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Review

Visceral responses to spinal manipulation

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ABSTRACT

While spinal manipulation is widely seen as a reasonable treatment option for biomechanical disorders of the spine, such as neck pain and low back pain, the use of spinal manipulation to treat non-musculoskeletal complaints remains controversial. This controversy is due in part to the perception that there is no robust neurobiological rationale to justify using a biomechanical treatment of the spine to address a disorder of visceral function. This paper therefore looks at the physiological evidence that spinal manipulation can impact visceral function. A structured search was conducted, using PubMed and the Index to Chiropractic Literature, to construct of corpus of primary data studies in healthy human subjects of the effects of spinal manipulation on visceral function. The corpus of literature is not large, and the greatest number of papers concerns cardiovascular function. Authors often attribute visceral effects of spinal manipulation to somato-autonomic reflexes. While this is not unreasonable, little attention is paid to alternative mechanisms such as somato-humoural pathways. Thus, while the literature confirms that mechanical stimulation of the spine modulates some organ functions in some cohorts, a comprehensive neurobiological rationale for this general phenomenon has yet to appear.

1. Introduction

Spinal manipulation is generally accepted as one reasonable treatment option in the management of musculoskeletal disorders such as low back pain and neck pain. Some evidence also exists that certain visceral disorders benefit from spinal manipulation (for example, see Bakris et al., 2007). However, the mechanisms by which spinal manipulation might alter visceral function, and so impact visceral disease, remain unclear. Therefore, in this paper, we review the currently available literature concerning visceral responses to the application of mechanical stimuli to the spine and paraspinal tissues. We specifically draw from human studies using high velocity, low amplitude manipulations, and also from research using biomechanically similar manoeuvres. Therefore, in this paper, the term 'spinal manipulation' may be interpreted liberally to include a range of related procedures.

To provide some clinical context for this review, it is to be noted that only a relatively small percentage of patients receive spinal manipulation specifically for the management of a non-musculoskeletal complaint. Numbers vary somewhat from survey to survey, but in Denmark, for example, the proportion of all patients presenting to chiropractors with non-musculoskeletal complaints apparently fell from 7% in 1966 to 3% in 1999 (Hartvigsen et al., 2003). Furthermore, the range of non-musculoskeletal complaints reported to be treated with spinal manipulation is quite limited. In fact, a previous review found that approximately half of the case reports and case series dealing with manipulative management of non-musculoskeletal complaints pertained to only a handful of disorders including gynecological complaints, visual deficits, asthma and enuresis (Budgell, 1999). Clinical trials of spinal manipulation in the treatment of non-musculoskeletal disorders are similarly restricted with the bulk of studies focused on cardiovascular disease, gynecological complaints, infantile colic and asthma (Hawk et al., 2007; Nakayama and Budgell, 2009). Given the restricted interests of clinical reports and controlled studies, as described above, we will therefore review basic physiological studies of what appear to be the most clinically relevant phenomena: cardiovascular, respiratory, gastrointestinal and female reproductive function.

2. Methods

Between April 25 and April 29, 2011, the PubMed and Index to Chiropractic Literature databases were searched, without date limitations, for the terms spinal manipulation or spinal manipulative therapy in combination with the terms somatovisceral, cardiovascular, respiratory, gastrointestinal, and gynecological. Thus, a representative search string would appear as: ("manipulation,

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spinal" [MeSH Terms] or ("manipulation" [All Fields] and "spinal" [All Fields]) or "spinal manipulation" [All Fields] or ("spinal" [All Fields] and "manipulation" [All Fields])) or ("spinal" [All Fields] and ("musculoskeletal manipulations" [MeSH Terms] or ("musculoskeletal" [All Fields] and "manipulations" [All Fields]) or "musculoskeletal manipulations" [All Fields] or ("manipulative" [All Fields] and "therapy" [All Fields]) or "manipulative therapy" [All Fields])) and somatovisceral [All Fields].

Titles of identified articles were reviewed to eliminate studies which were either clearly off-topic, not published in English or which did not appear to report original data (reviews, commentaries etc.). The abstracts were then reviewed for the articles which passed the first filtering process. The abstracts were further reviewed for the additional criteria that the articles reported original studies in healthy humans of physiological responses to manual treatment (spinal manipulation or mobilization) of the spine. Articles which satisfied these criteria (Fig. 1) were obtained as full text for data extraction and synthesis in this review.

Additionally, articles held in the authors' own collections but which were not identified by the electronic searches were included in this review if they satisfied the inclusion criteria. These have been marked with an asterisk in their respective tables and included nine articles pertaining to humoural or neurological responses to manipulation, 15 articles pertaining to cardiovascular responses, and one article each pertaining to respiratory and gastrointestinal function. On reading the full texts, some articles were excluded because it became apparent that the subjects were symptomatic patients. The sum of the numbers of articles located with each of the five searches does not equal the total number of articles subsequently analyzed since there was some duplication of results. That is to say that some studies investigated outcomes from more than one system, for example both cardiovascular and respiratory.

3. Results

3.1. Studies of cardiovascular function

Perhaps because of the limitations of available technology to record other physiological parameters and due to clinical relevance, the largest number of experimental studies of spinal manipulation and somato-visceral effects in humans has examined outcomes in cardiovascular function. A total of 18 articles which satisfied our inclusion criteria were retrieved (Table 1). The cardiovascular measures commonly reported were heart rate (HR), blood pressure (BP) and heart rate variability (HRV), from which changes in autonomic output to the heart may be implied. Earlier studies of effects of spinal manipulation on heart rate and blood pressure have employed less reliable technology. For example, in studies of effects of SMT on blood pressure in healthy young cohorts, McKnight and DeBoer (1988) and Tran and Kirby (1977a,b) employed single before and after measures obtained by auscultatory sphygmomanometry, whereas Nansel et al., using a similar cohort, did not describe their methods of measuring heart rate or blood pressure (Nansel et al., 1991). Automated methods of monitoring blood pressure and heart rate are demonstrably more reliable than manual methods (for example, see Pastellides, 2009). Earlier studies may also have eschewed statistical analysis of results in favor of the authors' subjective opinion of what constituted an important effect (for example, see Tran and Kirby, 1977a,b). Therefore, this review only considers in detail those studies that define both the outcome measure and statistical analysis used.

A few studies have employed arterial tonometry, a method which uses a force transducer placed over an artery to continuously measure blood pressure and, from the frequency of the pulse waves, heart rate. The tonometry equipment is costly but technically simple to apply and is a conventional method for monitoring blood pressure during surgery. The first pilot study using arterial tonometry to measure responses to spinal manipulation reported no significant changes or slight decreases in heart rate and blood pressure in alert healthy subjects ($n = 11$) receiving a series of mechanical cervical stimuli: direct pressure to cervical muscles, slow passive rotations of the neck and high velocity low amplitude manipulations, all of which were characterized as innocuous by the subjects (Fujimoto et al., 1999). Of these stimuli, cervical spinal manipulation produced the largest effects: decreases in systolic and diastolic pressures of 6.8 (S.D. ±1.9) mmHg and 6.6 (S.D. ±2.1) mmHg, respectively. While the authors of this study speculated that the cardiovascular changes seen were mediated primarily via the autonomic nervous system, they did not perform calculations in the time or frequency domains, for example power spectrum analysis, on their blood pressure and heart rate data

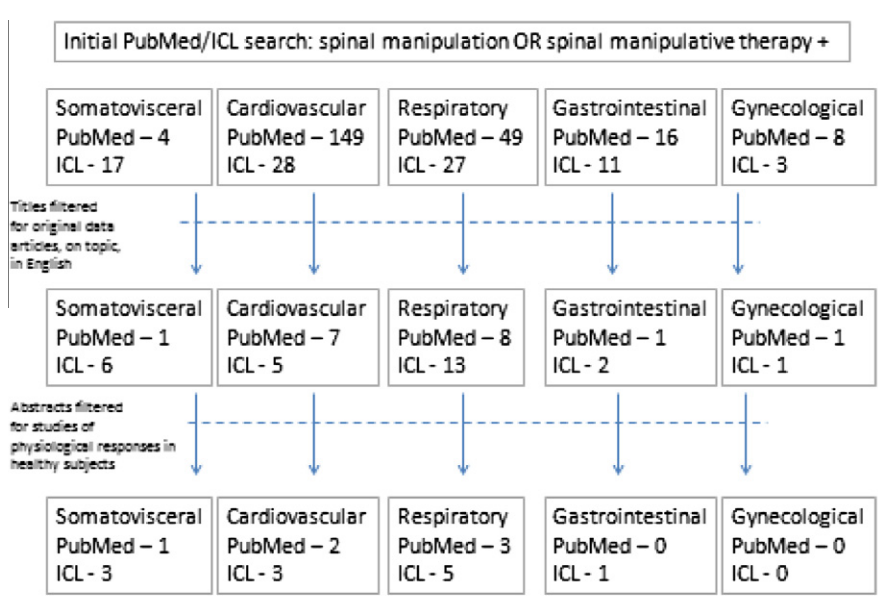

Fig. 1. Methods and results of searches in PubMed and Index of Chiropractic Literature (ICL).

Table 1
Studies of cardiovascular function.

Article	Setting	Demographics	Stimulation	Control	Outcome measure	Effect	Statistics	Notes
Budgell and Hirano (2001)[a]	Chiropractic college clinic	20 males, 5 females, 28.5 (S.D. ±6)years	Cervical (C/S) high-velocity low amplitude manipulation (HVLA)	Sham C/S HVLA	Heart rate(HR), HRV: low frequency (LF), high frequency (HF) components of power spectrum, and LF/HF	Decreased HR, LF, and LF/HF	Paired *t*-tests and Wilcoxon-signed rank test	Randomized crossover design
Budgell and Polus (2006)[a]	Chiropractic college clinic	23 males, 5 females, aged 18–45 (mean 29 ± 7) years	Thoracic (T/S) HVLA	Sham T/S HVLA	HR, HRV: LF, HF and LF/HF	Decreased HR, LF, and LF/HF	Paired *t*-tests and Wilcoxon-signed rank test	Randomized crossover design
Roy et al. (2009)[a]	Unknown	18 females and 15 males	Instrument-assisted HVLA of L5 ($n = 11$)	No intervention ($n = 11$), sham HVLA ($n = 11$)	HRV, including low frequency (LF), high frequency (HF) components of power spectrum, LF/HF and mean RR	Decreased HF, LF and increased LF/HF in manipulation cohort.	ANOVA with Tukey post hoc analyses	Non-randomized parallel cohort study. Marginal and barely significant difference between HVLA and sham groups
Tran and Kirby (1977a,b)[a]	Unknown	24 subjects, 20–30 years	Upper T/S HVLA	None	HR, systolic and diastolic BP	No significant effects of HVLA on HR or BP	None	Authors concluded HVLA decreased systolic and diastolic BP, but this is not supported by their data
Tran and Kirby (1977a,b)[a]	Unknown	18 males, 2 females, 20–30 years	C/S HVLA	None	HR, systolic and diastolic BP	No significant effects of HVLA on HR or BP	None	Authors concluded HVLA increased systolic and diastolic BP, but this is not supported by their data
McKnight and DeBoer (1988)[a]	Chiropractic college clinic	75 subjects, 20–35 years	C/S HVLA ($n = 53$)	C/S motion palpation ($n = 22$)	Systolic and diastolic BP	Decreased systolic and diastolic BP	Paired *t*-tests of pre- and post stimulation measures in 2 cohorts. No between group comparison.	Non-randomized parallel cohort study
Nansel et al. (1991)[a]	Laboratory	24 males, 22–37 years	C/S HVLA	Sham C/S HVLA	Systolic and diastolic BP, HR and plasma catecholamine levels	No significant effects of HVLA on HR, BP or catecholamines	Repeated measures ANOVA	Measures taken from 60 min before until 240 min after HVLA
McGuiness et al. (1997)	University	12 males, 11 females, 18–29 years	Grade III C/S mobilization	Placebo: contact with no mobilization. Control: no contact or mobilization	HR, systolic and diastolic BP	Increased HR, systolic and diastolic BP	ANOVA	Randomized repeated measures design
Fujimoto et al. (1999)[a]	Hospital laboratory	6 males, 4 females, 27–64 years.	C/S HVLA	Sham C/S HVLA	HR, systolic and diastolic blood pressure (BP)	No change in HR, decreased systolic and diastolic BP	Paired *t*-tests of pre- and post stimulation measures.	Some subjects fell asleep during long experiment and gave atypical results
Pastellides (2009)[a]	Chiropractic college clinic	40 males, 20–35 (mean 24) years	C/S and/or T/S HVLA	Sham C/S laser	Systolic and diastolic BP	C/S and T/S HVLA decreased systolic but not diastolic BP	ANOVA	Non-randomized crossover design, measures taken up to 30 min post HVLA
Harris and Wagnon (1987)[a]	Chiropractic college clinic	196 subjects of unknown age and gender	C/S,T/S or L/S HVLA	None	Hand skin temperature	Increased skin temperature with C/S HVLA, decreased skin temperature with T1-L3 HVLA	Paired *t*-tests of pre- and post stimulation measures.	Site of HVLA based on palpation of motion restriction in asymptomatic subjects

(continued on next page)

Table 1 (*continued*)

Article	Setting	Demographics	Stimulation	Control	Outcome measure	Effect	Statistics	Notes
Chiu and Wright (1996)[a]	University	16 males, 18–25 (mean 18.5) years	Grade III mobilization of C5 vertebra at 2 Hz vs. 0.5 Hz	Subject positioning without mobilization	Hand skin temperature	No change in skin temperature	ANOVA	Randomized crossover design
Vicenzino et al. (1998)[a]	Neurophysiology laboratory	13 females, 11 men, 49 (S.D. ±10) years	C/S oscillatory manipulation	Sham mobilization and no-intervention groups	Hand skin temperature and blood flow	Mobilization associated with decreased hand skin temperature and blood flow	Repeated measures ANOVA	Randomized cross-over design
Karason and Drysdale (2003)	Osteopathic college	20 males, 18–38 years	L/S HVLA	Sham HVLA	Skin blood in dorsum of foot	Increased skin blood flow in non-smokers	ANOVA with Tukey post hoc analyses	Six subjects who smoked gave atypical results
Roy et al. (2008)[a]	Private clinic	36 females, 30 males; unknown ages	Instrument-assisted HVLA of L4 or L5 ($n = 22$)	Sham ($n = 22$) or no treatment ($n = 22$)	Paraspinal skin temperature	Transient decreases in skin temperature at the point of contact	ANOVA	Demonstrated local cooling possible due to conductive heat loss to instrument
Licht et al. (1998)[a]	University hospital laboratory	9 males, 11 females, 22–36 (mean 24) years	C/S HVLA ($n = 10$)	Control not described ($n = 10$)	Vertebral artery peak flow velocity 3 min post HVLA	No change	ANOVA	Randomized parallel group design
Licht et al. (1999)	University hospital laboratory	20 subjects, unknown age and gender	C/S HVLA ($n = 10$)	Control not described ($n = 10$)	Volume of blood flow at 3, 10 and 15 min post HVLA	No change	ANOVA	Randomized parallel group design
Cagnie et al. (2005)[a]	University hospital	15 subjects, 21–48 (mean 26.5) yrs	C/S HVLA	None	Regional cerebellar blood flow per single photon emission computed tomography	Decreased blood flow in anterior lobe of ipsilateral cerebellum	Paired *t*-tests of blood flow pre- and post stimulation	Single cohort pre/post measures

[a] Articles from authors' collections.

which would have given some quantitative measure of changes in autonomic output to the cardiovascular system. Using a more complex design, four treatment paradigms over four successive days with measures of blood pressure pre-treatment and at 5, 15 and 30 min post treatment, Pastellides (2009) consistently showed decreases in systolic blood pressure in response to upper cervical manipulation, thoracic manipulation, and combined cervical and thoracic manipulation. Interestingly, McGuiness et al. (1997) referred to an increase in heart rate, and systolic and diastolic blood pressure following a 'grade III posteroanterior mobilization', although their paper does not report the actual data on heart rate and blood pressure.

While heart rate is a commonly used outcome measure, it is not constant even in a resting subject, but varies over a narrow range largely in response to changes in autonomic output to the cardiovascular system. Consequently analysis of heart rate variability has been used to indirectly assess relative autonomic drive to the heart (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). To explain the physiological mechanisms in brief, in humans relatively fast oscillations in heart rate, in the range of 0.25 Hz, are driven by the respiratory cycle (Grossman et al., 2004): as we inhale, thoracic pressure decreases, drawing blood pressure down slightly, in response to which baroreflexes attenuate vagal output to the heart somewhat, thereby permitting a slight rise in heart rate. The reverse process occurs as we exhale. Thus the relatively fast oscillations in heart rate reflect parasympathetic (vagal) output to the heart. Slower oscillations in heart rate, in the range of 0.15 Hz and lower, reflect a systemic ebbing and flowing of sympathetic output to the blood vessel walls creating low amplitude oscillations in blood pressure which again feed through the baroreflexes to modulate vagal tone. Thus, the slower oscillations in heart rate are ultimately driven by sympathetic tone but are dependent upon the integrity of the parasympathetic nervous system (Grasso et al., 1997). Nonetheless, computer algorithms can discriminate between fast and slow oscillations in R–R interval and generate numerical values which are broadly representative of sympathetic and parasympathetic cardiac tone.

Hence, based on HRV calculated from ECG recordings in healthy, pain-free young adults, it was reported that both cervical (Budgell and Hirano, 2001) and thoracic (Budgell and Polus, 2006) spinal manipulation were associated with increases in sympathetic output to the heart, even as heart rate decreased somewhat. Changes in HRV, and so autonomic output to the heart, have also been reported with lumbar manipulation (Roy et al., 2009). However, the small increases reported in parasympathetic tone in subjects without low back pain barely achieved the level of statistical significance.

Hence, while the numbers of studies and the sizes of their cohorts have been modest, there is some evidence that, in healthy subjects, high-velocity low-amplitude manipulation of the cervical, thoracic or lumbar spine modulates autonomic output to the heart. Cervical and thoracic manipulation have been associated with no changes or a shift in favor of sympathetic output to the heart in healthy young adults. Lumbar manipulation was associated with a small increase in cardiac parasympathetic output. Both cervical and thoracic manipulation have been associated with changes in heart rate and blood pressure. The actual magnitudes of changes in heart rate and blood pressure in the reports cited thus far have been modest – single digit decreases in HR (bpm), and systolic and diastolic blood pressures (mmHg) – and, in the healthy subjects employed, of course, of no clinical significance (but see Koch et al., 2002).

A number of authors have also reported effects of spinal manipulation on peripheral vascular physiology. Outcome measures have included such parameters as peripheral blood flow velocity and volume (Licht et al., 1998, 1999), skin temperature and skin blood flux (Harris and Wagnon, 1987; Chiu and Wright, 1996; Vicenzino et al., 1998; Karason and Drysdale, 2003; Roy et al., 2008). No statistically significant effects have been observed in the functions of the larger vessels; however, skin temperature and skin blood flow changes of various sorts have been reported in the upper limb (Harris and Wagnon, 1987; Chiu and Wright, 1996; Vicenzino et al., 1998), lower limb (Karason and Drysdale, 2003) and paraspinal region (Roy et al., 2008). Cervical mobilization has been associated with no (Chiu and Wright, 1996) or small (Vicenzino et al., 1998) decreases in skin temperature and blood flux (Vicenzino et al., 1998). Interestingly, Harris and Wagnon (1987) reported increases in hand skin temperature using what was likely a higher velocity manipulation (vs. Chiu and Wright's and Vicenzino's mobilization) of the cervical spine. Karason and Drysdale (2003) showed mixed results, with lumbar manipulation resulting in decreased blood flow in the dorsum of the foot in non-smoking subjects. In earlier studies, effects of manipulation on skin temperature have been interpreted based on the assumption that an increase in skin temperature reflected vasodilation driven by decreased sympathetic output to dermal blood vessels. This assumption is now known to be overly simplistic (see Hodges and Johnson, 2009), so that skin temperature and skin blood flow measurements cannot be regarded as surrogates for direct measurement of autonomic output. Hence, while it may be said with some confidence that spinal manipulation can affect peripheral cutaneous blood flow in certain cohorts, the underlying mechanisms remain to be resolved and there is no obvious explanation for why different studies should report changes of the opposite polarity (see Harris and Wagnon, 1987 vs. Vicenzino et al., 1998).

One published study used single photon emission computed tomography to examine the effects of spinal manipulation on central nervous system blood flow (Cagnie et al., 2005). No raw data were presented, but the authors stated that in a cohort of 15 subjects it was possible to identify one region of the cerebellum where blood flow decreased when recorded 30 min after a cervical spinal manipulation. The physiological significance of this finding is not clear, and no correlation could be drawn with symptomatology in what was, after all, a healthy cohort. The authors suggest, however, that cerebellar hypoperfusion could be one source of subjective side effects following spinal manipulation (Cagnie et al., 2005).

3.2. Studies of respiratory function

In comparison to the number of studies of cardiovascular function, investigations of the effects of spinal manipulation on respiratory function are rather sparse; only three papers were found which satisfied the inclusion criteria (Table 2). McGuiness et al. referred to an increase in respiratory rate following a 'grade III posteroanterior mobilization' (McGuiness et al., 1997), although their paper did not report the actual pre- and post-treatment respiratory rates. A study of an apparently well cohort of adults demonstrated that a 2 week course of upper cervical manipulation was associated with statistically significant increases in forced vital capacity of approximately 6% and forced expiratory volume of approximately 5%, although this study also had no control cohort (Kessinger, 1997). A small study with only five subjects in the intervention group also referred to increases in FVC and FEV-1 with manipulation (Engel and Vemulpad, 2007), but did not report the data on which these results were apparently based. The existing literature therefore is essentially phenomenological and provides little meaningful data about the effects of spinal manipulation on respiratory function in humans (but see, for example, Koch et al., 1998).

Table 2
Studies of respiratory function.

Article	Setting	Demographics	Stimulation	Control	Outcome measure	Effect	Statistics	Notes
McGuiness et al. (1997)	University	12 males, 11 females, 18–29 years	Grade III C/S mobilization	Placebo: contact with no mobilization. Control: no contact or mobilization	Respiratory rate	Increased respiratory rate	ANOVA	Randomized repeated measures design
Kessinger (1997)[a]	Private chiropractic clinic	24 males, 32 females, 18–80 years	C/S HVLA	None	Forced vital capacity (FVC) and forced expiratory volume in one second (FEV-1)	Increased FVC and FEV-1	Paired *t*-tests	Single cohort study with no control procedure
Engel and Vemulpad (2007)	Chiropractic college clinic	7 males, 10 females, 18–28 years	C/S and/or T/S HVLA ($n = 5$)	No intervention ($n = 4$); Exercise ($n = 4$); Exercise + HVLA ($n = 4$)	FVC and FEV-1	Increased FVC and FEV-1 with HVLA in comparison to other cohorts	Generalized linear model	Randomized parallel group design

[a] Article from authors' collections.

Table 3
Studies of gastrointestinal function.

Article	Setting	Demographics	Stimulation	Control	Outcome measure	Effect	Statistics	Notes
Wiles (1980)[a]	Chiropractic college	Four subjects	C/S HVLA (6 trials)	No HVLA (7 trials)	Frequency and amplitude of gastric contractions measured by electrogastrogram	Decreased frequency and increased amplitude with HVLA	Not described for pre- vs. post comparisons	Non-randomized parallel group design.

[a] Article from authors' collections.

Table 4
Studies of female reproductive function.

Article	Setting	Demographics	Stimulation	Control	Outcome measure	Effect	Statistics	Notes
Nogueira de Almeida et al. (2010)	University clinic	40 females, 20–40 (mean 33.6) years	Sacral HVLA	None	Phasic perineal contractions (PPC), Tonic perineal contractions (TPC) and Accessory muscle contractions (APC)	Increased PPC	Pre- vs. post *t* tests	Non-randomized uncontrolled single cohort design

3.3. Studies of gastrointestinal function

Notwithstanding the interest by practitioners in the effects of spinal manipulation on gastrointestinal function, basic physiological studies are all but absent (Table 3). One small study (13 trials in four subjects) reported that gastric tone, as determined by electrogastrogram wave amplitude, increased in response to upper cervical manipulation (6 trials) and in comparison to trials in which subjects (7 trials) did not receive spinal manipulation (Wiles, 1980). Raw data and the statistical methods for pre- vs. post-SMT comparisons were not described in detail.

3.4. Studies of female reproductive function

Our systematic searches of PubMed and the Index to Chiropractic Literature revealed only one study of spinal manipulation in humans with implications for female reproductive function (Table 4). Nogueira de Almeida et al. (2010) examined the effects of sacral manipulation on intravaginal and basal perineal tonus. In this uncontrolled, single cohort trial, manipulation was associated with increased phasic perineal contraction amplitude.

3.5. Human studies of somato-autonomic reflexes

Somato-autonomic reflexes are often invoked as the mechanisms underlying somato-visceral phenomena associated with spinal manipulative therapy. Therefore, to do justice to the topic of spino-visceral phenomena, it is also appropriate to review studies of changes in autonomic function, and changes in organ or tissue function which are reflective of autonomic activity but which do not yet have any clear clinical implications. Five papers which satisfied the inclusion criteria were identified (Table 5). Examples of autonomically-mediated responses to spinal manipulation include sweating, which has been measured indirectly by skin conductance (see for example, Moulson and Watson, 2006; Jowsey and Perry, 2010), static pupil diameter (Briggs and Boone, 1988) and edge light pupil cycle time (Gibbons et al., 2000).

The studies of skin conductance suggest that a sympatho-excitatory effect can be induced in the lower limbs with lumbar spinal manipulation (Perry et al., 2011), and perhaps in the hands following mobilization of the thoracic region (Jowsey and Perry, 2010). The study by Perry et al. (2011) compared two interventions, a ‘high-velocity low amplitude grade V manipulation’ of the lumbar spine, and a set of lumbar extension exercises (25 subjects per cohort). Both interventions produced a transient and statistically significant increase in skin conductance, with the response to manipulation being significantly larger than the response to exercise. The study by Jowsey and Perry (2010) compared the effects of a ‘grade III postero-anterior rotator joint mobilization technique applied to the T4 vertebra’ with the effects of sustained pressure to the same region (18 subjects per cohort). The sustained pressure resulted in no changes in hand skin conductance whereas the mobilization was accompanied by a slight increase in skin conductance in one hand ($p = 0.034$ per one way ANOVA) but not the other; these calculations based on percentage change from baseline.

Studies of the effects of spinal manipulation on the regulation of pupil diameter report mixed results. Upper cervical manipulation produced either increases or decreases in static pupil diameter in individuals within a cohort of eight subjects who received spinal manipulation, but no statistically significant change for the cohort as a whole, a control cohort of seven subjects who did not receive spinal manipulation also showed no change in pupillary diameter over the 4-day course of the study. (Briggs and Boone, 1988). On the other hand, in an uncontrolled study of a cohort of 13 young men, upper cervical manipulation was also associated with a decrease in edge light pupil cycle time ($p = 0.002$ per paired *t*-test);

Table 5
Human studies of somato-autonomic function.

Article	Setting	Demographics	Stimulation	Control	Outcome measure	Effect	Statistics	Notes
Moulson and Watson (2006)[a]	University	11 females, 5 males, 18–37 (mean = 23) years	C5/6 mobilization	Sham mobilization and no intervention	Hand skin conductance (SC) and skin temperature	No change in skin temperature, Increased SC with mobilization compared to no intervention	Repeated measures ANOVA	Randomized single group design, raw data not presented
Jowsey and Perry (2010)[a]	Unknown	13 males, 23 females, 18–35 (mean 23) years	Grade III T4 mobilization	Static pressure to T4	Skin conductance (SC)	Increased SC with HVLA in right hand but not left hand	ANOVA	Randomized parallel group design, raw data not presented
Briggs and Boone (1988)	Unknown	9 males, 6 females, 21–41 years	C/S HVLA ($n = 8$)	Sham HVLA ($n = 7$)	Pupillary diameter	Individual responses reported, but not mean group effects	No pre- vs. post comparison reported for groups	Non-randomized parallel group design
Gibbons et al. (2000)[a]	University	13 males, mean 18–29 (mean 24.2) years	C/S HVLA	None	Edge light pupil cycle time (ELPCT)	Decreased ELPCT with HVLA	*t*-Tests for pre- vs. post measures	Randomized, single group design
Perry et al. (2011)[a]	University	21 males, 29 females	L/S HVLA ($n = 25$)	Exercise ($n = 25$)	Skin conductance (SC)	Increased SC with HVLA vs. exercise	*t*-Tests for pre- vs. post measures	Randomized parallel group design

[a] Articles from authors’ collections.

Table 6
Somato-humoural studies.

Article	Setting	Demographics	Stimulation	Control	Outcome Measure	Effect	Statistics	Notes
Vernon et al. (1986)[a]	Chiropractic college	27 males, mean age 23 years	C/S HVLA ($n = 9$)	Sham HVLA ($n = 8$) and venipuncture control ($n = 10$)	Plasma beta-endorphin levels	Increased plasma endorphin level post HVLA in comparison to controls	Repeated measures ANOVA	Randomized parallel group design
Christian et al. (1988)[a]	Chiropractic college	20 males, 18–30 years	C/S or T/S HVLA ($n = 10$)	Sham HVLA ($n = 10$)	Plasma ACTH, beta-endorphin and cortisol levels	No change in ACTH, beta-endorphin, or cortisol levels in comparison to control group	Statistics not reported, Some missing data points	Non-randomized, parallel group design.
Brennan et al. (1991)	Chiropractic college	67 males, 32 females, mean 26.2 ± 5.5 years	T/S HVLA ($n = 42$)	Sham HVLA ($n = 38$) and soft tissue manipulation ($n = 19$)	Respiratory burst in polymorphonuclear neutrophils and monocytes, and plasma substance P	Increased respiratory burst and plasma substance P with HVLA versus control	Multiple *t*-tests	Randomized parallel group design
Brennan et al. (1992)	Chiropractic college	27 males, 19 females, mean age 25.9 ± 7.3 years	T/S HVLA	None	Respiratory burst in neutrophils ($n = 16$), and plasma substance P and TNF-a ($n = 30$)	Increased respiratory burst and plasma substance P and TNF-a	Paired *t*-tests of pre- and post measures	Two separate single cohort studies
Whelan et al. (2002)[a]	Chiropractic college	30 males of unknown age	C/S HVLA ($n = 10$)	Sham HVLA ($n = 10$), non-intervention control ($n = 10$)	Salivary cortisol	No significant differences in salivary cortisol levels between groups	Repeated measures ANOVA	Randomized parallel group design
Teodorczyk-Injeyan et al. (2006)[a]	Chiropractic college	36 females, 28 males, mean age 25 years	T/S HVLA ($n = 24$)	Sham HVLA ($n = 20$), Venipuncture control ($n = 20$)	Induced tumor necrosis factor, interleukin 1-beta and plasma substance P	Decreased tumor necrosis factor and interleukin 1-beta, no change in substance P	Paired *t*-tests of pre- and post measures	Randomized parallel group design
Teodorczyk-Injeyan et al. (2010)[a]	Chiropractic college	43 females, 31 males, mean age 25 years	T/S HVLA ($n = 27$)	Sham HVLA ($n = 25$), Venipuncture control ($n = 22$)	Pokeweed-induced and Interleukin-2-induced immunoglobulin G and M	Increased interleukin-2 induced immunoglobulin G and M production	Repeated measures ANOVA	Randomized parallel group design

[a] Articles from authors' collections.

i.e. the time it takes for the pupil to constrict and dilate following a brief exposure to light. Thus, the manipulative procedure appeared to accelerate the reflex response of the pupil, but it was not possible to resolve specific effects on the parasympathetic vs. sympathetic contributions to the reflex (Gibbons et al., 2000). While these are intriguing human studies involving direct measures of autonomically mediated responses to spinal manipulation, they provide little physiological insight into the therapeutic impact of spinal manipulation on visceral conditions.

3.6. Somato-humoural studies

The discussion so far has focused on studies of responses which are most often presumed to be mediated by the autonomic nervous system. However, responses to spinal manipulation may also be mediated by other mechanisms, and a few studies have specifically examined humoural and cellular mechanisms. Seven articles were identified which measured such responses to spinal manipulation in healthy cohorts (Table 6).

A controlled trial demonstrated that in a cohort ($n = 27$) of healthy young males cervical manipulation was associated with a statistically significant increase in plasma levels of the endogenous analgesic beta-endorphin at 5 min post-treatment when measured by radioimmune assay (Vernon et al., 1986). On the other hand, a study of the effects of lumbar manipulation with a cohort of asymptomatic subjects ($n = 20$) found no changes in beta-endorphin levels at 5 and 30 min following treatment, nor changes in serum cortisol (Christian et al., 1988). Whelan et al. (2002) also reported no changes in salivary cortisol levels attributable to cervical manipulation.

Early controlled studies also report that thoracic spinal manipulation was associated with increased immune function, as measured by zymosan-stimulated chemiluminescence, in neutrophils and monocytes, and increased production of substance P and tumor necrosis factor (TNF-α) at 15 min post treatment (Brennan et al., 1991, 1992). On the other hand, a later and larger ($n = 64$) controlled study using different methods of assay and a longer time frame (up to 2 h) found that in healthy adults thoracic manipulation was associated with a decrease in synthesis of TNF-α and interleukin (IL-1β), and no change in levels of substance P (Teodorczyk-Injeyan et al., 2006). The latter authors suggested that such down regulation of inflammatory cytokines as they observed was likely not mediated by substance P, but might have been the result of activation of the parasympathetic nervous system. Using a comparable design, they also demonstrated increased synthesis of immunoglobulin G and immunoglobulin M at 20 min and 2 h, respectively, following thoracic manipulation (Teodorczyk-Injeyan et al., 2010). Collectively, these results do not paint a cohesive picture of the effects of spinal manipulation on the complex interactions within the immune system. Nonetheless, they do demonstrate the phenomenon of immunological response to manual therapy in the cohorts described.

4. Conclusions

Notwithstanding substantial interest by manual medicine practitioners in somato-visceral disorders, there are relatively few basic physiological studies in humans to guide clinical practice. The corpus of somato-visceral studies is characterized by small cohorts of subjects, uncontrolled trials and one time pilot exercises with no subsequent follow-up. The field has been slow to adopt new technologies. Only recently have teams of researchers appeared with the sustained interest, expertise and resources to pursue meaningful programmes of research. The greatest number of physiological studies has focused on cardiovascular function, with few investigations of other organ systems. There is a justifiable interest in autonomically-mediated phenomena. However, somato-humoural and non-autonomic neural mechanisms of spino-visceral interactions remain largely unexplored.

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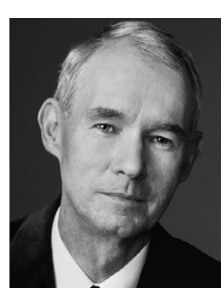

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