Determinants of Health Related Quality of Life among Adolescents with Migraine

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This thesis titled
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ABSTRACT

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This study examined data from 63 adolescents with migraine (45 female) between the ages of 11 and 17 (mean age=14.4) to compare the relative impact of migraine severity, associated symptom severity, internalizing symptoms and catastrophizing on health-related quality of life (HRQL). Participants kept a 4-week diary about their headaches and completed 3 different quality of life scales, a psychological assessment scale and a catastrophizing questionnaire. A hierarchical regression analysis revealed that associated symptoms of migraine and internalizing symptoms predicted adolescent functioning. This is the first study of its kind designed specifically for adolescents with migraine. Its results suggest there is a need for further research exploring the impact of associated symptoms of migraine and internalizing on HRQL of adolescents.

Approved: _____________________________________________________________

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INTRODUCTION

Migraine is a neurological disorder which causes episodes of moderate to severe head pain lasting from one hour to three days, as well as a variety of migraine associated symptoms including gastrointestinal disturbances (i.e. nausea), heightened sensitivity to light (photophobia) and noise (phonophobia) (The International Classification of Headache Disorders 2nd edition, 2004). Demographically, migraine is one of the most prevalent forms of chronic illness in adolescence, affecting up to 7% of adolescents worldwide (Bigal et al., 2007; Fendrich et al., 2007; Linet et al., 1989; Lu et al., 2000). Adolescents with chronic illness have been found to experience psychiatric, psychosocial, educational and emotional problems significantly more often than healthy populations and experience a significantly lower quality of life (Beck et al., 1986; Pless & Nolan, 1991). However, studies of adolescents with migraine have found great variability in overall health-related quality of life (HRQL) across different samples (Carlsson et al., 1996; Kernick and Campbell, 2009; Langeveld et al., 1996; Langeveld et al., 1997; Nodari et al., 2002; Powers et al., 2000). There has been little research on factors that might account for this variability.

The head pain associated with migraine can be debilitating to the adolescent. Increased headache severity and frequency have been linked to greater impairment in some studies (Fichtel and Larsson, 2002; Hunfeld et al., 2001; Langeveld et al., 1997), but not others (Tkachuk et al., 2003; Vannatta et al., 2007). Further evidence is necessary to determine under what conditions do migraine frequency and severity impact HRQL of adolescents.
Associated symptoms of migraine (nausea, photophobia and phonophobia) might also cause significant impairment, but little data is available on their impact on adolescent HRQL. One small (N=37) study has indicated that severity of migraine-associated symptoms is predictive of poorer adolescent quality of life independent of migraine severity and frequency (Tkachuk et al., 2003). Severity of migraine-associated symptoms also correlated with impaired quality of life in adults (Holroyd et al., 2007). In addition, where nausea, photophobia and phonophobia have been examined in other chronic conditions such as cancer, they have been found to impair adolescent wellbeing (Ballatori et al., 2007; Badell et al., 2006; Hockaday, 1988; Judd, 2007; Westbrook et al., 2002). Associated symptoms of migraine appear likely to impact adolescent quality of life, but further research is necessary.

Internalizing psychological disorders comorbid with migraine might also impact quality of life, although currently data for adolescents is available only from one study. Brna and colleagues (2008) collected data from a population sample of Canadian teenagers (N=994) and used the Canadian Community Health Survey to screen for migraines, anxiety and mood disorders. HRQL data was obtained from the Short Form Health Survey questionnaire (SF-36). A multivariate linear regression analysis which controlled for age, gender and the presence of migraines, found that mood disorders were predictive of lower scores on the emotional role, physical role, social functioning, vitality, mental health and general health domains of the SF-36. The presence of an anxiety disorder was predictive of lower scores on the emotional role and social functioning domains of the SF-36. Studies with physically healthy adolescents also indicate that internalizing symptoms impair quality of life (Beck et al., 1985). However,
based on findings from only one study, which did not use International Headache Society (IHS) or Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria to screen its participants, it is unclear whether internalizing symptoms impact HRQL of adolescents with migraine.

Negative cognitive patterns of responding to pain such as catastrophizing might also account for variability in HRQL (Crombez et al.; 2003), but currently there is no information on the relationship between catastrophizing and quality of life in adolescents with migraine. One recent study found catastrophizing had a significant negative impact on HRQL of adults with migraine, independent of migraine characteristics and depression (Holroyd et al., 2006). Catastrophizing has been described by multiple authors as one of the most important cognitive factors that influence fear of pain, determine pain variation and impact the functioning of patients with chronic pain disorders (Chaves and Brown, 1987; Spanos et al., 1979; Sullivan et al., 1995, 2001; Turner et al., 2000). Based on these findings, the impact of catastrophizing on HRQL is worth exploring with adolescents who experience migraines.

Overall, migraine is a multifarious disorder that might impact quality of life through a number of pathways. Although existing studies point to likely variables such as migraine frequency and severity, migraine-associated symptoms, internalizing symptoms and catastrophizing, little information is available about the role of these factors in impairing quality of life in adolescents. This study examined the impact of migraine frequency and severity, associated symptoms of migraine, internalizing symptoms and catastrophizing on HRQL. It was expected that each of the above variables would be associated with quality of life and independently predictive of variations in quality of life.
METHODS

Participants

Potential participants were identified by treating physicians at the Columbus Children’s Hospital outpatient headache clinics in Columbus, OH and referred to an onsite member of the study team. All participants were informed of the aim and purpose of the study before being invited to participate. IRB approval for this study was obtained from both the Columbus Children’s Hospital and Ohio University.

Data from a larger ongoing project aimed at examining the validity of multiple migraine-related adolescent questionnaires was used for the purposes of this study. A sample of 63 adolescents (45 female) between the ages of 11 and 17 (mean age=14.4) was available for analysis. Inclusion was based on: 1) pediatric neurologist IHS diagnosis of migraine with or without aura; 2) average migraine frequency of at least 1 migraine per month for each of the last 3 months; 3) Ability and willingness of both parent/caregiver and adolescent to give informed consent/assent; 4) English as primary language to ensure subjects’ ability to read and comprehend the questionnaires. Exclusion criteria included: 1) diagnosis of chronic daily headache (chronic migraine, chronic tension-type headache, new daily persistent headache) or medication overuse headache; 2) diagnosis of a pain disorder other than migraine as a primary diagnosis; 3) diagnosis of a medical or psychiatric conditions that in the opinion of the study staff might render the subject unable to participate in the study.

Written informed consent/assent was obtained from all participants and their parents/caregivers. Adolescents were screened by a neurologist and administered the questionnaires. Upon leaving the test setting, each participant was assigned an electronic
diary (Palm OS) to keep track of daily headaches for the next four weeks. Then participants were invited to visit the test setting again, submit the electronic diary and fill in the second round of questionnaires for other purposes. For their participation, each adolescent received $20 per accomplished surveying visit (total of two visits) and $10 after completing the electronic diary.

Measures

Quality of life

It has been suggested that assessment of HRQL through multiple measures can increase external validity (Holroyd et al., 2007). Following directions from Kernick and Campbell (2009), data from one generic (Pediatric Quality of Life Inventory) and two disease-specific (Pediatric Migraine Disability Assessment Score & Migraine Specific Quality of Life – Adolescents) self-report measures were used to measure migraine-related impairments in functioning and HRQL.

The Pediatric Quality of Life Inventory (PedsQL; Varni et al., 1999) measures both physical (8 items) and psycho-social health (15 items). The internal consistency estimates of reliability of PedsQL are very good to excellent (average Cronbach α = .89; Connelly and Rapoff, 2006). The same study estimated the test–retest values for the measure (2 week baseline interval) as very good (r = .86, p < .01). Validity of the PedsQL was demonstrated by using the known-groups method, by examining the correlations with indicators of morbidity and illness burden, and through factor analysis (Varni et al., 2001). The PedsQL successfully distinguished between healthy and pediatric populations, including children with acute or chronic health conditions. PedsQL scores were related to
indicators of morbidity and illness burden, and displayed a factor-derived solution largely consistent with the a priori conceptually-derived scales.

The Pediatric Migraine Disability Assessment Score (PedMIDAS, Hershey et al., 2001), is a simple validated disease-specific measure that focuses on functional status as defined by the child’s ability to perform daily activities that are essential to meet its basic needs, roles and wellbeing. It is comprised of six developmentally appropriate open-ended questions designed to give an accurate depiction of the impact of migraine on school-related and extracurricular performance and functioning of children and adolescents (i.e. How many full days of school were missed in the last 3 months due to headaches?; How many days were you not able to do things at home (i.e. chores, homework, etc.) due to a headache?). The PedMIDAS has a high test-retest reliability ($r=0.80$) and a Cronbach alpha range of $0.77 – 0.78$. Its scores have been found to correlate significantly with self-reported headache frequency, severity, and duration, with severity of associated symptoms of migraine and with school and home functional ability (Hershey et al., 2001). It has been found to be sensitive to treatment response among children with headaches, with mean scores improving in correspondence to reductions in migraine frequency, severity and duration following a pharmaceutical intervention.

Participants also completed the Migraine Specific Quality of Life – Adolescents scale (MSQ-A). The MSQ-A is a 14-item measure designed to measures the physical and emotional limitations which are typically associated with migraine headaches among adolescents with migraines (Martin et al., 2000). Internal consistency alphas for the MSQ-A range from .77 to .93 (Cottrell et al., 2006). Scores on the MSQ-A correlate significantly with self-reported migraine frequency, severity, duration, and associated
symptoms and have been found sensitive to variations in migraine related missed activities (Tkachuk et al., 2003).

**Independent variables**

Migraine characteristics and related symptoms were assessed by analysis of the recordings from the electronic daily diary (Holroyd & Chen, 2000). The electronic diary is a handheld computer capable of storing the daily entries of the participants. Entries include start and end time of headache, headache type, ratings of headache severity and each associated symptom and medication used. From these data, several items of particular interest to this study were computed including migraine frequency (number of migraine episodes with the requirement that distinct episodes be separated by 24 hour pain free period), migraine days (number of recorded days of migraine per 30 days), migraine severity (average severity of migraine episodes, range 0-3) and associated symptom severity (the sum of the three average severity ratings provided for nausea, phonophobia and photophobia provided for each migraine, ranging from 0-9, summed across migraine episodes). Out of this data, two severity indexes were computed to be used in the final analysis – migraine severity index (migraine days * migraine severity) and associated symptom severity index (migraine days * associated symptom severity). This transformation was done in the interest of better capturing the full effect of migraine episodes both across intensity and frequency, in a fashion similar to previous studies in the area (Holroyd et al., 2007). Migraine and associated symptom severity indexes were tailored to measure impact of pain with regards to both dimensions of pain intensity and pain frequency (as a frequency of twenty migraine episodes per month is likely to cause significantly more distress than a frequency of two, regardless of the severity of the
episodes). Another reason for the use of a combined severity index was the small size of this study’s sample. Frequency and severity indexes were combined into one in order to decrease number of variables in the regression analysis and improve power. Before constructing the severity indexes several frequency variables were examined including total number of migraines, migraine hours per month and migraine days per month. Time variables (migraine days & hours) were considered a better representation of frequency as they incorporated both rate and duration. Between the two time variables migraine days was chosen as its distribution was less skewed.

Internalizing symptoms were assessed by the internalizing scale of the Youth Self Report (YSR). The YSR provides self-ratings for twenty competence and problem items paralleling those of the Child Behavior Checklist (CBCL)/Ages 6-18 (Achenbach, 1991, 2001; Achenbach & Edelbrock, 1983). YSR contains 20 competence items that measure the child’s participation in hobbies, games, sports, jobs, chores, friendship, and activities, and 112 items that measure eight sub-scale symptoms: withdrawn, somatic complaints, anxiety and depression, social problems, thought problems, attention problems, aggressive and delinquent behaviors (Achenbach, 1991). Adolescents select their responses on a scale from 0 (not true) to 2 (Very true or often true). Scores from the withdrawn, somatic complaints, anxiety and depression subscales are then used to compute an ‘internalizing’ scale. The YSR has a test-retest reliability ranging from 0.47 - 0.79 and a Cronbach alpha range of 0.71 - 0.95 (Achenbach, 1991, 2001; Ferdinand & Verhulst, 1995; Song et al., 1994). Validity of the YSR was demonstrated by examining the correlations with indicators of depression and anxiety, and through factor analysis.
The YSR internalizing scale scores were found to be sensitive to variations in depression and anxiety symptoms and to treatment response among adolescents with depression.

Catastrophizing was assessed by administering the Pain Catastrophizing Scale (PCS) for adolescents (Sullivan, et al., 1995; Crombez, et al., 2003). PCS items assess how participants feel and what they think about when they are in pain. Questions are related to rumination (i.e. …can’t keep the headache out of my mind), magnification (i.e. …afraid the headache will get worse), and hopelessness (i.e. …can’t stand the headache anymore). The instrument has demonstrated sufficient reliability and construct validity (Cronbach α= .87; Sullivan, et al., 1995). PCS scores were found considerably correlated to pain intensity and functional disability (Crombez, et al., 2003).

Statistics

A Pearson r correlation analysis was performed to explore the relationships among independent variables, among HRQL measures and, finally, between independent and dependent variables. Because the distributions of migraine severity and associated symptom severity indexes were found to be significantly skewed, the analysis was repeated with nonparametric statistics (Spearman). A hierarchical multiple regression analysis was conducted to investigate whether the independent variables remained correlated to HRQL in the presence of one another. In the literature, multiple regression analysis is used to estimate models to describe the distribution of a response variable with the help of independent variables (Petrocelli, 2003). When a theoretical link exists between independent variables, a hierarchical regression is the most appropriate form of analysis. In hierarchical regression analysis independent variables are split into blocks based on theoretically-estimated relatedness (i.e. grouping catastrophizing and
internalizing in one block, as they both are maladaptive psychological variables). For the purposes of this study, the independent variables were split into three blocks. The first block of independent variables entered into the analyses was demographic variables (sex and age). These variables were entered into the equations first to control for possible relationships between the demographic variables and quality of life. Then, the associated symptom severity index was entered into the analyses to control for the effects of migraine characteristics. Finally, psychological variables (internalizing symptoms and catastrophizing) were entered in the analyses in the third block.

A multinomial logistic regression was attempted as an alternative to the hierarchical linear regression in order to control for issues related to the non-normal distribution of the associated symptom severity index. However, due to the small size of the sample, there were not enough individuals in the permanent plot to fill all matrix entries and no valid logistic analysis could be performed.

Power analysis

To date no research has been done exploring the relationship between migraine severity, associated symptoms of migraine, internalizing symptoms, catastrophizing and HRQL in the same study. A limited number of studies have been conducted exploring individual correlations between the independent variables of this study and HRQL measures. Where correlations between the proposed predictor variables of this study and quality of life measures are reported in the literature, correlation coefficients range from .29 to .40 (average $r^2=.35$; $|r|=0.59$), while squared multiple coefficients of determination are usually between .30 and .45 (average $r^2=.37$; $f^2=.59$).
Power analysis conducted with G*Power™ software revealed that for the bivariate correlations at least 22 participants would be needed in order to detect an effect size of .59 with a power of .95. For the regression analysis, it was estimated that in order to detect an effect size of .59 with a power of .95, with 3 predictors and 2 demographic variables, 40 participants would be needed.
RESULTS

Demographic information for the sample is displayed in Table 1. Headache diary data was unavailable for 15 out of the 63 participants in this study. Furthermore 8 of the participants who completed the migraine diary recorded no migraines. Because the impact of migraine on quality of life cannot be examined in adolescents who do not experience headaches, participants with no migraine data and participants who recorded no migraines were excluded from the analysis. Of the 40 participants that could be investigated for the purposes of this analysis, 7 adolescents recorded at least one migraine but reported no associated symptoms of migraine. As this absence of associated symptoms is likely to occur if a migraine is effectively treated early in the episode or if the migraine is mild in severity, it was decided to keep these participants in the analysis.

Means and standard deviations for all variables are displayed in Table 2. The distributions of the migraine severity index (M=12.5; SD=10.7) and associated symptom severity index (M=17.9; SD=23.4) were positively skewed. This was largely due to the fact that about 30% of all participants recorded less than 3 migraine days per 30 days. All other variables’ distributions appeared normal.

Psychiatric symptoms data was available for 39 of the 40 subjects in the study. The mean internalizing score on the Youth Self Report scale was 55.7 (SD=9.1). On average, the scores were within normal limits. However, about 30% (12 of 39) of subjects with available YSR data scored within the clinically relevant range of this instrument (>60). Data from the Pain Catastrophizing Scale was available for 37 of the 40 subjects in the study. The average catastrophizing score was 3.24 (SD=2.55). Compared to previous
studies with college age populations (M=20; Sullivan et al., 2000; Sullivan et al., 2006a), and children age 8-16 (M=16.79, Crombez, et al., 2003), scores from the present sample were unusually low.

Different numbers of subjects completed each of the three quality of life measures (PedsQL, N=37; PedMIDAS, N=36; MSQ-A, N=38). Average MSQ-A (M=36.5; SD=10.9) and PedsQL (M=71.1; SD=16.8) scores were within the range reported by other authors (Tkachuk et al., 2003; Varni et al., 2004). PedMIDAS scores (M=22.3; SD=15.4) were low compared to findings with migraine children and adolescents elsewhere in the literature (Hershey et al., 2001).

Relationships among variables

Correlations among quality of life measures are presented in Table 3.1. MSQ-A scores were significantly related to PedMIDAS and PedsQL scores. However, PedMIDAS and PedsQL scores were unrelated.

Correlations among independent variables and demographics are displayed in Table 3.2. There was a significant positive correlation between associated symptom severity index and catastrophizing (r=.38). Migraine severity index and severity of associated symptoms index were highly correlated (r=.87). In order to avoid multicollinearity and because it was uncorrelated with MSQ-A, PedsQL or PedMIDAS, the migraine severity index was dropped from the hierarchical regression. All other relationships between independent variables were found non-significant.

Correlations of the independent variables with HRQL measures are displayed in Table 3.3. Associated symptom severity and internalizing symptoms were each significantly related to MSQ-A scores. Internalizing was the only significant correlate of
PedsQL. PedMIDAS scores were unrelated to any of the independent variables. Despite being tailored to measure migraine disability in terms of days missed due to migraine episodes, PedMIDAS did not correlate with either number of migraines ($r=.07$) or number of migraines per 30 days ($r=.18$).

A Spearman r correlation analysis was performed to control for issues related from the non-normalcy of variables’ distributions. Correlations between HRQL scales are displayed in Table 6.1. Scores on PedsQL and MSQ-A were significantly related. Correlations between independent variables and demographics are displayed in Table 6.2. Migraine severity index and associate severity index were again found significantly correlated. Correlations between independent variables and HRQL measures are displayed in Table 6.3. Associated symptom severity, internalizing symptoms and catastrophizing were significantly related to MSQ-A scores. Internalizing was the only significant correlate of PedsQL. PedMIDAS scores were unrelated to any of the independent variables. Correlation coefficients were similar to the ones obtained from the Pearson analysis. The only exception was catastrophizing, which the Spearman analysis found uncorrelated with associated symptom severity index and correlated with MSQ-A. However, in both of these relationships the correlation coefficients were of similar magnitude to the ones obtained from the Pearson analysis. The similarity in the results obtained from Pearson and Spearman analyses suggests that the skewed distribution of migraine severity and associated symptom severity indexes doesn’t have a significant impact on their relationships with other variables in the study, and allows for regression analysis to be performed with at least one of the indexes included.
Regression analysis

Results of the hierarchical regression analysis examining the relationship between independent variables and MSQ-A is presented in Table 4. A total of 34 participants had submitted all data necessary for this analysis. Gender was significantly related to HRQL as measured by MSQ-A, with girls experiencing lower functioning than boys. Results from the second block indicated there was a significant positive relationship between the severity of the associated symptoms of migraine and HRQL as measured by MSQ-A. Although the third block was significant, no single psychological variable emerged as an independent predictor of HRQL.

Results from the hierarchical regression analysis that examined the relationship between independent variables and PedsQL are displayed in Table 5. A total of 32 participants had submitted all data necessary for this analysis. Results indicated there was a significant positive relationship between internalizing symptoms and HRQL as measured by PedsQL, even after controlling for the effects of demographics, associated symptom severity and catastrophizing. As some of the items on the psychosocial domain of PedsQL assess psychological distress, an exploratory analysis was performed to test if overlap in item content explains the significant relationship between the PedsQL and YSR internalizing scale. Internalizing scores were significantly correlated with both physical ($r=.34$, $p<.05$) and psychosocial ($r=.63$, $p<.01$) subscales of the instrument. Thus it can be inferred that although it may have increased the correlation between the Internalizing scale of the YSR and PedsQL, the overlap in item content is not the only factor which made their relationship significant.
DISCUSSION

This study examined the relationship of migraine severity, associated symptom severity, internalizing symptoms and catastrophizing with adolescent quality of life. It also tested whether these variables accounted for independent variance in adolescent HRQL.

Variations in migraine characteristics were a poor predictor of adolescent quality of life. None of the three HRQL scales correlated with the migraine severity index. These findings are consistent with authors who suggest that migraine frequency and severity do not represent as important an influence on quality of life of adolescents as previously thought (Thachuk et al., 2003; Vannatta et al., 2007). However, it is possible that factors specific to the sample and the methodology of the current study might have reduced the likelihood of detecting a significant relationship.

At the time of recruitment all participants in this sample presented with clinically diagnosable migraines, and reported an average migraine frequency of at least 1 migraine per month for each of the last 3 months, yet during the following month many of these adolescents experienced mild migraines or no migraines at all. Although in the adolescent literature it is not unusual to see significant fluctuations in the intensity and duration of migraines across time (Raieli et al., 1995), the low average scores, the restricted range of scores and the skewness of the migraine severity index may have made it difficult to detect relationships with the quality of life measures in this study.

The lack of relationship between migraine severity index and HRQL could also have been a result from the quality of life scales used in this study and the timing of their administration. Both MSQ-A and PedMIDAS were originally designed to measure
quality of life of clinical populations where high levels of migraine frequency and severity are the norm. Thus, they might not have been sensitive to the effects of mild or moderate migraines on adolescent functioning in this sample. Additionally, our quality of life scales were retrospective measures administered at a single occasion only. It is possible that different methodology for assessing quality of life, for example a daily diary measure, would yield different results. It is also possible that a diary methodology for assessing quality of life assessment would be more sensitive to the impact of mild or moderate migraines in adolescents. Similar retrospective measurement of quality of life has been related to migraine characteristics in adults with migraine, but never in samples where migraine severity and frequency were as low as in the present study.

Although in this study migraine severity and frequency, as measured by the migraine severity index were found unrelated to adolescent quality of life, a significant relationship was found between the severity of associated symptoms of migraine and HRQL (as measured by MSQ-A). This finding is important, as associated symptoms of migraine tend to be overlooked in the quality of life literature. One group of authors has found that in adolescents, associated symptoms of migraine have significant impact on quality of life, independently from migraine frequency and severity (Tkachuk et al., 2003). In the current study, the impact of migraine characteristics (severity, duration and frequency) and associated symptoms of migraine on HRQL could not be compared in a regression analysis due to issues of multicollinearity. Further research is necessary to confirm whether associated symptoms of migraine impact HRQL independently from migraine frequency and severity.
In the current study one third of all participants scored above the clinical cut-off on the internalizing scale of the Youth Self Report. The average rates of internalizing disorders in samples of adolescents with migraine reported in the literature are similar to the average rates for healthy adolescents. However, many authors have noted that large percentages of their samples (up to 30%) scored within the clinically significant range of their measures of depression and anxiety (Anttila et al., 2004; Just et al., 2003; Mazzone et al., 2005). Results from the present study confirm that there is a substantial minority of adolescents who are likely to present at a headache clinic with a clinically relevant psychological syndrome.

The comorbid presentation of migraine and internalizing symptoms is likely to result in impaired HRQL. The present study found that internalizing symptoms were a significant predictor of HRQL (as measured by PedsQL). The association remained strong even after controlling for the effects of associated symptoms of migraine, catastrophizing and demographics. Therefore, it is important to assess for internalizing symptoms when treating adolescents with migraines and address them when appropriate.

Participants in this sample reported few catastrophizing thoughts. The restricted range of the Pain Catastrophizing Scale limited our ability to detect relationships between catastrophizing and quality of life. Despite the low catastrophizing scores and the restricted range, the relationship between PCS and MSQ-A was of a meaningful size and approached statistical significance ($r=.3, p=.09$). A post-hoc power analysis to examine the likelihood of Type 2 error revealed that with the current sample size ($n=35$), there is approximately 40% chance of failing to detect a significant relationship between PCS and
Thus, it is worth exploring data from a larger sample which includes participants who experience more catastrophizing thoughts.

The three quality of life measures PedsQL, PedMIDAS and MSQ-A related differently with migraine variables, psychiatric comorbidity and catastrophizing. MSQ-A scores correlated significantly with internalizing symptoms and associated symptom severity index, while their relationship with catastrophizing was of meaningful size and would have likely been statistically significant if more participants were available for analysis. The relationship between MSQ-and the other two measures of HRQL was statistically significant. However, of these two correlations, only the relationship between MSQ-A and PedMIDAS was of meaningful size \( r = .56 \). Although statistically significant, the relationship between MSQ-A and PedsQL was too small \( r = .35 \), considering how both of these instruments were designed to measure similar concept. PedsQL and PedMIDAS did not correlate with one another or with the independent variables. The only exception was the relationship between PedsQL and internalizing symptoms, which was significant. It is unclear whether the difference in the way PedsQL, PedMIDAS and MSQ-A related to the independent variables of this study is due to variations in their statistical properties or differences in item content. Data from the three quality of life questionnaires has not been previously compared in the same adolescent sample. It is possible that even though all three measures aim to assess health-related impairments in functioning, the item content of PedsQL, PedMIDAS and MSQ-A differs sufficiently to result in discrepant quality of life scores for the same sample. While PedMIDAS assesses disability based only on time away from school activities and house chores, MSQ-A and PedsQL include social, recreational and emotional domains of
functioning and measure avoidance of activity out of fear a migraine will occur. The unusually low scores and the restricted range of the PedMIDAS scale in the present sample might be another explanation why no correlations were detected with the independent variables or the other two quality of life scales.

**Strengths and limitations**

There were several strengths to the current study. First and foremost the sample included only adolescents with clinically diagnosed migraine. In the literature there is a general lack of data specifically for adolescents with migraine (Karwautz et al., 1999). Studies tend to combine data from adolescents with data from younger children or pool data from participants with migraine and tension-type headache (Andrasik et al. 1988; Anttila et al., 2004; Fichtel and Larsson, 2002; Hunfeld et al., 2001; Langeveld et al., 1997). Authors have recently pointed out the need to consider adolescents separately from children when measuring HRQL (Frisen, 2007). Similarly, while migraine and tension-type headache share a number of characteristics, there are also important differences in their prevalence, prognosis and impact on adolescent HRQL (Borkum, 2007).

A second advantage was the methodology through which the data was collected. Migraine-related impairment in HRQL was measured through multiple instruments (PedsQL, PedMIDAS and MSQ-A) and unlike most studies in the area, a migraine specific measure of HRQL was used. The inclusion of an electronic headache diary was also valuable as migraine characteristics were recorded at the time of the headache. Finally, psychological symptoms were measured based on the adolescent’s own judgment, rather than being reported by the caregiver. Researchers have encouraged the
use of self-report assessment with adolescents, for the interest of providing the most accurate symptom description (Achenbach, 1991).

There were also several important limitations to this study. One such limitation was the relatively small sample size. Fewer than expected participants were available for the regression analysis, which resulted in low predictive power. The chance of Type 2 error was 36% when MSQ-A was the dependent variable and 14% when PedsQL was the dependent variable. Another limitation of the present study was the clinical nature of the sample. Although clinical samples allow for good monitoring and controlled data collection, studying participants who are currently being treated restricts the range of migraine frequency and severity and this makes it more difficult for significant relationships to be detected. Some problems were also encountered with the migraine and associated symptom severity indexes, which might have compromised the interpretation of this study’s results. First of all, the distributions of both were considerably skewed with many participants experiencing migraine episodes of low severity and few experiencing migraine episodes of very high severity. Additionally, bivariate correlation revealed the two indexes to be almost identical ($r=.874, p < .001$). The migraine severity index was omitted from the hierarchical regression analyses, as the presence of both indexes would have created issues of multicollinearity. Overall, considering that this was the first study to examine the relationship of migraine severity, associated symptom severity, internalizing and catastrophizing with HRQL specifically for adolescents with migraine, the analyses are to be considered exploratory and their results can not be over-generalized.
Implications

In this study, severity of associated symptoms of migraine and the presence of internalizing symptoms had a significant impact on adolescent HRQL. These findings demonstrate the need to assess migraine severity from a broader perspective, beyond intensity and frequency of head pain. Clinicians and researchers have long overlooked associated symptoms of migraine as a potential variable, but the existing research evidence and data from this study suggests they might be a considerable source of disability. Additionally, the findings of this study suggest that psychological functioning be evaluated when developing a treatment plan for adolescents with migraine, because it is often not only migraine-related symptoms that negatively impact functioning for this population. The combined clinical presentation of migraine and internalizing psychological disorders could complicate the treatment process, and demand that medical treatments be aided by psychological interventions. Future research needs to evaluate if HRQL of adolescents with migraine would be improved by such integrated treatment.
### TABLES AND FIGURES

Table 1

*Demographics Data*

<table>
<thead>
<tr>
<th></th>
<th>All participants (N = 63)</th>
<th>Participants included in the analysis (N = 40)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td>17 Males (27%)</td>
<td>10 Males (25%)</td>
</tr>
<tr>
<td><strong>Age range</strong></td>
<td>11-17</td>
<td>12-17</td>
</tr>
<tr>
<td><strong>Average Age</strong></td>
<td>14.3 Years</td>
<td>14.5 Years</td>
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</tbody>
</table>
Table 2

Means and Standard Deviations of Study Variables

<table>
<thead>
<tr>
<th></th>
<th>Frequency of Migraines/ Month</th>
<th>Total Duration of Migraines (hours)</th>
<th>Total Severity of Migraines (days)</th>
<th>Average Severity of Migraines</th>
<th>Associated Severity of Symptoms</th>
<th>MSQ-A</th>
<th>PedMIDAS</th>
<th>PedsQL</th>
<th>YSR</th>
<th>Internalizing Scale</th>
<th>PCS</th>
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<tbody>
<tr>
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<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>38</td>
<td>36</td>
<td>37</td>
<td>39</td>
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<tr>
<td>M</td>
<td>4.5</td>
<td>6.3</td>
<td>6.2</td>
<td>1.9</td>
<td>2.4</td>
<td>12.5</td>
<td>17.9</td>
<td>36.5</td>
<td>22.3</td>
<td>71.1</td>
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</tr>
<tr>
<td>SD</td>
<td>2.9</td>
<td>5.5</td>
<td>4.9</td>
<td>.4</td>
<td>1.8</td>
<td>10.7</td>
<td>23.4</td>
<td>10.9</td>
<td>15.4</td>
<td>9.1</td>
<td>2.5</td>
</tr>
</tbody>
</table>

*Note.* Migraine Severity Index = migraine days * average migraine severity

Associated Symptom Severity Index = migraine days * associated symptoms severity

MSQ-A=Migraine Specific Quality of Life – Adolescent Form

PedMIDAS= Pediatric Migraine Disability Assessment Score

PedsQL= Pediatric Quality of Life Questionnaire

YSR-Internalizing Scale=Youth Self Report – Internalizing Scale

PCS=Pain Catastrophizing Scale
Table 3.1

*Zero-Order Correlations between *HRQL* Measures*

<table>
<thead>
<tr>
<th>Variable</th>
<th>MSQ-A</th>
<th>PedMIDAS</th>
<th>PedsQL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. MSQ-A</td>
<td>---</td>
<td>.56**</td>
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<td></td>
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<td>N=33</td>
<td>N=31</td>
</tr>
<tr>
<td>2. PedMIDAS</td>
<td>---</td>
<td></td>
<td>.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N=32</td>
<td></td>
</tr>
<tr>
<td>3. PedsQL</td>
<td></td>
<td></td>
<td>---</td>
</tr>
</tbody>
</table>

*Note. MSQ-A=Migraine Specific Quality of Life – Adolescent Form
PedMIDAS= Pediatric Migraine Disability Assessment Score
PedsQL= Pediatric Quality of Life Questionnaire*
### Table 3.2

**Pearson R Zero-Order Correlations between Independent Variables**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Gender</th>
<th>Age</th>
<th>Migraine Severity Index</th>
<th>Associated Symptom Severity Index</th>
<th>Internalizing</th>
<th>Catastrophizing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=40</td>
<td>N=40</td>
<td>N=40</td>
<td>N=40</td>
<td>N=39</td>
<td>N=37</td>
</tr>
<tr>
<td>1. Gender</td>
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<td>.24</td>
<td>.22</td>
<td>-.10</td>
<td>.11</td>
</tr>
<tr>
<td>2. Age</td>
<td>---</td>
<td>.03</td>
<td>.08</td>
<td>.12</td>
<td>-.30</td>
<td></td>
</tr>
<tr>
<td>3. Migraine Severity Index</td>
<td>---</td>
<td>.87**</td>
<td>.10</td>
<td>.22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Associated Symptom Severity Index</td>
<td>---</td>
<td>.22</td>
<td>.38*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>---</td>
<td>.21</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Catastrophizing</td>
<td>---</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

*Note.* * = p < .05, ** = p < .001

Migraine Severity Index = migraine days * average migraine severity
Associated Symptom Severity Index = migraine days * associated symptom severity
Table 3.3

**Zero-Order Correlations between Independent Variables and HRQL Measures**

<table>
<thead>
<tr>
<th></th>
<th>Gender</th>
<th>Age</th>
<th>Migraine Severity Index</th>
<th>Associated Symptom Severity Index</th>
<th>Internalizing Symptoms</th>
<th>Catastrophizing</th>
</tr>
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<tr>
<td><strong>1. MSQ-A</strong></td>
<td>.38*</td>
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<td>.35*</td>
<td>.30</td>
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<td>N=35</td>
<td>N=35</td>
<td>N=35</td>
<td>N=35</td>
<td>N=35</td>
</tr>
<tr>
<td><strong>2. PedMIDAS</strong></td>
<td>.31</td>
<td>.18</td>
<td>.07</td>
<td>.16</td>
<td>.21</td>
<td>.21</td>
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<td>N=36</td>
<td>N=36</td>
<td>N=35</td>
</tr>
<tr>
<td><strong>3. PedsQL</strong></td>
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<td>N=36</td>
<td>N=35</td>
<td>N=36</td>
</tr>
</tbody>
</table>

*Note.* MSQ-A=Migraine Specific Quality of Life – Adolescent Form

PedMIDAS= Pediatric Migraine Disability Assessment Score

PedsQL= Pediatric Quality of Life Questionnaire

Migraine Severity Index= migraine days * average migraine severity

Associated Symptom Severity Index= migraine days * associated symptom severity
Table 4

Hierarchical Regression Results between MSQ-A and Independent Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Beta</th>
<th>df</th>
<th>ΔR²</th>
<th>t</th>
<th>F</th>
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<td></td>
<td></td>
<td></td>
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<td>Gender</td>
<td>.39</td>
<td>(2, 32)</td>
<td>.15</td>
<td>2.33*</td>
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<tr>
<td>Age</td>
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<td>Block 2</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Associated Symptom Severity Index</td>
<td>.33</td>
<td>(3, 31)</td>
<td>.10</td>
<td>2.10*</td>
<td></td>
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<tr>
<td>Block 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Internalizing</td>
<td>.24</td>
<td>(5, 29)</td>
<td>.075</td>
<td>1.50</td>
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<td>Catastrophizing</td>
<td>.12</td>
<td></td>
<td>.70</td>
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</table>

Note. * = p < .05, ** = p < .001

MSQ-A=Migraine Specific Quality of Life – Adolescent Form
Associated Symptom Severity Index= migraine days * associated symptom severity
Table 5

*Hierarchical Regression Results between PedsQL and Independent Variables*

<table>
<thead>
<tr>
<th>Variable</th>
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<th>ΔR²</th>
<th>t</th>
<th>F</th>
</tr>
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<td><strong>Block 1</strong> (2, 30)</td>
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<td>Age</td>
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<td>-1.25</td>
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<tr>
<td><strong>Block 2</strong> (3, 29)</td>
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<td>Associated Symptom Severity Index</td>
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<td>.22</td>
<td>.52</td>
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**Block 3** (5, 27)

| Internalizing             | -.60 |       |      | -3.65**|      |
| Catastrophizing           | .12  |       |      | .67   |      |

*Note.* * = p < .05, ** = p < .001

PedsQL= Pediatric Quality of Life Questionnaire
Associated Symptom Severity Index= migraine days * associated symptom severity
Table 6.1

Zero-Order Spearman Correlations between HRQL Measures

<table>
<thead>
<tr>
<th>Variable</th>
<th>MSQ-A</th>
<th>PedMIDAS</th>
<th>PedsQL</th>
</tr>
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<td></td>
<td></td>
<td>N=33</td>
<td>N=31</td>
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<tr>
<td>2. PedMIDAS</td>
<td>---</td>
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<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>N=32</td>
<td></td>
</tr>
<tr>
<td>3. PedsQL</td>
<td></td>
<td>---</td>
<td></td>
</tr>
</tbody>
</table>

*Note. MSQ-A= Migraine Specific Quality of Life – Adolescent Form
PedMIDAS = Pediatric Migraine Disability Assessment Score
PedsQL = Pediatric Quality of Life Questionnaire*
Table 6.2

Zero-Order Spearman Correlations between Independent Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Gender</th>
<th>Age</th>
<th>Migraine Severity</th>
<th>Associated Severity</th>
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<th>Catastrophizing</th>
</tr>
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<td></td>
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<td></td>
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<td>.11</td>
<td>.30</td>
<td>.31</td>
<td>-.10</td>
<td>.13</td>
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<tr>
<td>2. Age</td>
<td>---</td>
<td>-.10</td>
<td>-.06</td>
<td>.10</td>
<td>-.30</td>
<td></td>
</tr>
<tr>
<td>3. Migraine Severity Index</td>
<td>---</td>
<td>.78**</td>
<td>.08</td>
<td>.11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Associated Symptom Severity Index</td>
<td>---</td>
<td>.11</td>
<td>.14</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Internalizing</td>
<td>---</td>
<td>.22</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Catastrophizing</td>
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<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

*Note.* * = p < .05, ** = p < .001

Migraine Severity Index = migraine days * average migraine severity
Associated Symptom Severity Index = migraine days * associated symptom severity
Table 6.3

Zero-Order Spearman Correlations between Independent Variables and HRQL Measures

<table>
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<tr>
<th></th>
<th>Gender</th>
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<th>Associated Symptom Severity</th>
<th>Internalizing Symptoms</th>
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<td>-.10</td>
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<td>.35*</td>
<td>.34*</td>
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<td>PedMIDAS</td>
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<td>.19</td>
<td>.14</td>
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<td>.27</td>
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<td>PedsQL</td>
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<td>-.18</td>
<td>.06</td>
<td>.01</td>
<td>-.56**</td>
<td>.03</td>
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</table>

Note. MSQ-A=Migraine Specific Quality of Life – Adolescent Form

PedMIDAS= Pediatric Migraine Disability Assessment Score
PedsQL= Pediatric Quality of Life Questionnaire
Migraine Severity Index= migraine days * average migraine severity
Associated Symptom Severity Index= migraine days * associated symptom severity
REFERENCES


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Health related quality of life (HRQL)

According to the World Health Organization (WHO), health is defined as “the state of complete physical, mental, and social well being, and not merely the absence of disease or infirmity” (WHO, 1948). Over the years, this definition has had a significant influence on the way Health Related Quality of Life (HRQL) was conceptualized and measured (Spieth & Harris, 1996; Wilson et al., 1995). In its essence, HRQL was designed to capture the effects of an illness and its consequent therapy upon a subject, as perceived by the subject across several different domains of functioning. In other words, studying HRQL is an attempt to go beyond the precise physiological impact of a given disease on one’s well-being, as measured by a medical instrument (how bad one should feel given biological indications), to the level of subjectively experienced disruption in their everyday life which occurs due to the disease. Unlike a regular medical examination, HRQL is a multi-dimensional construct which covers four major areas of the individual’s well-being, including physical condition, functional status, psychological functioning and social functioning (Aaronson, 1988; Ware, 1984). This multidimensionality makes HRQL assessment a valuable addition to biological information, as it could potentially provide valuable information on the way variables within the dimension of health (i.e. a disease or its treatment) relate to particular dimensions of life and functionality (Ware, 1995).
Comorbidity of migraine and internalizing disorders

In a commentary on the prominent aspects of new research in the area of pediatric headache, Labbe (1999) suggested that children and adolescents with migraines are at a heightened risk of experiencing an internalizing psychological disorder, while children and adolescents with anxiety or depression are at increased risk of developing disabling headaches. Several authors have confirmed this idea (Egger et al., 1998; Pine et al., 1996).

In a longitudinal study Pine and colleagues (1996) obtained a large (n= 776) population sample of adolescents (ages 9-18) with and without clinical headache (migraine and chronic and impairing headache) and followed it in time to test the dynamics of the relationship between headache and depression/anxiety. The presence of clinical headache was initially diagnosed by a physician, while the adolescents’ psychological well-being was assessed through Diagnostic Interview Schedule for Children (child and caregiver forms). Results from the two follow-up assessments (three and nine years past the first assessment) indicated that headache was approximately twice as common in depressed adolescents compared with controls. Furthermore adolescents with no history of chronic impairing headache who experienced major depression were ten times more likely to develop impairing headaches at some time during the next 7 years.

Other authors studying clinical adolescent samples have found that migraine is associated with elevated levels of internalizing symptoms (Andrasik et al. 1988; Anttila et al., 2004; Just et al., 2003). However, these authors also reported that the average
levels of internalizing scores reported by their headache groups were lower than the clinical cutoff on their measures.

In the adult literature the comorbidity between migraine and internalizing disorders is a well-documented phenomenon (Breslau et al., 1994; Breslau et al., 2000; Hamelsky & Lipton, 2006; Lipton et al., 2000). Lipton et al. (2000) compared 389 adults with migraine from USA and UK (population sample) to 379 healthy controls based on their scores on the Short Form 12 and the Primary Care Evaluation of Mental Disorders scale. Migraine and depression were found to be highly comorbid. Other large scale population-based longitudinal studies have found that on average adults with migraine are 2.2 to 4.0 times more likely to experience elevated internalizing symptoms than healthy controls (Breslau et al., 1994; Breslau et al., 2000). In these studies the risk of migraine in people with pre-existing depression ranged from 2.8 to 3.5.

Overall, despite evidence from adolescent and adult studies, according to a recent review by Powers et al. (2006) the relationship between headache and psychological illness among children and adolescents continues to be “a well-recognized, but poorly understood phenomenon”. Further research is necessary to determine whether adolescent migraine is associated with clinical internalizing disorders, or rather with elevated internalizing symptoms.

Catastrophizing as a form of pain communication

Pain catastrophizing, has been found to be an important determinant of intrapersonal features of pain, including heightened pain intensity, distress and disability
(Sullivan et al., 2001). Because high levels of catastrophizing also have been found to be associated with a wide range of observable pain and illness behaviors (Bedard et al., 1997; Sullivan et al., 2000), Sullivan et al. (2001, 2006b) suggested that pain catastrophizing also has intrinsic interpersonal features. According to these authors, high catastrophizers feel threatened and helpless about their pain and seek social support by overt display of pain. As observers predominantly rely upon communicative pain behaviors to infer pain ratings (Deyo et al., 2004; Sullivan et al., 2006b), catastrophizers’ heightened pain expression might therefore function as social communications directed toward obtaining proximity and support.

Further elaboration by some researchers indicates that catastrophizing as a reaction to pain might be rooted in a curious self protective mechanism (Craig, 2004; Williams, 2002). Pain intensity is strongly connected to the associated sense of danger and avoidance from physical threat. An individual expressing pain might receive benefit when that expression is followed by protective actions by observers (Craig, 2004). However, pain expression is not merely the function of inner observation or recognition of private experiences. The interpersonal context might be essential in explaining how and when pain is expressed. The concept of pain is connected to pain behavior in circumstances of tissue damage or pathology, but also involves diverse social reactions, ranging from supportive or empathic responses to interpersonal distancing and loss of relatedness, punishment, or even exploitation of vulnerability (Williams, 2002). Alternatively, when negative reactions to pain behavior are anticipated, suppression of
pain expression might arise (Williams, 2002). In the presence of solicitous others, by contrast, one might expect robust pain expression (Morley et al., 2000).

To date, evidence for the association between pain catastrophizing and pain expression, in particular more communicative pain behavior, stems from studies with adults (Keefe et al., 2000; Sullivan et al., 2006b). However, the role of pain catastrophizing in pain expression might be of particular importance in children and adolescents (Vervoot et al., 2008). Vervoot et al. (2008) investigated the expressive dimensions of pain catastrophizing in school children and children experiencing clinically significant pain. They discovered that pain catastrophizing was predictive of verbal expression of pain experience independently from gender, age and experienced pain intensity. Parental perceptions of the child pain and paternal expression of protective behavior were significantly related to pain catastrophizing. Although children with chronic pain exhibited higher levels of catastrophizing, the above relationships were observed in both pain and healthy groups.

Catastrophizing as an independent predictor of disability

As a relatively young concept, the importance of catastrophizing as an independent contributor to HRQL has been called into question. Sullivan and D’Eon (1990) proposed that there is a significant conceptual and operational overlap between depression and catastrophizing. According to these authors the association between the two might limit the usefulness of catastrophizing as an independent explanatory construct for variations in pain among chronic pain patients.
However, the independent effects of catastrophizing and mood disorders on chronic-pain related quality of life have since been repeatedly confirmed (Geisser et al., 1994; Tripp et al., 2006). Catastrophizing has been found to influence pain perception through altering attention and anticipation, and heightening emotional responses to pain (Gracely et al., 2004). Their results were important because the relationship remained significant even after controlling for the effects of depression. Similar results were found by Seminowicz & Davis (2006). In a recent study Sullivan concluded that catastrophizing and depression seem to be influencing pain and emotional distress in qualitatively different ways (2001).

Catastrophizing was found to be a predictor of disability, independent from pain variation and demographic variables (Keefe et al., 1989). Keefe and colleagues (1989) studied patients with rheumatoid arthritis and compared catastrophizers to non-catastrophizers in terms of adjustment and coping (as measured by the Coping Strategies Questionnaire). The authors made special effort to control for a variety of potentially confounding factors (such as the initial physical, duration of the disease, age, socioeconomic status and others) found that that baseline catastrophizing was a stable predictor of levels of disability six months later. Similarly, in a population sample (N = 1,571) Picavet and colleagues found that, catastrophizing predicted the development of back pain in individuals who were pain free at baseline (2002). Catastrophizing has also been found to be a valid predictor of general health status even when the effects of pain intensity, age, gender, and chronicity were controlled for (Severeijns et. al., 2002).