Chapter 6

Pubertal status predicts back pain, overtiredness and dizziness in American and Dutch adolescents

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ABSTRACT

Objective: *Functional somatic symptoms (FSS), symptoms for which no organic pathological basis can be found, are more prevalent in girls than in boys and this difference tends to increase during adolescence. This might be explained, at least in part, by pubertal development. We hypothesized that pubertal maturation predicts the development of most FSS, and that this is especially true for girls.*
Method: *We used two longitudinal population based studies to examine our hypotheses, the Longitudinal Study of Pain in Adolescents in Seattle (N = 1996, 49.7% girls) and the Dutch Tracking Adolescents' Individual Lives Survey (N = 2230, 51.0% girls). Two assessment waves of each study were used. American adolescents were younger than Dutch adolescents at the first (11.6 versus 13.6) and second (14.5 versus 16.2) assessment wave, but they were in about the same pubertal development stage. FSS were measured by pain questions, the Symptom Checklist-90, and the Youth Self-Report. The Pubertal Development Scale was used to assess pubertal development on a continuous scale in both cohorts.*
Results: *Ordinal logistic regression analyses revealed that American and Dutch adolescents at a later pubertal status at baseline were more likely (odds ratios ranging from 1.24 to 1.61) to report back pain, overtiredness, and dizziness, but not stomach pain and headache two to three years later. Although these relations were not equally strong for boys and girls, no significant gender differences were found.*
Conclusion: *Pubertal status predicted the frequency of some, but not all, FSS at follow-up.*

INTRODUCTION

Functional somatic symptoms (FSS), symptoms for which no organic pathological basis can be found, are common in adolescents all over the world (Eminson, 2007;Perquin et al., 2000). These symptoms can have significant impact on adolescents' lives, by causing school-related problems, problems with peers, and problems in the family (Eminson et al., 1996). In general, girls experience more FSS than boys and this difference increases during adolescence (LeResche et al., 2005). It is unknown which factors are responsible for this increase in gender difference. One possibility is that pubertal development plays a role. Cross-sectional studies suggest that the association between pubertal development and FSS is different in boys and girls (LeResche et al., 2005;Oldehinkel et al., 2011;Rhee, 2005). However, research in this field is scarce and findings are sometimes contradictory. Most studies show that musculoskeletal symptoms,

headache, dizziness and fatigue increase during pubertal development in girls (LeResche et al., 2005;Oldehinkel et al., 2011;Rhee, 2005). Findings on the relationship between gastrointestinal symptoms and pubertal development in girls are less consistent, since some studies found a negative, some a positive and some did not find a significant association between the two (Kroner-Herwig and Vath, 2009;LeResche et al., 2005;Oldehinkel et al., 2011;Rhee, 2005). In boys, pubertal development is generally associated with a larger decrease in gastrointestinal symptoms, and with a smaller increase in musculoskeletal symptoms, headache, dizziness and fatigue than in girls, resulting in a lower overall prevalence of FSS in boys than in girls at the completion of pubertal development (LeResche et al., 2005;Oldehinkel et al., 2011;Rhee, 2005).

The relationship between specific FSS and pubertal development has, to the best of our knowledge, only been studied longitudinally for headache and stomach pain (Kroner-Herwig and Vath, 2009;Stanford et al., 2008). Consequently, it is unknown whether other FSS increase or decrease as adolescents proceed through pubertal development and whether this depends on gender. We hypothesized that: a) Pubertal maturation is a risk factor for development of back pain, headache, dizziness and overtiredness, but not for gastrointestinal symptoms, and b) The relationship between pubertal maturation and specific somatic symptoms is stronger in girls than in boys. To enlarge the robustness of our findings, we studied these hypotheses with longitudinal data from two samples, one consisting of Dutch and one of American adolescents.

METHODS

The Tracking Adolescents' Individual Lives Survey

The TRacking Adolescents' Individual Lives Survey (TRAILS) is a prospective cohort study of Dutch adolescents. The data reported here come from the second and third assessment wave of TRAILS, which ran from September 2003 to December 2004, and September 2005 to August 2008, respectively. The questionnaires used in the current study were all filled out by the adolescents at school under supervision of a TRAILS employee. TRAILS participants were selected from five municipalities in the North of the Netherlands, including both urban and rural areas. All children born between 10-01-1989 and 09-30-1990 (first two municipalities) or 10-01-1990 and 09-30-1991 (last three municipalities) were eligible for inclusion, provided that their schools were willing to cooperate and that they were able to participate in the study. Over 90% of the schools, accommodating 3,145 children, agreed to participate in the study. A small

proportion (6.7%) of these children was excluded because of mental or physical incapability or language problems. Of the remaining 2935 children, 76.0% (*N* = 2230, mean age= 11.1, *SD* = 0.6, range 10–12, 50.8% girls) were enrolled in the study. Information about the sample selection and differences between responders and non-responders at baseline has been described elsewhere (de Winter et al., 2005). Ten percent of the sample had at least one parent born in a non-Western country.

Of the 2230 baseline participants, 96.4% (*N* = 2149, mean age = 13.7, *SD* = 0.5, range=12-15, 51.0% girls) participated in the first follow-up assessment (T2), two to three years after assessment wave 1 (T1). At the third assessment wave (T3), two to four years after T2, the response was 81.4% (*N* = 1816, mean age = 16.3, *SD* = 0.7, range=15-18, 53.3% girls). Attrition at the second assessment was not associated with psychopathology (Huisman et al., 2008). Because the instruments used at T2 and T3 were most comparable to the instruments used in Seattle, data from these waves were used in the current study. The study was approved by the Dutch Central Committee on Research Involving Human Subjects. Parents' and adolescents' written informed consent was obtained.

The Longitudinal Study of Pain in Adolescents in Seattle

The Longitudinal Study of Pain in Adolescents in Seattle is a longitudinal cohort study in American adolescents. Subjects in this cohort study were boys and girls, initially all 11 years old, randomly selected from the enrollees of Group Health, a large non-profit integrated health care system in Washington State, USA. The study included a baseline interview (which ran from May 2000 to April 2001) and a three year follow-up interview (which ran from April 2003 to March 2004) each conducted by telephone. Both interviews were used for the current study. Children not sufficiently proficient in English to understand the interview questions, or whose parents were not sufficiently proficient in English to provide informed consent were considered ineligible.

Of all adolescents invited for this study 49% (*N* = 1996, mean age= 11.6, range 11.0-12.1, *SD* = 0.3, 49.7% girls) participated at baseline. Information about sample selection and differences between responders and non-responders at baseline can be found elsewhere (LeResche et al., 2005). The majority of adolescents (66.5%) described their race as White. At the three year telephone follow-up interview 91.0% of the adolescents (*N* = 1817, mean age= 14.5, *SD* = 0.3, 49.4% girls) participated again. All procedures were approved by the Institutional Review Boards of Group Health and the University of Washington.

Both the parent or legal guardian and the child provided informed consent (adults) / assent (children).

Measures

Functional somatic symptoms

Both studies assessed back pain, stomach pain and headache, the most prevalent types of pain in adolescents. The adolescents were asked how often they had experienced these symptoms during the past three months. In the Netherlands, adolescents filled out questionnaires with seven response categories: 'Not at all', 'Less than once a month', 'Once a month', 'Two to three times a month', 'Once a week', 'Two to six times a week', and 'Almost every day'. In the United States, adolescents could answer the interviewer with four response categories: 'Not at all', 'Fewer than half of the days', 'More than half of the days', and 'Almost every day'. There were few adolescents who reported having pain almost every day in either the Dutch or American sample. Therefore, in the Dutch sample this category was combined with the category 'Two to six times a week' and in the American sample with 'More than half of the days', resulting in six response categories in the Dutch and three in the American sample. In the United States, subjects were explicitly asked to report pains that lasted a whole day or more, or that they had several times in a year, and not to report little aches and pains that did not last very long. In the Netherlands no such restrictions were made.

In the Dutch study FSS other than pain symptoms were assessed with the Youth Self-Report (Achenbach et al., 2003), and in the American study, they were assessed during the telephonic interview with the Symptom Checklist-90 (Derogatis and Cleary, 1977). We used only items of both questionnaires that we considered comparable. These were: overtiredness and dizziness without obvious reason from the Youth Self-Report, which could be rated on a three point scale ('not at all', 'sometimes/a little bit', or 'often a lot'). In the Symptom Checklist, these items were feeling low in energy/slowed down and faintness/dizziness, which could be rated on a five point scale ('not at all', 'a little bit', 'moderately', 'quite a bit', or 'extremely'). The categories 'quite a bit' and 'extremely' were combined, because few adolescents reported experiencing these symptoms extremely. The time frame of the Youth Self-Report was six months, whereas that of the Symptom Checklist was one month.

Pubertal development

In both studies the Pubertal Development Scale, which is known to be a reliable instrument (Bond et al., 2006;Petersen et al., 1988), was used to measure pubertal development. The Pubertal Development Scale assesses development on five characteristics for each sex. These characteristics include growth spurt in height, skin change and body hair for both boys and girls; breast development and menarche in girls; and voice change and facial hair growth in boys. Subjects were asked to respond on a self-report questionnaire (Dutch) or in a telephone interview (American) to each item on a 4-point ordinal scale (no development=1, development barely begun=2, development definitely underway=3, development already completed=4). The menarche item was scored as 1 if pre-menarche and 4 if menstrual periods had begun. The mean item score of the five items was calculated and used as a continuous measure to increase the power to detect an effect (Streiner, 2002).

Statistical analyses

We performed ordinal logistic regression analyses to test our hypotheses. This analysis method is an extension of binary logistic regression, appropriate when the outcome variable contains more than two ordinal categories. An important assumption to perform these analyses is the proportional odds assumption. Violations of this assumption were tested by performing Brant tests (Long and Freese, 2005). By performing ordinal logistic regression analyses we examined whether pubertal status at the baseline of this study (i.e., at baseline in the American sample, and at T2 in the Dutch sample) predicted a specific FSS at follow-up (i.e., at three-year follow-up in the American sample, and at T3, which was two to three years after T2, in the Dutch sample). The analyses were adjusted for gender, because in general girls have more FSS (Eminson, 2007;Perquin et al., 2000) and are further along in pubertal development than boys at a given age (de Muinck Keizer-Schrama and Mul, 2001). We performed all analyses again, adjusting for age, to rule out that age, rather than pubertal status itself, predicted the relationship between pubertal status and FSS. To examine whether pubertal status truly predicted the direction of development of FSS, we performed the same analyses adjusting for the corresponding symptom at the first time point.

To test our second hypothesis that significant gender differences exist, an interaction term of gender and pubertal status at baseline was computed. We examined whether this interaction term, adjusted for the main effects of gender and pubertal status at baseline, predicted a specific FSS at follow-up. A result was considered statistically significant when the 95% confidence interval (CI) of the odds ratio (OR) did not include 1. Stata, Version 10, was used to perform all analyses.

RESULTS

Descriptive statistics

The Dutch boys and girls were older than the Americans, but the samples were fairly comparable with regard to mean pubertal development score (Table 1a and Table 1b). Adolescents from both cohorts were on average already in a mid-pubertal development stage at baseline. That American adolescents start their pubertal development earlier than European adolescents is in line with previous research (de Muinck Keizer-Schrama and Mul, 2001;Lee et al., 2001). Furthermore, American adolescents had slightly higher BMI scores than Dutch adolescents in keeping with known national differences (de Wilde et al., 2009;Freedman et al., 2006). Dutch adolescents reported having experienced pain more often than American adolescents.

Pubertal status as a predictor of FSS at follow-up

As is shown in Table 2, the higher the pubertal status of adolescents at baseline the more likely they were to report back pain, overtiredness and dizziness, but not stomach pain and headache at follow-up two to three years later. After adjusting for age, results were essentially the same. When we adjusted for the corresponding baseline FSS, results pointed in the same direction and remained statistically significant except for the relationship between pubertal development and dizziness in Dutch adolescents. The Brant test did not indicate the proportional odds assumption was violated for any of the analyses ($p > 0.05$).

Table 1a. Descriptive statistics of the Dutch and American girls at baseline and follow-up two to three years later

	American girls (BL)		Dutch girls (BL)		American girls (FU)		Dutch girls (FU)	
	Valid *N*	**mean (SD) / percentage**	**Valid *N***	**mean (SD) / percentage**	**Valid *N***	**mean (SD) / percentage**	**Valid *N***	**mean (SD) / percentage**
Mean age (*SD*)	992	11.6 (0.3)	1069	13.6 (0.5)	897	14.5 (0.3)	952	16.3 (0.7)
Mean pubertal status (*SD*)	911	2.3 (0.6) range: 1.0-4.0	1001	2.7 (0.7) range:1.0-4.0	880	3.5 (0.5) range: 1.6-4.0	866	3.3 (0.4) range:1.2-4.0
Mean BMI (*SD*)	904	19.6 (3.9)	1028	19.3 (3.3)	888	22.0 (4.2)	834	21.7 (3.2)
Headache	989	19.2 %*[a]	1069	56.7 %*[a]	897	21.4 %*[a]	871	51.6 %*[a]
Stomach pain	991	27.8 %*[a]	1068	46.9 %*[a]	897	16.7 %*[a]	875	35.9 %*[a]
Back pain	989	15.0 %*[a]	1068	30.5 %*[a]	896	25.2 %*[a]	874	35.6 %*[a]
Dizziness	992	33.3 %*[b]	1072	40.9 %*[c]	897	33.9 %*[b]	880	42.6 %*[c]
Overtiredness/ Lack of energy	991	57.3 %*[b]	1070	43.1 %*[c]	897	55.5 %*[b]	880	54.2 %*[c]

BL= at baseline, FU= at follow-up *Percentage of girls who experienced this symptom at least once during the, past three months[a], past month[b] or past six months[c]

Table 1b. Descriptive statistics of the Dutch and American boys at baseline and follow-up two to three years later

	American ♂ (BL)		Dutch ♂ (BL)		American ♂ (FU)		Dutch ♂ (FU)	
	Valid *N*	**mean (SD) / percentage**	**Valid *N***	**mean (SD) / percentage**	**Valid *N***	**mean (SD) / percentage**	**Valid *N***	**mean (SD) / percentage**
Mean age (*SD*)	1004	11.6 (0.3)	1018	13.6 (0.5)	920	14.5 (0.3)	867	16.3 (0.7)
Mean pubertal status (*SD*)	970	1.9 (0.4) range: 1.0-3.6	1006	2.1 (0.6) range: 1.0-4.0	915	2.7 (0.5) range: 1.0-4.0	768	3.0 (0.5) range: 1.0-4.0
Mean BMI (*SD*)	951	19.9 (4.3)	1000	18.7 (3.1)	914	22.3 (4.5)	759	20.9 (3.4)
Headache	1002	16.7 %*[a]	1013	44.5 %*[a]	920	13.5 %*[a]	769	34.9 %*[a]
Stomach pain	1002	22.0 %*[a]	1015	37.4 %*[a]	920	12.1 %*[a]	771	19.9 %*[a]
Back pain	998	11.1 %*[a]	1015	22.1 %*[a]	919	16.9 %*[a]	769	27.4 %*[a]
Dizziness	1002	32.0 %*[b]	1019	24.5 %*[c]	919	25.7 %*[b]	772	22.0 %*[c]
Overtiredness/ Lack of energy	1002	58.6 %*[b]	1016	29.0 %*[c]	919	47.6 %*[b]	772	29.5 %*[c]

BL= at baseline, FU= at follow-up *Percentage of boys who experienced this symptom at least once during the past three months[a], past month[b] or past six months[c].

Table 2. Longitudinal relationship between pubertal development at baseline and FSS at follow-up two to three years later analyzed with ordinal logistic regression analyses

		Headache (FU)	Stomach pain (FU)	Back pain (FU)	Overtiredness/ Lack of energy (FU)	Dizziness (FU)
American adolescents	**Pubertal status (BL)**	1.18 (0.94-1.48)[a]	1.26 (0.98-1.62)[a]	**1.61 (1.30-1.99)[a]**	**1.33 (1.12-1.58)[a]**	**1.35 (1.11-1.64)[a]**
		1.11 (0.87-1.41)[b]	1.25 (0.97-1.61)[b]	**1.52 (1.22-1.89)[b]**	**1.25 (1.05-1.49)[b]**	**1.26 (1.03-1.53)[b]**
Dutch adolescents	**Pubertal status (BL)**	1.07 (0.93-1.25)[a]	0.88 (0.75-1.04)[a]	**1.34 (1.13-1.57)[a]**	**1.30 (1.11-1.51)[a]**	**1.24 (1.05-1.46)[a]**
		1.07 (0.92-1.25)[b]	0.91 (0.76-1.08)[b]	**1.24 (1.04-1.46)[b]**	**1.26 (1.08-1.48)[b]**	1.16 (0.98-1.37)[b]

BL= at baseline, FU= at follow-up. Odds ratios and 95% confidence intervals are given. [a]adjusted for gender, [b]adjusted for gender and the corresponding baseline FSS. Bold numbers indicate a significant effect.

Table 3. Longitudinal relationship between pubertal development at baseline and FSS at follow-up two to three years later analyzed with ordinal logistic regression analyses stratified by gender

		Headache (FU)	Stomach pain (FU)	Back pain (FU)	Overtiredness/ Lack of energy (FU)	Dizziness (FU)
American ♀	**Pubertal status (BL)**	1.24 (0.94-1.61)	1.27 (0.94-1.72)	**1.50 (1.16-1.93)**	**1.44 (1.16-1.78)**	**1.29 (1.02-1.63)**
American ♂	**Pubertal status (BL)**	1.02 (0.66-1.59)	1.23 (0.78-1.93)	**1.90 (1.28-2.82)**	1.15 (0.86-1.53)	**1.47 (1.05-2.06)**
***p*-value of the interaction effect[a]**		0.61	0.90	0.34	0.19	0.55
Dutch ♀	**Pubertal status (BL)**	1.14 (0.95-1.37)	0.91 (0.74-1.10)	**1.31 (1.07-1.61)**	**1.29 (1.07-1.55)**	**1.30 (1.06-1.58)**
Dutch ♂	**Pubertal status (BL)**	0.96 (0.75-1.23)	0.83 (0.61-1.13)	**1.37 (1.05-1.79)**	**1.31 (1.00-1.70)**	1.11 (0.83-1.49)
***p*-value of the interaction effect[a]**		0.25	0.85	0.69	0.99	0.39

BL= at baseline, FU= at follow-up; Odds ratios and 95% confidence intervals are given. [a]p-value of the interaction effect of gender. Bold numbers indicate a significant effect.

Gender differences

Results of analyses of the relationships between pubertal status at baseline and specific FSS at follow-up stratified by gender pointed mostly in the same direction for each gender (Table 3). Although relationships were generally in the same direction for boys and girls, the results were not always equally strong for each gender and sometimes failed to reach significance in boys (Table 3). The interaction effects, however, indicated that these gender differences were not statistically significant (all *p*-values > 0.18, Table 3).

Growth spurt and back pain

Since pubertal status at baseline was only significantly related to back pain and not to headache and stomach pain, we wondered whether this association could be explained by growth spurt. We therefore examined whether growth spurt (i.e. the specific item from the PDS) at baseline predicted back pain at follow-up. Growth spurt at baseline was not a significant predictor of back pain at follow-up in the American sample (OR = 1.04, 95% CI = 0.89-1.21) or in the Dutch sample (OR = 1.13, 95% CI = 0.98-1.31).

DISCUSSION

This study indicates that Dutch and American adolescents who are in a later pubertal stage at baseline report more back pain, overtiredness, and dizziness, but not more stomach pain or headache two to three years later. We did not find any significant gender difference in the longitudinal relationship between pubertal development and FSS.

A strength of our research is that we used two large population-based studies, one of American and one of Dutch adolescents. This enhances the generalizability of our findings, since most of the findings were comparable in both studies despite racial and age differences. Furthermore, the use of two samples enhanced the robustness of our findings, because different instruments, e.g. different questionnaires with different response categories, were used in the two studies. Despite these methodological differences, results were fairly similar in both samples. Another advantage is that we had longitudinal data available, which allowed us to examine whether pubertal status, rather than age, was predictive of FSS at follow-up.

We have to acknowledge two limitations to our study. First, adolescents were already on average in a mid-pubertal development stage at the beginning of our

studies. Therefore, we might have missed some effects of early pubertal development. Another possible shortcoming is that we are not sure if the FSS measured were due to conventional medical conditions. In the Youth Self-Report it was stated that the symptoms had to occur without obvious cause, but in the other questionnaires used to assess FSS no such restrictions were made. However, medical conditions are seldom found in adolescents with common somatic complaints (Croffie et al., 2000;Goodman and Mcgrath, 1991). Moreover, findings in the two cohorts were largely comparable, and the prevalence of symptoms due to medical conditions is likely to be different in the two cohorts, because the Dutch adolescents were asked only to report symptoms without obvious cause. Therefore, medical conditions are not likely to have substantially influenced the associations between pubertal status and FSS.

Some differences between the samples have to be noted. Dutch adolescents reported having experienced pain much more often than American adolescents. Probably this difference can be explained by the restrictions made in the American questionnaire not to report minor pains and only to report pains that lasted one day or longer. Furthermore, in Seattle the data were collected by interviews, whereas the Dutch adolescents reported their symptoms on a questionnaire, which in general results in higher rates of symptom report. In addition to mean pain frequency, the response rates, response categories, the duration of the recall period of overtiredness and dizziness, follow-up time intervals and ethnicity differed between the samples. Despite all these methodological differences, results were essentially the same in each sample, which suggests that our findings are quite robust.

The longitudinal relationships we found between pubertal status and FSS are largely comparable to the cross-sectional associations in our prior studies (LeResche et al., 2005;Oldehinkel et al., 2011). In contrast to the Dutch baseline study (Oldehinkel et al., 2011) and a previous longitudinal study by Stanford et al. (Stanford et al., 2008), the current study did not find that adolescents in a lower pubertal stage report more stomach pain. Both previous studies indicated that lagging behind one’s peers in pubertal development is associated with reporting stomach pain. Since in the current study most adolescents were already in a mid-pubertal development stage, the effect of lagging behind one’s peers might have been missed. The largest difference with the American cross-sectional study (LeResche et al., 2005) is that the current study did not reveal a longitudinal positive association between pubertal status and headache in girls. An explanation might be the lack of older adolescents in the current study compared with the

cross-sectional study. It might take some time before having reached a mature pubertal status influences the frequency of headache in girls. This might also explain why no cross-sectional association was found between pubertal status and headache in girls in the Dutch baseline study when participants were on average even younger than in the American sample. The explanation is also in line with a previous study by Kröner-Herwig et al. (Kroner-Herwig and Vath, 2009) who found that reaching menarche two or more years ago was predictive of headache, whereas having reached menarche only one year ago was not associated with headache. Although intuitively plausible, growth spurt did not explain why we found a longitudinal association between pubertal development and back pain, but not the other pain symptoms. This is in keeping with previous studies that found that mechanical factors, like carrying backpacks and physical activity did not predict back pain at follow-up (Jones et al., 2003;Watson et al., 2003).

Although observed associations between pubertal development and FSS were not always equally strong for boys and girls, we found no statistically significant gender differences in the longitudinal relationship between pubertal status and specific FSS. Therefore, we did not find evidence to support the hypothesis that pubertal development causes girls to experience FSS more frequently than boys during early and mid adolescence (Fillingim et al., 2009;Paller et al., 2009). Gender differences due to pubertal development may become apparent during late adolescence, possibly because the sensitizing effects of the sometimes painful physiological signals associated with menstruation take some time to develop (Berkley, 1997). Psychological factors also likely contribute to the increasing difference in the amount of FSS reported by boys and girls during adolescence: growing into adulthood may increase the expectation for boys not to report and thereby decrease the willingness for boys to report FSS (Robinson et al., 2001).

Conclusion

Pubertal status was associated with some but not all FSS, suggesting that biological factors are differentially involved in the etiology of various FSS. It is tempting to speculate that back pain, dizziness, and overtiredness predominantly result from a different biological pathway than stomach pain and headache, but this needs to be further explored.