Combining fMRI and EEG: Unique multi-level neurosensory approach of tactile stimulation offered by creams

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Abstract

In today's global context, there has been a significant shift towards managing holistic well-being in the cosmetics industry. The texture of a product now plays a crucial role in shaping its emotional value. Formulation science enables an infinity of textures, within ingredients plays a pivotal role into the sensory benefits. Very few studies have explored the mental state induced by cosmetic creams through cerebral activity measurement and imaging, furthermore during the application specific step only. With the aim of investigating how pleasant touch can impact the wellbeing mental state, cerebral activity data have been collected with neuroscientific techniques focusing on the "after-feel" effect of creams.

Non-perfumed emulsions (Creams A and B) with the same formula except the emulsifier, have been tested on the back of the hand of 20 female participants by themselves following 3 tasks: application of the cream, penetration time, massage of the skin after penetration. ElectroEncephaloGraphy (EEG) and functional Magnetic Resonance Imaging (fMRI) data were collected during the massage block with no cream as a control, then compared to resting states to highlight significant differences. Cognitive opinions were investigated through a questionnaire.

Simple contrasts from fMRI compared to rest revealed consistent and robust activation of somatosensory related areas always larger for cream A by contracting regions of interests (ROI) related in memory, positive emotions, wellness, and reward circuity. Complex contrasts between conditions confirmed the significant additional impact of cream A, notably on the ROI involved in pleasant touch, the anterior cingulate cortex and the brainstem nuclei. In parallel, EEG evaluation highlighted for both creams, a relaxation decrease during task execution, anti-correlated to the mental load. Interestingly, while the emotional valence didn't change significatively, more panelists experienced an increase in attention for cream A, translation of the relative α power signal in parietal and frontal cortex.

For the first time, it was demonstrated that a tactile stimulus offered by skin after penetration of a cream promoted a high positive emotional experience over the cosmetic routine, highly influenced by the formulation. Only one ingredient shifted the tactile stimulation response by modification of the surface biomechanical properties of the skin, towards the pleasant touch. Combining high temporal and spacial resolution levels, EEG associated to fMRI unlocked the potential of some complex neuromarkers such as *attention* which is a cognitive process that selects some information and inhibits some other. Supported by fMRI, ROI activations revealed that the

distinguishing effect driven by cream A, was linked to positive sensations of well-being and reward outcomes. This dual approach offers a profound insight into consumers' emotional experiences, enabling a detailed grasp of product attractiveness during development, including texture refinement, and even laying the groundwork for formulating products based on their addictive potential.

Introduction

Current global context amplified the paradigm shift towards holistic well-being management in cosmetics, where the texture is an essential part of the emotional value of the product. The sense of touch a very important modality in this experience. Various types of mechanoreceptors are distributed on the hand, providing detailed tactile information about contact events to the brain through afferent nerves. It also provides sophisticated sensitivity to the shape and surface properties of objects. Measuring emotions and investigating neural responses induced by a tactile stimulus, outside the conscious individual sphere, is possible with neuroscience techniques. Most common methods for measuring brain activity are fMRI, PET and EEG.

Electroencephalography (EEG) is a method based on the record of the electrical activity generated by the synchronized activity of thousands of neurons by using electrodes placed on the scalp. Among the brain imaging techniques EEG offers the highest time resolution allowing the analysis even at sub-second timescale. The emotion recognition induced by various stimuli such as music, videos, photos, fragrances or virtual reality was largely explored by EEG. Some of papers focusing on the tactile perception of different substrates reported alpha (8-12Hz) and beta (12-28Hz) electric waves changes into the somatosensory cortex area. Furthermore, increased beta bands in the parietal-frontal regions were found to be associated to pleasant touch [1]. Among cosmetic purposes, 2 papers measured the cerebral activity via EEG occurring during application of creams or lip balms, highlighting the importance of textures on emotional responses during application [2,3].

Functional magnetic resonance imaging (fMRI) measures changes in cerebral bold flows and oxygenation in regions of strong neural activity. Its ability to acquire functional and reference anatomic images simultaneously are very useful in uncovering the neuroanatomical circuits underlying the sensation of hedonic valence with tactile stimuli. Although some complexities of combining the recording with the stimulation techniques due to the device environment, its high spatial resolution fills perfectly the gap to EEG method. Very few studies related have explored the effect of cosmetic texture on tactile perception with fMRI. Querleux *et al*., shown that the application of a cosmetic product on the skin activates different sensory areas compared to when the skin alone is touched, but the emotional responses were not examined [4]. Hirao *et al*. explored the neural process of associating a product texture application with the value provide by product information [5].

Until now, both fFMRI and EEG techniques have never targeted the mental state induced by tactile feedback following the application and penetration of a cream upon the skin, named the « after feel effect » of a texture. The aim of this study is firstly to investigate how the after-feel pleasant touch can impact the wellbeing mental state combining EEG and fMRI techniques and secondly explore how the formulation composition can modulate theses emotional responses.

Materials & Methods

1. Tested Products

Two cosmetic emulsions having the same composition excepted the emulsifier were evaluated by EEG and fMRI techniques. The emulsions contained no fragrance and exhibited the same aspect (white and fluid). The % of each emulsifier was chosen according to the formulation guidelines required to emulsify 20% of oil.

		Cream A Emulsion Test	**Cream B Emulsion Control**
Ingredient	**INCI**	**(%)**	**(%)**
Deionized Water	Water	71,95	72,95
Preservative system	Pentylene Glycol (and) glyceryl caprylate/caprate	2,5	2,5
Xanthan gum	Xanthan gum	0.50	0.50
Pickering emulsifier	Sodium starch Octenylsuccinate	5.00	0.00
Emulsifier Benchmark	Glyceryl stearate (and) PEG-100 stearate	0.00	4.00
Sweet almond oil	Prunus amygalus dulcis (sweet almond) oil	14.00	14.00
Shea butter	Shea butter ethyl esters	3.00	3.00
Coco-caprylate	Coco-caprylate	3.00	3.00
Anti-oxidant	Tocopherol(and)helianthus annuus (sunflower) oil	0.05	0.05

Table I: Formula composition of Cream A and cream B

2. EEG study

Seventeen healthy female subjects, aged between 22 and 55 years, participated to the clinical study. The purpose of the study and relevant information were provided to the participants. Informed written consent was obtained before the study.

a. EEG device

Cerebral electric signals have been detected and registered by means of a portable wireless EEG-system, the My BrainTech Q+ Headset. The headset consists of 4 data-collecting electrodes locating at AF3, AF4, P3, P4 following the American EEG Society standard. This headset did not require a moistened cap or gels to improve conduction.

b. Experimental procedure

SESSION 1						SESSION 2				
	CREAM A or B						CREAM B or A			
Resting state = Baseline	Application	Penetration	Touch	Resting state	BREAK	Resting state = baseline	Application	Penetration	Touch	Resting state
3min	15s	40s	20s	3min	5min	3min	15s	40s	20s	3min
Record			Record	Record		Record			Record	Record
	3 times repetitions						3 times repetitions			

Table II: EEG experimental procedure framework

The subjects were instructed to clean their hands with a neutral soap before and after the experiment and during the break between the sessions. Then, the headset was set up on the panelist head. The subject tested successively both creams according to a randomization within the population.

After the resting state with closed eyes recording, 80 µL of the cream was deposit on the back of the non-dominant hand and the volunteers were asked to apply the cream by rubbing it with the dominant hand, within a circle movement at the speed of 2sec/rotation, for 15s. Following the penetration time where they rested their arms on the table, the panelists were instructed to touch by massaging the back of their hand where the cream were applied. A final resting state with closed eyes ended the first session. After the break, the panelists were proceeded with the second session.

c. Data acquisition, processing, and analysis

My brain Technology platform (Heatset + data pre-processing and analysis) provided standardized measurement and analysis of cognitive and emotional EEG Biomarkers as Relaxation, Emotion, Attention and Mental load [6]. A proprietary algorithm extracted and merged the different frequency bands with a 0,5-40Hz pass band filter, average power for each channel according a 6sec-window.The sampling rate was 250Hz.

- Relaxation is a state of decreased alertness, muscle tone and nervous tension, resulting in a feeling of relaxation and well-being. It was quantified with the averaged paretial alpha power across subjects. A positive (negative) value indicates a relaxed (respectively exited) state.
- Mental workload is the amount of mental resources that a person mobilizes to perform a task. It was quantified with the averaged ratio between frontal theta power and parietal alpha power across subjects. A positive (negative) value indicates a high (respectively low) mental load.
- Emotional valence is a measure of the negative or positive nature of a felt emotion. It was quantified with the frontal alpha power asymmetry between the right and the left-brain hemispheres across subjects. A positive (negative) emotional valence represents positive (respectively negative) emotions.
- Attention is a cognitive process that selects some information and inhibits some other. Attention is attentional resources that task required to processing information but they are also demanded for perception process and memory accessing. It was quantified with a combination of delta, theta, alpha and beta powers across subjects [7]. A positive (negative) value indicates a high (respectively low) attentional level.

For each creams data from touch stimulation of all repetitions were grouped.

d. Statistics

Change of neuromarkers levels between the stimulation compared to the Baseline across sessions. Power activities were z-score normalized using baseline activity.

To define whether the evolution of the neuromarker between the baseline and the stimulation or the resting state is significant or not, a Wilcoxon signed-rank test have been used.

Number of subjects who experienced increases or decreases in their mental states between the baseline and the simulation was calculated by performing a non-parametric Mann-Whitney U statistical test on each individual session of subjects.

To determine whether there are significant differences between the sessions, a Friedman statistical test is first applied to determine whether at least one session is different from another.

3. fMRI study

a. fMRI Device

Functional magnetic resonance imaging was performed with a GE 3 Tesla SIGNA™ Premier MRI Scanner with a 48-Channel Head Coil. First, T2*-weighted echo-planar images was acquired with the following parameters: 2-mm slice thickness, TR = 1500 ms, TE = 30 ms, flip angle = 90 deg, FOV = 220 mm, voxel size 2x2x2 mm^3, ascending interleaved acquisition. Then, T1-weighted structural images were acquired with a resolution of 1x1x1 mm^3.

fMRI measures brain activity by detecting changes in the Blood Oxygenation Level Dependent (BOLD) signal. By comparing the BOLD signal during periods of rest and activation, regional changes in brain activity can be measured as a result of exposure to a stimulus. Data was collected throughout the experiment such that brain activity for each condition and step of the experiment was acquired, including during periods of rest.

b. Data acquisition, processing and analysis

Brain imaging data was preprocessed using fMRIprep (nipreps.org), a neuroimaging preprocessing tools application for task-based and resting state fMRI. Slice timing correction, motion correction and a high pass filter was applied to the functional images. Data was then co-registered to the structural images and normalized to the T1 standard template in the Montreal Neurological Institute and Hospital (MNI) space.

To assess the sensory effect of stimulations, simple contrasts analysis was carried out to measure differences in brain activation during the massage of skin after application and penetration of creams (or no cream, Control) compared to resting state records. Then, data obtained from the three blocks were contrasted (complex contrasts) to assess the added effects of the topical cosmetics to the massage alone. Brain region activity from the contrasts satisfying a false-discovery rate of $q(FDR) < 0.05$ and uncorrected $p < 0.01$ were reported.

c. Experimental procedure of the clinical study

20 healthy participants (female, 18-45 years of age) were informed about the experimental procedure and signed the informed consent form. Prior to scanning, 20 min of training was carried out to make sure the participants will be fluent in applying the creams.

3 experimental conditions, ie blocks, no cream, cream A, cream B, were performed in a pseudo-randomized order, always starting with the cream-free massage, followed by massage with cream A or B in a randomized order. At the beginning of each block, the experimenter cleans the volunteers' hands with a remover wipe, rinses them with a wet cotton pad and dries them with a

tissue. This will be followed by a 2-minutes rest period. Next, the experimenter applied 80µl of cream to 3 hand areas (hand back, inner wrist, outer wrist). The participants massaged successively these areas for 12s each, with 13 s of rest between. After this step, they asked to massage their hands for about 12s successively to feel the sensory effect of the cream on their skin.

The described procedure is under patent filling process.

Results

1. EEG study results
    a. Touch stimulus

The neural responses during the stimulation “touch phase” were firstly analyzed and compared to the baseline (=first resting state), basically when the subject massaged the skin which have received the creams (Figure 1). The effects and their significancy calculations, the number of subjects who experienced the change, were reported in the table III.

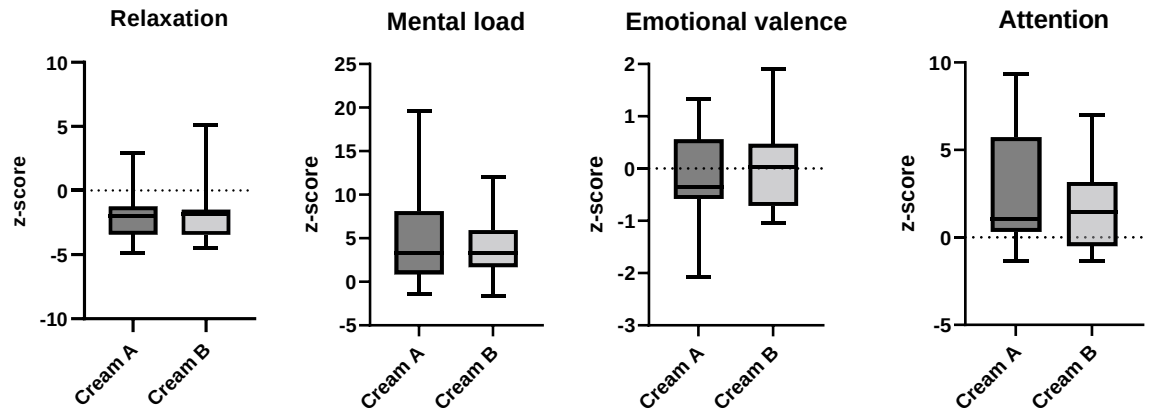

Figure 1: Neuromarkers change distribution during “touch” phase

	Cream A			Cream B		
	p-value	Difference (resting state vs stimulation)	Number of subjects affected	p-value	Difference (resting state vs stimulation)	Number of subjects affected
Relaxation	<0.001	-0.139	94%	<0.001	-0.135	94%
Mental load	0.002	0.274	94%	0.005	0.193	88%
Emotional valence	0.611	-0.004	-	0.927	0,0008	-
Attention	0.007	0.208	82%	0.080	0.140	59%

Table III: Effect of the stimuli, significancy (p-value) and number of subjects affected for cream A and cream B during the touch phase.

A significant difference was found in relaxation, anti-correlated to the mental load. For both creams, subjects were more excited and felt a higher mental load during the task “touch” compared to the resting state. The valence of emotional mental state remained the same as compared to the rest phase for cream A and B. Then, the attention biomarker is significantly increased for cream A (p-value<0,05) for 82% of the panelists in comparison to the cream B. This

result was partially driven by the task workload but involved others cerebral activity responses related to alertness and perception/memory processing meaning that cream A didn't leave the panelists indifferent.

b. Global session stimulus

By comparing the first and the last resting state data for both sessions, the emotional impact of the global experimental sequence, combining application, penetration time and touching the skin, was evaluated.

No significant differences were obtained regarding attention and emotional valence neuromarkers (Table IV) On the other side, the relaxation was significantly increased (Figure 2, Table IV), once again the opposite of the mental load.

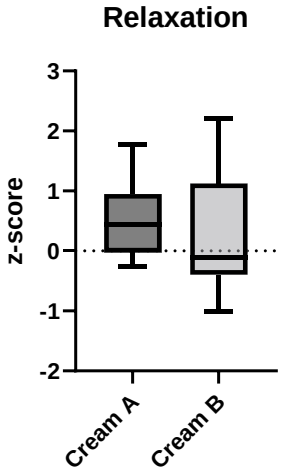

Figure 2: Relaxation change distribution between baseline and the final resting state.

	Cream A			Cream B		
	p-value	Difference (baseline vs resting state)	Number of subjects affected	p-value	Difference (baseline vs resting state)	Number of subjects affected
Relaxation	0.013	0.028	76%	0.487	0.013	-
Mental load	0.013	-0.021	82%	0.243	-0.071	-
Emotional valence	0.225	-0.007	-	0.818	0,004	-
Attention	1.000	-0.002	-	0.854	0.023	-

TABLE IV: Effect of the global session, significancy (p-value) and number of subjects affected for cream A and cream B.

The additional statistic test comparing cream A and B data confirmed that cream A significantly increased the relaxation level of the subjects after the session than the cream B ($F = 6.231$, $p=0.029$).

2. fFMRI study results

a. Simple contrasts

The activation for the contrast cream A vs resting state were always larger than those the massage free and cream B conditions. The cream-free condition results highlighted the strong impact of the creams at the surface of the skin on brain responses.

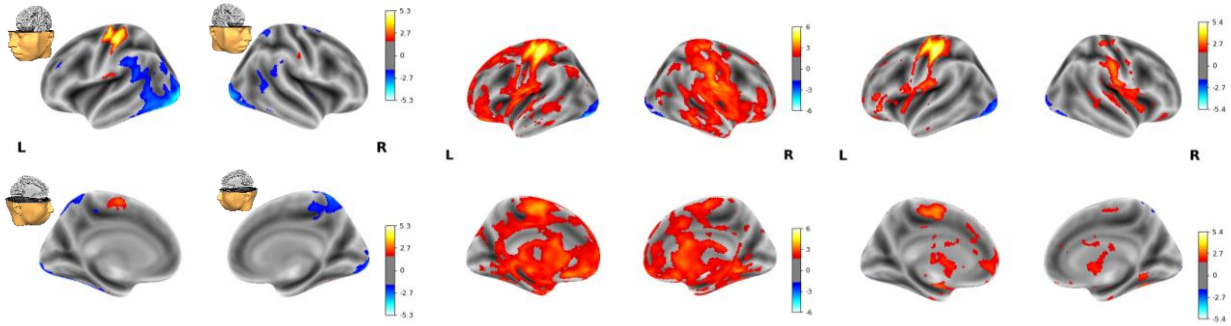

Figure 3: BOLD contrast for the massage the 3 conditions compared to rest: from right to left cream-free, Cream A, cream B. Brain activations (red label) and inhibitions (blue label) are represented through 4 brain views: inner and outer view of each brain lobes.

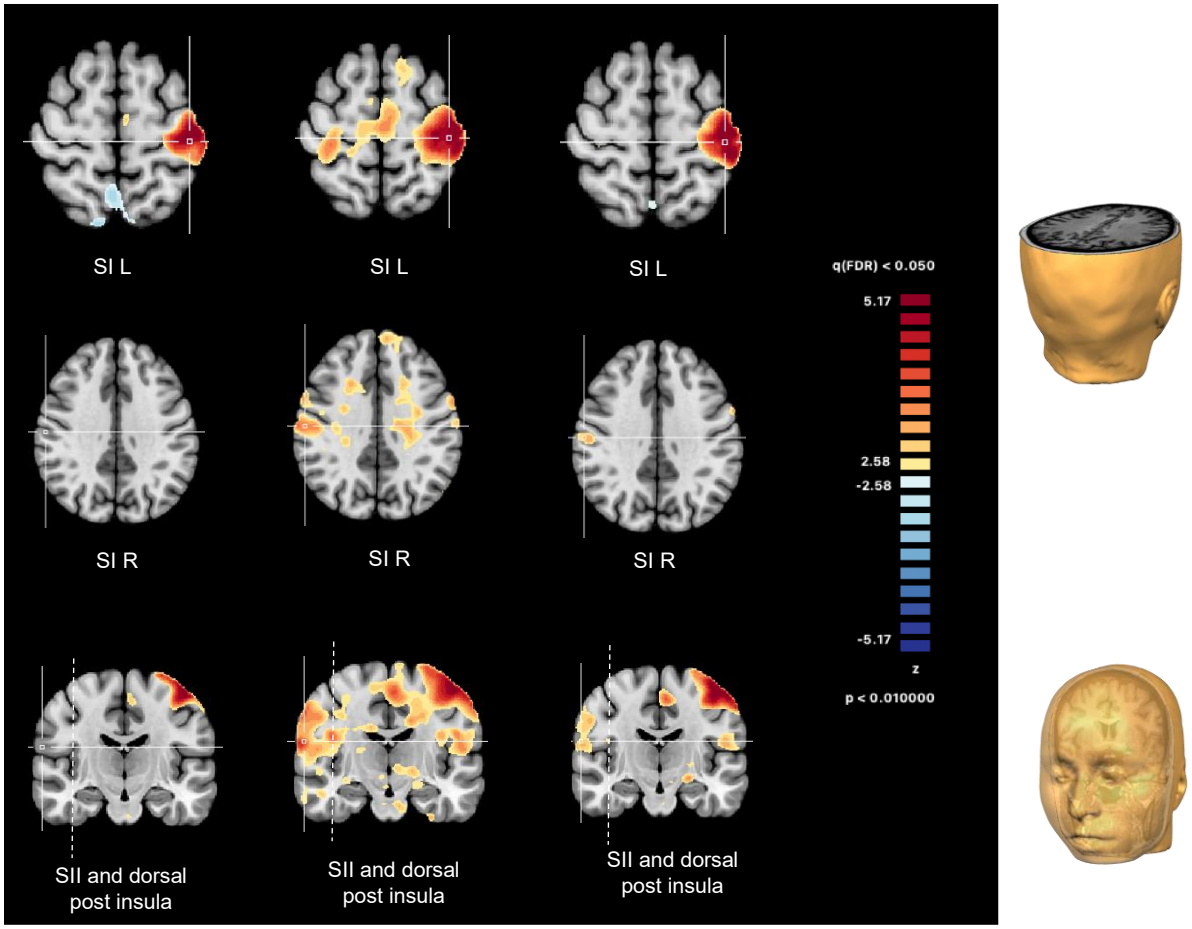

Figure 4: BOLD contrast for the massage the 3 conditions compared to rest: from right to left cream-free, cream A, cream B. Primary somatosensory cortex (SI), Secondary somatosensory cortex (SII) (solid line) and dorsal posterior insula (dotted line) BOLD mapping.

Consistent activations in somatosensory areas were got (Figure 4). In the left primary somatosensory cortex, activations are comparable in all three conditions. In the right one, as well as in the secondary somatosensory cortex, activation was stronger for Cream A compared to Cream B. In addition, cream A activated the region of the dorsal posterior insula. This suggested more interoceptive processing after the cream A application and a more positive impact on wellness in comparison of the cream B.

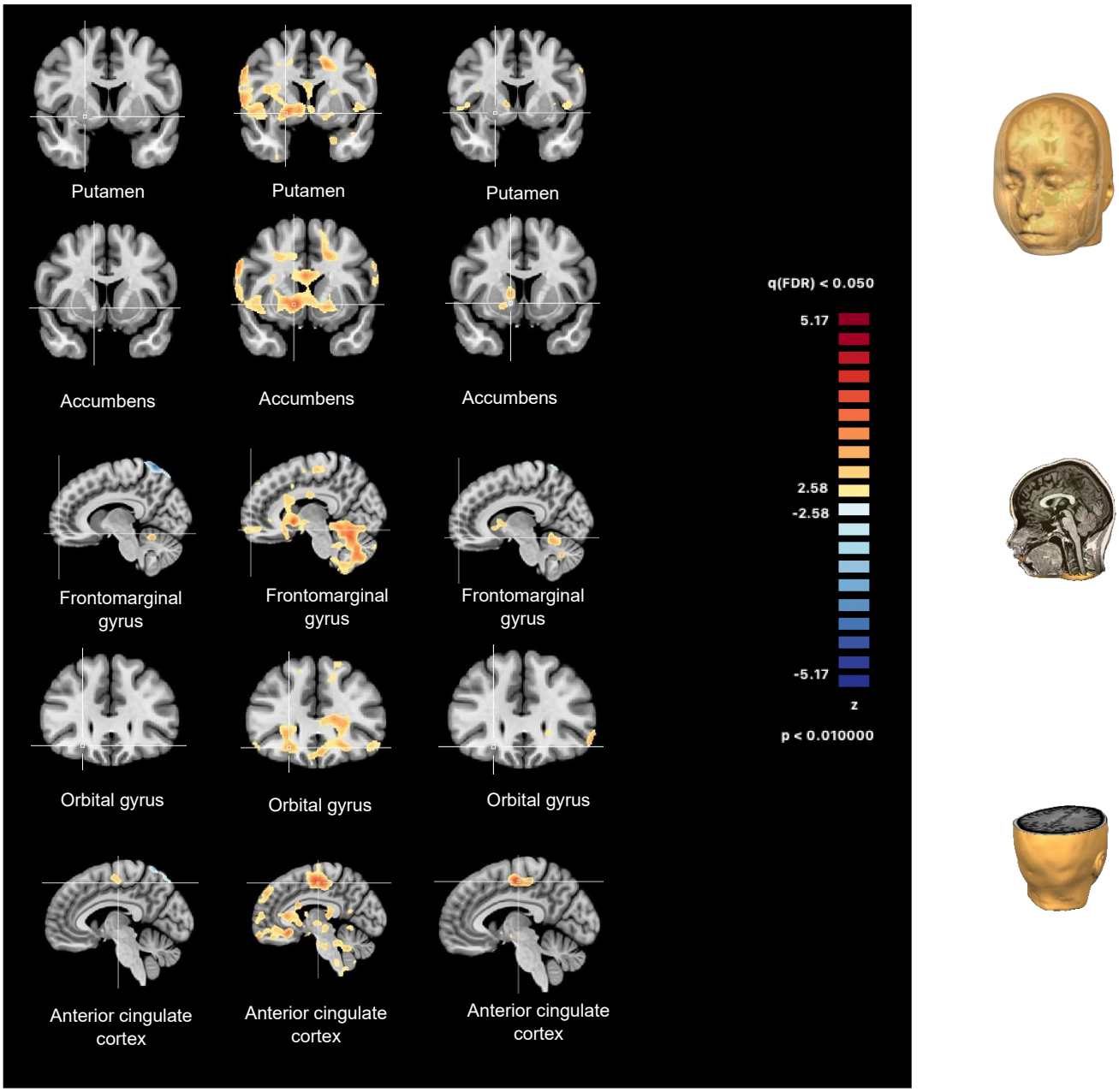

Figure 5: BOLD contrast for the massage the 3 conditions compared to rest: from right to left cream-free, cream A, cream B. Limbic areas (Putamen and Nc Accumbens) and Orbitofrontal cortex regions (Fronto marginal gyrus, orbital gyrus) and ACC (Anterior cingulate cortex) BOLD mapping.

Cream A showed larger responses in activation of the putamen and nucleus accumbens which plays an important role in reward (Figure 5). The accumbens region is also a key structure in mediating emotional and motivation processing.

Orbitofrontal regions like fronto-marginal and orbital gyri were strongly activated with the Cream A conditions only, while these areas have been shown to be implicated in the processing of pleasant touch [8,9]. Finally, the activation of the anterior cingulate cortex, strongly involved in well-being and emotional processing, was also larger from Cream A.

Others results non illustrated here highlighted a higher activation by Cream A into the ventral tegmental area and the ventral anterior thalamus, implicated in the reward circuity.

b. Complex contrasts

The complex contrasts were calculated by comparing the BOLD responses of the simple contrasts described above (Figure 6).

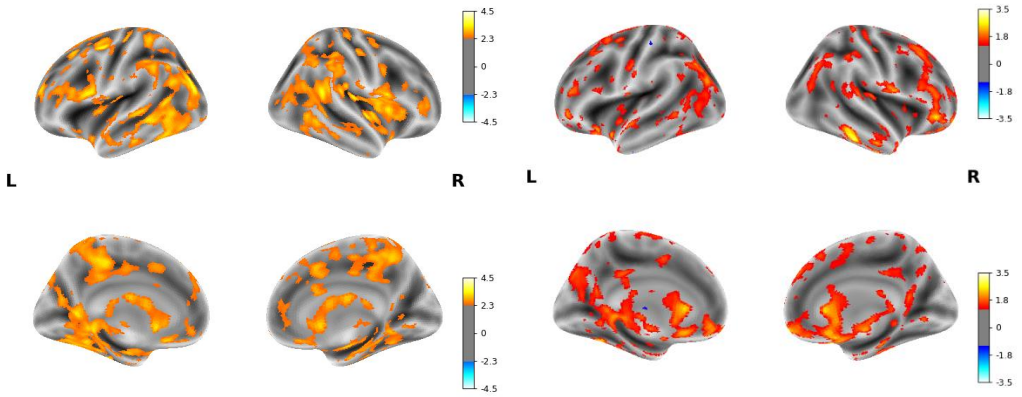

Figure 6: BOLD complex contrast of Cream A vs No cream (yellow label) conditions and Cream A compared to Cream B (red label)

The first contrast in yellow allowed to conclude that Cream A conditions had a significant and non negligeable additional impact on the tactile stimuli brain processing provoked by hand massage. The contrast in red allowed us to conclude that cream A had significantly more positive effects than cream B, and consequently that the emulsifier is the main promoter of the brain responses.

Discussion

The cerebral activity during the tactile stimuli of a skin after application of a product was for the first time investigated both EGG and fMRI. EEG data reveals a decrease in relaxation neuromarker expected because of motor activity related to the execution of a task. Whatever the cream, the classic analysis embracing frontal asymmetry alpha waves don't show a significant effect on emotional valence, whereas Gabriel *et al.* [3] demonstrated a difference during application, between 2 creams with different thickener. Interestingly, the neuromarker attention, involving the waves recorded into frontal and parietal zone, is emphasized with Cream A only. This neuromarker, which is a cognitive process that selects some information and inhibits some

other, is synonym to alertness. This indicates an arousal of the brain individual responses, unavoidable to notice within a consumer experience understanding, but could be difficult to translate into positive or negative perception. A first piece of explanation is given by the relaxation results obtained after the global routine of a cosmetic product; application penetration and touch the skin feel. The relaxation is significantly increased with Cream A compared to Cream B, meaning a wellbeing state reached by the panelists after this sequence.

fMRI study brings a new light of the tactile perception induces by creams on skin thanks to an exploration of all the brains areas, while EEG outcomes focused on 4 points in frontal and parietal lobes. Aligned with [3], the results reveal a bilateral activation of both primary and secondary somatosensory areas (anteriori parietal lobes), with a different gradient of activation between the 3 conditions. This unveils that somatosensory afferents like low-threshold mechanoreceptors are strongly stimulated in response to touching the skin which have received cream A. Overall, the brains zones coding for pleasant touch are activated such as ACC [8]. Furthermore, there is mounting evidence that one of these sub modalities-touch has another dimension, providing not only its well-recognized discriminative input to the brain, but also an affective input [10].The activation of the dorsal posterior insula, as well as other areas involved in emotional memory, or reward also suggest the affective dimension of the panelists sensation during the touch step of Cream A, through C-tactile afferents [11]. In addition, the tactile processing induced by cream A triggers neural activation correlated with well-being state according to King [12]. The review of 22 studies performed with EEG, PET or fMRI emphasizes a consistent and robust association between wellbeing and the prefrontal cortex, especially the ACC and the orbitofrontal areas, but as well into the temporal lobes.

Modification of the surface of the touching skin by different creams modulates the brain response and revealed that only one ingredient can increase the positive emotions related to affective memory, reward and well-being thank to a pleasant touch. The starch-based ingredient which emulsifies the cream A drives these sensory and emotional responses. It is well known that starches additives into cosmetics formulations provide softness, powdery and velvety skin feel benefits but never demonstrated with the reference contained into the cream A, what is more in neurosciences approach [13]. Extracting from quinoa, the starch is a smaller particle (2 µm) than other starches but remains at the surface of the skin after the cream penetration. Ensuring the emulsifying functionality during the formulation thanks to a lipophilic modification, it acts also as a unique sensorial promoter due to its morphology features and its physicochemical properties.

Ultimately, the amalgamation of EEF and fMRI methodologies allows us to underscore an intriguing observation. The escalation in mental exertion and vigilance, as evidenced by EEG readings during the tactile interaction phase, does not correlate with adverse sensations or emotions. Instead, it reveals an inherent allure of the product that resonates with the panelists.

Conclusion

While the multimodal property of the human somatosensory system is complex and continue to be unraveled, this study provides a novel exploration of cerebral activity during tactile stimuli following the application of a cosmetic product, comparing both EEG and fMRI methodologies. Each technique brings crucial information about emotions induced by the skin feel of cosmetic after application or during a routine. A cross-analysis between it, allows to clarify, validate, and emphasize some aspects like the alertness or the reward experienced by panelists. The modification of the skin’s surface by different creams modulates the brain response, revealing that

a single ingredient, like starch-based ingredient, can enhance positive emotions related to affective memory, reward, and well-being. This dual approach offers a profound insight into consumers' emotional experiences, enabling a detailed grasp of product attractiveness during development, including texture refinement, and even laying the groundwork for formulating products based on their addictive potential.

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Conflict of Interest Statement
Lucas Meyer Cosmetics is the supplier of the *sodium starch octenyl succinate*.

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