Surround Suppression in the Responses of Primate SA1 and RA Mechanoreceptive Afferents Mapped with a Probe Array

F. VEGA-BERMUDEZ AND K. O. JOHNSON
Department of Neuroscience and Krieger Mind/Brain Institute, Johns Hopkins University, Baltimore, Maryland 21218


INTRODUCTION

This is the second of two papers (Vega-Bermudez and Johnson 1999) describing the results of a study of slowly adapting type 1 (SA1) and rapidly adapting (RA) cutaneous mechanoreceptive afferents innervating the fingerpad employing a stimulus array with probes spaced 1 mm apart. The first paper reports an analysis of the responses evoked by single-probe indentations at 73 skin sites in each afferent’s receptive field (RF). This provided a detailed characterization of the RFs of single afferents, the effects of indentation amplitude, and estimates of the population responses evoked by single-probe indentations. The present paper reports an analysis of the responses evoked by multiple probes and the effects of changes in background indentation.

This study was motivated by previous studies in human and nonhuman primates that have shown that SA1 afferents respond much more vigorously to surface discontinuities, gradients, and curvature than to uniform skin indentation (Goodwin et al. 1995; Johansson et al. 1982; LaMotte and Srinivasan 1987b; Phillips and Johnson 1981a) and that they do so whether a surface is stationary (Cohen and Vierck 1993; Phillips and Johnson 1981a; Srinivasan and LaMotte 1987) or scanned across the skin (Blake et al. 1997; Johnson and Lamb 1981; LaMotte and Srinivasan 1987a,b). These SA1 response properties have been accounted for in quantitative detail by the assumption that their receptors respond to the local maximum compressive strain (Phillips and Johnson 1981b) or strain energy density (Grigg and Hoffman 1984; Khalsa et al. 1996; Srinivasan and Dandekar 1996), which are closely related strain components. In theory, sensitivity to these strain components confers response properties similar to those produced by surround inhibition in the CNS. In the present study we explore the suppressive effects of surrounding stimuli directly.

Previous studies of the responses of RA afferents to the same complex stimuli provide a less-consistent picture of their response properties. Some studies suggest that RA afferents respond simply to local skin indentation (Gardner and Palmer 1990; Goodwin et al. 1995; Phillips and Johnson 1981b) and that their responses are the same whether that indentation is part of a broad pattern of uniform indentation or is surrounded by regions of varying indentation. Other studies suggest that RA afferents, like SA1 afferents, are sensitive to some component of the spatial pattern of indentation (Goodwin et al. 1981; Johansson et al. 1982). Data from the study reported here support the conclusion that RAs are sensitive to spatial structure.

Both SA1 and RA afferents were studied with dual- and multiprobe stimuli whose indentation depths were generally limited to 10% of the probe spacing (i.e., to 100 μm) to minimize gross mechanical coupling between stimulus sites. Nonetheless, surrounding mechanical stimuli affected both SA1 and RA responses to a probe at the hot spot (HS, point of maximum sensitivity). Both afferent fiber types were also studied with a wide range of indentation patterns superimposed on varying degrees of background indentation, comparable to pressing a finger more or less firmly against a surface with raised surface features. The result was that background inden-
tation had no effect on SA1 and RA RFs or their responses over a wide range of background indentations.

METHODS

The neurophysiological and stimulus methods are described in detail in Vega-Bermudez and Johnson (1999). Briefly, experiments were performed on anesthetized monkeys (Macaca mulata) weighing between 3.0 and 5.0 kg. Single mechanoreceptive fibers were dissected from the median or ulnar nerves with methods described earlier (Mountcastle et al. 1972). Peripheral afferent fibers were classified as SA1, RA, or Pacinian according to their responses to a single, vibrating punctate probe (Talbot et al. 1968). Only fibers with RFs on the distal pads of the digits were studied.

The tactile stimulator consisted of probes, 0.5 mm in diameter, arrayed in a hexagonal pattern at 1.0-mm intervals (center to center). The entire array was 13 mm in diameter. All 155 probes except the central seven probes were stationary (see Fig. 1 in Vega-Bermudez and Johnson 1999); the central seven probes were driven by independent, servo-controlled linear motors (Schneider 1988), capable of 1,000-μm indentation with a 2-ms rise time. The array was lowered until all skin within a 4-mm radius around the central active probe (50 mm²) was in contact with the array; this background indentation was typically 1.6–2.0 mm below the point of first contact with the skin. The array was larger than any fingerpad, and no array placement resulted in contact with the edge of the array. Probes were indented for 200 ms followed by a 200-ms interstimulus interval. The first stimulus sequences, whose results are reported in a companion paper (Vega-Bermudez and Johnson 1999), established the location of the HS, which became the reference point for positioning the array in the studies reported here. Three stimulus sequences were used: a dual-probe sequence, a multiple-probe sequence, and a sequence aimed at studying the effects of background indentation.

Dual-probe sequence

The dual-probe stimulus sequence consisted of indentations by each of the seven active probes followed by simultaneous indentation with all possible pairs of the seven active probes (21) at each array placement. Indentation depths of 100 μm were used to minimize mechanical interactions between probes. This was repeated 10 times for a total of 280 trials at each placement of the array. The dual-probe sequence was presented 1) with the central active probe over the HS (Fig. 1A), 2) at six placements with one of six surrounding active probes over the HS (Fig. 1B), and 3) at six hexagonal placements with the central probe displaced from the HS by 577 μm (Fig. 1C). These placements sampled an area of 10 mm² with a resolution of 577 μm between adjacent points. All together there were 84 different paired stimulus sites separated by 1 mm, 42 by 1.7 mm, and 21 by 2 mm for a total of 147 different paired stimulus sites. In all of the analyses presented in this paper, R_{dual} represents the response evoked by two probes presented simultaneously, and R_{min} and R_{max} represent the minimum and maximum responses when the same two probes are presented singly.

Multiple-probe sequence

When the dual-probe sequence was completed, the array was re-centered on the HS (Fig. 1A), and the multiple-probe sequence was initiated. The stimulus sequence comprised indentations by the probe over the HS together with all 64 possible combinations of the surrounding 6 probes. Stimuli were presented in randomized blocks of 5 trials per stimulus (320 trials total; 64 probe combinations × 5 trials each). All indentation depths were 100 μm. After this, the multiple-probe sequence was repeated at four sites with the central probe displaced 1, 2, 3, and 4 mm from the HS along a line that included as much of the RF as possible.

Background-indentation sequence

The array was positioned with the central probe over the HS and lowered to the fiber’s initial background indentation as described previously. Stimuli were presented at this initial background indentation and again at background depths of 250, 500, 750, and 1,000 μm below the initial level. Three indentations (100, 200, and 300 μm) below the background depth were used.

The stimulus sequence at each background depth comprised 21 single-probe stimuli (7 probes × 3 indentation depths) and 81 dual-probe stimuli, each repeated 5 times for a total of 510 stimuli. The dual-probe stimuli comprised nine probe pairs (the central probe paired with each of the surrounding 6 probes and the 3 probe pairs straddling the central probe) presented at each of the nine possible pairings of 100-, 200-, and 300-μm indentation depths.

Indentation depth, force, and contact area

A large (20 × 30 mm), flat plate was driven into the skin of the distal pad of the index finger with a micrometer. Reaction force was measured with a digital force gauge (Omega Engineering DFG51–2, resolution 0.005 N). The difference between a flat plate and the array of densely spaced probes should be minimal insofar as the macroscopic biomechanics are concerned. Contact area at each indentation depth was measured by applying ink to the skin, sticking paper with adhesive on one side to the plate, and measuring the area of the
resulting fingerprint. The plate was retracted after every indentation and ink was reapplied. The plate was tilted distally just enough to avoid contact with the middle phalanx at maximum indentation. At that tilt angle (15–20°) the plate first contacted the skin at the midpoint of the distal pad, and the edge of the skin contact region came within 2–3 mm of the crease between the distal and middle phalanges.

RESULTS

Data were obtained from 24 SA1 and 26 RA afferents with RFs on the distal fingerpads. All stimuli were 200 ms long, and all stimuli involving two or more probes indented the skin by 100 μm unless stated otherwise to minimize mechanical interactions between probes. The total protocol was long, and some stimulus sequences were not run on all afferents. The numbers are specified when that was so.

Responses to two probes

Two probes were presented at a total of 540 locations within the RFs of 19 SA1s and 590 locations within the RFs of 21 RAs. The response to two probes (measured as impulse rate during the 200-ms stimulus period) was greater than the response evoked by either probe presented singly at only 10% of those locations. Eighty percent of all responses to two probes (called $R_{\text{dual}}$) lay between the minimum ($R_{\text{min}}$) and maximum ($R_{\text{max}}$) responses to the same two probes presented singly. The remaining 10% of dual-probe responses were less than $R_{\text{min}}$. These data are analyzed in greater detail subsequently.

DUAL PROBES WITH ONE PROBE AT THE HS. The effect of indentation with a second probe was studied with the array in 7 positions so that each of the seven active probes was over the HS (Fig. 1B). That yielded six different probe pairs where one was at the HS and the second probe was 1.0 mm from the HS, six where the second probe was 1.73 mm way, and six where the second probe was 2.0 mm away. All analyses were confined to probe pairs in which $R_{\text{min}}$ exceeded 5 impulses/s. Eighty-seven percent of all SA1 responses and 84% of all RA responses to two probes were suppressed relative to the response at the HS alone. Eleven percent of SA1 and 6% of RA responses to two probes were suppressed relative to the response at the HS alone. Eleven percent of SA1 and 6% of RA responses to two probes were even less than $R_{\text{min}}$. When the probe pairs were separated by 1.0 mm the response relative to a single probe at the HS was reduced 30% on average in SA1s and 23% in RAs (Fig. 2). The difference between SA1s and RAs was not large, but it was significant ($P < 0.01, t$-test). The distribution of $R_{\text{dual}}/R_{\text{max}}$ in single afferents is similar to the distribution for all afferents illustrated in Fig. 2.

The effects of probe separation and indentation depth were studied in 6 SA1s and 8 RAs. The effect of probe separation is illustrated in Fig. 3. As expected, the suppressive effect of a second probe is reduced when moved away from the primary probe. In these afferents $R_{\text{dual}}/R_{\text{max}}$ rose from 0.70 to 0.95 in SA1s and from 0.77 to 0.93 in RAs when the probe separation increased from 1 to 2 mm (ANOVA, $P < 0.003$).

It is surprising that at indentations of 100 μm, which are only one-tenth the spacing between probes, the interactions between probes should be so large. It is even more surprising that the effect was largely unaffected by the indentation depth for depths ranging from 100 to 300 μm. Response ratios ($R_{\text{dual}}/R_{\text{max}}$) for probes separated by 1.0 mm were compared at all nine combinations of 100, 200, and 300 μm at two probe sites (Fig. 4). A two-way ANOVA ($R_{\text{dual}}/R_{\text{max}}$ vs. fiber type and indentation depth) showed that indentation depth had no significant effect ($P = 0.19$) but fiber type did ($P < 0.001$), as expected from the previous analyses.

The overall result is that indentation by a second probe 1 mm from the HS reduces the responses of SA1 and RA afferents by 30 and 20%, respectively, and the effect is independent of the indentation magnitude at either probe ($\leq 300 \mu m$).

NEITHER PROBE ON THE HS. During the dual-probe stimulus sequence the tactile array was also placed with the central probe at six locations surrounding the HS so that no probe was directly on the HS (Fig. 1C). The suppressive effect of dual-probe stimulation was smaller when neither was at the HS (Fig. 5). The mean effects, $R_{\text{dual}}/R_{\text{max}}$, for all such probe placements were 0.890 and 0.885 for RAs and SA1s, respectively.
Responses to multiple probes

Next we studied how the response depended on the number of active probes. Twenty-two SA1 and 17 RA afferents were studied with the central probe positioned over the HS (Fig. 1A). Ten SA1s and 10 RAs were studied with the probe array positioned at varying distances from the HS (Fig. 1B). Probe indentation depth was 100 μm at all placements.

Central probe over the HS. When the array was positioned with the central probe directly over the HS, all possible combinations of seven probes that included the central probe (64 combinations) were presented (i.e., the central probe alone, 6 dual-probe stimuli comprising the central probe and the surrounding 6 probes, 15 triple-probe stimuli comprising the central probe and 2 of the surrounding 6 probes, etc.). All SA1 and RA responses were suppressed progressively by increasing numbers of probes (Fig. 6, top row). The SA1 suppressive effect was described much better as a multiplicative than as a subtractive effect (i.e., the relationship between impulse rates and number of probes was linear in logarithmic but not in linear coordinates, cf. Figs. 6 and 8). The RA suppressive effect was described approximately equally well as multiplicative or subtractive (cf. Figs. 6 and 8). The mean reductions in response per additional probe (the slopes of the curves in Fig. 6, bottom row) were 24 and 12% for SA1 and RA afferents, respectively. The decrement in response per additional probe ranged from 13 to 52% for SA1s and from 1 to 22% for RAS.

Central probe at varying distances from the HS. The stimulus sequence used at the HS was repeated with the central probe displaced by 1.0, 2.0, 3.0, and 4.0 mm from the HS along a line through the HS and the most distant point on the RF boundary. To remain consistent with the analysis at the HS, the analysis was restricted to multiple-probe stimuli that included the probe at the most active site (64 combinations). This was usually the probe nearest to the HS. The results for 10 SA1s and 10 RAs are shown in Fig. 7. A monotonic decline in SA1 and RA responses were suppressed progressively by increasing numbers of probes (Fig. 6, top row). The SA1 suppressive effect was described much better as a multiplicative than as a subtractive effect (i.e., the relationship between impulse rates and number of probes was linear in logarithmic but not in linear coordinates, cf. Figs. 6 and 8). The RA suppressive effect was described approximately equally well as multiplicative or subtractive (cf. Figs. 6 and 8). The mean reductions in response per additional probe (the slopes of the curves in Fig. 6, bottom row) were 24 and 12% for SA1 and RA afferents, respectively. The decrement in response per additional probe ranged from 13 to 52% for SA1s and from 1 to 22% for RAS.
and RA responses with increasing numbers of active probes persists to distances where there is little if any response to the 100-μm indentations. The average responses at each distance are shown in Fig. 8. A model based on exponential decline with increasing numbers of probes continued to fit the SA1 data closely for distances up to 3 mm; the effect of increasing probe numbers was constant at 24% per probe. The RA responses were fit well by a 12% reduction per probe at all distances.

Effects of background indentation depth

Before presenting the effects of background indentation on the neural responses, we present the results of a study of the relationships between indentation, contact force, and contact area in the human and the monkey. We do so for two reasons. First, although we manipulated the background indentation, background force is the more relevant variable because force is so commonly dictated by the manual task at hand. Therefore we need to understand the relationship between the indentation depths that we have used and contact force. Although many studies demonstrate the similarity in mechanoreceptive function between the two species, their fingerpad geometries are different.

The relationships between background indentation depth,
The effects of changes in background indentation depth were studied in 9 SA1 and 9 RA afferents by presenting 102 different stimuli at the array’s initial depth and then at background depths 250, 500, and 750 μm below the initial background depth. Some were studied at 1 mm below the initial depth as well. On the basis of the biomechanical data displayed in Fig. 9, we estimate that as the background indentation increased from 1.6 to 3.0 mm the reaction force increased from 0.3 to 3.0 N. The most important result was that both SA1 and RA responses to one and two probe stimuli were unaffected by background depth (ANOVA, SA1, $P = 0.76$; RA, $P = 0.27$). RF maps, based on indentation with a single probe were, like these quantitative results, unaffected by the background array depth. The RFs of a typical SA1 and RA afferent, mapped at three different background array depths, are shown in Fig. 10.

**DISCUSSION**

There were two main neurophysiological results. The first was that both SA1 and RA afferents are maximally responsive to indentation by a single point and that additional neighboring punctate stimuli have a graded, suppressive effect. The surpri-
followed by a noncompliant phase where reaction forces rose where indentation produced relatively slight reaction forces between the human and monkey force-displacement curves. To recognize complex, raised patterns (Loomis 1985), the skin is flattened and covers the entire stimulus area. Area of each • represents the impulse rate evoked at that point normalized by the impulse rate evoked at the HS.

The most interesting biomechanical result was the similarity between the human and monkey force-displacement curves. Both had a highly compliant phase between 0 and 2–3 mm where indentation produced relatively slight reaction forces followed by a noncompliant phase where reaction forces rose rapidly. The similarity suggests that this architectural feature is important in tactile sensing. We discuss this subsequently.

Previous studies

No previous neurophysiological studies of which we are aware have varied the number of probes or the background indentation. However, many studies have used complex spatial stimuli (Blake et al. 1997; Goodwin et al. 1995; Gardner and Palmer 1989; Goodwin et al. 1995; Johnson and Lamb 1981; LaMotte and Srinivasan 1996; Phillips and Johnson 1981a; Phillips et al. 1992; Sathian et al. 1989). All of those studies show that both SA1 and RA responses to a stimulus scanned across the HS are strongly suppressed by surrounding stimuli; Blake et al. (1997) showed that SA1 and RA responses to a single, raised scanned element begin to be suppressed when neighboring raised elements are closer than ~6 mm.

Three previous studies have indented the skin with stimuli more complex than a single point (Goodwin et al. 1995; Phillips and Johnson 1981a; Srinivasan and LaMotte 1987). The three studies show consistently that SA1 but not RA afferents encode the shape of the object indenting the skin, that SA1 afferents are very sensitive to spatial gradients close to the HS, and that RA afferents are sensitive only to the velocity of indentation over the HS. The study by Goodwin et al. (1995), in which the curvature of a spherical stimulus indenting the skin at the HS was varied, is perhaps most like the present study; gradually reducing curvature, as they did, causes the skin surrounding the HS to be stimulated progressively. They found that SA1 but not RA responses were affected by stimulus curvature. A surface with zero curvature (a flat surface) evoked an SA1 response that was, on average, one-sixth that evoked by a 3-mm diam spherical probe. If they had used a 0.5-mm diam probe as in this study the fraction would be even smaller.

A major difference between our results and these three previous studies is the RA surround suppression reported in this study. Goodwin et al. (1995) found that the responses of RAs were independent of stimulus curvature; the RAs in their study responded as vigorously to a flat surface as to a 3-mm diam probe. Phillips and Johnson (1981a) showed that RAs respond as vigorously to a flat surface as a narrow bar. The most likely explanation for the difference is that the indentation amplitudes in the previous studies were outside the RA dynamic range (the smallest indentation amplitude in the 3 previous studies was 500 μm). RA responses to rapid indentations >1–300 μm are strongly saturated (Blake et al. 1997; Vega-Bermudez and Johnhson 1999). The surround suppression may have appeared in this study but not in the others because of the small test amplitudes (100 μm) used in this study.

Biomechanics

The relationships between indentation depth, reaction force, and contact area when a flat surface is pressed into the skin of a fingerpad have been studied previously in the human (Pawluk and Howe 1999; Westling and Johansson 1987) and the monkey (Goodwin and Morley 1987). The human data shown in Fig. 9 are very similar to the previously published data. Goodwin and Morley’s data are restricted to indentations between 0.5 and 1.25 mm, but over that range their data and ours are similar.
The most interesting result in relation to tactile sensing is the similarity in the force-displacement curves between humans and monkeys. This curve has two phases, a highly compliant phase where the reaction forces are small and a noncompliant phase where the reaction forces rise very rapidly. The transition between these phases is ≤0.5 N. The subcutaneous hard tissues produce an absolute indentation limit of ~5 mm (unpublished observations). The tendency toward stiffening begins at small indentations, so factors other than compression against the underlying hard tissues evidently play a prominent role (Fung 1993). When subjects are asked to scan a surface the way they would ordinarily do so the skin is pushed into the noncompliant range (~1 N) (Johnson and Lamb 1981; Lederman 1974).

The significance of the highly nonlinear compliance function, we believe, the following. To sense the spatial pattern of a surface the skin must conform to the pattern. If the skin were stiff, we would have to press firmly to get the skin to conform to the pattern. Because the skin is so compliant over the first 2–3 mm, we can hold an object lightly and still sense surface form that varies by 2–3 mm. If a manual task requires high forces the skin is still free to protrude by 2–3 mm or possibly a bit more to follow the contours of the object held by the fingers. If monkeys were simply scaled-down humans the compliant range in the monkey would be less than one-half that in a human (the ratio of the volumes of the humans and monkeys in this study was $>10:1$, thus the linear scaling factor is $>2:1$), and the monkey’s ability to sense surface structure would be one-half that of a human. However, nonhuman primates and humans deal with the same tactile environment. The similarity of the force-displacement functions in the two species suggests that sensing features defined by elevations of 2–3 mm is important. A conspicuous difference between the monkey and human hand is the elevation of the distal pad. The exaggerated elevation of the distal pads of some prosimians is even more conspicuous (Jouffroy et al. 1993).

A significant outcome was the unexpected effect of ketamine. The decreased compliance may account for some ketamine effects on neurophysiological responses (Duncan et al. 1982). On biomechanical grounds alone, ketamine should not be used in neurophysiological experiments aimed at the normal response properties of neurons in the somatosensory system.

**Mechanisms**

Two different mechanisms might explain the attenuation observed when a second probe is placed in the RF. The attenuation could be caused by interactions between the neural signals arising in the distal branches of the afferent axon (Eagles and Purple 1974; Horch et al. 1974; Lindblom and Tapper 1966; Phillips and Johnson 1981b; Prosko and Gregory 1976). However, a strong argument against such a mechanism is that the suppressive effect of additional probes was as strong when the center of the array was 3 mm from the HS as when it was directly over the HS. At that distance the nearest active probe was within the RF of most SA1 afferents, but the rest were not.

The more likely mechanism is that both SA1 and RA afferents are responsive to some component of skin deformation other than simple indentation depth (Blake et al. 1997; Johnson et al. 1982; Johnson and Lamb 1981; LaMotte and Srini-vasan 1996) and that indentation with multiple probes distributes the stresses and strains required for the deformation and thereby reduces the stresses and strains at the transducer site(s) (Phillips and Johnson 1981b). When the probes are all at the same depth, the deformation is uniform, the shear strain is minimal, and the stress beneath each probe is only that required to deform the skin directly beneath the probe. When a single probe advances beyond the others it unloads neighboring probes, transfers the deformation load to itself, and creates a shear field around itself. If the transducer site(s) is within the strain field caused by the probe the result is a response to the displacement. When additional probes indent the skin the stresses and strains are redistributed. As the number of probes increases, the whole strain field tends toward that which prevails in uniform deformation. At first sight, it seems surprising that 100-μm indentations by probes spaced at ≥1 mm should interact so profoundly. On the other hand, it is clear that when one probe advances beyond the others by any amount it will progressively transfer the deformation load to itself, create an inhomogeneous strain field, and set up shear stresses and strains in the skin. Although 100 μm is a small displacement it is 10% of the probe spacing and therefore creates a substantial change in the geometry and the mechanics of deformation.


