ORIGINAL RESEARCH

Association of Subclinical Neck Pain With Altered Multisensory Integration at Baseline and 4-Week Follow-up Relative to Asymptomatic Controls

Bassem Farid, BHSc (Hons),[a] Paul Yielder, PhD,[a] Michael Holmes, PhD,[b] Heidi Haavik, PhD,[c] and Bernadette A. Murphy, DC, PhD[a]

ABSTRACT

Objective: The purpose of this study was to test whether people with subclinical neck pain (SCNP) had altered visual, auditory, and multisensory response times, and whether these findings were consistent over time.
Methods: Twenty-five volunteers (12 SCNP and 13 asymptomatic controls) were recruited from a Canadian university student population. A 2-alternative forced-choice discrimination task with multisensory redundancy was used to measure response times to the presentation of visual (color filled circles), auditory (verbalization of the color words, eg, *red* or *blue*), and multisensory (simultaneous audiovisual) stimuli at baseline and 4 weeks later.
Results: The SCNP group was slower at both visual and multisensory tasks ($P = .046$, $P = .020$, respectively), with no change over 4 weeks. Auditory response times improved slightly but significantly after 4 weeks ($P = .050$) with no group difference.
Conclusions: This is the first study to report that people with SCNP have slower visual and multisensory response times than asymptomatic individuals. These differences persist over 4 weeks, suggesting that the multisensory technique is reliable and that these differences in the SCNP group do not improve on their own in the absence of treatment. (J Manipulative Physiol Ther 2018;41:81-91)
Key Indexing Terms: *Reaction Time; Neck Pain; Superior Colliculi; Choice Behavior*

INTRODUCTION

Approximately 30% to 50% of people experience neck pain every year, which places a significant burden on the health care system.[1] A specific category of neck pain is subclinical neck pain (SCNP), which refers to lower-grade neck dysfunction in which individuals have recurrent flare-ups of neck pain but have not yet sought regular treatment.[2-4]

Altered afferent input through repetition and overuse changes the way that sensory information is processed by causing plastic changes in the central nervous system.[5-7] Several studies have provided evidence for altered proprioceptive and neuromuscular function in individuals with SCNP.[8-11] Further research has suggested that the altered afferent input arising from SCNP leads to altered sensorimotor integration (SMI), altered motor output, and impaired motor control.[5,12-14] It has been hypothesized that other sensory modalities such as visual and auditory inputs may also be processed differently in SCNP causing altered multisensory integration.[12]

When visual input is less clear (ie, "noisier"), less emphasis is placed on visual information and accuracy is decreased.[15] Adding haptic stimuli leads to improved accuracy and discrimination when visual input is less reliable.[15] However, when a sense is less reliable or provides contradictory information, combination of stimuli may not always enhance accuracy. Hogendoorn et al[16] reported that when there was contradictory input between proprioception of hand location and a visual afterimage, the visual afterimage of the hand disappeared. This suggests that when multisensory input is

[a] Health Sciences, University of Ontario Institute of Technology, Oshawa, Ontario, Canada.
[b] Applied Health Science, Brock University, St. Catherines, Ontario, Canada.
[c] Centre for Chiropractic Research, New Zealand College of Chiropractic, Auckland, New Zealand.
Corresponding author: Bernadette A. Murphy, DC, PhD, University of Ontario Institute of Technology, 2000 Simcoe Street North, Oshawa, ON, Canada, L1H 7K4. Tel.: +1 905 721 8668 ext 2778. (e-mail: *Bernadette.murphy@uoit.ca*).
Paper submitted July 17, 2017; in revised form September 12, 2017; accepted September 26, 2017.
0161-4754

https://doi.org/10.1016/j.jmpt.2017.09.003

contradictory, the central nervous system may try to arrange sensory information in relations to other sensory modalities, or even adapt motor output to muscles (eg, less contraction to more accurately reach the target).

In a study with mismatches between proprioception and vision, participants were asked to point toward a target with their unseen hand.[17] The relationship between proprioception and vision was manipulated by imposing erroneous visual feedback about the target's location.[17] With the distorted visual feedback, participants corrected their responses toward the adjusted visual image up to 60% of the distance of the incorrect visual feedback. When a sensory modality is less reliable or provides contradictory information, less weight is placed on the unreliable sense.[18,19] Proprioception is impaired in SCNP.[11,20] However, it is not clear exactly how proprioceptive mismatch affects integration of other senses. It is possible that SCNP may cause greater reliance on senses other than proprioception; however, it is also possible that the less reliable proprioceptive input in SCNP can negatively influence the processing of other sensory stimuli.

Previous research has indicated that multisensory integration in elderly populations is enhanced, as measured using a 2-alternative, forced-choice discrimination task involving measurement of response times.[21] Another study reported that the elderly have both altered SMI and altered multisensory integration.[22] Tasks such as temporal order judgements may not be effective at measuring multisensory integration in naïve participants because there is an experience component that "increases" intersensory synchrony ability.[23]

Areas in the thalamus integrate sensorimotor and multisensory processes.[24] The superior colliculus is 1 example of a multisensory site that has access to efferent projections of premotor and motor areas of the spinal cord and brainstem involved in superior colliculus–mediated attentive and orientation behaviors,[25] some that involve the saccadic movements of the eye, and neck movements, or "gaze shifts." In addition to 2 sensory modalities terminating in a target area, a cross-modal projection of 1 sensory modality can also converge onto a different sensory modality site.[26] Hairston et al[27] reported evidence for inverse effectiveness, where asymptomatic participants with artificially degraded vision (induced myopia) had their localization skills enhanced for audiovisual conditions, whereas in normal conditions the localization for multisensory conditions was similar to unisensory conditions. These papers suggest that a similar effect could occur in populations with altered sensory input from the neck, where that multisensory integration may be enhanced, as a result of ongoing alterations in sensory feedback from the neck joints and muscles that lead to degraded somatosensory input, similar to the degraded vision.

Numerous methods can be used to measure multisensory integration.[21,23,25,28] A popular task that uses behavioral enhancements from multisensory integration is a 2-alternative forced-choice discrimination task with semantically congruent, redundant, multisensory stimuli.[21,28] In some studies researchers accounted for the redundancy gain, a quickening of response times that occurs with redundant stimuli, by using the race model.[29] When measuring multisensory integration, temporal and spatial factors of the equipment used to present the stimuli must be carefully considered when designing a task, because both timing and location of stimuli may reduce or deplete multisensory activity.[30,31] Unfortunately, many studies fail to state or consider in detail the equipment being used in multisensory tasks, which can hinder interpretation of results,[21,23,28] a limitation that the present study tries to address.

The purpose of this study was to determine if there were differences in multisensory integration and unisensory and multisensory response times in individuals with SCNP compared with asymptomatic participants, and if the results were consistent over a 4-week interval in the absence of treatment for the SCNP group. It was hypothesized that individuals with SCNP would possess slower response times for both unisensory and multisensory conditions because of the ongoing effects of unreliable proprioceptive feedback from the neck.

Methods

Population

Participants were recruited from University of Ontario Institute of Technology campus using advertisements and word of mouth. The mean age for the asymptomatic controls (n = 13; 6 men) was 21.1 ± 2.1 years and for the SCNP group (n = 12; 5 men) was 22.0 ± 2.1 years. The Edinburgh handedness scale[32] was used to determine hand dominance because the responses in the protocol were developed for the right hand. This was important to ensure that the numbers of left-handed and ambidextrous individuals were similar between the neck pain and control groups to eliminate differences in movement or processing speed with the right limb. The asymptomatic control group had 7 right-handed, 4 ambidextrous, and 2 left-handed participants, and the SCNP group had 9 right-handed, 2 ambidextrous, and 1 left-handed participant.

A screening interview with questionnaires was performed to remove individuals with recent (last 5 years) history of epilepsy, any recent (last 5 years) history of head injury with loss of consciousness, stroke, brain surgery, Parkinson disease, attention-deficit/hyperactivity disorder, psychiatric disorders other than treated depression, diabetes, serious vision problems (other than refractive errors or astigmatism), color blindness, or uncorrected hearing problems that might affect their capacity to perform the experiment.

By definition, SCNP participants had not yet sought treatment at baseline, and they were required not to seek any treatment until after the 4-week measurement session had occurred. Participants were excluded if they had previously experienced whiplash. The participants had minimal to no neck pain on the actual testing days so that slower movements in response to pain would not confound the

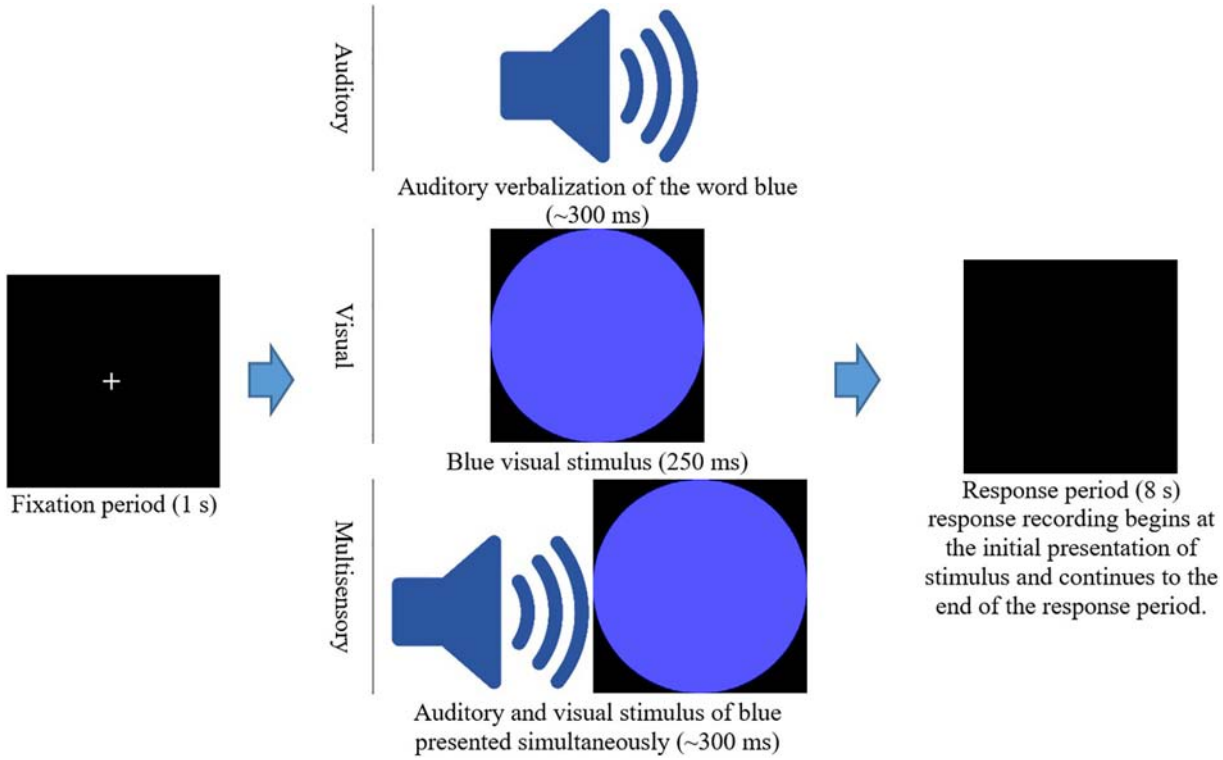

Fig 1. *The presentation process of blue is depicted. Each trial began with a fixation period for 1 second, followed by a pseudorandom presentation of the stimulus through auditory, visual, or multisensory conditions. The response period was a period with extra time allocated if there was no response detected during the presentation of the stimulus. A response would end the trial and initiate the next.*

response time measurements. A visual analog scale with minimal pain severity on the left and maximal pain severity on the right was used to test pain on the day of testing. A chronic pain grading scale was used to determine the severity of the neck pain in general (not specific to the day of testing).[33] Participants were asked to provide the history, frequency, duration, location, and severity on the day of testing and during neck pain in the previous 6 months. Ethical approval was received through the University of Ontario Institute of Technology's Research Ethics Board (07-073). All participants provided written consent before participating.

Two-Alternative Forced-Choice Type Discrimination Task With Multisensory Redundancy

Multisensory integration was measured using a 2-alternative forced-choice discrimination task that was similar to Laurienti et al.[21,28] A trial consisted of either an auditory stimulus alone, a visual stimulus alone, or a multisensory stimulus (auditory and visual), all in pseudo-random order. The participants were asked to discriminate between the colors blue or red, presented audibly through the verbalization of the colors for approximately 300 ms (a female voice says the word *blue* or *red*), visually through a circle filled with the corresponding color on a black background for 250 ms, or simultaneously presenting both stimulus modalities for 1 color (never conflicting colors). A trial began with a fixation cross in the center of a computer monitor for 1 second, followed by the stimulus, and lastly a response time screen for 8 seconds. From the onset of when the stimulus was presented by the program, the participant's key press was recorded. If after the stimulus presentation the participant had not responded, which was usually the case, an 8-second response period was provided. Once the participant responded, the trial was immediately terminated and the next trial was initiated. See Figure 1 for a visual representation of all 3 stimulus presentations.

The test began with a series of practice trials that were performed as many times as needed until both the participant and the researcher felt the participant understood the task and how to perform it correctly. For the task, participants were instructed to "respond as quickly and as accurately as possible." The participants were instructed to press "v" on the keyboard with their index finger when they saw and/or heard red, press "b" with their middle finger for blue, and to ignore the green stimulus. The unisensory stimuli were presented for 43 trials for each color (red or blue) within each stimulus type (auditory or visual), and the multisensory stimulus for red and blue was presented for 63 trials each. The green stimulus was presented for approximately 10% of the total trials, and responses were not

analyzed; this was to keep participants from anticipating the answer, which could have occurred if there were only 2 possible choices.

Apparatus

Great care was taken to ensure that there was minimal delay in the stimulus presentation by ensuring that the graphic and sound card and their drivers were as fast as possible, that the lag in the keyboard response time was as small as possible, and that the next stimulus to be presented by the E-prime 2.0 software (Psychology Software Tools, Sharpsburg, Pennsylvania) was stored in RAM, so that it was retrieved quickly on trial onset.

The task was created and recorded through the E-Prime 2.0 software (Psychology Software Tools) in a Windows 8.1 desktop computer (Dell Optiplex 7020; Dell, Round Rock, Texas). The responses were recorded on a 1000-Hz polling Razer BlackWidow Ultimate Stealth mechanical keyboard. The visual stimulus was presented using the integrated graphics for the Dell desktop on a 60-Hz monitor (SyncMaster 2220WM; Samsung, Suwon, South Korea) using a digital visual interface cable with a 5-ms gray-to-gray latency. The sound stimulus was presented on 2 speakers side by side to the monitor. The speakers were connected to a SoundBlaster Audigy FX soundcard with ASIO drivers (ASIO4ALL; Steinberg Media Technologies, Hamburg, Germany) integrated with E-Prime to maximally reduce sound latency. The volume of the speakers was adjusted to a comfortable and easily discriminable level for each participant. The participants were seated comfortably at a constant distance from the monitor and speakers. The test was conducted again after 4 weeks.

Data Analysis

Each participant's responses were analyzed separately. Outliers were removed from the response times, which were defined as responses greater than 2 standard deviations from the mean response time for each participant. Responses in less than 250 ms were not eliminated (unlike the study by Laurienti et al[21]), because participants continued to possess high accuracy in this low range. For example, 1 participant had 21 responses in less than 250 ms but only 1 incorrect. In keeping with the study by Laurienti et al[21] incorrect responses were included for response times. Response time and accuracy for the green stimulus were not analyzed because this stimulus was only used to keep participants from anticipating the stimulus.

Though the comparison of the mean accuracy was not the focus of the study, the mean accuracy was calculated for reference. All statistical tests were conducted using SPSS Version 23 (IBM Corp, Armonk, New York). The mean response time was analyzed using a 2-way (1 between-participants factor [participant groups = SCNP vs asymptomatic] × 1 within-participants factor [test time = baseline vs week 4] mixed analysis of variance (ANOVA) for each stimulus condition). To compare the multisensory gain between the 2 groups, the difference in response times between the fastest unisensory stimulus (visual) and multisensory stimulus was calculated for baseline and compared using an independent t test. If the 2 stimuli being compared in the multisensory gain possessed no difference at baseline and 4 weeks, the response time for the 2 were averaged in the test.

During preliminary data collection, it was noted that factors such as poor motivation, performance anxiety, inattention, and a lack of understanding of the task requirements all lead to prolonged response times that did not reflect true task performance. Therefore, participant outliers were calculated and removed for each group using boxplots with more than 1.5 box lengths from the edge of the box. Studentized residuals were then calculated to ensure all data were between –3 and +3 residual values. This ensured that individuals whose results were different from the group mean because they did not perform the task as required did not skew the genuine results. Shapiro-Wilks test was used to test for data normality. Mauchly test of sphericity to test for variance of the differences between groups did not apply because the dependent variable was only measured at 2 levels. To test homogeneity of error variance, Levene test of equality of error variances was used. Any significance in the homogeneity of covariances test, Box test for covariances, was noted, and thus interaction effects were not assessed. Partial η^2 was calculated for effect size, where small was interpreted as 0.01, medium as 0.06, and large as 0.14. To compare the multisensory gain, an independent 2-sample t test was conducted.

To control for the gain that may occur in multisensory data as a result of the redundant nature of the stimulus, cumulative distribution functions (CDFs) were plotted. Multisensory data were compared with the predicted gain from the redundancy of the stimulus to determine if the multisensory gain that may be seen was simply because the redundancy effect.[29] This model, known as the race model, is calculated from a CDF by joint probability of the unisensory conditions ([pAuditory + pVisual] – [pAuditory × pVisual]). If the probability of the multisensory conditions is larger than the joint probability of the unisensory conditions, then the race model is violated, which suggests a neural integration (multisensory integration) of the 2 unisensory stimuli.[29]

The CDF analysis was performed by analyzing each participant separately. Each participant's cumulative frequencies were placed into time bins, which were created starting from 100 ms with an increment of 10 ms up to 1600 ms. The percent frequency distribution for each bin was averaged for each group to ensure the results reflected the group and not outlying bins or participants. With the CDFs obtained for each unisensory stimulus, the race model was calculated for each participant. Deviations from the race model were calculated by subtracting the probability of the

Table 1. *Accuracy of Response Times Less Than 250 ms*

Stimulus (Total Responses)		Visual (86)		Auditory (86)		Multisensory (126)	
Week		0	4	0	4	0	4
SCNP responses <250 ms	No. of responses <250 ms	1	0.25	0	0	0.83	1.08
	Accuracy (% correct)	83	67	n/a	n/a	30	62
Control responses <250 ms	No. of responses <250 ms	1.42	2.92	0.08	0.08	3.33	3.42
	Accuracy (% correct)	76	86	100	0	78	98

SCNP, subclinical neck pain.
The mean number of responses that were less than 250 ms for each group's stimulus conditions, along with its accuracy of correct responses (%). There were a total of 86 audio and visual responses and 126 multisensory responses by default, not including green responses.

race model from the probability of the multisensory conditions for each bin. A 1-sample *t* test was conducted for each time bin in each group and was compared with zero (no gain), where significant ($P \leq .05$) deviations for each time bin were identified. A 2-sample *t* test was conducted to compare the deviations between the 2 groups, where significant ($P \leq .05$) deviations for each time bin between the groups were identified.

Results

The mean responses less than 250 ms and mean accuracy for these responses can be found in Table 1. The mean accuracy is reported in Table 2. The overall mean response time and accuracy for the asymptomatic controls and SCNP groups exceeded 95% in all stimulus conditions. In all conditions except 1 (week 4 visual), the SCNP group possessed larger variation than the control.

The mean response times for both SCNP and asymptomatic controls reported in Table 2 are also depicted in Figure 2 for baseline.

Auditory Stimulus

The 2-way mixed ANOVA for the auditory stimulus indicated no significant interactions between test week and participant group on auditory response time (SCNP week 0 [576 ± 64 ms] vs week 4 [550 ± 74 ms] and control week 0 [552 ± 43 ms] vs week 4 [533 ± 61 ms]; $F^{1, 21} = 0.082$, $P = .778$, partial $\eta^2 = 0.004$). The main effect of test week indicated a significant difference in mean auditory response time between week 0 and week 4 ($F^{1, 21} = 4.306$, $P = .050$, partial $\eta^2 = 0.170$). Response times for the auditory stimulus were slower for the group with SCNP by a mean difference of 24 ms at baseline and 17 ms at week 4; however, main effect of participant group indicated that this difference was not significant ($F^{1, 21} = 0.799$, $P = .382$, partial $\eta^2 = 0.037$).

Using the boxplot outlier feature in SPSS, the descriptive statistics identified 2 outliers (1 SCNP participant, 1 control participant) for values greater than 1.5 box lengths from the edge of the box; thus, these participants were excluded from this test. The studentized residuals for week 0 and 4 then produced no values <–3 or >3. All response times were normally distributed in all data cells, as assessed by Shapiro-Wilks test ($P > .05$). Levene test of equality of error variances was used to determine if there was homogeneity of variance and the assumption of homogeneity of variances was not violated ($P > .05$). Box test of equality of covariance matrices was used to test for homogeneity of covariances, where there was homogeneity of covariances ($P = .256$).

Visual Stimulus

The 2-way mixed ANOVA for the visual stimulus indicated no significant difference in mean visual response time at the different test weeks (SCNP week 0 [444 ± 69 ms] vs week 4 [433 ± 42 ms] and control week 0 [396 ± 35 ms] vs week 4 [396 ± 49 ms]; $F^{1,21} = 0.760$, $P = .393$, partial $\eta^2 = 0.035$). Response times for the visual stimulus were slower by 48 ms baseline and 37 ms at week 4, when compared with the control group. The main effect of participant group indicated that this difference was significant ($F^{1,21} = 4.490$, $P = .046$, partial $\eta^2 = 0.176$).

Using the boxplot outlier feature in SPSS, the descriptive statistics identified 3 outliers (1 SCNP participant, 1 control participant with 2 outliers) for values greater than 1.5 box lengths from the edge of the box, 1 of them being an extreme outlier with a value greater than 3.0 box lengths from the edge of the box; thus, these participants were excluded from this test. The studentized residuals for week 0 and 4 then produced no values <–3 or >3. All response times were normally distributed in all data cells, as assessed by Shapiro-Wilks test ($P > .05$). Levene test of equality of error variances was used to determine if there was homogeneity of variance and the assumption of homogeneity of variances was not violated ($P > .05$). Box test of equality of covariance matrices was used to test for homogeneity of covariances, where there was no homogeneity of covariances ($P = .004$). Because this test failed, the interaction effect between baseline and 4 weeks and stimulus condition was no longer assessed in this test.

Multisensory Stimulus

The 2-way mixed ANOVA for the multisensory stimulus indicated no significant difference in mean multisensory

Table 2. *Mean Response Time and Accuracy*

		Week 0			Week 4		
		Auditory	Visual	Multisensory	Auditory	Visual	Multisensory
SCNP	RT	576 (64)	444 (69)	450 (70)	550 (74)	433 (42)	443 (55)
	Accuracy	97.3 (3.0)	96.2 (5.0)	95.8 (4.4)	96.6 (4.4)	95.8 (4.7)	96.3 (5.2)
	n	11	11	12	11	11	12
Control	RT	552 (43)	396 (35)	396 (35)	533 (61)	396 (49)	392 (51)
	Accuracy	97.3 (2.3)	96.6 (2.9)	96.8 (2.6)	95.6 (2.7)	96.8 (1.7)	96.7 (3.6)
	n	12	12	12	12	12	12

RT, response time; *SCNP,* subclinical neck pain.
The mean RT in milliseconds, number of participants (n), mean accuracy in percentage, and their standard deviations (in parentheses) for each of the groups during baseline and the week 4 measurement. The numbers of participants are reported for each (stimulus condition) analysis of variance test.

response time at the different test weeks (SCNP week 0 [450 ± 70 ms] vs week 4 [443 ± 55 ms[and control week 0 [396 ± 35 ms] vs week 4 [392 ± 51 ms]; $F^{1,22} = 0.647$, $P = .430$, partial $\eta^2 = 0.029$). The response times for the multisensory stimulus were slower for the SCNP group by an average of 52 ms at baseline and 47 ms at week 4. The main effect of participant group indicated that this difference was significant ($F^{1,22} = 6.340$, $P = .020$, partial $\eta^2 = 0.224$).

Using the boxplot outlier feature in SPSS, the descriptive statistics identified 1 outlier (1 control participant) for values greater than 1.5 box lengths from the edge of the box; thus, this participant was excluded from this test. The studentized residuals for week 0 and 4 then produced no values <–3 or >3. All response times were normally distributed in all data cells, as assessed by Shapiro-Wilks test ($P > .05$). Levene test of equality of error variances was used to determine if there was homogeneity of variance and the assumption of homogeneity of variances was not violated ($P > .05$). Box test of equality of covariance matrices was used to test for homogeneity of covariances, where there was no homogeneity of covariances ($P = .004$). Because this test failed, the interaction effect between testing week and stimulus condition was no longer assessed in this test.

Multisensory Gain

The fastest mean response time for the unisensory stimuli for both groups was the visual stimulus, which almost matched the multisensory stimulus. The mean response time for visual stimulus was faster than multisensory for the group with SCNP. The comparison between the fastest unisensory response time mean to the multisensory response time mean (visual minus multisensory) between the control and the SCNP participants yielded times of 2.5 ms (± 2.5) and 4.2 ms (± 6.4), respectively, for the average of week 0 and week 4 measurements. An independent *t* test was conducted to compare multisensory gain between the 2 groups. Because the visual and multisensory stimuli indicated no significant change over time, the 2 values were averaged, to increase statistical power, and the difference calculated. There was no significant difference in mean multisensory gain between SCNP and control, with SCNP multisensory gain mean difference score being 1.78 higher than control multisensory gain (95% confidence interval [CI], –16.4 to 12.8), $t(14.373) = 0.261$, $P = .797$.

Outliers were recalculated separate from those of the ANOVA because the average of week 0 and 4 created new response time. Boxplots identified only 1 participant (control) as an outlier and was thus removed. Shapiro-Wilks test for normality yielded no significance for both the control ($P = .753$) and SCNP ($P = .717$) groups. The assumption of homogeneity of variances was violated, as assessed by Levene test for equality of variances ($P = .009$), and thus, a modified *t* test, the Welch *t* test, was used to compare multisensory gain between the 2 groups.

Redundancy Control

The race model was compared with the multisensory condition to determine if there was a gain in multisensory integration beyond what can be predicted as a result of the redundancy effect.[29] Even though no significant difference was identified in the weak multisensory gain between the groups in the earlier *t* test, a CDF to compare with the race model was conducted to determine if there were gain changes in some time bins that would not have been reflected when simply comparing the means using a *t* test. See Figure 3 for a graphical representation of the CDFs.

A clear difference can be identified for all the curves, where the asymptomatic group has their curves shifted to the left compared with the SCNP group, indicating that the asymptomatic group was faster in all aspects. However, it is unclear from visual inspection of the graph if there are significantly faster multisensory responses compared with either of the 2 unisensory conditions. Further analysis from the 1-sample *t* test identified no significant difference ($P > .05$) in deviations of the multisensory condition from the race model in all time bins for the asymptomatic group. There was, however, a significant deviation ($P \leq .05$) for the SCNP group in time bins 290 to 320 ms in the left direction (probability of multisensory integration > probability of race) and 430-480 ms in the right direction (probability of

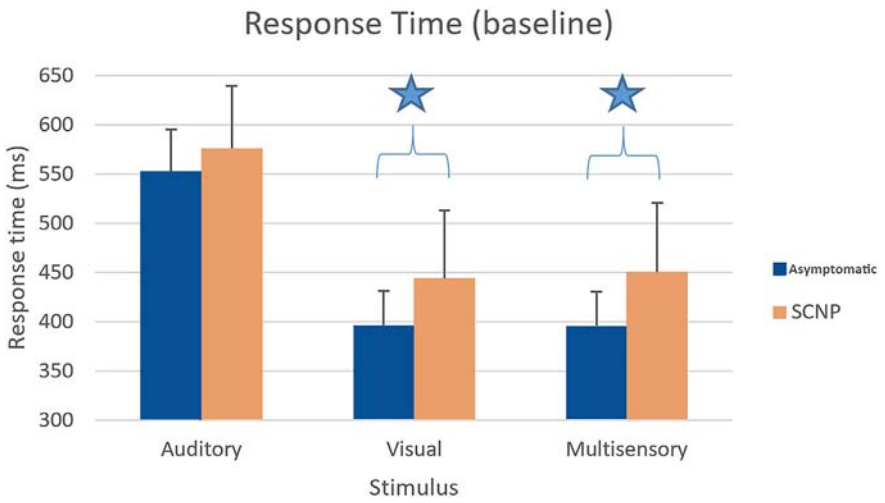

Fig 2. *The baseline mean response time for all the stimulus conditions presented with a comparison for each group alongside each stimulus. One standard deviation caps are presented for each stimulus condition and group. Stars indicate a significant difference.* SCNP, *subclinical neck pain.*

multisensory integration < probability of race). Thus, the SCNP group was the only group to have multisensory integration beyond the redundancy effect, and only for the 290- to 320-ms time bins. When the 2 groups were compared using the 2-sample *t* test to test for difference in deviations between the groups, no significant differences ($P > .05$) were identified.

Discussion

The results described are the first to reveal that there is a significant difference in response times for visual and multisensory stimuli in a 2-alternative forced-choice discrimination task between adults with SCNP and asymptomatic controls. These differences are not simply because of slower movement times in general, because previous studies of people with SCNP reported no difference in simple response times in this population but found that the SCNP group had slower response times in more complex tasks (mental rotation).[34]

Results from this study's SCNP group are similar to the slow unisensory response times reported in the elderly population in the study by Laurienti et al[21] Though identifying similar group differences between response times, the actual response time values did not match between the studies. All of our mean values and standard deviation for response times for each stimulus condition and were lower than those of Laurienti et al[21] possibly because we used equipment and drivers that produced a lower latency and variance than those of Laurienti et al. This is supported by the fact that our mean response times for visual conditions for the asymptomatic young adults (396 ± 35 ms) was lower than their young adult controls for the multisensory condition (485 ± 93 ms). We did not remove responses less than 250 ms; however, the large differences in response times between the 2 studies (eg, visual: 396 ± 35 ms vs 538 ± 117 ms) cannot solely be accounted for by this removal because it would only account for a minor difference (eg, <10 ms for visual).

Our standard deviations were almost one-third of the values reported by Laurienti et al[21] coupled with our faster response times, suggesting that our stimulus presentations were stronger because of a combination of smaller delays and lower variability in timing of stimulus presentation and recording parameters of the equipment used to collect the data. The multisensory gain was not as great as expected because the difference between the visual and multisensory stimulus was extremely small for the control group and SCNP group and there was no significant difference in the multisensory gain between the 2 groups for both the standard *t* test and CDF analysis. This is dissimilar to some earlier work,[21,28] which reported a large difference between their visual and multisensory stimuli for all groups. Researchers have pointed to the importance of spatial and temporal factors in the stimulus presentation required to create multisensory integration,[30,31] which may not have been effective enough in this experiment. However, Meredith and Stein[25] have reported multisensory integration when there is a delay of up to 100 ms between the 2 multisensory stimuli. The multisensory response times were similar to what the race model had predicted as simply being a redundancy gain. The race model predicts that the quickest response to combined audiovisual stimuli is a "redundant signal effect" that is explained by a summation of the probability of either stimulus being presented. Times faster than this are considered to represent true multisensory integration, rather than just interaction.[35] However, Juan et al[35]

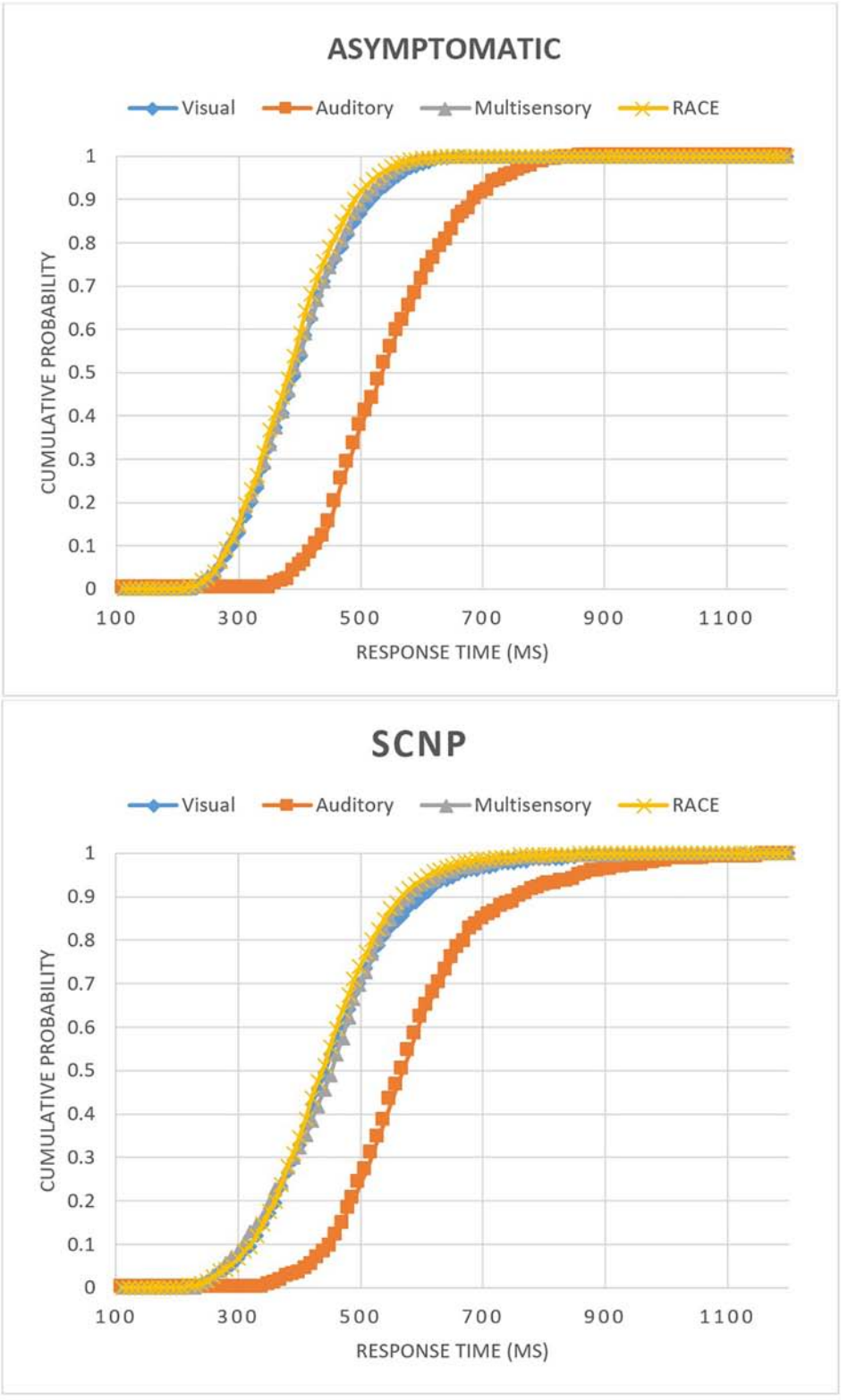

Fig 3. *A comparison of cumulative distribution functions for both asymptomatic and subclinical neck pain (SCNP) groups. The race model is depicted in addition to the visual, auditory, and multisensory conditions.*

recently conducted a study in both rhesus macaque monkeys and human participants. They used a large collection of both unimodal and bimodal audiovisual stimuli with semantic specificities that were presented at different saliencies (weightings). The authors reproduced the redundant signal effect; however, there were no systematic violations of the race model. The authors concluded that the redundancy effect at a neural level depends on how complex the stimuli are, with different consequences for unisensory vs multisensory brain areas.[35] This suggests that the reason that we did not identify enhanced multisensory gain may have been because our visual and auditory stimuli were not sufficiently complex for multisensory gain to provide any advantage, because our visual response times were already so fast relative to other studies as a result of careful attention to technical factors to minimize latencies of stimulus presentations.[21]

Most of the time bins revealed that the multisensory gain identified was solely based on the redundancy effect, because most bins did not violate the race model. However, the CDF from the SCNP group did identify multisensory integration beyond what was predicted by the race model between 290 and 320 ms, possibly reflecting increased gain in the SCNP group. However, a significant deviation below the race model prediction (eg, decreased multisensory gain) occurred between 430 and 480 ms, making it hard to draw definitive conclusions about differences in multisensory gain between the 2 groups. Additionally, the longer response times reported by Laurienti et al[21] suggest that the equipment they used may have had longer lag times in stimulus presentation and recording, which would have effectively acted as "noise," weakening the unisensory stimulus strength and causing increased reliance on multisensory integration. Noise would have the effect of obscuring the strength of the stimulus signal, paradoxically enhancing multisensory gain, which is strongest when the unisensory stimuli are weaker.[25]

Individuals with SCNP have altered SMI and altered motor responses.[5] Treatment of SCNP can improve somatosensory processing as well as elbow joint position sense.[36] Areas in the thalamus have been reported to be sites of interaction between multisensory integration and SMI.[24] The superior colliculus is a multisensory area with access to efferent projections of premotor and motor areas of the spinal cord and the brainstem involved in superior colliculus–mediated attentive and orientation behaviors.[25] A recent study[22] reported that seniors have altered sensorimotor feedback that may increase their risk of falling. Chiropractic treatment lead to improved sensorimotor and multisensory integration, reducing their risk of falls and suggesting a connection between altered sensorimotor and multisensory integration.

A recent study[37] reported that changing visual feedback altered the amount of pain-free neck rotation in a group of patients with chronic neck pain. This indicates an increased reliance on visual input in this group, possibly because their internal body schema or body map is not accurately calibrated, leading to altered integration of sensory input. SCNP participants also have worse mental rotation abilities, which likely reflects an altered egocentric frame of reference as a result of an altered body schema.[34] If patients with neck pain have an increased reliance on vision and their visual and multisensory processing response times are impaired, as indicated in the present study, it is problematic. Our study identified worse visual and multisensory reaction times in SCNP vs asymptomatic young adults, which was not compensated for by increased multisensory gain between the 2 groups, for both the standard *t* test and CDF analysis. The lack of change over 4 weeks suggests that left untreated, even subclinical neck pain can affect multisensory processing.

Another possibility for the differences in our results compared with previous work such as animal studies may relate to differences in upper level cortical processing. Felines possess efferent projections from the superior colliculus that were enhanced with multisensory input in behaviors involved with attention and orientation.[25] Our study suggests that additional factors, such as changes in projections from neck afferents, may interfere with upper-level cortical processing, affecting the initially quick response times of multisensory neurons. As mentioned in the introduction, the superior colliculus integrates sensory inputs that involve movement and orientation behaviors (eg, eye saccade, neck movement toward stimulus).[25] The altered sensory feedback from the neck in the SCNP group would have projected with other modalities onto these bimodal neurons, or through cross-modal projections onto other sensory sites, and affected multisensory processing. Our initial hypothesis was based on the concept that neck pain, like aging, would create a noisier system and longer unisensory response times, which we did find in the present study. However, we presumed that like the study by Laurienti et al[21] the multisensory neurons would have inverse effectiveness and greater gain to compensate. However, it is important to consider that neck pain is different from aging in that some neck afferents project directly to these same multisensory neurons, possibly altering their capacity to increase their gain to compensate for the slower unisensory processing. Previous work reported that spinal manipulation improved SMI in participants with SCNP.[5] It would be interesting to see whether spinal manipulation is able to improve response times of other unisensory and multisensory modalities.

Limitations

This study found that adults with SCNP have slower response times for visual and multisensory stimuli than asymptomatic controls, but differences in multisensory integration were inconclusive. The auditory component improved over time, suggesting a need to perform multiple

baseline tests to ensure that baseline performance has stabilized before including auditory stimuli in a longitudinal study. Although great care was taken to determine the technical specifications of all equipment, it is possible that technical factors such as screen refresh rates could have introduced delays in some of the response times. That being said, this would have been a random effect for both groups and thus would be unlikely to have affected the final results.

Conclusion

This is the first study to report that people with SCNP possess slower visual and multisensory response times. These differences persist over 4 weeks, suggesting that the measure is reliable over time and that differences caused by SCNP do not improve on their own in the absence of treatment.

Funding Sources and Potential Conflicts of Interest

The authors received funding from the Australian Spinal Research Foundation (LG 2013-22), Natural Sciences and Engineering Research Council of Canada Discovery Grants, and Canada Foundation for Innovation - John R Evans Leaders Fund. No conflicts of interest were reported for this study.

Contributorship Information

Concept development (provided idea for the research): B.F., M.H., H.H., B.A.M.
Design (planned the methods to generate the results): B.F., P.Y., B.A.M.
Supervision (provided oversight, responsible for organization and implementation, writing of the manuscript): B.F., P.Y., B.A.M.
Data collection/processing (responsible for experiments, patient management, organization, or reporting data): B.F.
Analysis/interpretation (responsible for statistical analysis, evaluation, and presentation of the results): B.F.
Literature search (performed the literature search): B.F., B.A.M.
Writing (responsible for writing a substantive part of the manuscript): B.F., B.A.M.
Critical review (revised manuscript for intellectual content, this does not relate to spelling and grammar checking): B.F., P.Y., M.H., H.H., B.A.M.

Practical Applications

- The ability of the brain to integrate sensory inputs is affected in those with recurrent neck pain.
- The response time to visual and combined audiovisual inputs was slower in the recurrent neck pain group at baseline and when measured again after 4 weeks.
- Altered sensory input from the neck appears to interfere with the ability to integrate inputs from other sensory stimuli.

References

1. Hogg-Johnson S, van der Velde G, Carroll LJ, et al. The burden and determinants of neck pain in the general population—results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine (Phila Pa 1976).* 2008;33(4 Suppl):S39-S51.
2. Lee HJ, Nicholson LL, Adams RD. Cervical range of motion associations with subclinical neck pain. *Spine.* 2004;29(1):33-40.
3. Lee HJ, Nicholson LL, Adams RD, Bae SS. Proprioception and rotation range sensitization associated with subclinical neck pain. *Spine.* 2005;30(3):E60-E67.
4. Lee HY, Wang JD, Yao G, Wang SF. Association between cervicocephalic kinesthetic sensibility and frequency of subclinical neck pain. *Man Ther.* 2008;13(5):419-425.
5. Haavik-Taylor H, Murphy B. Cervical spine manipulation alters sensorimotor integration: a somatosensory evoked potential study. *Clin Neurophysiol.* 2007;118(2):391-402.
6. Byl NN, Melnick M. The neural consequences of repetition: clinical implications of a learning hypothesis. *J Hand Ther.* 1997;10(2):160-174.
7. Haavik-Taylor H, Murphy B. Transient modulation of intracortical inhibition following spinal manipulation. *Aust.* 2007;37(3):106.
8. Gogia PP, Sabbahi MA. Electromyographic analysis of neck muscle fatigue in patients with osteoarthritis of the cervical-spine. *Spine.* 1994;19(5):502-506.
9. Bränström H, Malmgren-Olsson E, Barnekow-Bergkvist M. Balance performance in patients with whiplash associated disorders and patients with prolonged musculoskeletal disorders. *Adv Physiother.* 2001;3(3):120-127.
10. Falla D, Bilenkij G, Jull G. Patients with chronic neck pain demonstrate altered patterns of muscle activation during performance of a functional upper limb task. *Spine.* 2004; 29(13):1436-1440.
11. Paulus I, Brumagne S. Altered interpretation of neck proprioceptive signals in persons with subclinical recurrent neck pain. *J Rehabil Med.* 2008;40(6):426-432.
12. Taylor HH, Murphy B. The role of spinal manipulation in addressing disordered sensorimotor integration and altered motor control. *J Electromyogr Kinesiol.* 2012;22(5):768-776.
13. Taylor HH, Murphy B. The effects of spinal manipulation on central integration of dual somatosensory input observed after motor training: a crossover study. *J Manipulative Physiol Ther.* 2010;33(4):261-272.

14. Taylor HH, Murphy B. Altered central integration of dual somatosensory input after cervical spine manipulation. *J Manipulative Physiol Ther.* 2010;33(3):178-188.
15. Ernst MO, Banks MS. Humans integrate visual and haptic information in a statistically optimal fashion. *Nature.* 2002; 415(6870):429-433.
16. Hogendoorn H, Kammers MP, Carlson TA, Verstraten FA. Being in the dark about your hand: resolution of visuo-proprioceptive conflict by disowning visible limbs. *Neuropsychologia.* 2009; 47(13):2698-2703.
17. van der Kooij K, Brenner E, van Beers RJ, Schot WD, Smeets JB. Alignment to natural and imposed mismatches between the senses. *J Neurophysiol.* 2013;109(7):1890-1899.
18. Bresciani J-P, Dammeier F, Ernst MO. Tri-modal integration of visual, tactile and auditory signals for the perception of sequences of events. *Brain Res Bull.* 2008;75(6):753-760.
19. Oie KS, Kiemel T, Jeka JJ. Multisensory fusion: simultaneous re-weighting of vision and touch for the control of human posture. *Cogn Brain Res.* 2002;14(1):164-176.
20. Haavik H, Murphy B. Subclinical neck pain and the effects of cervical manipulation on elbow joint position sense. *J Manipulative Physiol Ther.* 2011;34(2):88-97.
21. Laurienti PJ, Burdette JH, Maldjian JA, Wallace MT. Enhanced multisensory integration in older adults. *Neurobiol Aging.* 2006; 27(8):1155-1163.
22. Holt KR, Haavik H, Lee ACL, Murphy B, Elley CR. Effectiveness of chiropractic care to improve sensorimotor function associated with falls risk in older people: a randomized controlled trial. *J Manipulative Physiol Ther.* 2016;39(4):267-278.
23. Zampini M, Brown T, Shore DI, Maravita A, Roder B, Spence C. Audiotactile temporal order judgments. *Acta Psychol.* 2005;118(3):277-291.
24. Cappe C, Morel A, Barone P, Rouiller EM. The thalamocortical projection systems in primate: an anatomical support for multisensory and sensorimotor interplay. *Cereb Cortex.* 2009; 19(9):2025-2037.
25. Meredith MA, Stein BE. Visual, auditory, and somatosensory convergence on cells in superior colliculus results in multisensory integration. *J Neurophysiol.* 1986;56(3):640-662.
26. Reinoso-Suarez F, Roda JM. Topographical organization of the cortical afferent connections to the cortex of the anterior ectosylvian sulcus in the cat. *Exp Brain Res.* 1985;59(2): 313-324.
27. Hairston WD, Laurienti PJ, Mishra G, Burdette JH, Wallace MT. Multisensory enhancement of localization under conditions of induced myopia. *Exp Brain Res.* 2003;152(3): 404-408.
28. Laurienti PJ, Kraft RA, Maldjian JA, Burdette JH, Wallace MT. Semantic congruence is a critical factor in multisensory behavioral performance. *Exp Brain Res.* 2004;158(4): 405-414.
29. Miller J. Divided attention: evidence for coactivation with redundant signals. *Cogn Psychol.* 1982;14(2):247-279.
30. Meredith MA, Stein BE. Spatial factors determine the activity of multisensory neurons in cat superior colliculus. *Brain Res.* 1986;365(2):350-354.
31. Nemitz JW, Meredith MA, Stein BE. Temporal determinants of multimodal interactions in superior colliculus cells. *Soc Neurosci Abstracts.* 1984;10(1):298.
32. Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia.* 1971;9(1):97-113.
33. Vonkorff M, Ormel J, Keefe FJ, Dworkin SF. Grading the severity of chronic pain. *Pain.* 1992;50(2):133-149.
34. Baarbé JK, Holmes MWR, Murphy HE, Haavik H, Murphy BA. Influence of subclinical neck pain on the ability to perform a mental rotation task: a 4-week longitudinal study with a healthy control group comparison. *J Manipulative Physiol Ther.* 2016;39(1):23-30.
35. Juan C, Cappe C, Alric B, et al. The variability of multisensory processes of natural stimuli in human and non-human primates in a detection task. *PLoS One.* 2017; 12(2)e0172480.
36. Haavik-Taylor H, Murphy B. Subclinical neck pain and the effects of cervical manipulation on elbow joint position sense. *J Manipulative Physiol Ther.* 2011;34(2):88-97.
37. Harvie DS, Broecker M, Smith RT, Meulders A, Madden VJ, Moseley GL. Bogus visual feedback alters onset of movement-evoked pain in people with neck pain. *Psychol Sci.* 2015;26(4):385-392.