JOURNAL
OF THE CANADIAN ACADEMY OF CHILD AND ADOLESCENT PSYCHIATRY / DE L'ACADÉMIE CANADIENNE DE PSYCHIATRIE DE L'ENFANT ET DE L'ADOLESCENT

RESEARCH ARTICLE

Mindfulness-based Intervention for Female Adolescents with Chronic Pain: A Pilot Randomized Trial

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Abstract:

Objective: To test the feasibility of a randomized-controlled trial measuring the impact of an adapted mindfulness-based intervention (MBI) in female adolescents with chronic pain. **Methods:** This was a single center, single-blind, prospective, experimental, longitudinal trial conducted in a pediatric tertiary care center. Participants had a history of chronic pain during at least three months. They were randomized into an intervention group or a wait-list control group. Both groups successively followed an adapted eight-week MBI designed specifically for adolescents with chronic pain. Pre-determined criteria were established to assess the feasibility, validity and acceptability of the study model. Data evaluating changes in quality of life, depression, anxiety, pain perception, psychological distress and salivary cortisol were collected throughout the 4-month study period. **Results:** Nineteen female participants completed the study and had a mean age of 15.8 years (range 13.9 -17.8). Attrition rate was low (17%). Attendance to mindfulness sessions (84%) and compliance to study protocol (100%) were high. All participants reported a positive change in the way they coped with pain. No changes in quality of life, depression, anxiety, pain perception, and psychological distress were detected. Significant reductions in pre- and post-mindfulness session salivary cortisol levels were observed ($p<0.001$). **Conclusions:** Mindfulness is a promising therapeutic approach for which limited data exist in adolescents with chronic pain. Our study indicates the feasibility of conducting such interventions in teenage girls. A large trial is needed to demonstrate the efficacy and bio-physiological impacts of MBIs in teenagers with chronic pain.

Key Words: *mindfulness, adolescent, chronic pain, feasibility, randomized, pilot*

Résumé

Objectif: Vérifier la faisabilité d'un essai randomisé contrôlé qui mesure l'effet d'une intervention de pleine conscience (IPC) adaptée chez des adolescentes souffrant de douleur chronique. **Méthodes:** Il s'agissait d'un essai monocentrique, à l'insu, prospectif, expérimental, longitudinal mené dans un centre soins tertiaires pédiatriques. Les participantes avaient des antécédents de douleur chronique durant au moins trois mois. Elles ont été randomisées soit dans un groupe d'intervention, soit dans un groupe témoin placé sur une liste d'attente. Les deux groupes ont suivi successivement une

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Submitted: May 1, 2016; Accepted: August 1, 2016

IPC adaptée de 8 semaines, conçue spécifiquement pour les adolescentes souffrant de douleur chronique. Des critères prédéterminés ont été établis pour évaluer la faisabilité, la validité et l'acceptabilité du modèle d'étude. Les données évaluant les changements touchant la qualité de vie, la dépression, l'anxiété, la perception de la douleur, la détresse psychologique et le cortisol salivaire ont été recueillies durant la période de 4 mois de l'étude. **Résultats:** Dix-neuf participantes ont participé à l'étude et leur âge moyen était de 15,8 ans (écart de 13,9 à 17,8). Le taux d'attrition était faible (17 %). L'assistance aux séances de pleine conscience (84 %) et l'observance du protocole de l'étude (100 %) étaient élevées. Toutes les participantes ont déclaré un changement positif de la façon dont elles traitaient avec la douleur. Aucun changement n'a été détecté en ce qui concerne la qualité de vie, la dépression, l'anxiété, la perception de la douleur, et la détresse psychologique. Des réductions significatives des taux de cortisol salivaire avant et après les séances de pleine conscience ont été observées ($p < 0,001$). **Conclusions:** La pleine conscience est une approche thérapeutique prometteuse pour laquelle il n'existe que des données limitées pour les adolescentes souffrant de douleur chronique. Notre étude indique la faisabilité de mener ces interventions auprès d'adolescentes. Il faut un vaste essai pour démontrer l'efficacité et les effets biophysiologiques des IPC chez les adolescentes souffrant de douleur chronique.

Mots clés: pleine conscience, adolescente, douleur chronique, faisabilité, randomisé, pilote

Author contributions

NC conceptualized and coordinated the study, performed data analysis, and drafted the initial manuscript. AM contributed to the design of the study, revised the protocol, taught and adapted the mindfulness-based intervention. MV and CMH revised the protocol. AD conducted cortisol analyses. PLD provided supervision and revised the mindfulness-based intervention. TML and JL revised the protocol and contributed to data analysis. NH revised the protocol and contributed to data collection. All authors contributed to data interpretation and revision of the manuscript.

Abbreviations

CBT	Cognitive Behavioral Therapy
MBI	Mindfulness Based Intervention
MBCT	Mindfulness Based Cognitive Therapy
MBSR	Mindfulness Based Stress Reduction

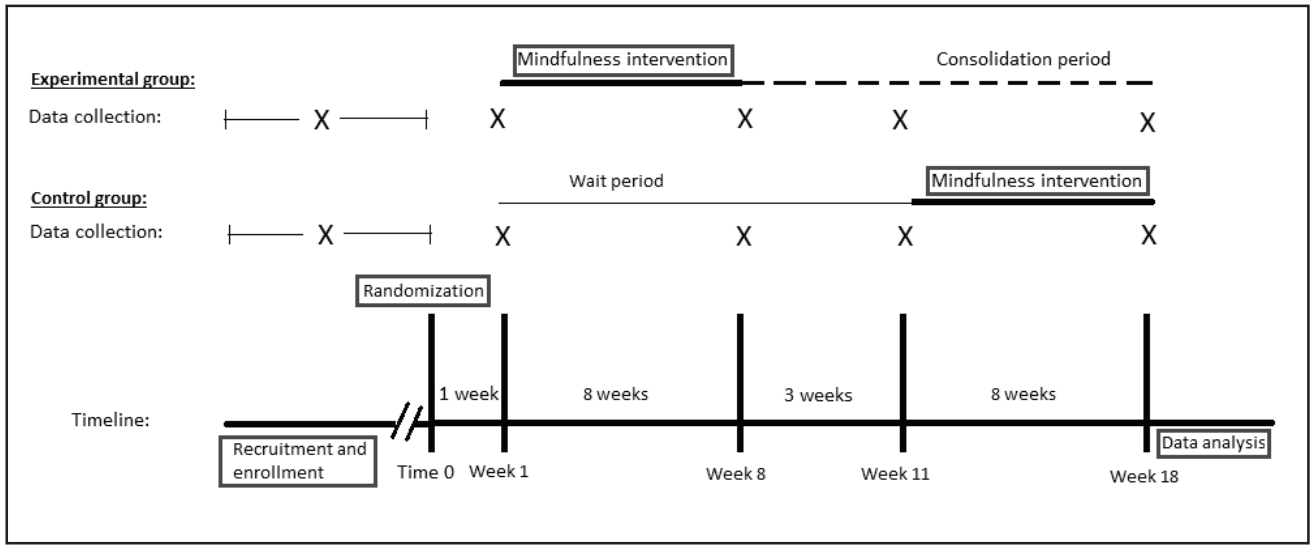
Introduction

Chronic pain in adolescents is a common condition, resulting in significant impacts on development and level of functioning. Although definitions vary widely, a review article on this topic suggests that: "[chronic pain] is overwhelmingly prevalent in children and adolescents and should be recognized as a major health concern" (King et al., 2011). The high emotional burden associated with chronic pain translates into a reduction in health-related quality of life (Warschburger et al., 2014). It has been suggested that interventions promoting the acquisition and strengthening of appropriate coping strategies could result in benefits for this group of adolescents for whom pain is often long-lasting and disabling (Kashikar-Zuck et al., 2013).

There has been a growing interest in the study of mindfulness-based interventions (MBIs) in children, adolescents and adults with various physical and mental health conditions including chronic pain (Gotink et al., 2015; Saunders, 2015). Drawing from meditation practices rooted in a number of Buddhist traditions, most contemporary forms of mindfulness meditation that are studied in the setting of clinical research seek to promote purposeful and non-judgemental awareness of one's thoughts, feelings and sensations (Kabat-Zinn, 1991). Since the early 1980s, when it was first studied clinically in groups of adults with refractory pain conditions (Kabat-Zinn, 1982), mindfulness has been taught through various structured and semi-structured programs to both clinical and non-clinical populations of children, adolescents and adults. Among the numerous and increasing number of available programs, the most widely studied interventions adopt a similar eight-week structure. These interventions include formal meditation practices, mindful movement and breathing as well as informal practices that can be integrated in daily life activities (Fjorback, Arendt, Ornbol, Fink, & Walach, 2011).

Evidence looking at the benefits of mindfulness in adult populations with chronic pain is increasing (Bawa et al., 2015; Lakhan & Schofield, 2013). A recent randomized controlled trial conducted in adults suggested that mindfulness has significant long-lasting impacts on dimensions of the experience of pain including pain acceptance, anxiety, depression and psychological well-being (la Cour & Petersen, 2015). Another study comparing the benefits of a MBI and cognitive behavioural therapy (CBT) for adults with somatoform disorders found that the MBI, derived from a well-studied mindfulness curriculum for adults, was comparable to CBT, with more rapid improvements for patients in the MBI group (Fjorback et al., 2013). The safety of conducting MBIs in clinical populations is still being studied at this time, but many authors have suggested that MBIs are safe, provided that adequate psychological support is available (Compson, 2014). A number of studies have explored the biological effects of mindfulness through the use of markers such as salivary cortisol (Matousek, Dobkin, & Pruessner, 2010). So far, reductions in cortisol levels have been shown in some studies, but results in randomized-controlled trials have been inconsistent (O'Leary, O'Neill, & Dockray, 2015).

Figure 1. Study design diagram



The body of evidence concerning MBIs in adolescents is less abundant than in the adult literature, but work in the area is emerging (Malboeuf-Hurtubise, Achille, Sultan, & Vadnais, 2014). Recent studies pertaining to a broad range of MBIs in youth indicate that mindfulness is a promising adjunct treatment for chronic pain conditions, anxiety and depression (Simkin & Black, 2014). Yet, although results are encouraging, it remains difficult to conclude on the magnitude of the effects of MBIs in youth due to the important heterogeneity of research methods used (Tan, 2015). Similarly, findings on biological correlates such as changes in salivary cortisol levels are promising, but lack reproducibility and large-scale validation (Schonert-Reichl et al., 2015; Sibinga et al., 2013).

With regard specifically to adolescents with chronic pain, data remains limited. To our knowledge, no large-scale randomized study has been conducted so far. A small pilot study (n=6) evaluating a MBI in youth with chronic pain reported numerous difficulties pertaining to recruitment and retention such that authors were unable to report any quantitative data (Jastrowski Mano et al., 2013).

Given the paucity of evidence for the study of MBIs in adolescents, we undertook a pilot trial to estimate the feasibility, acceptability and validity of a study looking at the efficacy of an adapted MBI in teenagers with chronic pain. We also collected pilot data to assess whether the MBI improved quality of life, depression, anxiety, pain perception, psychological distress and salivary cortisol levels among participants. We hypothesized that the intervention would be safe and well tolerated.

Methods

This study was approved by the Institutional Review Board of Sainte-Justine Hospital. Written consent was obtained from all participants and their parents. Potential advantages and disadvantages related to participation in the study were discussed with every participant during the recruitment interview.

Trial design

We report in this paper the pilot trial that serves to support the feasibility of conducting a large randomized controlled trial. Figure 1 depicts the timeline of the trial. Participants were randomly allocated to an experimental group or a wait-list control group, which subsequently received the eight-week adapted MBI designed for the project. The study was single-blind (to investigator only). During the course of the study, any treatment prescribed by the primary health care provider was maintained.

Participants

The pilot trial was conducted at Sainte-Justine Hospital, a pediatric tertiary care university-affiliated hospital located in Montreal, Canada. Participants were referred from seven different outpatient clinics: adolescent medicine, general pediatrics, adolescent psychiatry, pain clinic, gastroenterology, neurology and rheumatology. Patients between the ages of thirteen and eighteen who were followed by a physician for a condition resulting in chronic pain of at least three months duration were considered eligible for recruitment if their home was located less than a one-hour drive from the hospital and if they were fluent in French. Exclusion criteria included untreated psychosis or depression, active suicidal

Table 1. Primary outcome - feasibility, acceptability and validity criteria	
Indicator	Target
Recruitment rate	Less than 12 weeks to recruit target sample size (n=20)
Attrition rate	Less than 30% of loss to follow-up: with a difference in proportion < 20% between experimental and control groups
Compliance to the study protocol	At least 70% of study participants meeting both compliance criteria: - 75% attendance rate at mindfulness sessions - At least 1 documented home practice per week during the 8-week MBI training period
Adequate monitoring of the outcomes	Completion of all 4 questionnaire packages and saliva analyses
Quality control of the intervention	At least 70% of curriculum objectives completed during each of the 16 mindfulness sessions
MBI = Mindfulness-based intervention	

ideation unknown to the referral physician and intellectual limitation that could hinder study participation.

Patient screening and referral for recruitment were done by attending physicians in the seven outpatient clinics. Eligible participants and their parents met with a recruiting physician (NC and NH) for a 30-minute encounter. During the encounter, the recruiting physician re-evaluated eligibility criteria, explained the study program and commitment, and obtained consent from both the participant and her parent. Baseline data was collected after written consent was obtained from participants and parents. Recruitment was closed once a pre-determined convenient target sample size of 20 participants was reached.

Randomization and intervention

Randomization was done using a computer-generated randomization list and permuted block design, with block sizes of two or four. Participants were assigned to the experimental or the wait-list control group using a 1/1 ratio.

The MBI consisted of eight consecutive weekly group classes taught by two psychiatry residents (AM and EPM) with advanced mindfulness training and personal practice. Each session lasted 90 minutes. The curriculum was based primarily on elements taken from the two most widely used eight-week structured mindfulness programs for adults: Mindfulness-Based Stress Reduction (MBSR) (Kabat-Zinn et al., 1992) and Mindfulness-Based Cognitive Therapy (MBCT) (Teasdale et al., 2000). Content was specifically adapted to adolescent concerns and preferences as follows: smaller groups, mindfulness sessions shortened from 150 to 90 minutes, group meditations and individual practices capped at 15 to 20 minutes, simplification of vocabulary used for group inquiry, increased attention given to simpler and more accessible breathing practices, mindful movement and poetry. Content was inspired by the works of Vo (Vo, 2015), Dewulf (Dewulf, 2012), Deplus (Deplus, 2011) and Malboeuf-Hurtubise (Malboeuf-Hurtubise, Achille, Sultan, & Vadnais, 2013). Each weekly session was built around an overarching theme:

- Week 1: Present moment and body awareness
- Week 2: Introduction to pain and the five senses
- Week 3: Meditation and breathing, pleasant events and sensations
- Week 4: Stress reactivity, coping with pain and difficult sensations
- Week 5: Awareness of thoughts and stress response
- Week 6: Recognizing and responding to difficult emotions
- Week 7: Loving-kindness and compassion, integrative pain meditation
- Week 8: Continuity of practice and next steps

Mindfulness practices included: sitting meditations, walking meditations, love and kindness meditations, compassion and deep listening, body scan, mindful eating, breathing exercises, poetry readings, guided discussion and inquiry. Each mindfulness session was video-recorded and reviewed by an expert with Certification from the University of Massachusetts Medical School Center for Mindfulness, with extensive mindfulness teaching experience (PLD) (Dobkin, 2015) to ensure the courses were taught according to the protocol specifications and with embodied mindfulness on the part of the instructors.

Outcomes

Outcome measures of the pilot trial: Five criteria were selected by a multidisciplinary expert focus group in order to assess the feasibility of a large randomized controlled trial: recruitment rate; attrition rate; compliance; adequate monitoring of the outcomes and quality control of the intervention (see definitions in Table 1.)**.**

Other outcomes of interest: Health-related quality of life was measured using a validated self-administered 23-item

Table 2. Demographic and clinical characteristics of study participants

Indicator	Experimental group (n=10)	Control group (n=9)
Average age at randomisation – year (range)	16.1 (13.8-17.8)	15.6 (13.9-16.8)
Female gender	10	9
Race – number/total		
White	9	7
Hispanic	1	1
Black	0	1
Pain perception score at randomization /10 (range)	5.9 (3.5-7.8)	6.0 (4.8-7.4)
Medical history – number/total		
Somatoform disorder	5	5
Inflammatory/auto-immune disorder	1	3
Gastro-intestinal disorder	1	1
Migraine	4	3
Musculo-skeletal condition	3	3
Mental health history – number/total		
Current/past mood disorder	3	3
Current/past suicidal ideation	1	4
Current/past anxiety disorder	5	2
History of physical/sexual abuse	1	2
Medication		
Medication for pain (NSAIDs, acetaminophen, gabapentin, opiates)	6	8
Melatonin	5	2
Tricyclic antidepressant	2	4
Selective Serotonin Reuptake Inhibitors (SSRIs)	2	1
Combined hormonal contraceptive	4	3
Progesterone contraceptive	2	1
Adjunct therapy*	4	3
Substance use		
Tobacco use within last month	0	0
Alcohol use within last month	1	0
Drug use within last month	0	0
Previous mindfulness/yoga training	2	2

*Adjunct therapy included: physiotherapy, chiropractor, massage, acupuncture

questionnaire with Likert scales: the Pediatric Quality of Life Scale (PedsQL 4.0) designed for adolescents ages 13-18 years (Cronbach's alpha = 0.89) (Varni, Burwinkle, & Seid, 2006).

Depression, anxiety, pain perception and psychological distress were measured using patient-completed questionnaires: (1) the Beck Youth Depression and Anxiety Scales 2nd edition are Likert-type measurement scales that contain 20 questions for the evaluation of depressive and anxiety symptoms in adolescents (Cronbach's alpha ≥ 0.86) (Community-University Partnership for the Study of Children, 2011); (2) the Visual analogue pain scale composite score is a twelve centimeter vertical visual analogue scale that was used to assess the self-evaluated worse, average and best pain perception in the previous week; a composite score was created by using an average of the three measurements (Stinson, Kavanagh, Yamada, Gill, & Stevens, 2006); (3) the IDPESQ-14 Psychological distress scale is a fourteen-question-Likert-type measurement scale used to assess negative emotions leading to depression and anxiety in teens (Deschenes, 1998). For the purpose of this study, French validated versions of all scales were used.

Table 3. Comparison of mental health outcomes between the intervention and the control groups at week 8

Parameters (change from baseline values)*	Experimental group (n =10)	Control group (n =9)	Unadjusted comparison (P value)	Adjusted comparison for baseline score (P value)	Effect size (Eta square)
Quality of life	-1,30 (-7.95, 5.35)	-3.72 (-11.01, 3.57)	0.581	0.683	0.01
Depression	1.33 (-1.81, 4.48)	-2.78 (-9.45, 3.90)	0.217	0.446	0.13
Anxiety	0.35 (-4.24, 2.94)	-4.11 (-9.59, 1.37)	0.169	0.374	0.05
Pain perception	-0.55 (-1.25, 0.15)	0.36 (-1.39, 0.68)	0.721	0.723	0.01
Psychological distress	-0.50 (-5.61, 1.35)	-4.44 (-11.36, 2.47)	0.193	0.236	0.09

*Mean change over time (95% confidence interval)

Salivary cortisol was collected using Salivette® sampling devices, which consist of a plastic sampling vessel with a suspended insert containing a sterile neutral cotton wool swab (Vogeser, Durner, Seliger, & Auernhammer, 2006). Participants were questioned for oral bleeding or ulcers and were asked not to ingest any liquid or solid substances one hour prior to sampling. Swabs were placed under the tongue for 2.5 minutes and immediately returned to the insert. All samples were kept frozen until analysis at the end of the study period. Salivary cortisol was measured using immunoassay (Roche diagnostics, Cobas E410). Functional sensitivity was evaluated and established at 3 nmol/L (variability coefficient ≤20%). Within-run variability of the method was also verified (variability coefficient < 10%). Finally, the method was validated by mass spectrometry analysis of eight selected participant specimens including the lowest salivary cortisol value (0.65nmol/L). Linear regression analysis showed a high coefficient of determination (r^2 = 0.87).

Data management

Each participant was encouraged to maintain a study log book to document home practice frequency and duration. Instructors were asked to take attendance at the beginning of each session. Pre and post intervention questionnaires distributed at the first and eighth mindfulness sessions for both groups allowed gathering written feedback regarding participant satisfaction with the intervention.

Data for quality of life, depression, anxiety, pain perception and psychological distress were collected at baseline and at weeks 1, 8, 11 and 18 of the study period either on paper (during the mindfulness intervention) or online (before or after the eight-week MBI depending on participant groups). Questionnaire packages took approximately fifteen minutes to complete. Saliva samples for measurements of cortisol levels were collected at 17:30 and 19:00, immediately before and after a mindfulness session on the first and eighth week for both the experimental and the wait-list control groups (four saliva samples per participant). This was done to look at salivary cortisol change following a 90-minute mindfulness session, and also longer term modification following an eight-week intervention.

Statistical analysis

Descriptive statistics were used to report results on feasibility, acceptability, validity and cortisol measurements. We performed in the pilot trial the same statistical analyses that will be used in the large randomized controlled trial. All statistical analyses were done using an intention-to-treat strategy with version 22 of IBM SPSS software. Intention-to-treat analyses to compare the experimental and the control group on the five quantitative scales at week eight were performed using one-way ANOVAs and ANCOVAs to take into account baseline measures. Paired t-test analyses were performed pooling data from all nineteen retained participants to assess for pre-post MBI changes in mental health scores. Additional paired t-test analyses were performed to detect same-day variations (17:30 and 19:00) in cortisol at weeks one and eight of the MBI. No stratified data analysis was performed given the small population size.

Results

Baseline data

Table 2 presents the main demographic and clinical characteristics of study participants. All were female and their average age at randomization was 15.8 ±1.1 years. Baseline pain perception scores were comparable in both groups. Prevalence of mental health conditions, somatoform disorders and pain medication use was high in both groups.

Outcome measures of the pilot trial:

Results for each of the five feasibility, validity and acceptability criteria described in table 1 met or exceeded target goals. Twenty-three adolescents were recruited to participate in the study during a period of eleven weeks. Among the 23 participants, three left the study prior to randomization and one (control group) did not complete the eight MBI sessions (attrition rate: 17%). Main reasons for attritions were: living too far from the hospital (n=3) and

Table 4. Pre- and post-mindfulness salivary cortisol levels at week 1 and week 8

	Salivary cortisol (nmol/L)			
	Week 1		Week 8	
Participants	17:30	19:00	17:30	19:00
Intervention group				
1	1.81	0.79	1.71	0.66
2	4.14	1.06	2.04	2.34
3	/	/	0.54	0.57
4	/	1.24	/	1.81
5	4.37	1.53	4.03	1.83
6	5.17	3.04	3.5	2.55
7	1.36	1.14	2.46	2.66
8	/	0.94	/	3.12
9	/	1.65	7.08	3.17
10	1.57	1.1	2.83	1.35
Wait-list control group				
1	/	/	/	1.96
2	/	/	/	/
3	/	/	5.29	2.46
4	2.46	1.27	1.55	1.34
5	4.51	3.46	4.27	/
6*	4.04	4.55		
7	2.15	1.02	2.59	1.23
8	3.26	1.97	5.71	3.65
9	2.8	2.08	6.35	2.92
10	/	/	/	/

/ Insufficient saliva for analysis
*Participant did not complete the study

conflict with school hours (n=1). Among the nineteen participants who completed the MBI, sixteen (84%) met both attendance and home practice criteria (present at 6/8 MBI sessions and completed one home practice per week during the eight-week MBI period). All 19 participants were able to complete assessment questionnaires and provided the required saliva samples. Finally, curricular content was delivered in its entirety for both rounds of eight mindfulness sessions.

Mental health outcomes

Table 3 displays comparisons in mental health outcomes between the intervention and the control groups eight weeks post randomization. There were no significant changes in quality of life, depression, anxiety, pain perception and psychological distress, even after accounting for baseline status.

When combining data from all nineteen participants, no significant changes in mental health scores before and after completion of the MBI intervention were found.

Changes in salivary cortisol

Seventy-eight saliva samples were collected at four time points during the four-month study period. These were provided by the 20 randomized participants, including two samples from the participant who did not complete the trial as shown in table 4.

Among the 78 samples, 25 samples from ten participants could not be analyzed because of insufficient quantity of saliva. There was no difference in medical diagnosis, medication, age, or experimental vs. control group between participants with analyzed vs. non-analyzed samples. Data from the experimental and the wait-list control group were pooled for statistical analysis. Cortisol levels collected at 17:30 and 19:00 on the same day (from either the first or the eighth mindfulness session) were compared for fifteen participants who had at least one pair of analyzable saliva samples (experimental group n=8, control group n=7). For the ten participants who had more than one pair of analyzable samples, we selected the first available pair. Results show reduction in cortisol levels from an average of 3.37 (±1.72) nmol/L at 17:30 to an average of 1.95 (±1.13) nmol/L at

19:00 (Cohen's d 0.77, p value <0.001). No significant difference was found in 17:30 cortisol levels at week one vs week eight. There was also no significant difference in the magnitude of the decrease at week one vs week eight.

Satisfaction with the program and adherence:

Although participants were encouraged to keep a personal log for individual practice and personal reflections about the program, the use of log books was very inconsistent and did not allow for compilation of practice data. Comments were extracted from post intervention questionnaires and from notes taken by instructors during or immediately after mindfulness sessions based on group discussions. Study participants reported numerous benefits and positive outcomes with very few negative comments. For instance, one participant reported (translation from French): "My pain isn't less intense, but my relation to it has changed. Now I am able to live and respond to my pain more easily". Another wrote: "My biggest discovery during this program was to realize the impact that emotions can have on the body". One participant explained: "Before, I would drink to numb my pain. During the course of this program, I learned that there are other ways to cope and live with my pain. Since then, I stopped drinking and I can now stay with, accept and bring compassion to my pain". Finally, one participant mentioned: "I am less anxious and I feel that I have more tools to help me deal with stress. I don't think about my school exams two weeks ahead of time anymore; instead, I focus on what I can do now to prepare… and I breathe." Other cited advantages and emerging themes associated with the program included: making new friends through the program, getting to know other teenagers living with similar conditions, better social skills, increased school attendance and feeling less tired during the day, increased awareness and appreciation of the present moment, feeling more relaxed and having better self-regulation/emotion control.

Average number of weekly home practices reported in post-intervention questionnaires was four per week (range 1-10): 2/19 participants practiced on average once per week, 6/19 participants practiced two to three times per week, 9/19 participants practiced four to six times per week and 2/19 participants practiced seven or more times per week. Average duration of individual home practices was of eight minutes: one to five minutes for 7/19 participants, six to fifteen minutes for 8/19 participants, sixteen to twenty-five minutes for 2/19 participants and more than twenty-five minutes for 2/19 participants. The nature of practices was as follows (from most frequent to least frequent): informal practices during normal daily activities such as brushing teeth, waiting for the bus, formal sitting/walking meditations, body scan and mindful eating/breathing. All nineteen participants who completed the MBI reported a significant positive change in the way they coped with pain. This change was "small or medium" for 10/19 participants and "big or very big" for 9/19. Most participants reported a significant improvement in sleep quality (13/19) and the remaining six participants reported a small positive improvement. Nearly all participants indicated that they would be likely (5/19) or very likely (12/19) to recommend the program to a friend.

Discussion

This study showed that our adapted MBI was feasible and acceptable to teenagers who participated as demonstrated by the attainment of the five feasibility, acceptability and validity criteria detailed in table 1. Only one study had previously reported on a similar pilot trial in teenagers with chronic pain with less positive results (Jastrowski Mano et al., 2013).

Our success can be explained by some factors that were taken into account during study conception to overcome barriers observed in other studies. Meeting with parents and participants during the recruitment process might have encouraged commitment and adherence to the program. Results from other pilot studies conducted in youth with mental health problems or in other teenagers receiving MBIs at school or in the community were comparable to ours (Cotton et al., 2015; Tan & Martin, 2013; Zenner, Herrnleben-Kurz, & Walach, 2014).

One limitation of the study was that it was not powered enough to assess changes in mental health outcomes. Thus, drawing conclusions from these preliminary data is premature. Moreover, our study was too small to consider confounders that could have masked any potential short-term benefits of the intervention. Indeed, a larger trial could take into account seasonal effect on mood changes, time in the school year, individual factors such as change in primary treatment and medication, hospitalizations, surgery, vacation and psycho-social stressors. Other teams have opted for non-randomized or qualitative analyses with promising results (Monshat et al., 2013). However, these designs cannot address potential biases such as Hawthorne effect and unidentified confounders. Interestingly, the qualitative accounts recorded in post-intervention questionnaires were positive. The high number of individual practices, which for more than half of study participants took place on most days of the week, is impressive, suggesting a high level of adherence to mindfulness instructions.

Salivary cortisol has been studied as a surrogate marker for stress in a number of adult mindfulness trials with conflicting results (Gex-Fabry et al., 2012). It is important to note that mindfulness sessions took place in the evening, when baseline cortisol levels are low and at a time when physiologic variations are small. To ensure that changes observed were not due to normal physiological variation, we collected samples from ten young and healthy adults (laboratory employees). These adults were chosen for convenience and because they were engaging in activities requiring a similar level of activity as our study participants. Adult controls did not display any significant changes in their cortisol level

between 17:30 and 19:00 (data not shown). In our study, the significant reductions in salivary cortisol levels from 17:30 to 19:00 suggest that MBIs might have an important bio-physiological impact in youth with chronic pain. The lack of significant baseline change in pre-post MBI 17:30 cortisol levels between the first MBI session and the eighth session seem to indicate that these changes are of short duration. As mentioned in an early study of the original MBSR program by Kabat-Zinn (Kabat-Zinn, Lipworth, & Burney, 1985), our data support the assumption that participants would need to practice mindfulness on a regular daily basis to be able to see sustained benefits. Unfortunately, the large number of uninterpretable saliva samples could have impacted the data on cortisol. This could have been remediated by using Salivette® devices containing citrate to stimulate saliva production (Gallagher, Leitch, Massey, McAllister-Williams, & Young, 2006). Nevertheless, it is worth noting that the effect size for salivary cortisol was large, which strengthens our results.

There are other limitations to this study. First, we did not track long-term changes. The latest measurement, ten weeks post-MBI in the experimental group, did not show any significant changes in baseline measurement scores. Second, our design did not include a standardized assessment of mindfulness or daily practice measures which could have been useful to better describe the integration of mindfulness in daily life. Third, even though the study was open to both males and females, only females were enrolled, limiting external validity and suggesting a potential selection bias. Fourth, our clinical population (i.e. pain conditions) was highly heterogeneous. This could limit the conclusions and the reproducibility of this study. Fifth, due to budgetary and time limitations, control values for salivary cortisol levels were taken from young adults and not from adolescents. In addition, the number of samples per participant were limited: it would have been more informative to gather a larger number of saliva samples from each participant, throughout the day, on the first and last day of the MBI as suggested elsewhere (Matousek et al., 2010). Lastly, the lack of an attention-control group represents another important limitation of our study design. As a subsequent step, a head to head trial with CBT or dialectical behavioural therapy as a comparative group may have been informative (Hatchard, Lepage, Hutton, Skidmore, & Poulin, 2014) as the absence of an active control group makes it difficult to distinguish the therapeutic benefits of being in a group setting from the impact of the MBI itself.

Conclusion

Chronic pain in adolescents is a significant clinical problem with many comorbidities and significant impairments on quality of life. Although statistical analyses did not reveal significant differences between groups in this pilot, the promising feasibility, acceptability and validity data provided by our study as well as the high levels of appreciation among study participants prepare the grounds for further research including larger scale randomized studies on use of MBIs in adolescents with chronic pain. The reduction in salivary cortisol levels seen in study participants raises interesting questions about the bio-physiological underpinnings of mindfulness. More research is needed to understand the long-term impacts of MBIs and the magnitude of their effects on the developing brains of adolescents with chronic pain.

Acknowledgements / Conflicts of Interest

The research team wishes to acknowledge the contributions of Amelie Roch, Julien Bensoussan and Eveline Perrier-Menard. The research team also wishes to thank Dzung Vo and Jake Locke for their support and mentorship throughout the project. Finally, the authors would like to thank the American Academy of Pediatrics and the Bell Canada Mental Health Fund for their financial support as well as Roche Diagnostics for providing salivary cortisol measuring kits free of charge.

References:

Bawa, F. L., Mercer, S. W., Atherton, R. J., Clague, F., Keen, A., Scott, N. W., & Bond, C. M. (2015). Does mindfulness improve outcomes in patients with chronic pain? Systematic review and meta-analysis. *British Journal of General Practice, 65*(635), e387-400. doi:10.3399/bjgp15X685297

Community-University Partnership for the Study of Children, Youth, and Families. (2011). *Review of the Beck Youth Inventories – For Children and Adolescents 2nd Edition (BYIII)*. Retrieved from Edmonton, Alberta, Canada.

Compson, J. (2014). Meditation, trauma and suffering in silence: Raising questions about how meditation is taught and practiced in western contexts in the light of a contemporary trauma resiliency model. *Contemporary Buddhism, 15*(2), 274-297. doi:10.1080/14639947.2014.935264

Cotton, S., Luberto, C. M., Sears, R. W., Strawn, J. R., Stahl, L., Wasson, R. S.,...Delbello, M. P. (2015). Mindfulness-based cognitive therapy for youth with anxiety disorders at risk for bipolar disorder: A pilot trial. *Early Interventions in Psychiatry*. doi:10.1111/eip.12216

Deplus, S. (2011). *Pleine conscience et acceptation (chapter 3): Les interventions psychologiques basées sur la pleine conscience pour l'enfant, l'adolescent et leurs parents (original French version)*. Brussels, Belgium: De Boeck.

Deschenes, M. (1998). Study of the validity and the reliability of The Quebec Health Department's Psychological Distress Index (IDPSQ-14) in an adolescent population. *Canadian Psychology, 39*(4), 288-298.

Dewulf, D. (2012). *Mindfulness: la pleine conscience chez les ados (French transalation)*. Louvain-la-Neuve, Belgium: De Boeck.

Dobkin, P. (2015). Mindful Medical Practice: Clinical Narratives and Therapeutic Insights. Switzerland: Springer Press.

Fjorback, L. O., Arendt, M., Ornbol, E., Fink, P., & Walach, H. (2011). Mindfulness-based stress reduction and mindfulness-based cognitive therapy: A systematic review of randomized controlled trials. *Acta Psychiatrica Scandinavica, 124*(2), 102-119. doi:10.1111/j.1600-0447.2011.01704.x

Fjorback, L. O., Arendt, M., Ornbol, E., Walach, H., Rehfeld, E., Schroder, A., & Fink, P. (2013). Mindfulness therapy for somatization disorder and functional somatic syndromes: Randomized trial with

one-year follow-up. *Journal of Psychosomatic Research, 74*(1), 31-40. doi:10.1016/j.jpsychores.2012.09.006

Gallagher, P., Leitch, M. M., Massey, A. E., McAllister-Williams, R. H., & Young, A. H. (2006). Assessing cortisol and dehydroepiandrosterone (DHEA) in saliva: Effects of collection method. *Journal of Psychopharmacology, 20*(5), 643-649. doi:10.1177/0269881106060585

Gex-Fabry, M., Jermann, F., Kosel, M., Rossier, M. F., Van der Linden, M., Bertschy, G.,...Aubry, J. M. (2012). Salivary cortisol profiles in patients remitted from recurrent depression: One-year follow-up of a mindfulness-based cognitive therapy trial. *Journal of Psychiatric Research, 46*(1), 80-86. doi:10.1016/j.jpsychires.2011.09.011

Gotink, R. A., Chu, P., Busschbach, J. J., Benson, H., Fricchione, G. L., & Hunink, M. G. (2015). Standardised mindfulness-based interventions in healthcare: An overview of systematic reviews and meta-analyses of RCTs. *PLoS One, 10*(4), e0124344. doi:10.1371/journal.pone.0124344

Hatchard, T., Lepage, C., Hutton, B., Skidmore, B., & Poulin, P. A. (2014). Comparative evaluation of group-based mindfulness-based stress reduction and cognitive behavioral therapy for the treatment and management of chronic pain disorders: Protocol for a systematic review and meta-analysis with indirect comparisons. *Systematic Reviews, 3*, 134. doi:10.1186/2046-4053-3-134

Jastrowski Mano, K. E., Salamon, K. S., Hainsworth, K. R., Anderson Khan, K. J., Ladwig, R. J., Davies, W. H., & Weisman, S. J. (2013). A randomized, controlled pilot study of mindfulness-based stress reduction for pediatric chronic pain. *Alternative Therapies, Health and Medicine, 19*(6), 8-14.

Kabat-Zinn, J. (1982). An outpatient program in behavioral medicine for chronic pain patients based on the practice of mindfulness meditation: Theoretical considerations and preliminary results. *General Hospital Psychiatry, 4*(1), 33-47.

Kabat-Zinn, J. (1991). Full catastrophe living: Using the wisdom of your body and mind to face stress, pain, and illness. New York, NY: Dell Pub., a division of Bantam Doubleday Dell Pub. Group.

Kabat-Zinn, J., Lipworth, L., & Burney, R. (1985). The clinical use of mindfulness meditation for the self-regulation of chronic pain. *Journal of Behavior Medicine, 8*(2), 163-190.

Kabat-Zinn, J., Massion, A. O., Kristeller, J., Peterson, L. G., Fletcher, K. E., Pbert, L.,...Santorelli, S. F. (1992). Effectiveness of a meditation-based stress reduction program in the treatment of anxiety disorders. *American Journal of Psychiatry, 149*(7), 936-943.

Kashikar-Zuck, S., Sil, S., Lynch-Jordan, A. M., Ting, T. V., Peugh, J., Schikler, K. N.,...Lovell, D. J. (2013). Changes in pain coping, catastrophizing, and coping efficacy after cognitive-behavioral therapy in children and adolescents with juvenile fibromyalgia. *Journal of Pain, 14*(5), 492-501. doi:10.1016/j.jpain.2012.12.019

King, S., Chambers, C. T., Huguet, A., MacNevin, R. C., McGrath, P. J., Parker, L., & MacDonald, A. J. (2011). The epidemiology of chronic pain in children and adolescents revisited: A systematic review. *Pain, 152*(12), 2729-2738. doi:10.1016/j.pain.2011.07.016

la Cour, P., & Petersen, M. (2015). Effects of mindfulness meditation on chronic pain: A randomized controlled trial. *Pain Medicine, 16*(4), 641-652. doi:10.1111/pme.12605

Lakhan, S. E., & Schofield, K. L. (2013). Mindfulness-based therapies in the treatment of somatization disorders: A systematic review and meta-analysis. *PLoS One, 8*(8), e71834. doi:10.1371/journal.pone.0071834

Malboeuf-Hurtubise, C., Achille, M., Sultan, S., & Vadnais, M. (2014). Impact of a mindfulness-based randomized, wait-list controlled clinical trial intervention on mood, sleep and quality of life in teenagers with cancer. *Psychosomatic Medicine, 76*(3).

Malboeuf-Hurtubise, C., Achille, M., Sultan, S., & Vadnais, M. (2013). Mindfulness-based intervention for teenagers with cancer: Study protocol for a randomized controlled trial. *Trials, 14*, 135. doi:10.1186/1745-6215-14-135

Matousek, R. H., Dobkin, P. L., & Pruessner, J. (2010). Cortisol as a marker for improvement in mindfulness-based stress reduction. *Complementary Therapies in Clinical Practice, 16*(1), 13-19. doi:10.1016/j.ctcp.2009.06.004

Monshat, K., Khong, B., Hassed, C., Vella-Brodrick, D., Norrish, J., Burns, J., & Herrman, H. (2013). "A conscious control over life and my emotions:" Mindfulness practice and healthy young people. A qualitative study. *Journal of Adolescent Health, 52*(5), 572-577. doi:10.1016/j.jadohealth.2012.09.008

O'Leary, K., O'Neill, S., & Dockray, S. (2015). A systematic review of the effects of mindfulness interventions on cortisol. *Journal of Health Psychology*. doi:10.1177/1359105315569095

Saunders, D. C. (2015). Being mindful of mindfulness: Past, present, and future of mindfulness in child and adolescent psychiatry. *Journal of the American Academy of Child and Adolescent Psychiatry, 54*(6), 437-439. doi:10.1016/j.jaac.2015.03.006

Schonert-Reichl, K. A., Oberle, E., Lawlor, M. S., Abbott, D., Thomson, K., Oberlander, T. F., & Diamond, A. (2015). Enhancing cognitive and social-emotional development through a simple-to-administer mindfulness-based school program for elementary school children: A randomized controlled trial. *Developmental Psychology, 51*(1), 52-66. doi:10.1037/a0038454

Sibinga, E. M., Perry-Parrish, C., Chung, S. E., Johnson, S. B., Smith, M., & Ellen, J. M. (2013). School-based mindfulness instruction for urban male youth: A small randomized controlled trial. *Preventative Medicine, 57*(6), 799-801. doi:10.1016/j.ypmed.2013.08.027

Simkin, D. R., & Black, N. B. (2014). Meditation and mindfulness in clinical practice. *Child and Adolescent Psychiatry Clinics of North America, 23*(3), 487-534. doi:10.1016/j.chc.2014.03.002

Stinson, J. N., Kavanagh, T., Yamada, J., Gill, N., & Stevens, B. (2006). Systematic review of the psychometric properties, interpretability and feasibility of self-report pain intensity measures for use in clinical trials in children and adolescents. *Pain, 125*(1-2), 143-157. doi:10.1016/j.pain.2006.05.006

Tan, L., & Martin, G. (2013). Taming the adolescent mind: Preliminary report of a mindfulness-based psychological intervention for adolescents with clinical heterogeneous mental health diagnoses. *Clinical Child Psychology and Psychiatry, 18*(2), 300-312. doi:10.1177/1359104512455182

Tan, L. B. (2015). A critical review of adolescent mindfulness-based programmes. *Clinical Child Psychology and Psychiatry*. doi:10.1177/1359104515577486

Teasdale, J. D., Segal, Z. V., Williams, J. M., Ridgeway, V. A., Soulsby, J. M., & Lau, M. A. (2000). Prevention of relapse/recurrence in major depression by mindfulness-based cognitive therapy. *Journal of Consulting and Clinical Psychology, 68*(4), 615-623.

Varni, J. W., Burwinkle, T. M., & Seid, M. (2006). The PedsQL 4.0 as a school population health measure: Feasibility, reliability, and validity. *Quality of Life Research, 15*(2), 203-215. doi:10.1007/s11136-005-1388-z

Vo, D. (2015). *The Mindful Teen. Powerful Skill to Help You Handle Stress One Moment At a Time*. Vancouver, Canada: New Harbinger Publications.

Vogeser, M., Durner, J., Seliger, E., & Auernhammer, C. (2006). Measurement of late-night salivary cortisol with an automated immunoassay system. *Clinical Chemistry and Laboratory Medicine, 44*(12), 1441-1445. doi:10.1515/cclm.2006.244

Warschburger, P., Hanig, J., Friedt, M., Posovszky, C., Schier, M., & Calvano, C. (2014). Health-related quality of life in children with abdominal pain due to functional or organic gastrointestinal disorders. *Journal of Pediatric Psychology, 39*(1), 45-54. doi:10.1093/jpepsy/jst070

Zenner, C., Herrnleben-Kurz, S., & Walach, H. (2014). Mindfulness-based interventions in schools a systematic review and meta-analysis. *Frontiers in Psychology, 5*, 603. doi:10.3389/fpsyg.2014.00603