NEUROSCIENCE
INTERNATIONAL BRAIN IBRO RESEARCH ORGANIZATION

RESEARCH ARTICLE

L. Meier et al. / Neuroscience xxx (2018) xxx–xxx

Thirst-Dependent Activity of the Insular Cortex Reflects its Emotion-Related Subdivision: A Cerebral Blood Flow Study

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Abstract—Recent studies investigating neural correlates of human thirst have identified various subcortical and telencephalic brain areas. The experience of thirst represents a homeostatic emotion and a state that slowly evolves over time. Therefore, the present study aims at systematically examining cerebral perfusion during the parametric progression of thirst. We measured subjective thirst ratings, serum parameters and cerebral blood flow in 20 healthy subjects across four different thirst stages: intense thirst, moderate thirst, subjective satiation and physiological satiation. Imaging data revealed dehydration-related perfusion differences in previously identified brain areas, such as the anterior cingulate cortex, the middle temporal gyrus and the insular cortex. However, significant differences across all four thirst stages (including the moderate thirst level), were exclusively found in the posterior insular cortex. The subjective thirst ratings over the different thirst stages, however, were associated with perfusion differences in the right anterior insula. These findings add to our understanding of the insular cortex as a key player in human thirst – both on the level of physiological dehydration and the level of the subjective thirst experience.

Key words: dehydration, arterial spin labeling (ASL), insula, homeostasis.

INTRODUCTION

Thirst is fundamentally important for human survival. It is elicited by osmotic changes in the internal body milieu and it is processed by the interoceptive system. Like other homeostatic emotions (Craig, 2003a,b) such as hunger or air hunger, the feeling of thirst is associated with a homeostatic need and it is highly imperative for behavior. Basic physiological aspects of dehydration have been investigated extensively (Zerbe and Robertson, 1983; Thompson et al., 1986; McKinley and Johnson, 2004). Recently, however, there has been growing interest in the neurobiology of thirst (McKinley et al., 2006). Although results of early animal studies indicated that subthalamic parts of the brain are critically involved in the genesis of thirst (Andersson and McCann, 1955; Teitelbaum and Epstein, 1962), research over the last decade on human dehydration and perception of thirst has identified various telencephalic elements involved in the regulation of water intake. Imaging studies using positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) reported thirst-related brain activity in the cingulate cortex (anterior cingulate cortex (ACC) Brodmann area (BA) 32 and posterior cingulate cortex (PCC) BA 26/BA 29), the parahippocampal gyrus, the superior temporal gyrus, the middle temporal gyrus, the cerebellum, and the precuneus (Denton et al., 1999a,b; Parsons et al., 2000; de Araujo et al., 2003; Egan et al., 2003; Farrell et al., 2006; Farrell et al., 2008; Saker et al., 2014). Notably, some of these studies also identified the insular cortex to be involved in the human experience of thirst (Egan et al., 2003; Farrell et al., 2006; Saker et al., 2014).

The experience of thirst represents a state which slowly evolves over time. Therefore, extending the current knowledge of general neural correlates of thirst, the present study aims at systematically investigating cerebral perfusion reflecting the gradual progression of

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Abbreviations: ACC, anterior cingulate cortex; ASL, arterial spin labeling; BA, Brodmann area; BOLD, oxygenation level dependent; CBF, cerebral blood flow; fMRI, functional magnetic resonance imaging; pCASL, pseudo continuous ASL; PET, positron emission tomography.

https://doi.org/10.1016/j.neuroscience.2018.04.022
0306-4522/

thirst. To that end, we examined physiological dehydration and subjectively experienced thirst in healthy volunteers over varying levels of thirst. Focussing on the parametric aspect of thirst, we measured brain activity and subjective thirst ratings in four different hydration states: intense thirst, moderate thirst, subjective satiation, and physiological satiation. Assessing the neural correlate of a slowly evolving state with no apparent trigger is very challenging with conventional blood oxygenation level dependent (BOLD) neuroimaging techniques. Therefore, in case of thirst, the measurement of cerebral blood flow (CBF) seems a promising solution to overcome this putative limitation. CBF can be quantified by arterial spin labeling (ASL), a non-invasive imaging method using water molecules in arteries as intrinsic tracer. As a major advantage, ASL is sensitive to detect slow variations in neural activity (Wang et al., 2003). In a first study using ASL to examine neural correlates of thirst, CBF was investigated in a thirsty and a satiated state, and a control condition a few hours after drinking to satiation (Farrell et al., 2011). The experience of thirst was associated with alterations in perfusion in the cingulate cortex, prefrontal cortex, striatum, parahippocampus, and cerebellum. Additionally, differences in functional connectivity between the subcortical lamina terminalis and the cingulate cortex as well as to the insular cortex for the thirsty and the satiated state were found (Farrell et al., 2011). To extend these findings with a specific focus on the parametric progression of thirst, we measured cerebral perfusion in healthy subjects using ASL over four different thirst stages. With the aim to elicit an intense feeling of thirst as authentically as possible, we chose an extensive dehydration period of 18 h, during which the participants had to abstain from drinks and watery food products before taking part in the experiment.

EXPERIMENTAL PROCEDURES

Subjects

Twenty healthy male subjects with no psychiatric or neurological disorders, no active medical history, and no contraindications to MRI participated in the study. The number of subjects is in accordance with current recommendations for ASL studies (Mersov et al., 2015). All subjects were right-handed according to the Edinburgh Handedness Scale (Oldfield, 1971). Data of one subject were excluded due to pronounced inhomogeneity in intensity values in the ASL data, leaving 19 subjects for the statistical analysis with a mean age of 25.1 years, standard deviation *(SD)* = 2.9, range 20–31 years. All participants gave written consent, and ethical approval was obtained before the experiment (local ethics committee of the Kanton of Bern, Switzerland: KEK Bern, 081/12). The study conformed to ethical standards as outlined by the Declaration of Helsinki. We recruited subjects at the University of Bern and among the employees of the Insel University Hospital in Bern. The same subject group performed a study on emotional rivalry using an event-related BOLD fMRI paradigm, reported in Meier et al., 2015.

Procedure

The subjects were deprived from water for 18 h, during which they had to abstain from drinks (water and others) and watery food products. The water deprivation started at 8 p.m. and lasted the entire night and until the next day at 2 p.m. For safety reasons, subjects spent the morning of the water deprivation in the laboratory. There, they were offered a standardized breakfast and lunch (dry, salty snacks). At the level of intense thirst after 18 h of water deprivation, blood samples were taken in all subjects. Subsequently, the study session in the MR scanner was conducted, investigating CBF in four conditions: intense thirst (T1), moderate thirst (T2), subjective satiation (T3), and physiological satiation (T4) (Fig. 1). After the initial CBF measurement in the intense thirst condition, subjects drank 0.15 L of water. Then, the perfusion on the moderate thirst level (T2) was measured. After that, participants drank water *ad libitum* to satiation, followed by the cerebral perfusion measurement in the subjective satiation condition (T3). While the subjective feeling of thirst ends very quickly after drinking, normalization in serum electrolyte concentration needs more time. Therefore, the participants then left the scanner for one hour, during which they had free access to water. The exact amount of consumed water was measured for each subject. Also, the subjects were asked to go to the toilet during the break, in order to minimize potential confounds due to bladder distention. Then, in this physiologically satiated state (T4), another blood sample was drawn and the final cerebral perfusion measurement was performed. The subjects were instructed to keep their eyes closed throughout all imaging sequences. Before each perfusion measurement, subjects were asked for a subjective thirst rating on a 1–10 scale (1 = not thirsty at all, 10 = very thirsty). Blood samples were drawn from the antecubital vein, and levels of osmolality, sodium, chloride, and creatinine were analyzed for both the intense thirst (T1) and physiological satiation (T4) condition.

Magnetic resonance imaging

MR imaging was conducted on a 3 T whole-body MRI system (Magnetom Trio, Siemens Medical Systems, Erlangen, Germany) at the Inselspital, University of Bern with a standard 12-channel radiofrequency head coil.

Structural imaging. A high-resolution three-dimensional T1-weighted anatomical image (MDEFT) was obtained for every subject with the following parameters: echo time (TE), 2.48 ms; repetition time (TR), 7.92 ms; matrix size, 256 × 256; field of view, 256 mm^2; 176 slices; and slice thickness, 1 mm. The anatomical scan lasted approximately 14 min.

pCASL. For the measurement of CBF we used a pseudo continuous ASL (pCASL) technique (Wu et al., 2007; Dai et al., 2008). In this gradient-echo echo-planar imaging sequence alternating label and control images were acquired. Labeling was performed at 90

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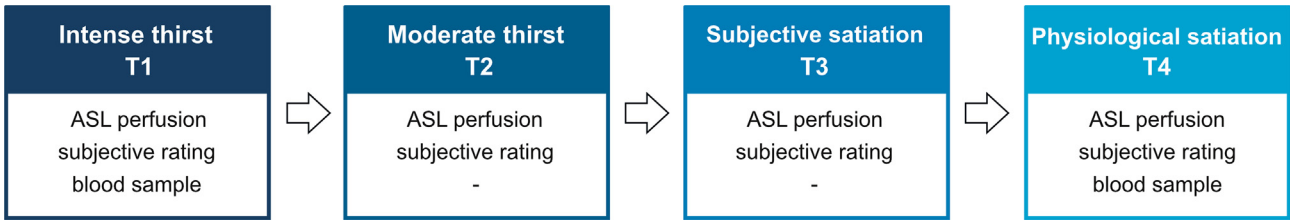

Fig. 1. Experimental paradigm. ASL perfusion and subjective thirst ratings were measured across four different hydration states. Blood samples were drawn in the intense thirst condition (T1) and the physiologically satiated state (T4).

mm below the isocenter of the imaging region and a post-labeling delay of 1.25 s was inserted (to allow the labeled water protons to enter the imaging slices), with a label time of 1.72 s. The images were acquired with the following parameters: TE, 18 ms; TR, 4000 ms; field of view, 230 mm^2; matrix size, 64 × 64; flip angle, 25°; voxel size, 3.6 × 1.8 × 6.0 mm. A total of 18 slices with 6-mm slice thickness were recorded from inferior to superior in a sequential order. The axial slices were placed in the line that was given by the intersection between the points of the anterior- and posterior commissure, perpendicular to the carotid artery. Each pCASL measurement comprised 110 acquisitions, and we measured every subject at four different hydration levels.

Data analyses

Subjective thirst ratings and serum parameters. Differences in thirst ratings over the four hydration states were analyzed with nonparametric Wilcoxon's signed-rank tests (Bonferroni corrected, $p < 0.05$). We used nonparametric tests because the ratings were not normally distributed (e.g. at T4 all subjects rated 1). To test for hydration effects on blood parameters, we calculated repeated measures *t*-tests for osmolality, sodium, chloride, and creatinine between T1 and T4 ($p < 0.05$). Differences in osmolality levels in intense thirst and physiological satiation were correlated with the amount of consumed water using Spearman's rank correlation ($p < 0.05$).

Preprocessing of ASL data. For the analysis of the ASL data, we used statistical parametric mapping (SPM8, Wellcome Department of Imaging Neuroscience, London, England; www.fil.ion.ucl.ac.uk/spm8) and MATLAB (The MathWorks Inc.; version R2014a). First, we realigned all ASL time series to correct for motion artefacts. Then, each subject's anatomical T1 image was segmented into gray matter, white matter and cerebrospinal fluid (CSF). Using an in-house MATLAB script, we calculated a flow-time series from the realigned ASL time series by subtracting the labeling images from the control images with a simple subtraction and computed whole-brain mean CBF images (temporal average of 55 volumes) for each subject (Federspiel et al., 2006). An intensity threshold of 300 (arbitrary units) was set for the raw images. Resulting mean CBF images of each subject and each hydration state were coregistered to the anatomical scans, normalized to the Montreal Neurological Institute (MNI) coordinate system and spatially smoothed with a Gaussian kernel (8 mm, full-width at half-maximum).

Statistical analysis. In order to investigate differences in cerebral perfusion across the four different hydration states, mean CBF images were entered into a one-way repeated measures ANOVA (within subjects) in SPM. The statistical model comprised regressors for intense thirst, moderate thirst, subjective satiation, and physiological satiation. Statistical comparisons were performed by contrasting the different hydration levels against each other.

Previous studies have shown that several brain regions are involved in neural responses to thirst. Based on previous literature indicating that the insular cortex (Farrell et al., 2011), the ACC (BA 32) (Denton et al., 1999b; Farrell et al., 2006, 2011), and the middle temporal gyrus (Farrell et al., 2011) are involved in neural responses to thirst, we conducted region of interest (ROI) analyses using explicit masks of the insular cortex, the ACC and the middle temporal gyrus, generated with the Wake Forest University (WFU) Pick Atlas Tool, version 2.4, (Maldjian et al., 2003).

To assess the relationship between CBF and subjective thirst ratings, we re-calculated the one-way repeated measures ANOVA with the subjective thirst ratings for all hydration states as covariate. Since we had no distinct hypothesis in which area in the brain we expected the relationship between CBF and subjective thirst ratings, this analysis was conducted as a ROI analysis for all the brain regions that are perfused by the middle carotid arteries.

An inspection of the whole-brain mean CBF values over all hydration states revealed a reduction of whole-brain CBF with decreasing thirst (Fig. 2B). Therefore, we conducted a systematic model fit analysis to investigate whether a linear or an alternative non-linear model would fit the relation between CBF and subjective thirst ratings most accurately. We investigated this by means of a goodness of fit analysis among the following four models, identifying the model with the highest explained variance:

$$Modelfunction0\ (linear)\ :f(x) = u_0 + u_1 \cdot x$$

$$Modelfunction1\ (quadratic)\ :f(x) = a_0 + a_1 \cdot x + a_2 \cdot x^2$$

$$Modelfunction2\ (cubic)\ :f(x) = b_0 + b_1 \cdot x + b_2 \cdot x^2 + b_3 \cdot x^3$$

$$Modelfunction3\ (logarithmic)\ :f(x) = c_0 + c_1 \cdot \log(x)$$

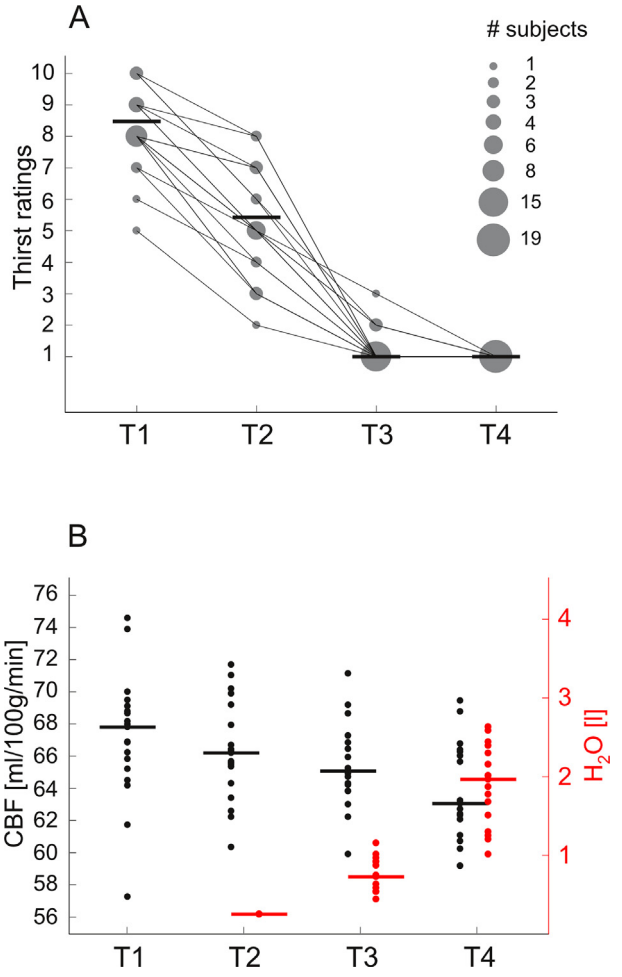

Fig. 2. Subjective thirst ratings, mean CBF values and consumed water. (A) *Thirst ratings*: The subjects rated their subjective feeling of thirst before each ASL measurement at T1–T4 on a scale of 1–10; 1 = not thirsty at all, 10 = very thirsty). The median of all subjects per time point is indicated by the black horizontal line: T1 *M(median)* = 8.5, *SD(standard deviation)* = 1.30; T2 *M* = 5.5, *SD* = 1.74; T3: *M* = 1.00, *SD* = 0.56; T4: *M* = 1.00, *SD* = 0.00. At T4, all subjects indicated being not thirsty (rating = 1). The size of the gray circles indicates the number of subjects for each rating at the different thirst levels. The connecting lines between the circles illustrate the progression of the thirst ratings (indicating which thirst level the respective subjects reported at the next time point). (B) Left axis: *Mean CBF*: This figure depicts whole-brain CBF values of each single subject at each time point (T1–T4). The median of all subjects per time point is indicated by the black horizontal line. Right axis (in red): *Amount of water consumed* at time points T2, T3 and T4. The median of all subjects per time point is indicated by the red horizontal line. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Both the subjective thirst ratings and the CBF values were repeated measures for each subject. Therefore, for each voxel the subjective ratings and the CBF values were treated as "within-subject" factors and subjects were treated as random effects.

RESULTS

Thirst ratings

Subjective thirst ratings at all four hydration states are depicted in Fig. 2A. Before the ASL measurement at the moderate thirst level (T2), subjects drank 0.15 L of water (fixed amount for all participants). At T3, the subjectively satiated condition, subjects were allowed to drink water *ad libitum* and consumed an average of 0.68 L (*SD* = 0.21). At T4, participants had consumed 1.89 L (*SD* = 0.5) (Fig. 2B, red). Significant differences in subjective thirst levels were observed between T1 and T2 ($Z = -3.85$, $p < 0.001$, Bonferroni corrected), T1 and T3 ($Z = -3.86$, $p < 0.001$, Bonferroni corrected), T1 and T4 ($Z = -3.86$, $p < 0.001$, Bonferroni corrected), and T2 and T3 ($Z = -3.84$, $p < 0.001$, Bonferroni corrected). There was no subjective difference in thirst ratings between T3 and T4 ($Z = -1.89$, $p = 0.354$, Bonferroni corrected). Both at T3 and T4 participants felt subjectively satiated.

Blood parameters

Analysis of blood samples revealed that serum osmolality was significantly higher when the subjects were highly dehydrated (T1) (*M* = 294.5 mOsm/kg, *SD* = 4.2) compared to the physiologically satiated state (T4) (*M* = 289.6 mOsm/kg, *SD* = 4.2). Further differences were observed for sodium and chloride levels, but not for creatinine (Table 1). Differences in osmolality levels between intense thirst (T1) and physiological satiation (T4) correlated with the amount of consumed water ($r(17) = 0.51$, $p = 0.028$).

One-way repeated measures ANOVA: ROI analyses

The repeated measures ANOVA revealed significant perfusion differences across hydration states for all three regions of interest: the (right) insular cortex (peak voxel: $x = 40$, $y = -20$, $z = 6$; $F(1,18) = 13.1$; *p(FWE-corrected)* = 0.003), the ACC (peak voxel: $x = 6$, $y = 48$, $z = 0$; $F(1,18) = 11.3$; *p(FWE-corrected)* = 0.006), and the (right) middle temporal gyrus (peak voxel: $x = 70$, $y = -34$, $z = 2$; $F(1, 18) = 15.64$; *p(FWE-corrected)* = 0.001). Contrasting the different hydration states against each other, we found that only the contrast of intense thirst vs. physiological satiation (T1 vs. T4) revealed significant perfusion differences in the ACC (peak voxel: $x = 6$, $y = 46$, $z = -2$; $T(18) = 5.14$, *p(FWE-corrected)* = 0.001) and the middle temporal gyrus (peak voxel: $x = 70$, $y = -34$, $z = 2$; $T(18) = 6.72$, *p(FWE-corrected)* = 0.001). In the insular cortex, however, differences in perfusion were found in all contrasts – not only for T1 vs. T4, but also for T1 vs. T2 and T1 vs. T3 (Table 2, Fig. 3).

Relation between CBF and subjective thirst ratings

This analysis, which was conducted as a ROI analysis for all brain areas perfused by the middle carotid arteries, revealed a significant cluster in the right insular cortex (peak voxel at $x = 38$, $y = 20$, $z = 0$, $T = 5.39754$, df = 17), which survived the FDR-corrected statistical threshold. The insular cluster is depicted in Fig. 4. Comparing these results based on a linear model with the results of a quadratic, a logarithmic and a cubic model function, the linear model explained the

Table 1. Blood parameters in intense thirst and physiological satiation

		T1 intense thirst (*SD*)	T4 satiation (*SD*)	*t (18)*	*p*
Osmolality	[mOsm/kg]	294.5 (4.2)	289.6 (4.2)	4.5	< 0.001
Sodium	[mmol/l]	143.9 (1.5)	141.8 (1.8)	5.1	< 0.001
Chloride	[mmol/l]	105.3 (1.4)	103.4 (1.2)	5.3	< 0.001
Creatinine	[μmol/l]	80.5 (8.8)	80.3 (10.9)	0.2	0.857

Table 2. MNI coordinates of significant peak voxels in the insular cortex

Contrast	Peak voxel coordinates *x*, *y*, *z* (MNI)			Cluster size	*T*	*p* (FWE-corrected)	Effect size	Hemisphere	Localization within insula
T1 vs. T2	−54	−38	18	14	4.38	0.029	1.1224	Left	Posterior
	38	22	2	8	4.36	0.031	1.5462	Right	Anterior
T1 vs. T3	38	22	2	7	4.52	0.019	1.6524	Right	Anterior
	−56	−32	20	24	4.01	0.041	1.2799	Left	Posterior
T1 vs. T4	−38	−20	4	151	5.24	0.002	1.7518	Left	Posterior
	40	−20	6	492	5.04	0.004	1.8364	Right	Posterior
	−42	−32	18	87	4.48	0.005	1.6799	Left	Posterior
	−34	22	2	34	4.42	0.026	1.1194	Left	Anterior
	58	−32	20	6	4.16	0.054	0.8564	Right	Posterior
T3 vs. T4	40	−18	8	364	5.10	0.003	1.9753	Right	Posterior
	−42	−4	−6	105	4.94	0.006	1.4891	Left	Posterior

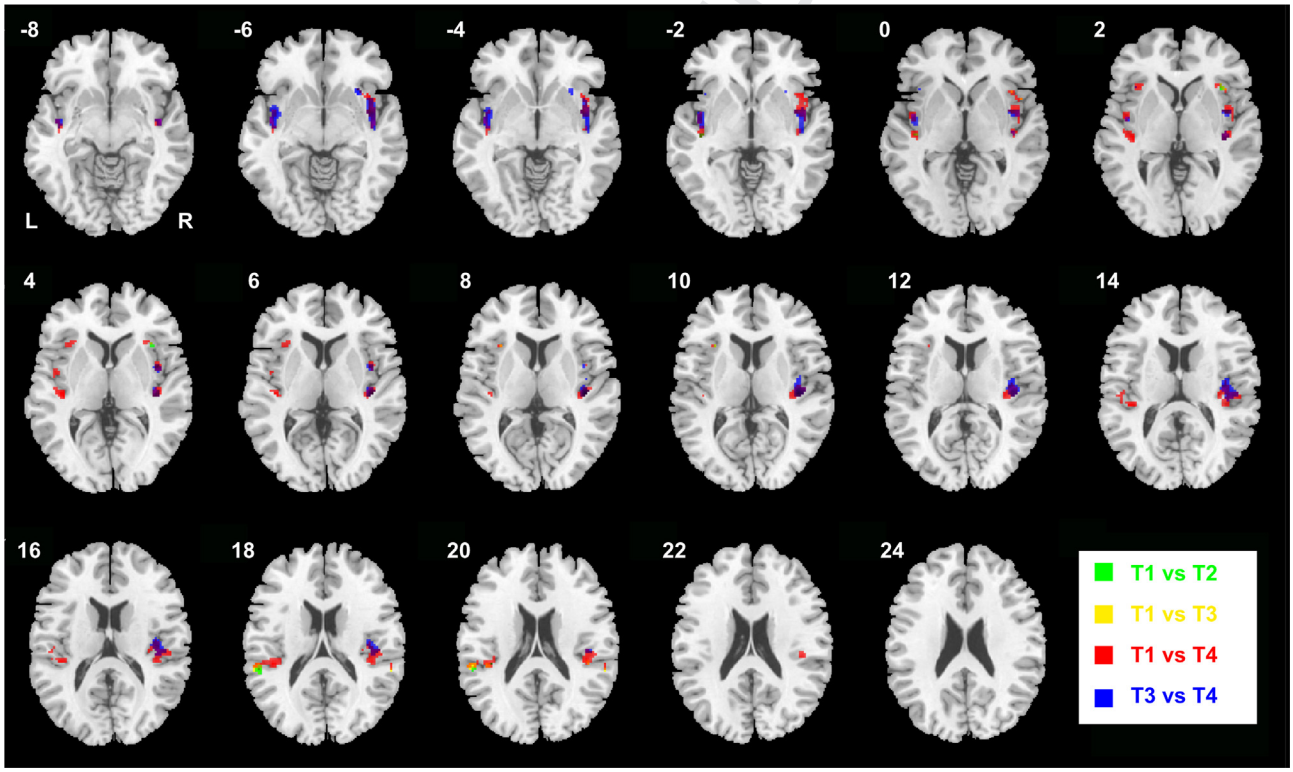

Fig. 3. Insular clusters across all thirst stages. This figure depicts all insular clusters identified by the one-way repeated measures ANOVA for all contrasts (T1 vs. T2, T1 vs. T3, T1 vs. T4 and T3 vs. T4). The image is depicted at $p = 0.001$ uncorrected.

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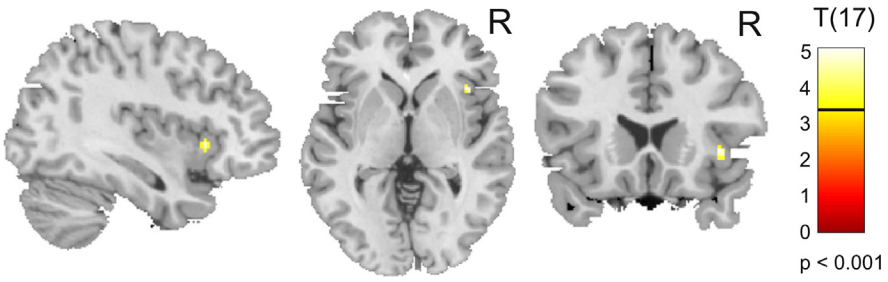

Fig. 4. CBF with subjective thirst ratings as covariate Insular cluster revealing a relation between CBF and subjective thirst ratings at peak voxel: $x = 38$, $y = 20$, $z = 0$, $T = 5.39754$, df = 17. The bar indicates *T*-values, image depicted at $p = 0.001$ uncorrected.

correlation between CBF and subjective ratings' best (goodness of fit $F(1, 4) = 8.03$, $p = 0.072$).

DISCUSSION

The main goal of this study was the investigation of cerebral perfusion reflecting the parametric progression of human thirst. To that end, we measured CBF, subjective thirst ratings and serum parameters across different levels of thirst. After an 18-h water deprivation, the subjects were highly dehydrated on a physiological level, reflected by the increased serum electrolyte concentration. In addition, the participants reported a subjective feeling of intense thirst. After drinking, the concentration of serum parameters decreased to normal levels and the subjects felt subjectively satiated.

In the CBF data we found thirst-related perfusion differences in all regions of interest: the ACC, the middle temporal gyrus and the insular cortex. However, parametric perfusion with significant differences across all four thirst stages (including the moderate thirst level), were exclusively found in the insular cortex. This finding is in line with results of previous imaging studies showing that the insula seems to play a core role in homeostatic functions, not only in thirst (Farrell et al., 2011), but also hunger (Tataranni et al., 1999; Wright et al., 2016), dyspnoea (Banzett et al., 2000; Herigstad et al., 2011) and urinary functions (Griffiths et al., 2007).

ACC and MTG

Previous studies have shown that not only the insula but also the ACC and the MTG are activated in thirsty participants (Denton et al., 1999b; Farrell et al., 2006, 2011), which is in line with the results of our study. However, we found the parametric changes exclusively in the insular cortex and not in the ACC and the MTG. A possible explanation for that could be that only an intense thirst level activates the entire thirst network with the aim to maximize the motivation to drink. From an evolutionary perspective it seems reasonable that a medium thirst level is perceived, but does not necessarily lead to the immediate action of drinking regardless of effort or potential risks. Intense thirst, however, signals the urge to drink in a more extensive network, including the ACC, which reflects not only the fact of being dehydrated, but also the motivational state of subjects (de Araujo et al., 2003). In line with this, it was reported that neural activity in the ACC correlated with pleasantness ratings of water (de Araujo et al., 2003), which maximizes the motivation to drink in a state of intense thirst. Other studies hypothesize that the neural activity in the ACC and the MTG could be subserving the consciousness of thirst, which decreases precipitously as soon as water is consumed (Egan et al., 2003; McKinley and Johnson, 2004). These brain areas do not seem to be activated at an early thirst stage, but may reflect cognitive processes taking place after thirst is well established (Egan et al., 2003). In that sense, the insular cortex seems to be closely involved in change detection, while the ACC/MTG monitor the current state and indicate if immediate action is needed in order to consume fluids.

Insular subdivision

Looking at the thirst-related perfusion differences in the insular cortex more closely, we found that perfusion was modulated predominantly in posterior parts of the insula. Previous studies have nicely shown that the insula can be divided in subparts with distinct functions (Craig, 2002; Cauda et al., 2011, 2012). The posterior insula has been reported to be involved in basic homeostatic processes and it has been shown that primary interoceptive inputs are represented in posterior parts of the insula (Craig, 2002), which is in line with our findings. Neuronal activity in the anterior insula, on the other hand, has been reported in the context of general emotional processing, cognitive and attention-related processes (Brass and Haggard, 2007; Mayer et al., 2007; Singer et al., 2009) and thus has been suggested to be crucial for human awareness in general (Craig, 2009). The fact that we found a positive correlation between CBF and subjective thirst ratings in the anterior insula concurs with this hypothesis. Furthermore, it is interesting that the correlation with subjective thirst ratings was lateralized to the right insula, which has been implicated in negative or distressful emotional processing (Craig, 2005, 2009), whereas the objective thirst differences were bilateral.

A recently published review extends the subdivision of the insular cortex in an anterior and a posterior part, but suggests an anatomical posterior-to-mid-to anterior progression of integration within the insula, from posterior primary interoceptive parts to the mid-insular integration area to the anterior representation of all feelings (Craig, 2009). If we integrate the results of the current study with our previously published results of a BOLD fMRI data set measured in the same subject group (Meier et al., 2015), the picture of the insular sub functions defined by Craig is completed. We reported that the sensory-evoked emotion disgust predominantly activated the anterior insula, while the interaction between disgust and the homeostatic emotion thirst (when both were perceived simultaneously) occurred in the mid insular cortex. Despite the limitation that only male subjects were included, which restricts generalization of the results, we

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can conclude the following. Within one subject group we could demonstrate that *(1)* the homeostatic input thirst activated the posterior insula; *(2)* the subjective awareness of thirst was represented in the anterior insula; *(3)* the sensory-evoked emotion disgusts activated the anterior insula; *(4)* the interaction between homeostatic and sensory-evoked input (thirst and disgust) occurred in the mid insula, which confirms its suggested function as integration area within the insular cortex.

Limitations

In the course of the discussion of the results, some limitations of the current study need to be considered. First of all, one subject group only was measured in a fixed order design. With this design the progression of unspecific factors over time (e.g. fatigue, stress hormone levels etc.) are not controlled for and make it difficult to rule out potential confounding factors. However, the study measured a very homogenous healthy subject sample going through a strictly standardized study procedure. Furthermore, measuring cerebral perfusion, serum parameters and subjective thirst ratings the impact of any cognitive or attention/motivation-related factors are limited to a minimum.

CONCLUSION

In conclusion, our findings confirm the role of the insular cortex as a central hub in the context of perception and emotional processing. Our results confirm that the insular cortex is a key player in the context of human emotional processing, because it comprises both specific representations of homeostatic and sensory-evoked emotions and it represents the site of cortical interaction between the two levels of emotions.

ACKNOWLEDGMENTS

We thank H. Friedrich, A. Nuoffer and S. Giezendanner for assistance with data collection and E. Michel for advice on blood parameters. Funding: This work was supported by the Swiss National Science Foundation (SPUM 33CM30-124114).

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(Received 13 October 2017, Accepted 17 April 2018)
(Available online xxxx)