Characteristics of autism spectrum disorders are associated with longer duration of anorexia nervosa: A systematic review and meta-analysis

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Abstract

Objective: Anorexia nervosa (AN) is associated with neuropsychological characteristics such as impairments in central coherence, cognitive flexibility, and emotion recognition. The same features also manifest in autism spectrum disorders (ASD) and have been suggested to be associated with illness prolongation in AN. The purpose of this meta-analysis was to examine whether pronounced neuropsychological characteristics related to ASD are associated with illness duration in AN.

Method: Four databases (Medline, PsycINFO, Scopus, PubMed) were searched for eligible studies. Search terms were (a) “anorexia nervosa” and (b) “cognitive flexibility” or “set-shifting” or “central coherence” or “emotion recognition” or “theory of mind”.

The final sample consisted of 53 studies. Duration of AN was divided into three categories in order to investigate differences between the groups with varying illness duration. The meta-analysis was performed with Review Manager using a random-effects model.

Results: Deficits in central coherence, cognitive flexibility, and emotion recognition were pronounced among individuals with prolonged AN compared to those with shorter illness duration.

Discussion: A prolonged course of AN appears to be associated with underlying neuropsychological characteristics that are also distinctive to ASD. Neuropsychological impairments may lead to prolonged AN, and prolonged illness may contribute to the subsequent “neurological scar effect,” further strengthening these impairments.
1 | INTRODUCTION

Anorexia nervosa (AN) is associated with neuropsychological characteristics that also manifest in autism spectrum disorders (ASDs). ASDs are neurodevelopmental disorders in which the core traits include problems in social communication and interaction, as well as repetitive and restricted behaviors and interests (American Psychiatric Association, 2013). Neuropsychological characteristics in AN that are associated with ASD include weak central coherence, cognitive inflexibility, and problems in emotion recognition (Anckarsäter et al., 2012; Oldershaw, Treasure, Hambrock, Tchanturia, & Schmidt, 2011; Westwood, Stahl, Mandy, & Tchanturia, 2016). These neuropsychological difficulties manifesting in ASD have been suggested to form an endophenotype of AN and to be associated with longer illness duration among individuals with AN (Kanakam, Raoult, Collier, & Treasure, 2013; Lang, Lopez, Stahl, Tchanturia, & Treasure, 2014; Lang, Stahl, Espie, Treasure, & Tchanturia, 2014; Tenconi et al., 2010; Zhou, McAdams, & Donnelly, 2018).

Unsurprisingly, a subgroup of individuals with AN have been found to fulfill the diagnostic criteria of ASD (Anckarsäter et al., 2012; Huke, Turk, Saedi, Kent, & Morgan, 2013). Elevation ASD traits in AN have been shown to be connected to a poorer outcomes, psychiatric symptoms, neuropsychological problems, increased eating disorder symptoms, longer treatment periods, and increased use of antipsychotic drugs (Nielsen et al., 2015; Stewart, McEwen, Konstantellou, Eisler, & Simic, 2017; Tchanturia, Adamson, Leppanen, & Westwood, 2017; Westwood, Mandy, & Tchanturia, 2017a, 2017b). Therefore, pronounced ASD characteristics appear to be associated with more severe and prolonged AN.

The most studied neuropsychological characteristics in AN associated with ASD include weak central coherence, problems in cognitive flexibility, and problems in emotion recognition. Central coherence describes the style of cognitive processing. Weak central coherence indicates that attention is focused on details, whereas global integration of information is poor (Happé & Booth, 2008). Weak central coherence is also associated with problems in understanding context (Happé & Booth, 2008). Weaker central coherence has been found in acutely ill and recovered individuals with AN, as well as in their healthy relatives (Kanakam et al., 2013; Lang et al., 2016; Roberts, Tchanturia, & Treasure, 2013; Tenconi et al., 2010). It has been suggested that weak central coherence in individuals with AN may sometimes contribute to the inability to benefit from conventional psychological treatment (Lang, Lopez, et al., 2014). Indeed, weak central coherence has been reported to relate to exaggerated obsessive–compulsive and perfectionistic personality traits, hampering behavioral change (Lang, Lopez, et al., 2014).

Cognitive flexibility refers to the ability to move flexibly from one task, thought, or strategy to another. Problems in cognitive flexibility are suggested to contribute to the restrictive and rigid behavior toward food and weight in individuals with AN (Kanakam & Treasure, 2013; Zhou et al., 2018). Adults with eating disorders have been shown to have impairments in cognitive flexibility (Roberts, Tchanturia, Stahl, Southgate, & Treasure, 2007; Tchanturia et al., 2012), whereas results among children and adolescents have been inconsistent (Lang, Stahl, et al., 2014). It has therefore been suggested that these findings reflect an association between longer illness duration and cognitive inflexibility (Lang, Stahl, et al., 2014). However, problems in cognitive flexibility have also been found in those who recovered from AN (Harrison, Tchanturia, Naumann, & Treasure, 2012; Lindner, Fichter, & Quadflieg, 2014) and in healthy relatives of individuals with AN (Holliday, Tchanturia, Landau, Collier, & Treasure,
2.5 | Categorization of the illness duration

There is no consensus of the threshold of prolonged AN, and previous studies have based cutoffs on experts’ judgement (Wildes et al., 2016). However, a recent review reported that the most used criteria for prolonged AN is a duration of at least 7 years (Broomfield, Stedal, Touyz, & Rhodes, 2017). Based on this, we decided to categorize prolonged illness as 7 years or over. Moreover, it has been shown that half of the individuals with AN recover within 4 years of illness (Keski-Rahkonen et al., 2007). Therefore, a recovery in less than...
4 years could be considered a short duration. Based on this, we decided to categorize an illness of under 4 years as short duration. In addition, mean duration of AN is reported to be approximately 6 years (Treasure, Schmidt, & Hugo, 2005). Based on the above evidence, duration categories in our study were defined as follows: mean illness duration of 0–3.99 years (short), mean illness duration of 4–6.99 years (average), and mean illness duration of more than 7.0 years (prolonged illness). Data were analyzed separately in each illness duration category in order to calculate the differences between the categories. Some studies also divided AN participants into subgroups and reported the results of the subgroups separately (e.g., AN-R and AN-BP or currently ill and recovered individuals), and because of this, we also divided the results of these studies into subgroups according to the original studies.

2.6 Quality assessment

We assessed the quality of the included studies using the Newcastle-Ottawa Scale for case-control studies (Wells et al., 2019). This instrument assesses the quality of case-control studies in three categories as follows: patient selection (four criteria), comparability of study groups (two criteria), and assessment of the outcome (three criteria). A study can obtain one star for each assessed criterion, with a maximum of nine stars. Fourteen studies received six stars, 19 studies obtained seven stars, and 20 studies received eight stars. Furthermore, a funnel plot was created to assess potential publication bias, as presented in Figure 2.
2.7 Data extraction

Data were extracted from the following variables: number of participants (individuals with AN and HC participants), AN subtype (restrictive, AN-R; or binge/purge, AN-BP), age and gender of the participants, illness duration (mean and standard deviation), stage of the illness (currently ill or recovered), body mass index, full-scale intelligence quotient of individuals with AN, age of illness onset in individuals with AN, potential comorbid psychiatric and neurologic diagnoses, potential medication of individuals with AN, methods, and results (mean and standard deviation). The extracted data were used to calculate the standard mean differences (SMDs) between the individuals with AN and HCs. The data were then entered into nine separate meta-analyses exploring central coherence, cognitive flexibility, and emotion recognition. In addition, every investigated characteristic was further divided into three different categories according to the mean illness duration of AN in each study.

2.8 Description of measures in studies

Central coherence: Most of the studies used the Rey-Osterrieth Complex Figure Test (Osterrieth, 1944), which is a visual copy-and-recall task that measures central coherence. One study used the Embedded Figure Test in which participants have to find a simple figure within a more complex figure (Fonville et al., 2013). One study used the Matching Familiar Figure Test, which is a visual search task that measures attention to details (Southgate, Tchanturia, & Treasure, 2008). In addition, in two studies, central coherence was measured using the Autism Quotient’s questions that measure focus on details (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001).

Cognitive flexibility: Most of the studies used the Wisconsin Card Sorting Task or Berg’s Card Sorting Task (Berg, 1948). In these tasks, participants are asked to classify cards according to criteria that change frequently without warning. One study used the Trail Making Task, which measures the ability to switch between two different conditions (Delis, Kaplan, & Kramer, 2001). One study used visual set-shifting tasks in which participants react to stimuli that change constantly (Bühren et al., 2012). Two studies used category learning tasks in which participants sort stimuli according to given rules (Filoteo et al., 2014; Shott et al., 2012). Three studies used the Intra Dimensional/Extra Dimensional Shift Task, in which participants shift their attention between two different conditions (Fowler et al., 2006; Galimberti, Martoni, Cavallini, Erzegovesi, & Bellodi, 2012; Télleus et al., 2015). Two studies used the Brixton task, in which participants have to predict rules that change frequently (Konstantakopoulos, Tchanturia, Surguladze, & David, 2011; Lounes, Khan, & Tchanturia, 2011). In addition, in two studies, set shifting was measured using the AQ’s subscale that measures attention switching (Baron-Cohen, Wheelwright, Skinner, et al., 2001).

Emotion recognition: Most of the studies used tasks measuring emotion recognition from faces or eyes. Ten studies used the “Reading the Mind in the Eyes” test (RMET) that measures the ability to recognize other people’s emotions from the eye area only (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001). The RMET includes many complex emotions such as jealousy and sarcasm and is therefore also considered a measure of a theory of mind. Six studies used emotion recognition tasks specifically designed for those studies. These studies measured the ability to recognize basic emotions such as sadness or happiness. One study used a movie task to measure emotional states (Brockmeyer et al., 2016). One study used a self-report questionnaire to measure emotion recognition (Morris, Bramham, Smith, & Tchanturia, 2014).

2.9 Data analysis

The Review Manager was used for statistical analyses (RevMan 2014). A random-effects model was chosen due to the heterogeneity of the neuropsychological measures and due to variation of results of individual studies (high heterogeneity). The SMD was estimated in each individual study (high heterogeneity). The SMD was estimated in each individual study (high heterogeneity). The SMD was estimated in each individual study (high heterogeneity). The SMD was estimated in each individual study (high heterogeneity).

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Participant characteristics</th>
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<tbody>
<tr>
<td></td>
<td>Individuals with anorexia nervosa (n = 2,142)</td>
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<tr>
<td>Age (range)</td>
<td>12.17–35.44</td>
</tr>
<tr>
<td>Gender</td>
<td>Females</td>
</tr>
<tr>
<td>2018 (94.2%)</td>
<td>18 (0.8%)</td>
</tr>
<tr>
<td>Type of anorexia nervosa (%)</td>
<td>Restrictive subtype</td>
</tr>
<tr>
<td>949 (44.3%)</td>
<td>349 (16.3%)</td>
</tr>
<tr>
<td>Not reported</td>
<td>785 (36.6%)</td>
</tr>
<tr>
<td>Illness stage</td>
<td>Currently ill</td>
</tr>
<tr>
<td>1,731 (80.8%)</td>
<td>329 (15.4%)</td>
</tr>
<tr>
<td>BMI (range)</td>
<td>Currently ill</td>
</tr>
<tr>
<td>13.3–17.6</td>
<td>18.1–21.2</td>
</tr>
<tr>
<td>Mean FSIQ (range)</td>
<td>97.8–116.84</td>
</tr>
<tr>
<td>Medication</td>
<td>With medication</td>
</tr>
<tr>
<td>227 (10.6%)</td>
<td>363 (16.9%)</td>
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</table>

Abbreviations: BMI, body mass index; FSIQ, Full Scale Intelligence Quotient.
<table>
<thead>
<tr>
<th>Study areas</th>
<th>Study characteristics</th>
<th>Participants</th>
<th>Age</th>
<th>IQ (AN)</th>
<th>Race (AN)</th>
<th>Type of AN</th>
<th>Duration of illness</th>
<th>Stage of illness</th>
<th>BMI of AN group</th>
<th>Age of AN onset</th>
<th>Medication (AN)</th>
<th>Comorbid diagnoses</th>
</tr>
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<tbody>
<tr>
<td>CF</td>
<td>Abbate-Daga et al. (2011)</td>
<td>30 AN</td>
<td>AN 24.13 (6.16)</td>
<td>100</td>
<td>NP</td>
<td>Caucasian</td>
<td>100% AN-R</td>
<td>5.20 (4.19)</td>
<td>III</td>
<td>15.62 (1.66)</td>
<td>18.12 (3.33)</td>
<td>NP</td>
</tr>
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<td>CF</td>
<td>Abbate-Daga, Buzzichelli, Marzola, Amianto, and Fassino (2014)</td>
<td>94 AN</td>
<td>AN 24.7 (7.25)</td>
<td>100</td>
<td>104.12 (13.06)</td>
<td>Caucasian</td>
<td>83.0% AN-R</td>
<td>7.13 (6.56)</td>
<td>III</td>
<td>15.17 (1.98)</td>
<td>NP</td>
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<td>Adenzato, Todisco, and Ardito (2012)</td>
<td>30 AN</td>
<td>AN 19.73 (6.03)</td>
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<td>NP</td>
<td>NP</td>
<td>53.3% AN-R</td>
<td>3.63 (5.27)</td>
<td>III</td>
<td>15.06 (1.74)</td>
<td>15.77 (3.74)</td>
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<td>NP</td>
<td>NP</td>
<td>NP</td>
<td>4.63 (5.39)</td>
<td>III</td>
<td>15.30 (1.23)</td>
<td>NP</td>
<td>16.0%</td>
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<tr>
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<td>28 AN</td>
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<td>108.8 (10.4)</td>
<td>Caucasian</td>
<td>NP</td>
<td>0.93 (0.62)</td>
<td>III</td>
<td>15.4 (1.2)</td>
<td>NP</td>
<td>75.0%</td>
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<td>85 AN</td>
<td>AN 23.73 (6.68)</td>
<td>100</td>
<td>NP</td>
<td>Caucasian</td>
<td>100% AN-R</td>
<td>6.24 (6.37)</td>
<td>III</td>
<td>15.06 (1.89)</td>
<td>NP</td>
<td>NP</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Study Areas</th>
<th>Participants</th>
<th>Age</th>
<th>Females (%)</th>
<th>IQ (AN)</th>
<th>Race (AN)</th>
<th>Type of AN</th>
<th>Duration of Illness</th>
<th>Stage of Illness</th>
<th>BMI of AN group</th>
<th>Age of AN onset</th>
<th>Medication (AN)</th>
<th>Comorbid Diagnoses</th>
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</thead>
<tbody>
<tr>
<td>SAURE ET AL.</td>
<td>23 AN</td>
<td>AN 13.48 (2.04)</td>
<td>100</td>
<td>VIQ 111.35 (14.44)</td>
<td>NP</td>
<td>100% AN-R</td>
<td>1.29 (0.99)</td>
<td>III</td>
<td>15.5 (1.24)</td>
<td>12.18 (2.21)</td>
<td>17.4%</td>
<td>34.8% have depression; 8.7% have depression and generalized anxiety disorder; 4.3% have OCD</td>
</tr>
<tr>
<td></td>
<td>46 HC</td>
<td>HC 13.48 (2.02)</td>
<td></td>
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<tr>
<td>ER</td>
<td>30 AN</td>
<td>AN 25.2 (7.2)</td>
<td>100</td>
<td>109.0 (8.8)</td>
<td>NP</td>
<td>NP</td>
<td>9.5 (6.4)</td>
<td>III</td>
<td>14.7 (1.4)</td>
<td>NP</td>
<td>43.3%</td>
<td>No bipolar disorder, schizophrenia, psychotic conditions, learning disability, or neurological disorders</td>
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<tr>
<td>ER</td>
<td>40 HC</td>
<td>HC 30.2 (16.7)</td>
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<tr>
<td>Castro-Fornieles et al. (2019)</td>
<td>30 AN</td>
<td>AN 14.9 (1.3)</td>
<td>100</td>
<td>105.4 (10.6)</td>
<td>96.7% white</td>
<td>73.3% AN-R</td>
<td>1.45 (1.3)</td>
<td>III</td>
<td>16.9 (1.0)</td>
<td>NP</td>
<td>33.3%</td>
<td>26.6% have anxiety disorder, 10% have adjustment disorder, 13.3% have depression, 10% have ADHD, 6.7% have oppositional defiant disorder</td>
</tr>
<tr>
<td>CF</td>
<td>30 HC</td>
<td>HC 15.3 (1.4)</td>
<td></td>
<td></td>
<td>3.3% asian</td>
<td>26.7% AN-BP</td>
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<td>Courty et al. (2013)</td>
<td>15 AN</td>
<td>AN 23.9 (4.7)</td>
<td>93.3</td>
<td>NP</td>
<td>NP</td>
<td>33.3% AN-R</td>
<td>4.0 (3.5)</td>
<td>III</td>
<td>16.4 (1.7)</td>
<td>19.8 (3.4)</td>
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<td>No autism spectrum disorders</td>
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<tr>
<td></td>
<td>15 HC</td>
<td>HC 24.0 (4.9)</td>
<td></td>
<td></td>
<td></td>
<td>66.7% AN-BP</td>
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<td>Danner et al. (2012)</td>
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<td>AN 25.63 (5.41)</td>
<td>100</td>
<td>NP</td>
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<td>62.5% AN-R</td>
<td>7.9 (4.0)</td>
<td>III</td>
<td>14.65 (1.70)</td>
<td>NP</td>
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<tr>
<td>CF, CC</td>
<td>15 HC</td>
<td>HC 25.80 (4.69)</td>
<td></td>
<td></td>
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<td>37.5% AN-BP</td>
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<tr>
<td></td>
<td>15 AN</td>
<td>AN 24.33 (4.72)</td>
<td>93.3</td>
<td>NP</td>
<td>NP</td>
<td>73.3% AN-R</td>
<td>4.0 (2.7)</td>
<td>Recovered</td>
<td>21.20 (1.82)</td>
<td>NP</td>
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<tr>
<td>CF, CC</td>
<td>15 HC</td>
<td>HC 25.80 (4.69)</td>
<td></td>
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<td></td>
<td>26.7% AN-BP</td>
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<td></td>
<td>35 AN</td>
<td>AN 27.54 (8.36)</td>
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<td>NP</td>
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<td>10.54 (9.16)</td>
<td>III</td>
<td>15.33 (1.74)</td>
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<td>NP</td>
<td>No psychosis or autism spectrum disorders</td>
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<td>42 HC</td>
<td>HC 26.98 (7.55)</td>
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</tbody>
</table>

(Continues)
<p>| Study areas | Participants | Age | Females (%) | IQ (AN) | Race (AN) | Type of AN | Duration of illness | Stage of illness | BMI of AN group | Age of AN onset | Medication (AN) | Comorbid diagnoses |  |
|-------------|--------------|-----|-------------|---------|-----------|------------|-------------------|-----------------|-----------------|----------------|----------------|-----------------|-----------------|-----|
| De Sampaio et al. (2013) | 24 AN | AN 24.6 (6.1) | 100 | 102.5 (19.8) | NP | 33.3% AN-R | 7.8 (5.9) | NP | 18.1 (1.8) | 16.8 (4.8) | 54.2% | No developmental disorder, psychosis, or substance dependence | CC, ER |
| 24 HC | HC 24.5 (5.7) | | | | | | | | |
| Degortes, Tenconi, Santonastaso, and Favaro (2016) | 51 AN | AN 24.6 (6.1) | 100 | NP | NP | 72.5% AN-R | 3.48 (4.425) | Recovered | 20.4 (2.0) | 16.5 (2.8) | NP | Bulimia nervosa 100% | CF, CC |
| 159 HC | HC 24.5 (5.7) | | | | | | | | | 27.5% AN-BP | |
| Dmitrzak-Weglarz et al. (2011) | 61 AN | AN 15.85 (2.16) | 100 | NP | NP | NP | 0.18 (0.15) | III | 14.35 (1.55) | 13.48 (2.16) | 0% | No schizophrenia, bipolar disorder, or serious somatic disorder | CF |
| 49 HC | HC 15.32 (2.16) | | | | | | | | |
| Favaro et al. (2012) | 29 AN | AN 25.8 (6.9) | 100 | NP | NP | NP | 6.21 (6.87) | III | 14.5 (2.3) | 18.2 (4.4) | 31.0% | No neurological problems, medical illness, depression, substance abuse, schizophrenia, or bipolar disorder | CC |
| 26 HC | HC 26.7 (6.7) | | | | | | | | |
| 16 AN | AN 23.8 (4.8) | 100 | NP | NP | NP | 2.3 (1.68) | Recovered | 19.2 (1.0) | 17.9 (2.8) | 18.6% | No neurological problems, medical illness, depression, substance abuse, schizophrenia, or bipolar disorder | CC |
| 26 HC | HC 26.7 (6.7) | | | | | | | | | (Continues) | |</p>
<table>
<thead>
<tr>
<th>Participants</th>
<th>Age</th>
<th>Females (%)</th>
<th>IQ (AN)</th>
<th>Race (AN)</th>
<th>Type of AN</th>
<th>Duration of illness</th>
<th>Stage of illness</th>
<th>BMI of AN group</th>
<th>Age of AN onset</th>
<th>Medication (AN)</th>
<th>Comorbid diagnoses</th>
<th>Study areas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filoteo et al. (2014)</td>
<td>19 AN</td>
<td>AN 29.7 (6.6)</td>
<td>100</td>
<td>NP</td>
<td>NP</td>
<td>63.2% AN-R</td>
<td>8.8 (6.5)</td>
<td>Recovered</td>
<td>21.2 (1.3)</td>
<td>14.5 (2.6)</td>
<td>0%</td>
<td>26.3% have depression; 5.3% have anxiety, no psychosis, substance abuse, or bipolar disorder</td>
</tr>
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<td>Fonville et al. (2013)</td>
<td>35 AN</td>
<td>AN 23 (9)</td>
<td>NP</td>
<td>110 (9)</td>
<td>NP</td>
<td>80.0% AN-R</td>
<td>8.9 (8.1)</td>
<td>III</td>
<td>16.0 (1.6)</td>
<td>NP</td>
<td>45.7%</td>
<td>NP</td>
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<td>Fowler et al. (2006)</td>
<td>25 AN</td>
<td>AN 16.9 (2.0)</td>
<td>100</td>
<td>108.3 (5.5)</td>
<td>NP</td>
<td>44.0% AN-R</td>
<td>2.1 (1.4)</td>
<td>III</td>
<td>15.3 (1.3)</td>
<td>NP</td>
<td>56%</td>
<td>No substance use disorder, psychosis, or mania</td>
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<td>Galimberti et al. (2012)</td>
<td>24 AN-R</td>
<td>AN-R 26.70 (9.58)</td>
<td>100</td>
<td>NP</td>
<td>NP</td>
<td>100% AN-R</td>
<td>6.56 (6.4)</td>
<td>III</td>
<td>14.26 (1.2)</td>
<td>19.34 (7.35)</td>
<td>100%</td>
<td>No other psychiatric disorders, medical diseases, or substance abuse</td>
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<td>Galimberti et al. (2013)</td>
<td>29 AN</td>
<td>AN 24.1 (6.8)</td>
<td>100</td>
<td>NP</td>
<td>NP</td>
<td>48.3% AN-R</td>
<td>5.95 (5.09)</td>
<td>III</td>
<td>16.21 (4.02)</td>
<td>18.13 (4.53)</td>
<td>0%</td>
<td>No neurological diseases, axis I diagnoses, or substance abuse</td>
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<tr>
<td>Hambrook et al. (2008)</td>
<td>22 AN</td>
<td>AN 26.73 (4.77)</td>
<td>100</td>
<td>NP</td>
<td>NP</td>
<td>9.5 (5)</td>
<td>III</td>
<td>15.27 (1.22)</td>
<td>17.3 (2.6)</td>
<td>NP</td>
<td>NP</td>
<td>CC, CF</td>
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<th>Race (AN)</th>
<th>Type of AN</th>
<th>Duration of illness</th>
<th>Stage of illness</th>
<th>BMI of AN group</th>
<th>Age of AN onset</th>
<th>Medication (AN)</th>
<th>Comorbid diagnoses</th>
<th>Study areas</th>
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<td>Harrison, Sullivan, Tchanturia, and Treasure (2009)</td>
<td>20 AN</td>
<td>AN 26.25 (5.73)</td>
<td>100</td>
<td>114.5 (4.61)</td>
<td>NP</td>
<td>NP</td>
<td>7.2 (3.2)</td>
<td>III</td>
<td>15.81 (1.15)</td>
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<td>Kanakam et al. (2013)</td>
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<td>AN 31 (25)</td>
<td>100</td>
<td>108 (14)</td>
<td>91% white British</td>
<td>NP</td>
<td>6 (12)</td>
<td>NP</td>
<td>20.6 (3.30)</td>
<td>17 (6)</td>
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<td>42 HC</td>
<td>HC 45 (22.75)</td>
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<tr>
<td>Kim, Eom, Yang, Kang, and Treasure (2015)</td>
<td>35 AN</td>
<td>AN 21.97 (8.41)</td>
<td>100</td>
<td>107.11 (12.38)</td>
<td>NP</td>
<td>NP</td>
<td>3.61 (0.18)</td>
<td>III</td>
<td>15.07 (2.41)</td>
<td>18.80 (5.52)</td>
<td>NP</td>
<td>No psychotic disorder or substance abuse or autism spectrum disorders</td>
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<td>33 HC</td>
<td>HC 22.64 (2.28)</td>
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<tr>
<td>King, Korb, Ehrlich, and Egner (2019)</td>
<td>22 AN</td>
<td>AN 23.03 (2.83)</td>
<td>100</td>
<td>112.41 (9.92)</td>
<td>NP</td>
<td>86.4% AN-R</td>
<td>3.17 (2.30)</td>
<td>Recovered</td>
<td>21.03 (1.48)</td>
<td>NP</td>
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<td></td>
<td>22 HC</td>
<td>HC 23.18 (2.73)</td>
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<td></td>
<td>13.6% AN-BP</td>
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<td>Konstantakopoulos et al. (2011)</td>
<td>25 AN</td>
<td>AN 28.6 (8.66)</td>
<td>100</td>
<td>111.85 (7.28)</td>
<td>Caucasian</td>
<td>64.0% AN-R</td>
<td>12.19 (3.77)</td>
<td>III</td>
<td>13.32 (1.15)</td>
<td>16.00 (1.15)</td>
<td>NP</td>
<td>No psychosis or substance abuse</td>
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<td>35 HC</td>
<td>HC 24.9 (4.77)</td>
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<td></td>
<td>36.0%</td>
<td>AN-BP</td>
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<td>Kucharska, Jeschke, and Mafi (2016)</td>
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<td>AN 27.1 (6.3)</td>
<td>100</td>
<td>NP</td>
<td>NP</td>
<td>NP</td>
<td>9.7 (6.6)</td>
<td>III</td>
<td>17.6 (2.2)</td>
<td>NP</td>
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<td>25 HC</td>
<td>HC 24.5 (5.2)</td>
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<tr>
<td>Kucharska-Pietura, Nikoulau, Masiak, and Treasure (2003)</td>
<td>30 AN</td>
<td>AN 20.2 (4.4)</td>
<td>100</td>
<td>NP</td>
<td>76.7% AN-R</td>
<td>23.3% AN-BP</td>
<td>2.83 (2.5)</td>
<td>III</td>
<td>15.2 (1.7)</td>
<td>NP</td>
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<td>30 HC</td>
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<td>Laghi et al. (2015)</td>
<td>40 AN</td>
<td>AN 14.93 (1.48)</td>
<td>100</td>
<td>NP</td>
<td>NP</td>
<td>NP</td>
<td>1.28 (1.04)</td>
<td>III</td>
<td>15.76 (1.45)</td>
<td>13.64 (1.50)</td>
<td>NP</td>
<td>45% have depression; 12.5% have generalized anxiety disorder, No psychotic symptoms, substance abuse, or significant medical instability</td>
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<td></td>
<td>40 HC</td>
<td>HC 14.88 (0.56)</td>
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<th>Duration of illness</th>
<th>Stage of illness</th>
<th>BMI of AN group</th>
<th>Age of AN onset</th>
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<th>Comorbid diagnoses</th>
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<td>Lang et al. (2015)</td>
<td>41 AN</td>
<td>15.07 (1.81)</td>
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<td>85.4% white</td>
<td>British</td>
<td>NP</td>
<td>1.7 (1.18)</td>
<td>III</td>
<td>16.16 (1.50)</td>
<td>13.80 (2.30)</td>
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<td>Lindner, Fichter, and Quadflieg (2013)</td>
<td>100 AN</td>
<td>34.49 (7.13)</td>
<td>100</td>
<td>NP</td>
<td>40.0% AN-R</td>
<td>3.88 (3.17)</td>
<td>Recovered</td>
<td>20.86 (1.31)</td>
<td>AN-R</td>
<td>3.88 (3.17)</td>
<td>40.0% AN-R</td>
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<td>Lindner et al. (2014)</td>
<td>100 AN</td>
<td>34.53 (7.26)</td>
<td>100</td>
<td>NP</td>
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<td>No psychiatric comorbidity or neurological problems</td>
<td>CF</td>
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<td>Lopez et al. (2008)</td>
<td>42 AN</td>
<td>28.4 (9.6)</td>
<td>100</td>
<td>112.8 (6.8)</td>
<td>69.0% AN-R</td>
<td>13.08 (11.2)</td>
<td>Ill</td>
<td>15.8 (1.7)</td>
<td>AN-R</td>
<td>11.9 (SD not told)</td>
<td>11.9 (SD not told)</td>
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<td>Lounes et al. (2011)</td>
<td>45 AN</td>
<td>27.6 (7.87)</td>
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<td>NP</td>
<td>57.8% AN-R</td>
<td>11.9</td>
<td>Ill</td>
<td>14.7 (1.26)</td>
<td>AN-R</td>
<td>11.9 (SD not told)</td>
<td>11.9 (SD not told)</td>
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<td>49 HC</td>
<td>24.1 (4.37)</td>
<td>42.2% AN-BP</td>
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<td>Study areas: CF = case findings, CC = case controls.</td>
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<td>Medina-Pradas, Navarro, Alvarez-Moya, Grau, and Obiols (2012)</td>
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<td>Mendlewics, Linkowski, Bazelmans, and Philippot (2005)</td>
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<tr>
<td>Morris (2014)</td>
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<td>Nakazato et al. (2008)</td>
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<tr>
<td>Nalbant, Kalayci, Akdemir, Akgül, and Kanbur (2019)</td>
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<th>Study areas</th>
<th>Participants</th>
<th>Age</th>
<th>Females (%)</th>
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<th>Race (AN)</th>
<th>Type of AN</th>
<th>Duration of illness</th>
<th>Stage of illness</th>
<th>BMI of AN group</th>
<th>Age of AN onset</th>
<th>Medication (AN)</th>
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<td>Oldershaw, Hambrook, Tchanturia, Treasure, and Schmidt (2010)</td>
<td>40 AN</td>
<td>AN 27.3</td>
<td>92.5</td>
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<td>NP</td>
<td>35.0% AN-R</td>
<td>7.4 (8.5)</td>
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<td>16.6 (1.3)</td>
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<td>47 HC</td>
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<td>24 AN</td>
<td>AN 29.9</td>
<td>95.8</td>
<td>114.4 (5.6)</td>
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<td>45.8% AN-R</td>
<td>5.6 (3.8)</td>
<td>Recovered</td>
<td>20.8 (2.0)</td>
<td>15.9 (3.6)</td>
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<td>47 HC</td>
<td>HC 29.8</td>
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<td>Ill</td>
<td>15.26 (1.2)</td>
<td>NP</td>
<td>No psychosis</td>
<td>ER</td>
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<td>Sato et al. (2013)</td>
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<td>3.6 (3.7)</td>
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<td>14.6 (1.5)</td>
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<td>26 AN</td>
<td>AN 15.2 (1.7)</td>
<td>100</td>
<td>106.6 (10.5)</td>
<td>NP</td>
<td>NP</td>
<td>1.3 (0.7)</td>
<td>Ill</td>
<td>15.4 (1.2)</td>
<td>34.6%</td>
<td>50% have depression; 8.0% have OCD; 3.8% have conduct disorder; 26.9% have anxiety disorder; 4.3% have panic disorder</td>
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<td>37 HC</td>
<td>HC 15.2 (1.7)</td>
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<th>Race (AN)</th>
<th>Type of AN</th>
<th>Duration of illness</th>
<th>Stage of illness</th>
<th>BMI of AN group</th>
<th>Age of AN onset</th>
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<td>0.9 (0.8)</td>
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<td>16.2 (1.1)</td>
<td>13.6 (2.1)</td>
<td>86.7%</td>
<td>33.3% have depression</td>
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<td>16 HC HC 14.0 (1.6)</td>
<td>NP</td>
<td>NP</td>
<td>AN-BP</td>
<td>13.3%</td>
<td>Ill</td>
<td>16.4 (1.3)</td>
<td>16.8 (0.4)</td>
<td>77.0%</td>
<td>53.9% have depression; 46.2% have anxiety disorder</td>
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<td>116.84 (4.84)</td>
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<td>NP</td>
<td>9.12 (7.4)</td>
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<td>16.31 (2.64)</td>
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<td>No substance abuse or neurological diseases</td>
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<td>NP</td>
<td>AN-BO</td>
<td>42.3%</td>
<td>Ill</td>
<td>15 (1.9)</td>
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<td>0%</td>
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<td>Spitoni, Aragona, Bevacqua, Cotugno, and Antonucci (2018)</td>
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<td>3.89 (1.51)</td>
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<td>4.3 (2.7)</td>
<td>Recovered</td>
<td>21.14 (2.0)</td>
<td>0%</td>
<td>No medical illness, neurological conditions</td>
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<td>10.8</td>
<td>Ill</td>
<td>19.0 (1.0)</td>
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<td>No medical illness or neurological conditions</td>
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<td>NP</td>
<td>NP</td>
<td>NP</td>
<td>7.7 (4.2)</td>
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<td>14.63 (1.7)</td>
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<td>100</td>
<td>NP</td>
<td>NP</td>
<td>4.3 (2.7)</td>
<td>Recovered</td>
<td>21.14 (2.0)</td>
<td>0%</td>
<td>No medical illness, neurological conditions</td>
</tr>
<tr>
<td>(Continues)</td>
<td></td>
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</tr>
<tr>
<td>Study areas</td>
<td>Participants</td>
<td>Age</td>
<td>Females (%)</td>
<td>IQ (AN)</td>
<td>Race (AN)</td>
<td>Type of AN</td>
<td>Duration of illness</td>
<td>Stage of illness</td>
<td>BMI of AN group</td>
<td>Age of AN onset</td>
<td>Medication (AN)</td>
<td>Comorbid diagnoses</td>
<td></td>
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<tr>
<td>Talbot, Hay, Buckett, and Touyz (2015)</td>
<td>24 AN</td>
<td>AN 21.0</td>
<td>95.8</td>
<td>109.46</td>
<td>NP</td>
<td>62.5% AN-R</td>
<td>4.0</td>
<td>II</td>
<td>14.99 (1.83)</td>
<td>16.5</td>
<td>58.3%</td>
<td>54.2% have some comorbid diagnoses</td>
<td></td>
</tr>
<tr>
<td></td>
<td>43 HC</td>
<td>HC 19.0</td>
<td>90.0</td>
<td>110.57</td>
<td>NP</td>
<td>37.5% AN-BP</td>
<td>5.0</td>
<td>Weight recovered</td>
<td>20.99 (1.40)</td>
<td>15.0</td>
<td>40.0%</td>
<td>60.0% have some comorbid diagnoses</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 AN</td>
<td>AN 21.5</td>
<td>100</td>
<td>111.23</td>
<td>NP</td>
<td>73.3% AN-R</td>
<td>4.0</td>
<td>Fully recovered</td>
<td>21.62 (2.00)</td>
<td>16.0</td>
<td>26.7%</td>
<td>46.6% have some comorbid diagnoses</td>
<td></td>
</tr>
<tr>
<td>Tchanturia et al. (2011)</td>
<td>215 AN</td>
<td>AN 26.9 (8.2)</td>
<td>100</td>
<td>109.1 (8.7)</td>
<td>NP</td>
<td>88.3% AN-R</td>
<td>1.2 (1.2)</td>
<td>II</td>
<td>15.8 (1.8)</td>
<td>NP</td>
<td>20.2% have affective disorder; 22.3% have anxiety disorder; 5.3% have psychosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>216 HC</td>
<td>HC 27 (7.9)</td>
<td>100</td>
<td>101.1 (16)</td>
<td>NP</td>
<td>73.3% AN-R</td>
<td>0.87 (0.56)</td>
<td>III</td>
<td>15.93 (0.70)</td>
<td>NP</td>
<td>26.7%</td>
<td>46.6% have some comorbid diagnoses</td>
<td></td>
</tr>
<tr>
<td>Télleus et al. (2015)</td>
<td>94 AN</td>
<td>AN 14.9 (1.8)</td>
<td>89.4</td>
<td>101.1 (16)</td>
<td>NP</td>
<td>73.3% AN-R</td>
<td>0.87 (0.56)</td>
<td>III</td>
<td>15.93 (0.70)</td>
<td>NP</td>
<td>26.7%</td>
<td>46.6% have some comorbid diagnoses</td>
<td></td>
</tr>
<tr>
<td></td>
<td>94 HC</td>
<td>HC 19.0</td>
<td>100</td>
<td>109.1 (8.7)</td>
<td>NP</td>
<td>11.7% AN-BP</td>
<td>0.84 (0.74)</td>
<td>III</td>
<td>14.39 (1.24)</td>
<td>NP</td>
<td>26.7%</td>
<td>46.6% have some comorbid diagnoses</td>
<td></td>
</tr>
<tr>
<td>Van Noort, Pfeiffer, Ehrlich, Lehmkuhl, and Kappel (2016)</td>
<td>30 AN</td>
<td>AN 12.17 (1.57)</td>
<td>NP</td>
<td>109.23 (14.35)</td>
<td>NP</td>
<td>93.3% AN-R</td>
<td>6.7% AN-BP</td>
<td>III</td>
<td>14.39 (1.24)</td>
<td>NP</td>
<td>26.7%</td>
<td>46.6% have some comorbid diagnoses</td>
<td></td>
</tr>
<tr>
<td></td>
<td>30 HC</td>
<td>HC 11.62 (1.29)</td>
<td>NP</td>
<td>108.72 (10.08)</td>
<td>NP</td>
<td>73.3% AN-R</td>
<td>0.87 (0.56)</td>
<td>III</td>
<td>15.93 (0.70)</td>
<td>NP</td>
<td>26.7%</td>
<td>46.6% have some comorbid diagnoses</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AN-R, anorexia nervosa restrictive subtype; AN-BP, anorexia nervosa binge-purge subtype; AN-B, anorexia nervosa binge subtype; AN-P, anorexia nervosa purge subtype; EDNOS-AN, eating disorder not otherwise specified anorexia nervosa subtype; HC, healthy controls; CF, cognitive flexibility; CC, central coherence; ER, emotion recognition; NP, not provided.
RESULTS

3.1 Study characteristics

Study characteristics are presented in Table 1. See Table 2 for details of every study. There were two studies in which the sample was duplicated, but because they presented results on different neuropsychological characteristics, both were included in the analyses. However, the number of participants was calculated only once in Table 1 (Lindner et al., 2013, 2014). In all studies, participants were almost exclusively female. Most of the studies did not report the race of the participants, and those that reported it almost exclusively included Caucasian. Most studies were based on currently ill participants, and among studies reporting illness subtype, most participants had AN-R. Many studies did not report whether the participants had comorbid illnesses or medication, and those that did reported diverse psychiatric comorbidity.

3.2 Central coherence

We identified 15 studies that measured central coherence and were eligible for the meta-analysis. The number of studies or subgroups in each of the three illness duration categories (0–3.99 years, 4.0–6.99 years, 7.0 years or over) was eight, four, and six, respectively. The meta-analysis...
FIGURE 4 A forest plot of studies investigating cognitive flexibility and including participants with anorexia nervosa (AN) with a mean illness duration of 0–3.99 years (top), a mean illness duration of 4.0–6.99 years (center), and a mean illness duration of 7.0 years or over (bottom). AQ, autism quotient; BCST, Berg’s Card Sorting Test; ID/ED, intradimensional/extradimensional; TMT, trail making task; WCST: Wisconsin Card Sorting Test [Color figure can be viewed at wileyonlinelibrary.com]
demonstrated a high degree of heterogeneity in the first two illness duration categories ($\chi^2 = 27.00, p = .0003; \chi^2 = 9.61, p = .02$, respectively), whereas in the third category, the heterogeneity was lower ($\chi^2 = 9.42, p = .09$). In the meta-analysis, weak central coherence was not found in studies with participants whose mean illness duration was less than 4 years ($p = .82, \text{SMD} = -0.03$). Weak central coherence was also not found in studies with participants whose mean illness duration was between 4.0 and 6.99 years ($p = .19, \text{SMD} = -0.37$). A meta-analysis of studies with participants whose mean illness duration was 7 years or longer (prolonged illness) found that these individuals had significantly weaker central coherence than HCs ($p < .00001, \text{SMD} = -0.72$). See Figure 3 for forest plots.

### 3.3 | Cognitive flexibility

We found 30 studies that measured cognitive flexibility and were eligible for the meta-analysis. The number of studies or subgroups in each illness duration category (0–3.99 years, 4.0–6.99 years, 7.0 years or over) was 14, 12, and 12, respectively. The meta-analysis showed a high degree of heterogeneity in the first category ($\chi^2 = 36.88, p = .0004$), whereas in the second and third categories, the heterogeneity was lower ($\chi^2 = 11.48, p = .40; \chi^2 = 12.83, p = .30$, respectively). In the meta-analysis of studies with participants whose mean illness duration was under 4 years (short illness), there emerged no significant differences in cognitive flexibility between individuals with AN and HCs.

**FIGURE 5** A forest plot of studies investigating emotion recognition and including participants with anorexia nervosa (AN) with a mean illness duration of 0–3.99 years (top), a mean illness duration of 4.0–6.99 years (center), and a mean illness duration of 7.0 years or over (bottom). RMET, Reading the Mind in the Eyes Test; SEQ, Socio-Emotional Questionnaire [Color figure can be viewed at wileyonlinelibrary.com]
A meta-analysis of studies with participants whose mean illness duration was 4.0–6.99 years and studies with participants whose mean illness duration was 7.0 years or over (prolonged illness) indicated that individuals with AN had significantly more problems in cognitive flexibility than HCs ($p < .00001$, SMD $-0.58$; $p < .00001$, SMD $-0.63$, respectively). See Figure 4 for forest plots.

### 3.4 Emotion recognition

We found 21 studies that measured emotion recognition and were eligible for the meta-analysis. The number of studies or subgroups in each illness duration category (0–3.99 years, 4.0–6.99 years, 7.0 years or over) was eight, three, and nine, respectively. The meta-analysis demonstrated a high degree of heterogeneity in all three categories ($\chi^2 = 16.70, p = .02$; $\chi^2 = 6.55, p = .04$; $\chi^2 = 23.37, p = .003$, respectively). In the meta-analysis, no significant differences in emotion recognition were found in studies in which participants had mean illness duration under 4 years (short illness) compared to the HCs ($p = .25$, SMD $-0.16$). In addition, in studies with individuals with mean illness duration between 4.0 and 6.99 years, there were no differences in emotion recognition when compared to HCs ($p = .75$, SMD $-0.09$).

A meta-analysis of studies of individuals with mean illness duration of 7 years or over (prolonged illness) showed that individuals with AN had significantly more problems in emotion recognition than HCs ($p < .0001$, SMD $-0.64$). See Figure 5 for forest plots.

### 3.5 Synthesis of the meta-analysis

Individuals with a short duration of AN (0–3.99 years) did not differ from HCs in central coherence, cognitive flexibility, and emotion recognition. Individuals with average duration of AN (4.0–6.99 years) did not differ from HCs in central coherence and emotion recognition, whereas they had significantly more difficulties in cognitive flexibility than HCs. Individuals with prolonged illness duration (7.0 years or over) had significantly weaker central coherence, more problems in cognitive flexibility, and more problems in emotion recognition when compared to HCs. See Table 3 for synthesis of results.

### 4 DISCUSSION

This study is the first systematic review with a meta-analysis reporting a relationship between illness duration in individuals with AN and neuropsychological characteristics related to ASD. The meta-analysis showed that problems in cognitive flexibility, weak central coherence, and difficulties in emotion recognition are evident among individuals with prolonged AN but not among those with shorter illness duration.

The nature of the relationship between AN illness duration and higher levels of cognitive inflexibility, weak central coherence, and problems in emotion recognition is not clear. Some researchers have suggested that prolonged illness amplifies neuropsychological...
characteristics (neurological scar effect, Lang, Stahl, et al., 2014). It has been suggested that reduction of brain volume observed in adults with AN could contribute to the neuropsychological difficulties and therefore reflect the neurological scar effect (Lang, Stahl, et al., 2014). Reduction of brain volume is also shown to correlate with illness duration, based on individuals with prolonged illness manifesting more brain abnormalities (Fonville, Giampietro, Williams, Simmons, & Tchanturia, 2014). However, reduction of brain volume and global cortical thinning are shown to be reversed after weight restoration, which could indicate that these abnormalities are unlikely to solely reflect the neurological scar (Fonville et al., 2014; King et al., 2015). In contrast, other studies suggest that neuropsychological characteristics become more pronounced (Fonville, Giampietro, Williams, Simmons, & Tchanturia, 2014). However, reduction of brain volume and global cortical thinning are shown to be reversed after weight restoration, which could indicate that these abnormalities are unlikely to solely reflect the neurological scar (Fonville et al., 2014; King et al., 2015). In contrast, other studies suggest that neuropsychological characteristics persist after recovery and that these characteristics are unlikely to solely reflect the neurological scar (Fonville et al., 2014; King et al., 2015). In contrast, other studies suggest that neuropsychological characteristics persist after recovery and that these characteristics also manifest in the healthy relatives of individuals with AN (Holliday et al., 2005; Roberts et al., 2013; Tenconi et al., 2010). These findings suggest that neuropsychological characteristics also associated with ASD constitute at least part of the endophenotype of AN (Holliday et al., 2005; Roberts et al., 2013; Tenconi et al., 2010).

The reality may lie somewhere between these two approaches. Individuals with AN with underlying neuropsychological features typical of ASD may benefit less from traditional treatments, leading to prolonged illness. This is supported by the fact that high levels of ASD traits are associated with a more severe clinical presentation and poorer outcome in AN (Nielsen et al., 2015; Stewart et al., 2017; Tchanturia et al., 2017). The prolonged illness may then cause the "neurological scar effect," further strengthening these underlying neuropsychological characteristics. As a result, due to these further exacerbated neuropsychological features, rehabilitation may become increasingly difficult as the illness endures. This model of the role of neuropsychological characteristics of AN is shown in Figure 6.

It is also important to pay attention to the possible underdiagnosing of ASD among individuals with AN and how it may be associated with prolonged illness duration. Previous studies report that 8–28% of individuals with AN receive a comorbid ASD diagnosis if careful diagnostic assessment of ASD is performed (Anckarsäter et al., 2012; Huke et al., 2013; Westwood et al., 2017b; Westwood, Mandy, Simic, & Tchanturia, 2018). In addition, a nationwide register-based study found that a family history of ASD was associated with an increased risk of AN, and a family history of AN was associated with increased risk of ASD (Koch et al., 2015). ASD itself is associated with various eating problems, such as highly selective eating, restricted diet, and food refusal (Råstam, 2008). Undetected comorbid ASD may be one factor for poor treatment outcome in some individuals with AN as their underlying problem is unrecognized ASD. Future studies should investigate treatment regimens for AN that also take into account pronounced ASD traits in individuals with this disorder.

5 | LIMITATIONS

This study has some limitations. An important limitation is that the categories of illness duration are based on the mean illness duration represented in each individual study, and therefore, it is likely that there are participants with varying illness duration. However, in our view, this was a reasonable way to conduct this meta-analysis as we did not have access to the raw data of each study. In addition, from a mathematical perspective, if illness duration is associated with the strength of neuropsychological deficits, the mean illness duration should reflect the mean strength of neuropsychological deficits in each study. Participants in the included studies were largely female, and the results of the meta-analysis are therefore not necessarily generalizable to males. The AN subtype (AN-R or AN-BP) was also not taken into account because most of the articles included both AN-R and AN-BP participants and did not analyze results separately. A previous review has suggested that there may be differences between AN-R and AN-BP regarding at least some neuropsychological characteristics (Van Autreve, De Baene, Baeken, van Heeringen, & Vervaet, 2013), so it is possible that this aspect could have affected the results. Finally, the illness stage (currently ill or recovered) and the age of the participants were not included in the analysis; as it has been reported that neuropsychological difficulties are independent of illness stage (e.g., Kanakam & Treasure, 2013; Roberts et al., 2007), this limitation may not cause bias in this meta-analysis.

6 | CONCLUSIONS

In this meta-analysis, we showed that prolonged course of AN is associated with neuropsychological characteristics, including problems in central coherence, cognitive flexibility, and emotion recognition. These characteristics are also characteristic of ASD, suggesting an overlap between the two disorders. We suggest that clinicians...
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