Human Tears Contain a Chemosignal

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Emotional tearing is a poorly understood behavior that is considered uniquely human. In mice, tears serve as a chemosignal. We therefore hypothesized that human tears may similarly serve a chemosignaling function. We found that merely sniffing negative-emotion-related odorless tears obtained from women donors, induced reductions in sexual appeal attributed by men to pictures of women's faces. Moreover, after sniffing such tears, men experienced reduced self-rated sexual arousal, reduced physiological measures of arousal, and reduced levels of testosterone. Finally, functional magnetic resonance imaging revealed that sniffing women's tears selectively reduced activity in brain-substrates of sexual arousal in men.

Charles Darwin suggested that expressive behaviors initially served emotion-relevant functions, before evolving to serve as emotion-signals alone (*1, 2*). Thus, the behavior of emotional tearing, considered uniquely human (*3*), is a paradox: Whereas tears clearly serve an emotional signal (*4*), tears were not related to any emotionally relevant function. Despite psychological theories on the meaning of tears (*5, 6*), and biological theories describing tears as an adaptation related to their eye-protective nature (*3*), or a mechanism for expelling toxic substances (*7*), the functional significance of emotional tears remains unknown (*8*).

Tears are drops of liquid produced by the lacrimal, accessory lacrimal, and Meibomian glands, that contain proteins, enzymes, lipids, metabolites, electrolytes and traces of drugs (*9*). In mice, tears contain a chemosignal or pheromone (*10-12*). Because the chemical makeup of human emotional tears differs from that of reflexive eye-protective tears (*13*), we hypothesized that human tears may similarly convey a chemosignal.

We first asked whether emotional tears have a discernable odor. We obtained negative-emotion tears from 2 donor women (ages 30 and 31) who watched sad films in isolation (Fig. 1A, SOM). We then tested whether 24 men (mean age 28.12 ± 4.05) could smell a difference between these fresh tears and saline. The saline was first trickled down the cheek of the donor women to account for any skin-bound odor sources. Participants failed to discriminate the smell of tears from the smell of saline (mean correct = $0.31\% \pm 0.14$, t (23) = 0.81, p < 0.659, Fig. 1C), i.e., emotional tears did not have a discernable odor.

We next asked whether sniffing such odorless tears influences perception. We compared two alternative hypotheses: Tears may contain a chemosignal related to their typical context of sadness (*14*). Indeed, seeing tears on faces renders the faces sadder in appearance (*4*). Alternatively, human tears may function like mouse tears, where they signal information related to sociosexual behavior (*10-12*).

Twenty four men (mean age 26.92 ± 3.13) first sniffed a jar containing a compound (fresh tears or trickled saline, 3 donor women mean age 30.33 ± 0.5), and then rated its intensity, pleasantness, and familiarity. To keep subjects exposed to the compound for the rest of the experiment, 100μl of the compound were deposited onto a pad pasted onto the subject's upper lip, directly under his nostrils (Fig. 1B). The jar was presented by an additional, non-crier female experimenter blind to jar contents (*15*). Subjects next viewed on-screen emotionally-ambiguous pictures of women's faces, and used a visual-analogue scale (VAS) to rate the sadness (24 faces, Fig. 2A) and sexual attraction (18 faces, Fig. 2B) attributed to each face. Interleaved with these ratings were 40 VAS questions from a standardized questionnaire that assesses empathy (*16*). Each subject participated twice, on consecutive days, once with tears and once with saline, counterbalanced for order across participants, and double-blind as to compound identity.

Tears did not differ from saline in perceived intensity, pleasantness, or familiarity (F(1,23) = 1.26, p = 0. 27) (Fig. 1, D to F). However, VAS ratings of faces differed after sniffing tears or saline (F(1,23) = 7.46, p < 0.02). This difference did not reflect a shift in sadness attributed to the faces (mean VAS tears = 572 ± 118, mean VAS saline = 592 ± 94, t (23) = 1.2, p = 0.23), but rather a shift in sexual attraction attributed to the faces, whereby the faces appeared less sexually attractive after sniffing tears than after sniffing saline for 17 of the 24 participants (mean VAS tears = 439 ± 118, mean

VAS saline = 463 ± 125, t (23) = 2.5, p < 0.02 (Fig. 2C). Sniffing tears did not influence empathy (mean VAS tears = 593 ± 56, mean VAS saline = 587 ± 56, t (23) = 1.2, p = 0.24).

Tears may have failed to influence sadness or empathy because the experimental context was not explicitly sad. We therefore studied 50 men (mean age 28.2 ± 3.8) using a paradigm that generates negative emotions (*15, 17*). We measured psychophysiological arousal (galvanic skin response (GSR); heart rate; respiration rate; skin temperature), VAS self-ratings of mood (*18*), and salivary levels of testosterone, before (baseline), during, and after subjects sniffed either tears (5 donor women mean age 29.2 ± 2.3) or saline. After sniffing, subjects watched a sad film. Each subject participated twice, on consecutive days, once with tears and once with saline, counterbalanced for order across participants, and double-blind (see SOM) as to compound identity.

Tears did not differ from saline in perceived intensity, pleasantness, or familiarity (F(1,49) = 0.36, p = 0.55) (Fig. 1, D to F). The paradigm successfully reduced positive mood (tears and saline combined, positive mood VAS change from baseline = -69.81 ± 99 , t(49) = 4.95 , p < 0.0001), and increased negative mood (negative mood VAS change from baseline = 50.57 ± 58.5 t(49) = 4.95 , p < 0.0001). Despite this negative emotional setting, VAS self-ratings of mood did not differ after sniffing tears compared to saline (F(1,49) = 0.1, p = 0.74). However, observing the response within each session revealed a modest effect whereby tears reduced self-ratings of sexual arousal (baseline mean VAS rating = 293.48 ± 173.3, after sad film mean VAS rating = 263.44 ± 140,: t(49) = 2.46, P < 0.01) (Fig. 3A), yet saline did not (baseline mean VAS rating = 260.96 ± 124, after sad film mean VAS rating = 251.8 ± 120.4,t(49) = 0.81, P = 0.29) (Fig. 3B).

Whereas the effect on subjective self-rated sexual arousal was modest (*19*), the effects on objective psychophysiology and hormonal expression were pronounced (all measures: F(1,49) = 4.27, p < 0.05). During sniffing, there was an increase in GSR, greater for tears than for saline (mean tears =0 .08 ±0 .03, mean saline = -0.05 ±0 .04, t(42) = 2.68, P < 0.02) (Fig. 4, C and D), yet after sniffing there was a progressive reduction in arousal, greater for tears than for saline. This was evident in several independent measures (Fig. S1), as well as in a conservative composite index (*17, 20*) (CPI) that equally weighted all recorded measures (end of experiment: CPI mean tears = -0.08 ± 0.02, mean saline = -0.01 ± 0.02, t(49) = 2.29, P <0 .03) (Fig. 4, E and F). Finally, and critically, levels of salivary testosterone were progressively lower after sniffing tears as compared to the baseline period (baseline testosterone = 151.96 ± 76 pg/ml, last testosterone = 132.66 ± 63.1 pg/ml, t(49) = 3.3, P < 0.001) (Fig. 3G), an effect not evident for saline (baseline

testosterone = 154.8 ± 74.4 pg/ml, last testosterone = 154.34 ± 101.8 pg/ml, t(49) = 0.81, P = 0.96) (Fig. 3H). Reductions in testosterone are a significant indicator of reductions in sexual arousal in men (*21*).

Brain imaging has uncovered brain activity associated with human chemosignals (*22-24*). Because sniffing women's odorless tears consistently reduced sexual arousal in men within a non-sexual setting (viewing pictures of faces and sad or neutral films), we next used fMRI to ask whether this was reflected in brain activity. We first presented sexually arousing pictures and movies in order to delineate sexual-arousal-related brain structures, and then separately measured the response within these regions to sad, happy and neutral movies after sniffing either tears or saline. Each of 16 male subjects (mean age 28 ± 2.67) participated twice, on consecutive days, once with tears and once with saline (5 donor women mean age 33.6 ± 7.5), counterbalanced for order across participants, and double-blind as to compound identity. In order to assure that subjects sniffed the compound, they were asked to provide estimates of intensity, pleasantness, and familiarity, that revealed no perceptible odor for tears (F(1,15) = 0.02, p = 0.88) (Fig. 1D-F).

Sexually arousing stimuli outlined a brain network consistent with that previously implicated in brain imaging studies of sexual arousal (*25*) (table S1, see fig. S2 for activity induced by tears alone), most notably the hypothalamus (Fig. 4A) and left fusiform gyrus (Fig. 4B). Within these regions, activity induced by the sad film was significantly lower after sniffing tears than after sniffing saline (hypothalamus, Area Under the Curve (AUC) % change tears = 0.04 ± 2.26, AUC % change saline = 2.33 ± 2.86, t(15) = 3.05, p < 0.008 (Fig. 4C; 4E); left fusiform gyrus, AUC % change tears = 13.42 ± 21.33, AUC % change saline = 17.27 ± 22.7, t(15) = 2.38, p < 0.031 (Fig. 4, D and F)).

Subjective ratings of attributed sexual appeal, together with objective measures of psychophysiological arousal, testosterone expression, and brain activity, jointly suggest that women's emotional tears contain a chemosignal that reduces sexual arousal in men. We have thus identified an emotionally relevant function for tears.

These effects materialized despite that subjects did not see a women cry, nor were they aware of the compound source. Moreover, in Western culture, exposure to tears is usually in close proximity. We hug a crying loved one, often placing our nose near teary cheeks, typically generating a pronounced nasal inhalation as we embrace. Such typical behavior entails exposure equal to or greater than that experienced here, hence the effects we observed in the laboratory are relevant to human behavior.

All mammals, including humans, use chemosignals. The most commonly studied carrier of human chemosignals is

sweat (*25-27*), yet most mammals don't sweat like humans do. Although cursory observation of non-human mammalian behavior suggests that most chemosignals are carried by urine or anal/vaginal secretions, careful observation reveals that mammals investigate facial chemosignals as well (*28*). Indeed, specific chemosignals have been identified in the lachrymal secretions of mice (*10, 12*), i.e., in the mouse equivalent of tears. Thus, although it is commonly stated that only humans shed emotional tears, our findings may serve to tie human emotional crying to tear-shedding in other species (*7, 29*).

The action of mammalian chemosignals can range from "releasers" that generate a response *de novo* (e.g., lordosis), to "primers" that modify a long-term process (e.g., sexual maturation), to "signalers" that provide information (e.g., kinship) and "modulators" that modify an ongoing response (*30*). In our view, "modulator", a term coined primarily to describe the action of human pheromones (*31*), best fits the effects of tears as measured here. Here, women's tears modulated (reduced) sexual arousal, physiological arousal, testosterone levels, and brain activity in men.

These findings pose many questions: What is the identity of the active compound/s in tears? Do chemosignals in women's tears signal anything else but sexual disinterest, and is this signaling restricted to emotional tears alone? Moreover, could the emotional or hormonal state (menstrual phase/oral contraceptives) of the crier/experimenter influence the outcome? In turn, what if any are the signals in men's tears (see SOM), in children's tears, and what are the effects of all these within, rather than across gender? Despite these open questions, the current results conclusively demonstrate a chemosignal in human tears. In this, we illustrate a novel functional role for crying.

References and Notes

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Supporting Online Material
www.sciencemag.org/cgi/content/full/science.1198331/DC1
Materials and Methods
Figs. S1 and S2
Tables S1
References

Fig. 1. Emotional tears are odorless. (**A**) To obtain tears, donor women watched sad films in isolation, using a mirror to capture tears into a vial. A typical donation contained ~1 ml. B. For continuous exposure, tears deposited onto a pad allowed ongoing nasal airflow exposure, but not tr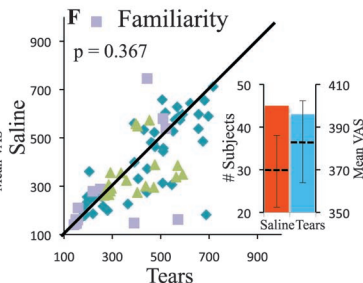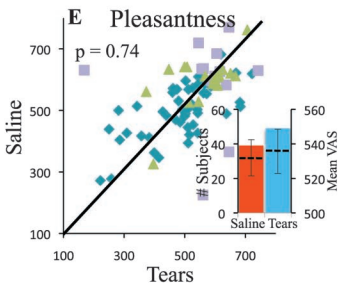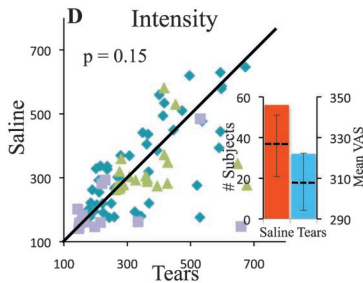ansdermal diffusion. Panels (A) and (B) are illustrations. (**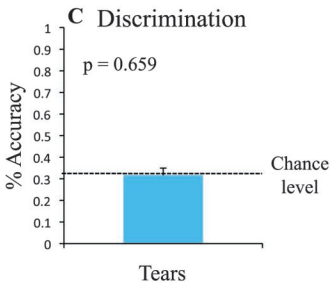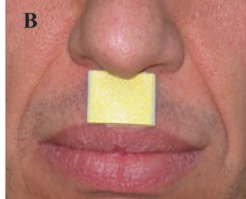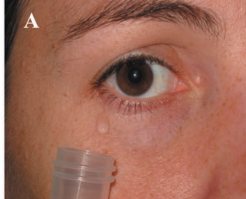C**) Discrimination accuracy of tears from saline. (**D** to **F**). Scatter-plots of: (D) intensity, (E) pleasantness, and (F) familiarity estimates of tears and saline in all experiments. Within-subjects comparisons [(D) to (F) here, and all other figures] are presented in scatter-plots along a unit slope-line (X = Y), where each point reflects a subject. If data accumulates under the line then values were greater for tears, if data accumulates above the line then values were greater for saline. If data accumulates on the line, then there was no difference between tears and saline. Inlay: Bars reflect the number of subjects on each side of the unit slope-line (left ordinate), and dashed line reflects the mean values and standard error (right ordinate).

Fig. 2. Sniffing tears reduces attributed sexual attraction. (**A** and **B**) Typical VAS questions from the face-rating experiment. (**C**) Attributed sexual attraction by 24 men. Data accumulated above the line, indicating reduced attributed sexual attraction after sniffing tears. Inlay: Bars reflect the number of subjects on each side of the unit slope-line (left ordinate), and dashed line reflects the mean values and standard error (right ordinate).

Fig. 3. Sniffing tears reduces arousal. (**A**) Shift in self-rated sexual arousal from baseline to ~5 minutes after sniffing tears, indicating a drop in arousal. (**B**) Shift in self-rated sexual arousal from baseline to ~5 minutes after sniffing saline, indicating no change. (**C** to **F**). Timeline of psychophysiological data. Data were aligned in time to the first sniff (dashed vertical line). Abscissa lists time in seconds, and experimental phases: BL = baseline, Q/S = VAS mood questionnaire followed by saliva sample, EE = experimenter enters room. Experimental phases are about (~) accurate in time, as subjects differed in questionnaire latency, resulting in a shift of a few seconds. Error bars reflect between-subjects variance, here displayed only to give a better sense of the data. The statistically relevant variance is the within-subjects variance displayed in the scatter plots (D) and (F). (C) Timeline of ongoing GSR amplitude, indicating greater GSR response for tears during sniffing only. (D) GSR change from sniffing to end of sad movie, indicating greater change for tears. (E) Timeline of the composite psychophysiological index (CPI), indicating reduced arousal after sniffing tears. (F) CPI at the final stage of the study, indicating significantly lower arousal following tears versus saline. (**G**) Shift in salivary levels of testosterone from baseline to last saliva collection after sniffing tears, indicating a drop from baseline. (**H**) Shift in salivary levels of testosterone from baseline to last saliva collection after sniffing saline, indicating no change. Inlay: Bars reflect the number of subjects on each side of the unit slope-line (left ordinate), and dashed line reflects the mean values and standard error (right ordinate).

Fig. 4. Sniffing tears reduces brain activity in substrates of sexual arousal. (**A**) Activity induced by an erotic film generated a region of interest (ROI) in the Hypothalamus. (**B**) Average activity time-course from 16 men within the previously identified hypothalamic ROI. This activity was induced by a sad film clip after sniffing either tears (blue) or saline (red). (**C**) Area under the curve of activation from (B), providing a measure of variance across subjects. (**D**) Activity induced by an erotic film generated an ROI in the left fusiform gyrus. (**E**) Average activity time-course from 16 men within the previously identified fusiform gyrus ROI. This activity was induced by a sad film clip after sniffing either tears (blue) or saline (red). (**F**) Area under the curve of activation from (E), providing a measure of variance across subjects. Inlay: Bars reflect the number of subjects on each side of the unit slope-line (left ordinate), and dashed line reflects the mean values and standard error (right ordinate).
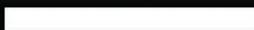
A

B

C Discrimination

% Accuracy

p = 0.659

Chance level

Tears

D Intensity

Saline

p = 0.15

Tears

Subjects

Mean VAS

Saline Tears

E Pleasantness

Saline

p = 0.74

Tears

Subjects

Mean VAS

Saline Tears

F Familiarity

Saline

p = 0.367

Tears

Subjects

Mean VAS

Saline Tears

▲ Face-Rating Experiment ◆ Physiological Monitoring Experiment ■ fMRI Experiment

A. To what extent is this face sad?

Not at all — Very

B. To what extent is this face sexually arousing?

Not at all — Very

C. p < 0.02

A Sexual arousal rating

p < 0.018

B Sexual arousal rating

p = 0.29

C GSR

D p < 0.02

E Composite psycophysiological index

F p < 0.0304

G Testosterone

p < 0.0018

H Testosterone

p = 0.96