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Cumulative effects of multiple pains sites in youth with chronic pain

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Abstract

Background—The experience of persistent pain in multiple locations is common in youth. Based on current literature, youth with multiple pain sites (MPS) are at risk of experiencing poorer emotional outcomes and a spread of symptoms into late adolescence and adulthood. Little is known regarding the association between MPS with physical and school functioning domains, particularly after initiation of multidisciplinary pain treatment. Therefore, the objective of this study was to examine the association of MPS with disability and school functioning among youth with chronic pain.

Methods—A total of 195 patients with chronic pain, aged 8–17, and their parents completed measures assessing patient distress and functioning at a multidisciplinary pain clinic evaluation and at 4-month follow-up.

Results—At evaluation, 63% of patients presented with MPS; 25% reporting MPS endorsed pain in five or more locations. When controlling for relevant demographic and emotional distress factors, MPS was associated with lower school functioning at evaluation with a persistent trend at follow-up. Although MPS was not a significant predictor of pain-related disability at evaluation, it emerged as significant at follow-up.

Conclusions—Potentially due to the MPS load and the inverse effects that such a pain state has on function, such patients may be at-risk for poorer health and school-related outcomes. The

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Conflicts of interest

The authors have no conflicts of interest to disclose.

Author contributions

LES oversaw the overall execution of the project. MCB, ETC, and LES had significant contributions to the conception, design, analysis, and interpretation of the data. MCB and LES wrote the manuscript. DEL, NLS, and DB discussed and contributed to the interpretation of the results and commented on the manuscript. All authors contributed to the drafting or revising and final approval of the manuscript.

mechanisms influencing these relationships appear to extend beyond psychological/emotional factors and warrant further investigation in order to aid in our understanding of youth with MPS.

Significance—Youth with MPS may be at risk for experiencing poorer physical and school functioning in comparison to single-site peers, despite treatment initiation. Further research is warranted in order to inform assessment and treatment approaches for this subgroup of patients.

Introduction

Multiple pain sites (MPS), defined as pain in more than one location, is common in youth, reaching prevalence rates of 32% (Auvinen et al., 2009). Frequently, MPS is recurrent, ranging from once a month to daily, and number of pain sites tends to increase with age (Petersen, Brulin, & Bergstrom, 2006). Furthermore, into late adolescence and adulthood, MPS demonstrates high rates of persistence (Andersson, 2004; Paananen et al., 2010; Stahl et al., 2008). Taken together, these data suggest that youth suffering with pain in more than one location are likely to experience a spread of symptoms over time with a high likelihood of endurance into adulthood.

Not surprisingly, youth with MPS exhibit deficits in health-related quality of life (Pellise et al., 2009). Most research highlights the association between chronic MPS and poorer emotional functioning outcomes. An adult study reported that the number of pain sites, not severity or persistence of pain, served as the best predictor of an individual experiencing depression (Dworkin, Von Korff, & LeResche, 1990). Another indicated that the prevalence of depressive and anxiety disorders increased across the continuum of individuals with no pain, a single pain site, and MPS (Gureje et al., 2008). Comparable results are found in studies with youth demonstrating associations between psychological symptoms and number of frequent pain sites (Ando et al., 2013; Larsson & Sund, 2007), as well as longitudinal studies suggesting that anxiety and depression symptomatology may predict MPS development and persistence (Paananen et al., 2010).

On the contrary, few studies exist demonstrating the association of MPS on physical and school functioning outcomes. Cross-sectional research has found an association between an increased number of pain sites in youth and greater functional impairment (Rabbitts, Holley, Groenewald, & Palermo, 2016) and perceived academic impairment (Ando et al., 2013). Research in youth has not clearly defined mechanisms for these relationships; however, adult research has demonstrated associations between an increased number of pain sites and increased difficulties with functional mobility and strength (Leveille, Bean, Ngo, McMullen, & Guralnik, 2007), as well as more work absences (Miranda et al., 2010).

Given the high occurrence of multiple chronic pains in youth and preliminary evidence of the association between MPS and physical and school functioning, it is important to further examine these relationships in comparison to youth with single pain sites. Additionally, longitudinal examination of these relationships is needed, particularly after initiation of multidisciplinary pain treatment, to understand the possible association of MPS with recovery trajectory.

We hypothesized that a greater number of pain sites would significantly predict higher functional disability and school dysfunction at the time of multidisciplinary pain treatment evaluation and at 4-month follow-up. In order to clearly determine the relationship between MPS and the outcomes, we found it necessary to control for clinically relevant demographic and psychological distress variables provided their known associations with MPS, as detailed earlier.

Methods

Participants and procedure

Patients with chronic pain aged 8 to 17 and an accompanying parent who attended an initial evaluation at an outpatient multidisciplinary pain clinic in the northeastern region of the United States from January 2012 to April 2014 were invited to participate in a larger IRB-approved study aimed at developing a Pediatric Pain Screening Tool (PPST; Simons et al., 2015). A research assistant asked both patients and their parents for written informed consent/assent to allow data from their clinic assessment to be used for research purposes. All measures used for the purposes of this paper were administered as part of a standard clinic battery that was completed at home prior to the evaluation appointment. Measures were completed at home on paper (mailed to the family) or electronically (via an email link). All participants were invited to participate in a four-month follow-up assessment and received phone call reminders from a member of the research team regarding the follow-up period. The four-month follow-up assessment occurred via REDCap software (Harris et al., 2009) and included the same measures that were administered at initial evaluation. For this study, we only included participants who completed measures at both time points.

Measures

Demographic and pain-related variables—Age, sex, and pain duration were collected from patients at the initial evaluation. Also during initial evaluation, children were asked to provide their average pain rating on a standard 11-point numeric rating scale from 0 (no pain) to 10 (most pain possible) (Castarlenas, Jensen, von Baeyer, & Miro, 2017) to the evaluating multidisciplinary team. These variables, including pain diagnoses, were obtained via medical chart review.

Pain sites—Patients reported pain locations in response to an open-ended question provided by the multidisciplinary team. Pain sites were coded from 1–5 with five or more locations, including those patients reporting ‘diffuse body pain,’ categorized as ‘5.’ All listed sites were considered to be separate (i.e., hand and wrist of the same extremity), and bilateral sites were always coded as separate. Any patient defined as having 2 or more pain sites was considered to have MPS. This variable was obtained via medical chart review.

Depressive Symptoms—The Children’s Depression Inventory (CDI-2; Kovacs, 1985) is a 28-item self-report assessment that measures child depressive symptoms. Higher scores are reflective of greater depressive symptoms. Internal reliability for the current sample was 0.90.

General Anxiety—The Revised Children’s Manifest Anxiety Scale (RCMAS; Reynolds & Richmond, 2008) is a 45-item self-report measure determining the source and level of a child’s anxiety. All items (excluding the lie scale) are summed for a raw total anxiety score. Higher scores are reflective of greater anxiety symptoms. Internal reliability for the current sample was 0.90.

School Functioning—The Pediatric Quality of Life Inventory (PedsQL; Varni, Seid, & Kurtin, 2001; Varni, Seid, & Rode, 1999) is a 23-item questionnaire that evaluates the health-related quality of life of a child. Five of the items comprise the School Functioning subscale. A higher PedsQL score indicates better functioning. The parent proxy report of PedsQL has been found to demonstrate more validity and reliability than the child self-report (Simons & Kaczynski, 2012), therefore, we used the parent proxy report as a measure of school functioning. The alpha reliability for this sample was 0.77.

Functional disability—The Functional Disability Inventory (FDI; Walker & Greene, 1991) is a 15-item self-report scale that assesses patients’ perceptions of how much difficulty in physical and psychosocial functioning they experienced in the last two weeks due to physical health. Scores are calculated by summing all of the items, with a higher total score indicating greater disability. A total score lower than 13 indicates low disability and a total score 30 or higher indicates high disability. The internal consistency in this sample was 0.90.

Statistical Analyses

Data was entered and analyzed using SPSS version 21.0 (SPSS IBM, New York, USA). Pearson product moment correlations were used to examine relationships between number of pain sites, child demographics and emotional factors, and proposed outcomes (i.e., functional disability and school functioning) to determine potential covariates. Independent samples t-tests were conducted to assess any pairwise statistical differences between the single site pain and MPS groups for the outcome variables at initial evaluation and follow-up. To examine the association of MPS on the outcomes of functional disability and school functioning at initial evaluation and follow-up, a series of stepwise hierarchical regression analyses were conducted. Total scores from the FDI and PedsQL constituted the dependent variables for each regression model. In the initial step of each regression, child age, sex, typical pain rating, and pain duration were entered. In step two, total raw scores from CDI and RCMAS were entered. In the final step, number of pain sites was entered in each equation to examine the incremental association of each on the functional outcomes.

Results

Participants

Of the 318 patients included in the larger study, 195 (61.3%) completed four-month follow-up measures and, therefore, were included in this analysis. There were no significant differences between the group of individuals who completed follow-up and those who did not on scores of disability and school functioning at the time of initial evaluation.

Among the 195, the majority of patients self-identified as Caucasian (92.9%) and female (76.4%). The mean age was 13.8 (SD=2.42). Reported primary pain locations were as follows: lower extremity (including leg, knee, ankle, and foot; 37.1%), upper extremity (including shoulder, arm, elbow, wrist, and hand; 11.3%), back/neck (19.2%), abdomen (including flank and chest; 14.2%), head (including jaw and face, 8.5%), hip/pelvis (5.7%), and diffuse body pain (4.1%). Duration of pain ranged from less than one month to over 15 years, with a median duration of 13 months; 8.8% reported pain duration of less than three months. Pain diagnoses spanned several categories and are detailed in Table 1. Within the total sample, 123 patients reported MPS (63%); 25% of those reporting MPS listed pain in five or more sites (Figure 1). ANOVA results revealed that youth with diffuse musculoskeletal [F (4, 190) = 31.625, $p < .001$] and headache pain [F (4, 189) = 12.738, $p < .001$] were more likely to have a greater number of pain sites than youth with other primary pain diagnoses. Means and standard deviations of individuals with a single pain site versus those with MPS on the proposed study outcomes, along with independent samples *t*-test statistics between groups at each time point are presented in Table 2. At initial evaluation, functional disability levels between patients with MPS and single site pain did not differ while school functioning was approaching significance ($p = .062$). At follow-up, patients with MPS had significantly higher functional disability compared to patients with single site pain, while school functioning did not differ between groups.

Parents were predominantly mothers (92%) and the majority was married (67%). Parents were generally well educated; 64% of mothers and 60% of fathers completed college with 22% of mothers and 27% of fathers obtaining a graduate degree.

Preliminary Correlation Analyses

Table 3 reports the correlations among study variables. In examining the association between pain sites and study variables, older age ($r = .16$, $p < .05$), longer pain duration ($r = .24$, $p < .01$), higher anxiety symptoms ($r = .16$, $p < .05$), and lower school functioning ($r = -.19$, $p < .01$) at initial evaluation were associated with a greater number of pain sites. At follow-up, higher functional disability ($r = .27$, $p < .01$) and lower school functioning ($r = -.27$, $p < .01$) were significantly associated with a greater number of pain sites.

Regression Analyses

To examine predictors of pain-related functioning, stepwise linear regression analyses were conducted. Functional disability and school functioning at initial evaluation and 4-month follow-up were the outcomes of interest. All stepwise models controlled for age, sex, typical pain rating, pain duration, depression and anxiety symptoms with number of pain sites entered at the final step. Multicollinearity statistics across predictor variables revealed values in the acceptable range (Tolerance = .781 – .933; VIF = 1.07 – 1.28) and normality assumptions were met. Results of the analyses are presented in Tables 4a–b and 5a–b.

Initial evaluation

Functional disability—After controlling for demographic pain-related and emotional distress variables, only pain duration ($\beta = -.19$; $p < .01$) and depressive symptoms ($\beta = .27$; $p < .01$) emerged as significant predictors of functional disability. In the final model, number

of pain sites was not a significant contributor to disability at the time of the pain clinic evaluation. Overall, this model explained approximately 25% of the variance in functional disability at initial evaluation.

School functioning—For school functioning, depressive symptoms ($\beta = -.30, p < .01$) was a significant predictor with number of pain sites ($\beta = -.16, p < .05$) also emerging as a unique predictor after controlling for several relevant demographic, pain-related, and emotional distress variables. The final model explained approximately 24% of the variance in school functioning at initial evaluation.

4-month follow-up

Functional disability—After including all variables in the model that were assessed at evaluation, age ($\beta = .20, p < .01$), functional disability at initial evaluation ($\beta = .30, p < .01$), and number of pain sites ($\beta = .15, p < .05$) all emerged as significant predictors of functional disability at 4-month follow-up. This final model explained approximately 26% of the variance in functional disability at follow-up.

School functioning—For school functioning at 4-month follow-up, only baseline school functioning ($\beta = .47, p < .01$) emerged as a significant predictor with a trend for number of pain sites ($\beta = -.13, p < .10$). Overall, this model explained approximately 32% of the variance in school functioning at follow-up.

Discussion

The current study utilized a brief longitudinal design to assess the potential association of MPS on pain-related disability and school functioning in youth who presented to a multidisciplinary chronic pain clinic. Approximately 63% of patients in this sample reported having pain in more than one site, with 25% of those with MPS reporting pain in five or more sites. These numbers are commensurate with rates that have been observed in the few prior studies examining this subgroup of patients, underscoring that this is a common problem presenting in a tertiary care pain clinic.

Bivariate associations between pain sites and several demographic and pain-related variables at initial evaluation were significant, including age, pain duration, anxiety symptoms, and school functioning. Four months later, number of pain sites continued to be significantly associated with school functioning in addition to functional disability. These data are supported by previous studies that have demonstrated increased prevalence in multiple pain symptoms with age as well as strong associations with multiple pain conditions and mood disorders (Petersen et al., 2006); (Gureje et al., 2008). Furthermore, functional ability has shown to decrease considerably with increasing number of pain sites (Kamaleri, Natvig, Ihlebaek, & Bruusgaard, 2008).

Contrary to hypotheses, hierarchical regression analyses revealed that pain sites was not a significant predictor of functional disability at the time of initial evaluation, although pain duration and depressive symptoms were significant predictors. This finding is consistent with literature demonstrating that living with pain for a longer period of time and

experiencing greater psychological comorbidity (i.e., depression) is associated with greater physical dysfunction (Kashikar-Zuck, Goldschneider, Powers, Vaught, & Hershey, 2001). Four months later, however, number of pain sites at evaluation did emerge as a predictor of functional disability, along with functional disability at initial evaluation and age. For school functioning at the time of the evaluation, number of pain sites was predictive, along with depressive symptoms. At four-month follow-up, school functioning at initial evaluation served as the only significant predictor of school functioning at follow-up; however, number of pain sites exhibited a trend toward significance.

To our knowledge, one previous study has documented the association of an increased number of pain sites with functional impairment in youth cross-sectionally; these researchers highlighted the importance of future studies continuing to investigate this association, particularly as it relates to recovery in youth (Rabbitts et al., 2016). As a follow-up, the results of the current study indicate that having MPS, in comparison to a single pain site, may place youth at-risk for experiencing poorer school functioning upon presentation to the pain clinic as well as greater functional disability after initiation of treatment. And although the association weakened, MPS may continue to influence school functioning even after the initiation of treatment. Based on our analyses, it appears that the mechanisms driving these associations between MPS with disability and school functioning are unique and may extend beyond the examined pain-related demographic and psychological/emotional factors. Given that this is the first study of its kind, future research should further examine the possible predictive nature of MPS on global functioning and academic domains after initiation of treatment. Additionally, consideration of the potential unique mechanisms driving this relationship is warranted to aid in our understanding of MPS, particularly given its high prevalence rates in youth.

Limitations and future directions

Limitations of the study are noteworthy. Foremost, the duration of the study is short, and long-term longitudinal studies are clearly required to define the epidemiology of multiple pain sites. Similarly, the 4-month window in which the patients have been captured can seem quite arbitrary, given the fact that the patient sample had experienced pain for a variable amount of time, although importantly pain duration was controlled for in all analyses. It was originally decided that the 4-month window from initial evaluation to follow-up would provide ample amount of time for treatment to display effectiveness, if possible. However, as stated previously, patients with MPS, who on average presented with experiencing pain for a longer duration of time, may require a wider follow-up window to allow for the full benefits of the provided treatment regimen. In future studies, it would be beneficial to include multiple follow-up time points beyond that which is included in the current study, such as 8 and 12 months, in order to better capture treatment outcomes and changes over time. Importantly, the authors were not able to assess patient engagement in the recommendations provided at the initial pain clinic evaluation. Therefore, it is possible that patients who displayed greater improvements in the proposed outcomes were those who were more adherent to recommendations. Future studies should examine treatment adherence as a means to clarify associations with outcome measures. Additionally, in the current study school functioning was measured via parent report, and it is possible that parents do not have

all of the information to accurately assess this domain. Lastly, it is important to note that the analyses of the current study produced small effect sizes; thus, it is imperative that future research attempt to replicate the findings and further our understanding of youth with MPS.

Conclusions

Chronic pain in childhood is a prominent issue in healthcare, and evidence is emerging that the presence of multiple pain complaints is associated with higher levels of disability and emotional disorders when compared to children with fewer pain complaints and those with pain in a single body part (Gureje et al., 2008; Rabbitts et al., 2016). Furthermore, research suggests that the coexistence of pain conditions, rather than location or type, has the largest impact on the functional, emotional, and social effects of the affected children and adolescents (Larsson & Sund, 2007). Given that these data and prior work (Auvinen et al., 2009) show that a significant percentage of youth with chronic pain are experiencing pain in multiple sites, further research examining this subgroup of patients is warranted, particularly involving longitudinal investigation after treatment initiation with the purpose of potentially informing assessment and intervention approaches.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Distribution of number of pain sites across the sample with a large proportion of patients having pain in a single location (37%) followed by those with pain in 5 or more sites (25%).

Table 1

Pain diagnoses of participants (n=195)

Group Name	Pain Diagnoses	Primary Pain (n)	Total Sample(n)
Localized Musculoskeletal	Single limb or joint, low back, chest pain	35.4% (69)	37.4% (73)
Neuropathic	CRPS, neuralgia	29.2% (57)	36.4% (71)
Diffuse Musculoskeletal	Widespread musculoskeletal pain, Postural Orthostatic Tachycardia Syndrome (POTS) with musculoskeletal pain, Ehler's Danlos Syndrome (EDS), joint hypermobility	11.3% (22)	17.9% (35)
Abdominal	Functional abdominal pain (FAP), Irritable Bowel Syndrome (IBS), Inflammatory Bowel Disease (IBD), Endometriosis	7.2% (14)	16.4% (32)
Headache	Migraine, tension, chronic daily headache, post-traumatic headache	16.9% (33)	28.4% (55)

Table 2

Study outcome means based on pain site group

Pain Site Group	Variable	n	Mean	SD	df	T-statistic
Single site	Functional disability at initial evaluation	69	21.0	11.7	190	-2.46
MPS		123	21.4	11.3		
Single site	Functional disability at follow-up	72	10.9	10.1	193	-2.55*
MPS		123	15.1	11.7		
Single site	School functioning at initial evaluation	67	55.4	26.2	182	2.84 [†]
MPS		117	45.0	22.4		
Single site	School functioning at follow-up	71	69.7	22.1	181	3.46
MPS		112	57.8	23.1		

Note.

* $p < .05$;

[†] $p < .10$

Table 3

Correlations between child factors.

Variable	1	2	3	4	5	6	7	8	9	10	11	Mean	SD	N
1. Number of pain sites	--	.24**	.16*	-.08	.00	.06	.16*	.09	-.20**	.27**	-.27**	2.63	1.61	195
2. Pain duration		--	.10	-.03	-.07	.04	.18*	-.12	-.10	.16*	-.19*	22.9	26.7	195
3. Age			--	.09	.08	-.04	.14	.08	-.04	.28**	-.02	13.8	2.42	195
4. Sex				--	-.02	-.11	.06	-.08	.20**	-.04	.14	0.76	0.43	195
5. Typical pain rating					--	.21**	.11	.23**	.15*	.10	-.11	6.03	2.11	179
6. Depression						--	.72**	.43**	-.43**	.28**	-.25**	57.4	12.7	189
7. Anxiety							--	.41**	-.35**	.30**	-.28**	49.6	11.2	184
8. Functional disability								--	-.32**	.37**	-.20**	21.3	11.4	192
9. School functioning									--	-.14	.53**	48.8	24.3	184
10. Functional disability follow-up										--	-.38**	13.6	11.3	195
11. School functioning follow-up											--	62.4	23.4	183

Note.

**
 $p < .01$,

*
 $p < .05$

Table 4a
Hierarchical stepwise regressions for predictors of functional disability at initial evaluation.

Variables	Step 1			Step 2			Step 3		
	B	SE B	β	B	SE B	β	B	SE B	β
Age	.591	.361	.127	.445	.341	.096	.408	.341	.088
Sex	-1.61	1.97	-.063	-.909	1.85	-.036	-.582	1.87	-.023
Typical pain rating	1.05	.407	.197*	.620	.381	.117	.629	.381	.119
Pain duration	-.055	.032	-.133 [†]	-.072	.029	-.175*	-.079	.030	-.193**
Depressive symptoms				.232	.097	.264*	.238	.097	.272*
Anxiety symptoms				.181	.110	.182	.166	.111	.167
Number of pain sites							.644	.509	.093
R ² Change		.076			.239			.247	
F for R ²		3.23**			16.7**			1.60	

Note.

* $p < .05$;

** $p < .01$;

[†] $p < .10$

Table 4b

Hierarchical stepwise regressions for predictors of school functioning at initial evaluation.

Variables	Step 1			Step 2			Step 3		
	B	SE B	β	B	SE B	β	B	SE B	β
Age	-.990	.777	-.101	-.771	.745	-.079	-.632	.739	-.065
Sex	9.83	4.31	.179*	7.70	4.13	.140 [†]	6.52	4.11	.119
Typical pain rating	-2.10	.886	-.185*	-1.24	.845	-.109	-1.30	.835	-.114
Pain duration	-.057	.069	-.066	-.028	.065	-.032	-.003	.065	-.003
Depressive symptoms				-.536	.214	-.286*	-.568	.212	-.302**
Anxiety symptoms				-.246	.242	-.116	-.184	.241	-.087
Number of pain sites							-.241	1.11	-.162*
R ² Change		.078			.213			.237	
F for R ²		3.22*			12.9**			4.72*	

Note.

* $p < .05$;

** $p < .01$;

[†] $p < .10$

Table 5a
Hierarchical stepwise regressions for predictors of functional disability at 4-month follow-up.

Variables	Step 1			Step 2			Step 3		
	B	SE B	β	B	SE B	β	B	SE B	β
Age	1.02	.346	.212**	.999	.355	.208**	.943	.353	.197**
Sex	-1.61	1.87	-.061	-1.53	1.93	-.058	-.980	1.92	-.037
Typical pain rating	.084	.394	.015	.017	.399	.003	.043	.395	.008
Functional disability (initial evaluation)	.379	.075	.367**	.327	.083	.316**	.309	.083	.299**
Pain duration	.072	.030	.171*	.064	.031	.151*	.050	.032	.118
Depressive symptoms				.060	.102	.067	.076	.101	.084
Anxiety symptoms				.064	.115	.062	.041	.115	.040
Number of pain sites							1.10	.526	.154*
R^2 Change		.227			.238			.259	
F for R^2		9.21*			1.13			4.41*	

Note.

* $p < .05$;

** $p < .01$;

† $p < .10$

Table 5b
Hierarchical stepwise regressions for predictors of school functioning at 4-month follow-up.

Variables	Step 1			Step 2			Step 3		
	B	SE B	β	B	SE B	β	B	SE B	β
Age	-.082	.708	-.008	.007	.735	.001	.087	.732	.009
Sex	4.58	4.04	.081	4.90	4.13	.087	4.39	4.12	.078
Typical pain rating	-.342	.801	-.031	-.342	.817	-.031	-.422	.813	-.038
School functioning (initial evaluation)	.502	.073	.501**	.490	.080	.489**	.467	.080	.466**
Pain duration	-.141	.068	-.147*	-.136	.069	-.142 [†]	-.110	.070	-.115
Depressive symptoms				.053	.217	.028	.000	.218	.000
Anxiety symptoms				-.133	.244	-.063	-.074	.245	-.035
Number of pain sites							-1.85	1.11	-.125 [†]
<i>R</i> ² Change		.303			.305			.319	
<i>F</i> for <i>R</i> ²		12.4**			.178			2.78 [†]	

Note.

* $p < .05$;

** $p < .01$;

[†] $p < .10$