Differential comorbidity profiles in avoidant/restrictive food intake disorder and anorexia nervosa: Does age play a role?

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Abstract

Objective: Research comparing psychiatric comorbidities between individuals with avoidant/ restrictive food intake disorder (ARFID) and anorexia nervosa (AN) is limited. ARFID often develops in childhood whereas AN most typically develops in adolescence or young adulthood. Understanding how age may impact differential psychological comorbidity profiles is important to inform etiological conceptualization, differential diagnosis, and treatment planning. We aimed to

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compare the lifetime frequency of psychiatric comorbidities and suicidality between participants assigned female at birth with ARFID (n=51) and AN (n=40), investigating the role of age as a covariate.

Method: We used structured interviews to assess the comparative frequency of psychiatric comorbidities/suicidality.

Results: When age was omitted from analyses, females with ARFID had a lower frequency of depressive disorders and suicidality compared to AN. Adjusting for age, only suicidality differed between groups.

Discussion: This is the first study to compare comorbidities using a relatively even split of ARFID and AN, and a structured clinical interview to confer ARFID and comorbidities, covarying for age, and the first to compare suicidality. Although suicidality is at least three times less common in ARFID than AN, observed differences in other psychiatric comorbidities may reflect ARFID's relatively younger age of presentation compared to AN.

Avoidant/restrictive food intake disorder (ARFID) and anorexia nervosa (AN) are characterized by dietary avoidance/restriction. While avoidance/restriction in ARFID can be motivated by sensory sensitivity, fear of aversive consequences, and/or lack of interest in eating, in AN, it is typically driven by shape/weight concerns (APA, 2013; Thomas & Eddy, 2019). Data comparing psychiatric comorbidities between ARFID and AN are limited. Such research is warranted to inform etiological conceptualization, differential diagnosis, and treatment planning.

Findings on the frequency of comorbidities in ARFID versus AN are mixed. Comorbid depressive disorders appear less common in ARFID (Aulinas et al., 2020; Bryson et al., 2018; Fisher et al., 2014; Keery et al., 2019; Lieberman et al., 2019; Nicely et al., 2014). No studies have compared suicidality. Anxiety and neurodevelopmental disorders appear more common in ARFID (Aulinas et al., 2020; Bryson et al., 2018; Fisher et al., 2014; Keery et al., 2019; Lieberman et al., 2019; Nicely et al., 2014; Ornstein et al., 201; Zanna et al., 2020). However, studies comparing psychiatric comorbidities are limited by unbalanced designs/small sample sizes, reliance on treatment-seeking samples, lack of structured interviews, use of retrospective chart reviews and self-report to confer diagnoses, and absence of diagnostic reliability information.

In the above studies, ARFID samples were younger than AN samples, highlighting the possibility that observed differences in comorbidities may be attributed to age. Indeed, only one study (Aulinas et al., 2020) adjusted for age. This is critical given the well-known ages of onset of specific psychiatric disorders, resulting from brain development/activation of pubertal hormones and age-related changes in psychosocial influences. In a large-scale

meta-analysis of epidemiological studies, Solmi and colleagues (2021) reported on peak ages of onset: neurodevelopmental disorders onset earliest in life (5.5 years), followed by anxiety disorders (5.5 years for specific phobia/separation anxiety disorder, 14.5 years for social anxiety disorder, and 15.5 years for panic/generalized anxiety disorder), and depressive disorders (20.5 years). Given younger age of onset for ARFID than AN (e.g., Becker et al., 2019), understanding how age may impact differential comorbidity profiles is important.

We compared the frequency of lifetime psychiatric comorbidities and suicidality between children/adolescents assigned female at birth with ARFID and AN, investigating the role of age as a covariate. For Aim 1, we omitted age as a covariate to replicate findings from extant research, forming hypotheses based on these findings. We also wanted to examine how findings compared with and without adjusting for age. We hypothesized that females with ARFID would demonstrate: (a) lower frequency of depressive and bipolar-related disorders ("depressive disorders") and suicidality; (b) higher frequency of anxiety, obsessive-compulsive, and trauma-related disorders ("anxiety disorders"); and (c) higher frequency of neurodevelopmental, disruptive, and conduct disorders ("neurodevelopmental disorders"). For Aim 2 (including age as a covariate), we had no a priori hypotheses and conducted exploratory analyses in the spirit of discovery (Kraemer, 2015).

Method

Participants

We recruited participants ($N = 91$; $n = 51$ ARFID; $n = 40$ AN), ages 10–23 years, for two studies of the neurobiology of eating disorders (EDs; $n = 9$ ARFID and $n = 40$ AN; R01MH103402) and ARFID ($n = 42$; R01MH108595). Participants had to be female and meet full criteria for ARFID or AN. Participant characteristics have been previously reported for a subset of participants (Aulinas et al., 2020; Becker et a., 2021; Breithaupt et al., 2020; Bryant-Waugh et al., 2019; Harshman et al., 2021; Harshman et al., 2019; Izquierdo et al., 2019; Kambanis et al., 2020; Kerem et al., 2021; Mancuso et al., 2020; Thomas et al., 2020; Wang et al., 2020) to test different hypotheses than explored in the current paper. Exclusion criteria for the parent studies included: (a) past-month active substance/ alcohol use disorders; (b) current/lifetime psychosis; and (c) intellectual disability (IQ < 70). Exclusion criteria pertaining to magnetic resonance imaging/neuroendocrine assessments are detailed elsewhere (Breithaupt et al., 2020; Mancuso et al., 2020); and (d) current active suicidality with plan/intent (current passive suicidality and history of active suicidality were allowed). Importantly, no participants had to be excluded due to current active suicidality with plan/intent.

Measures

Comorbid Psychiatric and ED Diagnoses—We used the Kiddie Schedule for Affective Disorder and Schizophrenia – Present and Lifetime (KSADS-PL) 2013 Working Draft (Kaufman et al., 2013) to assess history of depressive, anxiety, and neurodevelopmental disorders. We added questions keyed to *DSM*-5 ARFID criteria.

Percent agreement between raters conferring diagnoses ranged from 94–100% (Kambanis et al., 2020; random sample representing 14% of R01MH108595).

We used the Pica, ARFID, and Rumination Disorder Interview (PARDI; Bryant-Waugh et al., 2019) to confer ARFID diagnoses in R01MH108595. We used the Eating Disorder Examination (EDE) and KSADS-PL to confirm ARFID diagnoses in R01MH103402. Inter-rater reliability for a subset of the ARFID sample was excellent ($\kappa = 1.0$; Thomas et al., 2020).

We used the EDE Version 17.0 (Fairburn et al., 2008) to confirm AN diagnosis in R01MH103402. Inter-rater reliability for a subset of the AN sample was excellent ($\kappa = 1.0$; Wang et al., 2020).

Suicidality—We used the Children's Depression Inventory 2 (CDI-2; Kovacs, 2011; a score of 2 ["*I think about killing myself but I would not do it*"] on Item 8) and the Beck Depression Inventory II (BDI-II; Beck et al., 1996; a score of 1 or 2 ["*I have thoughts of killing myself, but I would not carry them out*" or "*I would like to kill myself*"] on Item 9) to classify individuals as endorsing suicidality.

Procedure

Procedures were approved by the Mass General Brigham Institutional Review Board. Research coordinators administered the KSADS-PL at participants' screening visit. During participants' primary visit, dietitians measured participants' height/weight and study staff administered the PARDI/EDE.

Statistical Analyses

We used SPSS 28.0 (IBM Corp., 2021) for analyses. We used age at study presentation ("age") as our age variable due to its increased reliability (e.g., many individuals did not have an ARFID diagnosis preceding the study, some had significant symptoms prior to an official diagnosis). Prior to our main analyses, we conducted a *t*-test comparing age; females with ARFID were significantly younger ($p < .001$, Cohen's $d = .94$; Table 1), supporting our inclusion of age as a covariate.

Aim 1 – Omitting Age as a Covariate—To test our hypotheses that females with ARFID would demonstrate: (a) lower frequency of depressive disorders and suicidality; (b) higher frequency of anxiety disorders; and (c) higher frequency of neurodevelopmental disorders, we conducted chi square tests of independence for broad lifetime KSADS-PL categories and suicidality.

Aim 2 – Including Age as a Covariate—For exploratory analyses that included age as a covariate, we performed logistic regression. We performed analyses when expected cell counts were > 1 with less than 20% of cells having expected frequencies < 5 (Tabachnick & Fidell, 2013; Table 2). We simultaneously entered diagnosis and age as covariates and absence/presence of each relevant diagnosis as the binary criterion variable. We were unable to perform logistic regression for lifetime neurodevelopmental disorders because the cell count assumption was not met.

Results

Demographics and clinical characteristics are presented in Table 1.

Omitting Age as a Covariate

Frequencies of lifetime psychiatric comorbidities are presented in Table 2. Consistent with our hypotheses, results from chi square tests of independence indicated that lifetime depressive disorders ($\chi^2[1] = 4.99$, $p = .025$, Cramer's $V = .23$) were significantly less frequent among females with ARFID than AN. The chi square cell count assumption for suicidality was not met; a Fisher's exact test demonstrated that suicidality was significantly less frequent among females with ARFID than AN ($\chi^2[1] = 8.89$, $p = .003$, Cramer's $V = .31$). Contrary to our hypothesis, there were no between-group differences in anxiety disorders ($\chi^2[1] = 1.58$, $p = .208$, Cramer's $V = .13$). Finally, neurodevelopmental disorders were four times as frequent in ARFID group, though this trend was non-significant ($\chi^2[1] = 3.42$, $p = .064$, Cramer's $V = .19$).

Including Age as a Covariate

Results from logistic regression analyses are presented in Table 2. When including age as a covariate, no between-group differences emerged in depressive (60% AN v. 37% ARFID; $p = .276$) or anxiety (65% AN v. 53% ARFID; $p = .938$) disorders. Females with ARFID still had a lower frequency of suicidality than AN (35% AN v. 10% ARFID; $p = .009$).

Discussion

Given different ages of onset of specific psychiatric disorders and that ARFID typically develops in childhood whereas AN typically develops in adolescence or young adulthood, we compared the frequency of lifetime psychiatric comorbidities and suicidality between females with ARFID and AN omitting (Aim 1) and including (Aim 2) age as a covariate to improve our understanding of the impact of age on differential comorbidity profiles. Omitting age as a covariate, females with ARFID had a lower frequency of depressive disorders and suicidality, which was consistent with our hypothesis. Only the result regarding suicidality remained significant when including age as a covariate. These data suggest that suicidality is at least three times less common in ARFID than AN irrespective of age. However, observed differences in other psychiatric comorbidities may reflect ARFID's relatively younger age at treatment presentation compared to AN.

Restrictive eating predicts suicidality (Forrest et al., 2016; Wang et al., 2018) and may increase risk of suicidal ideation even beyond risk associated with other eating behaviors (Wang et al., 2019). Restriction in AN functions to control shape/weight; however, research suggests that individuals with AN may also engage in restriction with intention to harm themselves (Fox et al., 2019). Suicidality in AN, then, may be tied to judging one's self-worth predominantly based on appearance. The absence of overvaluation of shape/weight among individuals with ARFID could account for their lower frequency of suicidality. Further, restriction in ARFID serves a different function than restriction AN; therefore, correlates of restriction may also differ. Since ours is the first study to compare suicidality

between ARFID and AN, future research should explore this finding across age ranges, given that both disorders can present across the lifespan.

No difference emerged in the frequency of overall anxiety disorders; these are common psychiatric comorbidities for both EDs. There was a non-significant trend for neurodevelopmental disorders to be more frequent in ARFID; however, we were unable to examine the extent to which age may have influenced this finding, warranting further research. Neurodevelopmental disorders are more common in males (Kessler et al., 2005), and past studies that reported a higher frequency in ARFID (i.e., Lieberman et al., 2019; Nicely et al., 2014) had higher proportions of males than females with ARFID than AN. Future studies should explore potential differences in both sexes. Additionally, future studies should examine illness duration as a covariate, which has implications for understanding the etiology of psychiatric comorbidities in ARFID and AN as well as the temporal relationship between onset and the development of comorbidities.

Limitations of this study include that exclusion criteria for the parent study prevented us from comparing certain comorbidities. Though no participants were excluded due to current active suicidality, it is possible that individuals with current active suicidality chose not to participate in the study. Our sample was homogeneous (i.e., primarily non-Hispanic and White). Future research should focus on minoritized youth with AN and ARFID, given the dearth of research in this area, despite unique risk factors at play for these populations (Goel et al., 2020; Egbert et al., 2020, 2022). Our sample size was modest ($N = 91$), making it challenging to ascertain whether our study was adequately powered to detect meaningful between-group differences. Some cell sizes were small, precluding logistic regression analyses for neurodevelopmental disorders. Finally, the inclusion of only females in our sample prevents the generalizability of our findings to males. Limitations notwithstanding, our findings suggest that previously reported differences in psychiatric comorbidities between ARFID and AN may be attributed, in part, to ARFID's younger age at clinical presentation. Suicidality appears to be the exception to this pattern of findings, being three times less common in ARFID than AN, regardless of age. Future research is needed to replicate these findings.

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Data availability statement:

All data will be made publicly available through the National Institute of Mental Health National Database for Autism Research at the conclusion of the study.

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Table 1

Demographics and clinical characteristics of 51 females with avoidant/restrictive food intake disorder and 40 females with anorexia nervosa

Demographic and clinical characteristics	ARFID	AN
	M (SD)	**M (SD)**
Age (years)[1]	16.61 (3.92)	19.59 (2.16)
	n, (%)	**n, (%)**
Race		
Black/African American	1 (2)	0 (0)
Asian	3 (6)	7 (18)
White	44 (85)	32 (80)
Other	4 (8)	1 (2)
Ethnicity		
Hispanic	7 (13)	4 (10)
Non-Hispanic	45 (87)	36 (90)
ARFID Profile[2]		
Sensory sensitivity	36 (69)	N/A
Fear of aversive consequences	13 (25)	N/A
Lack of interest in food/eating	29 (56)	N/A

Note. ARFID – avoidant/restrictive food intake disorder; AN – anorexia nervosa; M – mean; SD – standard deviation; N/A – not applicable.

[1] There was a statistically significant difference in age between ARFID and AN ($p < .001$, Cohen's $d = .94$).

[2] We used the PARDI to determine presence/absence of each ARFID profile for $n = 42$ individuals in study R01MH108595. The $n = 9$ individuals with ARFID who we recruited as part of study R01MH103402 are not represented in this table because we did not administer the PARDI to participants in this study. Combined percentages exceed 100% because, consistent with Thomas and colleagues' (2017) three-dimensional model of ARFID, participants could present with more than one profile.

Table 2

Frequency and results of logistic regression analyses, including age as a covariate, for lifetime psychiatric comorbidities and suicidal ideation in 51 females with avoidant/restrictive food intake disorder and 40 females with anorexia nervosa.

Lifetime KSADS-PL Diagnoses (Binary Criterion Variables)[1]	ARFID n (%)	AN n (%)	β	SE	Wald χ^2	p-value	OR [95% CI]
Depressive and Bipolar-Related Disorders**	19 (37)	24 (60)	−.52	.48	1.19	.276	.59 [.23, 1.52]
Major depressive disorder	15 (29)	24 (60)					
Other specified depressive disorder	3 (6)	0 (0)					
Persistent depressive disorder	1 (2)	0 (0)					
Anxiety, Obsessive-Compulsive, and Trauma-Related Disorders	27 (53)	26 (65)	.04	.51	.01	.938	1.04 [.39, 2.80]
Generalized anxiety disorder	18 (35)	18 (45)					
Panic disorder	7 (14)	3 (8)					
Specific phobia	5 (10)	5 (13)					
Social anxiety disorder	5 (10)	15 (38)					
Separation anxiety disorder	0 (0)	4 (10)					
Other specified anxiety disorder	1 (2)	0 (0)					
Obsessive compulsive disorder	3 (6)	2 (5)					
Posttraumatic stress disorder	4 (8)	2 (5)					
Neurodevelopmental, Disruptive, and Conduct Disorders[2]	7 (14)	1 (3)					
Oppositional defiant disorder	1 (2)	0 (0)					
Autism spectrum disorder	1 (2)	0 (0)					
Attention deficit/hyperactivity disorder	4 (8)	1 (3)					
Other specified attention deficit/hyperactivity disorder	2 (4)	0 (0)					
Suicidality[3]**	5 (10)	14 (35)	−1.75	.67	6.87	.009*	.18 [.05, .64]

Note. ARFID – avoidant/restrictive food intake disorder; AN – anorexia nervosa; KSADS-PL – Kiddie Schedule for Affective Disorders and Schizophrenia – Present and Lifetime Version; SE – standard error; OR – odds ratio. Anorexia nervosa is the reference group.

[1] Individual diagnoses with no test statistics reported indicate those that did not have sufficient representation in all cells for logistic regression (i.e., > 1 with less than 20% of cells having expected frequencies <5 [Tabachnick & Fidell, 2013]) or those under broad KSADS-PL categories that were not significant (i.e., Anxiety, Obsessive-Compulsive, and Trauma-Related Disorders) and were therefore not analyzed.

[2] Assumptions for logistic regression analysis were not met and therefore, this test was not performed on this category of disorders.

[3] The self-report measures we used to assess suicidality reflect the past two weeks.

*
Bolded *p*-values indicate those that met the threshold for statistical significance of *p* < .05.

**
Represents KSADS-PL categories that were statistically significant in chi-square tests of independence that omitted age as a covariate.