Autism Spectrum Disorder, Externalizing Behavior and Pubertal Status in Adolescents

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Abstract

Adolescents with ASD show more externalizing behavior, compared to their peers. Additionally, early pubertal development can increase the risk of showing externalizing behavior. Recent input indicates that females with ASD can show early pubertal development, which raises the question of whether early pubertal development could influence externalizing behavior amongst adolescents with ASD. Therefore, this study aimed to assess the possible moderating effect of pubertal status (PDS) on the association between the likelihood of ASD (ASD-scale) and externalizing behavior, in particular rule-breaking behavior, aggressive behavior (YSR, ASEBA), and the onset of alcohol use (general substance use questionnaire). The data from the baseline measurement from the observational prospective cohort study The iBerry Study was used, consisting of 500 male and 522 female high- and low-risk adolescents (2.5:1 ratio), age 12 to 18. Higher pubertal status was associated with higher externalizing, rule-breaking, and aggressive behavior for male and female adolescents, and a smaller chance of already having used alcohol for female adolescents. A higher likelihood of ASD was associated with higher externalizing and rule-breaking behavior for female adolescents and higher aggressive behavior and chances of already having used alcohol for male and female adolescents. However, there was no interaction effect of pubertal status and the likelihood of ASD on all studied externalizing behaviors, indicating no moderating effect. Results add to current knowledge by broadening previous findings beyond the clinical population to high-risk adolescents who show sub-clinical symptoms of ASD and better comprehension of symptoms that female adolescents with ASD experience.

ASD is a pervasive developmental disorder characterized by impairments in social interaction and communication, as well as repetitive patterns of behavior, interests, or activities, that are present from early childhood (American Psychiatric Association, 2013). The *Diagnostic and Statistical Manual of Mental Disorders* (DSM-V) (American Psychiatric Association, 2013) reports a 1% prevalence for ASD for both children and adults. In recent years, the prevalence of ASD increased to approximately 2% (Chiarotti & Venerosi, 2020). The DSM-V reports a 4:1 sex-based ratio of males to females. More recent research suggests a ratio closer to 3:1, where females with ASD might be underdiagnosed, which could be due to females being better at camouflaging their symptoms than males with ASD (Loomes, Hull & Mandy, 2017). Previous research shows that 70% of children and adolescents with ASD have at least one comorbid diagnosis, like social anxiety disorder, attention-deficit/hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), obsessive-compulsive disorder (OCD), and specific phobia (Simonoff et al., 2008; Leyfer et al., 2006). Adolescents with ASD often have fewer friendships, do not engage in social activities

as much as their peers, and are more likely to have learning difficulties in school (Montes & Halterman, 2006; Orsmond, Krauss & Seltzer, 2004).

Several studies demonstrate that children and adolescents with ASD engage in higher levels of externalizing behavior than typically developing peers (Kanne & Mazurek, 2011; Mahan & Matson, 2011; Matson, Wilkins & Macken, 2008; Mazurek, Kanne & Wodka, 2013). Externalizing behavior consists of a broad range of behaviors, like aggressiveness, impulsivity, noncompliance, and control problems (Bauminger, Solomon & Rogers, 2010). Children and adolescents with ASD show more hyperactivity and conduct problems compared to their peers (Mahan & Matson, 2011). Additionally, high rates of aggression towards caregivers and non-caregivers are found amongst children and adolescents with ASD (Kanne & Mazurek, 2011). A cross-sectional prevalence rate of aggression of 46.9% amongst 14- to 17-year-old adolescents with ASD was reported (Mazurek, Kanne & Wodka, 2013). Children who have more severe symptoms of ASD are shown to exhibit more challenging and problem behaviors than children with milder ASD symptoms (Matson, Wilkins & Macken, 2008). Regarding another type of externalizing behavior, substance use, it is argued that individuals with ASD mostly use substances to suppress social anxiety, reduce stress, and increase social abilities (Kronenberg et al., 2014). Individuals with ASD can also have dysfunctional coping styles, which can put them at greater risk of substance abuse (Kronenberg et al., 2015). Alcohol use is the most common substance of choice amongst individuals with ASD (Haasbroek & Morojele, 2021), and a positive association between autistic traits and alcohol dependence has been found (de Alwis et al., 2014). Since alcohol has an anxiolytic effect, is widely available, and overall socially accepted, drinking could be used as a coping strategy to handle social situations or for feelings of social isolation and deficits in executive functioning (Haasbroek & Morojele, 2021; Kaltenegger et al., 2021). Research looking into alcohol use amongst adolescents with ASD is still at an early stage, which calls for further research to explore this. Taken together, previous research shows overall more externalizing behavior amongst children and adolescents with ASD, compared to their typically developing peers.

In their meta-analytic review, Dimler & Natsuaki (2015) argued that early pubertal timing is a risk factor for externalizing behaviors. Puberty is characterized as the transition between childhood and adulthood; a period of substantial physical, cognitive, neuroendocrine, and social-emotional changes (Negriff & Susman, 2011). The development of secondary sexual characteristics is an indication of the onset of puberty, like the development of breasts in females and genital maturing in males. Both sexes also develop pubic hair. Biological changes are the result of a neuroendocrine process, which involves adrenarche (like dehydroepiandrosterone, DHEA), growth hormones, and gonadarche (the production of estrogen and testosterone). Next to physical and biological changes, adolescence encompasses a time

with changes in social-affective engagement, risk-taking, planning, goal flexibility, and decision-making (Crone & Dahl, 2012). Often, new social, cognitive, and emotional challenges are encountered. Research shows that early pubertal timing is a risk factor for externalizing behaviors in adolescents, like conduct problems, delinquency, and antisocial tendencies (Dimler & Natsuaki, 2015). In agreement, Negriff & Susman (2011) argued in their review that most of the literature shows a negative impact of early pubertal timing for externalizing behavior. For example, more symptoms of ADHD, ODD, and CD were found amongst adolescents who matured earlier (Ge et al., 2002). Early pubertal timing was also associated with rule-breaking, conduct disorder symptoms, and attention behavior problems for boys and relational aggression for girls (Susman et al., 2007). In line with this, early pubertal development was associated with elevated delinquency and physical aggression amongst early-adolescent females (Mrug et al., 2014).

Several hypotheses for explaining the relationship between early pubertal timing and externalizing behaviors have been developed. The developmental readiness hypothesis (also called the early timing or stage termination hypothesis), discusses the differences between physical, cognitive, social, and emotional maturity (Ge et al., 2002). It states that certain developmental tasks have to be completed before someone can sufficiently transition into adolescence. Following this reasoning, early puberty can bring difficulties, since there has been less time to acquire the skills necessary to handle the transition into puberty. Another explanation states that the hormonal changes associated with puberty could increase novelty-seeking behaviors, which could heighten the risk for developing externalizing behavior (Dimler & Natsuaki, 2015). The maturational deviance hypothesis states that any deviation from normal development is stressful, which increases exposure to mood and behavior problems (Negriff & Susman, 2011). Following this hypothesis, girls and boys who mature early will deviate from their peers, leading to different problems. All things considered, research indicates that early pubertal development is a risk factor for different kinds of externalizing behaviors.

In a recent article, the onset of puberty for individuals with ASD (age 10-13) was discussed (Corbett et al., 2020). Since the onset of puberty is marked by several physiological, psychological, and social changes (Negriff & Susman, 2011), and ASD is characterized by difficulties with change in routine or environment (American Psychiatric Association, 2013), the onset and course of puberty may be a crucial transition for adolescents with ASD. Some earlier studies report earlier pubertal timing in females (Harper & Collins, 1979; Mouridsen & Larsen, 1989; Yoshimura et al., 2005) and males (Tordjman et al., 1997;) with ASD. Other studies report a delayed pubertal onset (Hergüner & Hergüner, 2016; Knickmeyer et al., 2006; Whitehouse et al., 2011) in females with ASD. Importantly, most of these studies were uncontrolled and clinically referred, retrospective self-report studies or case studies. May et al. (2017) looked at

pubertal timing of males and females with ASD, age 8-15, compared to non-ASD peers. In contrast to earlier research, no difference was found in pubertal timing for males and females with ASD. In a more recent study, Corbett et al. (2020) looked at pubertal timing for adolescents with ASD or with typical development and across sexes. Pubertal onset was measured by genital/breast (GB) and pubic hair stage (PH), based on a physical examination carried out by a licensed physician. There were no differences in slopes of the GB-stage for typical developing adolescents, and results showed the expected developmental sex differences for PH-stage between males and females. For adolescents with ASD, significant sex differences were found. Females with ASD had significantly earlier pubertal onset, compared to males with ASD and typically developing females. Adolescent females with ASD showed an earlier onset of menses and breast development, but not for pubic development, compared to typically developing adolescent females (Corbett et al., 2020). The indication that the timing of pubertal development is already decreasing worldwide (Eckert-Lind et al., 2020), needs to be considered. Thus, even with an already declining pubertal onset, females with ASD showed earlier pubertal onset in this study (Corbett et al., 2020). Taken together, there is an indication that females with ASD can show earlier onset of puberty.

In summary, previous research firstly shows more externalizing behavior amongst adolescents with ASD, compared to their typically developing peers. In addition, research also indicates that early pubertal development can increase the risk to show externalizing behavior. Given the recent input of Corbett et al. (2020), there is an indication that females with ASD can show early pubertal development. This raises the question of whether early pubertal development could have an influence on externalizing behavior amongst adolescents with ASD. Until now, as far as is known, no study has looked at this association. Since challenging behaviors are the primary reason for referral and treatment amongst individuals with ASD (Matson & Smith, 2008), factors associated with these challenging behaviors are important to be aware of, to identify and treat these behaviors. Since no study has looked into the possible influence of pubertal status on externalizing behavior for adolescents with ASD, it is useful to explore this possible effect in full scope. Therefore, the focus of this study is on the likelihood of ASD. In 2013, when the DSM-V went into effect, the sub-group labels for autism that were used in the DSM-IV were combined to one: autism spectrum disorder (American Psychiatric Association, 2000; American Psychiatric Association, 2013). As the name suggests, one of the main features of this spectrum is the large variability in symptom severity in clinical populations (Bora et al., 2017). Focusing on the entire spectrum of severity of ASD symptoms gives ground for exploring the possible effect of pubertal status in full scope. Next to this, research suggests a possible diagnostic gender bias for ASD, where females with ASD might be better

at disguising their symptoms and therefore could be underdiagnosed (Loomes, Hull & Mandy, 2017). A better understanding of the total scope of symptoms that females with ASD experience, including the possible influence of pubertal development, could be helpful. Therefore, this study aims to investigate the possible moderating effect of pubertal status on the association between the likelihood of ASD and externalizing behavior in male and female adolescents.

Firstly, the association between the likelihood of ASD and externalizing behavior is explored. This will be assessed for externalizing behavior and more specifically rule-breaking behavior, aggressive behavior, and the onset of alcohol use. Based on previous research (Kanne & Mazurek, 2011; Mahan & Matson, 2011; Matson, Wilkins & Macken, 2008; Mazurek, Kanne & Wodka, 2013), it is expected that there will be an association between the measured likelihood of ASD and externalizing, rule-breaking and aggressive behavior. Namely, adolescents who measure higher on the likelihood of ASD will show more externalizing, rule-breaking, and aggressive behavior. Research looking at alcohol use amongst adolescents with ASD is still at an early stage. It is therefore interesting to explore the onset of alcohol use, namely: if the adolescent at the time of measurement ever used alcohol. Especially given that alcohol use could be a coping mechanism for individuals with ASD, who already show impairments in social interaction (American Psychiatric Association, 2013; Haasbroek & Morojele, 2021; Kaltenegger et al., 2021). Following this and the positive association found between autistic traits and alcohol dependence (de Alwis et al., 2014), it is expected that there will be an association between the measured likelihood of ASD and alcohol use. Namely, adolescents who measure higher on the likelihood of ASD will have a higher chance of already having used alcohol.

Next, the association between pubertal status and externalizing behavior is explored. This will be assessed for externalizing behavior and more specifically rule-breaking behavior, aggressive behavior, and the onset of alcohol use. The focus of this study lies on pubertal status, which indicates the level of development at a single point in time. For example, how far the development of breasts is for girls at the time measured. Based on previous research (Dimler & Natsuaki, 2015; Negriff & Susman, 2011), it is expected that there will be an association found between pubertal status and externalizing, rule-breaking and aggressive behavior, and the onset of alcohol use. Namely, adolescents with a higher pubertal status will show more externalizing behavior.

If there is an association found between the likelihood of ASD and externalizing behavior, rule-breaking behavior, aggressive behavior, and the onset of alcohol use, the possible moderating effect of pubertal status on these associations will be evaluated. Given that Corbett et al. (2020) only found early pubertal development amongst females with ASD, follow-up analyses will be conducted to assess the

effect of the sex of the adolescent. Based on the indication that females with ASD can show earlier onset of puberty (Corbett et al., 2020), and that early pubertal development is a risk factor for externalizing behaviors (Dimler & Natsuaki, 2015; Mrug et al., 2014; Negriff & Susman, 2011; Susman et al., 2007), it is expected that pubertal status will have a moderating effect on the association between the likelihood of ASD and externalizing behavior, rule-breaking behavior, aggressive behavior, and the onset of alcohol use.

Method

The iBerry Study

The participants in this study were part of the iBerry Study cohort (Grootendorst – van Mil et al., 2021). For the present study, the data of the baseline measurement was used. The iBerry Study is an observational prospective cohort study situated in Rotterdam-Rijnmond. The focus of this study lies on the observation and identification of the long-term course of subclinical psychiatric symptoms of adolescents and which genetic and psychosocial determinants can help explain the transition from subclinical psychiatric symptoms to evident psychiatric disorders. As part of this study, high-risk and low-risk adolescents and their parents were selected from the health research that the CJG (Centre for Youth and Family) Rijnmond carried out in 2015 and 2016. To form these high and low-risk groups, based on the risk of developing psychopathology, adolescents were screened with the Dutch version of the Strengths and Difficulties Questionnaire Youth (SDQ-Y) (van Widenfelt et al., 2003) in their first year of high school. The low-risk group was formed from the lowest 85% of the scores on the SDQ-Y (n=294). The high-risk group was formed from the highest 15% of the scores on the SDQ-Y (n=728), with a 2.5:1 ratio for high-risk to low-risk adolescents. The iBerry Study was approved by the Medical Ethics Research Committee of Erasmus University Medical Centre, Rotterdam (NL47209.078.14).

There were several inclusion criteria formulated. The adolescents were required to speak the Dutch language and there needed to be written permission to participate from both parents/caregivers and the participating adolescent. The adolescents also needed to screen positive (high-risk) or negative (low-risk), based on the inclusion criteria from phase one of the iBerry Study. Exclusion criteria were adolescents under the age of 12 or adolescents who already participated in the Generation R study, which is also located in Rotterdam-Rijnmond. Adolescents and/or their parents who indicated that they did not want to be approached, were also excluded.

Participants

A total of 1022 adolescents participated in the iBerry Study, 500 males (48.9%) and 522 females (51.1%). The mean age for all adolescents was 15.0 years, with a range from 12.7 to 18.4 years. Males were between the age of 12.7 and 18.4 (*M* =15.0, *SD* = 0.9). Females were between the age of 12.9 and 18.3 (*M* = 15.0, *SD* = 0.9). A total of 61 adolescents participated in the study without their parent or caregiver. Next to this, 961 parents or caregivers participated in the iBerry study, 162 males (15.9%) and 799 females (78.2%). The mean age of all parents/caregivers was 46.6 years, with a range of 29.0 – 70.5. Males were between the age of 34.8 and 68.0 (*M* = 49.7, *SD* = 6.2). Females were between the age of 29.0 and 70.5 (*M* = 45.9, *SD* = 5.3). Sociodemographic characteristics of the participants are presented in Table 1. The educational level describes the level of education followed during the time measured for the adolescent and the educational level achieved for the accompanying parent or caregiver.

Procedure

For the baseline measurement of the iBerry Study, the adolescents, together with one of their parents or caretakers, were invited to the research centre situated at the Erasmus Medical Centre (Erasmus MC) for a three-hour visit. All participants received information about the nature of the study and signed an informed consent form before their appointment. General instructions about the time schedule and anonymity of personal information were given at the beginning of the visit to the adolescent and parent/caregiver. During their visit, the adolescent and the parent/caregiver were interviewed separately by a trained (child)psychiatric care worker and were asked to fill in questionnaires. Participants verbally responded to the different questions from the interview. No direct feedback was given to them about their responses. Next to the interview, physical measurements and neuropsychological tasks were administered to the parent/caregiver and adolescent. In total, the interview and tests for the adolescent and parent/caregiver took about 90 minutes. In addition, there was a 30-minute break for filling in questionnaires. At no point during the appointment, the health or safety of the participants was at risk. There was an extensive protocol for identifying situations that are reason for concern and a psychiatrist was always available for consultation. As a reward for their participation, the adolescent received a gift card with five euros of credit.

Table 1

Sociodemographic Characteristics of the Participants

		Adolescent			Parent/caregiver	
		Frequency	Percent (%)		Frequency	Percent (%)
Ethnicity	Dutch	709	69.4		689	67.4
	Asian	30	2.9		35	3.4
	African	7	0.7		7	0.7
	South American	6	0.6		6	0.6
	Other Western	55	5.4		65	6.4
	Suriname	49	4.8		47	4.6
	Moroccan	12	1.2		12	1.2
	Turkish	12	1.2		13	1.3
	Dutch Antilles	19	1.9		12	1.2
	Cape Verdean	16	1.6		15	1.5
Educational level	SVO	36	3.5	Primary school	20	2.0
	VMBO 1,2,3	215	21.0	Secon. school**	515	50.4
	VMBO 4	215	21.1	HBO	195	19.1
	HAVO	219	21.4	WO	121	11.8
	VWO	186	18.2	Other	56	5.5
	Not specified*	88	8.6	Missing	115	11.3
	Missing	10	1.0			
Type of accompanying parent/caregiver				Biological	886	86.7
				Stepparent	1	0.1
				Adoption parent	5	0.5
				Foster parent	4	0.4
				Grandparent	2	0.2
				Missing	5	0.5

Note. Not specified*: class with combined educational levels. Secon. school**: Secondary school/ Vocational training.

Materials

Screening for autism spectrum disorder

ASD-scale (So et al., 2013)

To screen for autism spectrum disorder in our sample, an ASD-scale from So et al. (2013) was used, which is derived from the *Child Behavior Checklist* (CBCL) and the *Teacher's Report Form* (TRF). The CBCL and TRF are part of *The Achenbach System of Empirically Based Assessment* (ASEBA) and are parent-report and teacher-report questionnaires for assessing behavioral, social, and emotional problems in children and adolescents (Archenbach & Rescorla, 2000). Both questionnaires contain 113 items and the response is scored on a 3-point scale (0 = not true, 1 = somewhat or sometimes true and 2 = very true or often true). The CBCL and TRF are comprised of eight syndrome scales: Withdrawn/Depressed, Somatic Complaints, Anxious/Depressed, Social Problems, Thought Problems, Attention Problems, Rule-Breaking Behavior, and Aggressive Behavior. The aim of the study of So et al. (2013), was to test which of the items on the CBCL and TRF would be best to make a distinction between adolescents with ASD and adolescents from other diagnostics groups. Their study was based on a sample of 3853 children, age 6-18, consisting of referred children with ASD, referred children without ASD, and children from the general population. Based on their findings, a separate ASD-scale was formed of ten items from the CBCL/TRF (Appendix A). These ten items were significantly higher in the ASD group, compared to the other groups. The combined ASD-scale demonstrated high predictive values, based on a cut-off score of eight for the general population. They found a positive predictive value (PPV) of 95% and a negative predictive value (NPV) of 73%. Internal consistency with a Cronbach's alpha of .81 was found on the ASD-scale, which indicates good reliability. By using the CBCL and TRF combined, instead of using only the CBCL items, the accuracy of the prediction of ASD amongst adolescents increased by only 1-8% (So et al., 2013). As is argued in Deckers, Muris & Roelofs (2020), the additional value of including the TRF was quite limited. In combination with this reasoning and given the fact that there were a lot of missing TRF's in this sample, only the items from the CBCL were used for this study. The maximum time to fill in the CBCL was 20 minutes. The total score for each participant was calculated by adding the scores of the 10 selected items on the CBCL, which was used continuously. To determine who screened positive for ASD, a cut-off score of five was used, following Deckers, Muris & Roelofs (2020).

Measurement of pubertal status

Pubertal Development Scale (PDS)

To measure pubertal status, the Pubertal Development Scale (PDS) was used (Petersen et al., 1988). The PDS is a self-report instrument where physical development on five different aspects is indicated. For both girls and boys questions about growth in height, growth of body hair, and skin changes (pimples) were asked. Additionally, for boys, deepening of the voice and growth of facial hair were assessed. For girls, breast growth and menarche were also questioned. The state of development was assessed on a four-point rating scale with the following answer options: 'Not yet started' (1 point), 'Barely started' (2 points), 'Definitely started' (3 points), and 'Seems complete' (4 points), except for menarche (started: yes (4 points)/no (1 point) and if yes, at what age). The maximum time to fill in this questionnaire was 5 minutes. Petersen et al. (1988) report an internal consistency with a Cronbach's alpha between .68 and .83, which indicates questionable to good reliability. Carskadon & Acebo (1993) report strong correlations between self-report (PDS) and physician ratings of physical examination (Tanner stages) with r = 0.841 – 0.868. The Dutch translation of the items is presented in Appendix B. The mean score on the five items for boys and girls was computed to obtain an overall pubertal status score, where the higher scores point to further development of physical maturation. This score was used continuously.

Measurement of externalizing behavior

Externalizing, rule-breaking, and aggressive behavior (YSR)

To measure externalizing, rule-breaking and aggressive behavior, the Youth Self-Report (YSR) was used. The YSR is a general assessment instrument for behavioral and emotional problems of children and adolescents aged 6 – 18 and is part of ASEBA (Archenbach & Rescorla, 2000). The YSR is filled in by the adolescent and contains 112 items with a response score on a 3-point scale (0 = not true, 1 = somewhat or sometimes true and 2 = very true or often true). To measure externalizing behavior, the externalizing syndrome scale of the YSR is used. This subscale is comprised of two subscales: rule-breaking behavior (15 items) and aggressive behavior (17 items). The externalizing subscale contains 32 items in total, for example, 'steals outside home' (rule-breaking subscale) or 'threatens others' (aggressive subscale). Archenbach & Rescorla (2000) report test-retest reliability with a correlation of .89 for the externalizing subscale and internal consistency with a Cronbach's alpha of .90, which both indicate good reliability. The items from the externalizing syndrome scale and the Dutch translation are presented in Appendix C. For rule-breaking and aggressive behavior, total scores were calculated by summing the scores on the items

of the corresponding scale. The externalizing score was computed by summing the scores of the rule-breaking and aggressive behavior subscales. All scores were used continuously.

The onset of alcohol use

To screen for the onset of alcohol use at the time measured, different materials were used to ensure the most complete reporting: two self-reported items that were part of the questionnaires and one question that was part of the interview. Firstly, the iBerry Study used a general questionnaire consisting of 12 items about smoking, alcohol, and drug use (current and past use). The maximum time to fill in this questionnaire was five minutes. The Dutch translation of the following item was used in this study to screen for the use of alcohol: 'Did you ever drink a glass of alcohol?', with two answer options: 'Yes' and 'No/never'. Secondly, the Dutch translation of the following item, that is part of the Youth Self-Report (YSR) (Achenbach & Rescorla, 2000), was used: 'I drink alcohol without my parents' approval', with three answer options: 'Not true', 'Somewhat or sometimes true' and 'Very true or often true'. The participants filled both these questions in on their own. Thirdly, the Dutch translation of item 7 of the Self-reported early delinquency scale (SRED), which measures delinquent behavior, was used (Moffit & Silva, 1988). Namely: 'Did you ever drink alcohol?', with the following answer options: 'No/never', '1 time', '2-3 times', '4-6 times' and '7 times or more'. This question was asked during the interview. Following, the answers to all questions were used to form a dichotomous variable: did ever drink alcohol vs. did never drink alcohol. Participants who reported 'Yes' to the iBerry-questionnaire, and/or 'Somewhat or sometimes true' and/or 'Very true or often true' on the YSR, and/or reported '1 time' or more during the interview, were labeled as 'did ever drink alcohol'. Participants who reported 'No/never', both at the interview and on the questionnaires, were labeled as 'did never drink alcohol'.

Covariates

To control for potential confounding effects, several covariates were taken into account. Namely: IQ, ADHD symptoms, age, sex, and Socioeconomic Status (SES). Previous research shows that these variables are associated with at least one of the main variables. Namely: IQ with externalizing behavior (Lahey, Waldman & McBurnett, 1999), ADHD with externalizing behavior (Gaub & Carlson, 1997) and likelihood of ASD (Antshel et al., 2016), age with pubertal status (May et al., 2017), sex with pubertal status (Negriff & Susman, 2011), and SES with externalizing behavior (Ge et al., 2002). Pubertal status is also shown to be associated with SES (Corbett et al., 2020; Mendle et al., 2016). For example, James-Todd et al. (2010) showed that lower SES was associated with earlier age at menarche. Early pubertal

development is also related to factors that are associated with lower SES, like obesity and the composition of the family (Mendle et al., 2016). SES was measured using the net household income per month, with the following categories: < 1500 euro, 1600-2399 euro, 2400 – 4399 euro, and > 4400 euro. IQ was measured using the continuous SON-IQ score of the Snijders-Oomen-Nonverbale Intelligentietest (SON-R 6-40), which was corrected for the Flynn effect (Tellegen & Laros, 2011). ADHD symptoms were established using the DSM-subscale of the YSR (Archenbach & Rescorla, 2000). Both the IQ score and ADHD symptoms scores were used continuously.

Statistical analyses

All data processing and statistical analyses were done in IBM SPSS Statistics 25. For all analyses, a significance level of $\alpha = .05$ was used. A maximum of 25% missing items on the questionnaire was accepted for all materials used in this study. If any items were missing on a subscale, the score was multiplied by the total number of items per scale divided by the number of filled-in items.

To assess the association between the likelihood of ASD and externalizing behavior (Model 2), rule-breaking behavior (Model 7), and aggressive behavior (Model 12), multiple hierarchical regression analyses were performed. The models are presented in Tables 3-6. An interaction variable with sex and the likelihood of ASD was added to see if the sex of the adolescent was significantly influential. If significant, separate analyses were additionally performed to assess the associations for males and females. To assess the association between pubertal status and externalizing behavior (Model 3), rule-breaking behavior (Model 8), and aggressive behavior (Model 13), multiple hierarchical regression analyses were performed. An interaction variable with sex and pubertal status was added to see if the sex of the adolescent was significantly influential. If significant, separate analyses were additionally performed to assess the associations for males and females. To assess the possible moderating effect of pubertal status on the association between the likelihood of ASD and externalizing behavior (Model 4), rule-breaking behavior (Model 9), and aggressive behavior (Model 14), an interaction variable for the likelihood of ASD and pubertal status was computed for the multiple hierarchical regression analyses. An interaction variable with sex, pubertal status, and likelihood of ASD was added to see if the sex of the adolescent was significantly influential (Model 5, 10, and 15). If significant, separate analyses were additionally performed to assess the associations for males and females. The following covariates were taken into account: IQ, ADHD symptoms, SES, sex, and age. The R^2, *F*-statistic, *B*-value, and β-value with *p*-values were used for decision making.

For the above-mentioned analysis, multiple assumptions were checked. Linearity was met, as assessed by partial regression plots and a plot of standardized residuals against the standardized predicted values. There was homoscedasticity, which was assessed by visual inspection of the last-mentioned plots. Residuals were independent, as assessed by Durbin-Watson statistics which were all greater than 1 and smaller than 3. The assumption of normality was met, as assessed by Q-Q Plots. Influential cases and outliers were assessed using Cook's distance (no values above 1), leverage points (no values above 0.2), and casewise diagnostics (no standardized residuals greater than ±3 standard deviations). For some cases, the standardized residuals were greater than ±3 standard deviations, but for these cases, Cook's distance was below 1, and leverage points were below 0.2. No other notable signs were found for these cases, so these cases were included in the analysis. Multicollinearity was assessed by correlation (lower than 0.8), tolerance values (greater than 0.2), and VIF values (smaller than 10). There was evidence for multicollinearity of the ASD variable and the interaction variable of ASD and pubertal status. To overcome this, mean centering of these variables was used. After centering, no multicollinearity was detected.

To assess the association between the likelihood of ASD and the onset of alcohol use (Model 17), a binary logistic regression was performed. If significant, the rates of alcohol use amongst adolescents who screened positive on the ASD-scale were calculated. To screen for ASD, the cut-off score of five on the ASD-scale by So et al. (2013) was used, as suggested by Deckers, Muris & Roelofs (2020). Next, an interaction variable with sex and the likelihood of ASD was added to see if the sex of the adolescent was significantly influential. If significant, separate analyses were additionally performed to assess the associations for males and females. To assess the association between pubertal status and onset of alcohol use (Model 18), a binary logistic regression was performed. An interaction variable with sex and pubertal status was added to see if the sex of the adolescent was significantly influential. If significant, separate analyses were additionally performed to assess the associations for males and females. To assess the possible moderating effect of pubertal status on the association between the likelihood of ASD and onset of alcohol use (Model 19), an interaction variable for the likelihood of ASD and pubertal status was computed for the binary logistic regression. An interaction variable with sex, pubertal status, and likelihood of ASD was added to see if the sex of the adolescent was significantly influential (Model 20). If significant, separate analyses were additionally performed to assess the associations for males and females. The following covariates were taken into account: IQ, ADHD symptoms, SES, sex, and age. The Chi-Square-value (χ^2), R^2, *B*-value, and Wald-statistic with *p*-values were used for decision making.

Several assumptions were checked for the binary logistic regression. The Box-Tidwell (1962) procedure was used to determine the linearity of the continuous variables related to the logit of the

dependent variable. By using a Bonferroni correction, using all 16 terms in the model, statistical significance was accepted when $p < .003125$ (Tabachnick & Fidell, 2014). Following this, all continuous independent variables were linearly related to the logit of the dependent variable. Outliers were assessed using casewise diagnostics (standardized residuals greater than ±2 standard deviations). One case showed a standardized residual of 2.76, but no other notable signs were found, so it was included in the analysis. Multicollinearity was checked using linear regression. There was evidence for multicollinearity of the ASD variable and the interaction variable of ASD and pubertal status. To overcome this, mean centering of these variables was used. After centering, no multicollinearity was detected.

Results

Means, standard deviations, and percentages for all dependent variables, independent variables, and covariates are presented in Table 2. All results from the various regression analyses are presented in Tables 3, 4, 5, and 6.

Externalizing behavior

Results show a significant positive association between the likelihood of ASD and externalizing behavior, demonstrating that if the likelihood of ASD increases, externalizing behavior increases as well. The full model with covariates and the likelihood of ASD to predict externalizing behavior was statistically significant with $R^2 = .30$, $F(6, 818) = 58.72$, $p < .001$. The addition of the likelihood of ASD to the prediction of externalizing behavior led to a statistically significant increase in R^2 of .01, $F(1, 818) = 7.57$, $p = .006$. To assess the possible influence of sex on this association, the interaction between sex and the likelihood of ASD was added. The addition led to a statistically significant increase in variance explained, namely: R^2 change < .01, $F(1, 817) = 5.03$, $\beta = 0.09$, $p = .025$, demonstrating that the sex of the adolescent significantly contributes to the association between the likelihood of ASD and externalizing behavior, indicating a sex difference. The regression model was therefore run separately for males and females. For males, the addition of the likelihood of ASD to the model with covariates for the prediction of externalizing behavior did not lead to a statistically significant increase in variance explained, namely: R^2 change < .01, $F(1, 394) = 0.17$, $\beta = 0.02$, $p = .678$.

Table 2

Descriptive Statistics of Dependent and Independent Variables and Covariates

		Males		Females	
		M	SD	M	SD
ASD		2.87	2.59	2.69	2.41
Pubertal Status		12.50	2.95	15.87	2.33
IQ		97.51	13.86	97.65	12.22
ADHD symptoms		6.38	2.84	6.66	2.97
Rule-breaking behavior		4.63	2.96	4.26	3.09
Aggressive behavior		5.12	3.77	5.58	4.27
Externalizing behavior		9.7	5.99	9.83	6.63
		N	%	N	%
Onset of alcohol use	Yes	192	38.4	216	41.4
	No	247	49.4	249	47.7
	Missing	61	12.2	57	10.9
SES	< 1599	52	10.4	56	10.7
	1600 - 2399	61	12.2	77	14.8
	2400 - 4399	218	43.6	216	41.4
	> 4400	100	20.0	93	17.8
	Missing	69	13.8	80	15.3
ASD – SP	Yes	101	20.2	89	17.0
	No	341	68.2	369	70.7
	Missing	58	11.60	64	12.3

Note. ASD-SP = Screening positive for ASD. SES = Socioeconomic status, in euro. ASD-scale and ASD-SP: N = 900, PDS: N = 951, IQ: N = 966, ADHD symptoms: N = 968, Rule-breaking behavior: N = 969, Aggressive behavior: N = 967, Externalizing behavior: N = 969, Onset of alcohol use: N = 904, SES: N = 873.

For females, the addition of the likelihood of ASD did lead to a statistically significant increase in R^2 of .02, $F(1, 419) = 11.93$, $\beta = 0.14$, $p = .001$. This means that for females there is a significant positive association between the likelihood of ASD and externalizing behavior, indicating that if the likelihood of ASD increases, externalizing behavior increases as well.

Results show a significant positive association between pubertal status and externalizing behavior, demonstrating that if pubertal status increases, externalizing behavior increases as well. The full model with covariates and pubertal status to predict externalizing behavior was statistically significant with R^2 = .31, $F(6, 807) = 60.13$, $p < .001$. The addition of pubertal status to the prediction of externalizing behavior led to a statistically significant increase in R^2 of .01, $F(1, 807) = 16.80$, $p = < .001$. To assess the possible influence of sex on this association, the interaction between sex and pubertal status was added. The addition did not lead to a statistically significant increase in variance explained, namely: R^2 change < .01, $F(1, 806) = 0.90$, β = -0.19, $p = .344$. This demonstrates that the sex of the adolescent does not significantly contribute to the association between pubertal status and externalizing behavior, indicating no sex difference.

The full model of covariates, the likelihood of ASD, pubertal status, and the interaction between pubertal status and the likelihood of ASD to predict externalizing behavior, was statistically significant R^2 = .32, $F(8, 800) = 46.48$, $p < .001$. However, the addition of the interaction between pubertal status and the likelihood of ASD did not lead to a statistically significant increase in variance explained, namely: R^2 change < .01, $F(1, 800) = 2.57$, $p = .109$. This demonstrates that there is no moderating effect of pubertal status on the association between the likelihood of ASD and externalizing behavior. To explore possible sex differences for this possible moderating effect, the interaction of pubertal status, the likelihood of ASD, and sex was added. The addition did not lead to a statistically significant increase in variance explained, namely: R^2 change < .01, $F(1, 799) = 2.48$, $p = .116$. This demonstrates that the possible interaction effect of the likelihood of ASD and pubertal status on externalizing behavior is not dependent on the sex of the adolescent, indicating no sex difference.

Rule-breaking behavior

Results show a non-significant association between the likelihood of ASD and rule-breaking behavior. The full model with covariates and the likelihood of ASD to predict rule-breaking behavior was statistically significant with R^2 = .19, $F(6, 818) = 30.99$, $p < .001$. However, the addition of the likelihood of ASD to the prediction of rule-breaking behavior did not lead to a statistically significant increase in R^2 of < .01, $F(1, 818) = 2.15$, $p = .143$. To assess the possible influence of sex on this association, the interaction between sex and the likelihood of ASD was added. The addition led to a statistically significant increase in variance explained, namely: R^2 change < .01, $F(1, 817) = 4.16$, β = 0.09, $p = .042$, demonstrating that the sex of the adolescent significantly contributes to the association between the likelihood of ASD and rule-breaking, indicating a sex difference. The regression model was therefore run separately for males and

females. For males, the addition of the likelihood of ASD to the model with covariates for the prediction of rule-breaking behavior did not lead to a statistically significant increase in R^2 of < .01, $F(1, 394) = 0.16$, $p = .694$, with $B = -0.02$, $SE\ B = 0.05$, $\beta = -0.02$. For females the addition of the likelihood of ASD did lead to a statistically significant increase in R^2 of .01, $F(1, 419) = 6.47$, $p = .011$, with $B = 0.146$, $SE\ B = 0.06$, $\beta = 0.114$. This means that for females there is a significant positive association between the likelihood of ASD and rule-breaking behavior, indicating that if the likelihood of ASD increases, rule-breaking behavior increases as well.

Results show a significant positive association between pubertal status and rule-breaking behavior, demonstrating that if pubertal status increases, rule-breaking behavior increases as well. The full model with covariates and pubertal status to predict rule-breaking behavior was statistically significant with $R^2 = .20$, $F(6, 807) = 34.05$, $p < .001$. The addition of pubertal status to the prediction of rule-breaking behavior led to a statistically significant increase in R^2 of .02, $F(1, 807) = 19.13$, $p = < .001$. To assess the possible influence of sex on this association, the interaction between sex and pubertal status was added. The addition did not lead to a statistically significant increase in variance explained, namely: R^2 change < .01, $F(1, 806) = 0.38$, $\beta = -0.13$, $p = .539$. This demonstrates that the sex of the adolescent does not significantly contribute to the association between pubertal status and rule-breaking behavior, indicating that there is no sex difference.

The full model of covariates, the likelihood of ASD, pubertal status, and the interaction between pubertal status and the likelihood of ASD to predict rule-breaking behavior, was statistically significant $R^2 = .21$, $F(8, 800) = 25.88$, $p < .001$. However, the addition of the interaction between pubertal status and the likelihood of ASD did not lead to a statistically significant increase in variance explained, namely: R^2 change < .01, $F(1, 800) = 1.71$, $p = .192$. This demonstrates that there is no moderating effect of pubertal status on the association between the likelihood of ASD and rule-breaking behavior. To explore possible sex differences for this possible moderating effect, the interaction of pubertal status, the likelihood of ASD, and sex was added. The addition did not lead to a statistically significant increase in variance explained, namely: R^2 change < .01, $F(1, 799) = 0.96$, $p = .327$. This demonstrates that the possible interaction effect of the likelihood of ASD and pubertal status on rule-breaking behavior is not dependent on the sex of the adolescent, indicating no sex difference.

Aggressive behavior

Results show a significant association between the likelihood of ASD and aggressive behavior, demonstrating that if the likelihood of ASD increases, aggressive behavior increases as well. The full model

with covariates and the likelihood of ASD to predict aggressive behavior was statistically significant with R^2 = .31, F(6, 818) = 61.12, p < .001. The addition of the likelihood of ASD to the prediction of aggressive behavior led to a statistically significant increase in R^2 of .01, F(1, 818) = 9.81, p = .002. To assess the possible influence of sex on this association, the interaction between sex and the likelihood of ASD was added. The addition did not lead to a statistically significant increase in variance explained, namely: R^2 change < .01, F(1, 817) = 3.54, β = 0.08, p = .060, demonstrating that the sex of the adolescent does not contribute to the association between the likelihood of ASD and aggressive behavior, indicating no sex difference.

Results show a significant positive association between pubertal status and aggressive behavior, demonstrating that if pubertal status increases, aggressive behavior increases as well. The full model with covariates and pubertal status to predict aggressive behavior was statistically significant with R^2 = .31, F(6, 807) = 59.95, p < .001. The addition of pubertal status to the prediction of aggressive behavior led to a statistically significant increase in R^2 of .01, F(1, 807) = 8.21, p = .004. To assess the possible influence of sex on this association, the interaction between sex and pubertal status was added. The addition did not lead to a statistically significant increase in variance explained, namely: R^2 change < .01, F(1, 806) = 0.86, β = -0.182, p = .355. This demonstrates that the sex of the adolescent does not significantly contribute to the association between pubertal status and aggressive behavior, indicating no sex difference.

The full model of covariates, the likelihood of ASD, pubertal status, and the interaction between pubertal status and the likelihood of ASD to predict aggressive behavior, was statistically significant R^2 = .32, F(8, 800) = 46.66, p < .001. However, the addition of the interaction between pubertal status and the likelihood of ASD did not lead to a statistically significant increase in variance explained, namely: R^2 change < .01, F(1, 800) = 2.15, p = .143. This demonstrates that there is no moderating effect of pubertal status on the association between the likelihood of ASD and aggressive behavior. To explore possible sex differences for this possible moderating effect, the interaction of pubertal status, the likelihood of ASD, and sex was added. The addition did not lead to a statistically significant increase in variance explained, namely: R^2 change < .01, F(1, 799) = 2.84, p = .093. This demonstrates that the possible interaction effect of the likelihood of ASD and pubertal status on rule-breaking behavior is not dependent on the sex of the adolescent, indicating no sex difference.

The onset of alcohol use

Results show a significant association between the likelihood of ASD and the onset of alcohol use and the Odds Ratio (*OR*) of 1.13 indicates that as the likelihood of ASD increases, so do the odds of the

onset of alcohol use. The full model with covariates and the likelihood of ASD to predict the onset of alcohol use was statistically significant with $\chi^2(8) = 96.30$, $p < .001$. The addition of ASD significantly added to the fit of the model with $\chi^2(1) = 14.23$, $p < .001$. The model correctly classified 65.9% of cases, with Nagelkerke pseudo $R^2 = 0.15$. To assess the possible influence of sex on this association, the interaction between sex and the likelihood of ASD was added. The addition did not lead to a statistically better fit of the model, namely: $\chi^2(1) = 1.50$, $p = .221$, with $B = -0.08$ ($SE = 0.06$), $Wald = 1.49$, $p = .222$, $OR = 0.93$ [0.82, 1.05], demonstrating that the sex of the adolescent does not contribute to the association between the likelihood of ASD and the onset of alcohol use, indicating no sex difference.

To further explore the significant positive association between the likelihood of ASD and the onset of alcohol use found for male and female adolescents, the rates amongst adolescents who screened positive for ASD were calculated. Results showed that 59.1% of males and 49.4% of females who screened positive for ASD did ever use alcohol and 40.1% of males and 47.5% of females who screened negative for ASD did ever use alcohol.

Results show a significant negative association between pubertal status and the onset of alcohol use and the *OR* of 0.93 indicates that as pubertal status increases, the odds of the onset of alcohol use decreases. The full model with covariates and pubertal status to predict the onset of alcohol use was statistically significant with $\chi^2(1) = 6.16$, $p = .013$. The model correctly classified 65.1% of cases, with Nagelkerke pseudo $R^2 = 0.14$. To assess the possible influence of sex on this association, the interaction between sex and pubertal status was added. The addition of the interaction led to a significantly better fit of the model with $\chi^2(1) = 6.90$, $p = .009$, with $B = -0.16$ ($SE = 0.06$), $Wald = 6.66$, $p = .010$, $OR = 0.85$ [0.76, 0.96]. This demonstrates that the sex of the adolescent significantly contributes to the association between pubertal status and the onset of alcohol use, indicating a sex difference. The regression model was therefore run separately for males and females. For males, the addition of pubertal status to the model with covariates for the prediction of onset of alcohol use did not lead to a statistically significant better fit of the model, $\chi^2(1) = 0.83$, $p = .362$, with $B = -0.04$ ($SE = 0.04$), $Wald = 0.83$, $p = .363$, $OR = 0.96$ [0.89, 1.04]. For females, the addition of pubertal status did lead to a statistically significant better fit of the model, $\chi^2(1) = 10.45$, $p = .001$, with $B = -0.17$ ($SE = 0.05$), $Wald = 9.73$, $p = .002$, $OR = 0.85$ [0.76, 0.94]. This means that for females there is a significant negative association between pubertal status and alcohol use, where the *OR* of 0.85 indicates that as pubertal status increases, the odds of the onset of alcohol use decreases.

The full model of covariates, the likelihood of ASD, pubertal status, and the interaction between pubertal status and the likelihood of ASD to predict the onset of alcohol use, was statistically significant

with $\chi^2(10) = 101.61$, $p < .001$. The model correctly classified 65.3% of cases, with Nagelkerke pseudo $R^2 = 0.16$. However, the addition of the interaction between pubertal status and the likelihood of ASD did not lead to a statistically significant better fit of the model, $\chi^2(1) = 0.37$, $p = .542$. This demonstrates that there is no moderating effect of pubertal status on the association between the likelihood of ASD and the onset of alcohol use. To explore possible sex differences for this possible moderating effect, the interaction of pubertal status, the likelihood of ASD, and sex was added. The addition did not lead to a statistically significant better fit of the model, $\chi^2(1) = 3.10$, $p = .078$. This demonstrates that the possible interaction effect of the likelihood of ASD and pubertal status on the onset of alcohol use is not dependent on the sex of the adolescent, indicating no sex difference.

Table 3

Results of Multiple Hierarchical Regressions Predicting Externalizing Behavior

		Externalizing Behavior														
		Model 1			Model 2			Model 3			Model 4			Model 5		
Variable		B	SE B	β	B	SE B	β	B	SE B	β	B	SE B	β	B	SE B	β
Constant		-10.92*	3.77	-	-10.22*	3.76	-	-8.60*	3.80	-	-8.04*	3.80	-	-7.75*	3.81	-
Covariates	Sex	-0.21	0.37	-0.02	-0.16	0.37	-0.01	-1.29*	0.45	-0.10	-1.26*	0.45	-0.10	-1.26*	0.45	-0.10
	Age	0.95**	0.21	0.14	0.92**	0.21	0.14	0.57*	0.23	0.08	0.53*	0.23	0.08	0.52*	0.23	0.08
	IQ	< -0.01	0.01	-0.01	< -0.01	0.01	-0.01	-0.01	0.01	-0.02	-0.01	0.01	-0.02	-0.01	0.01	-0.02
	SES	-0.28	0.21	-0.04	-0.24	0.21	-0.04	-0.28	0.21	-0.04	-0.25	0.21	-0.04	-0.24	0.21	-0.03
	ADHD	1.16**	0.06	0.54	1.13**	0.07	0.52	1.15**	0.06	0.53	1.13**	0.07	0.52	1.12**	0.07	0.52
ASD					0.21*	0.08	0.08	-	-	-	0.20*	0.08	0.08	0.06	0.11	0.02
PS								0.32**	0.08	0.16	0.32**	0.08	0.16	0.32**	0.08	0.16
ASD x PS											0.04	0.03	0.05	0.01	0.03	0.01
ASD x PS x Sex														0.02	0.01	0.08

Note. * $p < .05$, ** $p < .001$. Sex is for females compared to males. ASD = Likelihood of ASD. PS = Pubertal Status.

Table 4

Results of Multiple Hierarchical Regressions Predicting Rule-breaking Behavior

		Rule-Breaking Behavior														
		Model 6			Model 7			Model 8			Model 9			Model 10		
Variable		B	SE B	β	B	SE B	β	B	SE B	β	B	SE B	β	B	SE B	β
Constant		-6.07*	1.95	-	-5.87*	1.95	-	-4.79*	1.96	-	-4.65*	1.97	-	-4.56*	1.97	-
Covariates	Sex	-0.47*	0.19	-0.08	-0.46*	0.19	-0.08	-1.06**	0.23	-0.18	-1.06**	0.24	-0.17	-1.06**	0.24	-0.18
	Age	0.62**	0.11	0.19	0.61**	0.11	0.19	0.40*	0.12	0.12	0.40*	0.12	0.12	0.39*	0.12	0.12
	IQ	-0.01	0.01	-0.04	-0.01	0.01	-0.04	-0.01	0.01	-0.05	-0.01	0.01	-0.05	-0.01	0.0	-0.05
	SES	-0.12	0.11	-0.04	-0.10	0.11	-0.03	-0.11	0.11	-0.03	-0.11	0.11	-0.03	-0.10	0.11	-0.03
	ADHD	0.40**	0.03	0.39	0.40**	0.03	0.38	0.40**	0.03	0.38	0.39**	0.03	0.38	0.39**	0.03	0.38
ASD					0.06	0.04	0.05	-	-	-	0.05	0.04	0.04	0.01	0.06	0.01
PS								0.17**	0.04	0.18	0.17**	0.04	0.18	0.17**	0.04	0.18
ASD x PS											0.02	0.01	0.04	0.01	0.02	0.02
ASD x PS x Sex														0.01	0.01	0.06

Note. * $p < .05$, ** $p < .001$. Sex is for females compared to males. ASD = Likelihood of ASD. PS = Pubertal Status.

Table 5

Results of Multiple Hierarchical Regressions Predicting Aggressive behavior

		Aggressive Behavior													
		Model 11			Model 12			Model 13			Model 14			Model 15		
Variable		B	SE B	β	B	SE B	β	B	SE B	β	B	SE B	β	B	SE B	β
Constant		-4.80*	2.40	-	-4.29	2.39	-	-3.77	2.43	-	-3.34	2.43	-	-3.14	2.43	-
Covariates	Sex	0.25	0.24	0.03	0.28	0.24	0.04	-0.23	0.29	-0.03	-0.20	0.29	-0.03	0.13	0.14	0.03
	Age	0.34*	0.13	0.08	0.31*	0.13	0.07	0.16	0.15	0.04	0.14	0.14	0.03	< 0.01	0.01	0.01
	IQ	0.01	0.01	0.02	0.01	0.01	0.02	< 0.01	0.01	0.01	< 0.01	0.01	0.01	-0.13	0.13	-0.03
	SES	-0.17	0.13	-0.04	-0.14	0.13	-0.03	-0.17	0.13	-0.04	-0.14	0.13	-0.03	0.73**	0.04	0.53
	ADHD	0.76**	0.04	0.55	0.74**	0.04	0.53	0.75**	0.04	0.54	0.74**	0.04	0.53	0.05	0.07	0.03
ASD					0.15*	0.05	0.09	-	-	-	0.14*	0.05	0.09	0.14*	0.05	0.11
PS								0.14*	0.05	0.11	0.40*	0.05	0.11	< 0.01	0.02	< 0.01
ASD x PS											0.02	0.02	0.04	-0.21	0.29	-0.03
ASD x PS x Sex														0.01	0.01	0.09

Note. * $p < .05$, ** $p < .001$. Sex is for females compared to males. ASD = Likelihood of ASD. PS = Pubertal Status.

Table 6

Results of Binary Logistic Regressions Predicting Alcohol use

		Alcohol use								
		Model 16			Model 17			Model 18		
Variable		B (SE)	Wald	OR [95% CI]	B (SE)	Wald	OR [95% CI]	B (SE)	Wald	OR [95% CI]
Constant		8.07	19.61**	3200.80	8.75	22.32**	6338.73	6.97	14.57**	1058.53
		(1.82)			(1.85)			(1.83)		
Covariates	Sex	0.15	1.01	1.16	0.18	1.41	1.20	0.42	4.95*	1.52
		(0.15)		[0.87, 1.56]	(0.15)		[0.89, 1.62]	(0.19)		[1.05, 2.19]
	Age	-0.64	36.04**	0.53	-0.68	39.17**	0.51	-0.51	20.18**	0.60
		(0.11)		[0.43, 0.65]	(0.11)		[0.41, 0.63]	(0.13)		[0.48, 0.75]
	IQ	0.02	14.22**	1.02	0.02	13.72**	1.02	0.02	15.09**	1.02
		(0.01)		[1.01, 1.04]	(0.01)		[1.01, 1.04]	(0.01)		[1.01, 1.04]
	SES		6.67			8.05*			6.92	
	SES 1	-0.52	3.19	0.60	-0.56	3.63	0.57	-0.60	4.19*	0.55
		(0.29)		[0.39, 1.05]	(0.29)		[0,32, 1.02]	(0.29)		[0.31, 0.98]
	SES 2	-0.43	3.05	0.65	-0.43	2.88	0.65	-0.42	2.90	0.66
		(0.25)		[0.40, 1.05]	(0.25)		[0.40, 1.07]	(0.25)		[0.41, 1.07]
	SES 3	-0.07	0.07	0.93	-0.01	< 0.01	0.99	-0.09	0.12	0.91
		(0.27)		[0.55, 1.59]	(0.28)		[0.58, 1.69]	(0.27)		[0.54, 1.55]
	ADHD	-0.11	15.80**	0.90	-0,12	20.72**	0.88	-0.11	16.29**	0.90
		(0.03)		[0.86, 0.95]	(0.03)		[0.84, 0.93]	(0.03)		[0.85, 0.95]

ASD					0.12	13.85**	1.13	-	-	-
					(0.03)		[1.06, 1.20]			
PDS								-0.08	6.07*	0.93
								(0.03)		[0.87, 0.98]

		Model 19			Model 20		
Variable		B (SE)	Wald	OR [95% CI]	B (SE)	Wald	OR [95% CI]
Constant		7.71	16.81**	2233.38	7.66	16.43**	2110.16
		(1.88)			(1.89)		
Covariates	Sex	0.45	5.65*	1.57	0.46	5.73*	1.58
		(0.19)		[1.08, 2.27]	(0.19)		[1.09, 2.94]
	Age	-0.55	22.45**	0.58	-0.55	21.97**	0.58
		(0.12)		[0.46, 0.72]	(0.12)		[0.46, 0.72]
	IQ	0.02	14.70**	1.02	0.02	14.86**	1.02
		(0.01)		[1.01, 1.04]	(0.01)		[1.01, 1.04]
	SES		7.98*			8.62*	
	SES 1	-0.62	4.45*	0.54	-0.69	5.29*	0.50
		(0.30)		[0.30, 0.96]	(0.30)		[0.28, 0.90]
	SES 2	-0.40	2.48	0.67	-0.42	2.79	0.66
		(0.25)		[0.41, 1.10]	(0.25)		[0.40, 1.08]
	SES 3	-0.03	0.01	0.97	-0.07	0.06	0.93
		(0.28)		[0.57, 1.67]	(0.28)		[0.54, 1.61]
	ADHD	-0,13	20.59**	0.88	-0.12	19.93**	0.88
		(0.03)		[0.84, 0.93]	(0.03)		[0.84, 0.93]

ASD	0.13	14.93**	1.13	0.20	13.59**	1.22
	(0.03)		[1.06, 1.21]	(0.05)		[1.10, 1.36]
PDS	-0.08	6.38*	0.92	-0.08	6.39*	0.92
	(0.03)		[0.87, 0.98]	(0.03)		[0.87, 0.98]
ASD x PDS	0.01	0.37	1.01	0.02	2.68	1.02
	(0.01)		[0.99, 1.03]	(0.01)		[1.00, 1.05]
ASD x PDS x				-0.01	3.05	0.99
Sex				(0.01)		[0.98, 1.00]

Note. * $p < .05$, ** $p < .001$. For sex, reference category is male. For SES, reference category is < 1599 euro. SES 1 = 1600-2399 euro. SES 2 = 2400-4399 euro. SES 3 = > 4400 euro. OR = Odds Ratio, 95% CI = for OR. ASD = Likelihood of ASD.

Discussion

This study aimed to assess the possible moderating effect of pubertal status on the association between the likelihood of ASD and externalizing behavior, in particular rule-breaking behavior, aggressive behavior, and the onset of alcohol use. Firstly, results indicated that a higher likelihood of ASD was associated with higher aggressive behavior and higher chances of already having used alcohol for male and female adolescents. Results also showed that a higher likelihood of ASD was associated with higher externalizing and rule-breaking behavior for female adolescents, where no association was found for male adolescents. Additionally, higher pubertal status was associated with higher externalizing behavior, rule-breaking behavior, and aggressive behavior for male and female adolescents. Results also indicated that higher pubertal status was associated with a smaller chance of already having used alcohol for female adolescents, where no association was found for male adolescents. Lastly, results demonstrated that no moderating effect of pubertal status on the associations between the likelihood of ASD and externalizing behavior, rule-breaking behavior, aggressive behavior, and the onset of alcohol use was found for male and female adolescents.

Previous research shows consensus about higher levels of externalizing behavior amongst children and adolescents with ASD, compared to their peers (Mahan & Matson, 2011; Matson, Wilkins & Macken, 2008). For example, higher externalizing behavior, comprising of hyperactivity, aggression, and conduct problems, was found in children and adolescents with ASD, compared to typically developing peers (Mahan & Matson, 2011). Current results are partly in line with this, where a higher likelihood of ASD was associated with higher externalizing and rule-breaking behavior for female adolescents. Interestingly, results only show significant positive effects for female adolescents, but not for male adolescents. This is in contrast with Kozlowski, Matson & Rieske (2012), who found that children and adolescents with ASD showed more externalizing challenging behaviors than individuals without ASD, regardless of sex. Noteworthy, in their study, children and adolescents between the age of 2-17 with a mean age of eight years were assessed, while the current study looked at adolescents between the age of 12 -18 with a mean age of 15 years (Kozlowski, Matson & Rieske, 2012). Since previous research reports a decrease of externalizing behavior, specifically aggression, over time in children and adolescents with ASD between the age of 2-17 (Mazurek, Kanne & Wodka, 2013), it is therefore possible that the difference in age of the children and adolescents that were part of the studies could partly account for the incongruence of the results. But this decrease of externalizing behavior was not assessed for males and females separately (Mazurek, Kanne & Wodka, 2013), so no conclusions can be drawn from this. Additionally, the intellectual functioning of the adolescents was not considered in the study of Kozlowski,

Matson & Rieske (2012). ASD is frequently comorbid with intellectual disability, and more challenging behaviors are found when IQ goes down (Matson & Shoemaker, 2010). It is therefore possible that adding or leaving the intellectual functioning out of the analyses could partly explain the incongruence in results. Based on the above, replication of the current findings is necessary and recommended.

The finding that female adolescents who show a higher likelihood of ASD, also show higher levels of externalizing behavior and rule-breaking behavior in adolescence, is highly relevant. Research suggests a possible diagnostic gender bias for ASD, where females are at greater risk of their ASD being misdiagnosed, diagnosed later, or not at all (Loomes, Hull & Mandy, 2017). There is a possible female autism phenotype with distinct female symptoms of ASD, which could be partly different from the current conceptualization of ASD (Bargiela, Steward & Mandy, 2016). As the DSM-V mentions, females could show a more subtle expression of social and communication difficulties (American Psychiatric Association, 2013). This points to the concept of 'camouflaging', where females with ASD are more likely to mask the difficulties they experience because of their ASD (Loomes, Hull & Mandy, 2017). The current findings contribute to learning more about this possible female autism phenotype and the symptoms that females with ASD experience. The results implicate that for the development of better diagnostics and interventions for females with ASD, more attention has to be paid to externalizing and specifically rule-breaking behavior for females with (possible) ASD. Since timely diagnostics can improve quality of life, for example by getting access to the right interventions and reducing self-criticism, learning more about symptoms of females with ASD is especially beneficial (Bargiela, Steward & Mandy, 2016; Portway & Johnson, 2005).

Higher likelihood of ASD was associated with higher levels of aggressive behavior for both male and female adolescents, which is in line with Kanne & Mazurek (2011), who found that aggression was higher amongst children and adolescents who showed more ASD related symptoms in communication, social environments, and restricted and repetitive behaviors. Complementary, previous research also found that aggression was equally common amongst young males and females with ASD (Kanne & Mazurek, 2011; Kozlowki, Matson & Rieske, 2012; Mazurek, Kanne & Wodka, 2013). Empathy may play a role in explaining the positive association between the likelihood of ASD and aggressive behavior. Individuals with ASD show heightened empathic arousal when seeing others in distress, but have an impaired social understanding of this situation (Fan et al., 2014). The combination of insufficient emotion regulation and poor understanding of emotions of other individuals, seem to be associated with aggressive behavior in children with ASD (Pouw et al., 2013). Fur future studies it is interesting to explore if and how the concept of empathy is connected to aggressive behavior amongst adolescents with ASD.

Additionally, results indicated that a higher likelihood of ASD was associated with higher chances of already having used alcohol, both in male and female adolescents. Research looking into alcohol use amongst adolescents with ASD is still at an early stage, which makes this finding meaningful. Where some reasoning might suggest that since adolescents with ASD have poor contact with their peers and have deficits in social connections, individuals with ASD might be less exposed to social settings where alcohol is used and therefore less prone to alcohol use (Kaltenegger et al., 2021), the results of this study point to an increased chance of already having used alcohol before the legal drinking age when the likelihood of ASD increases. Specifically, results show that 59.1% of males and 49.4% of females who screened positive for ASD, already used alcohol. In comparison, 47.8% of males and 45.4% of females of the general population between the age of 12 and 16 in the Netherlands did already use alcohol (*Cijfers alcoholgebruik jongeren*, 2020). The rates found are comparable to rates of alcohol use reported amongst adolescents (age 13-18) with anxiety disorders (45.3%) and lower than adolescents with mood disorders (67.1%) and eating disorders (68.2%) (Mangerud et al., 2014). Interestingly, they report a 7.7% rate of alcohol use amongst adolescents with ASD, which is a lot lower compared to the current results. But, alcohol use was reported as using alcohol presently versus having never used alcohol or not using presently, while in the current study it was reported as having ever versus never used alcohol, which could partly explain the incongruence in rates of alcohol use found in both studies. Since the participants in the current study were under the age of 18 and therefore under the legal drinking age in The Netherlands, this finding is relevant, especially following the detrimental effect alcohol can have on our physical and mental health (Rehm et al., 2003). Therefore, the long-term effects of alcohol for individuals with ASD are interesting to explore. For future studies, it is necessary and interesting to replicate and expand the current findings by differentiating between the types of alcohol use, like the early and later stages of alcohol use, the amount of alcohol used, the number of times ever used, and what age alcohol use started.

Next, results show that higher pubertal status is associated with higher levels of externalizing, rule-breaking and aggressive behavior. These results are somewhat in line with previous research, where Dimler & Natsuaki (2015) and Negriff & Susman (2011) show that early pubertal timing is associated with higher levels of externalizing behavior, for both males and females. In other words, individuals who showed further physical development at an earlier age compared to their peers also showed higher levels of externalizing behaviors. Current results show that further physical development, regardless of age, is associated with higher levels of externalizing behaviors. But, this comparison needs to be treated with caution, since pubertal status with correction for the age of the adolescent that is used in the current study, is not fully the same construct as pubertal timing, which indicates if pubertal development is early,

on time or late. The cross-sectional nature of the data in the current study limits the ability to assess the full changes in pubertal development. Since the age of this cohort is between 12 to 18 years, and puberty can start as early as 8 years old for girls (Eckert-Lind et al., 2020), it is difficult to state if pubertal development at the time measured, is early, on-time or late. For this reason, it is recommended for future research to follow children and adolescents over a longer period, to fully measure pubertal development and specifically pubertal timing.

Interestingly, results show that as the pubertal status of female adolescents increases, the odds of ever used alcohol decreases. No association was found for males. This result is surprising and not easy to interpret. Social anxiety may play a role here. Research shows that early-maturing adolescent females show significantly higher social anxiety, compared to girls who mature on time and boys who mature early (Blumenthal et al., 2011). Research also indicates that female adolescents who are more susceptible to social stress, show an earlier onset of alcohol use, which could be due to an incompetent coping mechanism (Cloutier et al., 2019). It is possible that female adolescents who are less physically developed, regardless of age, therefore show a higher chance of already having used alcohol. More research is necessary to replicate and further explore the current finding.

Looking at the main focus of this study, no significant interaction effects for pubertal status and the likelihood of ASD were found for the externalizing behavior, rule-breaking behavior, aggressive behavior, and the onset of alcohol use for male and female adolescents. This shows that pubertal status did not moderate the association between the likelihood of ASD and the externalizing behaviors in this study. It appears that the associations between ASD and the assessed externalizing behaviors are separate phenomena, independent of the pubertal status of the adolescent. But, this statistical null effect does not mean that there is no effect in the population, since there is no conclusive evidence for the absence of an effect (Nickerson, 2000). To affirm the current findings, replication is necessary. Based on the discussion points mentioned above and the recent finding of Corbett et al. (2020) that females with ASD show early pubertal timing, it is recommended to further explore the role pubertal development plays for adolescents with ASD. A longitudinal study is suggested to be able to look at pubertal development, timing, and tempo of this development to fully explore its possible effect.

It should be noted that results showed that 17.0% of female adolescents and 20.2% of male adolescents screened positive for ASD on the ASD-scale. This seems a lot higher than the general population, where prevalence rates between 1 to 2% are reported (American Psychiatric Association, 2013; Chiarotti & Venerosi, 2020). But, the study was oversampled with high-risk adolescents, with a high-

risk to low-risk ratio of 2.5:1, which could explain the higher rates of adolescents who screen positive on ASD (Grootendorst – van Mil et al., 2021).

The decision to add ADHD symptoms as a covariate needs to be considered. On the one hand, the focus of this study lied on the likelihood of ASD, and since ADHD is a very common comorbid diagnosis for children with ASD (comorbidity rates between 40 -70% are reported) (Antshel et al., 2016), controlling for this is necessary to assess the true effect of the likelihood of ASD on externalizing behavior. Nonetheless, ADHD symptoms and externalizing behaviors are very much intertwined (Gaub & Carlson, 1997). Following this, the possibility of too much correction cannot be ruled out. But, as this study explored the possible moderating effect of pubertal status on the association between the likelihood of ASD and externalizing behavior for the first time, preference was given to examine the true effect of the likelihood of ASD and therefore correct for ADHD symptoms. This needs to be kept in mind while interpreting the abovementioned results.

The possibility of a multiple testing problem needs to be addressed too. Since the measurement of externalizing behavior consists of the two subscales aggressive and rule-breaking behavior, which were also assessed separately, there is a possibility of false-positive results (Sainani, 2009). Because of the explorative character of this study, no correction was applied. This also needs to be kept in mind while interpreting the abovementioned results.

Important to review as well, is the measurement of pubertal status that is used, the PDS (Petersen et al., 1988), since this is often a discussion point in studies looking into pubertal development (Dimler & Natsuaki, 2015). As Negriff & Susman (2011) report, not all measures of pubertal development seem to tap onto the same underlying processes. The strength of the observed association between pubertal maturation and externalizing behavior could therefore be dependent on the type of measurement used. Using the Tanner stages for measurement of pubertal development (Marshall & Tanner, 1969; Marshall & Tanner, 1970) is considered to 'golden standard' if it is done by a trained healthcare worker (Negriff & Susman, 2011). But, Koopman-Verhoeff et al. (2020) found that the PDS generally maps onto the same changes of pubertal development of the Tanner stages that are measured with physical examination. Additionally, as Pompéia et al. (2019) argue, the PDS also incorporates puberty-related changes like growth in height and skin changes, in contrast to the Tanner stages. Following this, Dimler & Natsuaki (2015) found that although different measures of pubertal development describe different underlying processes, they did not find a moderating effect of measurement on the association between early pubertal timing and externalizing behaviors. This confirms the correct use of the PDS for the pubertal status measurement in this study.

While in the current study no evidence was found of a moderating effect of pubertal timing, the concept of perceived pubertal timing of the adolescent, namely, if they feel their physical changes are occurring before, at the same time, or after their peers, could be interesting to explore (Mendle, 2014). The self-perception of feeling physically different from their peers could influence their behavior, to seek out experiences or an environment that corresponds to their impression of their physical maturation. For example, Lynne et al. (2007) showed that adolescents who reported feeling that they matured earlier compared to their peers, showed higher levels of aggression and delinquency. For future studies it is interesting to assess the possible moderating effect of perceived pubertal timing on the association between the likelihood of ASD and externalizing behaviors, and how this relates to the assessment of pubertal development by a trained professional. Self-perception is especially important since children and adolescents with ASD can experience lower self-esteem (McCauley et al., 2019).

Concluding, this study shows that a higher likelihood of ASD is associated with higher externalizing and rule-breaking behavior for female adolescents and higher aggressive behavior and chances of already having used alcohol for male and female adolescents. These results are especially relevant since the current study looked at the likelihood of ASD, which extends previous research only looking at diagnosed individuals, by broadening previous findings beyond the clinical population to high-risk adolescents who show sub-clinical symptoms of ASD. New insights were also gained about the use of alcohol, where the results of the study point to an increased chance of already having used alcohol when the likelihood of ASD increases. Next to this, the current study expands the comprehension of symptoms that adolescents, and specifically females, with ASD experience, which adds to the understanding of the possible female autism phenotype. The results indicate that within the youth care system, it is relevant to look out for externalizing behaviors while screening for ASD, specifically for rule-breaking behavior for females and aggressive behavior for male and female adolescents. While no moderating effect of pubertal status on the assessed externalizing behaviors was found, looking into the role of pubertal development for adolescents with ASD is recommended.

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Appendix A

Table A7

The Dutch Translation of the Items of the ASD-scale by So et al. (2013)

Item number	Item description
1	Doet te jong voor zijn/haar leeftijd
9	Kan bepaalde gedachten niet uit zijn/haar hoofd zetten, obsessies
17	Dagdromen of gaat op in zijn/haar gedachten
42	Is liever alleen dan met anderen
62	Onhandig of stuntelig
66	Herhaalt bepaalde handelingen steeds maar weer, dwanghandelingen
79	Spraakprobleem
80	Kijkt met een lege blik
84	Vreemd gedrag
111	Teruggetrokken, gaat niet met anderen om

Table A8

The Items of the ASD-scale by So et al. (2013)

Item number	Item description
1	Acts too young for his/her age
9	Cannot get his/her mind off certain thoughts; obsessions
17	Daydreams or gets lost in his/her thoughts
42	Would rather be alone than with others
62	Poorly coordinated or clumsy
66	Repeats certain acts over and over
79	Speech problem
80	Stares blankly
84	Strange behavior
111	Withdrawn, does not get involved with others

Appendix B

Table B11

The Dutch Translation of the Items of the PDS (Petersen et al., 1988)

Girls and boys	Hoe is het met je lichaamsgroei in de lengte (de zogenaamde groeispurt)? Hoe is het met de groei van je oksel- en schaamhaar? Hoe is het met de veranderingen in je huid (vet, puistjes)?
Girls	Menstrueer je al? Zo ja, hoe oud was je toen je je eerste menstruatie kreeg? …….. jaar en ……. maanden Is de borstgroei al begonnen?
Boys	Is je stem al veranderd (lager geworden)? Heb je al baardgroei?

Appendix C

Table C9

The Items of the Externalizing Syndrome of the CBCL (Archenbach & Rescorla, 2000)

Rule-breaking behavior	2. Drinks alcohol 26. Lacks guilt 28. Breaks rules 39. Bad friends 43. Lies, cheats 63. Prefers older kids 67. Runs away 72. Sets fires 81. Steals at home 82. Steals outside home 90. Swearing 96. Thinks of sex too much 99. Uses tobacco

	101. Truant
	105. Uses drugs
Aggressive behavior	3. Argues a lot
	16. Mean
	19. Demands attention
	20. Destroys own things
	21. Destroys others' things
	22. Disobedient at home
	23. Disobedient at school
	37. Gets in fights
	57. Attacks people
	68. Screams a lot
	86. Stubborn, sullen
	87. Mood changes
	89. Suspicious
	94. Teases a lot
	95. Temper
	97. Threatens others
	104. Loud

Table C10

The Dutch Translation of the Items of the Externalizing Syndrome Scale (Archenbach & Rescorla, 2000)

Regelovertredend gedrag	2. Drinkt alcohol zonder dat zijn/haar ouders dat goed vinden.
	26. Lijkt zich niet schuldig te voelen na zich misdragen te hebben.
	28. Houdt zich niet aan de regels thuis, op school of ergens anders.
	39. Gaat om met jongens of meisjes die in moeilijkheden raken.
	43. Liegt of bedriegt.
	63. Gaat liever om met oudere jongens of meisjes.

	67. Loopt weg van huis. 72. Sticht branden. 81. Steelt van huis. 82. Steelt buitenshuis. 90. Vloekt of gebruikt vieze woorden. 96. Denkt te veel aan seks. 99. Rookt tabak. 101. Spijbelt, blijft weg van school. 105. Gebruikt drugs.
Aggressief gedrag	3. Maakt veel ruzie. 16. Wreed, pesterig of gemeen tegen anderen. 19. Eist veel aandacht op. 20. Vernielt eigen spullen. 21. Vernielt spullen van gezinsleden of van anderen. 22. Is thuis ongehoorzaam. 23. Is ongehoorzaam op school. 37. Vecht veel. 57. Valt mensen lichamelijk aan. 68. Schreeuwt veel. 86. Koppig, stuurs of prikkelbaar. 87. Stemming en gevoelens veranderen plotseling. 89. Achterdochtig. 94. Pest veel. 95. Driftbuien of snel driftig. 97. Bedreigt mensen. 104. Meer dan gewoon luidruchtig.