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Salt taste inhibition by cathodal current

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Abstract

Effects of cathodal current, which draws cations away from the tongue and drives anions toward the tongue, depend on the ionic content of electrolytes through which the current is passed. To address the role of cations and anions in human salt tastes, cathodal currents of -40 to -80 μA were applied to human subjects' tongues through supra-threshold salt solutions. The salts were sodium chloride, sodium bromide, potassium chloride, ammonium chloride, calcium chloride, sodium nitrate, sodium sulfate, sodium saccharin, sodium acetate and sodium benzoate, which taken together encompass *salty*, *bitter*, *sour* and *sweet* taste qualities. The taste of NaCl, the *salty* and *bitter* tastes of the other chloride salts and the taste of NaNO_3 were inhibited, suggesting the current displaced stimulatory cations from *salty* and *bitter* receptors. However, *bitter* tastes of non-halide sodium salts were not inhibited, likely because other *bitter* receptors respond to anions. A discharge current at cathode-off ubiquitously evoked a *metallic* taste reminiscent of anodal taste used in clinical electrogustometry. Analogous effects on ambient NaCl responses were recorded from the hamster chorda tympani nerve. Increases in tastes of the saccharin and benzoate anions were not evoked during current flow, suggesting that cathodal current does not carry stimulatory anions to *sweet* receptors. Cathodal current may selectively inhibit *salty* and *bitter-salty* tastes for which proximal stimuli are cations.

Keywords

human gustation; taste inhibition; ionic stimulus coding; cathode-on; cathode-off

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1. Introduction

Although there is general acceptance of Tas2R and Tas1R G-protein coupled receptors for bitter and sweet tastes in humans and other mammals [1,2,3,4], a consensus has not emerged for receptors involved in human ionic tastes. Acid taste is associated with intracellular acidification and transient receptor (TRP) channel PDK2 [5,6,7]; but, species diversity has made the human *salty* and *bitter* tastes of salts more difficult to study. Rodent salt tastes include a prominent, specific Na^+/Li^+ component that depends on a functional epithelial Na^+ channel, ENaC [8,9]; but, ENaC plays little role in human *salty* taste transduction [10,11,12]. Moreover, rodent “bitter” contains perceptually distinct taste qualities, one for ionic stimuli that are bitter to humans and others for non-ionic stimuli that are also bitter to humans [13,14].

There are no human *salty*-taste inhibitors other than chlorhexidine, a substantive bitter bis-biguanide that may disrupt lingual epithelial ion flow [15,16,17]. Another way to disrupt ion flow is to apply electric currents to the tongue. Perceptions evoked by weak electric currents, “electric tastes” [18], depend on the direction of ion flow; that is, whether the anode (+) or cathode (−) contacts the tongue. Two questions still arise in the electric-taste literature. One is whether it is the current or electrolysis products, acids and bases, at anode and cathode (respectively) that are the actual electric-taste stimuli [19]. The other is whether the electrically evoked perception is a pure taste or combined activation of sensory nerves for taste (e.g., chorda tympani) and other sensory modalities (e.g., trigeminal) [20].

Localized clinical testing is conveniently done with the anode [21,22]. Short pulses of weak anodal current evoke a *sour-metallic*, *battery* taste whether current is applied through metal electrodes [23] or passed through a *salty* NaCl bridging solution [24,25]. Bridging solutions between electrode and tongue prevent accumulation of H^+ on the tongue surface, and revealed that current flow, not electrolysis products, generates battery taste. However, the ion non-specificity and ubiquitous battery taste quality of anodal current suggest that the current either non-specifically activates multiple receptors-channels and/or directly activates taste nerve endings.

Weak anodal current may stimulate the trigeminal nerve [20,26], which richly innervates taste-bud containing fungiform papillae on the tip of the tongue [27,28]; and a brief, anode-like, *metallic* taste appears at cathode-off when the current is only slightly higher [18]. The reaction to cathode-off is likely generated by a brief “anodal” capacitive discharge current [29]. The cathode itself evokes tastes only at much higher currents, making trigeminal involvement even more of a concern [18]. Remarkably, the possibility that weak cathodal currents would inhibit ongoing tastes of salt solutions was overlooked. Here, we present the results of three human studies on the ion-specificity of cathodal inhibition of salts with *salty*, *sour*, *bitter* and *sweet* taste qualities [30,31] to identify cation-dependent human tastes.

We also present, for comparison, the effects of weak electric currents applied through an ambient stimulating NaCl solution on neural activity of the hamster chorda tympani nerve. Rodent chorda tympani nerves contain mostly taste fibers and neural activity may be affected by application of current through sub-threshold bridging solutions; invariably, after release of cathodal current, an excitatory neural burst occurs [32,33,34,35].

2. Materials and methods

2.1. Human subjects

Thirty-four subjects, 12 women and 22 men, reporting normal taste function and mean age of 26 (S.D. 6) years, volunteered to participate. Subjects were recruited from students and staff of the University of Connecticut Health Center. The research protocol was approved by the

Institutional Review Board of the University of Connecticut Health Center. Subjects gave informed consent.

2.2. Stimulus and response variables

Stimulus chambers were used to contain ionic solutions in three experiments (A, B and C). Experiment A addressed cation specificity by having subjects simultaneously rate total intensity and identify NaCl, KCl, NH₄Cl, and CaCl₂ quality (Table 1). Experiments B and C addressed anion specificity with different psychophysical methods. In experiment B, subjects separately rated *salty*, *sour*, *sweet* and *bitter* intensities of NaCl, NaNO₃, Na⁺-acetate and Na⁺-saccharin (Table 2). In Experiment C, subjects separately rated total intensity and identified 0.5 M NaCl, NaBr, Na₂SO₄ and Na⁺ benzoate quality (Table 3).

A modified, portable, battery-operated electrogustometer (RION TR-06) provided 2-seconds of direct electrical current of $-40\ \mu\text{A}$ and $-80\ \mu\text{A}$. The two currents were used in Experiment A, $-80\ \mu\text{A}$ was used in Experiment B and $-40\ \mu\text{A}$ was used in Experiment C. Experiment A showed that the 2 currents had indistinguishable effects. The $-80\ \mu\text{A}$ was used in Experiment B to compensate for lower current density, given the larger area stimulated [21,36].

In Experiments A and C, salt solutions were presented in a 5 mL plastic tube with a 12-mm diameter opening to 10 subjects (mean age: 26.4 yrs, 7 men and 3 women) and 12 subjects (mean age: 27.3 yrs, 6 men and 6 women), respectively. In Experiment B, salt solutions were presented in a 28 mL plastic cup with a 4-cm diameter opening to 12 subjects (mean age: 24.1 yrs, 9 men and 3 women). The cathode contacted solutions via a steel screw inserted through the bottom of the vessels. The anode was held in the hand or skin-tact[®] to the wrist. The electric circuit was completed when the subject's tongue tip was placed into the solution. On each trial, subjects made 3 judgments within a short time—before, when the tongue tip was inserted into the solution, during the 2-second current application, and immediately after current termination. The experimenter vocally specified the time point for each decision. Stimuli and current levels were presented in random order in each session.

Experiment A, Chloride Salts. Without training, subjects simultaneously rated total intensity and identified quality [Figure 1] on each trial. Subjects, instructed to choose all appropriate qualities on the list, selected one quality 74%, two qualities 21% and three qualities 5% of the time. Two replicates for two salts were obtained in one session and 2 replicates for the other two salts in a second session. Subjects indicated choices and the experimenter recorded responses at the end of each trial.

Experiment B, Sodium Salts. After presentation of a reference solution (0.1 M NaCl for *salty*, 3.2 mM citric acid for *sour*, 0.1 M sucrose for *sweet* and 0.1 mM quinine-HCl for *bitter*), subjects rated *salty*, *sour*, *sweet* and *bitter* intensities separately for all four salts [Table 2] in each of 2 sessions. Subjects indicated choices and the experimenter recorded responses at the end of a trial.

Experiment C, 0.5 M Sodium Salts. After training with 0.3 M and 2.5 mM NaCl, subjects rated 2 replicates of total intensity [Figure 1] in one session. After presentation of reference solutions (0.3 M NaCl for *salty*, 10 mM citric acid for *sour*, 0.5 M sucrose for *sweet* and 1 mM quinine-HCl for *bitter*), subjects separately identified 2 replicates of each quality [Figure 1 list minus *burn*] in a second session. Subjects, instructed to choose all appropriate qualities, selected one quality 89%, two qualities 10% and three qualities 1% of the time. Subjects recorded choices on data sheets during a trial.

2.3. Data analysis

For each experiment, intensity data were analyzed with repeated-measures analysis of variance (ANOVA) and, if appropriate, followed by ANOVA for data subsets. For Experiment A—time, current, compound, concentration and replicate were the 5 factors. For Experiment B—time, current, compound, quality and replicate were the 5 factors. For Experiment C—time, current, compound, and replicate were the 4 factors. A significant interaction between time and current revealed that intensity ratings depended on current. A significant interaction between the factors of time, current and compound (or quality) revealed that the 4 compounds (or qualities) were affected differently by current. Post-hoc comparisons, $\alpha = 0.05$, used Neuman-Keuls (NK) tests.

Quality identities *during* and *after* current were compared to the same control time epochs; identities *during* and *after* current were also compared. Numbers of subjects who identified each individual quality (whether alone or in a doublet or triplet) for each stimulus replicate were counted. The *salty* identity was expected to decrease and, correspondingly, *no-taste* expected to increase *during* current. *Metallic* was expected to increase after cathode-off. *Salty*, expected to decrease *during* current, was expected to rebound with current release. Average numbers of subjects identifying qualities chosen by > 10% of the subjects were compared with within-subjects *t* tests. The α level, 0.05, was adjusted for multiple comparisons with a Bonferroni correction [37].

2.4 Hamster chorda tympani nerve

Using an animal protocol approved by the Animal Care Committee of the University of Connecticut Health Center, electrophysiological recordings were obtained from the whole chorda tympani nerve (CT) of the golden hamster (*Mesocricetus auratus*) [38]. Male hamsters (>100 grams) obtained from Charles River Laboratories (Wilmington MA) were deeply anesthetized with sodium pentobarbital (7.5 mg/100 g, initially, plus 25% supplements). The nerve, approached from beneath the mandible, was dissected free and looped over a nichrome-wire recording electrode positioned above musculature contacted by the reference electrode. Rectified, squared, integrated records of differentially amplified neural responses were displayed on a strip chart recorder. Solutions were delivered to the anterior portion of the tongue, enclosed in a glass chamber, from an overhead funnel at ~1.5 mL/sec. Constant current was applied across a nichrome-wire electrode inserted into the chamber, above but not in contact with the tongue, and a stainless steel pin inserted into rear leg musculature [39]. Water and 0.1 M NaCl, a bridging solution, were alternately flowed through the tongue chamber, covering tongue and electrode. Five-second epochs of anodal (+9 μ A) or cathodal (−9 μ A) current were applied during ongoing NaCl-evoked CT neural activity, which has an initial transient and, notably, a lengthy tonic component in rodents [39].

3. Results

3.1. Chloride salts, total intensity and quality identity— Experiment A

Before current was applied, high concentrations of the four chloride salts had a *medium* average intensity of $5.8 \pm .5$ and low concentrations had a *weak* average intensity of $2.6 \pm .5$, $F(1,9) = 159.4$, $p < .000001$ (Figure 1, Table 1). As the initial 5-way ANOVA revealed no difference between −40 μ A and −80 μ A, data for the two currents were combined. Two 4-way ANOVA were used to separately evaluate data for high and low stimulus concentrations because of the interaction between concentration, compound, time and current ($F(6, 54) = 3.98$, $p = .002$).

High concentration–Intensity (Figure 2–red circles)—Although intensities differed before current application (Table 1), $F(3, 27) = 4.84$, $p = .008$ (0-sec time points), cathodal current similarly affected the intensity of high concentrations of the 4 salts ($F(2,18) = 35.08$,

$p = .000001$). During current (2-sec time points), average intensity ratings decreased from a control value of 4.6 (gray line) to 3.3 ($p = .0002$) and, after current was released (4-sec time points), average intensity increased above the control of 5.0 to 5.4 ($p = .01$).

Low concentration–Intensity (Figure 2–blue squares)—Intensities differed before current application, $F(3, 27) = 4.28$, $p = .01$, (Table 1) and average intensity was affected by current ($4,36 = 10.62$, $p < .00001$), decreasing ($p = .01$) during current from 2.0 to 1.6 (2-sec time points) and increasing ($p < .0008$) above the 2.2 control to 2.9 after current was released (4-sec time points). Current affected low concentrations of the 4 compounds somewhat differently, $F(6,54) = 3.90$, $p = .003$; all four stimuli increased in intensity after current release, but only KCl (2.4 to 1.8) and NaCl (2.2 to 1.6) decreased significantly in intensity during current. Note individual significant comparisons are encircled by gray ovals

Stimulus Quality–During current (Figure 3)—Counts of quality identifications by the 10 subjects for the 8 salts revealed that *salty*, *bitter*, *no-taste*, and *tingle* identities were chosen by more than 10 % of the subjects (per presentation) in the during current (0, –40 or –80 μ A) epoch. Each common identity was affected during current. Average numbers of subjects identifying either *salty* or *bitter* decreased $t(7) = 6.09$, $p = 0.0005$; and *no taste*, $t(7) = 7.23$, $p = .0002$, and *tingle*, $t(7) = 8.62$, $p = .0003$, increased compared to the 0- μ A control (Figure 3). Also, *no taste* ($4.0 \pm .37$ vs. $2.1 \pm .22$, $t(7) = 3.72$, $p = .007$) and *tingle* ($5.2 \pm .28$ vs. $4.0 \pm .34$, $t(7) = 2.81$, $p = .03$) were identified more often for low than high concentrations.

Stimulus Quality–After current—The average number of subjects identifying *metallic*, 0.81 during current, increased from a 0.88 control to 2.94 subjects after current release, $t(7) = 6.19$, $p = .0005$. There was no change in the subjects' use of *salty*, *bitter*, and *tingle* in the *after* epoch. Neither *sweet*, *sour* nor *burn* was used by more than 10 % of the subjects *after* or *during* current.

Thus, effects of current on chloride salts did not depend on the counter cation. During cathodal current, total intensity of the *salty-bitter* NaCl, KCl, NH_4Cl , and CaCl_2 decreased by 25%, *salty-bitter* was identified less often, and *no-taste* and *tingle* were identified more often, especially at low concentrations. After current release, intensity increased by 16% and *metallic* was identified more often.

3.2. Sodium salts, quality intensity–Experiment B

The sodium salts had distinct quality profiles before current was applied; saccharin was moderately *sweet* and weakly *bitter*; the other stimuli were *salty*, *sour* and *bitter*. NaCl had a medium-strong *salty* intensity, higher than the salty intensity of either NaNO_3 or Na acetate ($p = .0001$) (Table 2). The initial 5-way ANOVA revealed that compound and quality interacted with time and current ($F(18,198) = 3.11$, $p = .00005$); therefore, two sets of 4, 3-way repeated measures ANOVA were run. One set separately evaluated the 4 taste qualities. The 2nd set separately evaluated the 4 sodium salts.

Taste Quality Intensity—The effect of current on *salty*, $F(2,22) = 14.8$, $p = .00009$, depended on the salt, $F(6,66) = 9.19$, $p = .000001$ (Figure 4). During current (2-sec time points), NaCl, Na acetate and NaNO_3 were less *salty* ($p < .01$), and, after current release (4-sec time points), NaCl was significantly more salty ($p = .03$) than respective 0- μ A controls. The four salts average *sour* intensity was reduced from 2.3 to 1.8 during current, $F(2,22) = 5.30$, $p = .01$; whereas, the four salts average *bitter* intensity increased after current release from 2.5 to 3.0, $F(2,22) = 5.62$, $p = .01$. Average *sweet* intensity was unaffected.

Salt Intensity—The effect of current on NaCl, $F(2,22) = 12.9$, $p = .0002$ (Figure 5A), depended on the quality, $F(6,66) = 7.52$, $p = .000004$. The strong *salty* taste of NaCl was decreased most during current and rebounded after current release (Figure 4). During current, weaker *sour* (from 2.9 to 1.6, $p = .0001$), *sweet* (from 1.4 to 0.6, $p = .0005$), and *bitter* (from 2.6 to 2.2, $p = .02$) tastes of NaCl also decreased. The effect of current on NaNO_3 , $F(2,22) = 3.94$, $p = .03$, did not depend on quality; the average four-quality taste of NaNO_3 decreased during current but did not rebound after current release (Figure 5A). In contrast, unaffected during current, the four-quality intensities of Na-acetate, $F(2,22) = 6.84$, $p = .005$, and Na-saccharin, $F(2,22) = 4.01$, $p = .03$, increased after current release (Figure 5B).

Thus, the effects of cathodal current on sodium salts depended on the counter anion. Combined, NaCl and NaNO_3 taste intensity decrements during current were *salty*, *sour* and *sweet*; whereas, combined Na-acetate and Na-saccharin taste intensity increments after current release were *bitter*, *sour* and *salty*.

3.3. 0.5 M Sodium salts, total intensity and quality identity—Experiment C

Before current was applied, NaCl and NaBr had *medium* average intensities, Na_2SO_4 and Na-benzoate had *weak* average intensities, $F(3,33) = 14.4$, $p < .000004$; and subjects most often identified NaCl, NaBr and Na_2SO_4 as salty, and Na-benzoate as sweet (Table 3).

Total Intensity (Figure 6)—Salt intensity depended on current ($F(2,22) = 10.85$, $p = .0005$); but the individual salts were affected differently ($F(6,66) = 2.48$, $p = .03$). Average halide intensity decreased from 5.1 to 3.5 during current ($p = .001$) (Figure 6A); but average non-halide intensity, unaffected during current, increased above the 2.9 control to 4.6 ($p = .0002$) after current release (Figure 6B).

Stimulus Quality— during and after current epochs—A control average 7.8 subjects identified NaCl, NaBr and NaSO_4 as *salty* (Table 3); during current this was reduced to 4.0 subjects ($t(5) = 4.8$, $p = .005$); *salty* identities rebounded to 6.5 subjects after current release ($t(5) = 7.3$, $p = .0007$) (Figure 7A). *Tasteless* identities rose to an average $3.5 \pm .2$ subjects during current compared to control $1.3 \pm .3$ subjects, $t(5) = 7.05$, $p = .0009$. *Bitter* identities, used by more than 10 % of the subjects before current for NaBr, Na_2SO_4 and Na-benzoate, were unaffected by current. And, neither *metallic* nor *tingle* was used by more than 10 % of the subjects before or during current. The *metallic* identity appeared after current release; it was used by 2.8 subjects on average, compared to the average control 0.4 subjects ($t(7) = 9.0$, $p = .00004$) (Figure 7B).

Thus, effects of current on 0.5 M sodium salts depended on the counter anion. During cathodal current, total intensity of NaCl and NaBr decreased 39%, salty was identified less often, and *no-taste* was identified more often. After current release, *salty* identifications rebounded. The intensity of Na_2SO_4 and Na-benzoate were unaffected during current, but after current release, increased by 59% when a *metallic* identity appeared.

3.4. Chorda tympani nerve recording

A near duplicate of the protocol that we used in humans was applied to the hamster taste nerve, with the highly effective salt solution serving as the current bridge. Figure 8 presents the recording of 2.4 minutes of neural activity elicited in the hamster CT by 0.1 M NaCl, upon which 5-sec epochs of anodal (+9 μA) or cathodal (−9 μA) current were superimposed. Especially note the neural activity decrements during cathodal current: 2, 5-sec. inhibitions to baseline (green dotted line) for the 2, 5-sec. −9 μA applications. Thus, inhibition of hamster neural taste activity occurs during cathodal current application as did perceptual inhibition in humans (Figure 2A, Figure 5A, Figure 6A). Also note the transient increases in CT neural

activity, above the tonic response to NaCl (red dotted line), occurring after current was turned off. The neural off-response transiently overshoot the 0-current, tonic ambient response of the nerve. Likewise, in humans, the perceptual intensity of NaCl overshoots the 0-current control (Figure 6A). The epoch after current release is associated with emergence of metallic taste and return of salty taste (Figure 4, Figure 7) in humans. The 5-second, +9 μ A anodal current through 0.1 M NaCl elicits additional initial transient and tonic neural responses superimposed on NaCl elicited tonic activity, anodal responses quite similar to neural responses elicited without tonic activity evoked by a bridging solution [33].

4. Discussion

This is the first study of the inhibition of ongoing ionic tastes by cathodal current. Cathodal inhibition is stimulus-specific, primarily affecting electrolytes with a salty taste; and after current release, a rebound in *salty* taste identity is accompanied by a transient *metallic* taste, likely due to an “anodal,” tissue-capacitance discharge current [29]. Cathodal effects are unlike the singular, *metallic* identity elicited with anodal stimulation [18,23] used to map regional taste dysfunction in humans [22,36]. Furthermore, despite species differences, surprisingly similar effects were for the first time illustrated in ambient responses of the hamster chorda tympani nerve (CT). Human CT NaCl responses to continuous stimulation adapt much more rapidly toward baseline [40] than hamster CT responses (Figure 8); and humans do not share with rodents a strong Na^+/Li^+ -specific taste where hamsters equate the tastes of NaCl and NaNO_3 , which are quite distinct to humans [15,41,42].

4.1. During cathodal current– Inhibition of salt tastes

Application of cathodal current inhibited the human strong *salty* taste epitomized by NaCl and NaBr. The *salty* identity and weak *salty* intensity of NaNO_3 and Na-acetate; and the strong intensity and *salty-bitter* identity of KCl, NH_4Cl and CaCl_2 were also consistently inhibited. Yet, the weak *salty-bitter* taste of NaSO_4 ; *sour* tastes, generally; and *sweet* tastes of Na-saccharin and Na-benzoate were unchanged. Thus, cathodal current inhibits a subset of the multiple salt tastes experienced by humans when sampling ionic stimuli.

Rodent CT nerve recordings of weak cathodal current applied through subliminal NaCl and Na-acetate show marginal inhibitory effects (33, 39); cathodal current likewise has only a marginal effect on weak-tasting chloride salts (Figure 2). Cathodal current imposed on subliminal Na-saccharin and Na-*m*-nitrobenzene sulfonate [34,35,39], however, may elicit rodent CT neural excitation. To hamsters, Na-saccharin and Na-*m*-nitrobenzene-sulfonate taste like sucrose [43,44,45]. Also, –10- μ A imposed on 1 mM saccharin elicited bursting activity in hamster single CT nerve fibers specific to sugar and saccharin [34]. Bursting CT responses are associated with sweet stimuli in hamsters [46]. We saw no increment in intensity or sweet identity of supra-threshold Na-saccharin or Na-benzoate during weak cathodal current in humans. Either the supra-threshold sweet chemicals’ tastes obscured cathode-evoked increments or the difference is due to species variation, which is not likely to be as strong for sweet receptors as for bitter receptors [48].

Besides humans not having the Na^+ -specific taste that hamsters and other rodents have, we do not make distinctions among the bitter tastes of ionic and non-ionic compounds that hamsters do [13]. Perhaps, distinguishing sodium salts from all other salts and distinguishing among ionic and non-ionic bitters are more important for survival in granivorous hamster than in the omnivorous human.

4.2. After release of cathodal current–Metallic taste and Recovery of Salt taste

The tissue-capacitance discharge current at cathode-off evoked a *metallic* taste like the non-specific taste at anode-on [23]. This cathode-off effect, long known for humans [18] and occurring in the response of rodent CT nerves [32,33, Figure 8] was ubiquitous, observable with stronger stimuli but especially clear for weaker chemical stimuli (Figure 2), and was present whether or not significant inhibition of the stimulus occurred during current flow. *Metallic* taste elicited at cathode-off, like anode-on [24,25] is independent of the solution through which current flows. Its prominence with weaker ambient stimuli may relate to its purity, given the little inhibition and, as a result, potential recovery from inhibition, for weak salt stimuli. The “cathode-off” phenomenon helps explain why humans perceive similar tastes with 1-sec. electric stimuli of either polarity; subjects may be detecting *metallic* with anode at “on” or with cathode at “off” [48].

In addition to a *metallic* taste to the cathode-off current of opposite polarity, inhibited tastes would be expected to recover after release of inhibition [24]. For NaCl, *salty* intensity (Figure 4, Figure 6) and identity (Figure 7) increases accompanied the emergent *metallic* identity. Return of inhibited cationic tastes after current release were not seen in other cases. Perhaps the post-current increments were weak compared to the sharp *metallic* burst, or *metallic* and returning cationic tastes may have been confused. In experiment B, in which intensities of *sweet*, *salty*, *sour* and *bitter* taste qualities were rated and *metallic* was not an option, subjects identified the sensation at cathode-off as *bitter-sour-salty* (19%, 14% and 7% increments, respectively), identities also chosen for anodal taste, albeit less frequently than *metallic* [23].

4.3 Opposite polarities impact taste reception in distinct ways

Both anode and cathode likely exert their effects by conduction of ions in the vicinity of the receptors. Nevertheless, there is a fundamental difference between anode and cathode effects in electric taste. The anode is always stimulatory while the cathode has no effect or inhibits responses to stimulatory cations. The anode is stimulatory without chemical stimuli present, while the cathode inhibits ongoing tastes of specific salts. The non-specific positive anode taste, which is not due to electrolysis products, may directly depolarize taste receptor cells (TRC) or activate nerve endings. The negative cathode draws effective cations away from receptors located on TRC apical membranes and, at cathode-off, TRC are depolarized by a capacitive positive current surge, identical to the anode.

Cathode inhibition established NaCl, NaBr, KCl, CaCl, NH₄Cl₂ and NaNO₃ as adequate cationic taste stimuli that likely utilize cation channels for transduction. Other salts, Na-acetate, Na-saccharin, Na-benzoate and Na₂SO₄, hardly inhibited by the cathode, may stimulate Tas1R or Tas2R G-protein coupled receptors, or both [3,4,49]. To accommodate multiple perceptual qualities, several mechanisms likely serve as human salt taste receptors, which are likely distinct from one or another of the several candidate rodent receptors [6,50,51].

Inhibition of taste responses during cathodal current identifies cationic salt tastes; whereas, the *metallic* quality evoked by anode-on and cathode-off is likely a bypassing of normal taste mechanisms that is associated with gustatory dysfunction [52].

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Figure 1.

A. The 10-point fixed interval scale used for intensity rating and B. the closed label list used for quality identification of chloride salts in Experiment A and, with *burn* omitted, quality identification of 0.5 M sodium salts in Experiment C.

Figure 2.

The taste intensities of (A) 0.05 M and 0.5 M NaCl, (B) 0.05 M and 0.5 M KCl, (C) 0.4 M NH₄Cl and (D) 0.2 M CaCl₂ decrease with application of -40 or -80 μ A through the solutions and the intensities the chloride salt solutions increase after current release. The gray control lines show 0 μ A adaptation with time and the red and blue points are mean intensity values, $\pm$ standard errors of differences from control values. Gray ovals encircle individual significant differences. Timing: 0 sec = before current, 2 sec = during current, 4 sec = after current released.

Figure 3.

Ten subjects identified the sensory qualities of 8 chloride-salt solutions as *salty* and *bitter* less frequently, but *tasteless* and *tingle* more frequently during flow of -40 or $-80 \mu\text{A}$ current through the solutions, compared to a $0\text{-}\mu\text{A}$ control. Means $\pm$ standard errors of the number of subjects identifying the qualities are plotted.

Figure 4.

The salty taste of 0.3 M NaCl, 0.5 M Na-acetate and 0.5 M NaNO₃ were reduced during application of $-80 \mu\text{A}$. The salty taste of 0.01 M Na saccharin did not rise significantly above zero. Gray control lines show $0 \mu\text{A}$ adaptation with time for each compound and the colored points are mean intensities $\pm$ standard errors of differences from control values. Gray ovals encircle individual significant differences. Timing: 0 sec = before current, 2 sec = during current, 4 sec = after current.

Figure 5.

A. Average, composite quality intensities of 0.3 M NaCl and 0.5 M NaNO₃ are reduced by application of -80 μ A through the solution. B. Whereas, composite quality intensities for 0.5 M Na acetate and .01 M Na saccharin increase after release of current. Gray control lines show 0- μ A adaptation with time for each compound and colored points are mean intensities $\pm$ standard errors of differences from control values. Note Y-scale is expanded compared to other similar plots. Gray ovals encircle individual significant differences. Timing: 0 sec = before current, 2 sec = during current, 4 sec = after current released.

Figure 6.

A. Total taste intensities of 0.5 M NaCl and NaBr were reduced during application of -40 μ A through the solution. B. Whereas, taste intensities for 0.5 M Na_2SO_4 and Na Benzoate increased after release of current. Gray control lines show 0- μ A adaptation with time for each compound and colored points are mean intensities $\pm$ standard errors of differences from control values. Gray ovals encircle individual significant differences. Timing: 0 sec = before current, 2 sec = during current, 4 sec = after current released.

Figure 7.

Twelve subjects identified the (A) *salty* and (B) *metallic* qualities of 3 *salty* sodium-salt solutions.

A. Compared to a 0- μ A control, *salty* was less frequently identified during a -40 μ A current, but rebounded after current release. B. A metallic quality appeared after current release. Means $\pm$ standard errors of numbers of subjects identifying the qualities are plotted.

Figure 8.

The response of the chorda tympani nerve of a hamster (*Mesocricetus auratus*) to 0.1 M NaCl is affected by imposition of +9 μ A anodal and -9 μ A cathodal current. The dotted red line tracks adaptation of the tonic neural response to NaCl, the dotted green line tracks baseline neural activity to water. Note, during cathodal current neural activity is reduced to baseline and after release of cathodal current briefly increases above the tonic neural response to NaCl. Composite neural activity is plotted vertically and time is graphed horizontally.

EXPERIMENT A: CHLORIDE SALTS

TABLE 1

Initial, Before Current Application, Intensity Ratings & Percent Identifications

Stimulus	Total Intensity			Identification	
	High [M]	Rating	Low [M]	Rating	% Salty/% Bitter
NaCl	0.5	5.74 ± .56	0.05	2.96 ± .57	86 ± .07 05 ± .03
KCl	0.5	5.16 ± .60	0.15	2.80 ± .58	72 ± .05 34 ± .04
NH ₄ Cl	0.5	6.50 ± .51	0.05	2.95 ± .43	61 ± .05 36 ± .04
CaCl ₂	0.2	5.84 ± .48	0.03	1.90 ± .43	32 ± .10 51 ± .09

Means of 10 subjects' average total intensity and average percent (%) identification combined for high and low stimulus concentrations.

TABLE 2

EXPERIMENT B: SODIUM SALTS

Initial, Before Current Application, Ratings

Stimulus	Taste Quality Intensity			
	Salty	Sour	Bitter	Sweet
0.3 M NaCl	6.69 ± .51	3.10 ± .67	3.06 ± .72*	1.35 ± .55
0.5 M NaNO ₃	2.94 ± .43	2.79 ± .45	2.81 ± .37*	0.75 ± .28
0.5 M Na-acetate	3.94 ± .49	4.06 ± .58	3.27 ± .58*	1.10 ± .45
0.01 M Na-saccharin	1.04 ± .53*	1.64 ± .62	1.98 ± .55	5.83 ± .38
				2.62 ± .40

Means of 12 subjects' average intensity for each quality and four-quality average.

* Zero falls within 99% confidence intervals of values.

TABLE 3

EXPERIMENT C: 0.5 M SODIUM SALTS

Initial, Before Current Application, Intensity Ratings & Percent Identifications

Intensity	Percent Identification					
	Salty	Sour	Bitter	Sweet	None	Tingle
NaCl [5.73 ± .51]	79.2 ± 4.2	14.6 ± 5.2	4.2 ± 4.2	6.2 ± 4.0	2.1 ± 2.1	0
NaBr 5.75 ± .53	85.4 ± 6.3	2.1 ± 2.1	10.4 ± 4.0	4.2 ± 2.4	0	0
Na ₂ SO ₄ [3.29 ± .47]	43.8 ± 4.0	22.9 ± 4.0	16.7 ± 6.8	10.4 ± 4.0	12.5 ± 4.2	0
Na-benzoate [3.17 ± .53]	10.4 ± 5.2	4.2 ± 2.4	14.6 ± 2.1	18.3 ± 7.6	16.7 ± 3.4	2.1 ± 2.1

Means of 12 subject's average total intensity and mean percent quality identification. None = Tasteless, Metal = Metallic.