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## ► To cite this version:

Kathryn Hudson, Melia Condon, Rochelle Ackerley, Francis M Mcglone, Håkan Olausson, et al.. Effects of changing skin mechanics on the differential sensitivity to surface compliance by tactile afferents in the human finger pad. *Journal of Neurophysiology*, 2015, 114 (4), pp.2249-2257. 10.1152/jn.00176.2014 . hal-01599613

**HAL Id: hal-01599613**

**<https://hal.science/hal-01599613>**

Submitted on 2 Oct 2017

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# Effects of changing skin mechanics on the differential sensitivity to surface compliance by tactile afferents in the human finger pad

Kathryn M Hudson<sup>1,2</sup>, Melia Condon<sup>1,2</sup>, Rochelle Ackerley<sup>3</sup>, Francis McGlone<sup>4</sup>, Håkan Olausson<sup>3</sup>, Vaughan G Macefield<sup>1,5,6</sup> & Ingvars Birznieks<sup>2,5,6</sup>

<sup>1</sup>School of Medicine & <sup>2</sup>School of Science & Health, University of Western Sydney; <sup>3</sup>Dept of Clinical Neurophysiology, Göteborg University, Sweden; <sup>4</sup>Liverpool John Moores University, Liverpool, UK; <sup>5</sup>Neuroscience Research Australia; <sup>6</sup>MARCS Institute, University of Western Sydney;

Address for correspondence:

Prof Vaughan G Macefield

School of Medicine, University of Western Sydney, Locked Bag 1797 Penrith, NSW 2751, Australia

Phone: +61 2 4620 3779

Email: v.macefield@uws.edu.au

**Running title:** Responses of human tactile afferents during venous occlusion

## ABSTRACT

It is not known how changes in skin mechanics affect the responses of cutaneous mechanoreceptors in the finger pads to compression forces. We used venous occlusion to change the stiffness of the fingers and investigated whether this influenced the firing of low-threshold mechanoreceptors to surfaces of differing stiffness. Unitary recordings were made from 10 SAI, 10 FAI and 9 SAII units via tungsten microelectrodes inserted into the median nerve at the wrist. A servo-controlled stimulator applied ramp-and-hold forces (1, 2, 4 N) at a constant loading and unloading rate (2 N/s) via a flat 2.5 cm-diameter silicone disc over the centre of the finger pad. Nine silicone discs (objects), varying in compliance, were used. Venous occlusion, produced by inflating a sphygmomanometer cuff around the upper arm to  $40 \pm 5$  mmHg, was used to induce swelling of the fingers and increase the compliance of the finger pulp. Venous occlusion had no effect on the firing rates of the SAI afferents, nor on the slopes of the relationship between mean firing rate and object compliance at each amplitude, but did significantly reduce the slopes for the FAI afferents. Although the SAII afferents possess a poor capacity to encode changes in object compliance, mean firing rates were significantly lower during venous occlusion. The finding that venous occlusion had no effect on the firing properties of SAI afferents indicates that these afferents preserve their capacity to encode changes in object compliance despite changes in skin mechanics.

## INTRODUCTION

Compliance is the ability of an object to deform when subjected to a force; the perceptual attribute of this characteristic is referred to as softness. Humans require knowledge of the softness of objects, which they perceive via the activation of a population of low threshold mechanoreceptors in the skin of the hands. Sensory input from tactile afferents codes for the physical properties of handled objects (roughness, smoothness, softness, etc.) and controls the motor commands necessary to apply precisely the forces required to manipulate handled objects. The perception of softness is based on interactions between the compliance of the object and tactile afferents in the finger pad and must therefore depend on the relative differences in compliance of the object and the skin of the finger pad. We know that skin mechanics of the human finger pad alter as we age; this may be attributed to disorders producing edema of the extremities, or to the dehydration of the skin with age (Verrillo *et al.* 1999; Lévêque *et al.* 2000). Interestingly, as an individual ages there is a decrease in tactile spatial acuity, yet this is improved by application of moisturiser to the skin, indicating that changes in skin mechanics can indeed affect tactile sensibility (Lévêque *et al.* 2000). Recently, Friedman *et al.* (2008) performed a psychophysical study that investigated how humans perceive the softness of an object when silicone discs of differing compliance were passively applied to the the finger pad, i.e. relying on sensory information from the skin alone: subjects rated the object as ‘soft’ when the compliance of the silicone surface was less than that of the finger pad. Evidently, there is a relationship between perceptual softness, the ability of an object to conform to the finger pad and the encoding of tactile information related to object compliance.

We recently explored the capacities of tactile afferents located in the glabrous skin of the hand to encode differences in the compliance of objects brought into contact with the finger pad (Condon *et al.*, 2014). We showed that, of the four classes of tactile afferent in the glabrous skin of the human hand, the SAI afferents are the most sensitive class for signaling differences in compliance of an object: they exhibit a linear relationship between compliance and the number of spikes generated during the loading and plateau phases of a ramp-and-hold stimulus. Moreover, they have a high density in the finger pads (Johansson & Vallbo, 1979). The FAI afferents - which also have a high density in the finger pads (Johansson & Vallbo, 1979) - do contribute, but the slope of the relationship between the number of spikes generated during the loading phase and compliance is significantly lower than that of the SAI afferents. Conversely, the FAII and SAII afferents appear to play negligible roles in signaling changes in object compliance (Condon *et al.*, 2014).

The pulp of the finger pad undergoes considerable compression during contact and the application of force to/by an object, with the pulp being fairly compliant at low forces but becoming stiffer with higher forces (Westling & Johansson, 1987; Serina *et al.*, 1997; Pawluk & Howe, 1999). Because the pulp exhibits viscoelastic properties, including stress relaxation, creep and creep recovery, any change in compliance of the pulp will potentially influence the fingertip deformation that occurs with any stimulus (Pubols, 1982a-b; Serina *et al.*, 1997; Pawluk & Howe, 1999; Jindrich *et al.*, 2003). Given the interactions between the compliance

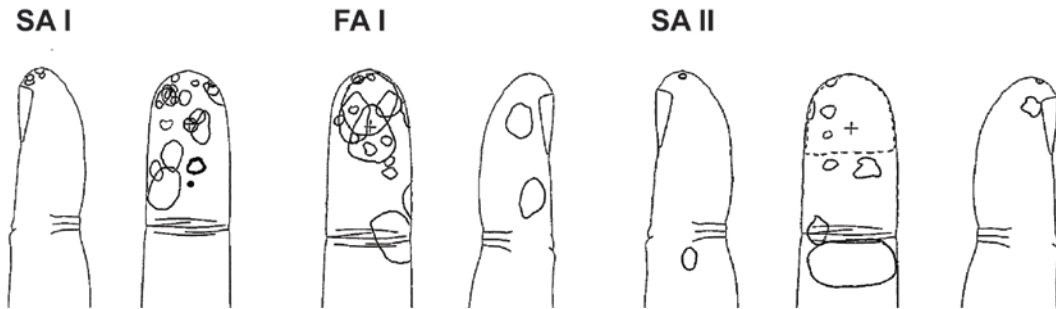
of an object and the finger pad referred to above, the purpose of the present study is to determine the effects of a change in finger pad compliance on the encoding of object compliance by cutaneous mechanoreceptors. We altered finger pulp compliance experimentally by inflating a sphygmomanometer cuff on the upper arm to a pressure of  $40 \pm 5$  mmHg. This will lower the rate of venous return from the upper limb, consequently altering the mechanical properties of the finger pulp by engorging the highly vascularised finger pads and thereby increasing their compliance. Given that mechanoreceptors in the finger pad eventually respond to deformation of the receptor-bearing tissue we propose that a change in skin mechanics produced by venous occlusion will affect the sensitivity of tactile afferents to controlled compression stimuli, and thereby affect their capacity to encode changes in object compliance.

## METHODS

A total of 23 (18-28 years) subjects (9 males) participated in the study, which was conducted with the approval of the Human Research Ethics Committee of the University of Western Sydney and undertaken in accordance with the Declaration of Helsinki. Each subject was seated in a comfortable, semi-reclined position throughout the duration of the experiment. The median nerve at the level of the wrist was located by application of weak cathodal stimuli (1.0-4.5 mA, 0.2 ms, 1 Hz), delivered by a 2 mm diameter probe via an optically isolated constant-current stimulator (Stimulus Isolator, ADInstruments, Sydney, Australia). A surface Ag/AgCl electrode placed on the dorsum of the wrist served as the anode. An insulated tungsten microelectrode, with a shaft diameter of 200  $\mu$ m and an exposed tip of  $\sim 5$   $\mu$ m (FHC, Bowdoin, Maine, USA) was then inserted percutaneously into the nerve at the level of the wrist; an uninsulated microelectrode inserted subcutaneously  $\sim 1$ cm away served as the reference electrode. Intraneural stimulation (0.02-1 mA, 0.2 ms, 1 Hz) via the recording microelectrode was then used to guide the microelectrode into a cutaneous fascicle of the nerve, as judged by the subjects' reports of radiating paraesthesiae. Once the tip of the microelectrode had entered a fascicle, indicated by cutaneous sensations at  $\leq 0.02$  mA, neural activity was amplified (20,000 X, 0.3-5.0kHz) using a low-noise headstage (NeuroAmpEX, ADInstruments, Australia) and the fascicular innervation zone explored by stroking and tapping the skin until a single mechanoreceptor was identified, the location of which was identified and marked on the subject's finger pad.

Afferents were classified as fast-adapting (FA) or slowly adapting (SA) to a sustained indentation, their receptive field size determined and mechanical thresholds measured by applying calibrated deformable monofilaments (Semmes-Weinstein Aesthesiometers, Stoelting, Chicago). Afferents were further classified as type I afferents, having small, well-defined receptive fields, or type II, with large, poorly-defined receptive fields: FAI afferents were particularly sensitive to stroking across the receptive fields, while FAII afferents responded to blowing across the receptive field and to mechanical percussion remote from the site; SAI afferents possessed a higher dynamic sensitivity than the SAII afferents and often responded with an off-discharge during withdrawal of indentation, while SAII afferents were sensitive to tensile strain in the skin produced by tangential stretch of the skin applied

manually remote to the receptive field (Macefield & Birznieks, 2009). The present data represents a subset of neural data obtained previously (Condon et al., 2014) in which we have specifically examined the effects of venous occlusion. The receptive field locations of all afferents are shown in Fig. 1.



**Fig. 1:** Receptive field locations for the FAI, SAI and SAII afferents.

### Stimuli

Nine silicone surfaces of linearly decreasing compliance (softness) were used – these were the same as those used in the magnitude estimates of softness study undertaken by Friedman and colleagues (2008). The surfaces (obtained from R.H. LaMotte) were made from two-component silicone rubber compounds mixed with varying amounts of diluent in order to achieve specimens of differing compliance, as described by previously (Friedman *et al.*, 2008) and embedded in 36 mm-diameter Petri dishes. The exposed surfaces were then powdered with talc to eliminate stickiness. In turn, each was applied to the surface of the finger pad using a holder attached to the shaft of a linear motor (Baldor, USA), mounted on the vertical (Z) axis of a three-axis linear gantry (Baldor, USA) that was used to locate the position of the stimulating motor in the X and Y axes. Displacement in the Z axis was measured via a linear variable displacement transducer (LVDT) and force was measured at the base of the silicone rubber holder using a sensitive tri-axial transducer (Nano F/T transducer, ATI Industrial Automation, USA). The compliance of the silicone surfaces was determined as the ratio of the amount of surface deformation to an applied force of 1 N (mm/N), and measured in progressive log units of 1.3, ranging from 0.21-7.59 mm/N (Friedman et al. (2008).

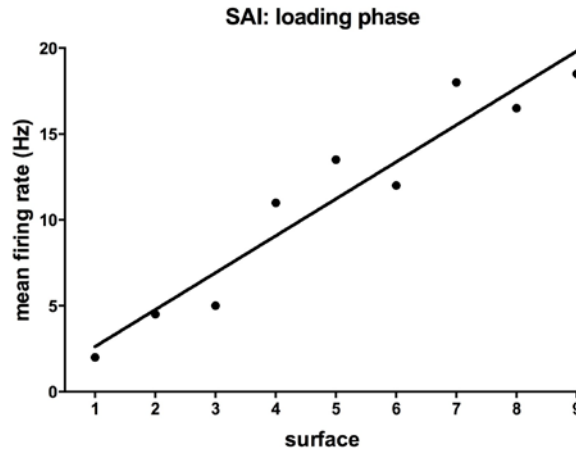
The surfaces, ranging from the softest (surface 1) to the hardest (surface 9), were presented in the following order: 9, 1, 5, 7, 3, 8, 2, 6 and 4. Each surface was presented to the centre of the finger pad of the receptor-bearing digit. The surface was first brought to within 0.5 mm of the finger pad under position control using the LVDT. The control system was then engaged in a force-control mode, in which the Z force at the probe tip provided the feedback to the control circuitry, and the first stimulus was presented causing the surface to contact the finger pad with a light contact force <0.2 N. Stimuli were then delivered under force-feedback control at a constant rate of 2 N/s and at three amplitudes - 1, 2 and 4 N, returning to the light contact force between the trapezoidal force profiles. The duration of the loading and unloading ramp was 0.5, 1 and 2 s for the 1, 2 and 4 N loads, with the duration of the plateau phase being 1 s for all loads; the interval between the three loads was 3.5 s. The entire sequence, including the generation of the initial contact force, was repeated for all surfaces, such that the time

between the end of one run of three amplitudes and the commencement of the next run required at least 50 s; this time included changing the stimulus surfaces. Each surface was applied once in the control condition and once in the occluded condition. Neural activity was sampled at 10 kHz and stored with force, torque and displacement signals (each at 400 Hz) using a computer-based data acquisition and analysis program (LabChart 7 software and PowerLab16S hardware, ADInstruments, Australia).

Venous occlusion was applied after a control sequence had been recorded. A sphygmomanometer cuff, fitted around the arm during the experimental setup, was inflated to a pressure of  $40 \pm 5$  mmHg. This pressure was chosen to prevent ischaemia of the hand while maintaining a force sufficient to retard venous return, thereby resulting in engorgement of the fingers and hence increasing the compliance of the fingerpad. A full sequence of stimuli was delivered five minutes following the commencement of venous occlusion, during which the cuff remained inflated. Once the sequence of stimuli was applied, the pressure was released from the sphygmomanometer cuff. Changes in compliance (mm/N) were measured from the recorded force and displacement signals during the plateau phase during the constant-force indentations at each of the three amplitudes (1, 2 and 4 N).

### **Data Analysis**

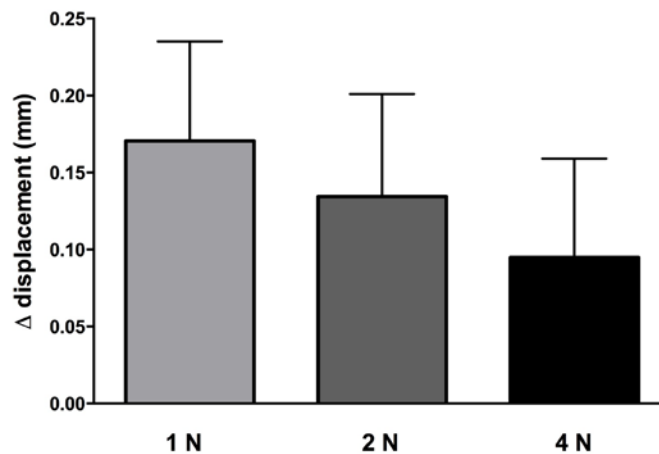
Spike activity was analysed using IGORPro 6.2 (WaveMetrics, Inc.). Single units were discriminated and an instantaneous frequency plot generated. Spontaneous activity was measured as the number of impulses during a one second epoch prior to the onset of the stimulus. The number of spikes was counted during the loading, plateau and unloading phases and the peak instantaneous frequency (the inverse of the shortest interspike interval), and the latency at which this occurred, was determined. Finally, the first spike latency was determined as the time difference between the onset of the ramp stimulus and the first detected impulse. For the spontaneously active SA II afferents, this was taken as the latency corresponding to the first short interspike interval following the onset of the ramp. The number of spikes was counted for each phase of the stimulus by collapsing the data into (i) baseline, (ii) loading phase, (iii) plateau phase and (iv) unloading phases. The loading and unloading ramp rates were constant (2 N/s) but because the amplitudes differed (1, 2, 4 N), the duration of the loading ramp increased with increasing amplitude (0.5, 1.0, 2.0 s). Accordingly, mean firing rates during the loading and unloading phases were estimated by dividing the total number of spikes by duration of the stimulation phase (normalized mean firing rate). An example of the relationship between normalized mean firing rate and surface compliance is shown for one SA I afferent in Fig. 2.



**Fig. 2:** Relationship between normalized mean firing rate and surface compliance during the loading phase for a single SAI afferent during delivery of the 4 N force ramps to the receptor-bearing finger pad at 2 N/s. The linear regression calculated for the data points is shown.

### Statistical Analysis

All analyses were performed using Prism 6 for Mac OS X (GraphPad Software, USA). Two-way analysis of variance (ANOVA) was performed to establish differences between the control and occlusion conditions at each amplitude, and any interaction between the two conditions and the nine silicone surfaces of differing compliance. Linear regression was used to measure the slopes of the relationship between normalized firing rate and object compliance.

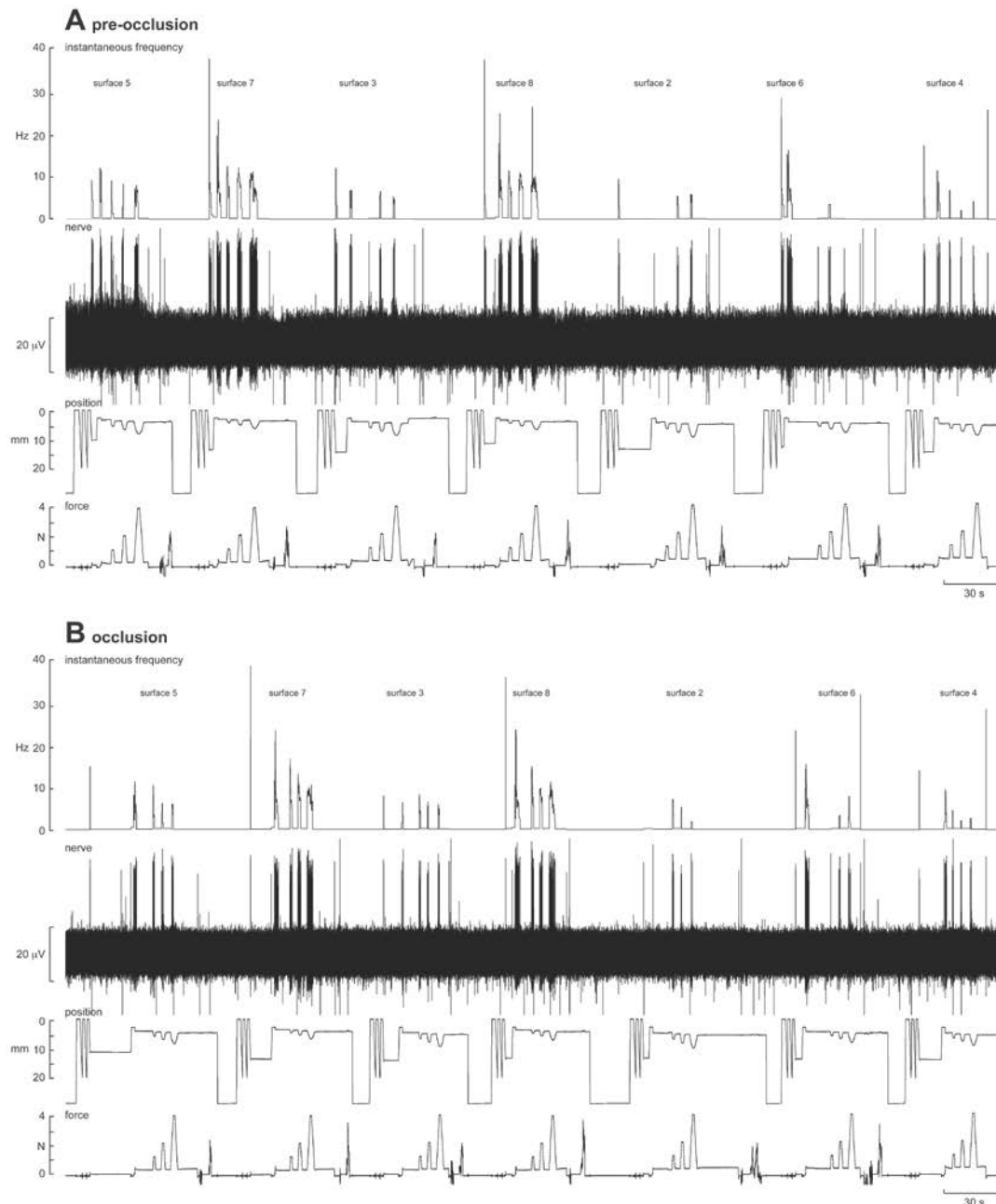


**Fig. 3:** Increase in displacement, measured during the plateau phase of the stimuli, following venous occlusion to 40 mmHg; data obtained from 9 subjects.

## RESULTS

Single unit recordings were made from 31 tactile afferents in the median nerve at the wrist, a subset of those reported previously (Condon et al., 2014): 10 slowly-adapting type I (SAI), 9 fast-adapting type I (FAI), 10 slowly-adapting type II (SAII) and two fast-adapting type II (FAII) afferents; the FAII afferents will not be considered further. Recordings were made before and five minutes following the onset of venous occlusion of the arm ( $40 \pm 5$  mmHg). Occlusion caused an overt engorgement of the finger pads but no subject reported discomfort.

The displacement of the stimulator probe required to reach the target force (1, 2 or 4 N) across the nine surfaces - ranging from the most compliant silicone disc (surface 1) to the least compliant (surface 9) - increased during venous occlusion (paired t-test;  $p=0.0012$ ,  $n=27$ ), indicating that compliance of the finger pulp had increased. After pooling all surfaces, the increase in displacement following venous occlusion could be seen to be higher for the 1 N than for the 4 N forces (Fig. 3); this can be explained by non-linear viscoelastic properties of the finger pulp, which is less compliant at higher forces.



**Fig. 4:** Experimental records from an SAI afferent to sets of trapezoidal compression ramps delivered to the pad of the receptor-bearing digit at 2 N/s via flat silicone discs of differing compliance. Responses to 1, 2 and 4 N forces are shown for seven of the nine compliant



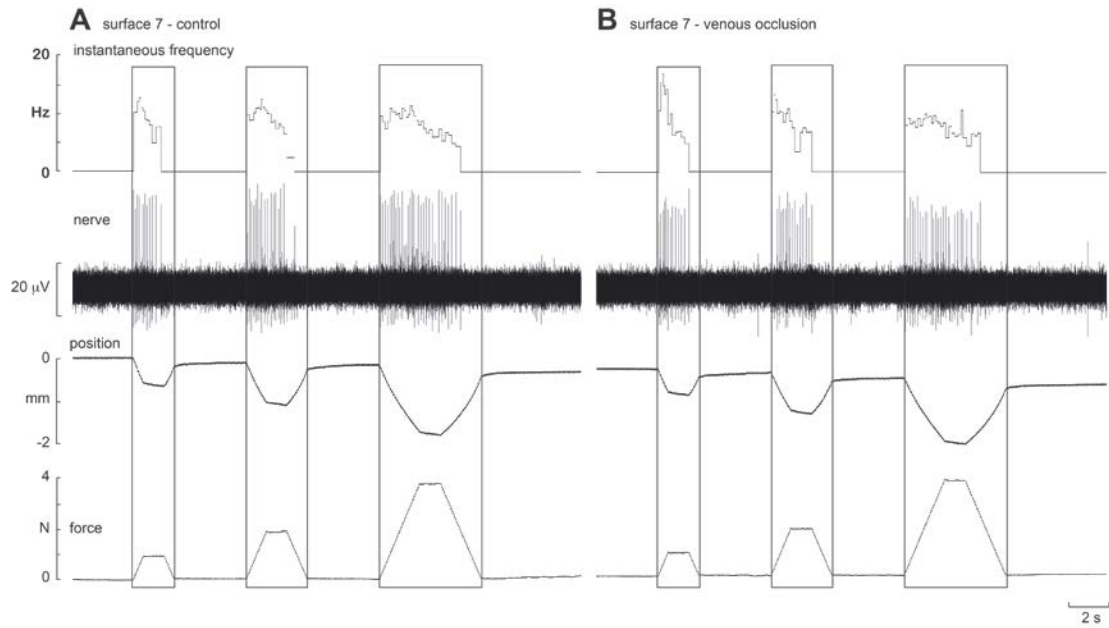
surfaces; the softest [surface 1) and hardest [surface 9] are not shown. Data are shown before (**A**) and after venous occlusion (**B**). The position trace, obtained from the LVST signal of the linear motor, indicates part of the initial searching paradigm, by which the control system operated under position control prior to engaging in force feedback on contact with the finger pad. Artifacts in the force trace after the three force ramps indicate manual exchange of one silicone disc to the next one.

<b>Force</b>	<b>Control 1 N</b>	<b>Occlusion 1 N</b>	<b>Control 2 N</b>	<b>Occlusion 2 N</b>	<b>Control 4 N</b>	<b>Occlusion 4 N</b>
<b>SAI</b>	0.94 $\pm 0.29$	0.93 $\pm 0.25$	0.84 $\pm 0.29$	0.99 $\pm 0.25$	0.81 $\pm 0.31$	0.92 $\pm 0.26$
<b>p</b>	<b>0.0019</b>	<b>0.0004</b>	<b>0.0048</b>	<b>0.0002</b>	<b>0.0108</b>	<b>0.0006</b>
<b>FAI</b>	0.39 $\pm 0.41$	0.08 $\pm 0.52$	0.67 $\pm 0.29$	0.23 $\pm 0.43$	0.66 $\pm 0.21$	0.34 $\pm 0.29$
<b>p</b>	0.3361	0.8769	<b>0.0221</b>	0.6031	<b>0.0028</b>	0.2415
<b>SAII</b>	0.36 $\pm 0.49$	0.20 $\pm 0.44$	0.35 $\pm 0.57$	0.48 $\pm 0.41$	0.50 $\pm 0.62$	0.70 $\pm 0.41$
<b>p</b>	0.4691	0.6508	0.5454	0.2437	0.4247	0.0948

**Table I:** Slopes of the relationship between surface compliance and mean firing rate during the loading phase for SAI (n=10), FAI (n=9) and SAII (n=10) afferents, before (control) and during venous occlusion. Significant p values are indicated in bold. Slopes were significant before and after occlusion for the SAI afferents, and were not affected by occlusion, while for the FAI afferents slopes were lower following occlusion. Slopes were flat for the SAII afferents and were not affected by occlusion.

### SAI Afferents

Experimental records from one SAI afferent, located in the finger pad of the index finger are shown before (A) and during (B) venous occlusion in Fig. 4. Three ramp-and-hold stimuli (1, 2 & 4 N) were applied via seven of the nine silicone discs. Occlusion had little effect on the responses to each of these surfaces. An example from another SAI afferent, also located in the finger pad of the index finger, is shown on an expanded time-base before and during venous occlusion in Fig. 5. Three ramp-and-hold stimuli (1, 2 & 4 N) were applied via one silicone disc (surface 7). Again, it is clear that occlusion had little effect on the responses to this surface; the same was true for the other 8 surfaces.

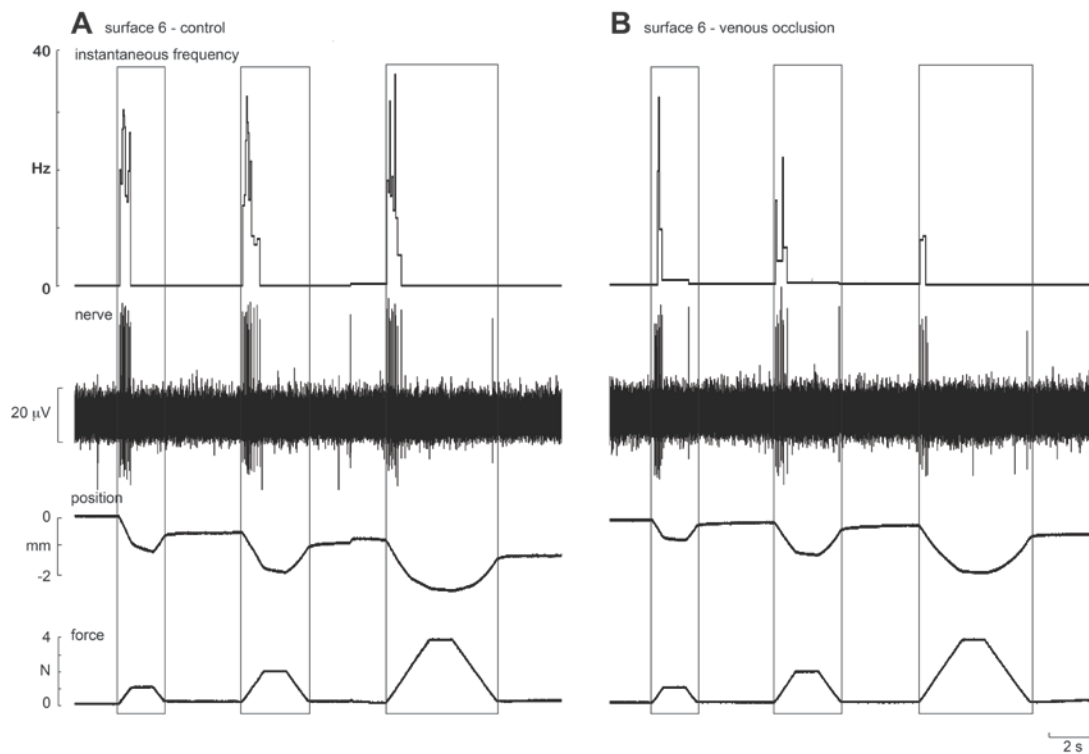


**Fig. 5:** Experimental records from an SAI afferent to trapezoidal compression ramps delivered to the pad of the receptor-bearing digit at 2 N/s. Responses to 1, 2 and 4 N forces are shown for a firm surface (surface 7) before (**A**) and after venous occlusion (**B**). Venous occlusion had no effect on the sensitivity of the afferent.

Source of Variation	% of total variation	p
<b>Mean Frequency (loading phase)</b>		
Interaction	0.91	>0.99
Surface	11.56	<b>&lt;0.0001</b>
Control vs. Occlusion	0.28	0.91
<b>Peak Frequency</b>		
Interaction	8.94	0.99
Surface	0.89	0.89
Control vs. Occlusion	1.62	0.27
<b>First Spike Latency</b>		
Interaction	5.96	0.9079
Surface	8.04	<b>&lt; 0.0001</b>
Control vs. Occlusion	6.53	<b>&lt; 0.0001</b>
<b>Peak Frequency Latency</b>		
Interaction	3.61	0.9862
Surface	3.16	0.0134
Control vs. Occlusion	34.63	<b>&lt; 0.0001</b>

**Table II:** Analysis of the influence of the 9 compliant surfaces, and the presence or absence of occlusion, and their interaction, for the firing parameters indicated. Two-way ANOVA for 10 SAI afferents. Significant p values are indicated in bold.

As described previously (Condon *et al.*, 2014), as a population the SAI afferents could faithfully encode changes in the compliance of an object brought into contact with the finger pad. Linear relationships between normalized mean firing rate and surface compliance at each amplitude were calculated from individual data as shown in Fig. 2. Quantitative data from the SAI afferents during the loading phase are shown in Table I. Mean normalized firing rate increased with increasing stiffness (decreasing compliance) of the surface during the loading phase, but at all amplitudes there were no differences in slope of the relationships before and during venous occlusion. Two-way ANOVA showed that there was no interaction between mean firing rate during the loading phase and the compliance of the surfaces and occlusion; however, venous occlusion did produce significant decreases in first spike onset latency, and the latency at which the peak frequency occurred (Table II). As expected, mean firing rates during the plateau phase were proportional to the amplitude of the force, but at each force venous occlusion had no significant effect on either average firing rate (calculated across all surfaces) or the slope of the linear regression between firing rate and compliance. Slopes during the unloading phase were flat (not significantly different from zero) and were not affected by venous occlusion.



**Fig. 6:** Experimental records from an FAI afferent to trapezoidal compression ramps delivered to the pad of the receptor-bearing digit at 2 N/s. Responses to 1, 2 and 4 N forces are shown for a firm surface (surface 7) before (A) and after venous occlusion (B). Venous occlusion reduced the sensitivity of the afferent.

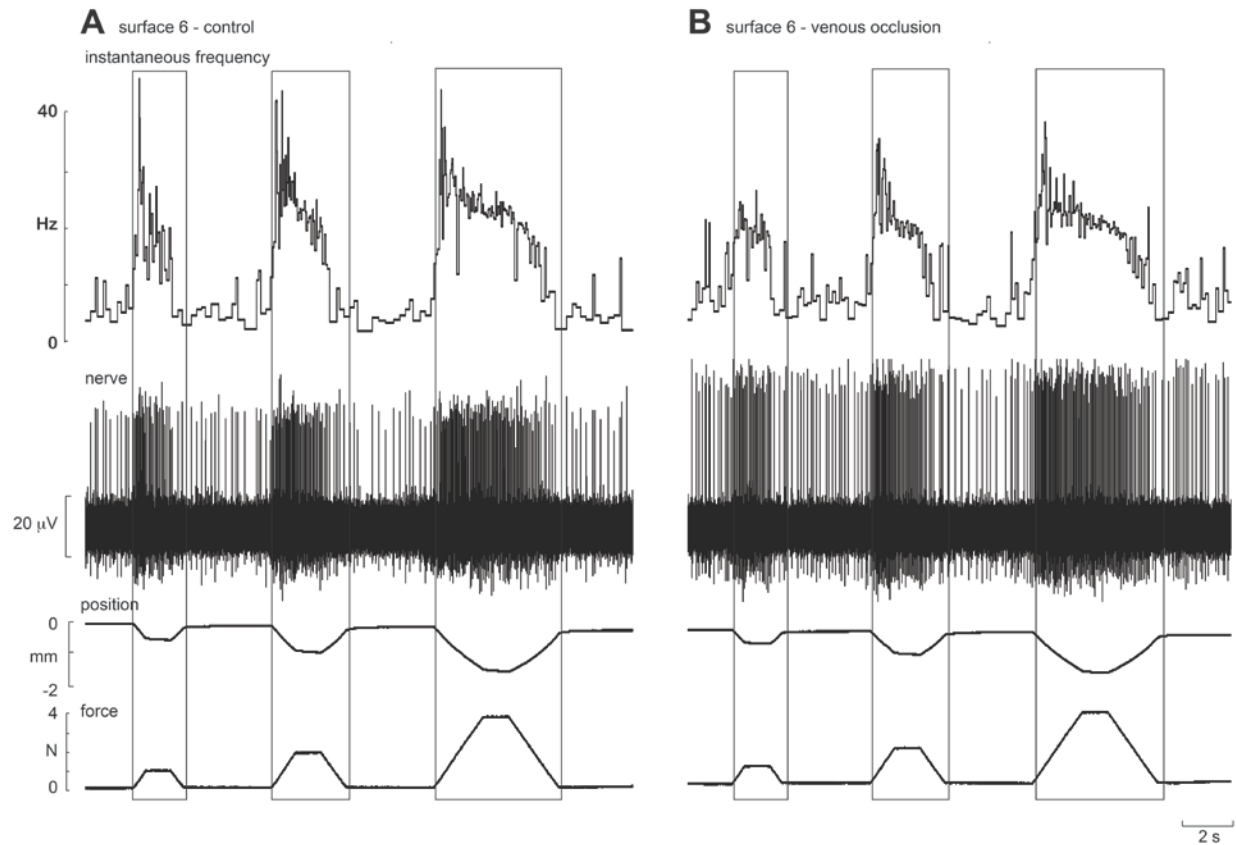
Source of Variation	% of total variation	p
<b>Mean Frequency (loading phase)</b>		
Interaction	1.33	> 0.9999
Surface	2.01	0.4241
Control vs. Occlusion	6.42	<b>0.0001</b>
<b>Peak Frequency</b>		
Interaction	2.90	> 0.9999
Surface	1.07	0.9275
Control vs. Occlusion	5.91	<b>0.0051</b>
<b>First Spike Latency</b>		
Interaction	4.88	0.9990
Surface	0.92	0.9146
Control vs. Occlusion	6.48	<b>0.0005</b>
<b>Peak Frequency Latency</b>		
Interaction	6.81	0.9672
Surface	1.92	0.5444
Control vs. Occlusion	16.05	<b>&lt; 0.0001</b>

**Table III:** Analysis of the influence of the 9 compliant surfaces, and the presence or absence of occlusion, and their interaction, for the firing parameters indicated. Two-way ANOVA for 9 SAI afferents. Significant p values are indicated in bold.

### FAI Afferents

Like the SA afferents, FAI afferents increased their discharge as a function of increasing stiffness during the loading phase; they were silent during the plateau phase. Figure 6 shows experimental records from one FAI afferent, located in the finger pad of the middle finger, during stimulation with one silicone disc (surface 6) before and after venous occlusion. At each amplitude it can be seen that firing rates were lower following occlusion. While more spikes were generated during the loading phase for the 4 N than the 2 or 1 N ramps, the normalized mean firing rates were actually higher for the 1 N loads. This can be explained by the fact that for a constant ramp rate (2 N/s), the 4 N loading ramp takes 2 s and the 1 N ramp 0.5 s, the normalized mean firing rate being calculated over different times. Given that most of the spikes occurred within the first 0.5 s, normalizing the firing rate will result in artificially different mean values. Nevertheless, it is apparent from Table I that venous occlusion significantly reduced the slopes at each amplitude (although the slope at the 1 N load was not significantly different from zero before occlusion, it was reduced by the occlusion). There was a significant increase in first spike latency ( $P=0.0005$ ), but two-way ANOVA uncovered no significant interaction between spike latency and surface or occlusion; the same was true for the latency at which the peak frequency occurred during the

loading phase (Table III). As noted above, there was a significant decrease in firing rate following venous occlusion ( $P=0.001$ ), but no significant interactions between surfaces and occlusion. Interestingly, peak frequencies during the loading phase were significantly higher during occlusion ( $P<0.0001$ ).



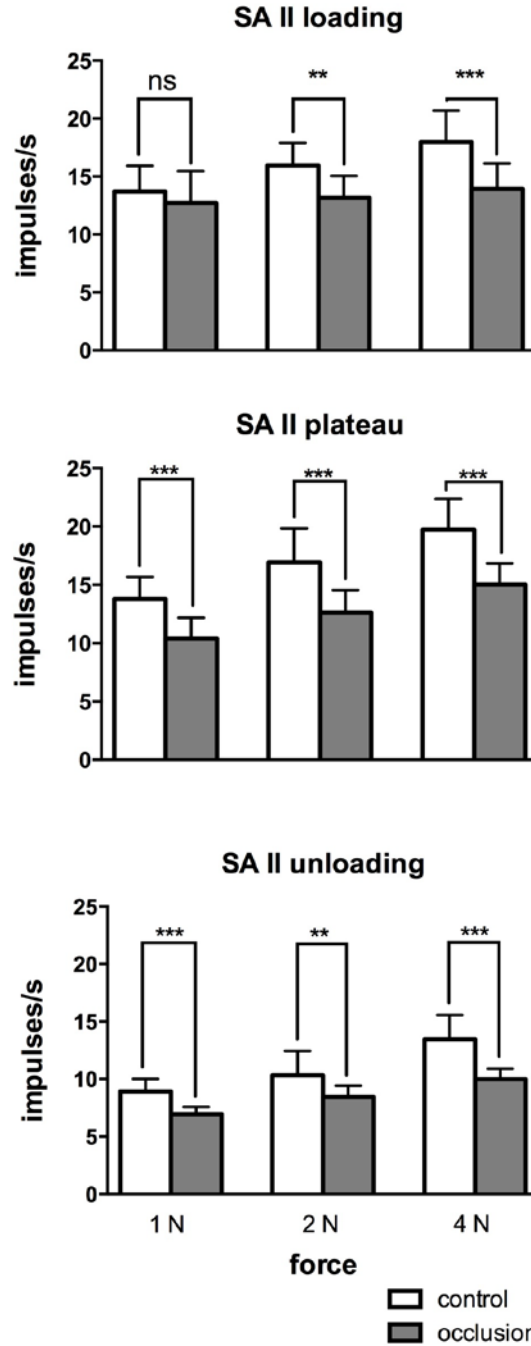
**Fig. 7:** Experimental records from an SAIL afferent to trapezoidal compression ramps delivered to the pad of the receptor-bearing digit at 2 N/s. Responses to 1, 2 and 4 N forces are shown for a firm surface (surface 7) before (A) and after venous occlusion (B). Venous occlusion reduced the sensitivity of the afferent. Note that the spike amplitude was slightly higher following occlusion due to a mechanical shift in the tip of the microelectrode.

Source of Variation	% of total variation	p
<b>Mean Frequency (loading phase)</b>		
Interaction	1.516	>0.9999
Surface	2.086	0.3753
Control vs. Occlusion	2.434	0.0752
<b>Mean Frequency (plateau phase)</b>		
Interaction	1.007	>0.9999
Surface	1.510	0.4942
Control vs. Occlusion	17.91	<b>&lt;0.0001</b>
<b>Mean Frequency (unloading phase)</b>		
Interaction	2.15	>0.9999
Surface	2.50	0.2058
Control vs. Occlusion	3.55	<b>0.0088</b>
<b>Peak Frequency</b>		
Interaction	2.62	> 0.9999
Surface	0.74	0.9346
Control vs. Occlusion	3.43	<b>0.0181</b>

**Table IV:** Analysis of the influence of the 9 compliant surfaces, and the presence or absence of occlusion, and their interaction, for the firing parameters indicated. Two-way ANOVA for 10 SAI afferents. Significant p values are indicated in bold.

### SA II Afferents

The SAI afferents showed the greatest changes during venous occlusion. Experimental records from one SAI afferent - located adjacent to the nail bed of the middle finger - during stimulation with one silicone disc (surface 6), before and after venous occlusion, are shown in Fig. 7. Like the FAI afferent illustrated in Fig. 6, firing rates of the SAI afferent were lower following occlusion. While the slope of the relationship between normalized mean firing rate and compliance was not significantly affected by occlusion, which was not significantly different from zero at any amplitude (Table I), at each amplitude the slopes were shifted downwards during the loading, plateau and unloading phases. This was because mean firing rates at each phase of the stimulus were lower during occlusion, as shown in Fig. 8. Two-way ANOVA showed that mean frequencies during the plateau and unloading phases were significantly lower following occlusion; mean firing rates were also lower during the loading phase, although this failed to reach statistical significance, and peak frequencies were significantly lower. At all phases there were no interactions between surfaces and occlusion (Table IV). Peak frequencies generated during the loading phase were also significantly lower during occlusion. There was no significant change in background discharge rate of the spontaneously active SAI afferents during occlusion.



**Fig. 8:** Mean ( $\pm$ SE) normalized firing rates of the SAI afferents before and during venous occlusion. Significant differences during the loading (A), plateau (B) and unloading (C) phases are indicated: \* =  $p < 0.05$ , \*\* =  $p < 0.01$ , \*\*\* =  $p < 0.001$ , ns = not significant (paired t-tests).

## DISCUSSION

We have shown that increases in the compliance of the finger pads, produced by vascular engorgement of the finger pulp by application of venous occlusion, affect the firing properties of some, but not all, classes of low threshold mechanoreceptor in the finger pad. SAI afferents were not affected by this manipulation whereas at all amplitudes the slopes of the relationship between mean firing rate and surface compliance were significantly reduced

for the FAI afferents, and significantly shifted downwards for the SAII afferents. That there were significant changes in the firing properties of the FAI and SAII afferents during venous occlusion indicates that there were indeed physiological changes in skin mechanics. We do not believe a change in blood flow *per se* will affect cutaneous mechanoreceptors, given that there is no change in blood delivery: no subjects reported paresthesiae either during or following release of the cuff, and pulsatile blood flow was maintained during the occlusion. A similar approach, inflation of a sphygmomanometer cuff proximal to the hand to 40 mmHg was used by Bowden & McNulty (2013) to increase compliance of the finger pad; these authors also reported no neural signs indicative of ischaemic block. We have previously shown that many tactile afferents in the finger pad exhibit pulse-related modulation of their discharge, owing to their proximity to blood vessels (Macefield, 2006), and demonstrated that any sympathetically-mediated effects on the firing properties of tactile afferents are exerted indirectly through changes in skin blood flow (Macefield & Elam, 2004).

We should point out that increasing the hydration of the outer layer of the skin, through application of a cosmetic moisturizer, has been shown to decrease the estimation of roughness (Verrillo *et al.*, 1999), but decrease two-point discrimination thresholds (Lévêque *et al.*, 2000; Bowden and McNulty, 2013). Moreover, moisturising the skin has been shown to reduce the mean firing rates of FA I afferents to brushing stimuli and of SA I afferents to sinusoidal indentation, at least in the hairy skin of the leg (Lévêque *et al.*, 2000); the authors suggested that hydration decreased the mechanical transfer function of the skin by reducing the elasticity of the stratum corneum. This is, of course, a different means of looking at the effects of skin compliance on tactile function than the approach adopted in the current study: we did not directly influence the softness of the outer layers of the skin but rather changed the compliance of the underlying pulp. Nevertheless, both studies emphasise the importance of skin mechanics on the transduction of a mechanical stimulus into a pattern of neural impulses by cutaneous mechanoreceptors.

### **Effects of changes in finger pad compliance on SA I afferents**

SAI afferents have small receptive fields and are found in high densities in the fingertips (Johansson & Vallbo, 1979), thereby enabling their ability to discriminate the shape, friction and texture of an object. Given their small receptive fields, engorgement of the finger pads during venous occlusion may not be expected to have as great an effect as seen in afferents with larger receptive fields (i.e. SAII afferents). The regression lines between mean firing rate and object compliance were not significantly different in control conditions and during venous occlusion conditions. This indicates that the firing rate of SAI afferents may be a very sensitive measure of changes in object compliance (Condon *et al.*, 2014) – one that is evidently not affected by changes in compliance of the finger pad itself. It may be that the histological structure and tissue environment of the Merkel discs, which are innervated by the SAI afferents, renders these mechanoreceptors less sensitive to changes in mechanical properties of the skin (Halata *et al.*, 2003).



### **Effects of changes in finger pad compliance on FAI afferents**

We had previously shown that the sensitivity of FAI afferents to changes in object compliance is lower than that for the SAI afferents (Condon et al., 2014). Moreover, unlike the SAI afferents - which can also encode static levels of object compliance (i.e. during the plateau phase) - the FAI afferents only respond during the loading phase, and to a lower extent during the unloading phase. The current data show that any contribution provided by the FAI afferents to encoding changes in object compliance is lost when the compliance of the fingers is increased: the slope of the regression line between mean firing rate and compliance became flat during venous occlusion. Additionally, the intersection of the linear regression lines (occurring between surfaces 4 and 5) is very interesting given the psychophysical investigation conducted by Friedman *et al.* (2008); these authors showed that when the finger pad of a subject was subjected to the same silicone surfaces used in the current study, the subject frequently identified the compliance of a surface as 'soft' when the true compliance of the surface was less than that of the subject's finger pulp. Within the range of stimuli used in the current study, the silicone surfaces that were approximately equivalent to the compliance of the human finger pulp were surfaces 4 and 5, at which point the regression lines intersect each other during the loading phase. Thus it can be assumed that the perception of softness/hardness of an object would not change due to the changes in mechanical properties of the fingertip pulp. This finding supports the results obtained by Bowden and McNulty (2013), who showed that venous occlusion to 40 mmHg had no effect on two-point discrimination.

### **Effects of changes in finger pad compliance on SA II afferents**

Occluding the venous return increased the compliance of the finger pads through engorgement of the finger pulp, in turn increasing the circumference of the finger pad; this would be expected to have had an effect on the background spontaneous discharge rate of the Ruffini organs (the mechanoreceptor endings of the SAII afferents) due to their sensitivity to tensile strain in the skin (Iggo & Muir 1969). However, although there was a small fall in the background firing rate of these afferents this was not significant. Nevertheless, venous occlusion did reduce the overall firing rates during the application of the stimulus, and shifted the slopes of the linear regressions between mean firing rate and compliance downwards. The net result of venous occlusion therefore was to decrease the responsiveness of the Ruffini organs to the mechanical stimuli. It is clear that venous occlusion caused an alteration in the skin mechanics of the finger pads, which will have caused a change in the internal environment surrounding the Ruffini organs. A detailed histological and mechanical model built to fit with our neurophysiological data would be required to address this. However, given that venous occlusion emulates what occurs in edema, it is likely that the sensitivity of SAII afferents to forces applied to the skin would be reduced in oedema. A recent psychophysical study tested the hypothesis that altering the skin mechanics using venous occlusion would affect the ability of a subject to perceive different forces applied by punctate stimuli (von Frey hairs) applied with varying forces: Bowden and McNulty (2013) concluded that venous occlusion had no significant effect on how humans perceive such stimuli. However, the results from the current investigation may be able to explain why Bowden and McNulty (2013) reached this conclusion. The stimuli these investigators used (von Frey

hairs) were more suited to stimulate type I afferents (i.e. SAI and FAI), which have small receptive fields and lower mechanical thresholds. SAII afferents have the highest threshold to mechanical stimulation, have very large receptive areas and respond to lateral skin stretch, so would have been less likely to be stimulated during this psychophysical study. Accordingly, it is likely that the results obtained by Bowden and McNulty primarily reflected the effects of venous occlusion on type I afferents, which – as we have seen – are little affected.

## **Conclusions**

This study has shown that experimentally-induced changes in skin mechanics affects the firing of some, but not all, classes of low-threshold cutaneous mechanoreceptor during the application of controlled compression stimuli to the finger pad. Specifically, we have shown that increasing the compliance of the finger pad by venous occlusion had no effect on the capacity of the SAI afferents to encode changes in object compliance, whereas the FAI afferents were no longer able to encode changes in compliance following venous occlusion. The SAII afferents exhibited a decrease in sensitivity to forces applied to the finger pad but, given that these afferents are insensitive to changes in object compliance, this would have little consequence. Whether these changes in skin mechanics affect the capacity to discriminate differences in softness remains to be determined.

## **Acknowledgements**

We are grateful to Prof Robert H LaMotte for providing the compliant surfaces.

## **Grants**

This work was supported in part by an NHMRC/ARC Thinking Systems grant to VGM. The authors declare no conflicts of interest.

## **REFERENCES**

- Birznieks I, Jenmalm P, Goodwin AW, Johansson RS. Encoding of direction of fingertip forces by human tactile afferents. *J Neurosci* 21: 8222-8237, 2001.
- Birznieks I, Macefield VG, Westling G, Johansson RS. Slowly adapting mechanoreceptors in the borders of the human fingernail encode fingertip forces. *J Neurosci* 29: 9370-9379, 2009.
- Blake DT, Hsiao SS, Johnson KO. Neural coding mechanisms in tactile pattern recognition: the relative contributions of slowly and rapidly adapting mechanoreceptors to perceived roughness. *J Neurosci* 17: 7480-7489, 1997.
- Bowden J, McNulty PA. Age-related changes in cutaneous sensation in the healthy human hand. *Age (Dordr)* 35:1077-89, 2013.
- Cauna N. Nerve supply and nerve endings in Meissner's corpuscles. *Am J Anat* 99: 315-350, 1956.
- Condon M, Birznieks I, Hudson K, Chelvanayagam DK, Mahns D, Olausson H, Macefield VG. Differential sensitivity to surface compliance by tactile afferents in the human finger pad. *J Neurophysiol.* 2014 111:1308-1317
- Darian-Smith I. *The Sense of Touch: Performance and Peripheral Neural Processes*, in *Comprehensive Physiology*, John Wiley & Sons, Inc. 2011.

Friedman RM, Hester KD, Green BG, LaMotte RH. Magnitude estimation of softness. *Exp Brain Res* 191: 133-142, 2008.

Goodwin AW, Browning AS, Wheat HE. Representation of curved surfaces in responses of mechanoreceptive afferent fibers innervating the monkey's fingerpad. *J Neurosci* 15: 798-810, 1995.

Goodwin AW, Wheat HE. Sensory signals in neural populations underlying tactile perception and manipulation. *Annu Rev Neurosci* 27: 53-77, 2004.

Greenspan JD, LaMotte RH. Cutaneous mechanoreceptors of the hand: experimental studies and their implications for clinical testing of tactile sensation', *J Hand Ther* 6: 75-82, 1993.

Hagbarth KE, Vallbo ÅB. Mechanoreceptor activity recorded percutaneously with semi-microelectrodes in human peripheral nerves. *Acta Physiol Scand* 69: 121-122, 1967.

Halata Z, Grim M, Bauman KI. Friedrich Sigmund Merkel and his "Merkel cell", morphology, development, and physiology: review and new results. *Anat Rec A Discov Mol Cell Evol Biol* 271: 225-239, 2003.

Iggo A. An electrophysiological analysis of afferent fibres in primate skin. *J Neural Transmiss* 24: 225-240, 1962.

Iggo A, Muir AR. The structure and function of a slowly adapting touch corpuscle in hairy skin. *J Physiol* 200: 763-796, 1969.

Jenmalm P, Birznieks I, Goodwin AW, Johansson RS. Influence of object shape on responses of human tactile afferents under conditions characteristic of manipulation', *Eur J Neurosci* 18: 164-176, 2003.

Jenmalm P, Johansson RS. Visual and somatosensory information about object shape control manipulative fingertip forces. *J Neurosci* 17: 4486-4499, 1997.

Jindrich DL, Zhou Y, Becker T, Dennerlein JT. Non-linear viscoelastic models predict fingertip pulp force-displacement characteristics during voluntary tapping. *J Biomech* 36: 497-503, 2003.

Johansson RS. Receptive field sensitivity profile of mechanosensitive units innervating the glabrous skin of the human hand. *Brain Res* 104: 330-334, 1976.

Johansson RS, Birznieks I. First spikes in ensembles of human tactile afferents code complex spatial fingertip events. *Nat Neurosci* 7: 170-177, 2004.

Johansson RS, Flanagan JR. Coding and use of tactile signals from the fingertips in object manipulation tasks. *Nat Rev Neurosci* 10: 345-359, 2009.

Johansson RS, Vallbo ÅB. Tactile sensibility in the human hand: relative and absolute densities of four types of mechanoreceptive units in glabrous skin. *J Physiol* 286: 283-300, 1979.

Johansson RS, Vallbo ÅB. Tactile sensory coding in the glabrous skin of the human hand. *Trends Neurosci* 6: 27-32, 1983.

Jones LA, Hunter IW. A perceptual analysis of stiffness. *Exp Brain Res* 79: 150-156, 1990.

Knibestöl M. Stimulus-response functions of slowly adapting mechanoreceptors in the human glabrous skin area. *J Physiol* 245: 63-80, 1975.

Knibestöl M, Vallbo ÅB. Single unit analysis of mechanoreceptor activity from the human glabrous skin. *Acta Physiol Scand* 80: 178-195, 1970.

LaMotte RH. Softness discrimination with a tool. *J Neurophysiol* 83: 1777-1786, 2000.

Lévêque JL, Dresler J, Ribot-Ciscar E, Roll JP, Poelman C. Changes in tactile spatial discrimination and cutaneous coding properties by skin hydration in the elderly. *J Invest Dermatol* 115: 454-458, 2000.

Lindblom U. Properties of touch receptors in distal glabrous skin of the monkey', *J Neurophysiol* 28: 966-985, 1965

Lindblom U, Lund L. The discharge from vibration-sensitive receptors in the monkey foot. *Exp Neurol* 15: 401-417, 1966.

Macefield VG. Cardiovascular and respiratory modulation of tactile afferents in the human finger pad. *Exp Physiol* 88, 617-625, 2003.

Macefield VG, Birznieks I. Cutaneous mechanoreceptors, functional behaviour, in MD Binder, N Hirokawa & U Windhorst (eds), *Encyclopedia of Neuroscience*, Germany, Springer, pp. 914-922, 2009.

Macefield VG, Elam M. Does sympathetic nerve discharge affect the firing of myelinated cutaneous afferents in humans? *Autonom Neurosci* 111: 116-126, 2004.

Mountcastle VB, Talbot WH, Sakata H, Hyvarinen J. Cortical neuronal mechanisms in flutter-vibration studied in unanesthetized monkeys. Neuronal periodicity and frequency discrimination. *J Neurophysiol* 32: 452-484, 1969.

Pawluk DT, Howe RD. Dynamic lumped element response of the human fingerpad. *J Biomech Eng* 121: 178-183, 1999.

Pubols BH Jr Factors affecting cutaneous mechanoreceptor response:I. Constant force versus constant displacement stimulation. *J Neurophysiol* 47: 515-529, 1982a.

Pubols BH Jr Factors affecting cutaneous mechanoreceptor response:II. Changes in mechanical properties of skin with repeated stimulation. *Journal of Neurophysiology* 47: 530-542, 1982b.

Serina ER, Mote CD Jr, Rempel D. Force response of the fingertip pulp to repeated compression - effects of loading rate, loading angle and anthropometry. *J Biomech* 30: 1035-1040, 1997.

Purves D, Augustine GJ, Fitzpatrick D. *Mechanoreceptors specialized to receive tactile information*, 2nd edn, Sinauer Associates, Sunderland (MA), 2001.

Srinivasan MA, LaMotte RH. Tactile discrimination of softness: abilities and mechanisms. in OJ Franzen, R.; Terenius, L. (ed.), *Somesthesia and the Neurobiology of the Somatosensory Cortex.*, Birkhauser Verlag, Basel, 1996.

Talbot WH, Darian-Smith I, Kornhuber HH, Mountcastle VB. The sense of flutter-vibration: comparison of the human capacity with response patterns of mechanoreceptive afferents from the monkey hand. *J Neurophysiol* 31: 301-334, 1968.

Vallbo ÅB, Johansson RS. Properties of cutaneous mechanoreceptors in the human hand related to touch sensation. *Hum Neurobiol* 3: 3-14, 1984.

Verrillo RT, Bolanowski SJ, Checkosky CM, McGlone FP. Effects of hydration on tactile sensation. *Somatosens Mot Res* 16: 352-360, 1999.

Westling G, Johansson RS. Responses in glabrous skin mechanoreceptors during precision grip in humans. *Exp Brain Res* 66: 128-140, 1987.