxiety. ANOVAs tested differences between AN and HC groups, and mediation models with IU as a mediator between behavioural inhibition and trait anxiety were run.

Results: AN adolescents reported significantly higher levels of behavioural inhibition, IU and trait anxiety compared to their peers. In both AN and HC, a direct and a total effect of behavioural inhibition on trait anxiety was found. However, only in the AN group IU partially mediated the relation between behavioural inhibition and trait anxiety.

Limitations: Data is cross-sectional and longitudinal studies are required. A mean illness duration of nearly 2 years may mean early effects of malnourishment and habituation and future studies should include patients with shorter illness duration.

Conclusions: Results highlight that behavioural inhibition and IU may contribute to anxiety in AN whilst their peers may have developed better executive and social-emotional skills to manage uncertainty. Adolescents with AN may benefit from interventions targeting behavioural inhibition and IU.

1. Introduction

1.1. Anorexia nervosa

AN is characterized by a restriction of energy intake, weight loss, fear of weight gain and distorted body image (APA, 2013). Whilst prevalence rates of AN are relatively low (1–4 %, Hoek, 2016), this devastating disorder has among the highest mortality rates of all psychiatric disorders and suicidality is common (Arcelus et al., 2011). AN-related psycho-social consequences are severe, with individuals with AN report a low quality of life (Sy et al., 2013; Treasure et al., 2020 (Importantly, the prognosis for AN is poor, with high rates of relapse and with up to 20 % of patients developing a chronic course (Dobrescu et al., 2020; Hay et al., 2012; Smink et al., 2012). Unfortunately, current treatments are suboptimal, which may be contributable to our still poor understanding of the disorder's etiology and to the relative scarcity of evidence-based theoretical models for AN (Van den Berg et al., 2019). This scarcity is likely a consequence of the complicated interplay between biological, socio-cultural and psychological factors in AN (Crow et al., 2009).

Recently, a temperament-based treatment for AN has been proposed (Kaye et al., 2015), based upon a growing body of empirical evidence highlighting the importance of certain temperamental traits for the

* Corresponding author at: Department of Clinical Psychology, PO Box 80140, 3508 TC Utrecht, the Netherlands.
E-mail address: L.C.Sternheim@uu.nl (L.C. Sternheim).

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development and maintenance of AN. Temperament Based Therapy (TBT; Kaye et al., 2015) aims to increase the development of AN-focused constructive coping strategies on the one hand and to focus on carer-focused strategies to manage these temperament traits on the other. Kaye and colleagues describe 3 groups of temperament constructs; 1) anxiety; 2) reward insensitivity; and 3) interoceptive awareness. The current study focusses on two key anxious temperamental traits, namely behavioural inhibition and intolerance of uncertainty (IU) in adolescents with and without AN.

Investigating temperament traits in adolescents is particularly valuable, as the peak of onset in AN is during adolescence, when the brain is still very much developing. This means that at that stage the neural pathways that process emotion regulation and executive function and which integrate life experience with temperament and behavioural traits to form character and personality are still very much in development. Moreover, earlier in the illness the starvation effects are relatively minimal.

Whilst the rather elaborate TBT incorporates a large number of traits, identifying key factors and drivers will allow for a more focused and efficient treatment approach. Additionally, the current study aims to investigate how these traits relate to levels of anxiety in both groups. For our clinical practice, understanding relations between behavioural inhibition, IU and anxiety in AN is important as it will allow us to modify intervention objectives and treatment methods to target anxiety in AN.

1.2. Anxiety in anorexia nervosa

For those clinically working with AN patients, it is evident that anxiety is inherent to AN. Patients with AN frequently report an overwhelming fear of eating and weight gain (APA, 2013; Steinglass et al., 2011). Additionally, patients often report anxieties that are not specific to AN but relate to a much wider scope and may include symptoms of social anxiety, trauma-related anxiety and frequently generalized anxiety (i.e., school performance, interpersonal relations, health; Sternheim et al., 2012; Thornton et al., 2011). Indeed, comorbidity with anxiety disorders is up to 80 %, with 20–30 % for generalized anxiety disorder (GAD), and > 50 % for social anxiety disorder (Giovanni et al., 2011; Ulfvebrand et al., 2015). Moreover, biological studies confirm a shared genetic variation between anxiety disorders and AN (Dellava et al., 2011).

Whilst for some AN patients levels of anxiety seem to ameliorate with weight recovery and during AN treatment, for a large group of patients levels of anxiety remain unacceptably high, even after (weight) recovery, or are even perceived as heightened compared to the underweight state (Kezelman et al., 2015). Moreover, research shows that anxiety disorders often are present before the onset of AN (Dellava et al., 2011; Godart et al., 2000; Swanson et al., 2011). In other words, for a group of AN patients, anxiety may be present independent of AN and starvation, and as such be contributable to a so-called pre-morbid anxious temperament. Importantly, higher levels of anxiety are associated with a higher treatment drop-out rate and poorer outcomes (Lockwood et al., 2012). Thus, a better understanding of anxiety and anxious temperamental traits in AN is urgently required and may pave the way for innovative interventions for AN.

1.3. Anxiety traits in AN

Anxiety-related personality characteristics are common in those with AN, i.e., a need for certainty and control, harm avoidance, worry, cognitive avoidance and avoidance behaviour (Frank et al., 2012; Pallister and Waller, 2008). A handful of studies have examined anxious traits in AN and show that compared to those without eating disorders, individuals with AN report higher levels of harm avoidance and lower self-directedness as well as novelty seeking (Buelens et al., 2020; Frank et al., 2012; Klump et al., 2000; Marzola et al., 2017; Marzola et al., 2020). Neurobiological studies confirm the relevance of these anxious personality traits and relay them to altered function of executive dorsal caudate (DC) and limbic regions, including altered dopamine (DA) and serotonin (5-HT) function (Kaye et al., 2013). Further evidence of the importance of anxiety-related (brain) processes in AN is that research has found increased fear learning (i.e. a faster response to associating fear with a stimulus in a conditioning experiment) in those with AN, similar to those with anxiety disorders (Cardi et al., 2019).

Despite the relevance of these temperamental and personality traits and high levels of anxiety comorbidity (Kaye, 2000; Riquin et al., 2021), the anxious temperament in AN is understudied with regard to course and outcome of AN. The handful of available studies confirm relations between an anxious temperament and altered eating psychology in AN (Jérolon et al., 2022; Marzola et al., 2020). Anxious traits are associated with core AN body-related psychopathology such as eating restraint and eating, shape, and weight concerns (Jérolon et al., 2022; Marzola et al., 2020), and with lowest lifetime BMI (Marzola et al., 2020). One other study showed that anxiety-related personality traits are still present in individuals with AN after recovery (Wagner et al., 2006).

The majority of studies into temperament in AN are conducted in adults. Whilst very little data is available for adolescents with AN, one study found evidence of anxiety traits in the form of high harm avoidance in adolescents with AN (Buelens et al., 2020). A second study shows associations between intolerance of uncertainty and weight and shape concerns in adolescents with AN (Bijsterbosch et al., 2021). It has been suggested that long-term malnourishment and anxiety are reciprocal processes, and consequently, maintain each other (Mattar et al., 2011). It is thus an important step to investigate the anxious temperament in patients with a relatively short duration of illness (i.e. adolescents) as in this group the effects of AN are less ingrained and less habitual. In this study we focus on two key anxious traits, namely behavioural inhibition and IU, in adolescents with and without AN.

1.4. Behavioural inhibition in AN

Behavioural inhibition is a child temperamental trait characterized by a fearful reactivity to novelty, uncertainty and ambiguity; this is expressed in a relatively consistent pattern of behavioural and emotional responses to unfamiliar people and novel stimuli and situations (i.e., motivated avoidance of aversive experiences) (Kagan et al., 1984). This may be driven by a physiological vulnerability at birth for a lower activation threshold of the sympathetic nervous system, whereby those children with high behavioural inhibition require less intense stimuli (e.g., situations that are novel or uncertain) than children with lower behavioural inhibition to activate this system (Kagan et al., 1987). Children high in behavioural inhibition tend to avoid novel situations and appear to be very shy when meeting new people. Higher levels of behavioural inhibition in childhood have been acknowledged as a risk factor for anxiety and anxiety disorders in both childhood and adolescence (Lahat et al., 2011). Research shows an increased prevalence of anxiety disorders among children who are behaviorally inhibited and higher behavioural inhibition in childhood is associated to higher levels of psychopathology in adulthood (Hirshfeld-Becker et al., 2008; Muris et al., 2011).

Various studies confirm high levels of self-reported behavioural inhibition in adults with AN (Harrison et al., 2011; Harrison et al., 2011; Jappe et al., 2011). Clinically, we observe behavioural inhibition in individuals with AN in that they often evaluate new stimuli and situations as fearful and unpleasant and that they employ both cognitive and behavioural avoidance strategies when faced with novelty. These avoidant behaviours typically interfere when AN treatments require patients to engage in new situations. Additionally, behavioural inhibition seems to be of stable nature in adults: One study found that after specialized outpatient treatment for AN adults self-reported behavioural inhibition scores did not change (Harrison et al., 2016). These behavioural data are supported by brain studies highlighting an important role for neural correlates of behavioural inhibition in adults with AN (e.g. impaired

inhibitory control; Kullmann et al., 2014). Regarding adolescents with AN, there is a lack of research into behavioural inhibition. One study using a self-report measure of behavioural inhibition in adolescents and young adults found higher levels of behavioural inhibition in those with AN compared to non-ED controls (Matton et al., 2013). More data on behavioural inhibition in adolescents with AN is much needed.

1.5. Behavioural inhibition, intolerance of uncertainty and anxiety

A second anxiety-related trait that may be important in understanding anxiety in AN is intolerance of uncertainty (IU), which refers to "*The tendency to react negatively to uncertainty on cognitive, behavioral, and emotional levels*" (Dugas et al., 1998). IU has been defined as a tendency to overestimate the possibility of threat and severity of this threat (Grupe and Nitschke, 2013; Gu et al., 2020). Indeed, individuals with high IU interpret stimuli more often as uncertain and evaluate this uncertainty as more negative than individuals with low IU (Carleton et al., 2007; Dugas et al., 2005; Heydayati et al., 2003). IU is considered a temperamental personality trait and a key contributor to anxiety. Originally studied in the context of GAD, a wealth of research confirms IU as a transdiagnostic factor across anxiety and other psychological disorders in both adults and adolescents (Carleton et al., 2012; Carleton, 2016; Osmanağaoğlu et al., 2018).

Our understanding of how IU arises is limited, however, a recent study suggested that behavioural inhibition may play a role in the development of IU (Zdebik et al., 2022). Namely, children with behavioural inhibition are at increased risk to react intensely to novel or uncertain situations at a physiological level. However, as they tend to avoid these uncertain and novel situations, in order ease their initial anxious reaction, they curb the habituation to such situations. Consequently, these children do not build on their experiences to disconfirm their fear for novelty and uncertainty. In fact, they hold on to their strong beliefs that the world is uncertain and threatening, which in turn places the child at risk for IU (as these beliefs forms the core of IU). Indeed, a longitudinal study showed that higher behavioural inhibition at the age of 6 years old was associated to higher IU when they were 21 years old (Zdebik et al., 2018). Additionally, IU may mediate the relation between BI and anxiety. Namely, IU is key in how novel and uncertain stimuli are processed and evaluated.

It has been suggested that both intrinsic and extrinsic factors may moderate the relation between behavioural inhibition and anxiety (Lahat et al., 2011). These may include executive functions such as attention shifting and attention biases, inhibitory control, learning processes, and coping strategies such as self-monitoring. Research on adults with AN shows abnormalities in these functions (Hirst et al., 2017; Villa et al., 2009), and there is some evidence of these abnormalities in adolescents (Hirst et al., 2017; Sternheim et al., 2021). So, whilst for the HC group well-developed executive functions may ameliorate the effect of behavioural inhibition on anxiety, for adolescents with AN, impairments in these areas may in fact create a vulnerability for associations between behavioural inhibition, IU and anxiety.

1.6. Intolerance of uncertainty in AN

IU seems to be a prominent factor in those with AN; studies report elevated levels of IU in individuals with AN, and higher IU is associated to more severe AN pathology (Brown et al., 2017; Bijsterbosch et al., 2022; Frank et al., 2012; Kesby et al., 2017). In a qualitative study, AN patients described a severe dislike for uncertainty; their attempts to avoid uncertainty at all costs and their engaging in AN behaviours to reduce uncertainty (Sternheim et al., 2011). One study found that higher IU was associated to higher anxiety in AN (Sternheim et al., 2015). Research into IU in adolescents with AN is more scarce; in one qualitative study adolescents with AN reported perceiving uncertainty as something negative and associating a lot of anxiety and stress with uncertainty (Konstantellou et al., 2019). Similar to adults, adolescents described how ED behaviours were given a functional role in reducing uncertainty. Two quantitative studies found that higher levels of IU were associated to more weight and shape concerns (Bijsterbosch et al., 2021). A third study found levels of IU comparable to adults with IU (Sternheim and Harrison, 2018). To our knowledge there is no study examining the contribution of IU to anxiety in adolescents with AN.

1.7. The current study

This study aimed to study interactions of anxiety related traits in AN in order to determine which traits drive other traits so as to ultimately develop a mechanism model of anxiety in AN. Results can be utilized to inform and adapt clinical interventions for anxiety in AN. These interventions may include the TBT (Kaye et al., 2015), but also other treatment schedules such as cognitive-behavioural techniques (i.e. exposure; Steinglass et al., 2011) or pharmacological approaches. Specifically, we examine two key anxiety temperament factors in adolescents with AN; behavioural inhibition and IU, and their relation with anxiety. It has been suggested that behavioural inhibition in childhood may increase the risk for IU (Zdebik et al., 2018) and is a powerful predictor for anxiety disorders in youth (Johnson et al., 2003). Moreover, previous research shows IU to play a mediating role between various psychological and concepts (e.g. looming cognitive style; Carnahan et al., 2021) and anxiety, and seeing that IU is key in how novel and uncertain stimuli are processed and evaluated, it is likely that IU mediates the relation between behavioural inhibition and anxiety.

1.8. Aims of the study

In this study we investigated behavioural inhibition, IU, and trait anxiety in adolescents with AN. First, we hypothesized that adolescents with AN report higher levels of behavioural inhibition, IU and trait anxiety compared to their peers without AN. Second, we examined the mediating role of IU in association between behavioural inhibition and trait anxiety in both adolescents with and without AN. In the AN group, we expected that higher levels of behavioural inhibition and higher levels of IU would be associated to higher levels of trait anxiety. Additionally, a positive indirect association between behavioural inhibition and trait anxiety through IU was expected. For the HC group we expected higher that levels of behavioural inhibition and higher levels of IU would be associated to higher levels of trait anxiety but that there would be no mediating effect of IU on the relation between behavioural inhibition and anxiety.

2. Methods

2.1. Participants

Participants were recruited from two different sites (the Netherlands - NL, United States of America - USA). Elaborate description of study groups has been described in a previous paper (Sternheim et al., 2021).

NL sample: adolescents with a current diagnosis of AN according to DSM 5 criteria were recruited from a Dutch specialized eating disorders center (AN-NL group). Healthy control (HC) adolescents were recruited in the Utrecht (NL) area through local advertisement flyers posted in a number of high schools, sports clubs and community centers (HC-NL group).

USA sample: adolescents with a diagnosis of AN (AN-USA group) were recruited through an eating disorders program at a children's hospital and a specialized eating disorder center. HC (HC-USA group) were recruited through local advertisements in the Denver metropolitan areas (USA).

This study was approved by the respective Dutch or USA (medical) ethical committee or institutional review board. All participants received information and signed informed consent prior to the start of the study.

2.1.1. Assessment measures

Demographic variables such as age and BMI were collected for all participants, and age of start illness and duration of illness in addition for the AN sample.

2.1.2. BMI

The NL-AN group's BMI was assessed before participation, by measuring weight on a digital Tanita scale (Tanita Cooperation of America, Inc., Arlington Heights, IL) and height with a stadiometer. The NL-HC group's BMI was assessed by asking participants to state their height and weight. All BMI were then calculated into kg/m2 using CDC.gov BMI calculator (BMI Calculator Child and Teen | Healthy Weight | CDC).

The USA-AN group's BMI (kg/m2) was obtained from their hospital chart (weight was measured on a digital scale daily). The weight date was on the day of the testing session, which was between 1 and 2 weeks into treatment. The USA-HC group's BMI (kg/m2) was assessed immediately before the testing session by weighing them on a digital Detecto scale (Detecto, Webb City, Missouri) and measuring their height with a Seca stadiometer.

2.1.3. Behavioural Inhibition

Behavioural inhibition was assessed with the Behavioural Inhibition subscale (BIS) of the BIS/BAS scales (Carver and White, 1994). The BIS contains 7 items with a total score ranging from 4 to 28 points. Each statement is rated on a 4-point Likert-type scale ranging from 1 (very false for me) to 4 (very true for me). An example of an item is "If I think something unpleasant is going to happen, I usually get pretty 'worked up'". The BIS is well validated and provides good test-retest reliability (Campbell-Sills et al., 2004). In the present sample a Cronbach's alpha of 0.70 was found, which is considered adequate reliability.

2.1.4. Intolerance of uncertainty

Intolerance of Uncertainty was assessed with the Intolerance of Uncertainty Scale-12 (Carleton et al., 2007). The items are rated on a 5-point Likert scale ranging from 1 (not at all characteristic of me) to 5 (entirely characteristic of me) with higher scores of IU indicating higher levels of IU. Examples of items include "Uncertainty makes me uneasy, anxious, or stressed", "Unforeseen events upset me greatly". The IUS-12 has good convergent and discriminant validity and good test-retest reliability (Buhr and Dugas, 2002). In the present sample a Cronbach's alpha of 0.90 and was found which is deemed excellent.

2.1.5. Anxiety

Anxious traits were assessed with the Trait subscale of the Spielberger State and Trait Anxiety Inventory (STAI; Spielberger, 1989). The STAI-trait has 20 items that are rated on a 5-point Likert scale ranging from 1 (not at all characteristic of me) to 5 (entirely characteristic of me) with higher scores representing higher levels of trait anxiety. Items include "I worry too much over something that really doesn't matter." In the present sample a Cronbach's alpha of 0.95 was found which is deemed excellent.

2.2. Data analyses

Outliers, multicollinearity and other assumptions were checked. Statistical analyses were performed using IBM SPSS Statistics Version 26 (IBM Corp., 2019) and PROCESS for SPSS v3.0 (Hayes, 2017). Scores on IUS, BIS and STAI-T were normally distributed.

Pearson correlation coefficients were calculated to analyse bivariate associations between the study variables. Before combining the AN groups and the HC groups, ANOVAs were carried out within the AN and HC groups to test for differences between USA and NL groups on clinical and model variables. Then, ANOVAs were run to test for differences between AN and HC on clinical and model variables. Thirdly, a mediation analysis with behavioural inhibition as predictor, IU as mediator and trait anxiety as outcome was conducted. The mediation analysis comprises the following steps (Hayes, 2017): First, in order to estimate the unique effects of behavioural inhibition on IU, a multiple regression analysis was calculated. Second, a hierarchical regression analysis was calculated in order to estimate the unique total effects of behavioural inhibition (Step 1) and the unique direct effects of behavioural inhibition as well as IU (Step 2) on trait anxiety. Third, the unique indirect effects of behavioural inhibition on trait anxiety through IU were determined by means of bootstrap analyses with 5000 bootstrap samples (Hayes, 2017). Standardized coefficients are reported.

3. Results

A total of 214 participants entered into the study. After excluding those who did not have complete datasets ($n = 49$) the total number of participants was 165 (AN $n = 94$, HC $n = 71$; see Table 1). All participants were CIS females. In terms of ethnicity, the NL sample consisted of Caucasian participants only. In the USA AN sample there were 1 Latino, 1 American Indian, 2 Asian and 72 Caucasian (non-Hispanic) participants. In the USA HC sample there were 5 Latino, 5 African American and 45 Caucasian (non-Hispanic) participants. In terms of education, for participants in the NL sample, school years varied between 6 and 12 years, with nearly 55 % of AN participants and 40 % of HC participants having completed at least 10 years of education. In the USA participants the number of school years varied from 6 to 12 years, with nearly 63 % of AN participants and 43 % of HC participants having completed at least 10 years of education.

3.1. Group differences USA vs NL

ANOVA's confirmed no significant differences between USA and NL participants on clinical or study variables.

3.2. Group differences AN vs HC

ANOVAs showed significant differences between the AN and HC groups on BMI, BIS, IUS, STAI with the AN participants reporting higher behavioural inhibition, higher intolerance of uncertainty and higher trait anxiety (see Table 1). As expected, AN participants had lower BMI. The AN group was slightly older than the HC group, but controlling for age made no difference to the results.

In the AN group, higher levels of behavioural inhibition were moderately positively associated to higher levels of IU ($r = 0.32$, $p = .002$) and higher levels of trait anxiety ($r = 0.36$, $p < .001$). Higher IU was associated to higher trait anxiety ($r = 0.55$, $p < .001$). In the HC group higher levels of behavioural inhibition were only associated to higher anxiety ($r = 0.33$, $p = .005$), not to higher IU. Higher IU was associated to higher trait anxiety ($r = 0.53$, $p < .001$). BMI, age of onset and illness duration were not associated to scores on the BIS, IUS-12 or

Table 1
Means and standard deviations of the study's variables across groups.

	AN		HC		*F*	*p*	ηp2
	M	*SD*	*M*	*SD*			
Age	15.05	1.67	14.48	1.84	5.44	0.02	0.03
BMI	16.66	1.72	20.55	2.43	142.09	<0.001	0.47
Age of onset[a]	13.17	1.96	–	–	–	–	–
Illness duration[a]	1.83	1.90	–	–	–	–	–
BIS	22.97	4.59	18.92	2.89	41.79	<0.001	0.21
IUS	34.78	10.36	23.82	7.88	55.75	<0.001	0.26
STAI-T	54.27	13.87	31.58	7.72	153.89	<0.001	0.49

Note. BMI = Body Mass Index, BIS = Behavioural Inhibition Scale, IUS = Intolerance of Uncertainty Scale-12, STAI-trait = Spielberger State and Trait Inventory – Trait.

[a] In years.

STAI-T.

3.3. Total, direct, and indirect effects of behavioural inhibition on trait anxiety through IU

In the AN group, the multiple regression analysis revealed a significant effect of behavioural inhibition on IU (see Fig. 1). A total of 10.3 % of the variance in IU could be explained, $F(1, 92) = 10.540$, $p < .002$.

The hierarchical regression revealed in step 1 a significant positive total effect and in step 2 a significant positive direct effect of behavioural inhibition on trait anxiety. This indicates that more behavioural inhibition is associated with more trait anxiety, before and after controlling for IU. Furthermore, step 2 of the hierarchical regression analysis yielded a significant positive effect of IU on trait anxiety, indicating that more IU is associated with more trait anxiety. In step 1, 33.57 % of the variance in trait anxiety could be explained by IU, $F(2, 92) = 22.89$, $p < .001$. In step 2, behavioural inhibition and IU explained a total of 12.7 % of the variance in trait anxiety, $F(1, 92) = 13.37$, $p < .001$.

The bootstrap analyses revealed a significant indirect effect of behavioural inhibition on trait anxiety via IU (0.47; 95 % confidence interval, 0.084–0.956). This indicates that more behavioural inhibition is associated with more trait anxiety through more IU.

In the HC group, the simple regression analysis revealed a non-significant positive effect of behavioural inhibition on IU, indicating that more behavioural inhibition is not associated with more IU. The hierarchical regression revealed in step 1 a significant positive total effect and in step 2 a significant positive direct effect of behavioural inhibition on trait anxiety. This indicates that more behavioural inhibition is associated with more trait anxiety, before and after controlling for IU. Furthermore, step 2 of the hierarchical regression analysis yielded a significant positive effect of IU on trait anxiety, indicating that more IU is associated with more trait anxiety. In step 1, 32.6 % of the variance in trait anxiety could be explained by IU, $F(2, 67) = 16.23$, $p < .001$. In step 2, behavioural inhibition and IU explained a total of 10.9 % of the variance in trait anxiety, $F(1, 68) = 8.30$, $p < .01$.

The bootstrap analyses revealed a non- significant indirect effect of behavioural inhibition on trait anxiety via IU (0.23; 95 % confidence interval, −0.124–0.705). IU thus did not mediate the relationship between behavioural inhibition and trait anxiety in the HC group (Fig. 2).

4. Discussion

The present study investigated the anxious temperament in AN by firstly comparing levels of behavioural inhibition, IU and trait anxiety between adolescents with and without AN. Secondly, we examined the relationships of behavioural inhibition with IU and trait anxiety. More specifically, we examined the mediating role of IU in the relation between behavioural inhibition and trait anxiety. We found that adolescents with AN reported higher levels of behavioural inhibition, IU and anxiety compared to their non-affected peers. Additionally, we found that higher levels of behavioural inhibition and higher levels of IU were associated to more trait anxiety in both groups. Furthermore, as expected, only in the AN group, we found an association between behavioural inhibition and IU and that IU mediated the association between behavioural inhibition and trait anxiety. We found no associations between BMI, age of onset or illness duration and behavioural inhibition, IU and trait anxiety in either group.

Elevated levels of behavioural inhibition, IU and trait anxiety in adolescents with AN are in line with adult studies (Brown et al., 2017; Frank et al., 2012; Matton et al., 2013) and contribute to the growing body of evidence highlighting the importance of these anxiety traits in both adolescents and adults with AN (Jérolon et al., 2022; Kaye, 2000; Marzola et al., 2020). Previous studies link anxiety-related personality characteristics to core AN body-related psychopathology (Frank et al., 2012; Jérolon et al., 2022; Marzola et al., 2020; Pallister and Waller, 2008). Moreover, anxiety and anxiety traits are related to suboptimal executive processes (e.g. social problem solving, implicit learning and decision making) in AN (Adoue et al., 2015; Fornasari et al., 2014; Shott et al., 2012 Sternheim et al., 2021; Sternheim et al., 2020, Van Elburg et al., 2021). Furthermore, anxiety traits seem to play a role in the emotion processing impairments known to AN (Hambrook et al., 2012). Moreover, evidence highlighting the contribution of trait anxiety to neurobiological facets of AN is growing. A scanning study found trait anxiety was directly related to how expectation drives taste stimulus receipt brain response and as such may play an important role in food approach in AN (Frank et al., 2023). So, findings corroborate the importance of anxiety-related traits and suggest a potential benefit of the Temperament Based Treatment (TBT) (Kaye et al., 2015) for individuals with AN, which aims to increase the development of AN-focused constructive coping strategies for managing anxiety traits.

Furthermore, results provide novel insights into the developmental processes of anxiety in adolescents with AN. Higher behavioural inhibition and IU were indeed associated with higher trait anxiety, which confirms literature proposing behavioural inhibition and IU as risk factors for anxiety and anxiety disorders (Carleton, 2016; Lahat et al., 2011). Interestingly, only in the AN group did we find that the relation between behavioural inhibition was enhanced when mediated by IU. This finding may help us strengthen our perspective on a potential developmental model for anxiety in AN. Namely, imagine a child with high behavioural inhibition in early childhood (i.e. an intense physiological response to novelty and uncertainty), who by using behavioural strategies such as the avoidance of novel and uncertain situations embeds strong beliefs that novelty and uncertainty must be negative and threatening (the cognitive IU component). Subsequently, this child

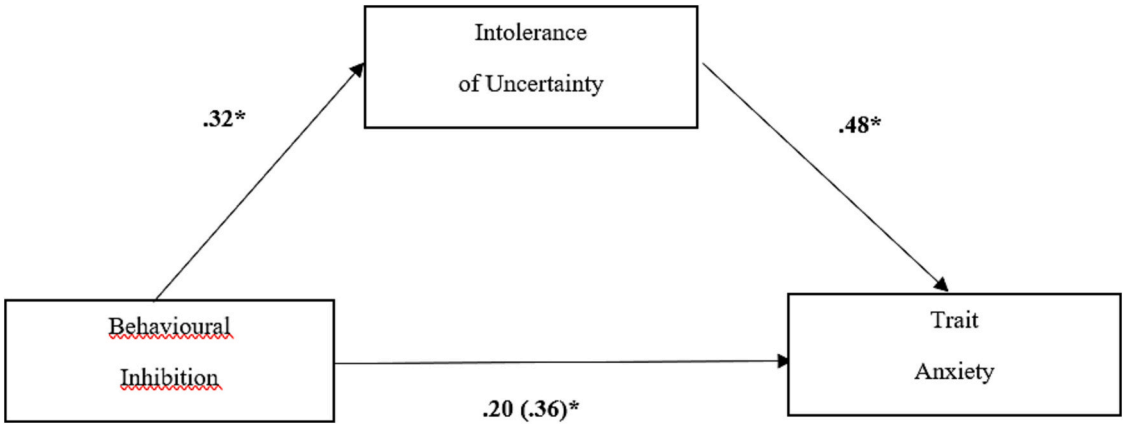

Fig. 1. AN group: significant mediating role of IU on the association between behavioural inhibition and trait anxiety.
N.B. Results of the regression analyses. The total effect derived from step 1 of the hierarchical regression analysis is displayed in parentheses. * $p < .01$.

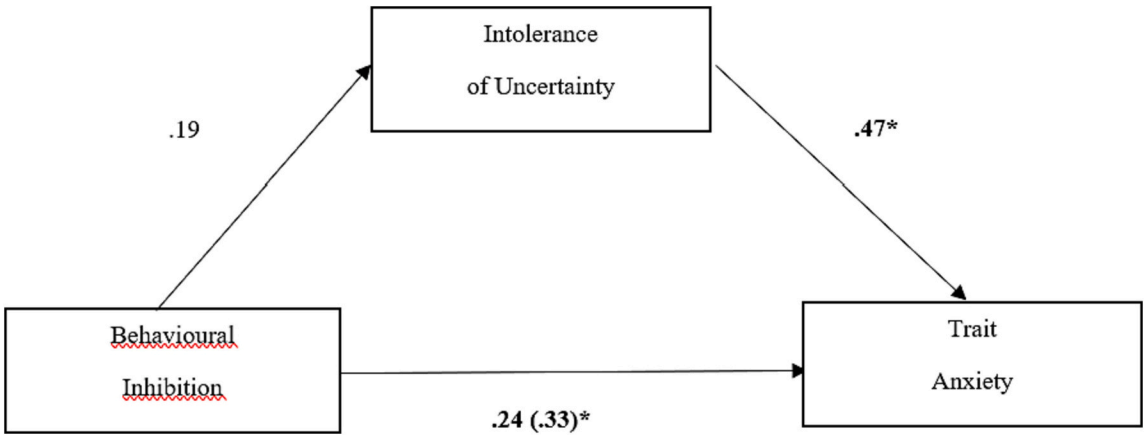

Fig. 2. HC group: non-significant mediating role of IU on the association between behavioural inhibition and trait anxiety.
N.B. Results of the regression analyses. The total effect derived from step 1 of the hierarchical regression analysis is displayed in parentheses. * $p < .01$.

experiences increased uncertainty-related anxiety, which then leads into more avoidance and inhibition. Whilst these behaviours may reduce anxiety in the short term, it may worsen the negative associations with uncertainty and related behaviours in the long run and in fact lead to even higher anxiety.

Literature from clinical non-eating disorder groups shows that the relationship between behavioural inhibition and anxiety is ameliorated by good executive functions (i.e. attention shifting, inhibitory control, attention bias) and good coping strategies (i.e. self-monitoring) (Lahat, 2011). Research shows weaker executive functions and poor coping in adults with AN (Hirst et al., 2017; Villa et al., 2009) and there is also some first evidence of abnormal executive functioning in adolescents with AN (Hirst et al., 2017; Sternheim et al., 2021). This speaks to the idea that altered brain-related processes may not just be a consequence of starvation, but rather it is likely that the brain development of those with AN differs from their peers. Which in itself is a risk for AN. Indeed a recent study found that individual differences in self report IU were reflected in the engagement in the prefrontal cortical regions known to be involved in safety-signaling and conscious threat appraisal during cue-signaled uncertainty of threat (Morriss et al., 2021).

In other words, adolescents with AN may simply not have the tools their healthy peers have to navigate uncertainty and self-regulate negative emotions associated to uncertainty. Consequently, these adolescents develop maladaptive behaviours to reduce uncertainty-related anxiety, such as avoidance and excessive information seeking. Indeed, it has been speculated before that AN behaviours, which are commonly developed in early adolescence, may also serve to reduce uncertainty and associated anxiety (Pallister and Waller, 2008; Sternheim et al., 2011). All in all, this fits with our finding that in the HC group there was no association between behavioural inhibition and IU. It may thus be that this group has developed the required skills to manage uncertainty.

Of course, this pathway of behavioural inhibition to anxiety may be particularly relevant in those with AN. Namely in AN onset commonly is in early adolescence, a developmental stage full of uncertainties across all life domains (i.e. bodily changes, social context) and where the brain's development is hindered by malnutrition. It has been proposed that anxiety is central to the heightened reinforcement of starvation, leading to its excessive repetition, and goal-directed system abnormalities in AN, both important maintenance processes of AN (Lloyd et al., 2017). A recent study shows that general anxiety in fact predicts highest clinical severity in AN (Riquin et al., 2021). As anxiety is also related to eating behaviour and reduced food intake (Lloyd et al., 2021), it is likely that those with high anxiety are doing worse in a treatment that requires changes and thus uncertainty in eating behaviour (e.g., increases in food intake). Indeed, higher anxiety is associated to a higher treatment drop-out rate and poorer outcomes (Lockwood et al., 2012). In other words, targeting anxiety seems an essential step in the treatment of AN.

4.1. Clinical implications

Findings confirm the relevance of anxiety traits in AN and their contribution to anxiety in AN. Seeing that both anxiety traits and anxiety have a detrimental effect on both treatment outcomes and long term outcomes (Lockwood et al., 2012), it is crucial to develop intervention strategies that focus on anxiety traits and anxiety. The TBT (Kaye et al., 2015), which focusses on teaching individuals with AN and their carers to recognize temperament patterns and develop strategies to manage these personality traits is a promising new avenue to improving AN treatment.

With the TBT expected to be a relatively time intensive treatment requiring experienced therapists (Kaye et al., 2015), it is important to also look at more simple and costs-effective interventions for anxiety. A handful of studies have shown successful reductions in IU using 12–20 cognitive and behavioural therapy session targeting IU in individuals with anxiety and other emotional disorders (Boswell et al., 2013; Dugas et al., 2022). Seeing existing studies highlighting the contribution of IU to AN pathology, a potentially large group with AN may benefit from targeting IU alongside AN treatment. A pilot study showed reductions in IU in adolescent in-patients with AN after receiving 12 sessions of group-based cognitive-behavioural intervention targeting IU (Sternheim and Harrison, 2018). Targeting IU can be a relatively simple avenue to increase readiness for treatment and to optimize existing AN treatment interventions.

Secondly, results suggest an important role for behavioural inhibition and IU on the development of anxiety and potentially AN and future studies should examine whether early intervention programmes targeting these anxiety traits in childhood and early adolescence may contribute to reducing AN, anxiety and IU-related psychological problems during later adolescence.

4.2. Limitations

Seeing that the age of our groups was middle adolescence, rather than early adolescence, and the duration of illness was nearly 2 years, it is possible that there are already effects of malnourishment and habituation. We did not control for BMI or age of onset or illness duration. This decision was based on previous research- showing that these variables are likely not associated to our model's variables. One study found that BIS scores were not associated to changes in BMI or other AN-related outcomes (Harrison et al., 2016). Studies also report no relations between IU and BMI (Brown et al., 2017). Corroborating this, we did not find any associations between BMI and the model variables.

However, future research may benefit from examining our model in adolescents with a very short duration of illness to avoid illness effects. Moreover, future research should aim to identify at what point (the use of) suboptimal executive skills and coping forms into maladaptive (AN) behaviours to reduce uncertainty-related anxiety. This may inform early intervention strategies for AN. Of note, whilst the US AN sample was recruited from both eating disorder centers and hospital wards, the NL AN sample was recruited from eating disorder centers only. This may pose a possible bias seeing that those in hospital wards are likely to have a poorer physical status quo, which may have interfered with participant's cognitive abilities. Secondly, we did not include pharmacological data, yet we are aware of the potential relation between anxiety (processes) and some pharmacological treatments (i.e. Olanzapine may increase anxiety whilst fluoxetine may decrease anxiety). We recommend future studies to include information on (anxiety) medication. We also recommend future studies to use more elaborate anxiety measures, e.g. the Hamilton Anxiety Rating Scale (HAM-A; Hamilton, 1959), which assesses both psychic and somatic states of anxiety. Indeed future research should include validated diagnostic instruments such as the Structured Clinical Interview for DSM (APA). Moreover, we did not screen for or excluded anyone with an anxiety or a depressive disorder. However, Jappe et al. (2011) found that the BIS total score as well as BIS-anxiety scores were similar between AN with and without anxiety disorder, suggesting that those effects are less relevant in this context. There are some limitations to the demographics of our sample that need to be considered. Our sample consisted of cis gender females only and we can thus not draw any conclusions on male patients. Moreover, the large majority of participants were of Caucasian origin. This may represent a selection bias and results may thus not be translatable to other cultural or ethnical groups. Lastly, we have no data on religious beliefs or factors such as previously diagnosed internal diseases and drug abuse and cannot exclude the possibility that these factors contribute to study outcomes.

4.3. Conclusion

Taken together, these results provide evidence for an anxious temperament in AN and highlight the importance of anxiety traits in adolescents with AN, specifically IU. Adolescents with AN may benefit from interventions managing these traits and targeting IU.

Prevention interventions in early adolescence targeting behavioural inhibition and IU may prevent AN, anxiety and related psychological problems in later adolescence and emerging adulthood.

Author statement

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CRediT authorship contribution statement

Lot C. Sternheim: Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Validation, Writing – original draft. **Jojanneke M. Bijsterbosch:** Conceptualization, Methodology, Writing – review & editing. **Mirjam C.M. Wever:** Data curation, Methodology, Writing – review & editing. **Annemarie A. van Elburg:** Data curation, Writing – review & editing. **Guido Frank:** Conceptualization, Supervision, Writing – review & editing.

Declaration of competing interest

None.

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