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RESEARCH ARTICLE

The impact of depressive and anxious symptoms on quality of life in adults on the autism spectrum

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Abstract

Quality of life (QoL) is lower in adults on the autism spectrum (AS) compared with typically developing (TD) adults. In this context, recent studies have examined the role of depression and anxiety in reducing QoL in AS adults. The aim of this study was to (1) replicate these findings of lower QoL and (2) assess the negative influence of depressive and anxious symptoms on QoL in an adult AS ($N = 86$) and TD ($N = 87$) German sample with a broad age range (18–70 years). For this, we used questionnaires that have been validated for the AS and TD population: the World Health Organization Quality of Life Brief Version, the Autism-Specific QoL items, and the Hospital Anxiety and Depression Scale. We replicated previous findings and extended them to autism-specific QoL. Our AS sample had lower QoL compared with the TD adults. However, depressive symptoms were the largest contributor to lower QoL in both samples, more so than group membership and anxious symptoms. We conclude that interventions to improve QoL in AS adults should specifically target depressive symptoms and for this, improvements to the diagnostic process and treatment of depression in AS are necessary.

Lay Summary

Adults on the autism spectrum reported lower quality of life (QoL) in comparison to typically developing adults. Depressive symptoms were a more relevant aspect in reducing QoL in both study groups than group membership or anxious symptoms. We conclude that interventions to improve QoL in adults on the autism spectrum should specifically address depressive symptoms. For this, improvements in recognizing and treating depression in autism spectrum are necessary.

KEYWORDS
adults, anxiety, autism spectrum, depression, quality of life

INTRODUCTION

The World Health Organization defines quality of life (QoL) as "individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" (World Health Organization, 1998, p. 3). QoL represents personal well-being, combining domains like interpersonal relationships, social inclusion, personal development, physical well-being, self-determination, material and emotional well-being in one construct (Schalock, 2004). Mental health problems have been found to be of relevance in terms of QoL in the general population with especially individuals being diagnosed with anxiety or depression experiencing poorer QoL (e.g., IsHak et al., 2011;

Olatunji et al., 2007; Saarijärvi et al., 2002) compared with healthy individuals.

Individuals on the autism spectrum (AS), often recognized in early childhood (American Psychiatric Association, 2013), experience challenges beyond childhood and adolescence, for instance poor social integration and mental health problems in adulthood (Barneveld et al., 2014; Howlin & Magiati, 2017). Prevalence rates of coexisting psychiatric conditions are increased in AS compared with typically developing (TD) adults (Croen et al., 2015; Joshi et al., 2013; Lai et al., 2019). Anxiety disorders and depression are very common (Lever & Geurts, 2016), with Hollocks et al. (2019) reporting a pooled lifetime prevalence rate of 42% for anxiety disorders and 37% for depression in adults on the AS. Studies in AS children suggest an association between anxiety, depression, and QoL (e.g., Adams et al., 2019; van Steensel et al., 2012). However, findings on the influence of depressive and anxious symptoms on QoL in AS adults are still rare and inconsistent, which makes more research necessary.

The World Health Organization Quality of Life Brief Version (WHOQoL-BREF; WHOQOL GROUP, 1998) is most commonly used to assess QoL in AS and TD samples (Ayres et al., 2018; Kim & Bottema-Beutel, 2019; McConachie et al., 2018, 2020). It evaluates QoL in four domains: physical, psychological, social, and environment. As some essential aspects for AS individuals, such as the influence of sensory issues on QoL, are left out, additional facets of QoL have been explored to better depict their experience (McConachie et al., 2018). The result were Autism-Specific Quality of Life Items (ASQoL; McConachie et al., 2018) evaluating AS-specific facets of QoL like friendship, AS identity, perceived support, sensory overload, and barriers in accessing services. These items describe experiences more relevant to an AS population but are not exclusive or necessarily unique to AS and, therefore, justify a comparison of AS and TD groups on these items. To our knowledge, only few other studies have used the ASQoL, for instance to validate a measure of alexithymia (Williams & Gotham, 2021a), but not yet to investigate QoL in a German AS sample or to compare AS and TD adults. In this study, we used it as an add-on module to the WHOQoL-BREF.

AS adults' self-reports on their subjective QoL were found to be reliable and internally consistent (Hong et al., 2016), which is essential, as the concept of QoL requires personal appraisal and an individual's subjective perception (World Health Organization, 1998). Further, studies showed that parent-reports might rather be an evaluation of their children's perceived impairment and functioning than their QoL (for further discussion see Knüppel et al., 2018). For instance, AS individuals rate their social QoL higher than their parents do (Hong et al., 2016; Knüppel et al., 2018), which further highlights the importance of the subjective perspective. Since autistic individuals often struggle not only with mental health issues but also with the difficulties in society that are brought by the diagnosis, it is important to evaluate their QoL to indicate where change is needed, to assess it as an outcome measure in adulthood and to evaluate diagnostic and treatment effects.

Subjective QoL in AS adults has been highly researched in recent years and was found to be lower across all domains when compared with TD samples and normative populations (Ayres et al., 2018; Graham Holmes et al., 2020; Lin & Huang, 2019; Mason et al., 2019; Oakley et al., 2021). In comparison to other QoL domains, the social domain has been reported as lowest in AS adults (Ayres et al., 2018; Knüppel et al., 2018; Lin & Huang, 2019; Mason et al., 2018), which represents one of the main areas of difficulties in AS (American Psychiatric Association, 2013). Other studies suggested that the greatest impairment is in the psychological domain (Hamm & Yun, 2019; Mason et al., 2019; Vincent et al., 2020), which is consistent with elevated distress and impaired mental health in AS (Park et al., 2019).

However, there is considerable variability, as not all AS individuals experience lower QoL (Hong et al., 2016; Moss et al., 2017; Oakley et al., 2021). This might be due to a variety of factors that potentially influence QoL, such as age, gender, AS core-symptoms, mental health, social, and intellectual functioning (Graham Holmes et al., 2020; Kim & Bottema-Beutel, 2019; Mason et al., 2018; Smith et al., 2019; van Heijst & Geurts, 2015). While a recent meta-analysis reported inconsistent and nonsignificant findings for the relationships between QoL and aspects, such as age, AS core-symptoms, and intelligence (Kim & Bottema-Beutel, 2019), impaired mental health and coexisting psychiatric conditions seem to be important factors responsible for reducing QoL in AS (Knüppel et al., 2018; Lawson et al., 2020; Mason et al., 2018, 2019; Oakley et al., 2021; Park et al., 2019; Smith et al., 2019). The results of four of these studies are of particular interest for the current investigation and will be described in detail below. Mason et al. (2019) reported on data of 69 autistic adults (48 men, 21 women), aged 55 years and above with a mean age of 61.5 years (SD = 5.27). The authors used the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) to investigate Anxiety ($M = 12.29$, SD = 4.32) and Depression ($M = 9.26$, SD = 4.31). Non-autistic individuals were included. Testing a larger sample with a much broader age-range, Lawson et al. (2020) included 244 autistic (15–80 years) and 165 non-autistic individuals (15–77 years). Park et al. (2019) assessed 96 autistic and 944 non-autistic young adults (16–30 years). Non-autistic adults either had a diagnosis of Depression ($N = 343$), Bipolar disorder ($N = 132$), Psychosis ($N = 166$), or Anxiety ($N = 303$). Finally, Oakley et al. (2021) reported on autistic ($N = 344$) and non-autistic ($N = 229$) individuals

between 6 and 33 years including 106 autistic and 86 non-autistic adults (both groups 18–30 years).

While Mason et al. (2019) and Lawson et al. (2020) found depressive symptoms to be associated with lower QoL across all domains in AS adults, Park et al. (2019) and Oakley et al. (2021) reported this association for all domains except for social and environment QoL, respectively. Regarding anxious symptoms, Park et al. (2019) only found a correlation with overall QoL but not with the individual domains. In line with this, Oakley et al. (2021) did not find a relation between anxious symptoms and lower QoL domain scores in AS adults. In contrast, Mason et al. (2019) reported that high levels of anxious symptoms had a negative impact on QoL in an AS sample, except for the social domain. Additionally, results by Smith et al. (2019) suggested that clinical levels of anxious symptoms had a significant impact on the social and psychological domains of QoL in AS adults. In sum, the evidence to date suggests relatively consistent and pervasive influences of depressive symptoms on multiple dimensions of QoL in AS adults, with anxiety playing a more circumscribed role. Although the specific pattern of findings varies across studies, this is likely due to the varying tools used to assess anxiety and depression as well as the complex bidirectional relationship between anxiety and depression over time (e.g., Jacobson & Newman, 2017), which is likely to be subject to considerable individual differences.

The current study builds on existing studies of QoL in autistic adults by considering the role of depression and anxiety in relation to autism-specific as well as more general dimensions of QoL and by examining these relationships in both an AS and TD group. As noted above, autism-specific aspects of QoL are not necessarily unique to autism and it is therefore of interest to explore their etiology also in the general population. In addition, it is of interest to establish whether the relative contributions of depression and anxiety to such autism-specific aspects of quality of life follow a similar pattern to that relating to more general aspects. To address this, we followed Mason et al. (2019) in using the HADS (Zigmond & Snaith, 1983) as a measure of depressive and anxious symptoms because it is a validated measure in AS adults (Uljarević et al., 2018). It is also worth noting that we used a German AS and TD sample with a broad age range (18–70 years) thereby adding to the replication of findings beyond English speaking samples.

Our two main hypotheses were the following: (1) Consistent with previous research, we expected the QoL in our AS sample to be lower than in our TD sample. We expected this for all domain scores of the WHOQoL-BREF as well as the ASQoL total. Due to inconsistencies in the literature, we did not draw any further expectations about between-group differences in certain domains. (2) We expected depressive and anxious symptoms to have a negative impact on QoL in AS and TD adults. We expected this to be the case for the WHOQoL-BREF subscales and the ASQoL total. Again, we did not draw any further predictions about between-group differences.

METHODS

Participants

Participants were recruited between May 2020 and May 2021 as part of a larger project aiming to improve the diagnostic process of anxiety in AS. The sample consisted of 173 individuals, including 86 AS[1] (24.4% female; age range = 18–67 years) and 87 matched TD adults[2] (24.1% female; age range = 18–70 years; Table 1). Groups were matched on chronological age, gender, and education status showing no significant differences in either of these variables: chronological age, $t(171) = -0.42$, $p = 0.675$, $d = -0.06$, 95% CI [−0.36, 0.23], gender, $\chi^2(1) = 0.002$, $p = 0.966$, $V = 0.003$, and education status, $U = 3218.50$, $p = 0.097$, $r = -0.13$, [−0.27, 0.02]. All participants received the German Autism-Spectrum Quotient (AQ; adapted from Baron-Cohen et al., 2001; Freitag et al., 2007) assessing AS-like traits within the typical population. The AS group showed higher scores than the TD sample, $t(171) = 12.56$, $p < 0.001$, $d = 1.91$, 95% CI [1.55, 2.27]. Specific data on ethnicity and socioeconomic status were not recorded.

Autistic participants were patients at the autism outpatient clinic of the university hospital Carl Gustav Carus in Dresden, Germany. As this is a specialized clinic with an interdisciplinary program for children, adolescents, and adults experiencing AS symptoms, patients visit for diagnosis and/or service. They received a clinical diagnosis of F84.0, F84.1, or F84.5 according to the International Statistical Classification of Diseases and Related Health Problems, Tenth Edition (ICD-10; World Health Organization, 1992). Diagnoses were obtained prior participation using the gold standard for autism diagnostic, that is, the Autism Diagnostic Observation Schedule (ADOS; Poustka et al., 2015; Rühl et al., 2004) and the Autism Diagnostic Interview-Revised (ADI-R; Bölte et al., 2006). Diagnostic assessments included the evaluation of intelligence using the German versions of the Wechsler Intelligence Scale for adults (Petermann, 2012; Tewes, 1991; von Aster et al., 2006) and children (Petermann & Petermann, 2008; Tewes et al., 1999) or the Cultural Fair Intelligence Test Scale 1 (Weiß & Osterland, 1997) depending on the age of participants at diagnosis. Participants were recruited through telephone calls, e-mails, their therapists, and flyers at the clinic. We only included individuals who could answer the questionnaires in self-report, excluding individuals

[1]Another 28 autistic adults were recruited but did not return their questionnaires: 24 did not specify a reason, three indicated a lack of time and one felt overwhelmed.
[2]Another 10 TD adults were recruited but did not return their questionnaires: eight did not specify a reason and two withdrew due to a lack of time.

TABLE 1 Descriptive statistics for the autism spectrum (AS) and typically developing (TD) sample.

	AS (65 m, 21 f)		TD (66 m, 21 f)	
Continuous variables	***M***	**SD**	***M***	**SD**
Age (years)	33.5	13.3	34.4	14.2
AQ[a]	32.8	8.9	17.5	7.1
FSIQ[b]	103.9	15.6		
ADOS				
C[c]	4.1	1.9		
RSI[d]	7.8	3.3		
Total[e]	11.7	4.3		
Im[f]	1.2	0.7		
SB[g]	1.1	1.1		
ADI-R				
SI[h]	17.0	5.0		
CL[i]	11.7	3.9		
RRB[j]	4.0	2.6		
Categorical variable	***n***	**%**	***n***	**%**
Education status[k]				
No degree	4	4.7	0	0
Nine years of school	5	5.8	5	5.7
Ten years of school	37	43.0	27	31.0
Higher education entrance qualification	17	19.8	29	33.3
University or college degree	19	22.1	24	27.6
Postgraduate degree	4	4.7	2	2.3

[a]Autism-spectrum quotient (AQ)—Total.
[b]Full-scale intelligence quotient (FSIQ; $n = 71$) assessed by German versions of the Wechsler Intelligence Scale for adults (Petermann, 2012; Tewes, 1991; von Aster et al., 2006) and children (Petermann & Petermann, 2008; Tewes et al., 1999) or the Cultural Fair Intelligence Test Scale 1 (Weiß & Osterland, 1997).
[c]Autism diagnostic observation schedule (ADOS)—Communication subscale ($n = 73$).
[d]ADOS—Reciprocal social interaction subscale ($n = 73$).
[e]ADOS—Total (Communication subscale + Reciprocal social interaction subscale; $n = 74$).
[f]ADOS—Imagination/Creativity subscale ($n = 72$).
[g]ADOS—Stereotyped behaviors and restricted interests subscale ($n = 72$).
[h]Autism diagnostic interview-revised (ADI-R)—Social interaction subscale ($n = 60$).
[i]ADI-R—Communication and language subscale ($n = 58$).
[j]ADI-R—Restricted and repetitive behaviors subscale ($n = 58$).
[k]Highest degree according to the German education system.

with an intelligence quotient (IQ) below 75. Overall, 23 AS adults (26.7%) had no coexisting psychiatric diagnoses in their lifetime, while 36 (41.9%) had one and 27 (31.4%) two or more. Mood disorders and neurotic, stress-related and somatoform disorders were the most common in our AS sample (see Table S1 for details).

Typical adults were recruited from a hospital-wide database of participants from past research through telephone calls and e-mails, flyers, and advertisement on eBay and Facebook. Further, we invited participants through letters sent to addresses provided by the resident registration office and the hospital's website and mailing list. Prospective participants answered an initial screening questionnaire and were included if they reported no personal or family history of AS or other related developmental or psychiatric diagnoses. Participants were included if they reported a history of anxiety or depression but it was not possible to recruit enough individuals with the relevant clinical diagnoses (only $n = 11$) to comprise a separate clinical comparison group vis-à-vis an AS and TD group. Participants who described elevated substance consume, for example more than five uses of cannabis or more than two uses of other illegal substances per year, were also excluded.

Procedure

Individuals gave written informed consent to participate and if there was a legal guardian, they agreed as well. Participants chose to answer the questionnaires paper based or took the online survey on LimeSurvey (Version 2.72.3, LimeSurvey GmbH, 2003), which they accessed via participant codes. Completing this project's twelve

TABLE 2 Descriptive statistics for the WHOQoL-BREF, ASQoL, and HADS.

	AS		TD				
Continuous variables	***M***	**SD**	***M***	**SD**	***t* (171)**	***d***	**95% CI**
WHQoL-BREF[a]							
Physical	66.8	14.5	79.5	13.2	6.03	0.92*	−1.23, −0.60
Psychological	56.3	17.1	71.5	15.7	6.12	0.93*	−1.24, −0.62
Social	52.4	22.5	66.1	21.9	4.06	0.62*	−0.92, −0.31
Environment	68.6	14.9	77.8	11.6	4.55	0.69*	−1.00, −0.38
ASQoL[b]					*t*(160.23)		
Total	63.5	17.4	77.5	13.5	5.95	0.91*	−1.22, −0.59
HADS[c]							
Depression	7.0	4.5	4.8	3.9	3.47 (166.86)	0.53*	0.23, 0.83
Anxiety	7.8	3.9	5.8	3.8	3.51 (171)	0.53*	0.23, 0.84
Categorical variables	***N***	**%**	***N***	**%**			
HADS—Depression[c]							
Normal	49	57.0	69	79.3			
Marginal	13	15.1	10	11.5			
Clinically significant	24	27.9	8	9.2			
HADS—Anxiety[c]							
Normal	47	54.7	61	70.1			
Marginal	17	19.8	16	18.4			
Clinically significant	22	25.6	10	11.5			

Abbreviations: AS, autism spectrum; TD, typically developing.
[a]World Health Organization Quality of Life Brief Version (WHOQoL-BREF).
[b]Autism-Specific Quality of Life Items (ASQoL).
[c]Hospital Anxiety and Depression Scale (HADS). *Statistically significant at $p < 0.001$.

questionnaires took approximately 60 min, including 20 min for the questionnaires reported here. After completion, the participants were compensated with €10. There was no community involvement in the reported study.

Materials

The WHOQoL-BREF (WHOQOL GROUP, 1998) is a 26-item questionnaire assessing subjective QoL on four domains: (1) physical, (2) psychological, (3) social, and (4) environment. Two global items evaluate overall QoL and satisfaction with health. Items were answered on a 5-point scale and subscale totals were transformed to scores ranging from 0 to 100 as described in the manual (World Health Organization, 1998) with higher scores indicating a higher QoL. The German WHOQoL-BREF has good internal consistency for the subscales ($\alpha = 0.77$–0.87; Gunzelmann et al., 2002). In an English-speaking AS sample, internal consistency was good for the subscales ($\alpha = 0.84$–0.87), except the social domain, where it was acceptable ($\alpha = 0.68$; McConachie et al., 2018). We used the global items and subscale scores for analysis.

The *ASQoL* (McConachie et al., 2018) evaluates facets of QoL that are essential to AS individuals. The questionnaire comprises one factor consisting of eight items on a 5-point scale and one global item asking about AS identity. We conducted the same score transformation for the total score as mentioned above. The internal consistency was excellent ($\alpha = 0.82$) in an English-speaking AS sample (McConachie et al., 2018). In this study, we used a self-translated German version of the ASQoL in consultation with the original authors (McConachie et al., 2018). We used the total scores across the 8 core items of the scale for analysis in both groups and the global item to describe the AS sample's relation with their autistic identity.

Depressive and anxious symptom were assessed using the 14-item German HADS (Herrmann-Lingen et al., 2010). The depression and anxiety subscales contain seven items rated on a 4-point scale with each subscale ranging from 0 to 21, higher scores indicating more severe levels of depressive and anxious symptoms. For analysis, we used cutoff scores proposed by Zigmond and Snaith (1983): ≤7—normal, 8–10—marginal, ≥11—clinically significant. Thereby, participants could reach clinically significant levels of symptoms in either depression, anxiety, or both. Internal consistency for the German version was good for both subscales ($\alpha = 0.80$–0.81; Herrmann-Lingen et al., 2010). The HADS was validated in an English-speaking adolescent and young adult AS

sample (Uljarević et al., 2018), finding good and acceptable internal consistency for the anxiety ($\alpha = 0.83$) and depression subscale ($\alpha = 0.65$), respectively.

Statistical analysis

Less than 1% of items were missing (5 for the WHOQoL; 3 for the ASQoL; 0 for the HADS), which were replaced by means of the corresponding subscales. Following, the data was analyzed using IBM SPSS Statistics (Version 27). Independent samples *t*- and Mann–Whitney U-tests tested for between–group differences. We then analyzed the combined impact of group and levels of depressive and anxious symptoms on the QoL subscales of the WHOQoL-BREF by using a MANOVA and a separate univariate ANOVA to evaluate their impact on autism-specific QoL assessed by the ASQoL. Since participants distributed unevenly over the levels of depressive and anxious symptoms, significant findings by MANOVA and (follow-up) ANOVA were analyzed by Scheffé posthoc tests. Cohen's *d*, Pearson's correlation coefficient *r* and partial eta squared (η_p^2) described effect sizes. All significance levels were set at 0.05, to which Bonferroni correction was applied for multiple comparisons.

RESULTS

Between-group differences for QoL, depressive, and anxious symptoms

First, we compared QoL scores between groups without accounting for different levels of depressive and anxious symptoms. Independent samples *t*-tests showed lower scores for AS compared with TD adults in all QoL domains as well as in the ASQoL total (see Table 2).

The distribution of the WHOQoL-BREF's global QoL item differed between groups, $U = 2255.00$, $p < 0.001$, $r = -0.37$, 95% CI [−0.49, −0.23]. Most AS adults rated their overall QoL as good, but many also indicated it to be neither poor nor good. In comparison, most TD participants reported their global QoL to be (very) good. The distribution of the WHOQoL-BREF's global satisfaction with health item also differed between groups, $U = 2671.00$, $p < 0.001$, $r = -0.26$, 95% CI [−0.40, −0.12]. Only half of the AS participants were (very) satisfied with their health compared with three-quarters of TD adults. Additionally, most AS adults reported being mostly or totally comfortable with their AS diagnosis on the ASQoL's global item, while 13 participants reported to be not at all or only a little content with AS as part of their identity (see Table S2 for details on the global items).

Independent samples *t*-tests showed higher HADS raw scores for AS compared with TD adults in the depression and anxiety subscales as can be seen in Table 2. Overall, the distribution of cutoff-scores differed between the two groups in the depression, $U = 2837.50$, $p < 0.001$, $r = -0.25$, 95% CI [−0.39, −0.11], and anxiety subscales, $U = 3071.50$, $p = 0.018$, $r = -0.18$, [−0.32, −0.03]. Around a fourth of AS adults met the cutoff for clinically significant levels in the depression subscale compared with around a tenth in the TD group—with similar distributions in the anxiety subscale (Table 2). Further, 12 AS (14.0%) compared with four TD adults (4.6%) met the criteria for clinically significant levels in both subscales.

Combined impact of group, depressive, and anxious symptoms on QoL

Table 3 sets out the correlations among the QoL, anxiety, and depression measures along with associations with age, AQ and for the ASD group also the available IQ data. Correlations for the ASD group are shown below the diagonal and those for the TD group above diagonal. Age was not correlated with any of the WHOQoL, ASQoL, or HADS measures in either group and in the ASD group this was also true for the available IQ measure, in line with recent findings (Kim & Bottema-Beutel, 2019). Autism-related traits, as measured by the AQ, was also not correlated with any of the QoL, depression, or anxiety measures in the ASD group, whereas in the TD group these associations were significant with exception of the WHOQoL environment subscale. As expected, the WHOQoL/ASQoL subscales and the two HADS subscales, were closely interrelated in both groups (light-shaded areas), and in both groups the HADS anxiety and depression subscales also demonstrated close associations with all QoL subscales (dark-shaded areas).

Due to the multidimensional construct of quality of life, we first examined the influence of AS diagnosis, depression, and anxiety by calculating a three-way MANOVA using the factors "group" (AS, TD), "depression" (normal, marginal, and clinically significant) and "anxiety" (normal, marginal, and clinically significant) as independent variables and all four subscales of the WHOQoL-BREF (physical, psychological, social, and environment) as dependent variables. There was a medium-sized effect of "group" on the combined dependent variables, Pillai's trace = 0.07, $F(4, 152) = 2.79$, $p = 0.028$, $\eta_p^2 = 0.07$. AS participants had lower QoL scores than TD individuals. However, separate follow-up ANOVAs revealed no "group" effects on the individual subscales of the WHOQoL-BREF after applying Bonferroni correction ($p_{\text{Bonferroni}} \leq 0.0125$; $F_{\max} \leq 6.15$, $p_{\min} \geq 0.014$, $\eta_p^2{}_{\max} \leq 0.04$).

Further, "depression" had a large-sized effect on the combined QoL subscales, Pillai's trace = 0.34, $F(8, 306)$

TABLE 3 Correlations among quality-of-life, anxiety, and depression measures and participant's age, IQ, and AQ for the ASD (below diagonal) and TD (above diagonal groups).

		1	2	3	4	5	6	7	8	9	10
1	FSIQ		N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
2	Age (years)	0.275		0.147	−0.053	−0.090	−0.159	−0.166	−0.192	0.206	−0.006
3	AQ	0.231	0.381*		−0.351*	−0.426*	−0.416*	−0.243	−0.502*	0.402*	0.403*
4	WHQoL physical	0.050	−0.218	−0.319		0.716*	0.513*	0.633*	0.535*	−0.526*	−0.460*
5	WHQoL psychological	0.129	−0.081	−0.212	0.715*		0.663*	0.534*	0.582*	−0.721*	−0.691*
6	WHQoL social	0.133	−0.133	0.035	0.205	0.399*		0.459*	0.620*	−0.669*	−0.482*
7	WHQoL environment	0.125	−0.164	−0.090	0.495*	0.516*	0.397*		0.595*	−0.473*	−0.398*
8	ASQoL total	−0.010	−0.240	−0.350*	0.519*	0.583*	0.526*	0.694*		−0.558*	−0.545*
9	HADS depression	−0.031	0.164	0.223	−0.558*	−0.784*	−0.297	−0.457*	−0.472*		0.590*
10	HADS anxiety	−0.014	0.025	0.214	−0.465*	−0.613*	−0.195	−0.317	−0.438*	0.591*	

*Statistically significant at Bonferroni corrected $p < 0.001$. Light shaded areas highlight correlations among sub-factors of the quality-of-life measures and HADS anxiety and depression subscales; dark shaded areas the correlations across these scales.

TABLE 4 Means and standard deviations of quality of life (QoL) measures by group and level of depressive/anxious symptoms.

	Depression[a]						Anxiety[a]					
	Normal		Marginal		Clinically significant		Normal		Marginal		Clinically significant	
Measures	***M***	**SD**	***M***	**SD**	***M***	**SD**	***M***	**SD**	***M***	**SD**	***M***	**SD**
Physical QoL[b]												
AS	72.4	12.5	65.4	14.2	56.1	12.8	70.4	13.0	68.3	12.3	57.7	16.0
TD	81.8	12.3	74.6	11.5	65.6	13.8	82.3	12.8	75.2	11.8	68.9	11.3
Psychological QoL[b]												
AS	66.2	11.5	54.2	5.9	37.0	13.5	63.3	15.0	53.5	10.0	43.4	18.0
TD	76.0	11.7	62.1	16.5	44.8	13.5	77.0	12.4	63.8	12.9	50.4	15.6
Social QoL[b]												
AS	55.9	21.2	50.6	26.5	46.2	22.5	55.7	20.7	47.1	15.9	49.4	29.4
TD	72.2	17.6	50.8	15.9	32.3	22.9	72.0	17.5	58.9	19.8	41.7	29.4
Environment QoL[b]												
AS	74.6	11.4	59.6	16.5	61.2	15.2	72.6	12.6	66.4	13.6	61.8	18.0
TD	79.6	10.4	77.8	10.7	62.5	12.4	80.1	10.8	73.6	12.6	70.6	1d0.8
Autism-specific QoL[c]												
AS	69.0	14.4	60.2	15.6	53.9	19.8	69.2	14.0	62.7	16.0	51.8	19.6
TD	80.7	11.3	73.1	8.4	56.1	16.4	81.3	11.1	70.1	13.4	66.5	17.1

Abbreviations: AS, autism spectrum; TD, typically developing.
[a]Depression and anxiety measured by the Hospital Anxiety and Depression Scale (HADS).
[b]QoL measured by the World Health Organization Quality of Life Brief Version (WHOQoL-BREF).
[c]QoL measured by the Autism-Specific Quality of Life Items (ASQoL).

$= 7.95$, $p < 0.001$, $\eta_p^2 = 0.17$. Subsequently, univariate ANOVAs revealed main effects of "depression" on all four QoL subscales—physical, $F(2, 155) = 8.13$, $p < 0.001$, $\eta_p^2 = 0.10$, psychological, $F(2, 155) = 36.49$, $p < 0.001$, $\eta_p^2 = 0.32$, social, $F(2, 155) = 7.09$, $p = 0.001$, $\eta_p^2 = 0.08$, and environment QoL, $F(2, 155) = 10.13$, $p = < 0.001$, $\eta_p^2 = 0.12$. Scheffé posthoc tests showed differences in QoL between the subgroups defined by normal, marginal, and clinically significant levels of depressive symptoms ($p_{max} \leq 0.012$). Thereby, highest QoL was found in the subgroup with normal levels of "depression," while QoL was lower in the subgroup with marginal and lowest in the subgroup with clinically significant levels for physical and psychological QoL (Table 4). Only the differences in the social and environment subscales of QoL between marginal and clinically significant levels of depressive symptoms were non-significant ($p_{min} \geq 0.198$).

"Anxiety" also had a medium-sized effect on the combined QoL variables, Pillai's trace $= 0.11$, $F(8, 306)$

TABLE 5 Regression analyses examining the combined effects of AQ, depression and anxiety on WHOQoL and ASQoL quality of life measures.

Dependent	Model (adjusted R^2; F test)	Predictors	Beta	t	p
WHOQoL physical	$R^2 = 0.47$ ($F(3,160) = 49.48$; $p < 0.001$)	AQ	−0.298	4.68	<0.001
		Depression	−0.380	5.23	<0.001
		Anxiety	−0.181	2.47	0.15
WHOQoL psychological	$R^2 = 0.67$ ($F(3,160) = 111.18$; $p < 0.001$)	AQ	−0.185	3.67	<0.001
		Depression	−0.522	9.09	<0.001
		Anxiety	−0.278	4.8	<0.001
WHOQoL social	$R^2 = 0.25$ ($F(3,160) = 18.84$; $p < 0.001$)	AQ	−0.153	2.01	0.046
		Depression	−0.387	4.47	<0.001
		Anxiety	−0.063	0.72	0.474
WHOQoL environment	$R^2 = 0.26$ ($F(3,160) = 20.41$; $p < 0.001$)	AQ	−0.119	1.58	0.115
		Depression	−0.381	4.45	<0.001
		Anxiety	−0.121	1.40	0.165
ASQoL	$R^2 = 0.47$ ($F(3,160) = 20.41$; $p < 0.001$)	AQ	−0.376	5.90	<0.001
		Depression	−0.270	3.72	<0.001
		Anxiety	−0.221	3.30	0.003

$= 2.31$, $p = 0.020$, $\eta_p^2 = 0.06$. Univariate ANOVAs indicated an effect of "anxiety" on psychological subscale of QoL, $F(2, 155) = 7.58$, $p = < 0.001$, $\eta_p^2 = 0.09$, but not on the other subscales ($p_{\text{Bonferroni}} \leq 0.0125$; $F_{\max} \leq 1.47$, $p_{\min} \geq 0.232$, ${\eta_p^2}_{\max} \leq 0.019$). Using Scheffé posthoc-tests, we identified differences in QoL between the three levels of "anxiety" in relation to the psychological subscale ($p_{\max} < 0.001$) with highest, lower, and lowest QoL at normal, marginal, and clinically significant levels of "anxiety," respectively (Table 4).

There was a interaction between "group" and "depression," Pillai's trace $= 0.10$, $F(8, 306) = 2.01$, $p = 0.045$, $\eta_p^2 = 0.05$. However, separate ANOVAs for the individual QoL subscales did not find this effect after applying Bonferroni correction ($p_{\text{Bonferroni}} \leq 0.0125$; $F_{\max} \leq 3.71$, $p_{\min} \geq 0.027$, ${\eta_p^2}_{\max} \leq 0.05$). No other interaction effects were significant ($F_{\max} \leq 1.59$, $p_{\min} \geq 0.067$, ${\eta_p^2}_{\max} \leq 0.04$).

The ASQoL total was entered as the dependent variable in a 2 ("group" [AS, TD]) × 3 ("depression" [normal, marginal, and clinically significant]) × 3 ("anxiety" [normal, marginal, and clinically significant]) ANOVA. There was a small main effect of "group," $F(1, 155) = 7.68$, $p = 0.006$, $\eta_p^2 = 0.05$ with AS adults showing lower QoL than TD participants. The main effect of "depression" was also medium-sized, $F(2, 155) = 8.90$, $p < 0.001$, $\eta_p^2 = 0.10$. Scheffé posthoc tests indicated that AS-specific QoL was highest at normal, lower at marginal and lowest at clinically significant levels of "depression" ($p_{\max} \leq 0.011$). Neither the main effect of "anxiety," nor any of the interactions were significant ($F_{\max} \leq 2.23$, $p_{\min} \geq 0.111$, ${\eta_p^2}_{\max} \leq 0.03$).

Complementing the above analyses that treated diagnostic group, anxiety, and depression as categorical variables, we also carried out regression analyses to examine the combined influence of AQ, depression and anxiety as continuous variables on the individual quality of life measures across both groups combined. The results are summarized in Table 5, and help to further clarify the pattern of results above. Specifically, depression was again the strongest and most consistent predictor across all dimensions of QoL. Autism-related traits (AQ), explained further unique variance only in the physical and psychological dimensions of the WHOQoL as well as the ASQoL, whilst anxiety played a unique role primarily in the psychological dimension of the WHOQoL and the ASQoL.

DISCUSSION

Autistic adults experience poorer QoL compared with TD adults (Ayres et al., 2018; Graham Holmes et al., 2020; Lin & Huang, 2019). Recent studies in the AS population have drawn a link between low QoL, poor mental health and a high prevalence of coexisting psychiatric conditions, particularly depressive and anxious symptoms (Lawson et al., 2020; Mason et al., 2019; Oakley et al., 2021; Park et al., 2019). The aim of this study was to investigate general and AS-specific QoL, depressive and anxious symptoms in an adult AS and matched TD German sample with a broad age range by using questionnaires that have been validated for AS adults.

Initially, we compared QoL between the groups without accounting for depressive and anxious symptoms. Consistent with our first hypothesis and past research (Ayres et al., 2018; Graham Holmes et al., 2020; Lin & Huang, 2019; Oakley et al., 2021), group (AS or TD) had a large influence on general QoL, that is all domains of

the WHOQoL-BREF had lower scores in AS compared with TD adults. This was also the case for QoL measured by the ASQoL, which has not been used before to compare QoL between AS and TD adults. However, when also considering the impact of depressive and anxious symptoms on QoL, the effect of group (AS or TD) became less pronounced, explaining unique variance only in relation to physical and psychological dimensions of the WHOQoL measure, as well autism-specific facets of quality of life captured by the ASQoL. This finding is important as it highlights the role of internalizing symptoms in relation to QoL in both AS and TD populations and it emphasizes the importance of early diagnosis and treatment of (co-occurring) mental health problems.

As expected, depressive symptoms had a negative influence on general and AS-specific QoL in AS and TD adults. Consistent with Lawson et al. (2020) and Mason et al. (2019), we found that depressive symptoms had a negative effect on all domains of general QoL, while Park et al. (2019) and Oakley et al. (2021) did not find this for the social and environment domains, respectively. Interestingly, these are the two QoL domains that did not demonstrate an effect of AQ in our regression analyses. Park et al. (2019) reported a relatively high social QoL for their AS sample. This differs from findings in our and abovementioned studies and might explain, why depressive symptoms did not reduce social QoL in their study. Oakley et al. (2021) reported fewer participants for the environment domain compared with the other domains of QoL in their study and due to this, the influence of depressive symptoms might have stayed undetected. To our knowledge, our study was the first to show that depressive symptoms also negatively affects aspects of QoL that are especially important to AS individuals as measured by the ASQoL.

The relevance of depressive symptoms in both groups is consistent with findings by Lawson et al. (2020), but might seem surprising, since we excluded TD participants with one or more psychiatric diagnoses. However, approximately one fifth of TD adults still reported increased levels of depressive symptoms, which explains why depressive symptoms had substantial negative influence on QoL in both AS and TD adults. While depressive symptoms reduce QoL independent of group, we also found an interactive effect of group and depressive symptoms on general QoL, which is clarified by the pattern of results in the regression analysis. Specifically, while physical and psychological dimensions of the WHOQoL demonstrated independent effects of depression and autism-related traits (AQ), this was not the case for social and environmental dimensions. This may seem counterintuitive given that social-communication difficulties are a core clinical characteristic of AS, and it is worth noting that the effect of AQ on the social WHOQoL sub-domain was marginal. Depressive symptoms can present themselves atypically in AS or interact with and influence AS core-symptoms (Stewart et al., 2006). For example, depressive symptoms might further reduce interest in social interaction or engagement with previously preferred routines (Chandrasekhar & Sikich, 2015). It is possible that such interactions between AS and depressive symptoms contribute to greater individual differences in relation to QoL than is the case for other dimensions, thus contributing to the pattern of findings reported here as well as the differences in findings across previous studies. Future studies could explore this issue, by probing mental health aspects that might be relevant for AS-specific QoL in more detail. For example, there is only one broad item in the WHOQoL-BREF assessing "negative feelings" including depressive symptoms and it might be beneficial to add more specific items to the ASQoL, seeing the impact depressive symptoms play in reducing QoL (for further discussion see McConachie et al., 2018, 2020).

Similar to depressive symptoms, we expected anxiety to negatively influence QoL, which was recently found in autistic adults (Mason et al., 2019; Smith et al., 2019). This hypothesis was largely confirmed although anxiety had a unique negative effect only on ASQoL and the psychological dimension of WHOQoL once depression and AQ were accounted for. This helps to explain some of the differences in findings in the existing literature. Specifically, unlike Mason et al. (2019) and Smith et al. (2019), other studies reported no influence of anxiety on QoL (Lawson et al., 2020; Oakley et al., 2021). Smith et al. (2019), however, only investigated anxious, but not depressive symptoms, and Mason et al. (2019) examined the impact of anxious and depressive symptoms on QoL separately rather than accounting for their interrelations. Lawson et al. (2020) and Oakley et al. (2021), on the other hand, investigated depressive and anxious symptoms in one analysis as was the case here. Given the complex bidirectional relationship between anxiety and depression over time (e.g., Jacobson & Newman, 2017), it is unsurprising that findings will differ depending on whether one or both of these internalizing symptoms are taken into account.

Taken together with existing literature, our results suggest that depressive symptoms were primarily responsible for reduced QoL in our sample, more so than anxious symptoms and autism-related traits, which may play a more circumscribed role in relation to psychological well-being and autism-specific facets of QoL. This implies that large group differences in QoL between AS and TD adults could partially be explained by high prevalence rates of coexisting psychiatric conditions in the AS population, particularly depressive symptoms. In line with this, depressive symptoms have increasing relevance in AS adults compared with AS children and adolescents (Hollocks et al., 2019). The severity of depressive symptoms in AS adults even appears to be comparable to individuals with primary diagnoses of mood disorders (Lever & Geurts, 2016; Park et al., 2019). Combined with these findings, our results suggest that programs to improve QoL should specifically target depressive symptoms. While QoL is already an important outcome measure of

psychosocial interventions (National Institute for Health and Care Excellence, 2012), empirical evidence for effective treatments of depressive symptoms or full-blown depression in AS adults is still insufficient (Menezes et al., 2020). There are studies supporting the effectiveness of cognitive behavioral therapy for treating anxious symptoms or anxiety in AS (White et al., 2018), but findings for depressive symptoms are inconsistent. Russell et al. (2020) assessed the feasibility of adapting a self-help intervention in cognitive behavioral therapy for autistic adults and showed promising results in that more individuals attended all sessions of the self-help intervention compared with treatment as usual, completed follow-up assessments and indicated the helpfulness of the therapy. More research in this direction is needed. There is, however, emerging empirical evidence suggesting the efficacy of mindfulness-based therapy (Chandrasekhar & Sikich, 2015; Menezes et al., 2020). Effective treatments against depressive and anxious symptoms would likely benefit AS adults most in psychological QoL. This domain was most strongly reduced by depressive symptoms compared with the other subscales and the only aspect negatively affected by anxious symptoms.

In this context, it is important to point out the difficulties in assessing depressive and anxious symptoms due to their co-occurrence and overlap with core-symptoms of AS (South et al., 2017; Stewart et al., 2006; Uljarević et al., 2018). Many AS adults, who meet criteria for depression, also meet criteria for anxiety and vice versa, while also scoring higher on AS specific measures like the AQ and ADOS (Lever & Geurts, 2016). Possibly, high levels of depression or anxiety could be related to higher levels of autistic-like traits (Albantakis et al., 2020). However, contrary to depressive symptoms, the influence of AS characteristics on QoL itself stays questionable and with contradicting results (Kim & Bottema-Beutel, 2019). It is possible though that depressive and anxious symptoms have a different impact on QoL depending on the level of autistic-like symptoms or vice versa. For example, Smith et al. (2019) found that AS social functioning only predicts social QoL if the level of anxiety is low. Future studies could further investigate this interaction regarding depressive symptoms and in relation to AS-specific QoL. In practice, this overlap of symptoms can lead to problems when core-symptoms of AS mask signs of depression and anxiety and therefore complicate their recognition (Mazzone et al., 2012). For example, reduced engagement in repetitive behaviors can be interpreted as an "improvement," while it can also be indicative of depression (Stewart et al., 2006). Therefore, diagnostic tools developed for the general population might not be appropriate, but there is still a lack of standardized assessment tools for depression in AS adults (Chandrasekhar & Sikich, 2015; Mazzone et al., 2012) as well as a lack of research in this area. The little evidence that there is indicates the need for adaptation of existing tools (Cassidy et al., 2018).

This is problematic, given the large influence depressive symptoms have on QoL in AS adults. It is hence not only essential to address depressive and anxious symptoms in interventions to improve QoL but also to further develop the diagnostic process of coexisting psychiatric problems up to disorders in the AS population.

The following limitations of this study need to be considered. First, our AS sample did not include participants with IQs below 75, which was due to the nature of this study using subjective measures in self-report. However, this limits the findings to adults with average and high intelligence on the AS, where intellectual disabilities are highly prevalent (Fombonne, 2003; La Malfa et al., 2004). A recent meta-analysis of studies examining the relationship between IQ and internalizing symptoms of anxiety and depression in ASD (Edirisooriya et al., 2021), highlighted some inconsistent findings across a still limited literature (15 relevant studies were identified), which was in part attributed to methods of measurement. For example, studies using self-report to examine anxiety found a negative association between anxious symptoms and IQ, which was not found in studies using informant-report measures. This may suggest that internalizing symptoms in autistic individuals with intellectual disabilities may sometimes be underestimated and more efforts should be directed at further developing appropriately tailored and adapted measurement tools through which autistic individuals with intellectual disabilities can effectively self-report on their mental health and wellbeing. Second, participants of the TD group were excluded if they reported psychiatric diagnoses. Therefore, the comparison between the groups only allows conclusions about differences between AS individuals and TD adults without mental disorders. While past studies have already compared the QoL of AS adults and individuals with other primary psychiatric and neurodevelopmental diagnoses (Barneveld et al., 2014; Park et al., 2019), future research should systematically compare AS and TD adults with and without diagnoses of depression and anxiety respectively to better assess their specific impact on QoL. Additionally, while depressive and anxious symptoms are very common in autistic adults, other diagnoses like ADHD are highly prevalent as well (Joshi et al., 2013; Lai et al., 2019) and most likely also contribute to differences in QoL between the groups. Further, demographic factors, such as employment, relationship, and socioeconomic status as well as ethnicity have been shown to have associations with internalizing symptoms (Akhtar-Danesh & Landeen, 2007; Everson et al., 2002) as well as QoL in TD individuals (Thumboo et al., 2003). These factors were not recorded in the current study but should be considered in future research. Further, it is important to note that the percentage of women included in this study was quite low to represent the ratio of men and women in autism. However, there might be differences in the

relation between anxiety, depression, and QoL in men and women in autism (Mason et al., 2018). Future studies should, therefore, ideally collect samples large enough to be able to compare subgroups of men and women. When doing this, one should be aware of two recent studies testing the psychometric properties of questionnaires on QoL in autism. In a first study, Williams and Gotham (2021b) assessed the ASQoL and reported on a gender bias underestimating the QoL of autistic women. The authors emphasize the importance of a revision of the ASQoL to be sensitive to these gender differences. Since we did not intend to compare autism-specific QoL between men and women, this bias seems not too problematic for the current study. Nevertheless, more research is needed to revise and validate the measure. In another study, Williams et al. (2023) developed an autism-specific scoring method for the Patient-Reported Outcomes Measurement Information System Global–10 (PROMIS global-10), which might also be a good tool to assess QoL in autistic adults. However, more research is needed to support these first important findings. Regarding the current study, because of the cross-sectional assessment, differences in QoL could be due to depressive and anxious symptoms, but it is also possible that individuals with lower QoL are more vulnerable to psychological distress and developing mental disorders. Ultimately, this study took place during the COVID-19 pandemic, which might have influenced QoL, depressive and anxious symptoms measured in this study (Ferreira et al., 2021; Hyland et al., 2020; Oomen et al., 2021).

Despite these limitations, the key strength of the study is to explore autism-specific aspects of QoL in AS adults and also the general population, as they are not necessarily unique to autism. hTe current study showed the substantial negative impact of depressive symptoms on autism-specific as well as more general dimensions of QoL in both AS and TD adults, which surpassed the negative influence of anxious symptoms or group. An early diagnosis and effective treatment of depressive symptoms should be an important part in interventions improving QoL in adults on the AS.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

This study was approved by the ethics committee of the Technische Universität Dresden (Processing number: EK 356092018) and adhered to the guidelines of Helsinki.

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