THE ROLE OF DISTRACTION ON FLAVOR PERCEPTION, INTERACTIONS WITH SATIETY AND NEURAL RESPONSES TO FAT

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ABSTRACT

THE ROLE OF DISTRACTION ON FLAVOR PERCEPTION, INTERACTIONS WITH SATIETY AND NEURAL RESPONSES TO FAT

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Overeating and obesity are becoming more prevalent in the contemporary world. To treat obesity, it is essential to evaluate the environmental, behavioral, social, and emotional factors that contribute to its development. Habitual distracted eating, fat intake, and satiety are aspects associated with the development of obesity. The mechanisms behind these are still unknown. This thesis evaluates how distraction due to engagement in a concurrent working memory task impacts flavor perception. Then, the role of fat content (high fat, low fat, tasteless) on neural responses to flavor stimuli is evaluated, as well as correlations between neural responses and flavor suppression caused by distraction. Finally, the role of satiety in flavor suppression by distraction is explored. The results indicate that suppression of fat by distraction happens only when participants taste high-fat stimuli. Neural responses to high-fat and low-fat drinks vs. tasteless drinks are observed in the mid-dorsal insula/frontal operculum, precentral gyrus, thalamus, and cerebellum. We found no difference between the neural activation of low-fat versus high-fat drinks in the brain. However, we did observe positive brain-behavior correlations, such that a greater response to flavor in fusiform and amygdala responses was related to greater fat suppression by distraction in the flavor perception tasks. Satiety robustly affects working memory performance (a mixture of positive and negative effects on response times and accuracy), but not flavor perception nor distraction-mediated flavor suppression.

Keywords: fMRI, distraction, satiety, cognitive load, flavor perception

ÖZ

DİKKAT DAĞILMASININ AROMA ALGISI ÜZERİNDEKİ ROLÜ, DOYMA HİSSİ İLE ETKİLEŞİMLERİ VE YAĞ ORANINA KARŞI SİNİRSEL TEPKİLER

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Aşırı yeme ve obezite çağdaş dünyada giderek daha yaygın hale gelmektedir. Obezitenin tedavisi için bu hastalığın gelişimine katkıda bulunan çevresel, davranışsal, sosyal ve duygusal faktörlerin değerlendirilmesi önem taşımaktadır. Dikkat dağınık yemek yeme alışkanlığı, yağlı beslenme ve doyumsuzluk hissi obezitenin gelişimine katkıda bulunan temel etkenler arasında sıralanmakla beraber, bu etkenlerin arkasındaki mekanizmalar hala tam olarak bilinmemektedir. Bu tez çalışmasında, eş zamanlı bir işleyen bellek görevine dahil olmanın getirdiği dikkat dağınıklığının aroma algısını nasıl etkilediği araştırılmıştır. Buna ek olarak, yağ içeriğinin (yüksek yağ, düşük yağ, tatsız) aroma uyaranlarına verilen sinirsel tepkiler üzerindeki etkisi ve ayrıca sinirsel tepkiler ile dikkat dağınıklığının neden olduğu aroma bastırma düzeyi arasındaki muhtemel ilişkiler incelenmiştir. Bulgular dikkat dağınıklığı nedeniyle yağ etkisinin bastırılmasının yalnızca katılımcılar yüksek yağlı uyaranları tattığında gerçekleştiğini göstermiştir. Tatsız içeceklerle kıyaslandığında yüksek yağlı ve az yağlı içeceklerin oluşturduğu sinirsel tepkilerin orta dorsal insula/frontal operkulum, precentral gyrus, talamus ve serebellum bölgelerinde farklılaştığı gözlenmiştir. Az yağlı ve yüksek yağlı içeceklerin sinirsel izdüşümleri arasında anlamlı bir farklılık gözlenmemiş, ancak fusiform ve amigdala bölgelerinde görülen aroma algısı yanıtlarıyla dikkat dağınıklığına bağlı yağ baskılaması düzeyi arasında pozitif bir ilişki olduğu görülmüştür. Ayrıca, doyum durumunun çalışma belleği performansını belirleyen tepki süreleri ve doğruluk düzeyi gibi bağımlı değişkenleri güçlü bir şekilde etkilediği, fakat aroma algısı veya dikkat dağıtma yoluyla bastırılan aroma algısı üzerinde anlamlı bir etkisinin olmadığı gözlenmiştir.

Anahtar Sözcükler: fMRI, dikkat dağınıklığı, tokluk, bilişsel yük, Aroma algısı

To my family …

and

To the courageous people of my country, Iran, who are fighting for freedom…

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TABLE OF CONTENTS

ABSTRACT iv
ÖZ v
ACKNOWLEDGMENTS ix
TABLE OF CONTENTS xi
LIST OF TABLES xiv
LIST OF FIGURES xv
LIST OF ABBREVIATIONS xvii

CHAPTERS

1. GENERAL INTRODUCTION 1
    1.1. Obesity 1
    1.2. The role of distraction on flavor perception 1
    1.3. Eating and Flavor perception 5
    1.4. Neural responses to flavor and fat 5
    1.5. Satiety 7
    1.6. Aim of the Study 8
    1.7. Research questions and hypothesis 8
2. DISTRACTION SUPPRESSES HIGH FAT FLAVOR PERCEPTION 11
  2.1. INTRODUCTION 12
  2.2. MATERIALS AND METHODS 15
    2.2.1. Participants 15
    2.2.2 Device and Software 15
    2.2.3. Chocolate coconut drinks 16
    2.2.4. Pilot study for cognitive load conditions 16
    2.2.5. Main experiment design and procedure 17
    2.2.6. Data analysis 21
  2.2. RESULTS 23
    2.3.1. Working memory task outcomes: response time and accuracy 23
    2. 3.2. Flavor perception task outcomes: intensity and fattiness ratings 24

2.3.3. A longer time between working memory task and making ratings is related to the intensity of sensations. 25
2.3. DISCUSSION 26
3. INSTANT NEURAL RESPONSES TO DIFFERENT FAT CONTENT DRINKS AND THEIR CORRELATION WITH FAT SUPPRESSION CAUSED BY DISTRACTION 29
3.1. INTRODUCTION 30
3.2. MATERIALS AND METHODS 33
3.2.1. Participants 33
3.2.2. Device and software 33
3.2.3. Taste stimuli 36
3.2.4. Experimental procedures 37
3.2.5. Data analysis for fMRI data 39
3.2.6. Analysis of concurrent flavor perception task during distraction 41
3.3. RESULTS 42
3.3.1. Neural response to flavored drinks vs tasteless 42
3.3.2. No difference in neural responses between high-fat and low fat 49
3.3.3. Fat suppression by distraction 49
3.3.4. Correlation between neural responses to flavored drinks and distractibility 50
3.4. DISCUSSION 52
3.4.1. Neural responses to flavors regardless of fat content 52
3.4.2. Neural correlates of different fat contents in flavors 53
3.4.3. Relation between fusiform and amygdala responses and fat suppression by distraction 54
4. EFFECTS OF SATIETY ON PERFORMANCE IN DUAL TASK PARADIGM WITH FLAVOR PERCEPTION AND WORKING MEMORY 57
4.1. INTRODUCTION 58
4.2. MATERIALS AND METHODS 62
4.2.1. Participants 62
4.2.2. Device and Software 62
4.2.3. Drinks 62

    - 4.2.4. Experimental design and procedure 63
    - 4.2.5. Data analysis 65
  - 4.3. RESULTS 66
    - 4.3.2. Influence of preload on flavor perception: fat and intensity perception ... 71
  - 4.4. DISCUSSION 76
- 5. GENERAL DISCUSSION 81
  - 5.1. Concurrent working memory and flavor perception tasks 81
  - 5.2. Distraction suppresses high fat flavor perception 82
  - 5.3. Instant neural responses to different fat content drinks and their correlation with fat suppression caused by distraction 83
  - 5.4. Effect of satiety on performance in dual task paradigm with flavor perception and working memory 84
  - 5.5. Updated working model 85
  - 5.6. Continuing Studies 86
  - 5.7. Further studies 87
  - 5.8. Limitations 87
- REFERENCES 89
- APPENDICES 100
  - APPENDIX A. Supplementary Materials for Chapter 2 100
  - APPENDIX B. Supplementary Materials for Chapter 4 103
- CURRICULUM VITAE 107

LIST OF TABLES

Table 1.1: Summary of the results WM articles…………...…………………….….…... 3
Table 3.1: Significant cluster of BOLD response to (high-fat+low-fat)-tasteless drink……………………………………………………………………….……44
Table 3.2: Significant cluster of BOLD response to high-fat-tasteless……………....46
Table 3.3: Significant clusters of BOLD response to low-fat-tasteless drinks…....….48
Table 4.1: Statistics for working memory tasks…….……………………..…...……68
Table 4.2: Statistics for flavor perception tasks……………….……….……….…....72

LIST OF FIGURES

Figure 1.1: The general mechanisms proposed for the thesis…………….……….. 10

Figure 2.1: Model of the influence of distraction on eating behavior……………… 13

Figure 2.2: Four different cognitive load for distraction pilot tasks………………... 16

Figure 2.3: Response accuracy and response times in the pilot study for the WM tasks………………………………………………………………………… 17

Figure 2.4: Position of participants in the MR simulator with a gustometer system.... 18

Figure 2.5: Procedure of sending drink to the mouth of participants………………… 18

Figure 2.6: The cut-off in the bore and the distance between eyes and screen……… 19

Figure 2.7: Covered MRI Simulator………………………………………………… 19

Figure 2.8: Distraction task with low cognitive load………………………………… 20

Figure 2.9: Distraction task with high cognitive load………………………………… 21

Figure 2.10: A timeline for concurrent working memory and flavor perception tasks. 21

Figure 2.11: Conditions for each run of a distraction task…………………………... 22

Figure 2.12: Design of Distraction tasks……………………………………………. 22

Figure 2.13: Response accuracy and response times in the WM task………………. 23

Figure 2.14: Intensity and fat ratings in the flavor perception task……………...... 25

Figure 3.1: The fMRI scanning room at UMRAM and the 32-channel head coil…… 34

Figure 3.2: The setup cart for a gustometer system and pipes for cleaning objects.… 35

Figure 3.3: The procedure of sending a drink to the mouth of a participants………. 35

Figure 3.4: Timeline of the fMRI block design……………………………………… 35

Figure 3.5: TANITA scale…………………………………………………………… 36

Figure 3.6: MRI scanning while presenting drinks with pumps………………..……. 38

Figure 3.7: Neural responses to (high-fat+low-fat)- tasteless………………………… 43

Figure 3.8: Neural responses to high-fat-tasteless………………………………... 45

Figure 3.9: Neural responses to low-fat-tasteless drinks…………………………… 47

Figure 3.10: Fat rating in the flavor perception task…………………………….…… 50

Figure 3.11: Correlation between neural responses to drinks and distractability….… 51

Figure 4.1: Proposed model for the effect of satiety on flavor perception and WM tasks…………………………….………………………………………………. 61

Figure 4.2: Timeline for an ER scan and distraction task ………………………….... 64

Figure 4.3: Timeline for consumption scans followed by distraction tasks………… 64

Figure 4.4: Impact of preload type on the proportion of correct answers……………. 70

Figure 4.5: Impact of preload type on response time………………….…………… 71

Figure 4.6: Impact of preload type on fat perception……………………………..... 74

Figure 4.7: Impact of preload type on intensity perception.…………..…………… 75

Figure 5.1: General model for the study……………………..…….…..…………… 86

LIST OF ABBREVIATIONS

AC: Anterior Commissure

ACC: Anterior Cingulate Cortex

aDCN: Anterior Deep Cerebral Nuclei

AFNI: Analysis of Functional Neuro Images

BIA: Bioelectrical Impedance Analysis

BIDS: Brain Imaging Data Structure

BMI: Body Mass Index

BOLD: Blood Oxygen Level Dependent

CNS: Central Nervous System

CSV: Comma Separated Values

DCI: Daily Calorie Intake

DICOM: Digital Imaging and Communications in Medicine

DLOFC: Dorsolateral Orbitofrontal Cortex

EEG: Electroencephalography

fMRI: Functional Magnetic Resonance Imaging

FFA: Fusiform Face Area

FOV: Field of View

FSL: FMRIB’s Software Library

GRAPPA: Generalized Autocalibrating Partially Parallel Acquisition

iPAT: Integrated Parallel Image acquisition Technique

JSON: JavaScript Object Notation

MB: Multiband

MPRAGE: Magnetization-Prepared Rapid Gradient -Echo

MR: Magnetic Resonance

MVPA: Multivoxel Pattern Analysis

NIFTI: Neuroimaging Informatics Technology Initiative

OFC: Orbitofrontal Cortex

PC: Posterior Commissure

PTB: Psychtoolbox

PWS: Prader-Willi Syndrome

ROI: Region of Interest

SD: Standard Deviation

SEM: Standard Error of the Mean

SNR: Signal to Noise Ratio

SPM: Statistical Parametric Mapping

ST: Slice Thickness (mm)

TA: Time of Acquisition

TR: Repetition Time

UMRAM: National Magnetic Resonance Research Center

VAS: Visual Analogue Scale

VN: Vagus Nerve

VPMpc: Ventroposteromedial Nucleus

WM: Working Memory

CHAPTER 1

GENERAL INTRODUCTION

1.1. Obesity

Obesity is becoming more prevalent in modern society. (Makaronidis and Batterham, 2018). It is also rising in Turkey (Pekcan et al., 2017). Basically, the imbalance between energy intake and expenditure causes obesity (Nijs and Franken, 2012; Tepper & Yeomans, 2017). As obesity causes many other diseases, it imposes high expenditures on governments and health care systems; in the meantime, it reduces quality of life and life expectancy among people. Obesity is affected by environmental, social, and emotional aspects (Makaronidis and Batterham, 2018). Evaluating these aspects with the purpose of curbing obesity is an urgent need that motivates this study, and it can also help bring down the costs for societies.

Many factors are associated with the development of obesity and overeating (Vandenbroeck et al., 2007). Habitual distracted eating, fat intake, and satiety are identified as prominent contributors to obesity and overeating. In three different chapters of this study, we evaluate the role of distraction on flavor perception. Besides, we inspect brain responses for different fat contents and their interrelation with flavor suppression as well as the role of satiety on the dual task paradigm of working memory tasks and flavor perception tasks.

1.2. The role of distraction on flavor perception

Modern, fast-paced life often includes multitasking during meals and other food consumption. Meals are habitually consumed in front of a television (Gore et al., 2003), computer screen, or with a mobile device in hand (Carrier et al., 2015), while steering the wheel of a car (Stutts et al., 2005), or while having social interactions (van Meer, 2022a). Multitasking impacts the performance of cognitive tasks as attentional resources compete with each other and there is limited capacity for attentional resources (Yantis, 2000). According to Kochs et al. (2023), the role of attention in food perception is particularly important. They proposed that brain responses to food are triggered by attentional focus rather than the calorie amount or palatability of the food. Performing other tasks while eating may change how food is perceived and how much is consumed. A representative cross-sectional study showed that watching TV while consuming food was associated with a higher BMI (van Meer et al., 2022a). Experimental studies provided causal evidence for the effect of distraction on food consumption. In children, Temple et al. (2007) showed an increase in food consumption while distracted. Consistently, Robinson et al. (2014) and Veit et al. (2020) found a decrease in food consumption and portion size in mindful eating. There are also studies that demonstrate the role of television (Brunstrom & Mitchell, 2006; Bellissimo et al., 2007; Temple et al., 2007) or other distracting conditions like driving or social eating (Ogden et al., 2013) in increasing food intake. Although distracted eating is related to an increase in food intake, the mechanism behind it is not that clear.

One mechanism by which distracted eating may lead to an increase in food intake is by suppressing perception of the chemosensory stimuli, triggering overconsumption to reach a desired sensory stimulation level (Van der Wal & van Dillen, 2013). To test this hypothesis, various studies used an experimental dual-task paradigm with a concurrent working memory task and a visual or chemosensory food perception task. Generally, in these tasks, to evaluate the possible suppression of food perception, low and high cognitive loads are manipulated for WM tasks. These tasks mostly have been done with the memorizing and rehearsal of alphanumeric strings (with one character versus seven characters for low and high cognitive loads, respectively). But a few studies used different manipulations, for example, a high-speed tetris game vs. a low-speed tetris game. In the food perception task, visual stimuli (food pictures) or chemosensory stimuli are presented. Food perception is usually evaluated on intensity ratings, but also on detection rates and categorization accuracy. Often, the food stimuli are presented at varying concentration levels or stimulus types (for example, stimuli associated with low-calorie vs. high-calorie foods). I summarized the different study methods in Table 1.1.

Notably, it was found that distraction suppresses the food stimulus perception. For instance, the detection rates of peri-threshold sweet and bitter pure taste solutions (Liang et al. 2018) and intensity ratings of sweet, sour, and salty foods (van der Wal & van Dillen, 2013) were reduced under distraction. Schadll et al. (2021) found a decrease in the intensity perception of food and non-food odors under the faster version of the game Tetris that was played by participants as a distraction. Less uniform effects of distraction have also been observed: van Meer et al. (2022a) observed that intensity and desirability were suppressed only in high sweet rather than low sweet glucose solutions. van Dillen & van Steenbergen (2018) observed the suppression of only high-calorie food pictures versus low-calorie or object pictures, and Hoffman et al. (2017) observed only the suppression of low-calorie food odors. Finally, Duif et al. (2020) found a reduction in taste neural responses under higher cognitive loads of categorizing objects and that the degree of neural response in the right insula to low-sweet stimuli under high distraction predicted subsequent consumption. Importantly, van der Wal & van Dillen (2013) and van Meer et al. (2022a) were able to prove that the suppression mechanism is indeed related to overconsumption because, in their studies, participants consumed more food under higher cognitive loads in ad libitum tasks and/or preferred higher concentrations of sugar under higher cognitive loads.

Table 1.1 Summary of the results WM articles

Article first author (year)	**WM task**	**WM levels**	**WM response (timing)**	**WM outcomes**	**Food stimulus task**	**Food stimulus response timing**	**Food stimulus modality**	**Food stimulus levels**	**Food stimulus outcomes**	**Internal state**
Wal & van Dillen (2013)	Digit + consonant span	1 vs 7	Handwritten (after food stimulus presentation)	-	Rate sweetness (during WM maintenance period)	After WM response	Gustatory in food Study 1: lemon juice Study 2: grenadine lemonade Study 3: butter on crackers	Study 1: 10 vs 30 % lemon juice in water Study 2: 0 vs 10 vs 30% lemonade in water Study 3: salt-free vs salted butter on crackers	Study 1: sourness rating Study 2: Sweetness rating Study 3: Saltiness ratings, amount consumed	Not reported
Van Dillen & van Steenbergen (2018)	Digit span	1 vs 6	Same/different forced choice (after food stimulus presentation)	Proportion correct and response times	Edibility categorization (During WM maintenance period)	During picture viewing (before WM response)	Visual (food pictures)	Low vs high calorie	Response time, proportion correct	1-3 hours after food intake
Van Meer et al., (2022a)	Digit span	1 vs 7	Same/different forced choice (after food stimulus presentation)	Proportion correct	Study 1: Rate intensity (VAS 0-8) Study 2: Rate preference (too sweet, just right, not sweet enough)	After WM response	Pure gustatory solutions with glucose in water	Study 1: Weak vs strong Study 2: 5 concentrations	Taste intensity preference	2 hours after food intake
Liang	Digit + consonant span	0 vs 2 vs 4 vs 6 vs 8	Verbal free recal (after food stimulus presentation)	-	Detect quality (-1,0,1) -1 for bitternes,0 nor bitter nor sweet,1 sweet	Unclear	Pure gustatory solutions of sucrose and phenylthourea	5 peri threshold concentrations + water	Taste detection ratio = proportion correct	1 hr after food intake
Hoffman et al., (2017)	Consonant span	1 vs 7	Forced choice recall (after food stimulus presentation)	Proportion correct	Rate intensity (VAS 0-100)	After WM response	Orthonasal odors	No odor/low caloric/high caloric	Odor intensity	Minimum 1 hr after food intake

Schadll et al. (2021)	Tetris video game	1 sq/0.47 s vs 1 sq /0.10 s	Move blocks with arrow keys (during food stimulus presentation)	Number of rows solved in 56 seconds, perceived difficulty (VAS 1-10)	Rate intensity (VAS 1-10)	After game ends	Orthonasal odors	No odor/food odor/non-foodor	Odor intensity	Minimum 1 hr after food intake
Duif	Object categorization	75 ms vs 750 ms presentation	Button press if picture matches instructed category (furniture, tools, toys)	d’	Not on trials only before and after test	-	Chocolate milk	Low vs high sweetness from non-caloric sweetener	Neural responses	Standardized meal 3 hr before the test

There do not appear to be any resources that explicitly look at the effects on holistic intensity ratings in the more complex chemosensory system of flavor yet. Therefore, the first aim of this thesis is to see how distraction affects the perception of flavor. I chose to ask participants to give overall intensity ratings of the stimuli in the flavor perception task. And since the previous work summarized above showed differences between high vs. low calories or high vs. low sweets in other studies, I wanted to focus on such a dimension too. I chose a high vs. low fat variation in the flavor stimuli because some of the methods used in this thesis are also used in a project aimed at evaluating the role of vagus nerve modulation on fat perception. To complement the variation in fat content, I also asked participants to rate the fattiness of the stimuli in the flavor perception task.

Concerning the working memory task, I modeled the design closely after Hoffman et al. (2017). However, I wanted to take an agnostic approach to the cognitive load conditions in the consonant span task, as a span of one consonant only may have unintended effects besides being low in cognitive load. This low span of one consonant may lead to boredom and underperformance, which may act as confounding factors besides cognitive load. Therefore, I first conducted a pilot study (reported in the methods section of Chapter 2) to assess suitable alternatives with low and high cognitive loads.

1.3. Eating and Flavor perception

The sequence of perceptual events when eating is that the food is first perceived visually and then by sniffing (orthonasal olfaction). Then, when the food is taken into the mouth, there is oral stimulation that involves multiple sensory systems (taste, somatosensory, and retronasal olfactory) (Piqueras-Fiszman and Spence, 2016). Processing flavor involves merging sensory inputs with simultaneous temporal and spatial occurrences and the assignment of attention (Small and Prescott, 2005). Then post-ingestive consequences involve interactions with receptors in the gut and the release of hormones in the bloodstream. These then affect the brain on a slower timescale. Together with the sensory signals, these slower responses affect the hedonic processing of food, wherein wanting, liking, and learning step in and impact food consumption (Piqueras-Fiszman and Spence, 2016). Flavor perception refers to the method by which our brain processes and interprets sensory information such as odor, taste, temperature, and texture (Hanci and Altun, 2016; Tepper & Yeomans, 2017). According to de Graaf and Boesveldt (2017), there are similarities between taste and smell perceptions, but they serve different purposes. This review article also highlights that humans can distinguish five or six tastes but more than a trillion smells.

1.4. Neural responses to flavor and fat

Based on Small and Prescott (2005), the neural activities of flavor perception are associated with the activation of chemosensory areas such as the anterior insula, frontal operculum, orbitofrontal cortex, and anterior cingulate cortex (ACC). Also, the areas for the integration of flavor are supposed to be in the posterior parietal cortex and ventral lateral prefrontal cortex. The insular cortex is recognized as a primary taste cortex (Small, 2010). And based on a meta-analysis of taste (Neurosynth, n.d.), flavors are expected to activate the insula. According to a meta-analysis by Huerta et al.

(2014), the left anterior insula is activated by various kinds of food stimuli, like taste, odor, or visual representation. Veldhuizen et al. (2011) showed that with taste stimuli, insular areas become activated together with the operculum. Consistently, Roll et al. (2011) also reported the joint activation of the insula and operculum for taste. Referring to the review article by Lundstorm et al. (2011), taste activates the brain stem, insula, and orbitofrontal cortex (OFC), and smell activates a set of areas in the frontal and medial anterior temporal lobes: “anterior olfactory nucleus, the olfactory tubercle, the anteromedial part of the entorhinal cortex, the periamygdaloid cortex, the anterior cortical nucleus, and the nucleus of the lateral olfactory tract of the amygdala”. Consistent with Small and Prescott (2005), Lundstorm et al. (2011) highlight that the dorsal anterior part of the insular cortex with the overlying frontal operculum is the area that becomes activated regardless of the type of chemosensory stimuli in response to the integrated chemical senses of smell, taste, and trigeminal perception that merge to form flavor perception. It should be noted that trigeminal perception, is a chemical sense that receives chemosensory information from the environment and is referred to as” intensity, warmth, coldness, and pain” (Filou et al., 2015).

Fat intake is one of the contributors to weight gain and, consequently, obesity. Animal studies show the role of high fat consumption in the development of obesity (Hariri and Thibault, 2010); human studies also associate obesity with higher energy intake from a high-fat diet (Hill et al., 2000; Schrauwen and Westerterp, 2000). Therefore, it is important to evaluate the role of fat content on the brain to be able to prevent obesity and develop treatments and prevention plans for it. Chapter 3 inspects the role of different fat contents on the neural response and evaluates the correlation of neural responses with fat perception suppression in a separate task.

According to Running et al. (2015), different attributes of fat are involved in the neural responses of the brain. There is consensus that fat may be considered a basic taste that is perceived in the mouth first (Tucker et al., 2014). Then the texture of fat triggers somatosensory receptors, volatiles from fat may also stimulate olfactory receptors through the retronasal route, and finally, neuropad receptors in the gut become engaged. Heinze et al. (2015) hypothesized observing neural responses to fat in sensory areas, including gustatory and somatosensory areas, together with reward areas. Only a few studies have directly investigated how fat content affects brain responses using the fMRI paradigm.

De Araujo et al. (2004) used high-fat vegetable oil versus a matched viscous drink, and they showed responses in the mid and anterior insula, hypothalamus, and ACC. Grabenhorst et al. (2010) presented strawberry and vanilla flavored high-fat and low-fat drinks, and they found neural activation in the lateral hypothalamus and amygdala. Eldeghaidy et al. (2011) evaluated brain responses to four different fat concentrations, and they observed a linear relationship of fat content in the ACC, anterior insula, frontal operculum, amygdala, and somatosensory areas. However, in another study, Eldeghaidy et al. (2012) found no difference in the activation of the brain in high-fat versus no-fat conditions. In the same way, Stice et al. (2013) could not find a robust difference in the activation of high-fat versus low-fat. It should be considered that the studies that observed neural responses mostly used high fat concentrations above what is found in daily food, and many of these studies were done before the latest breakthroughs in Generalized Autocalibrating Partially Parallel Acquisition

(GRAPPA, Griswold et al., 2002; Larkman & Nunes, 2007) and multiband (MB) scanning (Larkman et al., 2001). Besides, it seems that in these studies the spatial resolution was 3 mm or more; by using a higher spatial resolution, we can detect smaller volumes better. Besides, across these research studies, event-related design is used, whereas block design appears to show more efficiency in detecting neural responses (Birn et al., 2002). Considering all these studies, we used new advances in fMRI with a multiband scanning sequence and grappa to observe neural responses to different fat contents (tasteless, low-fat, and high-fat) in an interleaved fashion block design. It is hypothesized to observe activations and differences regarding fat contents in the brainstem, thalamus, insula, overlying operculum, hypothalamus, amygdala, and orbitofrontal cortex.

Fat perception varies remarkably among individuals (Tucker & Mattes, 2013). Personal differences in responsiveness to gustatory stimulations are driven by gustatory network activity, including the amygdala (Veldhuizen et al., 2020). It may be that individual differences in sensitivity to chemosensory stimuli are related to individual differences in distractibility. In chapter 3, we therefore examine the correlation between neural responses and participants' distractibility from fat suppression. In this respect, we presume the activation of the amygdala, which is commonly acknowledged to play a role in the process of salience of stimuli (Kong and Zweifel, 2021). Other gustatory and reward areas also might be involved.

1.5. Satiety

Given the not-uniform effect of distraction on the dual WM-chemosensory perception task reported in the literature, it may be that the saliency of the chemosensory stimuli influences how impactful distraction is. It may be that some stimuli are more salient than others and therefore more resistant to distraction. For instance, Hoffman et al. (2017) evaluated the role of cognitive load on low-calorie and high-calorie food odor perception. They used orange and apple odors for the low-calorie case versus chocolate and caramel for the high-calorie case, which confirmed that perception was suppressed for low-calorie food odor stimuli but not for high-calorie food odor stimuli. But the physiological state of the participant may also play a role. For example, when hungry, because of the salience of food stimuli, there might be less suppression in food perception. Referring to the column of internal state in Table 1, in most of the studies, the participants were (at least somewhat) hungry, and they were asked not to eat for 1-3 hours before the tests, hence, the level of hunger probably varied in those studies. For example, most people would be at least moderately hungry after not eating for 4 hours, and it would fit with goal-directed behavior to perceive flavor stimuli with greater acuity. Conversely, an hour after a meal, you might be quite full and not interested in anything perceived through the chemical senses. Blundell & Bellisle (2013) also highlighted that satiety influences the emergence and maintenance of obesity. Satiety is defined as the process of prohibiting appetite after eating, while satiation is about the process of terminating food intake in an ongoing meal (Tepper & Yeomans, 2017). Sensory cues and cognitive cues also play a role in satiety (McCrickerd, K. 2017). On the other hand, satiety also influences flavor perception. The available evidence in this regard presents a conflicting picture. Zverev (2004) reported that when hungry, participants had lower detection thresholds for sugar and salt *tastes* than when they were full. However, for bitters, there was no effect of hunger or satiety. Besides Shanahan and Kahnt, (2022) demonstrated the role of satiety and hunger on *odor* perception, and pleasant odors impact food intake by influencing selection and liking of foods. In the study of Cabanac (1971), where the impact of glucose was under scrutiny, when people were hungry, citrus odors rated more pleasant than when they consumed 100 gr of glucose. They also highlighted that the satiated condition reduces the platability ratings of food. In a reviewing article, Nie et al. (2022) demonstrated that in fasted versus full conditions, odor perception increases. It was consistent with Ramaekers et al.'s (2016) findings. Hanci and Altun (2016) investigated the impact of satiety on *taste and odor*. Their results were consistent with other studies in a way that when hunger increased, odor perception and taste perception for sweet, savory, and salty foods increased, while it decreased for bitter taste. There is a lack of studies to show the role of satiety on *flavor*. Siep et al. (2009) found interferences between hunger and neural responses for energy content. Satiety can be manipulated with preloads, the controlled consumption of food before other experimental procedures. Chapter 4 evaluates the role of preloads with different fat contents on distracting working memory performance and flavor perception under high and low cognitive loads for WM tasks.

1.6. Aim of the Study

The overarching aim is to investigate the role of working memory tasks in concurrent flavor perception tasks. Additionally, we investigate the neural responses to different fat contents and their correlation with fat suppression perceived due to distraction. Finally, we explore how satiety with different fat contents affects performance in dual paradigm tasks. The current study is being conducted to pursue the research questions below:

1.7. Research questions and hypothesis

Chapter 2) The role of distraction on flavor perception

RQ1) How does cognitive load (high versus low) in working memory tasks impact the response time and accuracy of participants?

H1) If cognitive load impacts participants' performance, then we should observe a higher proportion of correct answers and a lower response time under low cognitive load than high cognitive load.

RQ2) How is flavor perception (fat and intensity ratings) affected by distraction caused by working memory tasks?

H2) If attentional resources for working memory are competing with those allotted for flavor perception, it is expected to see more suppression of fat and intensity perception under high cognitive load than under low cognitive load.

Chapter 3) Instant neural responses to different fat content drinks and their correlation with fat suppression caused by distraction.

RQ1) Which brain areas respond to sips of drinks with different fat contents (tasteless, low-fat, and high-fat)? Is there any difference between neural responses to high-fat and low-fat drinks.

H1) It is expected to observe neural responses in taste and somatosensory areas, like the brainstem, thalamus, insula, overlying operculum, hypothalamus, amygdala, and orbitofrontal cortex, and differences in activation for different fat contents.

RQ2) What is the correlation between neural responses to flavor stimulation contents and the degree of flavor suppression caused by distraction in a subsequent task?

H2) We expect to find some areas of activation like the amygdala, dorsolateral or ventral prefrontal cortices related to the fat suppression caused by distraction.

Chapter 4) Effect of satiety on performance in dual task paradigm with flavor perception and working memory.

RQ1) How does satiety (manipulating the fat content of preloads on different experimental days) impact the performance of participants in a working memory task? And how does it affect flavor perception (fat and intensity perception) and the suppression of flavor perception caused by distraction?

H1) If satiety influences selective attention between competing stimuli, then we should observe stronger flavor perception in the hungry case than the full case. And we also expect hunger conditions to make chemosensory stimuli less vulnerable to the effects of distraction.

1.8. General outline of the thesis:

Overall, Chapter 1 provides a general introduction to the current study. Chapter 2 investigates how distraction while performing a flavor perception task influences it. Hence, working memory tasks with low and high cognitive loads are used while perceiving the fat and intensity of high-fat and low-fat drinks to determine the role. Chapter 3 examines how the central nervous system (CNS) responds to different fat-content drinks and what the correlation is with fat suppression caused by distraction, and Chapter 4 evaluates the possible effect of satiety on both flavor perception and flavor suppression caused by working memory tasks. Different preloads on different experimental days are applied to trace the effect. And Chapter 5 presents general achievements and discussion for the study. Figure 1.1 below shows the general proposed mechanism for this research over three chapters.

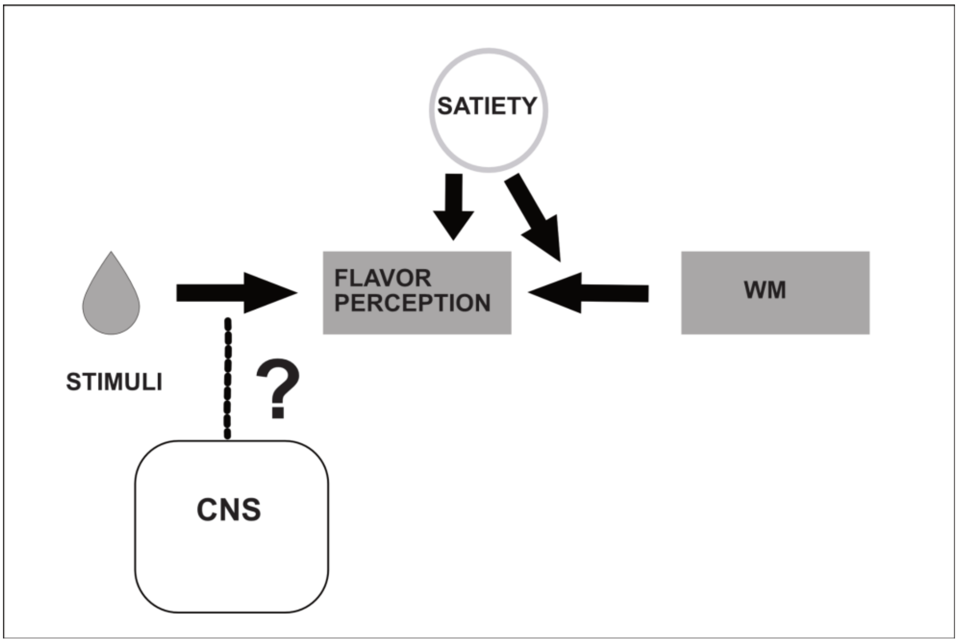


Figure 1.1. The general mechanisms proposed for the thesis. The impact of distraction by a working memory task on flavor perception; neural responses to drinks with different fat contents and their correlation with the distractibility factor; and the effect of satiety on flavor perception and flavor suppression caused by distraction.

CHAPTER 2

DISTRACTION SUPPRESSES HIGH FAT FLAVOR PERCEPTION

ABSTRACT

Distraction during eating contributes to overeating, and when habitually eating with distraction, this may contribute to the development of obesity. One of the proposed mediating mechanisms is the suppression of intensity perception in odor and taste. The effect of distraction on the fat intensity perception of flavor, the multisensory combination of odor, taste, and other sensory aspects, is still unknown.

In this study, 32 participants (22 women) performed a flavor perception task while also performing a distracting working memory task. In each trial, participants were instructed to observe and memorize a string of 3 (low cognitive load) or 7 (high cognitive load) consonants. Then they received a small quantity of high-fat or low-fat chocolate drinks, and after that, they were asked to select the string they tried to memorize from three options. Lastly, they rated the intensity and fattiness of the flavor.

As intended, in the working memory task, we observed that with the high cognitive load (relative to the low cognitive load), accuracy was decreased, and response times were increased. Regarding perception of the flavors, we observed that overall, high-fat drinks were rated as more intense and fattier. Cognitive load and fat content interacted such that for the low-fat drink, fattiness ratings were similar under both cognitive loads; however, under high cognitive load (relative to the low cognitive load), fattiness ratings for the high-fat drink were lower.

Our results show that distraction can impact the perception of fat in high-fat drinks. If distraction primarily reduces perception of the unhealthy macronutrients in high calorie foods, this may pose a particular risk to overeating unhealthy foods.

Keywords: Attention, Distraction, Cognitive load, Flavor perception, Fat perception

2.1. INTRODUCTION

Universally high rates of overweight and obesity are risks for health and reduce the quality of life (World Health Organization, 2022). Many factors contribute to the development of overweight and overeating, as captured in an arresting complex systems map (Vandenbroeck et al., 2007). An important contributor—the force of dietary habits—is influenced by psychological and food consumption factors, including television watching (Vandenbroeck et al., 2007), Indeed, modern fast-paced life often includes multitasking during meals and other food consumption. Many meals are consumed in front of a television (Gore et al., 2003), computer screen, or with a mobile device in hand (Carrier et al., 2015), while steering the wheel of a car (Stutts et al., 2005), or while having social interactions (van der Meer, 2022a). A representative cross-sectional study showed that watching TV while consuming food was associated with a higher BMI (van Meer et al., 2022a). Multitasking is known to affect performance on cognitive tasks due to the competition for limited attentional resources (Yantis, 2000). Such multitasking during food consumption would decrease food perception and affect food consumption. Experimental studies provided causal evidence for the effect of distraction on food consumption. For example, Temple et al. (2007) showed that in children, distraction or shifting attention during eating results in more food intake. Conversely, mindful eating reduces food consumption (Robinson et al., 2014) and portion size (Veit et al., 2020). Multiple studies have shown that satiety can be delayed, and that food consumption can increase while watching television (Brunstrom & Mitchell, 2006; Bellissimo et al., 2007; Temple et al., 2007). Higgs and Woodward (2009) reported vague recall of a meal when distracted by TV versus a control group, and subsequent increased snack intake. When consuming meals with others, particularly with family and friends (De Castro, 1994), food intake is facilitated, which is not compensated for in subsequent days (Ruddock et al., 2022). Lastly, Ogden et al. (2013) showed that any distraction increased snack consumption when participants were allocated to 4 different competing tasks (driving, watching TV, interacting with others, or the control task of eating alone). Summarizing, distraction during eating contributes to overeating, and when habitually eating with distraction, this may contribute to the development of obesity.

A few studies have investigated a potential mechanism for the role of distraction during eating. The model generally proposed is that increased cognitive load reduces the perception of the food stimulus (Fig. 2.1), which then presumably results in a compensatory mechanism that leads to overeating. The reduction in perception may result from decreased attentional resource availability (van Meer et al., 2022a) and/or decreased information transmission between brain areas (Duif et al., 2020). In support of the intensity suppression model, van der Wal & van Dillen (2013) reported that sour, sweet, and salty foods are eaten more and are rated as less intense when sampled during a working memory task with a high cognitive load (7-digit/consonant) versus a low cognitive load (1-digit/consonant). Moreover, higher sucrose concentrations in food are favored in an ad libitum task under a higher memory load (van der Wal & van Dillen, 2013). Van Meer et al. (2022a) reported that cognitive load decreases intensity perception and food desire for only strong sweet glucose drinks compared to weak sweet drinks under the working memory task of 1 versus 7-digit numbers. Liang et al. (2018) replicated and extended these findings. They used a distracting working memory task with different cognitive loads (0, 2, 4, 6, and 8 alphanumeric items) and six different concentrations of sweet or bitter solutions (near the threshold). They observed that distraction decreases both sweet and bitter detection ratios and that a higher cognitive load is associated with a greater decrease in detection ratios. Hoffman et al. (2017) used two distraction levels with a similar working memory task (low cognitive load: strings with 1 consonant, high cognitive load: strings with 7 consonants) and two food odors representing foods with different caloric densities (low/high). They showed that odor perception for high caloric odors didn't change under distraction, but that the high cognitive load specifically decreased intensity ratings for low caloric odors. This result was replicated in a more naturalistic task by Schadll et al. (2021), who probed the role of playing a Tetris game on olfactory intensity perception. They reported reduced odor intensity perception under high (faster dropping of Tetris stones) versus low (slower) difficulty levels of the game for both edible and inedible odors. Summarizing, the proposed mechanism for the effect of distraction on overeating is through a reduction in the perception of gustatory and/or olfactory components of the food stimulus.

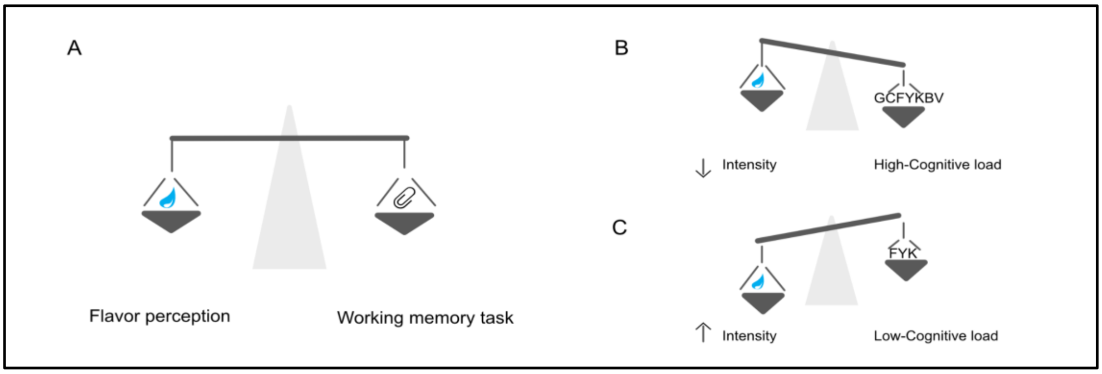


Figure 2.1. **model of the influence of distraction on eating behavior.** This model assumes limited and flexible attentional resources, which are divided over two tasks performed in parallel (panel A). When one of the tasks places a greater demand on the resources, less resources will be available for the other task, resulting in decreased perception and performance. For example, in panel B, there is a difficult competing memory task that decreases the resources available for the flavor perception task, leading to decreased intensity perception relative to flavor perception with an easier competing memory task (panel C).

These studies either evaluate taste or odor perception separately in model stimuli (Liang et al., 2018; Hoffman, 2017; Schadll et al., 2021), or focus only on taste aspects of more complex stimuli (van der Wal & van Dillen, 2013; Duif et al., 2020, van Meer, 2022a). The effect of distraction on flavor perception - the holistic combination of taste, odor, and other sensory aspects- is still unknown. Moreover, considering the role of calories of associated foods that Hoffman et al. (2017) observed in the intensity suppression of odors, it is important to investigate the interaction with calories in flavor stimuli too. Here we used a palatable chocolate-coconut milk drink with two different levels of fat to address the effect of calories. We asked participants to evaluate the intensity and fattiness of the drinks while doing memory tasks with low and high cognitive loads. If distraction suppresses perception of flavor, we expect to observe reduced fat and intensity perception under higher cognitive load relative to lower cognitive load.

2.2. MATERIALS AND METHODS

2.2.1. Participants

32 participants (10 men, 22 women) with an average BMI of 22.01 (+/- 1.95 standard deviation) were recruited for the experiments. Their average age is 23.70 (+/- 5.54 standard deviation). These participants were not the same as those in the pilot task. All participants reported having no known taste, smell, neurological, psychiatric (including eating disorders), cardiological, metabolic, or other pathological disorders. Participants were screened for common cold symptoms and COVID-19 symptoms before attending lab sessions. They had normal eyesight, or their eyesight was corrected to normal with glasses. Participants gave informed consent and were instructed and trained before starting the experiment. The study protocol (numbers 7807789 / 050.01.04 / 1152384) is approved by the Mersin University Committee for Clinical Research. This study was part of a larger study which included neuroimaging of neural responses to food with functional MRI. Some participants received monetary compensation for their participation in the larger study, others volunteered without monetary compensation (which is commonly done in research studies in Türkiye). The study was done at the National Magnetic Resonance Research Center (UMRAM) at the Aysel Sabuncu Brain Research Center of Bilkent University in Ankara, Turkey. Tasks are performed in a room with a quiet atmosphere that is equipped with an MR simulator scanner and gustometer system.

2.2.2 Device and Software

The main experiment data collection was done inside an MRI simulator, which includes a laptop monitor for displaying instructions and strings (Fig.2.4). Drinks are sent inside the simulator to the mouths of participants with a gustometer system (Figs 2.4 and .2.5). The gustometer is a computer-controlled syringe pump system used to deliver liquids to the mouths of participants. Three pumps are serially connected. Each pump was loaded with a syringe holding either a low-fat or high-fat coconut-chocolate drink or water. Each syringe is connected to a tube, which attaches to the mouthpiece (Fig. 2.5). We used MATLAB (R2021a) and Psychtoolbox-3 (PTB-3) (Brainard & Vision (1997)) code for delivering drinks to the mouths of participants, displaying strings on the screen, and for VAS rating of fattiness and intensity. For each trial, we recorded the following: length of the target string, target string, alternative string options, selected string, trial starting time, response time, accuracy, flavor solution, intensity VAS cursor position, and fattiness VAS cursor position. These variables were saved in a comma separated file. The screen distance is set to be 67 cm from the eye of the participant, which matches the comfort distance evaluations based on participants' preferences reported in Taptagaporn et al. (1995); Jaschinshi-Kruza (1990); and Jaschinski (1998). A Tanita (BC-601F) scale (Japan), which also measures bioelectrical impedance analysis (BIA), was used to measure the body mass index (BMI in kg/m2) of participants.

2.2.3. Chocolate coconut drinks

Two different levels of fat are used for preparing drinks: low-fat drinks (3.5% fat and 10% sugar) and high fat drinks (15% fat and 10% sugar). Vegan materials are used in the experiments. For the low-fat drink, 424 g of Alpro almond milk, 37 g of Thai Coco coconut cream, 40 g of sucrose, 6 g of Dr. Oetker cacao powder, and 1.25 g of vanilla sugar were heated and mixed (~70 kcal per 100 ml). For the high-fat drink, 252 g of Alpro almond milk, 206 g of Thai Coco coconut cream, 42 g of sucrose, 6 g of Dr. Oetker cacao powder, and 1.25 g of vanilla sugar were heated and mixed (~137 kcal per 100 ml). Both drinks were then cooled for half an hour at room temperature before being placed in the refrigerator. To match the coconut flavor in both drinks, we added extra coconut flavoring to the low-fat drink. Half an hour before tests, drinks are taken out of the refrigerator, tubes and syringes are filled with drinks, and they are placed in pumps.

2.2.4. Pilot study for cognitive load conditions

To determine the two cognitive loads (high and low) for the distracting working memory task, we first performed a pilot study with four different conditions in 30 participants (17 women) with an average age of 24.1 (+/- 3.96 SD). The aim was to observe how cognitive load affects response time and performance (proportion of correct answers). In this within-subjects design, participants observed strings of (1/3/5/7) consonants, and they were asked to memorize them. Then, from three options, they selected the string they memorized. For strings, 18 common consonants between the English and Turkish languages are used. To avoid mnemonic or visual pattern strategies, repeated letters were not used, and only capital letters were used. The same combination of letters as the target was used for three answer options. In each of the two incorrect alternatives, the positions of two of the letters were swapped within the string (randomly selected). The position of the target within the three answer options was also randomly determined. Fig 2.2. indicates the timeline of four different conditions for pilot tasks.

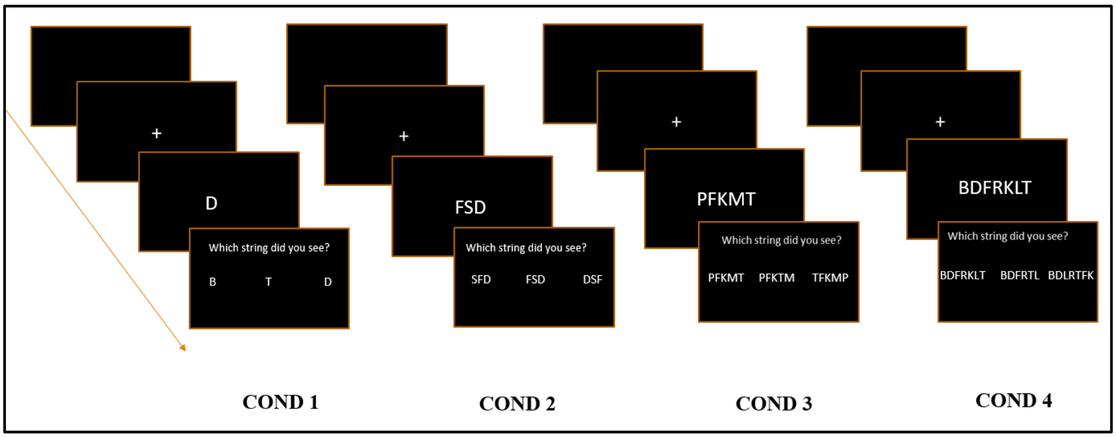


Figure 2.2: Four different cognitive load for distraction pilot tasks

There were four blocks for each condition, each containing 12 trials. The order of the blocks was randomized among the participants. Participants did not receive any drinks in this pilot task. A repeated measures ANOVA showed a main effect of condition on both response time (F (3,87) = 39.05, p <.001, $\eta^2 = 0.574$) and the proportion of correct answers (F (3,87) = 13.17, p <.001, $\eta^2 = 0.312$) shown in Fig 2.3. Post-hoc pairwise t-tests showed significant differences in response time between all conditions, except conditions 1 and 3. For accuracy, all conditions were different from condition 7. As there was more variance in the 1 letter condition than in the 3-letter condition, and to avoid potential boredom effects, we selected the 3-letter condition for the low cognitive load in the main experiment. For the high cognitive load in the main experiment, we chose the 7-letter condition, as this showed a clear decrease from perfect performance with 86% correct responses, which was still above chance performance (~33%). Summarizing, our pilot study showed that selecting three-letter long strings for the low cognitive load condition and seven-letter long strings for the high cognitive load condition would lead to clear differences in difficulty while avoiding boredom and ceiling effects in performance.

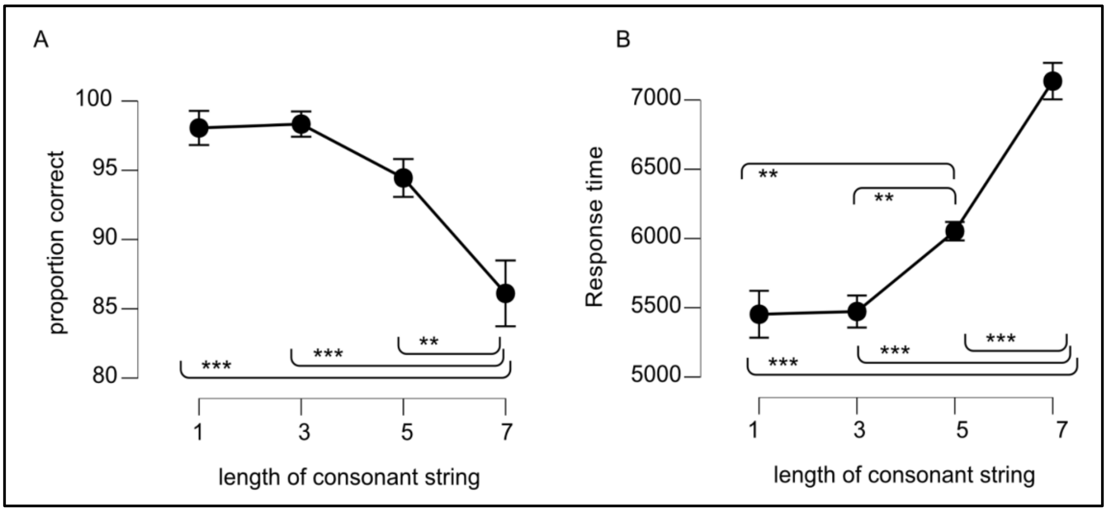


Figure 2.3. **Response accuracy and response times in the pilot study for the working memory task.** Graphs show averages ± standard errors of the mean (SEM) across participants with respect to each length of a consonant string (on the x-axis). Panel A depicts the proportion of accurate responses (from 0-100%), and Panel B depicts the response time in milliseconds. Significant planned follow-up t-tests are indicated with asterisks (* p < .05, ** p < .01, *** p < .001, Bonferroni corrected for multiple comparisons).

2.2.5. Main experiment design and procedure

To avoid the influence of satiety, we asked participants not to eat (except drinking water) for 3–4 hours before arriving at the lab. They are also asked not to use cigarettes, e-cigarettes, or nicotine-containing products for 2 hours before the test and not to have energy drinks or caffeine-containing drinks from the night before the test. The distraction task was performed after a task in which neural responses to the same low-fat and high-fat drinks and a tasteless control solution were measured in an MR scanner (results to be reported separately, addressing a research question unrelated to cognitive manipulations). During this scan, participants passively (no cognitive task) received the drinks, for a total of ~40 ml of each of the coconut-chocolate drinks, and ~40 ml of control solution, and ~40 ml of rinsing solution. Several participants (n=18) that did not meet the safety criteria for fMRI performed the experiment without a preceding MRI scan. Participants were brought to the fMRI simulator and outfitted with the taste delivery system. The simulator MRI and taste delivery system are shown in Figs 2.4. and 2.5. below.

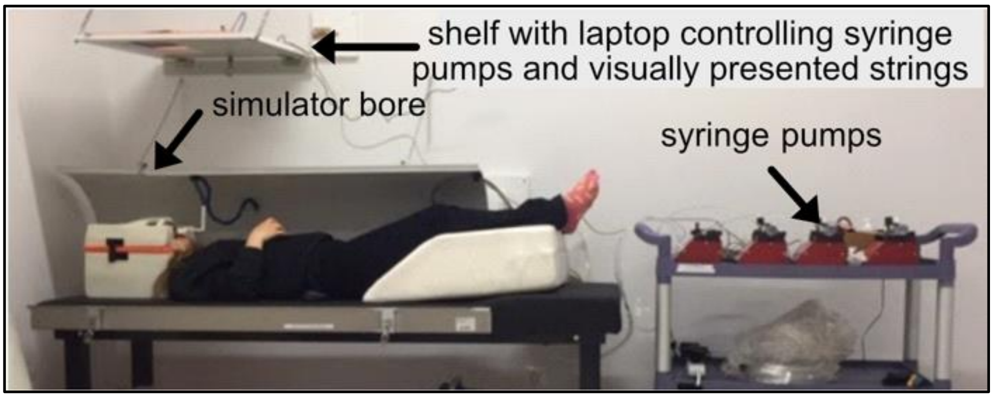


Figure 2.4: Position of participants in the MR simulator with a gustometer system

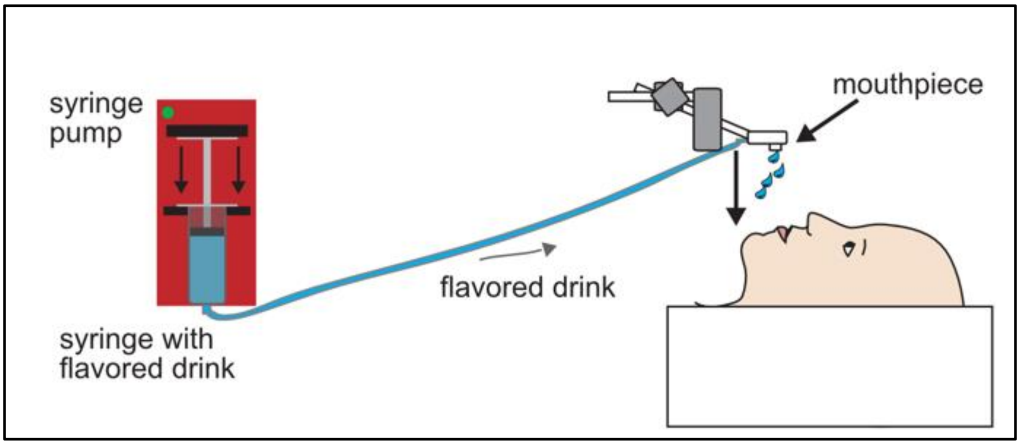


Figure 2.5: Procedure of sending drink to the mouth of participants via tubes connected to the computer-controlled pumps (Veldhuizen et al., 2007)

We used the gustometer system and fMRI stimulator to precisely control drink delivery and memory task performance. The bore has a rectangular cut-out section above the participant’s head so they can see out of the bore. Suspended above the bore is a shelf with a rectangular cut-out the size of the laptop screen. The laptop is fully opened at a 180° angle and placed with the screen facing down over the cut-out. The position of the simulator’s head coil is adjusted so the participant can see the screen. The screen's distance from the participants' eyes has been set to 67 cm, which matches the comfort distance evaluations based on participants’ preferences reported in Taptagaporn et al.

(1995); Jaschinshi-Kruza (1990); and Jaschinski (1998). The distance between the screen shelf and eye is shown below in Fig. 2.6.

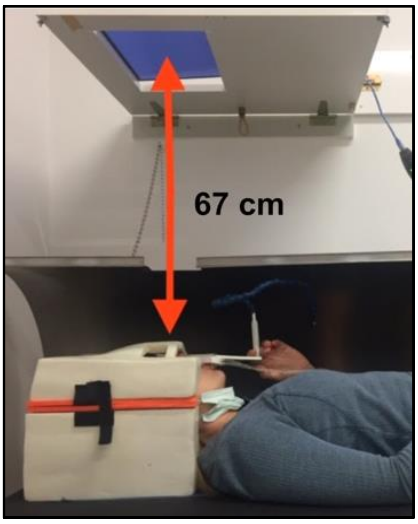


Figure 2.6: The cut off in the bore and the distance between eyes and screen.

Then the mouthpiece used for the delivery of liquids (Veldhuizen et al., 2007) was lowered into a comfortable position between the participant's lips (Figs. 2.4, 2.5). Then the other half of the MRI stimulator was attached to the wall-hung part. Neither the participants nor the experimenters saw each other. The covered MRI simulator is shown below in Fig. 2.7. To mimic the MRI conditions and mask the sounds of the computer-controlled syringe pumps, we played sounds similar to the sounds an MR scanner makes when collecting BOLD data.

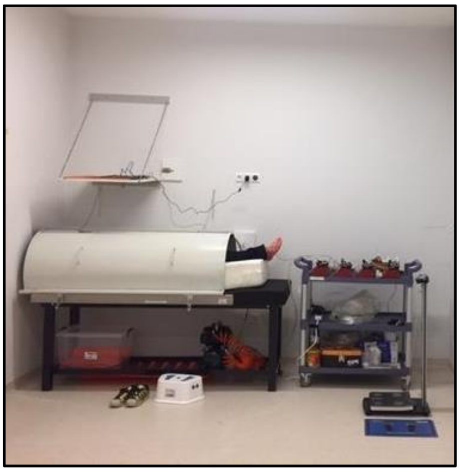


Figure 2.7: Covered MRI simulator

Participants used a mouse that was connected to the laptop. First, they read instructions on how to perform the working memory task and ratings. The timelines for low and high cognitive load are shown in Figs 2.8. and 2.9. A more specific timeline, considering the concurrency of tasks for events in a high cognitive load trial, is shown in Fig 2.10. At the start of each trial, the participants first see a fixation cross (0.5s), followed by the target string (2s), and a blank page (2s). Next, they received one of the two drinks (1 ml over 4 seconds). They are instructed to swallow this solution (1s). Then they see the three options for strings on the screen and are asked to click on the string that they memorized previously. Subsequently, we displayed a VAS scale for rating overall flavor intensity, followed by a VAS scale for rating the fattiness of the flavor. These scales both consisted of a horizontal 101-point line scale with the labels “no sensation” at the lower anchor point and “strongest imaginable” at the upper anchor point. Above the scale, the instruction “rate intensity” or “rate fattiness” was displayed. After completing the ratings, 1 ml of water is dispensed for the participant to rinse their mouth in 3s, followed by an 11-second pause until the next trial. Each session consisted of two blocks of 16 trials each. In each block, each combination of drink and cognitive load was presented in 4 trials (randomized order), leading to a total of 8 repeats per combination of drink and cognitive load. Overall, there are 32 trials in each experiment. Between the two blocks, there was a 3-minute break. Participants completed the task in about 25 minutes.

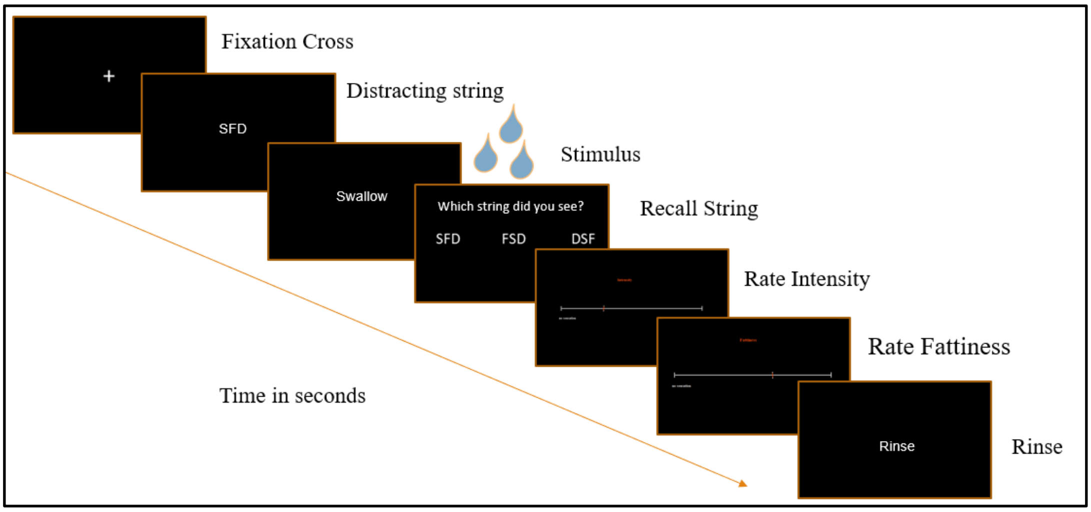


Figure 2.8: Distraction task with low cognitive load

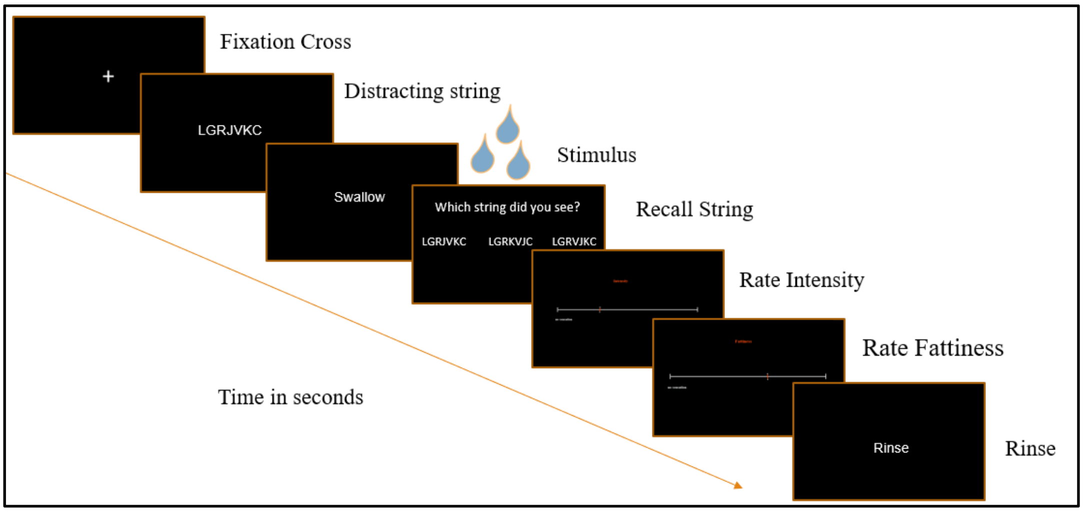


Figure 2.9: Distraction task with high cognitive load

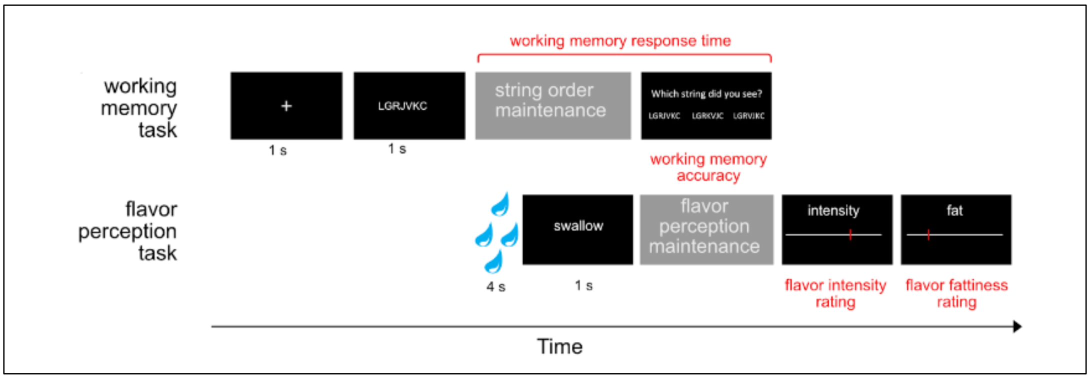
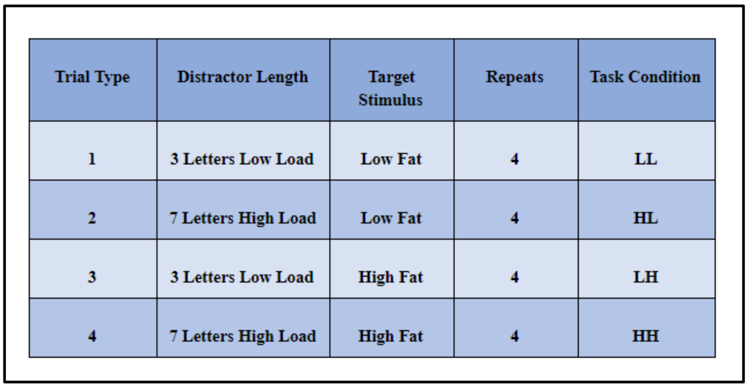


Figure 2.10: A timeline demonstrates the concurrency of working memory and flavor perception task

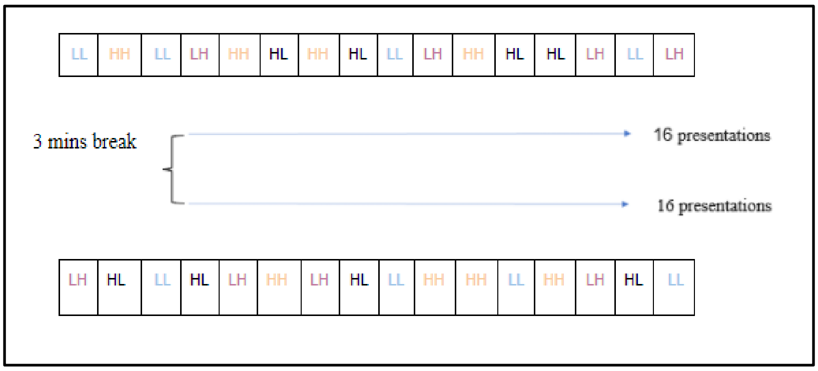
2.2.6. Data analysis

A visual inspection of the distribution of response times showed outliers above RT = 25 s (total number of excluded trials was 44, or 4.3%). We then averaged over the (up to) 8 repeats within each of the four different combinations of the fat content and cognitive load combinations. The conditions for each run of a working memory task and the design of the distraction task along two runs are shown in Figs. 2.11 and 2.12. To test the effect of the independent variables on the dependent variables, we used JASP software (version 0.16.3) to run a 2x2 repeated measures ANOVA with within-subject factors “fat content” (low fat vs. high fat) and “cognitive-load” (low load vs. high load) separately for each of the dependent variables (response time and proportion correct answers of the memory task, flavor intensity and flavor fattiness in the flavor perception task). We created a dummy variable to indicate which participants did not perform this experiment after an MRI scan and included this variable as a covariate in all analyses. We conducted planned follow-up t-tests (Bonferroni-corrected for 6 comparisons). We also ran Pearson correlation analyses between the response times and the intensity and fat ratings (no averaging across repeats). Alpha was set at 0.05. Figures were also created with JASP software.



Trial Type	Distractor Length	Target Stimulus	Repeats	Task Condition
1	3 Letters Low Load	Low Fat	4	LL
2	7 Letters High Load	Low Fat	4	HL
3	3 Letters Low Load	High Fat	4	LH
4	7 Letters High Load	High Fat	4	HH

Figure 2.11: Conditions for each run of a distraction task



LL	HH	LL	LH	HH	HL	HH	HL	LL	LH	HH	HL	HL	LH	LL	LH

LH	HL	LL	HL	LH	HH	LH	HL	LL	HH	HH	LL	HH	LH	HL	LL

Figure 2.12: Design of Distraction tasks

2.2. RESULTS

2.3.1. Working memory task outcomes: response time and accuracy

To evaluate whether the high cognitive load condition was more difficult than the low cognitive load, we evaluated accuracy (proportion correct, Fig. 2.13A) and response times (Fig. 2.13B) in the working memory task. Cognitive load had a main effect on response times (F (1,30) = 34.06, p <.001, η^2=0.06) and accuracy (F (1,30) = 18.163, p <.001, η^2=0.121), such that under high cognitive load response times were longer and more mistakes were made. Fat content had no effect on response times (F (1,30) = 3,203, p =0.084, η^2=0.04), but we note that there is a trend for a higher fat content to lead to longer response times. There was no effect of fat content on accuracy (F (1,30) < .001, p =0.992, η^2 < .001). We observed no interaction effect of fat * cognitive load on response times (F (1,30) = 0.537, p =0.469, η^2 < .001) or accuracy (F (1,30) = 0.984, p =0.329, η^2<0.006). Summarizing, these results show that, as intended, the high cognitive load task is more difficult than the low cognitive load task. Interestingly, it also shows hints that a higher fat content in the drink in the flavor perception task may interfere with the working memory task.

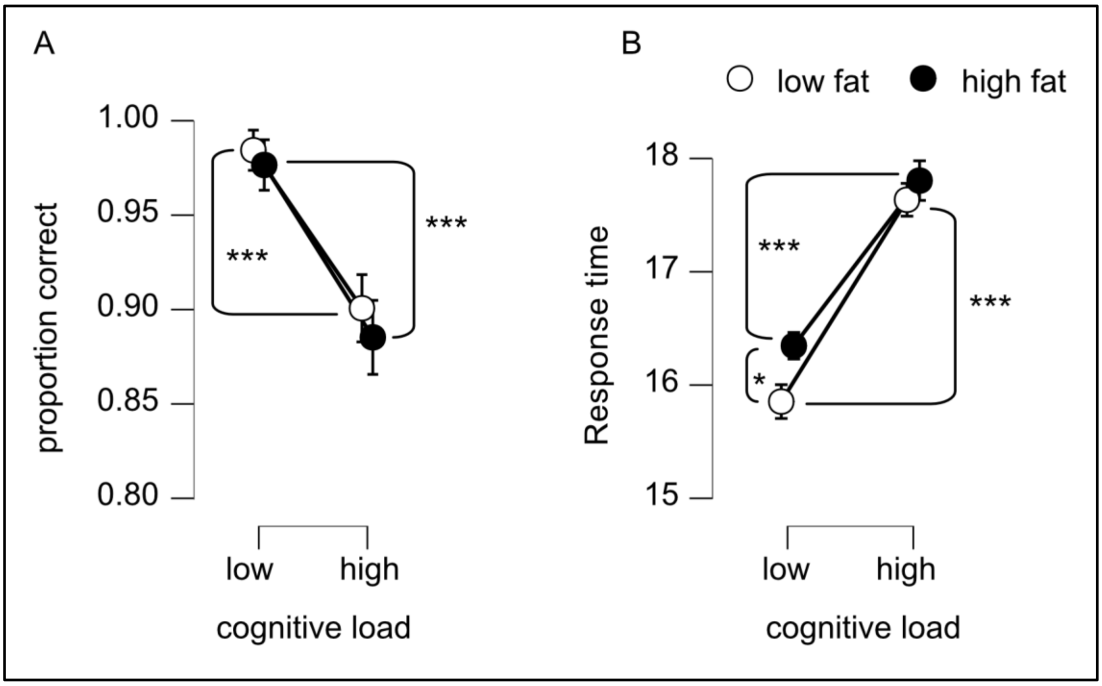


Figure 2.13. **Response accuracy and response times in the working memory task.** Graphs show averages ± standard error of the mean (SEM) across participants with respect to each cognitive load (on the x-axis). The different fat contents of the drinks are indicated with symbols: open circles indicate a low-fat content, filled circles a high fat content. Panel A depicts the proportion of accurate responses (from 0-1), and Panel B depicts the response time in seconds. Significant planned follow-up t-tests are

indicated with asterisks (* $p < .05$, ** $p < .01$, *** $p < .001$, Bonferroni corrected for multiple comparisons).

2. 3.2. Flavor perception task outcomes: intensity and fattiness ratings

To test whether distraction affects flavor perception, we evaluated intensity (Fig. 2.14A) and fat (Fig. 2.14B) ratings. Contrary to our expectation, cognitive load did not have a main effect on intensity ratings (F (1,30) = 4.08, p = .052, η^2=0.003), but we do note a trend for intensity to be lower for the higher load conditions (see also supplementary table x for post-hoc pairwise comparisons, which were significant between the low and high condition load conditions within each drink). Cognitive load had a significant effect on fat ratings (F (1,30) = 5.195, p = .03, η^2=0.003), such that under a high cognitive load, fat ratings were reduced. As expected, we also observe effects of fat content on intensity (F (1,30) = 20.25, p <.001, η^2=0.027) and fat (F (1,30) = 10.07, p =.003, η^2=0.016) ratings, such that higher ratings are given to the drink with the higher fat content. Interestingly, for fat ratings, we also observed an interaction between cognitive load and fat content (F (1,30) = 5.043, p = .032, η^2=0.002). When inspecting Fig.2.14B, the interaction seems to be driven by a greater effect of cognitive load in the drink with the higher fat content. In other words, a high cognitive load suppresses fat perception in the drink with only 15% fat content. Since within the high cognitive load there is no significant difference (in the post hoc t-test) between the low and high fat drinks, the perception of fat may be suppressed by distraction to such a degree that there is no longer a significant perceived difference between the two fat contents. This is remarkable because there is a more than 4-fold difference in fat content between the two drinks, which is demonstrably perceived in a low cognitive load condition. Summarizing, these results show that distraction specifically suppresses high fat flavor perception.

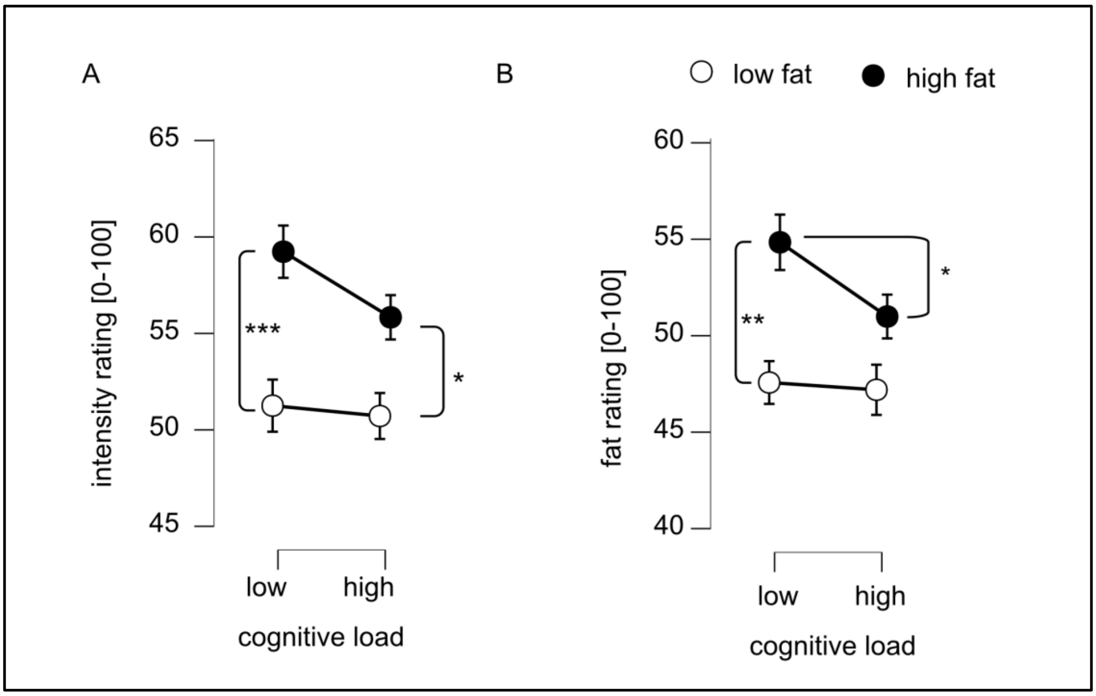


Figure 2.14. **Intensity and fat ratings in the flavor perception task.** Graphs show averages ± standard error of the mean (SEM) across participants with respect to each cognitive load (on the x-axis). The different fat contents of the drinks are indicated with symbols, open circles indicate low fat content, filled circles indicate high fat content. Panel A depicts intensity ratings (0-100) and panel B depicts fat ratings (0-100). Significant planned follow-up t-tests are indicated with asterisks (* p < .05, ** p < .01, *** p < .001, Bonferroni corrected for multiple comparisons).

2.3.3. A longer time between working memory task and making ratings is related to the intensity of sensations.

The difficulty of the higher cognitive load leads to more incorrect responses and longer response times. To examine if variation in the delay in responding to the working memory task is related to reductions in flavor perception, we examine correlations between ratings and response times. When we examine correlations across all combinations of the independent factors cognitive load and fat content, we observe negative correlations, such that the longer the RT, the lower the intensity ratings ($r = -0.130$, $p < .001$) and fat ratings ($r = -0.126$, $p < .001$). This indicates that when attention is switched back to the flavor perception task sooner, the intensity and fat ratings are higher.

2.3. DISCUSSION

We predicted that if distraction suppresses perception of flavor, we should observe reduced fat and intensity perception under higher cognitive load relative to the lower cognitive load of the competing working memory task. We observed robust effects of the cognitive load on accuracy and response times of the working memory task, confirming we achieved different levels of distraction from the flavor perception task. Contrary to our expectations, we did not observe uniform effects of distraction on flavor perception. We observed a trend for reduced intensity ratings regardless of fat content, and we observed reduced fat ratings for the high-fat drink only.

Although we observed a trend for a suppression of the intensity of chemosensory stimuli by distraction, we did not observe the robust effects on intensity perception (van der Wal & van Dillen, 2013) or detection ratios (Liang et al., 2018) that were previously reported. Another departure from other studies was the observation of the effect of cognitive load on fattiness ratings for the high-fat stimulus only, an asymmetry that depends on fat concentration. There may be various explanations for the marginal effects of intensity reductions. We asked participants to rate the intensity of the flavor stimulus as a whole, as well as the fattiness of the flavor. Both these perceptual tasks may be harder to perform than rating the intensity of a taste component of a food, of a pure taste solution, or of an odor presented to the nostrils. It is also possible that our experimental procedure was conducive to smaller effects. We controlled both the working memory task and the flavor perception task with a computer to ensure precise timing of stimulus presentation and measurement of responses. With the use of a gustometer, where the participant is in a supine position, orally presented samples are usually much smaller than in regular behavioral experiments that use whole-mouth stimulation. For example, we present only 1 ml of the flavored drink on each trial. In the study by van Meer et al. (2022a), a reduction in sweetness was observed only for the stimulus with a higher glucose concentration. This was a neuroimaging study that also employed small quantities of liquids. Other studies that focused on oral stimuli and used whole-mouth sampling procedures tend to show more uniform effects across concentrations (van der Wal & van Dillen, 2013; Liang et al., 2018), although it should be noted that there were variations across concentrations there too. For example, van der Wal et al. (2022a) showed that both a weak and strong taste were reduced, but the effect was larger for the higher concentration of sucrose. Liang et al. used relatively low (near threshold) sweet and bitter taste solutions and showed that the effect on detection ratios was not uniform across concentrations. For example, at the lowest concentrations, there was no effect of memory load, and the highest concentration of sucrose also showed no effect. In other studies, we note that the distraction effects depend on caloric value; for example, Hoffman et al. (2017) observed effects of distraction on ratings of odors associated with low-calorie foods (orange/apple odor), not high-calorie foods (chocolate-caramel). van Dillen & van Steenbergen (2018) showed that the effects of distraction over time are stronger for high-calorie food pictures. Taken together, ours and others' observations suggest that intensity and/or salience matter for the robustness of the distraction effect.

We observed that a high cognitive load suppresses fat perception in the drink with only 15% fat content, such that with a high cognitive load there is no significant perceived difference in fat between the low and high fat drinks. The more than 4-fold difference in fat content is demonstrable and perceived in the low cognitive load condition. This indicates that distraction can meaningfully reduce the perception of fat. If distraction primarily reduces perception of the unhealthy macronutrients in high calorie foods, this may pose a particular risk to overeating unhealthy foods. Future studies should directly assess whether there is a subsequent compensatory overeating response, and whether overeating affects high-calorie foods and/or specific macronutrient intake directly, for example by employing a modified bogus taste test (Robinson, 2017) to measure effects on food intake.

If limited resources are the mechanism for perception changes in distracted food sampling, then we should also consider the influence of the flavor perception task on the working memory task. For example, if in an experiment chemosensory perception is unaffected by competition for resources, that may be explained by a complete dedication of all resources to the working memory task, which could be reflected by a ceiling effect in performance on the working memory task. The inclusion of performance in the working memory task may also reveal other surprising response patterns. For example, here we observed that in the low cognitive load condition, the delivery of a high-fat flavor is associated with longer response times than the delivery of a low-fat flavor. This means that the converse of the canonical distraction effect may happen too; the flavor perception task interferes with the working memory task. If the higher fat solution is more salient than the lower fat solution, then it may capture more attentional resources, which affects performance on the working memory task. To this point, van Dillen et al. observed a shift in the speed-accuracy trade-off with higher calorie food trials. We propose that, to fully understand the effects of distraction on chemosensory perception, the effect of chemosensory perception on the distracting task should also be evaluated. If resources can flexibly be allocated between working memory and flavor perception, then we may expect flavor perception to be favored when the flavor stimulus is more salient, for example, when hungry vs. when full. Future studies may directly investigate this prediction.

Concluding, we observed that distraction and fat content interacted such that fattiness ratings for the high-fat drink were lower when distracted and not distinguishable from the low-fat drink. This meaningful reduction in fat perception due to distraction may pose a particular risk for overeating. Given the common and habitual tendency to be distracted during meal consumption, this may eventually form a risk factor for (unhealthy) weight gain.

Data availability

The data and the analysis files are accessible at https://osf.io/ewjm2/

CHAPTER 3

INSTANT NEURAL RESPONSES TO DIFFERENT FAT CONTENT DRINKS AND THEIR CORRELATION WITH FAT SUPPRESSION CAUSED BY DISTRACTION

ABSTRACT

Obesity and overeating are on the rise globally. Fat intake and habitual distraction during eating are two of many contributors. Preventing and treating obesity require more in-depth research into the interactions between these two factors. Here, we measured immediate brain activations after drinking various fat-content drinks (low, high, tasteless) and examined their correlations with suppression of fat perception during distraction. Functional magnetic resonance imaging was used in 19 healthy participants (14 women and 5 men) to measure BOLD responses to low-fat and high-fat chocolate flavors and a tasteless control solution. After MRI scanning, participants performed a flavor perception task that included fat ratings during a distracting working memory task. We observed neural responses to both fat drinks relative to the tasteless mid-dorsal insula and overlying operculum, precentral gyrus, and cerebellum. We did not observe regions that showed a stronger activation for high-fat drinks compared to low-fat drinks (or vice versa).

We observed that greater responses in the fusiform gyrus and amygdala corresponded to less suppression of fat perception during a distraction task. These results suggest that individual differences in neural sensitivity to fat perception and/or distractibility from flavor perception may indirectly contribute to risk factors for overeating.

Keywords: fMRI, flavor, fat perception, distractibility, insula, thalamus, fusiform, amygdala

3.1. INTRODUCTION

The modern lifestyle facilitates overeating and obesity, which are becoming more common worldwide (Makaronidis and Batterham, 2018; Jéquier, 2002). Obesity is influenced by environmental, behavioral, social, and emotional aspects. Considering environmental aspects, fat intake, and insufficient physical activity associated with the increment of obesity. In animals, high-fat food intake causes obesity (Hariri and Thibault, 2010), and in human studies, a high-fat diet contributes to obesity with an increase in energy intake (Hill et al., 2000; Schrauwen and Westerterp, 2000). Hence, to curb obesity and develop treatments and strategies for it, it is necessary to evaluate the role of fat content in the brain.

Fat has multiple properties that may affect brain responses (Running et al., 2015). First, it has a taste, which is detected in the mouth by gustatory receptors. Also in the mouth, fat will activate somatosensory receptors as it has texture. Lastly, in the gut, fat affects neuropod receptors, but the time scale of such responses that happen after minutes is outside the scope of this paper. Heinze et al. (2015) suggest that neural responses to fat can be expected to be observed in sensory areas such as gustatory and somatosensory brain networks as well as reward areas, as fat is a primary reinforcer. To date, there are only a few studies that have explicitly examined neural responses to different fat contents with fMRI. De Araujo et al. (2004) compared vegetable oil (~90% fat) to a matched viscous solution and observed increased responses in the mid and anterior insula, hypothalamus, and anterior cingulate cortex (ACC). Grabenhorst et al. (2010) compared strawberry and vanilla flavored high (18%) and low (0.1%) fat solutions, and increased responses were observed in the lateral hypothalamus and amygdala. Eldeghaidy et al. (2011) performed correlations with 4 fat solutions (5, 10, 20, and 30%) and observed positive linear relationships with fat content in the ACC, anterior insula, frontal operculum, amygdala, and somatosensory areas. In another study, Eldeghaidy et al. (2012) compared responses to flavored fat (22%) and non-fat (0%) and observed no significant activations. Stice et al. (2013) compared neural responses to 2.4% and 9% fat milkshakes and observed not-significant activations. Of note, in an EEG study of stimuli with varying fat content, only scalp responses to 0% (skim milk) and 38% fat (cream) dairy solutions could reliably be discriminated (Andersen et al. 2020). The studies above that did observe neural responses to varying fat content typically looked at a big difference in fat concentration, beyond what may be expected for regular foods.

Summarizing, understanding fat perception and neural processing is important for understanding food consumption patterns and weight gain, yet the neural responses to fat content have remained elusive, with indications that reward, and gustatory areas are involved, such as the orbitofrontal cortex, hypothalamus, insula and overlying operculum, secondary somatosensory cortex, and amygdala playing a role. These previous studies were done before some of the newest advances in the field of fMRI that might improve sensitivity to neural responses to fat. For example, advances in fMRI scanning parameters such as Generalized Autocalibrating Partially Parallel Acquisition (GRAPPA, Griswold et al., 2002; Larkman & Nunes, 2007) and multiband (MB) scanning allow for higher spatial or temporal resolution (Larkman et al., 2001). The studies mentioned above all used a spatial resolution of 3 mm or more, and it is possible that with a higher spatial resolution, activity in areas with a smaller volume can be detected better. In addition, most previous studies used event-related designs (with the exception of Stice et al.). In event-related designs, stimuli are presented randomly, while in block designs, the same stimulus is repeated a few times. Block designs tend to be more powerful at detecting neural responses (Birn et al., 2002). Therefore, our first research question is whether ecological variation in fat content can be detected with BOLD responses to flavor stimuli with improved fMRI scanning parameters and design.

Among the behavioral factors that can influence weight gain and obesity is habitual distraction during eating. Distracted eating is thought to promote overconsumption through suppression of the perception of the food stimulus. Several studies have found that by watching television, satiety can be postponed, and food consumption can increase (Brunstrom & Mitchell, 2006; Bellissimo et al., 2007; Temple et al., 2007). In controlled experimental studies, it has been shown that when performing a high-load memory task, taste or smell intensity suppression is greater than when performing a low-load memory task (van der Wal & van Dillen, 2013; Van Meer et al., 2022a; Liang et al., 2018; Hoffman et al., 2017; Schadll et al., 2021). We previously observed that distraction impacts the perception of fat in high-fat drinks but not in low-fat drinks. If distraction primarily reduces perception of the unhealthy macronutrients in high-calorie foods, this may pose a particular risk to overeating unhealthy foods.

The perception of fat shows considerable variation across subjects, which is reflected in sensory fat detection thresholds spanning over 4 orders of magnitude and initial thresholds being hard to establish in about half of participants (Tucker & Mattes, 2013). Likewise, in our previous study, we observed considerable variations across participants in fat suppression by distraction, where some participants showed none or even slight enhancement and others showed over 25 points of suppression on a 101-point VAS scale (Chapter 2). There are also large individual differences in sensitivity to gustatory stimulation in general, which is driven by activity in a network including the amygdala (Veldhuizen et al., 2020). Moreover, the amygdala is well-known to be involved in the encoding of stimulus saliency (Kong and Zweifel, 2021). This means that individual differences in distraction-induced fat suppression may result from individual differences in sensory processing in the amygdala. It is also possible that other areas in the gustatory and food reward brain networks may be involved. Therefore, our second research question is whether neural responses to fat stimuli show variation related to attention to flavor.

The aim of this study is to see if, with improved fMRI scanning parameters and design, differential neural responses to fat content can be observed. In addition, we assessed whether individual variation in distractibility from fat perception is related to sensory processing differences as expressed by neural activation in the brain. Here, we measured the instant BOLD responses to low-fat, high-fat, and tasteless chocolate drinks in 19 healthy participants with a multiband scanning sequence with grappa and a block design. In a separate session, we measure participants' distractibility from fat perception. We operationalized distractibility as the degree of suppression of fat ratings between a high and low cognitive load of concurrent working memory tasks. We expect to observe differences in activation in taste and somatosensory areas, including the brainstem, thalamus, insula, overlying operculum, hypothalamus, amygdala, and orbitofrontal cortex, between the different fat contents.

3.2. MATERIALS AND METHODS

3.2.1. Participants

19 participants, consisting of 14 women and 5 men, were recruited for the scans. Their average BMI was 22.12 (+/- 1.56 SD), and their average age was 25.05 (+/- 6.22 SD). From the 22 participants who took part in scans, one was excluded due to vertigo, and two others had a BMI > 24. Based on Who (2004), in the US and Europe the cut-off for a healthy BMI is 25, while in Turkey it is defined as 23, because lower body weight is higher, and it increases health risks. The participants were not identified as having specific illnesses; however, more information about their payment, exclusion, and inclusion criteria can be found on page 15 (part 2.2.1). For the correlation of distractibility and neural response analysis, data for 18 participants is evaluated. Their average BMI was 22.53 (+/- 1.65 SD), and their average age was 25.22 (+/- 6.36 SD). The Mersin University Committee approved the study protocol for clinical research with these details (numbers 7807789 / 050.01.04 / 1152384). Experiments were carried out at the National Magnetic Resonance Research Center (UMRAM) at Bilkent University's Aysel Sabuncu Brain Research Center in Ankara, Turkey. It is Turkey's only research center with a full-time magnetic resonance imaging (MRI) device dedicated to research purposes. Participants in the study are individuals who have voluntarily agreed to participate after reading and signing consent forms, and they have the right to discontinue their participation at any time if they wish to do so. Participants were fluent in Turkish, and they were given detailed information about the experiments in advance. Participants took part in four scanning sessions in total, and they were financially compensated for completing each scanning session of the project.

3.2.2. Device and software

MRI device: A Siemens 32-channel 3.0T Trio TIM scanner is used for this study. fMRI scanning room at UMRAM, and the 32-channel head coil is shown in Fig. 3.1 (A and B):

(A) (B)

Figure 3.1: A) The fMRI scanning room at UMRAM B) The 32 channel head coil

The technique of functional MRI is used to isolate brain areas that respond differently to low-fat, high-fat, tasteless, and water stimuli. It is aimed at measuring Blood Oxygen Level Dependent (BOLD) responses, which quantify oxygenated vs. deoxygenated blood flow and are regarded as indicative of neural activity.

Gustometer: It is a system used for conveying liquid drinks to the mouths of participants. In brief, this system consists of computer-controlled syringe pumps that infuse liquids from syringes filled with flavor solutions into an fMRI-compatible, custom-designed gustatory manifold via 25-foot lengths of Tygon beverage tubing (Saint-Gobain Performance Plastics, Akron, OH, USA). Pumps are serially connected, and pipes are sent from them to the mouthpiece in the scanner. The gustatory manifold is mounted on the MRI head coil, and the tubes anchor into separate channels that converge into a silicone tube, which rests just inside the subject's mouth. When a pump is triggered, liquid drops from the channel into the tube and comes in contact with the tongue. The parts of the system that are touched by participants will be cleaned in between participants with chloride solutions at concentration standards for medical cleaning procedures. The gustometer system is used for sending drinks while scanning and also for working memory tasks. The set-up and the procedure for sending chocolate drinks are shown below in Fig. 3.2 and Fig. 3.3. The time line of fMRI block design is shown in Fig. 3.4.

Figure 3.2: The setup cart for a gustometer system and pipes for cleaning objects

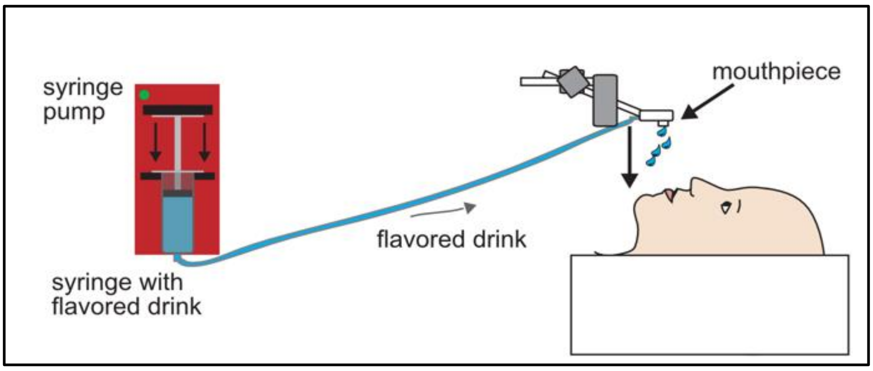


Figure 3.3: The procedure of sending a chocolate drink to the mouth of a participant (Veldhuizen et al., 2007).

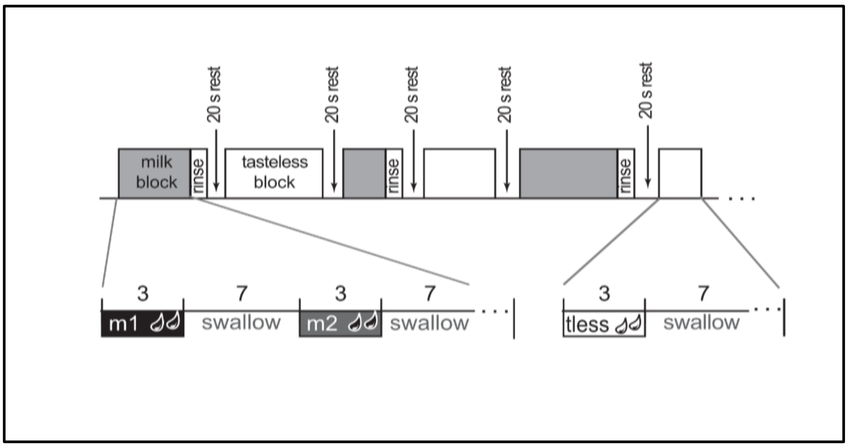


Figure 3.4: timeline of the fMRI block design

TANITA Scale

For measuring the body mass index (BMI) of participants, we use the TANITA scale, which uses bioelectrical impedance analysis (BIA). Safe electrical signals are passed through electrodes to the body to calculate body composition. In particular, it has a segmental body composition analyzer that provides detailed information about the distribution of fat or muscle in different body parts. Prominently, it also gives information about total body water percentage, bone mass, and daily calorie intake (DCI). The data for height and weight of participants is also collected, and the application categorises participants based on their BMI into underfat, healthy, overfat and obese groups. When participants' BMI is within borders, we use body type forms and ask participants to select their body types based on the pictures shown to them in the forms before their arrival. Fig.3.5 shows the scale for weight and height measurement.

Figure 3.5: TANITA scale

3.2.3. Taste stimuli

Vegan ingredients are used in the preparation of drinks in the scanner to ensure a low viscosity and easy flow through the tubes. A low-fat drink contains (3.5% fat and 10% sugar) with (70 kcal per 100 ml), while a high-fat drink contains (15% fat and 10% sugar) with (137 kcal per 100 ml). Artificial saliva is made from a combination of KCL, NAHCO3, and water for tasteless drinks. The recipes for chocolate drinks are the same as those used for distraction tasks. Detailed information regarding the ingredients and recipes for the chocolate drink can be found on page 16 (part 2.2.3.)

3.2.4. Experimental procedures

The objective of this study is to observe the immediate brain responses of participants to drinks with varying fat contents that are delivered into their mouths through the gustometer system. During fMRI runs, participants receive alternating sips of drinks, including high-fat, low-fat, tasteless, and rinsing water, via the mouthpiece that is connected to the pumps on one side and the head coil on the other. Participants are trained and shown illustrations of the experiment ahead of time. They are instructed to exhale through their noses after swallowing the drinks to ensure retronasal olfactory perception. They are asked not to eat for 3–4 hours before scanning. They are also told not to use nicotine-containing products for two hours before the test and not to drink energy drinks or caffeine-containing beverages the night before. They are also asked to remove metal parts in advance. Prior to participants' arrival, syringes and tubes are filled with drinks, the setup is arranged, and tubes are sent into the MRI room. When participants arrive, they are weighed on a scale, followed by ratings of their internal state and the drinks they are given with droppers. Then participants are outfitted in special clothes. Following that, the metal check is done, and they are instructed to put on ear plugs to protect themselves from the MRI sounds, and then they are directed to lie on the moveable bed that goes inside the magnetic bore. Later, the mouthpiece is adjusted between the lips of the participants in a way they can drink easily, and each drink is sent once or twice to ensure that they receive it. After that, participants are sent inside the MRI bore, and we constantly communicate with them via an intercom to confirm that they are comfortable. There is a handle button to notify the experimenter in case the participant needs assistance. After the scan, participants again performed ratings. There were two functional runs during which we measured the BOLD response to the drinks. Within each run, there are four blocks of repeated presentations of each drink. The four blocks for each drink consisted of 3, 3, 4 and 5 repetitions. A block starts with 3 seconds of stimulus delivery (flow rate, volume), followed by 7 seconds of time to swallow, which is then repeated. At the end of each block, we present a rinse. In total, participants get almost 40 ml of each of the drinks and 30 ml of rinsing water during the two runs. The order of blocks within a run is counterbalanced. As water activates the taste cortex (Fery & Petrides, 1999; Zald & Pardo, 2000) and has a taste (Bartoshuk et al., 1964), we make “artificial saliva” with KCL and NAHCO3 and water as a tasteless baseline. Each run takes nearly 12 minutes, and the whole scan takes 30 minutes. As well as two functional runs scans, scan sessions also include structural scans such as T1 MPRAGE, T1 FLASH, and TOPUP scans. After completing the scan, participants are directed to an MRI simulator in another room to perform working memory tasks for the other section of this study. The procedure for the distraction task is explained on page 17 (part 2.2.5). Fig. 3.6 below indicates the set-up for a fMRI session.

Figure 3.6: MRI scanning while presenting drinks with pumps. Pumps are serially connected and are controlled via a MATLAB program to deliver tasteless, low-fat, high-fat, and water to the mouths of participants.

fMRI scanning details

Images are acquired with an MRI scanner; the properties of the scanner are described on page 33 (Part 3.2.2 above). Multiband echoplanar imaging (EPI) was used for measuring BOLD signals as a marker of brain activation. To image the regional distribution of the BOLD signal, the PAT mode of GRAPPA, and the multiband acceleration factor PE = 2 are used with the following parameters: TR = 2319 ms, TE = 35 ms, flip angle = 60°, slice thickness = 2.10 mm, number of slices = 60, the FOV read is 230 mm, and the voxel size is 2.1*2.1*2.1 mm. To correct distortion, the reverse phase encoding direction sequence was used with the same parameter as the EPI sequence above (P>>A means posterior to anterior, whereas it was A>>P in the BOLD sequence). For structural scans, T1-MPRAGE (T1-weighted magnetisation-prepared rapid gradient-echo) with TR = 2150 ms, TE = 2.97 ms, flip angle = 12°, FOV = 230 mm, voxel size = 0.9*0.9*0.9 mm, slice thickness = 0.90, PAT mode = GRAPPA, Accel. Factor PE = 4 parameters and T1-flash (fast low-angle shot magnetic resonance imaging) with TR = 2000 ms, TE = 2.46 ms, flip angle = 90°, FOV = 240 mm, voxel size = 0.9*0.9*0.5 mm, number of slices = 24, and slice thickness = 5 mm parameters are used.

3.2.5. Data analysis for fMRI data

Preprocessing: initially, for analysing individual data, we used a script to convert DICOM (Digital Imaging and Communications in Medicine) files to NIFTI (Neuroimaging Informatics Technology Initiative) in BIDS (Brain Imaging Data Structure format), which is a standard template used for arranging and explaining neuroimaging brain study outputs (Gorgolewski, 2016). We used a Windows 10 Pro workstation and the MATLAB (R2019b, MathWorks) toolbox SPM 12 (SPM, 1994; Penny et al., 2011) to remove the faces of participants from the high-resolution anatomical scan to make participants unidentifiable. Subsequently, TOPUP as a part of FSL (Flippi, 2016; Smith, S.M., et al., 2004), is used for field distortion correction. After that, the origin of the images is manually aligned to the anterior commissure, and the line from AC-PC is adjusted to be horizontal to reduce individual differences for normalisation. Then we used SPM 12 to perform preprocessing (realignment, coregistration, segmentation, normalization, detrending, and smoothing). In detail, the images are first realigned to the average of all functional images and then coregistered with the participants' own T1 image. A unified segmentation procedure (Ashburner and Friston, 2005) combining segmentation, bias correction, and special normalization was used to process the anatomic T1 image. The same normalization parameters were then applied to the functional images. Then, at each voxel, all functional images were determined by removing any linear components that matched the global signal (Macey, P. M., et al., 2004). Finally, functional images were smoothed with a gaussian kernel with an FWHM of 6 mm. The movements of participants are plotted and evaluated based on their translation and rotation tables. If it is less than 1 mm, it indicates that the participant did not move much. Participants with more than 3 mm of movement are excluded. The ART toolbox (NITRC, 2008) is used to calculate outlying images based on movement regressors and image intensities. Then the movement regressors and a set of regressors for outliers are created.

First level analysis

Following preprocessing, we create a design matrix by matching the two sessions' block onsets and durations of events of interest. For the time-series analysis on all participants, a high-pass filter (300s) was included in the filtering matrix (adjusted from the convention in SPM12 to reflect the maximal period between two blocks of tasteless) to remove low-frequency noise and slow drifts in the signal. Condition-specific effects at each voxel were estimated using the general linear model (Friston et al., 1995; Worsley and Friston, 1995). The response to events was modeled using a canonical hemodynamic response function included in SPM12. The temporal derivative of the hemodynamic response function was also included as part of the basis set to account for up to 1 s shifts in the timing of the events (Henson et al., 2002). The events of interest are the three different stimuli: high fat, low fat, and tasteless. We also specified onsets of rinses (at the end of each block). The duration for rinses was specified as 0 (following convention for events of no interest). Motion parameters were included as regressors in the design matrix at the single-subject level. In addition, image volumes in which the z-normalized global brain activation exceeded 3 SDs from the mean of the run or showed 1 mm of composite (linear plus rotational) movement were flagged as outliers and deweighted during SPM estimation. After estimating the first level design matrix, we specified the following contrasts: low fat-tasteless, high fat-tasteless, high fat-low fat, (high fat+low fat)-tasteless. Finally, we evaluate the contrast (high fat+low fat)-tasteless at a low threshold ($p > .05$) to check if the data quality is acceptable. If no halo (shifting of voxels in and out of the brain) is observed and if we can see some active voxels in the usual areas that respond to flavor stimulation, such as the insula and oral somatosensory, the participant is included for group-level analysis. None of the participants were excluded for data quality concerns.

Second-Level Analysis of Average Responses: To localize brain regions responding to the chocolate drinks, we entered the parameter estimate contrasts of the first level analyses into a one-sample t-test. In this, and all subsequent contrasts, the resulting t-map was thresholded at $p < 0.005$ (uncorrected) and 5 or more contiguous voxels. Peaks were then considered significant if the p-value was less than 0.05 following family wise error correction for multiple comparisons at the cluster level across the whole brain (denoted P_{FWE}). Anatomical labels for the significant locations are manually labeled using atlases of the human brain (Mai et al., 2015; Najdenovska et al., 2018). We used JASP software (version 0.16.3) to plot the magnitude of the estimated response for each of the drinks in the maximally responsive voxel of a cluster. We also used those responses in equivalence t-tests to confirm the absence of a significant difference between stimuli. Equivalence t-tests were done with the “Two One-Sided Tests” (TOST; Lakens et al., 2018) procedure implemented in JASP, using the default equivalence region (-0.05–0.05).

3.2.6. Analysis of concurrent flavor perception task during distraction

We excluded response times above 25 seconds. We then averaged over the (up to) 8 repeats within each of the four different combinations of the fat content and cognitive load combinations. To test the effect of the independent variables on fat ratings, we used JASP software (version 0.16.3) to run a 2x2 repeated measures ANOVA with within-subject factors “fat content” (low fat vs. high fat) and “cognitive-load” (low load vs. high load). We conducted planned follow-up t-tests (Bonferroni-corrected for six comparisons). Alpha was set at 0.05. Figures were created with JASP software.

Second-Level Analysis of the Correlation with Fat Suppression by Distraction:

To determine if fat suppression due to distraction is related to reduced neural responses to the chocolate drinks, we regressed the difference between fat ratings in the high cognitive load condition relative to the low cognitive load condition against the BOLD response evoked by the stimuli. We ran two regression analyses. For the first regression analysis, we used the average of the fat ratings of the low and high fat chocolate drinks. For the second regression, we used the fat ratings of the high fat chocolate drink only, as we observed more fat suppression in the high fat stimulus in Chapter 2. For the regression analyses, we used a whole brain regression analysis in SPM12. This analysis was used to test *whether* and *where* we observe significant correlations in the neural response to the drinks and fat suppression by distraction from those drinks. Peaks were considered significant if the p-value was less than 0.05 following family wise error correction for multiple comparisons at the cluster level across the whole brain (denoted P_{FWE}). Predicted peaks in our regions of interest were considered significant if the p-value was less than 0.05 following family wise error correction for multiple comparisons at the peak level across the small volume search of 10 mm around peak voxels identified in a meta-analysis for the search term “food” in Neurosynth (denoted $P_{SVC\text{-}FWE}$). For example, for the amygdala, we used these coordinates: -30 -2 -22 and 36 -2 -22. We calculate the magnitude of the correlation (r) in the peak voxel of each cluster for post-hoc illustrative purposes. Scatterplots were created with JASP.

3.3. RESULTS

3.3.1. Neural response to flavored drinks vs tasteless

To isolate brain regions that respond to both chocolate drinks relative to tasteless stimuli, we conducted a one-sample T-test of (high-fat+low-fat)-tasteless. We observed clusters in the mid-dorsal insula/frontal operculum, precentral gyrus, VPMpc in thalamus, and cerebellum (Fig. 3.7, Table 3.1).

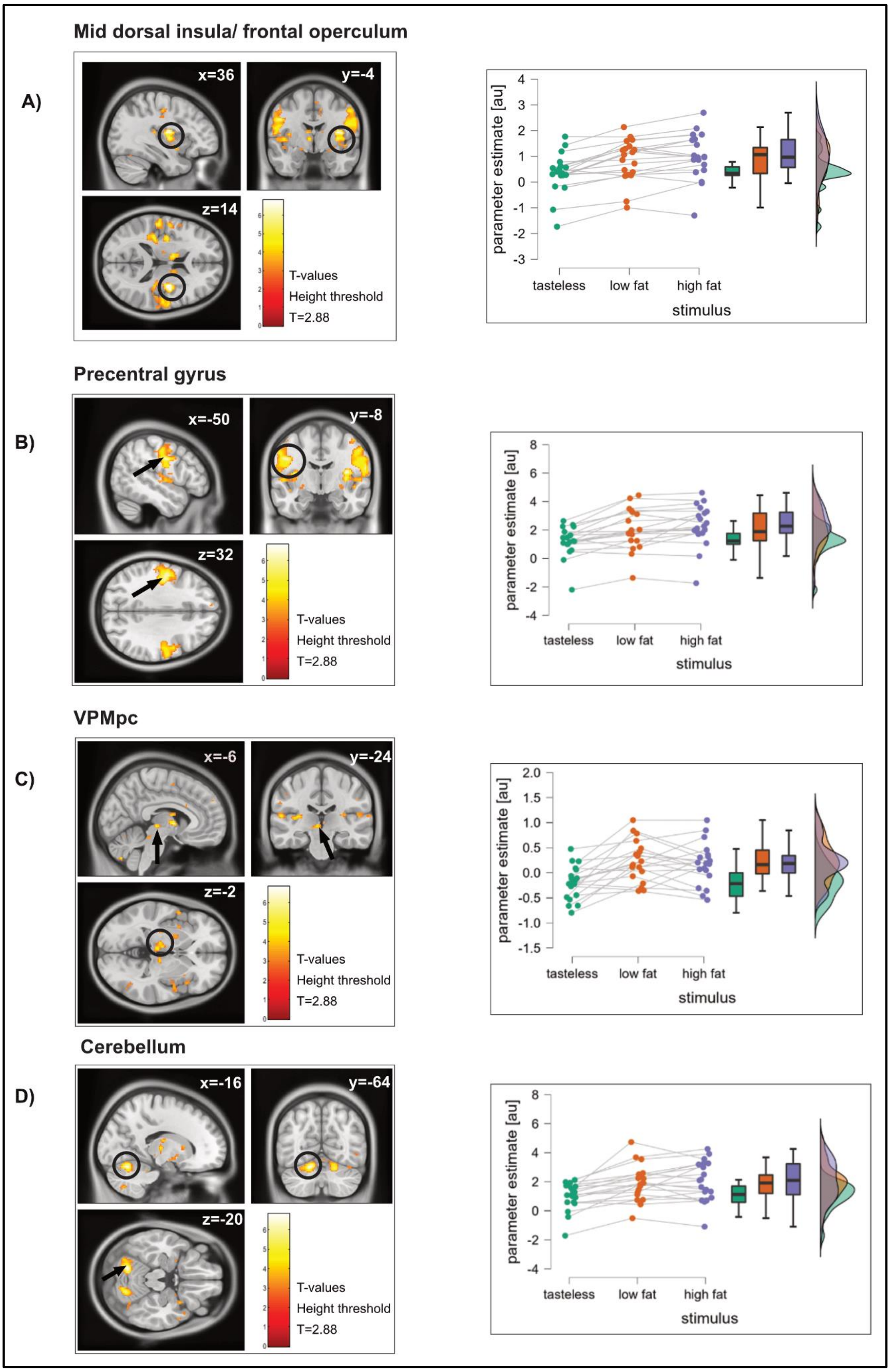
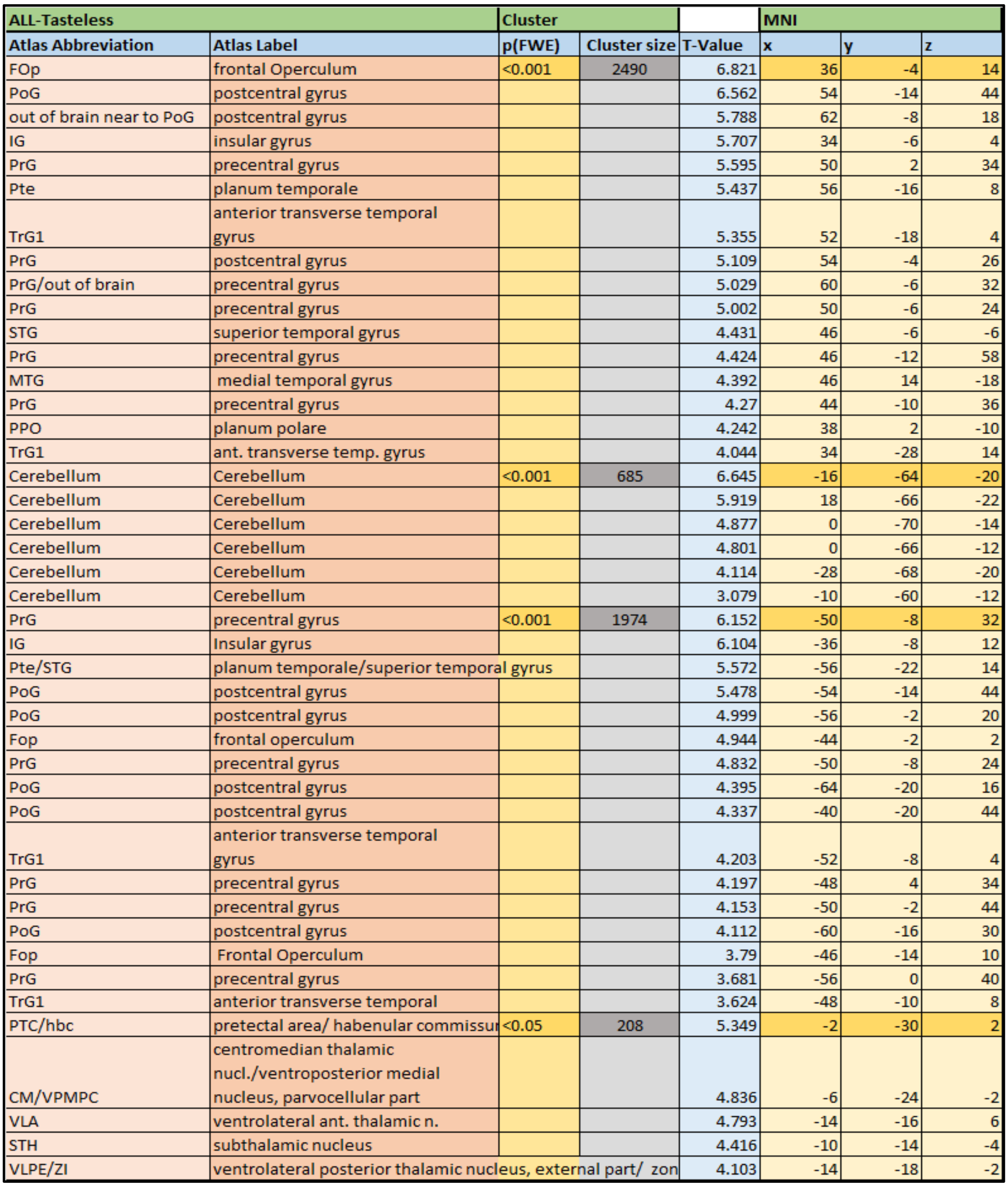


Figure 3.7: Neural responses to (high-fat+low-fat)- tasteless in mid dorsal insula/frontal operculum, precentral gyrus, VPMpc, and cerebellum (from top to bottom). In the left panel, we display the sagittal, coronal, and transversal planes of a template brain (slice location indicated in MNI coordinates) with

the SPM T-map overlaid, thresholded at puncorrected < 0.005, and a minimum of five contiguous voxels. The color gradient of the clusters depicts suprathreshold t values. In the right panel, we display the parameter estimate of the peak voxels within a significant cluster. The dot-line plot shows the parameter estimate for each participant, with the different stimuli for a given participant connected by lines. The boxplot graphs show the median (center line), first and third quartiles (lower and upper hinges), and 1.5 as the interquartile range (top and bottom whiskers). The half violin plots show the distribution density of the observations for each stimulus. Neural response to tasteless is plotted in green, to low fat in orange, and to high fat in purple.

Table 3.1: Significant cluster of BOLD response to (high-fat+low-fat)-tasteless drinks



ALL-Tasteless		Cluster			MNI		
Atlas Abbreviation	Atlas Label	p(FWE)	Cluster size	T-Value	x	y	z
FOp	frontal Operculum	<0.001	2490	6.821	36	-4	14
PoG	postcentral gyrus			6.562	54	-14	44
out of brain near to PoG	postcentral gyrus			5.788	62	-8	18
IG	insular gyrus			5.707	34	-6	4
PrG	precentral gyrus			5.595	50	2	34
Pte	planum temporale			5.437	56	-16	8
TrG1	anterior transverse temporal gyrus			5.355	52	-18	4
PrG	postcentral gyrus			5.109	54	-4	26
PrG/out of brain	precentral gyrus			5.029	60	-6	32
PrG	precentral gyrus			5.002	50	-6	24
STG	superior temporal gyrus			4.431	46	-6	-6
PrG	precentral gyrus			4.424	46	-12	58
MTG	medial temporal gyrus			4.392	46	14	-18
PrG	precentral gyrus			4.27	44	-10	36
PPO	planum polare			4.242	38	2	-10
TrG1	ant. transverse temp. gyrus			4.044	34	-28	14
Cerebellum	Cerebellum	<0.001	685	6.645	-16	-64	-20
Cerebellum	Cerebellum			5.919	18	-66	-22
Cerebellum	Cerebellum			4.877	0	-70	-14
Cerebellum	Cerebellum			4.801	0	-66	-12
Cerebellum	Cerebellum			4.114	-28	-68	-20
Cerebellum	Cerebellum			3.079	-10	-60	-12
PrG	precentral gyrus	<0.001	1974	6.152	-50	-8	32
IG	Insular gyrus			6.104	-36	-8	12
Pte/STG	planum temporale/superior temporal gyrus			5.572	-56	-22	14
PoG	postcentral gyrus			5.478	-54	-14	44
PoG	postcentral gyrus			4.999	-56	-2	20
Fop	frontal operculum			4.944	-44	-2	2
PrG	precentral gyrus			4.832	-50	-8	24
PoG	postcentral gyrus			4.395	-64	-20	16
PoG	postcentral gyrus			4.337	-40	-20	44
TrG1	anterior transverse temporal gyrus			4.203	-52	-8	4
PrG	precentral gyrus			4.197	-48	4	34
PrG	precentral gyrus			4.153	-50	-2	44
PoG	postcentral gyrus			4.112	-60	-16	30
Fop	Frontal Operculum			3.79	-46	-14	10
PrG	precentral gyrus			3.681	-56	0	40
TrG1	anterior transverse temporal			3.624	-48	-10	8
PTC/hbc	pretectal area/ habenular commissu	<0.05	208	5.349	-2	-30	2
CM/VPMPC	centromedian thalamic nucl./ventroposterior medial nucleus, parvocellular part			4.836	-6	-24	-2
VLA	ventrolateral ant. thalamic n.			4.793	-14	-16	6
STH	subthalamic nucleus			4.416	-10	-14	-4
VLPE/ZI	ventrolateral posterior thalamic nucleus, external part/ zon			4.103	-14	-18	-2

The main effect of a high-fat- tasteless drink was demonstrated in a similar manner in the precentral gyrus, cerebellum, and frontal operculum/insular gyrus (Fig. 3.8, Table 3.2).

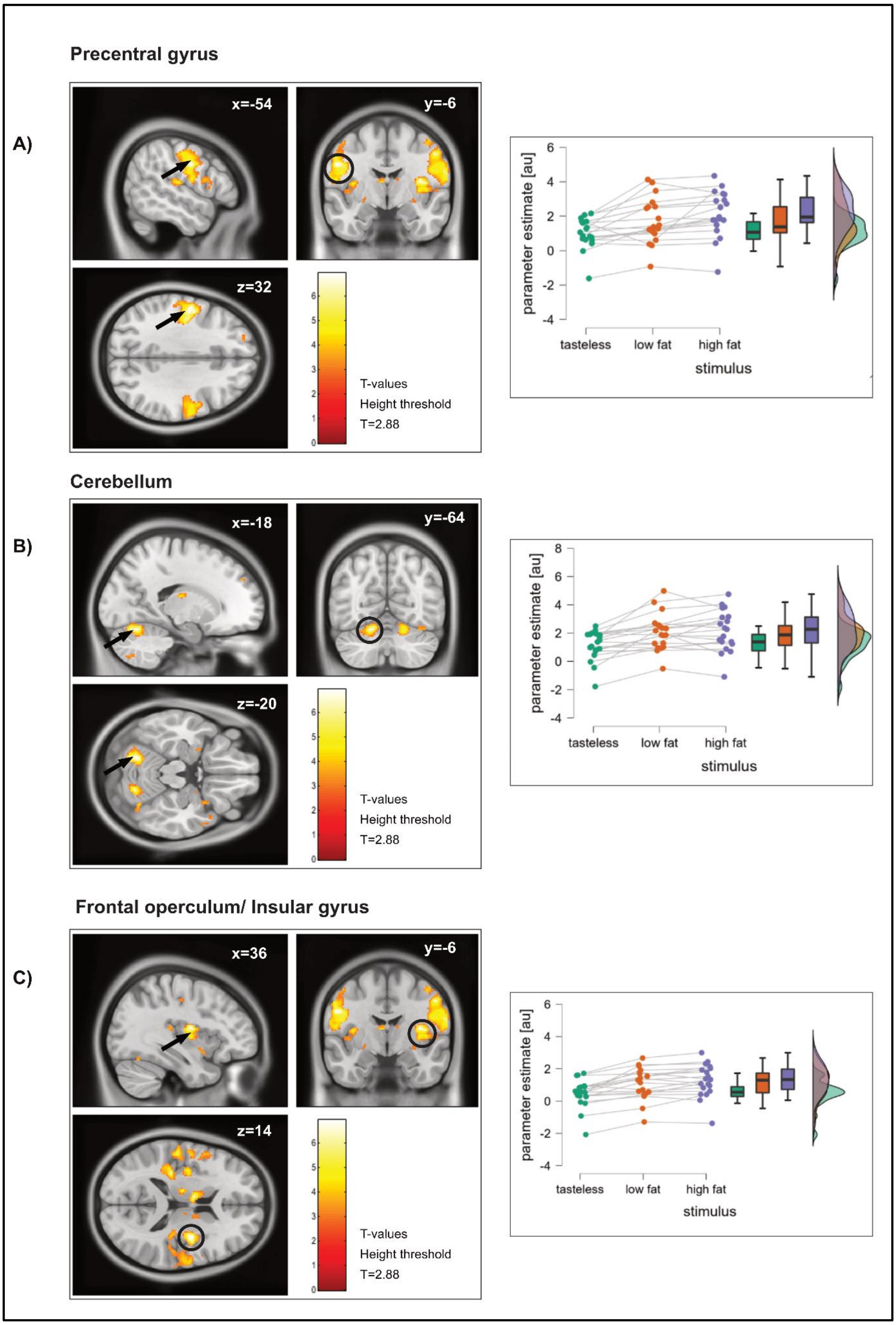
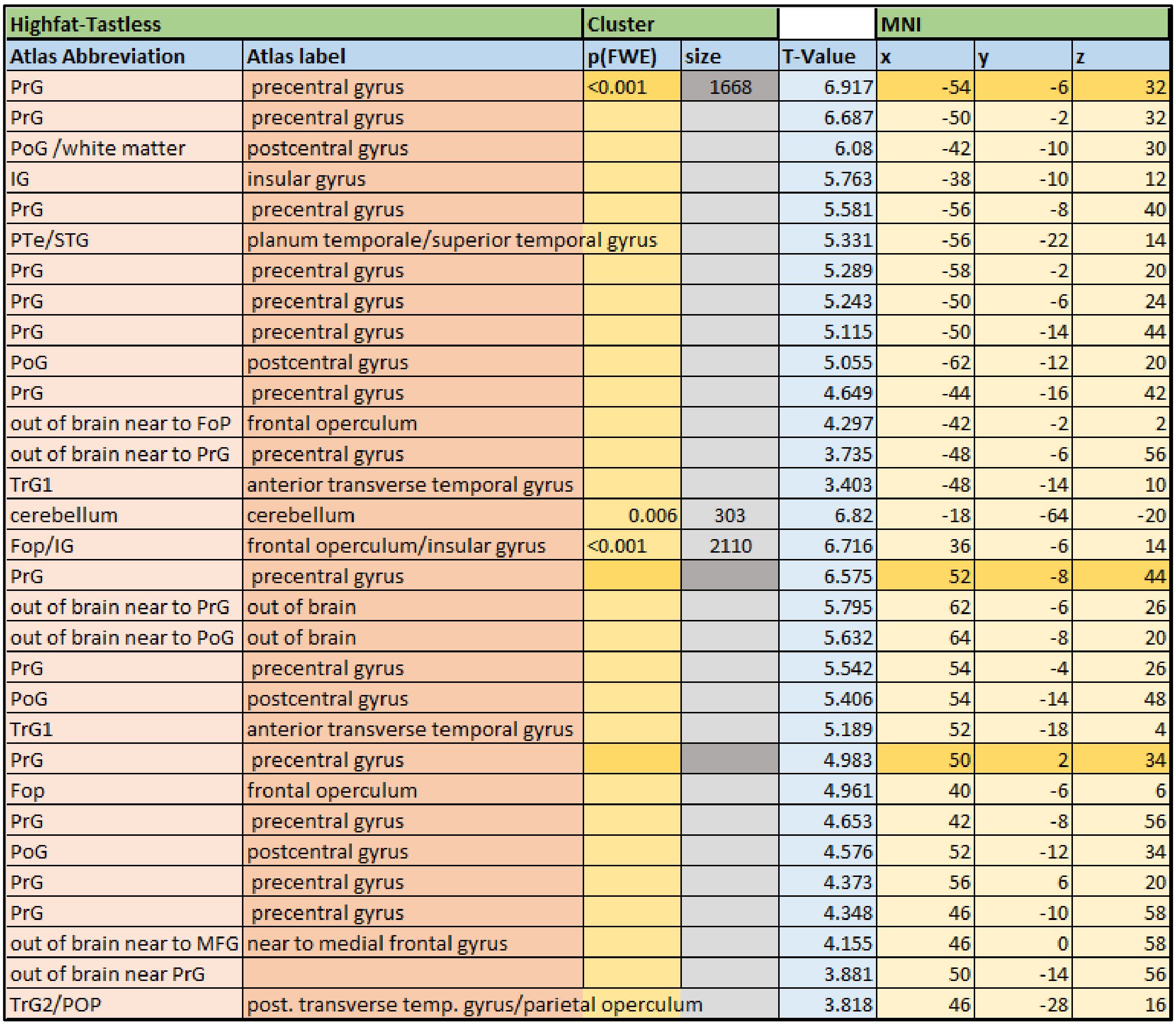


Figure 3.8: Neural responses to high-fat-tasteless, in the frontal operculum/insular gyrus, precentral, and

cerebellum. In the left panel, we display the sagittal, coronal, and transversal planes of a template brain (slice location indicated in MNI coordinates) with the SPM T-map overlaid, thresholded at puncorrected < 0.005, and a minimum of five contiguous voxels. The color gradient of the clusters depicts suprathreshold t values. In the right panel, we display the parameter estimate of the peak voxels within a significant cluster. The dot-line plot shows the parameter estimate for each participant, with the different stimuli for a given participant connected by lines. The boxplot graphs show the median (center line), first and third quartiles (lower and upper hinges), and 1.5 as the interquartile range (top and bottom whiskers). The half violin plots show the distribution density of the observations for each stimulus. Neural response to tasteless is plotted in green, to low fat in orange, and to high fat in purple.

Table 3.2: Significant cluster of BOLD response to high-fat-tasteless



Highfat-Tastless		**Cluster**			**MNI**		
Atlas Abbreviation	**Atlas label**	**p(FWE)**	**size**	**T-Value**	**x**	**y**	**z**
PrG	precentral gyrus	<0.001	1668	6.917	-54	-6	32
PrG	precentral gyrus			6.687	-50	-2	32
PoG /white matter	postcentral gyrus			6.08	-42	-10	30
IG	insular gyrus			5.763	-38	-10	12
PrG	precentral gyrus			5.581	-56	-8	40
PTe/STG	planum temporale/superior temporal gyrus			5.331	-56	-22	14
PrG	precentral gyrus			5.289	-58	-2	20
PrG	precentral gyrus			5.243	-50	-6	24
PrG	precentral gyrus			5.115	-50	-14	44
PoG	postcentral gyrus			5.055	-62	-12	20
PrG	precentral gyrus			4.649	-44	-16	42
out of brain near to FoP	frontal operculum			4.297	-42	-2	2
out of brain near to PrG	precentral gyrus			3.735	-48	-6	56
TrG1	anterior transverse temporal gyrus			3.403	-48	-14	10
cerebellum	cerebellum	0.006	303	6.82	-18	-64	-20
Fop/IG	frontal operculum/insular gyrus	<0.001	2110	6.716	36	-6	14
PrG	precentral gyrus			6.575	52	-8	44
out of brain near to PrG	out of brain			5.795	62	-6	26
out of brain near to PoG	out of brain			5.632	64	-8	20
PrG	precentral gyrus			5.542	54	-4	26
PoG	postcentral gyrus			5.406	54	-14	48
TrG1	anterior transverse temporal gyrus			5.189	52	-18	4
PrG	precentral gyrus			4.983	50	2	34
Fop	frontal operculum			4.961	40	-6	6
PrG	precentral gyrus			4.653	42	-8	56
PoG	postcentral gyrus			4.576	52	-12	34
PrG	precentral gyrus			4.373	56	6	20
PrG	precentral gyrus			4.348	46	-10	58
out of brain near to MFG	near to medial frontal gyrus			4.155	46	0	58
out of brain near PrG				3.881	50	-14	56
TrG2/POP	post. transverse temp. gyrus/parietal operculum			3.818	46	-28	16

The main effect of low-fat-tasteless is reported in the insular gyrus, mediodorsal thalamus, and cerebellum (Fig. 3.9, Table 3.3).

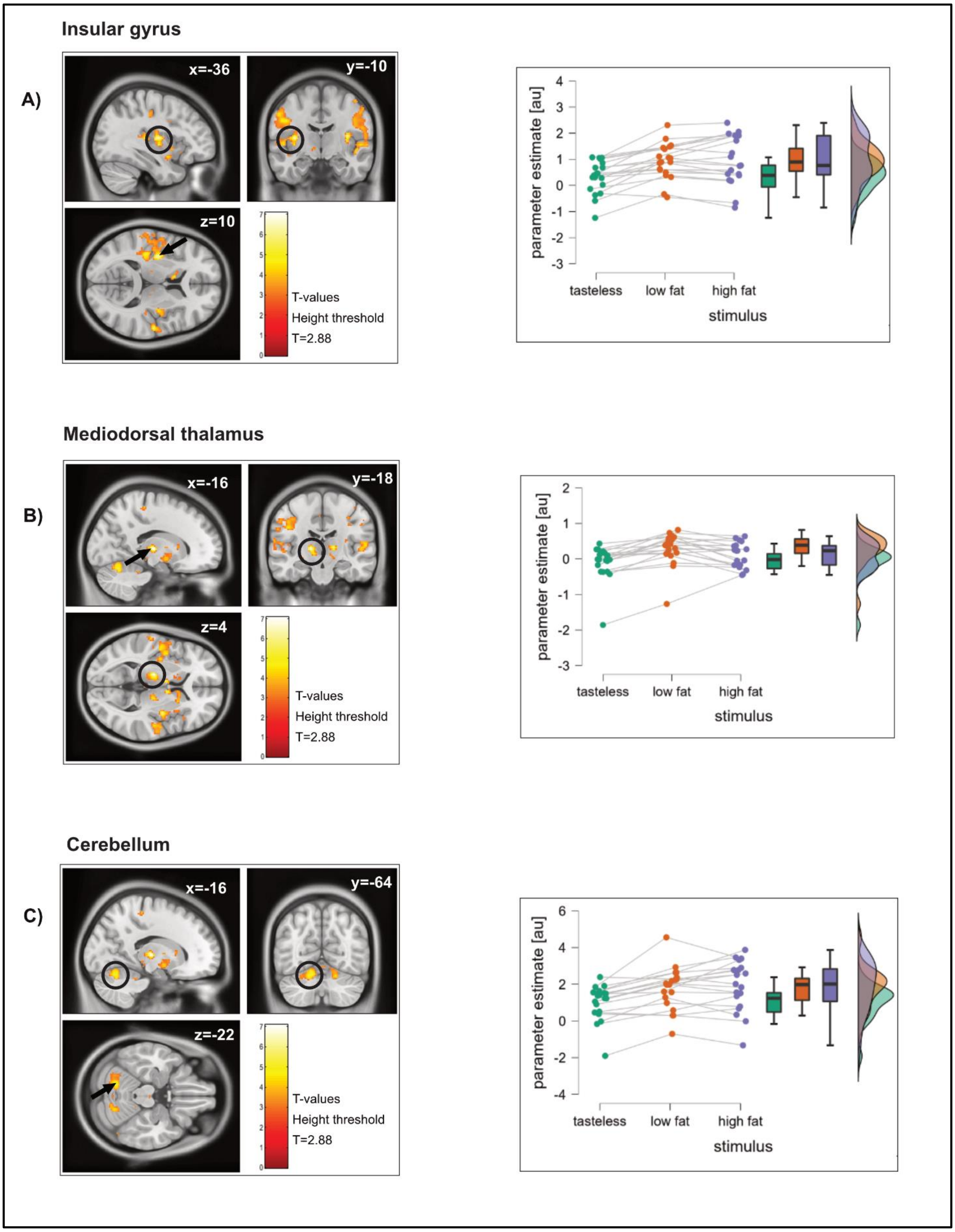
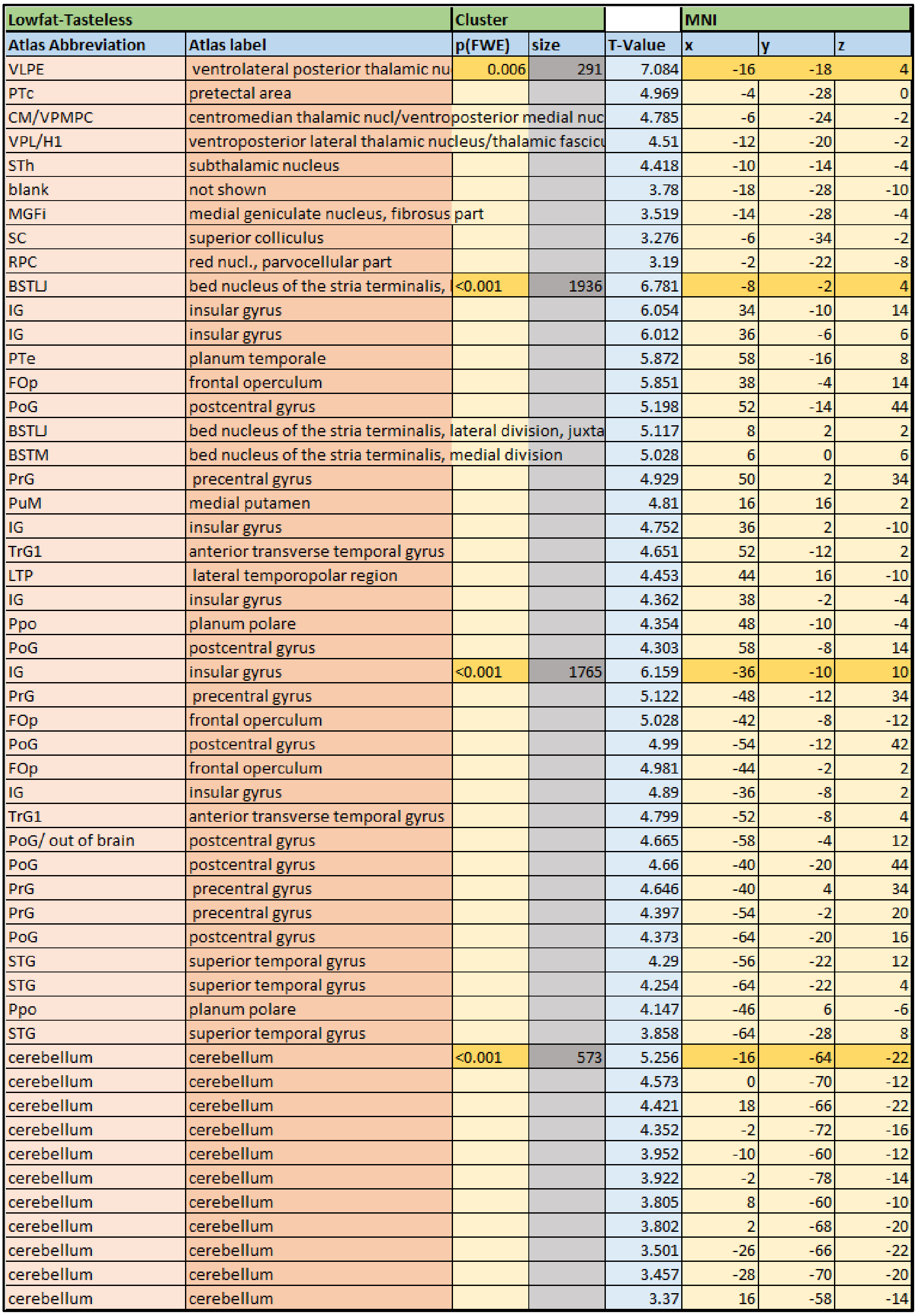


Figure 3.9: Neural responses to low-fat-tasteless drinks are found in the insular gyrus, mediodorsal thalamus, and cerebellum. In the left panel we display the sagittal, coronal, and transversal planes of a template brain (slice location indicated in MNI coordinates) with the SPM T-map overlaid, thresholded at puncorrected < 0.005, and a minimum of five contiguous voxels. The color gradient of the clusters depicts suprathreshold t values. In the right panel, we display the parameter estimate of the peak voxels within a significant cluster. The dot-line plot shows the parameter estimate for each participant, with

the different stimuli for a given participant connected by lines. The boxplot graphs show the median (center line), first and third quartiles (lower and upper hinges), and 1.5 as the interquartile range (top and bottom whiskers). The half violin plots show the distribution density of the observations for each stimulus. Neural response to tasteless is plotted in green, to low fat in orange, and to high fat in purple.

Table 3.3: Significant clusters of BOLD response to low-fat-tasteless drinks



Lowfat-Tasteless		Cluster			MNI		
Atlas Abbreviation	**Atlas label**	**p(FWE)**	**size**	**T-Value**	**x**	**y**	**z**
VLPE	ventrolateral posterior thalamic nu	0.006	291	7.084	-16	-18	4
PTc	pretectal area			4.969	-4	-28	0
CM/VPMPC	centromedian thalamic nucl/ventroposterior medial nuc			4.785	-6	-24	-2
VPL/H1	ventroposterior lateral thalamic nucleus/thalamic fascicu			4.51	-12	-20	-2
STh	subthalamic nucleus			4.418	-10	-14	-4
blank	not shown			3.78	-18	-28	-10
MGFi	medial geniculate nucleus, fibrosus part			3.519	-14	-28	-4
SC	superior colliculus			3.276	-6	-34	-2
RPC	red nucl., parvocellular part			3.19	-2	-22	-8
BSTLJ	bed nucleus of the stria terminalis, l	<0.001	1936	6.781	-8	-2	4
IG	insular gyrus			6.054	34	-10	14
IG	insular gyrus			6.012	36	-6	6
PTe	planum temporale			5.872	58	-16	8
FOp	frontal operculum			5.851	38	-4	14
PoG	postcentral gyrus			5.198	52	-14	44
BSTLJ	bed nucleus of the stria terminalis, lateral division, juxta			5.117	8	2	2
BSTM	bed nucleus of the stria terminalis, medial division			5.028	6	0	6
PrG	precentral gyrus			4.929	50	2	34
PuM	medial putamen			4.81	16	16	2
IG	insular gyrus			4.752	36	2	-10
TrG1	anterior transverse temporal gyrus			4.651	52	-12	2
LTP	lateral temporopolar region			4.453	44	16	-10
IG	insular gyrus			4.362	38	-2	-4
Ppo	planum polare			4.354	48	-10	-4
PoG	postcentral gyrus			4.303	58	-8	14
IG	insular gyrus	<0.001	1765	6.159	-36	-10	10
PrG	precentral gyrus			5.122	-48	-12	34
FOp	frontal operculum			5.028	-42	-8	-12
PoG	postcentral gyrus			4.99	-54	-12	42
FOp	frontal operculum			4.981	-44	-2	2
IG	insular gyrus			4.89	-36	-8	2
TrG1	anterior transverse temporal gyrus			4.799	-52	-8	4
PoG/ out of brain	postcentral gyrus			4.665	-58	-4	12
PoG	postcentral gyrus			4.66	-40	-20	44
PrG	precentral gyrus			4.646	-40	4	34
PrG	precentral gyrus			4.397	-54	-2	20
PoG	postcentral gyrus			4.373	-64	-20	16
STG	superior temporal gyrus			4.29	-56	-22	12
STG	superior temporal gyrus			4.254	-64	-22	4
Ppo	planum polare			4.147	-46	6	-6
STG	superior temporal gyrus			3.858	-64	-28	8
cerebellum	cerebellum	<0.001	573	5.256	-16	-64	-22
cerebellum	cerebellum			4.573	0	-70	-12
cerebellum	cerebellum			4.421	18	-66	-22
cerebellum	cerebellum			4.352	-2	-72	-16
cerebellum	cerebellum			3.952	-10	-60	-12
cerebellum	cerebellum			3.922	-2	-78	-14
cerebellum	cerebellum			3.805	8	-60	-10
cerebellum	cerebellum			3.802	2	-68	-20
cerebellum	cerebellum			3.501	-26	-66	-22
cerebellum	cerebellum			3.457	-28	-70	-20
cerebellum	cerebellum			3.37	16	-58	-14

Neural responses to low fat - tasteless generally includes more voxels (numerically greater spatial extent) than high fat - tasteless in the clusters. We also noted that only with low fat - tasteless we observe significant responses in the thalamus.

3.3.2. No difference in neural responses between high-fat and low fat

To isolate brain regions that respond to fat concentration, we conducted a one-sample T-test of high-fat *minus* low-fat. We observed no clusters that were significant when corrected for multiple comparisons in our regions of interest, nor in unpredicted areas. We did observe a small cluster in the left middorsal insula that was not significant when corrected for multiple comparisons (-34, 0, 16, $t = 3.83$, $p_{uncorrected} = 0.001$). This agrees with the general pattern of responses as can be observed in Fig.3.7; the distributions of neural responses to low and high fat generally overlap, and the average magnitude of the response looks similar. There were also no regions that displayed a significantly stronger response to low fat relative to high fat. To explicitly confirm that responses in our regions of interest are equivalent, we inspected equivalence t-tests for the extracted parameter estimates for the peak voxels of the significant clusters in Table 1. Equivalence tests did not explicitly confirm the absence of a difference between low and high fat in the mid-dorsal insula/frontal operculum ($t = -2.048$, $p = .055$), precentral gyrus ($t = -1.892$, $p = .075$), thalamus ($t = 0.685$, $p = .502$), and cerebellum (t -0.652, $p = 0.522$). We note that a few of these tests are marginally significant, so we cannot conclude that the responses are different nor that they are similar.

3.3.3. Fat suppression by distraction

Here, we used behavioral data for a subset of participants (N = 18) from Chapter 2 that also have fMRI data. To test whether in this subset of participants we can replicate the interaction of cognitive load and fat content, we evaluated fat ratings (Fig.3.10). Cognitive load did not have a main effect on fat ratings ($F(1,17) = 1,613$, $p = .221$, $\eta^2 = 0.015$). We observed a main effect of fat content on fat ratings ($F(1,17) = 9.128$, $p = .008$, $\eta^2 = 0.259$) , such that higher ratings are given to the drink with the higher fat content. Critically, for this subset of participants, we still observed the interaction between cognitive load and fat content ($F(1,17) = 6.983$, $p = .017$, $\eta^2 = 0.024$) that we also reported in Chapter 2. Post-hoc paired t-test indicates that this is driven by a suppression of fat perception under high cognitive load for the high fat stimulus ($t(17) = 2.322$, $p = 0.033$, uncorrected for multiple comparisons).

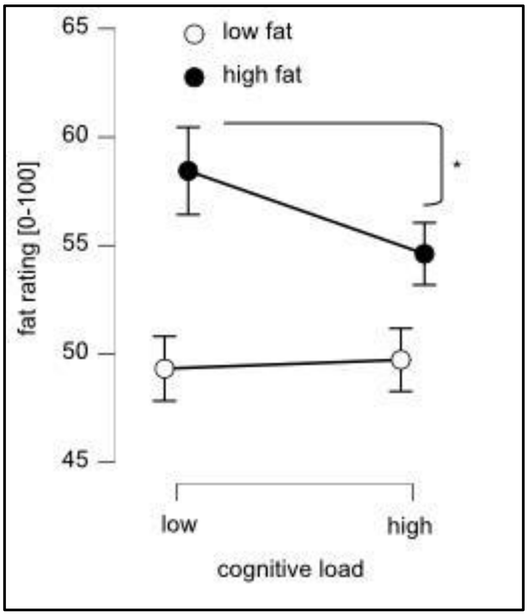


Figure 3.10: Fat rating in the flavor perception task. The graph shows averages ± standard error of the mean (SEM) across participants with respect to each cognitive load (on the x-axis). The different fat contents of the drinks are indicated with symbols, open circles - low fat content, filled circles - high fat content. The figure depicts the fat ratings (0-100). Significant planned follow-up t-tests are indicated with asterisks (* p < .05).

3.3.4. Correlation between neural responses to flavored drinks and distractibility

To assess whether individual variation in distractibility from fat perception is related to sensory processing differences as expressed by neural activation in the brain, we regressed the degree of suppression of fat ratings between a high and low cognitive load of working memory tasks (measured in a separate session) against neural responses to both high and low fat vs. tasteless. We observed a cluster in the fusiform gyrus that shows a relation with fat suppression, such that the more fat is suppressed, the lower activity in this area (Fig.3.11, 32,-68,-12, t=7.48, k = 345, $P_{FWE\ cluster} = 0.002$). We also noted a cluster in the left amygdala, which was significant when we used a small volume search (-28, -8, -14, t=6.05, k =115, $p_{FWE\ peak\ level} = 0.009$).

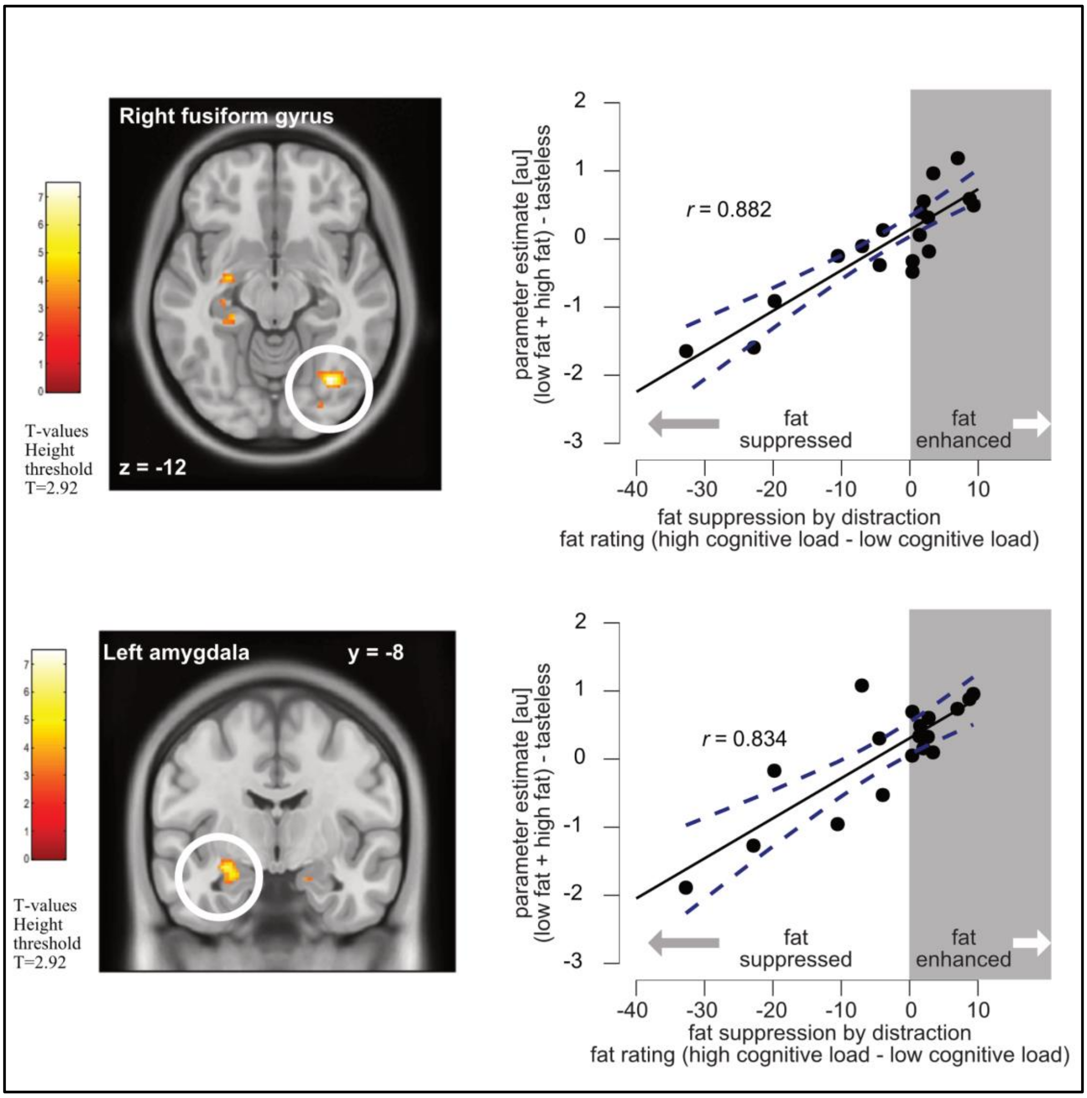


Figure 3.11: Correlation between neural responses to drinks and distractability for (high fat + low fat) - tasteless. The upper left image shows fusiform gyrus activation, and the right image shows their correlation (the more fat suppressed, the less activation in fusiform gyrus). The lower picture on the left shows the activation of the amygdala, and the right one shows the correlation between activation of the amygdala and fat suppression. Scatterplots show fat suppression by distraction (fat ratings for high cognitive load minus low cognitive load averaged over the low and high fat stimuli) on the x-axis and parameter estimates of the peak voxel (high fat+ low fat) - tasteless in arbitrary units (au) on the y-axis. Each dot stands for a participant. The solid line indicates the linear regression line, and the r value is the Pearson correlation. Dashed lines indicate the 95\percentage_sign confidence intervals.

3.4. DISCUSSION

In the current study, neural responses to varying fat contents are evaluated by employing new advances in fMRI analysis. We found significant responses to high-fat and low-fat drinks vs. tasteless drinks in the mid-dorsal insula/frontal operculum, precentral gyrus, VPMpc of the thalamus, and cerebellum. There was no significant difference between low-fat and high-fat drinks in the neural responses. We also looked to see whether there was any correlation between brain responses and perceived fat suppression caused by distraction. The distractibility factor is determined by the difference in fat perception for both high-fat and low-fat drinks under high versus low cognitive loads. Results indicated a robust relation between sensory responses in the fusiform gyrus and fat suppression, in such a manner that there is a greater response when fat suppression is less. We observed a similar pattern of responses in the amygdala.

3.4.1. Neural responses to flavors regardless of fat content

We observed responses in the insula, as expected, because the putative primary taste cortex is in the insula (Small, 2010). Meanwhile, flavors are expected to evoke responses in the insula according to an automated meta-analysis based on neuroimaging studies of “taste” (https://neurosynth.org/analyses/terms/food/, accession date 10/03/2023). Huerta et al. (2014) reported the meta-analysis result that the left anterior insula is the region that is activated by all types of food cues, such as taste, odor, or image. In our study, we observed the activation of the insular gyrus and overlying operculum, which is consistent with Veldhuizen et al. (2011), wherein they pointed out that gustatory stimuli activate these two areas; in addition, they demonstrated activation of various other insular areas. The frontal operculum is known for controlling cognitive procedures (Higo et al., 2011). In line with Veldhuizen et al. (2011), the frontal operculum accompanies the activation of the insula for taste stimuli in most other studies (Roll et al., 2011). Besides taste responses, the frontal operculum is also involved in the processing of oral somatosensory aspects such as fat texture, viscosity, and temperature (Verhagen et al., 2004).

This study also demonstrated the activation of the precentral gyrus. This area was associated with managing intentional motor movements in the previous studies (Banker & Tadi, 2019). However, Huerta et al. (2014) also reported the activation of this region for food stimuli in a meta-analysis. In our study, activation of the precentral gyrus could be related to swallowing, mouth, and tongue movements, but as the area is not activated in tasteless-flavored drinks, it might also be related to taste rather than motor function, or it might happen because drinking tasteless drinks might involve fewer motor activities than drinking viscous (low-fat or high-fat) drinks.

Previously, the cerebellum was thought to be the region associated with motor and movement control; however, recent studies demonstrate the nonmotor contributions of this region to the various aspects of behavior like attention, working memory, learning, and emotion as well as motor controls (Strick et al., 2009). According to Low et al.

(2021), the cerebellum is activated by food cues, and this region has a prominent role in adjusting satiety and satiation. It is also noted that hunger increases cerebellum responses to food stimuli in both humans and mice. They found that activation of the anterior deep cerebellar nuclei (aDCN) inhibits food consumption. Strikingly, they reported that people with Prader-willi Syndrome (PWS) who have satiation problems have a deficiency in cerebellar activity. Our participants are asked not to eat anything three hours before scans that might emphasize the significant activation of the cerebellum.

The ventroposteromedial nucleus (VPMpc) nucleus of the thalamus is the first cortical relay of gustatory and somatosensory information, which then projects to primary sensory areas in the insula, overlying the operculum and pre- and postcentral gyrus. Olfactory information projects to the primary olfactory cortex in piriform from the olfactory bulb, bypassing the thalamus (Gottfried, 2006; Small, 2006). However, later in the sensory processing network, there are projections to the mediodorsal thalamus. The thalamus also connects cortical areas and forms links between sensory and motor neural circuits in the brain (Basso et al., 2005). Huerta et al. (2014) showed activation of the thalamus in response to food cues in a meta-analysis. In the case of (low-fat + high-fat) - tasteless, we observed responses in the VPMpc and mediodorsal nuclei of the thalamus. Veldhuizen et al. (2020) showed that the amygdala modulates VPM and the mediodorsal thalamus in taste responses. Tham et al. (2009) noted the role of the mediodorsal thalamus in processing olfactory attention, and Veldhuizen et al. (2011) highlighted the activation of the mediodorsal thalamus in response to food cues. This suggests that both primary gustatory and higher-order flavor processing are reflected in thalamic responses here.

Previous studies showed that the taste of fat activates the OFC and amygdala, as well as the primary taste cortex. However, our findings showed no activation of the amygdala or OFC. We also expected to see activation in the brainstem as a pathway from the tongue to the thalamus, but there was no activation in that area at the group level, although we observed it in at least a few individual participants.

3.4.2. Neural correlates of different fat contents in flavors

High fat and low fat did not create significantly different responses in the brain. We expected to observe responses in, for example, the insula and overlying operculum, as was previously observed (De Araujo et al. (2004) and Eldeghaidy et al. (2011)). However, other studies have also not found differential responses, for example Eldeghaidy et al. (2012) and Stice et al. (2013). We note that the studies that observed differences tended to use very high concentrations of fat, which are not usually consumed on their own, and for ecological reasons, many studies want to use lower concentrations. We cannot definitively conclude there are no differences in neural responses to lower range fat concentrations, as equivalence tests also gave inconclusive results, but clearly the current methods are not sensitive enough to detect differences. Maybe MVPA (multivoxel pattern analysis; Avery et al., 2020), higher temporal resolution (following early discrimination with EEG (Electroencephalography; Andersen et al., 2020), or consumption designs might be used.

However, it is also possible that this lack of response to fat concentration is all due to individual variation in sensitivity, and our correlation with distractibility gives a suggestion for that. Perhaps some participants are just very distracted by auditory noise and other sensations in the scanner. One approach may be to only include participants who have lower fat detection thresholds in future studies.

3.4.3. Relation between fusiform and amygdala responses and fat suppression by distraction

Fusiform is located inside the ventral visual stream; commonly, it involves face recognition (especially through the subregion of the Fusiform Face Area (FFA)). There are also studies showing the activation of fusiform in object identification (Gauthier et al., 1999) and categorization (Gauthier et al., 2000; Xu, 2005). This suggests that there are fusiform subregions, that are specialized for salient categories. Indeed, one salient category that has recently been associated with the fusiform gyrus is food. Adamson and Troiani (2018), demonstrated bilateral activation with food and categorizing food in the fusiform. They also reported that faces and food activate the left fusiform in exactly the same way. In their meta-analysis, Van der Laan et al. (2011) proved the robust activation of bilateral fusiform in response to food images. Khosla et al. (2022) found sensitivity of the ventral visual pathway to faces, scenes, bodies, and words as well as food categorization. It was also shown that activation of the fusiform gyrus is affected by hunger and the calorie content of food images (Frak et al., 2010; Siep et al., 2009; Uher et al., 2006). All of these studies used visual cues with food images, not real food; inside fMRI, we used realistic drink stimuli (high-fat, low-fat, and tasteless flavored drinks). Regarding the correlation between neural responses and fat suppression under distraction, we found that the more the fusiform is activated, the less fat suppression occurs. We speculate that perhaps stronger responses in fusiform reflect categorization of the stimulus as food. A more holistic processing may make the flavor more resistant to reductions by distractions. We can deduce that not only visual triggers like food images but also the flavors of drinks can be associated with the fusiform food object area. Frak et al. (2010) demonstrated a gender effect on the activation of the fusiform gyrus in a way that the activation was higher in women, and since our study is predominantly with women, this may be a partial explanation.

Recently, the amygdala has been proposed as a central source of gain adjustments to modulate sensitivity to gustatory stimuli (Veldhuizen et al. 2020). Van der Laan et al. (2011) also discuss the role of the amygdala in reward processing and remark that, when hungry, activation of the amygdala is higher for food images. Kong and Zweifel (2021) reported the role of the amygdala in processing the prominence of stimuli. In the current study, we observed that individual variation in distractibility from fat perception is related to sensory processing of fat tastes in the amygdala, such that stronger neural responses correlate positively with less fat suppression due to distraction (in a separate session). A possible explanation for this observation is that some people are perceptually less sensitive to fat and require more attentional resources to perceive it, which, when distracted, will affect their perception of fat more negatively. Adamson and Troiani (2018) highlight a network that includes fusiform and amygdala in the processing of face and food cues. Since we found co-activation of the amygdala and fusiform in the correlation with fat suppression, this may also reflect food reward network processing. Future studies may focus specifically on deciphering the connectivity between these areas with attention to food.

In conclusion, flavored drinks versus tasteless drinks activated the mid-dorsal insula/frontal operculum, precentral gyrus, ventral posterior medial thalamus, medio-dorsal thalamus, and cerebellum. Neural responses were not significantly different for low-fat and high-fat drinks. Fat suppression caused by distraction was negatively associated with the activation of the fusiform gyrus and amygdala. We recommend screening participants for fat sensitivity in future studies trying to assess neural processing of fat content.

CHAPTER 4

EFFECTS OF SATIETY ON PERFORMANCE IN DUAL TASK PARADIGM WITH FLAVOR PERCEPTION AND WORKING MEMORY

ABSTRACT

The contemporary lifestyle promotes overeating and obesity. One such lifestyle factor is habitual distracted eating. In the context of limited cognitive resources, distracted eating is thought to promote overconsumption through suppression of perception of the food stimulus. It is unknown if goals or physiological demands allow a flexible reassignment of resources in favor of food perception. For example, when hungry, there may be less suppression of food perception by competing tasks. The aim of this study is to observe how preloads with different fat contents change participants' distraction behavior and flavor perception under high and low cognitive loads.

15 participants (11 women) took part in this study. Participants consumed different preloads of fat content (water, low-fat chocolate drink, and high-fat chocolate drink) on three different days, as well as interleaved sips of tasteless, low-fat, high-fat on a fourth day, before performing concurrent flavor perception and working memory tasks. In each trial, participants are asked to memorize a string of either three (low cognitive load) or seven (high cognitive load) consonants that appear on the screen in the distraction task. Then they received a high-fat or low-fat chocolate drink. Next, they are asked to choose the string they recall among three options. Finally, they rated the flavor intensity and fattiness of the drinks they received.

The results showed a significant influence of preload on participants' response time and accuracy in the working memory task but not on their fat and intensity perceptions. We observed a complicated pattern of effects of preload on the performance of the working memory tasks, where the interleaved preload (which was also always the first session) affected performance most negatively. We observed neither a main effect of preload on flavor perception nor an interaction between preload and the suppression of fat by distraction. Surprisingly, we observed robust effects of flavor stimulus fat content on working memory task performance, which suggests bidirectional effects should be evaluated in future studies.

Keywords: satiety, distraction, cognitive load, flavor perception, fat perception

4.1. INTRODUCTION

The rate of obesity is increasing in contemporary life (Makaronidis and Batterham, 2018), and it is associated with a variety of factors. Environmental, social, and emotional factors all have an impact on obesity. There are experimental studies that propose that distraction during eating causes overconsumption of food. These experiments are explained on page 12 with more details. Temple et al. (2007) demonstrated that distraction during eating increases food intake in children. Focused eating, on the other hand, reduces both food consumption (Robinson et al., 2014) and portion size (Veit et al., 2020). Several studies have found that by watching television, satiety can be postponed, and food consumption can increase (Brunstrom & Mitchell, 2006; Bellissimo et al., 2007; Temple et al., 2007). Beside the role of television, other distracting conditions such as driving or interacting with others facilitated food intake when compared to mindful eating alone (Ogden et al., 2013). Other studies have investigated the effects of distraction in a more formal experimental approach where distraction is manipulated by performing concurrent tasks with higher and lower cognitive loads. When performing a high-load memory task, taste or smell intensity suppression is greater than when performing a low-load memory task (van der Wal & van Dillen, 2013; Van Meer et al., 2022a; Liang et al., 2018; Hoffman et al., 2017; Schadll et al., 2021). More information can be found on pages (12, 13, 14).

Focused or distracted food consumption relies on shifts in attentional resources. Attention involves filtering irrelevant information with a focus on specific actions. Attention is directed via two techniques: top-down (voluntary) and bottom-up (involuntary). There are limited attentional resources (Yantis, 2000), and these resources interact and compete with each other, and they play a role in attentional processes (Corbetta and Shulman, 2002). In the case of food consumption, a shift in goals may affect distractibility from food consumption. For example, when hungry, finding and consuming food is an important goal, and this may affect the way the sensation of food stimuli is processed. Thus, satiety (or the absence of hunger) may alter the way stimuli or concurrent tasks compete with one another. Another aspect that should be considered is that there may be systemic effects from the physiological state; for example, when people are hungry, they might be prone to more mistakes and slower responses. Afridi et al. (2019) investigated the role of school meals on students' short-term performance. They had participants solve mazes before and after meals and discovered that the post-meal conditions improved attention and cognitive efficiency. Their performance (number of mazes solved correctly) improved by 13%–16% in post-meal conditions. Importantly, the mechanisms involved in satiety are linked to the development and persistence of obesity (Blundell & Bellisle, 2013). Therefore, it is critical to understand the interplay between distraction and satiety in food perception and consumption.

Satiety is the process of suppressing appetite after eating, whereas satiation is related to the process of terminating food intake (Tepper & Yeomans, 2017). Satiety influences the time between meals and when the next meal is served, whereas satiation influences when to stop eating an ongoing meal. Sensory cues such as taste and smell, as well as food color and texture, influence the food termination and appetite suppression processes. Cognitive cues, in addition to sensory cues, play a role. For example, knowledge about the consequences of food intake, beliefs, food labels, and attention are some prominent examples (McCrickerd, K. 2017). Sensory perception not only influences satiety, but in turn, satiety also impacts the perception of flavors. We now turn to the mechanisms and a brief literature overview of the effect of satiety on perception.

There are various ways a person's physiological state may influence food stimulus processing. Because a food stimulus is more salient when people are hungry, it should be given priority in terms of attentional resource allocation. In contrast, when people are satiated, food stimuli are less important to goals, which implies less competition between resources. There is also the possibility that when satiated, food stimuli become unpleasant, thus again demanding resources, but now with the goal of avoiding these stimuli.

There is mixed evidence for a physiological state influencing the sensory processing and perception of gustatory, olfactory, and flavor stimuli. Zverev (2004) investigated how short-term caloric restriction and satiety impact *gustatory* recognition thresholds. Participants had lower detection thresholds for sugar and salt when they were hungry than when they were full. On the contrary, hunger and satiety had no effect on the taste perception of bitter substances. Meanwhile, hunger and satiety also have an impact on how *odors* are perceived. Palatable odors have a significant impact on food consumption by directing food choices and preferences (Shanahan and Kahnt, 2022). Referring to several articles, they reported that when hungry, the pleasant smell of food is more attractive and more intense than when satiated. Notably, beside physiological factors, behavioral factors such as mood, sleep deprivation, and circadian states have a significant impact on odor perception. Cabanac (1971) evaluated the role of glucose on the odor perception of citrus fruits. Participants rated odor more graceful when fasted than when they had 100 gr of glucose. Their group found that having a meal decreased the pleasantness of food. Similarly, Nie et al. (2022) reviewed the role of fasted and fed conditions on olfactory perception in 13 studies involving 550 participants and concluded that olfactory perception increased when fasted versus satiated. The effect was stronger for non-food odors. Fasting time was also a prominent factor; the longer the fast, the greater the sensitivity to odor. In another study (Ramaekers et al., 2016), odor threshold perception was investigated under three different types of preloads: very hungry (control condition), sweet lunch, or savory lunch. Results indicated that regardless of the type of food, participants' sensitivity to odor was higher in the hungry case than in the satiated case. Lastly, Hanci and Altun (2016) examined the impact of hunger and fullness on 123 participants' smell and taste perception. In line with other studies, their findings showed increased olfactory perception in hunger and increased taste perception for sweet, savory, and salty foods in hunger. In contrast, sensitivity to bitter taste was higher in the full condition.

Flavor is the result of the collective effects of odor, taste, temperature, and texture that influence appetite and food intake (Hanci and Altun, 2016; Tepper & Yeomans, 2017). The effect of satiety on taste, odor, and flavor perception is investigated further below. Graaf and Boesveldt (2017) highlighted that even though there are similarities between these two perceptions, they have different functionalities. It is also noted that humans can differentiate five or six tastes but more than a trillion odors. According to the study, taste is mostly responsible for satiation, while odor plays a role in selecting and anticipating food.

Despite studies that show the influence of satiety on chemosensory perception, there is a scarcity of resources for the role of satiety on flavor perception in terms of fat content, as well as the role on distraction. Siep et al. (2009) looked at the interaction of satiety, food energy content, and distraction on the neural processing of food pictures. They noted that hunger interferes with neural processing of food energy content: activity in the posterior cingulate cortex, medial OFC, insula, caudate putamen, and fusiform gyrus is modified. They also showed that in satiated healthy women, the processing of reward improved while presenting low-calorie food pictures; however, in fasted participants, it rose for high-calorie foods. The article highlights the complex interaction that may occur between attention, calorie-richness, and satiety in the food reward process in the human brain. Further research in this area could have significant implications for understanding how we make food choices and developing strategies to promote healthy eating habits.

In our previous study (Chapter 2), distraction specifically suppressed the fat perception of high-fat drinks. The overarching aim here is to investigate how manipulating satiety with different preloads affects distraction and flavor perception. Here, we use four distinct preload conditions on four distinct days, and then participants perform concurrent working memory tasks and flavor perception tasks. From the literature review above, we propose that satiety may influence both distraction and flavor perception independently.

The proposed mechanism here is that satiety might impact flavor perception and working memory tasks. It is estimated that when people are hungry, they have a stronger flavor perception than when they are full. It is also expected to see a decrease in the performance of working memory tasks in terms of response time and accuracy (the proportion of correct answers) in a hungry state versus a full state. Fig 4.1 indicates the proposed mechanism for the effect of satiety on both flavor perception and working memory tasks.

It is also expected to see more correct and faster answers in full condition (at least when people are not very hungry). We also predict that high versus low cognitive load will have a greater impact when people are hungry.

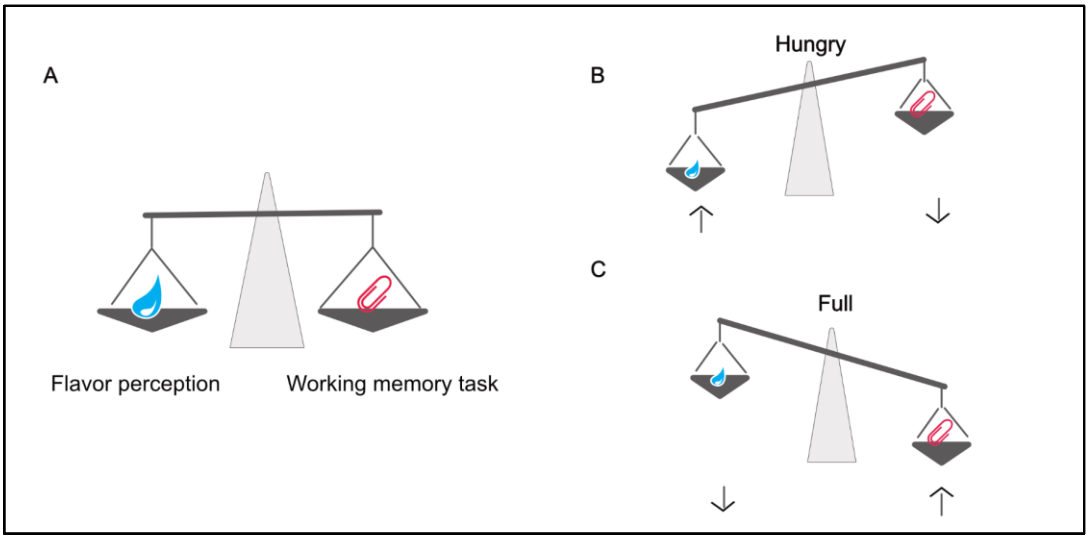


Figure 4.1: Proposed model for the effect of satiety on flavor perception and working memory tasks. A) indicates the allocation of attentional resources for concurrent flavor perception and working memory tasks. B) When hungry, the salience of food places more demand on flavor perception than working memory tasks. C) In the full condition, the salience of food is less, and more resources are allocated for the working memory task than the flavor perception task, and as a result, it is expected to see an increase in the performance of participants on the working memory task.

4.2. MATERIALS AND METHODS

4.2.1. Participants

15 participants (4 men, 11 women) with an average BMI of 22.44 (+/- 1.78 SD) and an average age of 24.46 (+/- 5.81 SD) are recruited for the experiments. These participants were among those who attended for the first distraction task. The experiment included 19 participants; one was excluded due to vertigo, another due to pregnancy, and two others because they had not completed all preload sessions.

In short, participants are not recognized as having specific illnesses, more detailed information about participants and their payment, exclusion, and inclusion criteria is explained in page 15. The protocol of the study for clinical research with these details (numbers 7807789 / 050.01.04 / 1152384) affirmed by the Mersin University Committee, and experiments were conducted at the National Magnetic Resonance Research Center (UMRAM) at the Aysel Sabuncu Brain Research Center of Bilkent University in Ankara, Turkey. Participants are volunteers who agree to take part after reading and signing consent forms. The current study is a part of a bigger research project for functional MRI of neural responses to food, and participants got financial compensation for completing scanning parts of the project.

4.2.2. Device and Software

The device and software used for collecting data were similar to the previous distraction study Figs (2.4, 2.5, 2.6) on pages (18-19). Briefly, the MRI simulator has a shelf above that houses a laptop that displays strings and performs VAS scale ratings for fat and intensity of drinks. The gustometer system is used to send drinks to the mouths of participants while they are lying supine inside the simulator. Three serially connected pumps with syringes filled with water, low-fat, and high-fat drinks and connected to tubes are controlled with scripts. There is also a mouthpiece connected to the ends of the tubes. The strings and ratings are presented on the screen through the scripts in MATLAB and Psychtoolbox-3 (PTB-3) (Brainard & Vision (1997)), and detailed data for trials is collected and documented in CSV file format.

4.2.3. Drinks

Two types of drinks are prepared for this study. Preload drinks and gustometer drinks to assess the rate of fat and intensity under cognitive loads.

Preload: To evaluate the role of satiety on distraction, four types of preloads are used: an interleaved preload of low-fat, high-fat, tasteless, and water drinks on one day, and preloads of water, low-fat drinks, and high-fat drinks on the other three days. On interleaved preload days, participants get a combination of blocks of 40 ml of each of the three drinks and 30 ml of rinsing water along two runs. On each of the other three days, participants drink 355 ml of one of the drinks in a randomized order, and then they perform distraction tasks. Two different levels of fat are used in making drinks:

low-fat drinks with (3.5% fat and 10% sugar) and high-fat ones with (15% fat and 10% sugar).

Drinks for preloads (except interleaved sessions): For the low-fat drink, 412 g of SEK (full fat ~ 3.5%) milk, 8g of Içim “Sef Krema” 35% fat cream, 60g of chocolate base, 28g of sugar, and 5g of corn starch were mixed and heated (~106 kcal per 100 ml). For a high-fat drink, 230g of SEK (full fat ~3.5%) milk, 188g of Içim “Sef Krema " 35% fat cream, 60g of chocolate-base, and 30g of sugar were mixed and heated (~ 189 kcal per 100 ml). Drinks are cooled at room temperature and then put in the refrigerator. Half an hour before the tests, they are taken out of the fridge.

Drinks for the taste perception task and interleaved sessions: For preparing ER and distraction task drinks, vegan ingredients were used (coconut cream, almond milk, coconut oil, cacao). Water and two different fat contents are used: a low-fat drink contains (3.5% fat and 10% sugar) with (~70 kcal per 100 ml) while a high-fat drink contains (15% fat and 10% sugar) with (~137 kcal per 100 ml). For tasteless drinks, artificial saliva is made with a combination of KCL, NAHCO3, and water. The detailed information for the chocolate drink ingredients and the recipes can be found on page 16.

4.2.4. Experimental design and procedure

In the current study, distraction tasks are done over 4 separate days after MR scanning sessions, each with a different type of preload. Two cognitive load conditions (low and high) with three and seven consonants, respectively, are determined based on the pilot study with four different cognitive load conditions among 30 participants. On Chapter2 pages (17, 22), the details of this study and its findings are explained.

In order to assess the role of satiety, participants are asked not to eat for 3–4 hours before the tests. They are also informed not to use nicotine-containing products for 2 hours prior to the test and not to consume energy drinks or caffeine-containing beverages the night before.

The procedure is that each session is done with a different preload on different days. For the first session, they received interleaved drinks (nearly 40 ml of each high-fat, low-fat, tasteless drink, and 30 ml of rinsing water) while scanning inside the MRI, and after scans, they were directed into the MR simulator. For the other three sessions, each day participants go inside the scanner and a baseline scan is done, then they have 355 ml of one of the preload drinks (water, low fat, high fat), which is randomly selected for that day, followed by after-consumption scans, and then outside the scanner they are directed to the MR simulator to perform distraction tasks. Experiment days do not have to be consecutive. In consumption sessions, participants' ingestive neural responses to drinks are collected, while in ER sessions, their instant neural responses to drinks are collected inside the scanner. For the ER preload, drinks are delivered via gustometer system pumps to the mouths of participants, and for the consumption preload, the experimenter takes the glass of drink inside the MR room, and participants receive it via straw in a supine position inside the scanner. After getting a drink, in the consumption sessions, they stay inside the scanner for 20 minutes (5 minutes for rating internal states and 15 minutes for BOLD scans). For the ER session, participants are inside the scanner for 30 minutes; there are two BOLD scans, each with almost 12 minutes in which they receive drinks along with it, and there are also other short scans in between the two BOLD scans. Out of the scanner, they do another internal state rating for 5 minutes and then go inside the MR simulator. For distraction and flavor perception tasks, and to have better control over participants' behavior, the gustometer system is used to deliver drinks to the mouths of participants inside the MR simulator. Figs 4.2 and 4.3 indicate the timelines for ER and consumption days in sequence.

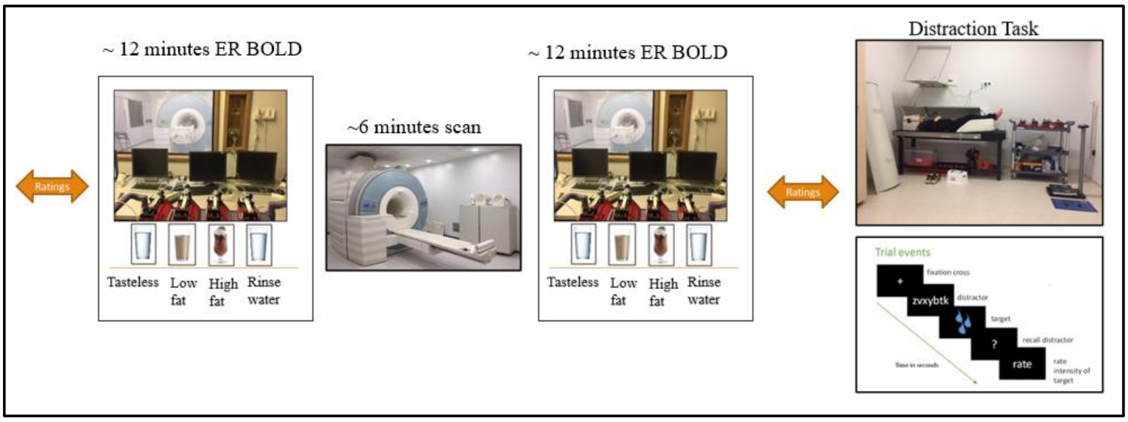


Figure 4.2: Timeline for an interleaved scan and distraction task

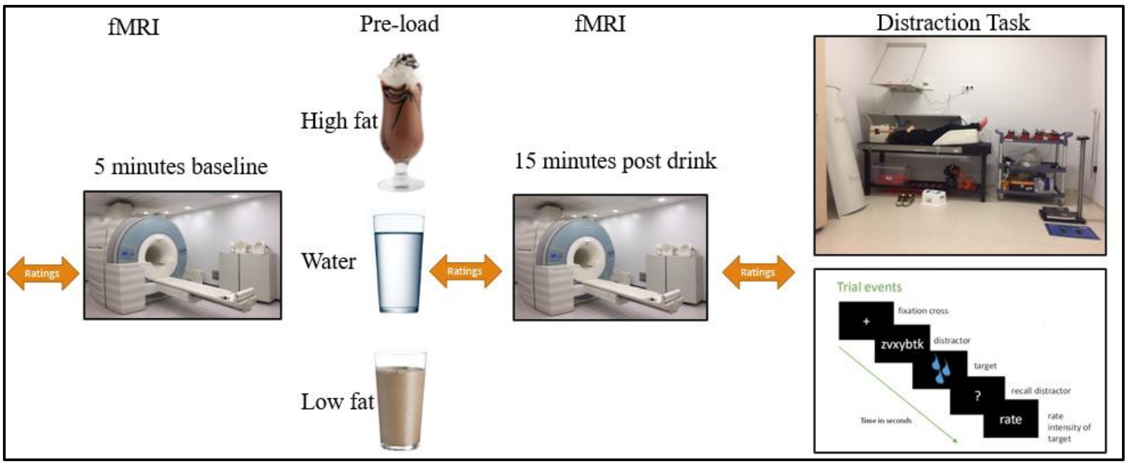


Figure 4.3: Timeline for consumption scans followed by distraction tasks, one of the preloads is used every day in a random order.

The procedure for locating the participant in the MR simulator and details about the procedure are described on pages (18-19) and in Figs (2.4, 2.5, 2.6). In brief, participants lie inside the simulator, and the position of the simulator head coil is adjusted so that they can see the screen above the bore appropriately. The mouthpiece is also set in the mouth of the participant and tested before the main task. Each experiment takes nearly 25 minutes and consists of two distraction tasks, each with 16 trials and a 3-minute break in between. Each distraction task has four different combinations of drinks and cognitive load, that will be repeated four times. Each trial begins with a 0.5-second fixation-cross presentation and continues with a 2 second target string and 2 second blank page display. Then participants get one of the drinks via the mouthpiece (1 ml in 4s). After that, the swallow command is displayed for 1 second, and then they are asked to choose the string they memorized among three options shown on the screen. Finally, they use VAS scales to rate the fat and intensity of the drink they received. The VAS scales are horizontal, continuous lines with 101 points labeled from “no sensation” to “strongest imaginable”. After rating, 1 ml of water is supplied to rinse in 3 seconds. And between trials, there is an 11-second break.

4.2.5. Data analysis

Trials with a RT greater than 25 seconds were excluded from the analysis, as was done in the previous study. The study has a within-subject design, and all participants take part in all four sessions. For the data analysis, we used five ANOVAs per dependent variable (response time, proportion of correct answers in the memory task, flavor intensity, and flavor fattiness). First, we used a 2x2x4 repeated measures ANOVA, with independent variables fat content (low fat vs. high fat), cognitive load (low load vs. high load), and preload (“interleaved” vs. water vs. low-fat vs. high-fat). Then, for each of the preloads, we used 2x2 repeated measures ANOVAs, with independent variables fat content (low fat vs. high fat) and cognitive load (low load vs. high load). If we observed a significant interaction between fat content and cognitive load, we conducted post-hoc paired-comparison t-tests to examine the interaction between fat content and cognitive load. We specifically inspected the comparison of high fat-low load vs high fat-high load to assess whether the effects in Chapter 2 replicated, for which we report uncorrected p-values. Version 0.16.3 of JASP software was used to produce summary statistics, tests, and plots.

4.3. RESULTS

4.3.1. Influence of preload on working memory task outcomes: response time and accuracy

In Table 4.1 and Figs 4.4 and 4.5, we show summary statistics for the working memory outcomes (response time and accuracy) for each factorial combination of preload, cognitive load, and fat content. To assess the effect of satiety on distraction, we looked at how preload affected response time and accuracy in working memory tasks. Response times are numerically longest for the interleaved preload, followed by the water preload, the high fat preload, and lastly the low-fat preload (Table 1 in Appendix B). The proportion of correct answers (accuracy) is numerically greatest for water preload, followed by high fat preload, then low fat preload, and last interleaved preload. There is a significant effect of preload on both response times and the proportion of correct answers (for statistics of the factorial ANOVAs, see Table 4.1). Inspection of post-hoc paired t-tests showed that the effect on response times is primarily driven by differences between the interleaved preload versus high-fat and low-fat preloads and marginally by differences between the water preload versus the low-fat preloads (Table 2 in Appendix B). For the proportion of correct answers, it is less clear which difference between preloads drives the effect, but post-hoc paired t-tests show marginal differences between interleaved vs. water preloads and water versus low-fat preloads (Table 2 in Appendix B).

Response time and accuracy are significantly influenced by cognitive load and fat content as well. As intended, with a higher cognitive load, we observed longer response times and a lower proportion of correct responses. Unexpectedly, the fat content of the stimulus in the flavor perception task also influenced response times and proportion correct, such that when the fat content of the stimulus was low, participants produced more accurate and faster answers than for the high-fat stimulus.

For accuracy, we observed an interaction between fat content and cognitive load. Inspection of post-hoc paired t-tests showed that this interaction effect is driven by a difference between low and high cognitive load in the high fat stimuli ($T(14) = 4.711$, $p = <.001$), which is much smaller between the low and high cognitive load in the low fat stimuli ($T(14) = 2.216$, $p = 0.221$). None of the other interactions: fat content*preload; cognitive-load*preload; cognitive-load*fat content*preload effect on accuracy or response time.

Summarizing, as we intended, a high cognitive load was more difficult than a low cognitive load, as evidenced by slower response times and more incorrect answers. Overall, we also observed effects of preload on the outcome measures of the working memory task. Generally, the interleaved and water conditions differed from the other two preloads. The interleaved preload was always on the first test day, so longer response times and lower accuracy relative to the other preloads may reflect improvements from learning. However, the order of the other preloads was randomized and here the order effect presumably does not contribute to differences in performance. After a water preload, the working memory task tended to be performed relatively slowly but also with relatively few errors compared to the other preloads. Unexpectedly, we observed that a flavor stimulus with a higher fat content was associated with slower responses and more errors relative to the low-fat content flavor stimulus.

We next turned to the factorial ANOVAs with cognitive load and fat content factors for each preload separately, to confirm more explicitly under which preloads we replicated our previous observations of interactions between cognitive load and fat content of the flavor stimuli in the flavor perception task.

Table 4.1. Statistics for working memory tasks. Significant results are presented in bold.

Dependent variable	**Independent variable (df)**	**F**	**p**	**η^2**
Response time	**Preload**	**7.306**	**< .001**	**7.179**
	Fat content	**19.765**	**< .001**	**0.024**
	Cognitive load	**74.020**	**< .001**	**0.206**
	Preload* Fat content	2.034	0.124	0.009
	Preload * Cognitive load	1.872	0.149	0.009
	Fat content * Cognitive load	0.497	0.492	2.399e-4
	Preload * Fat content * Cognitive load	0.240	0.868	7.345e-4
Proportion correct	**Preload**	**3.300**	**0.029**	**0.022**
	Fat content	**11.561**	**0.004**	**0.047**
	Cognitive load	**16.462**	**0.001**	**0.203**
	Preload* Fat content	1.291	0.290	0.007
	Preload * Cognitive load	0.972	0.415	0.006
	Fat content * Cognitive load	**5.741**	**0.031**	**0.026**
	Preload * Fat content * Cognitive load	0.420	0.740	0.004

Working memory outcomes for each of the preloads: First, to assess whether our observations in Chapter 2 are similar in this subset of 15 participants, we examined the effect of fat content and cognitive load in the "interleaved" preload. For the **interleaved preload**, there is a main effect of cognitive load on accuracy (F (1,14) = 18.056, p< .001, η^2= 0.325), and response time (F (1,14) = 34.221, p< .001, η^2= 0.552). There is a marginal effect of fat content (F (1,14) = 4.054, p = 0.064, η^2= 0.031) on response times, but no effect on accuracy. We observed no interaction effect of fat content and cognitive load on accuracy or response time

When the preload is **water** there is a significant effect of fat content (F (1,14) = 9.494, p = 0.008, η^2= 0.066), cognitive load (F (1,14) = 9.202, p = 0.009, η^2= 0.230) and their interaction (F (1,14) = 4.884, p = 0.044, η^2= 0.066) on the accuracy. Performing a Post-hoc paired t-test demonstrated that this interaction effect is driven by a difference in cognitive load in high-fat stimuli (T(14) =3.376, p=0.005). In addition, there is a significant effect of fat content (F (1,14) = 15.214, p = 0.002, η^2= 0.139), cognitive load (F (1,14) = 28.149, p = < .001, η^2= 0.407) but not their interaction, on the response time.

When the preload is **low-fat,** there is a main effect of fat content (F (1,14) = 10.141, p = 0.007, η^2= 0.104), and a main effect of cognitive load (F (1,14) = 5.544, p = 0.034, η^2= 0.133) on accuracy, their interaction on accuracy has a marginally significant effect (F (1,14) = 3.524, p = 0.081, η^2= 0.057). Post-hoc paired t-test showed that the effect is steered by the difference in cognitive load where fat content is high (T (14) = 2.626, p=0.020). Similarly, there is a main effect of fat content (F (1,14) = 10.773, p = 0.005, η^2= 0.072) and cognitive load (F (1,14) = 33.697, p< .001, η^2= 0.540) but not their interactions on response time.

When the preload is **high-fat** there is a main effect of fat content (F (1,14) = 5.503, p = 0.034, η^2= 0.057) and cognitive load (F (1,14) = 16.569, p = 0.001, η^2= 0.270) on accuracy, with no effect of interaction. Besides, there is a main effect of cognitive load (F (1,14) = 19.566, p< .001, η^2= 0.309) but no main effect of fat-content and their interaction on response time. Results for the impact of preload on the proportion of correct answers and response time are shown in Figs 4.4 and 4.5 below.

Summarizing, when evaluating the effect of cognitive load and fat content in each of the preloads separately, we observed the expected effects of cognitive load in each of the preloads, such that the high cognitive load was always slower and less accurate than the low cognitive load. The unexpected effect of the high-fat flavor stimuli leading to slower and less accurate working memory performance than the low-fat flavor stimuli was observed in some of the preloads, with less pronounced effects in the interleaved and high-fat preloads. Additionally, the interaction of fat content and cognitive load on accuracy was only observed for the water condition and only marginally so for the low-fat condition.

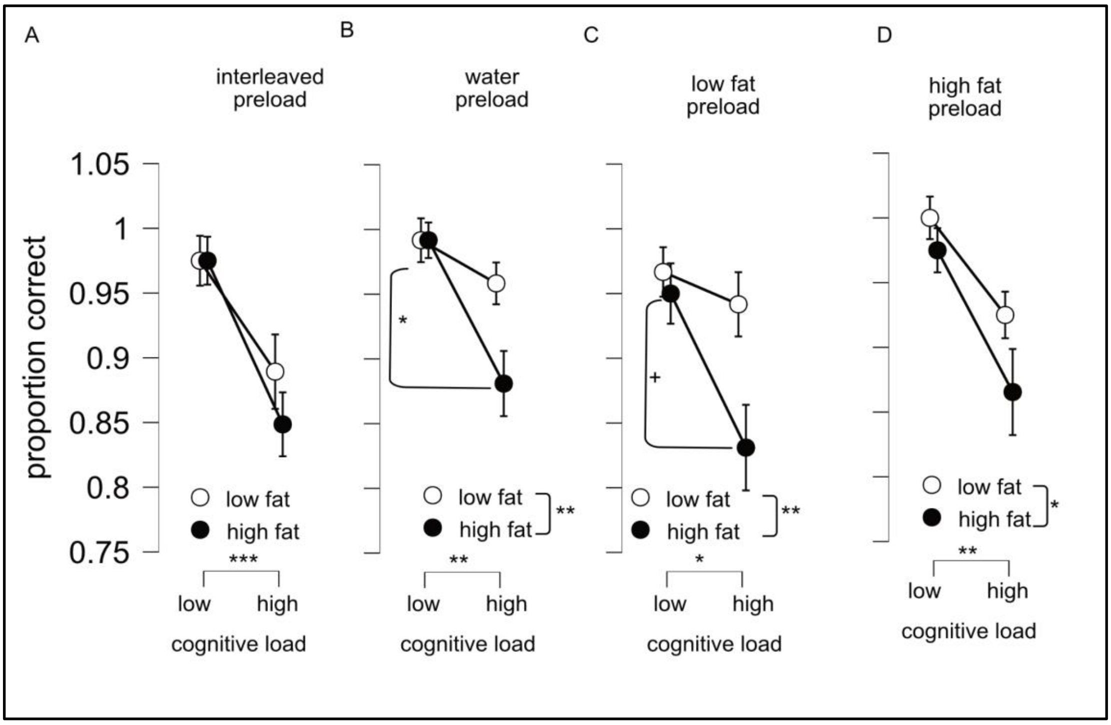


Figure 4.4: Impact of preload type on the proportion of correct answers. The graph shows averages ± standard error of the mean (SEM) across participants with respect to each cognitive load (on the x-axis). The different fat contents of the drinks are indicated with symbols, open circles - low fat content, filled circles - high fat content. The figure depicts the proportion of correct (0-1) for A) interleaved preload, B) water preload, C) low fat preload, and D) high fat preload. Graphs also show the main effects of fat contents (low vs. high, indicated next to the legends) and cognitive loads (low vs. high, indicated right above the x-axis). Significant effects are indicated with asterisks (* $p < .05$, ** $p < .01$, *** $p < .001$, + $0.05 < p < 0.1$).

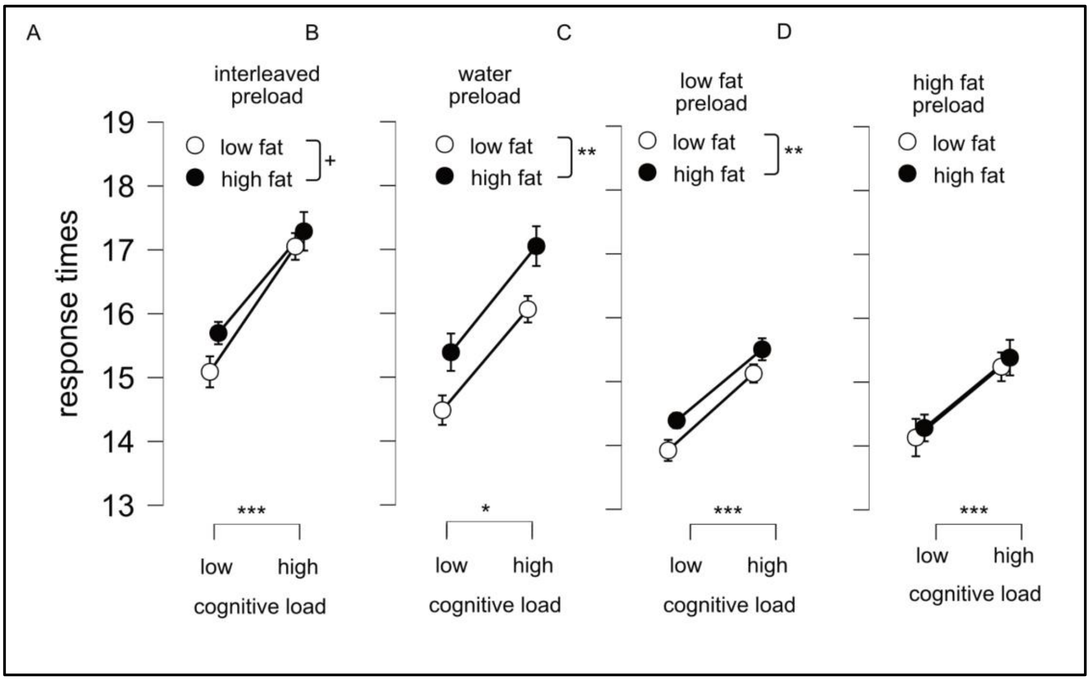


Figure 4.5: Impact of preload type on response time. The graph shows averages ± standard error of the mean (SEM) across participants with respect to each cognitive load (on the x-axis). The different fat contents of the drinks are indicated with symbols, open circles - low fat content, filled circles - high fat content. The figure depicts the response times in seconds for A) interleaved preload, B) water preload, C) low fat preload, and D) high fat preload. Graphs also show the main effects of fat contents (low vs. high indicated above the graphs) and cognitive loads (low vs. high indicated right above the x-axis). Significant effects are indicated with asterisks (* $p < .05$, ** $p < .01$, *** $p < .001$, + $0.05 < p < 0.1$).

4.3.2. Influence of preload on flavor perception: fat and intensity perception

Table 4.2 indicates the statistical summary for the flavor perception task (fat perception and intensity perception) regarding each factorial combination of preload, cognitive load, and fat content. To evaluate the effect of satiety on flavor perception, we investigated the role of preload on fat and intensity perception. There was no main effect of preload on fat and intensity perception of the flavors. There is a main effect of fat content on fat perception and a marginal effect of fat content on intensity perception. Cognitive load has no main effect on fat and intensity perception. Contrary to our expectations, we could not find the interaction effect of preload* cognitive load on fat perception and intensity perception. We also didn't observe any other significant interaction effects.

Summarizing, as intended, high-fat drinks are rated as fattier and marginally more intense than low-fat drinks by participants. We did not observe a difference in sensitization between different preloads. In addition, cognitive load had no effect on how participants rated the fat and intensity of the drinks, and there was no interaction between fat content and cognitive load. We next turned to the factorial ANOVAs with cognitive load and fat content factors for each preload separately, to more explicitly confirm under which preloads we replicated our previous observations of interactions between cognitive load and fat content.

Table 4.2. Statistics for flavor perception tasks. Significant results are presented in bold.

Dependent variable	**Independent variable (df)**	**F**	**p**	**η^2**
Fat perception	Preload	1.765	0.168	0.075
	Fat content	**6.159**	**0.026**	**0.064**
	Cognitive load	1.025	0.328	0.001
	Preload * Fat content	0.028	0.994	1.096e-4
	Preload * Cognitive load	0.416	0.742	8.081e-4
	Fat content * Cognitive load	1.297	0.274	3.684e-4
	Preload * Fat content * Cognitive load	0.919	0.440	0.001
Intensity perception	Preload	1.055	0.378	0.053
	Fat content	3.731	0.074	0.026
	Cognitive load	1.056	0.322	0.002
	Preload* Fat content	0.774	0.515	0.002
	Preload * Cognitive load	0.919	0.441	0.001
	Fat content * Cognitive load	2.231	0.157	6.397e-4
	Preload * Fat content * Cognitive load	0.319	0.812	5.384e-4

Flavor perception outcomes for each of the preloads: Considering the **interleaved condition**, there is a main effect of fat content (F (1,14) = 5.971, p = 0.028, η^2= 0.241), no main effect of cognitive load (F (1,14) = 1.207, p = 0.291, η^2= 0.010) , and an interaction effect of cognitive load * fat content (F (1,14) = 5.158, p = 0.039, η^2= 0.019) on fat perception. When we inspect post-hoc paired comparison t-tests between low and high cognitive load within drink, we observed a marginal effect for the high-fat drinks (T(14)= 1.861, p = 0.084 uncorrected), but not for the low-fat drinks (T(14) = 0.450, p = 0.660 uncorrected). This is in line with the effects reported in Chapter 2. There is a marginal effect of fat content on intensity perception (F (1,14) = 4.504, p = 0.052, η^2= 0.118), no main effect of cognitive load, and no interaction between fat content and cognitive load on intensity perception.

When the preload is **water**, there is a main effect of fat content on both fat (F (1,14) = 5.643, p = 0.032, η^2= 0.248) and intensity (F (1,14) = 4.951, p = 0.043, η^2= 0.190) perceptions. Other effects were not significant.

When the preload is **low-fat**, there is a significant effect of fat content (F (1,14) = 6.126, p = 0.027, η^2= 0.191) on fat perception but not on intensity. The other effects were not significant.

For **high-fa**t preload, there is no main effect of fat content and cognitive load on both fat and intensity perception. Other effects were not significant. Results for the impact of preload on fat and intensity perceptions are shown in Figs 4.6 and 4.7 below.

Summarizing, generally, the pattern of result for fat and intensity perception is similar across preloads. Surprisingly, generally, distraction doesn’t suppress fat perception, except when the stimulus is a high-fat flavor, and then only after the interleaved preload.

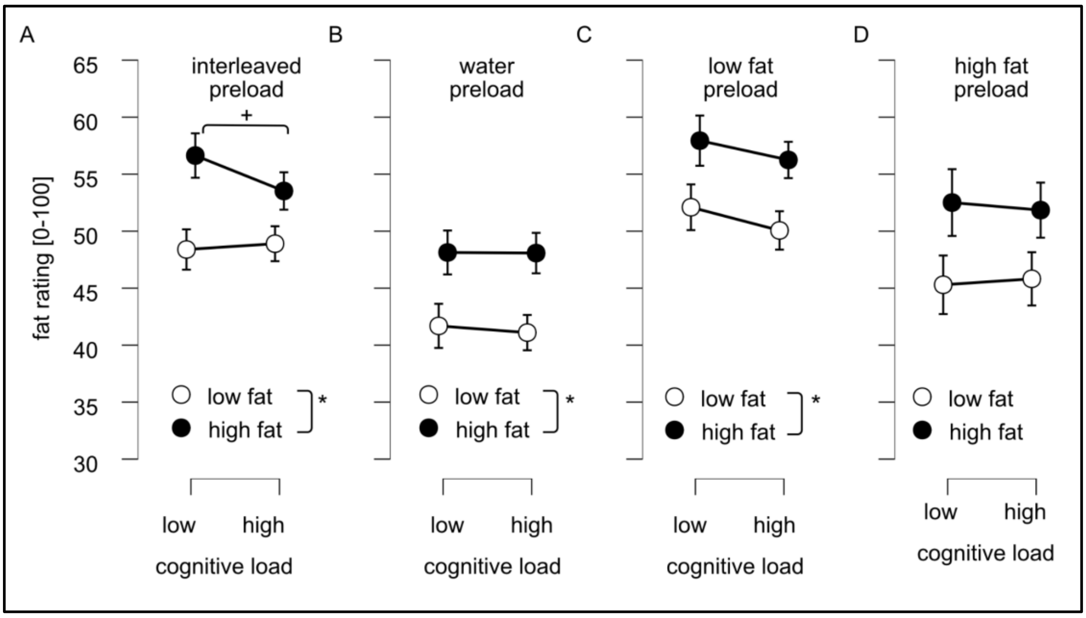


Figure 4.6: Impact of preload type on fat perception. The graph shows averages ± standard error of the mean (SEM) across participants with respect to each cognitive load (on the x-axis). The different fat contents of the drinks are indicated with symbols, open circles - low fat content, filled circles - high fat content. The figure depicts the fat ratings (0-100) for A) interleaved preload, B) water preload, C) low fat preload, and D) high fat preload. Graphs also show the effects of fat contents (low vs. high) and cognitive loads (low vs. high). Significant effects are indicated with asterisks (* $p < .05$, + $0.05 < p < 0.1$).

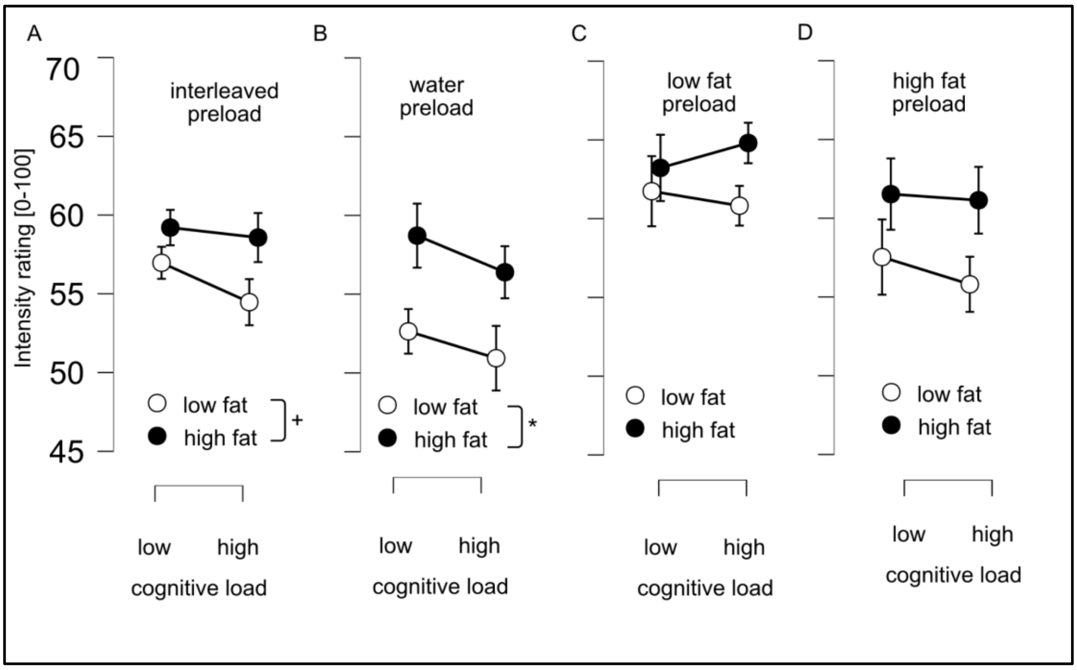


Figure 4.7: Impact of preload type on intensity perception. The graph shows averages ± standard error of the mean (SEM) across participants with respect to each cognitive load (on the x-axis). The different fat contents of the drinks are indicated with symbols, open circles - low fat content, filled circles - high fat content. The figure depicts the intensity ratings (0–100) for A) interleaved preload, B) water preload, C) low fat preload, and D) high fat preload. Graphs also show the effects of fat contents (low vs. high) and cognitive loads (low vs. high). Significant effects are indicated with asterisks (* $p < .05$, + $0.05 < p < 0.1$).

4.4. DISCUSSION

In this study, we tested whether a concurrent working memory task would affect flavor perception and whether this is modulated by satiety. We manipulated satiety by preceding the concurrent working memory and flavor perception tasks with a preload; 150 ml of interleaved stimuli vs. 355 ml of water vs. 355 ml of low-fat chocolate drink vs. 355 ml of high-fat chocolate drink. We did not observe an effect of preload on fat or intensity perception, nor did we observe an effect of preload on fat or intensity suppression by distraction. However, we did observe clear effects of preload on response time and accuracy in working memory tasks. In addition, the fat content of the stimuli in the flavor perception task and the cognitive load also interacted to influence the proportion of correct answers in the working memory task. Overall, satiety as manipulated by preload seemed to have a more pronounced effect on the working memory task than on the flavor perception task.

Working memory task observations in context

First, we note that, as we intended, the high cognitive load task was consistently more difficult than the low cognitive load task, regardless of the preload and fat content of the stimuli in the flavor perception task.

Second, and unexpectedly, the fat content of the preloads affected the performance on the working memory task in terms of response time and accuracy, such that after water and low-fat preloads, their overall performance was different from when the preloads contained high fat. In more detail, we observed that participants had a relatively higher proportion of correct answers but a slower response when the preload was water. After a high-fat preload, participants were less accurate than after a water preload but faster, and more accurate than after a low-fat preload but slower. The interleaved preload condition was the slowest and least accurate of the conditions tested; this could be explained by the fact that it was the first day of the experiment for the participants, and performance improved on the subsequent days. However, the order of the other preloads was randomized, and here the order effect presumably does not contribute to differences in performance. We speculate that flexible trade-off patterns between response time and the proportion of correct answers are responsible for these complex results. In the working memory task, we didn't have a maximum delay for participants to respond (i.e., the response options were shown on screen until an answer was given). It is possible that participants favored giving correct responses at the cost of having longer response times more after low-fat and water preloads and that they favored faster but less accurate responses after the interleaved and high-fat preloads. Future studies may use a maximum allowed response time of, for example, 15 seconds to observe if encouraging participants to give faster responses will lead to different observations regarding the effect of preload on working memory performance.

Third, we observed an unexpected effect of the fat content of the stimuli in the flavor perception task on the working memory task. Specifically, the high-fat flavor stimuli led to slower and less accurate working memory performance than the low-fat flavor stimuli after water and low-fat preloads, with less pronounced effects after the interleaved and high-fat preloads.

Lastly, we were specifically interested in the interaction of fat content and cognitive load on performance, since in our previous report (Chapter 2) we observed that this interaction affected fat perception. Here, the interaction of fat content and cognitive load on accuracy was only observed for the water condition and only marginally so for the low-fat condition.

These last two observations both suggest that after a preload that contains no high-fat drinks, i.e., the water and low-fat preloads, performance on the working memory task is different. We will go into this aspect in greater detail in the paragraph "working memory modulations" below.

Flavor perception task observations in context

Despite our expectations, we did not observe an interaction between preload and cognitive load on fat and intensity perception. Previous studies showed that when participants were hungry, their perception of sweet and salt increased in comparison to when they were full (Zverev, 2004; Hanci and Altun, 2016). We hypothesized that when hungry, for example after a water preload, the distraction task may be less effective since the perception of stimuli might be heightened. That our expectations were not carried out may be related to inconsistent sensory enhancement of fat taste by satiety (similar to what has been reported for bitter foods). As intended, there was a main effect of fat content on fat perception, and high-fat drinks were rated as fattier and sometimes more intense. After the water and low-fat preloads, the effect of fat content on perception was most pronounced. After a high-fat preload, participants appeared less sensitive to differences in fat perception. This is in line with the study of Costanzo et al. (2018), where they found that habitual high-fat eating decreases the responsiveness to fat, potentially due to interference with the communication pathways between the gut and brain. Intensity ratings were not always higher for the more fatty stimulus. This may be because the intensity concept is more vague than fat perception, and participants might be more focused on sweet, bitter, chocolate, or coconut perception. We observed no main effect of cognitive load on fat and intensity perception, and there is also no interaction effect of fat content or preload on intensity or fat ratings. These findings were unexpected. There can be various explanations. First, the sample size here is relatively small compared to our previous study, and with the known large variation in fat perception across participants, the design here may not have been sensitive enough for small effect sizes. Second, flavor perception may be relatively more robust to distraction compared to the findings using unisensory chemosensory stimuli. Future studies may focus on directly comparing the effects of satiety on distraction from unisensory chemosensory stimuli vs. complete chemosensory stimuli.

Working memory modulations

In this study and many similar studies, distraction is operationalized as a relatively difficult task compared to an easier baseline task. Some studies explicitly evaluate whether this manipulation was successful by comparing response times and accuracy

(Duif et al., 2020; Schadll et al., 2021; Van Dillen et al., 2018; van Meer et al., 2022a), but others only make the assumption that they are different in difficulty and don’t report working memory task-related outcomes (van der Wal & van Dillen, 2013; Liang et al., 2018). Sometimes in those analyses, the authors collapse across the various chemosensory stimulus identities, and thus the influence of the chemosensory task on the working memory task is not evaluated (Hoffman et al., 2017; Schadll et al., 2021). Among the studies that explicitly evaluate the difficulty of manipulation, we know of three studies that also evaluated the effect of the chemosensory stimulus on working memory. The first is Van Dillen et al. (2018), who observed an interaction between stimulus type (high-calorie vs. low-calorie) and time (first vs. second block), such that accuracy for the digit-span task decreased for high-calorie food images in the later block. Second, van Meer et al. (2022a) showed that sweet concentration did not influence accuracy rates on a digit span task. Last, Duif et al. (2020) also observed no effect of sweet concentration on the performance of the visual detection task. In chapter 2, we noted a trend toward longer response times in the working memory task when tasting a higher fat stimulus. In the current report, we observed robust effects of the fat content of flavor stimuli on the performance in the distraction task, such that when the fat content of the stimulus was low, participants produced more accurate and faster answers in the working memory task than for the high-fat stimulus. This effect was most pronounced after the water and the low-fat preloads. This may be explained by a bottom-up effect, such that a salient stimulus, the high-fat stimulus in this case, increases response times and reduces accuracy, and it does so mostly after the participant has not yet consumed a high-fat drink in the preceding preload. This suggests that satiety influences performance on the two concurrent tasks, but in a somewhat unexpected fashion. Specifically, on the one hand, satiety leaves the effects of distraction on the flavor perception task relatively unaffected. On the other hand, satiety influences performance on the distraction task itself. We speculate that this shows that working memory and flavor tasks are not simply reciprocal parts of a constant total attentional resource, but that they are (at least partially) independent processes. This is an important methodological consideration for future studies of distraction in chemosensory perception: the distraction task may be more or less distracting depending on the stimulus identity in the other task and the state of the participant. In other words, depending on the circumstances, the flavor perception task may provide a distraction from the working memory task more so than the working memory task distracts from the flavor perception task. Why did not all previous studies observe an effect of chemosensory stimuli on working memory (Van Meer et al., 2022a; Duif et al., 2020), while another study (Van Dillen et al., 2018) did observe effects of chemosensory stimuli on working memory performance? Van Meer et al. (2022a) and Duif et al. (2020) both used sweet concentration differences, while our study used differences in fat content. Van Dillen et al used high vs. low calorie food pictures, where fat content and sugar content may have differed. Perhaps fat signals have a stronger bottom-up effect than sugar signals in influencing dual-task performance.

Limitations

First, our sample size was relatively small, and these results should be confirmed with a larger sample size. Second, because we used vegan material for the fat content in the flavor perception task and the amounts were small, the perceptual differences between the low-fat and high-fat drinks in the fat and intensity perception tasks were small. For future studies, we also recommend assessing more behavioral state factors. For example, since circadian state also affects satiety, doing tests at the same time of day when possible is best, and additionally, mood and sleep deprivation should be measured and/or controlled (Shanahan and Kahnt, 2022).

Summarizing, this study evaluated how concurrent working memory and flavor perception tasks can be impacted by satiety. We observed that response time and the proportion of correct answers in the working memory task are affected by preload. Unexpectedly, cognitive load and fat content interacted to affect the performance of participants in a working memory task, such that participants were slower and more prone to mistakes in the working memory task if the flavor stimulus was high-fat, but only if they didn't have a preload containing high-fat stimuli. We conclude that fat suppression by distraction is not robust. We speculate that the strength of distraction may depend in part on the state of the participant, such that when high-fat food has already been consumed, the saliency of the high-fat stimulus is decreased, thereby reducing interference from the flavor perception task on the performance of the working memory task.

CHAPTER 5

GENERAL DISCUSSION

Briefly, chapter 2 of the current study evaluates the role of distraction on flavor perception by manipulating the cognitive load of a working memory task that is simultaneously performed by flavor perception tasks in which participants rate the intensity and fat of low-fat and high-fat drinks. Performance on working memory tasks is assessed by participants' response time and accuracy. Besides, chapter 3 investigates the neural brain responses to drinks with different fat contents (tasteless, low-fat, and high-fat) and their correlation with perceived fat suppression caused by distraction. Chapter 4 explores the role of satiety as another contributor to overeating by manipulating the amount of fat on different preloads (water, low-fat, high-fat, interleaved) in advance of a dual paradigm working memory task and a flavor perception task. Each of the preloads is examined on a different experimental day.

5.1. Concurrent working memory and flavor perception tasks

I developed a working memory task that can be performed concurrently with a flavor perception task to evaluate the interplay between them. Prior to this study, the results of the pilot study with 4 different conditions of 1, 3, 5, and 7 consonants for working memory tasks were compared to determine the two main cognitive loads (high and low). The experiments were conducted among 30 participants who did only working memory tasks, and no drink was delivered. There were four blocks in random order, each with 12 trials. Based on the results, the 3 and 7 consonant conditions were selected for low and high cognitive loads, respectively.

Working memory tasks and flavor perception tasks are performed concurrently inside the MR simulator. Participants lie supine to have better control over their behavior. First, they read the instructions for both WM tasks and flavor ratings. Then, they see a fixation cross followed by a target string with low or high cognitive loads (3 or 7 spans of consonants). They are asked to memorize the string that appears on the screen. Next, they get one of the drinks (low fat or high fat). Then they are instructed to swallow the drink, and after that, they see three options on the screen and are asked to click on the string they memorized in advance. Lastly, we display the VAS scales for rating the fat and intensity of the drinks they received. They get water for rinsing after completing each rating, and there is a pause between trials. Overall, there are 32 trials, which are presented in two blocks (each with 16 trials), and between two blocks there is a 3-minute break.

Based on previous work, we expected to observe fat and intensity suppression under high cognitive load relative to low cognitive load. However, we only found the effect on fat perception when the flavor stimuli were high in fat. Meanwhile, it was also assumed to see differences in neural responses for drinks with fat content versus tasteless drinks in taste and somatosensory areas, such as the brainstem, thalamus, insula, overlying operculum, hypothalamus, amygdala, and orbitofrontal cortex, and differences in activation for different fat contents. Although we found activations of the insula, overlying operculum, and thalamus, we also found activations in the precentral gyrus and cerebellum areas and no activations of the hypothalamus, brainstem, or orbitofrontal cortex. And we could not find differences between high-fat and low-fat neural responses. Regarding the correlation between neural responses and flavor suppression caused by distraction, we anticipated activation in areas such as the amygdala, dorsolateral, or ventral prefrontal cortex. We found activation in the amygdala and in the fusiform gyrus as well. Lastly, we expected to see the role of satiety with manipulation of preload on the performance across both concurrent WM and flavor perception tasks, to some extent, in the hungry case rather than the full case, we predicted to experience more flavor perception, however, unexpectedly, we found no effect of satiety on flavor perception, but we found the impact on the performance of participants in WM tasks, and prominently, we noticed the bilateral interferences between flavor perception and WM tasks.

5.2. Distraction suppresses high fat flavor perception

The second chapter investigates the role of distraction with different cognitive loads (low and high) in flavor intensity perception (fat and intensity ratings) with two different fat content stimuli (low and high). Performance on the working memory task was evaluated by response time and the proportion of correct answers. Intensity perception was investigated by VAS scale ratings of fat and intensity of the drinks. As expected, we observed an effect of cognitive load on response time and accuracy. High cognitive load (a more difficult condition) causes less accurate and slower responses than low cognitive load. Fat content of flavor perception did not affect performance, but there was a trend for longer responses with high fat, which could be an indication of interference from high-fat flavor stimuli on working memory performance. Considering flavor perception, cognitive load has no effect on intensity ratings, with a trend showing that under high cognitive load intensity ratings were lower. Remarkably, cognitive load had an effect on fat ratings; under high cognitive load, fat ratings decreased. The difference between fat and intensity rating results might be because intensity is a more general concept, reflecting the perception of sugar, chocolate, and coconut, which all remained constant across the two drinks. Fat content affects both intensity and fat ratings significantly, and ratings for high fat content were higher. There was also an interaction between fat content and cognitive load for fat ratings, and that was driven by cognitive load for high-fat drinks in such a manner that under high cognitive load versus low cognitive load, participants perceived high fat as less intense. This could highlight the role of distraction in decreasing the perception of unhealthy food and compensating for more food consumption. These findings were consistent with the results of Van Meer et al. (2022a), who showed that higher concentrations of glucose were perceived as less sweet under distraction. van Dillen & van Steenbergen (2018) also confirmed a more powerful effect of distraction on food pictures with high caloric content. However, Hoffman et al. (2017) find a reduction of odor perception only in low-calorie foods and van der Wal et al. (2022a) reported reductions in both low and high taste, although the effect was larger for the higher sweet content. These findings highlight the role of intensity, caloric content, and salience of content on the effectiveness of distraction. Besides, we evaluated the correlation between response time and flavor ratings, and we found that longer response times are connected to lower ratings. Hence, it could be inferred that when participants' attention was switched back to flavor perception earlier, they rated the intensity and fat of drinks higher.

This study stressed that not only does distraction affect flavor perception, but flavor perception also influences performance in a working memory task. And it coined the idea that if attentional resources are competing between working memory and flavor perception tasks, flavor perception could be more involved when stimuli are salient, for instance when people are hungry. In chapter 4, the role of satiety on dual paradigm tasks is evaluated by manipulating fat contents at different preloads. Chapter 3 inspects the neural responses for different fat contents also assesses the possible correlation with fat suppression caused by distraction.

5.3. Instant neural responses to different fat content drinks and their correlation with fat suppression caused by distraction

The third chapter of the study evaluated the neural responses of drinks with different fat contents by using the cutting-edge technologies of fMRI scanning. Main effects of both high-fat and low-fat drinks compared to tasteless drinks are observed in the mid-dorsal insula/frontal operculum, precentral gyrus, thalamus, and cerebellum areas. The neural responses to high and low fat did not differ significantly. Besides, the study investigated correlations between neural responses and fat suppression due to distraction, wherein distractability is defined as the subtraction of fat perception in low cognitive load from high cognitive load (including both high-fat and low-fat drinks). We found robust activation of the fusiform gyrus and amygdala related to fat suppression. With more fat suppression, participants demonstrated less activation in the fusiform gyrus and in the amygdala.

In our study, the activation of the insula along with the activation of the opperculum is in line with the other studies in response to taste stimuli (Huerta et al., 2014; Roll et al., 2011; Veldhuizen et al., 2011). Operculum is also involved in managing cognitive behavior (Higo et al., 2011). Thalamus is also activated by food cues (Huerta et al., 2014) and has a role in relaying olfactory and gustatory signals for further processes (Basso et al., 2005). Activation of the precentral gyrus and cerebellum in high-fat and low-fat drink conditions but not in tasteless drink conditions puts forward the possibility that, as well as motor activities (Banker & Tadi, 2019; Strick et al., 2009), they might be involved in taste perception. This is consistent with the approaches of Huerta et al. (2014) for the precentral gyrus and Low et al. (2021) for the cerebellum. Although these differences might also be due to the differences in viscosity between tasteless and flavored drinks, which cause less involvement of the motor area in the tasteless conditions. In further studies, the effect of drinks' viscosity on the activation of motor areas can be evaluated to confirm that these regions are involved in taste perception.

In line with Eldeghaidy et al. (2012) and Stice et al. (2013), we did not experience different neural responses with low-fat and high-fat stimuli. However, De Araujo et al. (2004) and Eldeghaidy et al. (2011) found differences when using high densities of fat.

More sensitive methods of scanning might be used in the future, or individual differences regarding their sensitivity to fat perception can be used to select more sensitive participants.

The current research found a correlation between perceived fat suppression caused by distraction and neural responses in the fusiform gyrus and amygdala. The fusiform gyrus is known for face and object recognition and categorization (Gauthier et al., 1999; Gauthier et al., 2000; Xu, 2005). There are some studies that find traces of fusiform activation for food image responses (Adamson and Troiani, 2018; Khosla et al., 2022; Van der Laan et al., 2011) as well as the activation of the amygdala with food cues (Veldhuizen et al., 2020), and notably, Adamson and Troiani (2018) also proposed a connectivity network between the amygdala and fusiform for food cues, which is congruent with our findings wherein these two areas are coactivated.

5.4. Effect of satiety on performance in dual task paradigm with flavor perception and working memory

Chapter 4 investigated the possible role of satiety as another contributor to the suppression of flavor perception caused by distraction. On different experimental days, preloads of interleaved sips of water, low-fat, and high-fat and preloads of different fat contents of water, low-fat, and high-fat were applied before doing simultaneous flavor perception and working memory tasks. A robust influence of preload on the proportion of correct answers and response times of participants in working memory tasks is observed, while there is no influence of preload on fat and intensity perception or on the suppression of flavor caused by distraction. Participants presented the worst performance on the interleaved condition. That might be because the interleaved preload is always performed on the first session, while the others were randomized, and participants might benefit from a learning effect on the other days. Noteworthy, participants were relatively slow but more accurate after drinking water. There seems to be a trade-off between response time and accuracy of participants after preloads. This trade-off might be triggered because we did not define a maximum delay for their answers; participants seem to prefer to answer more accurately at the cost of time. Notably, the fat content of stimuli in the flavor perception tasks impacted the working performance of participants in such a way that, with high-fat stimuli in perception tasks, participants were less accurate and slower than low-fat stimuli. This was pronounced more when the preload was water and low-fat and not high-fat. The reason behind this might be because of the salience of high fat in the bottom-up effect. Meanwhile, fat content also affected fat perception, and participants were more sensitive to fat after a low-fat and water preload rather than a high-fat preload. These findings can be supported by Costanzo et al. (2018), who found that regular high-fat intake reduces fat perception.

In contrast with our expectations, there was no interaction between preload and cognitive load on flavor perception. However, Zverev (2004) reported lower taste detection thresholds of participants for sweet and salt when they were hungry than sated and no significant difference for bitter stimuli. For odor perception, there was also evidence that hungry participants rated food more intensely than in the sated condition (Cabanac, 1971; Hanci and Altun, 2016; Nie et al., 2022). The unexpected result might have occurred because of the inconsistent rise of the fat taste sensation, as also reported in the bitter stimulus above. In essence, we observed a more prominent effect of satiety on the working memory performance of participants in terms of response time and accuracy than the flavor perception task.

5.5. Updated working model

All in all, we ended up with a different mechanism than what we expected. Fig 5.1 below indicates the prominent findings across three chapters. Firstly, we found that not only does working memory affect flavor perception but that the inverse relationship also exists. We conclude that working memory and flavor perception tasks interfere with each other. Hence, the hypothesis of a one-way effect of WM on flavor perception is rejected and adjusted to be bilateral. Subsequently, we evaluated the role of different fat contents in drinks on the neural brain responses, and we found activations of the insular and operculum, cerebellum, thalamus, and precentral gyrus for (high-fat + low-fat)-tasteless drinks. Our findings couldn't support robust differences between low-fat and high-fat activations in the brain. Considering the correlation between neural responses and the fat suppression that is caused by distraction, we found that the activation of the fusiform gyrus and amygdala occurred in such a way that these areas became activated more when fat suppression was less. So, the CNS part is added to the model, wherein we can see the areas activated by fat content versus tasteless stimuli and also the areas that are associated with fat suppression. Lastly, we evaluated the role of satiety by manipulating the fat content of drinks of different preloads on different experimental days and performing concurrent working memory and flavor perception tasks. We found a robust effect of satiety on the performance of participants in working memory tasks in terms of response time and accuracy; however, we couldn't find the impact of satiety on the flavor perception of participants or on the fat suppression caused by distraction. Therefore, the hypothesised model is adjusted in such a way that, despite our expectations, there is no impact of satiety on flavor perception but there is on the WM task.

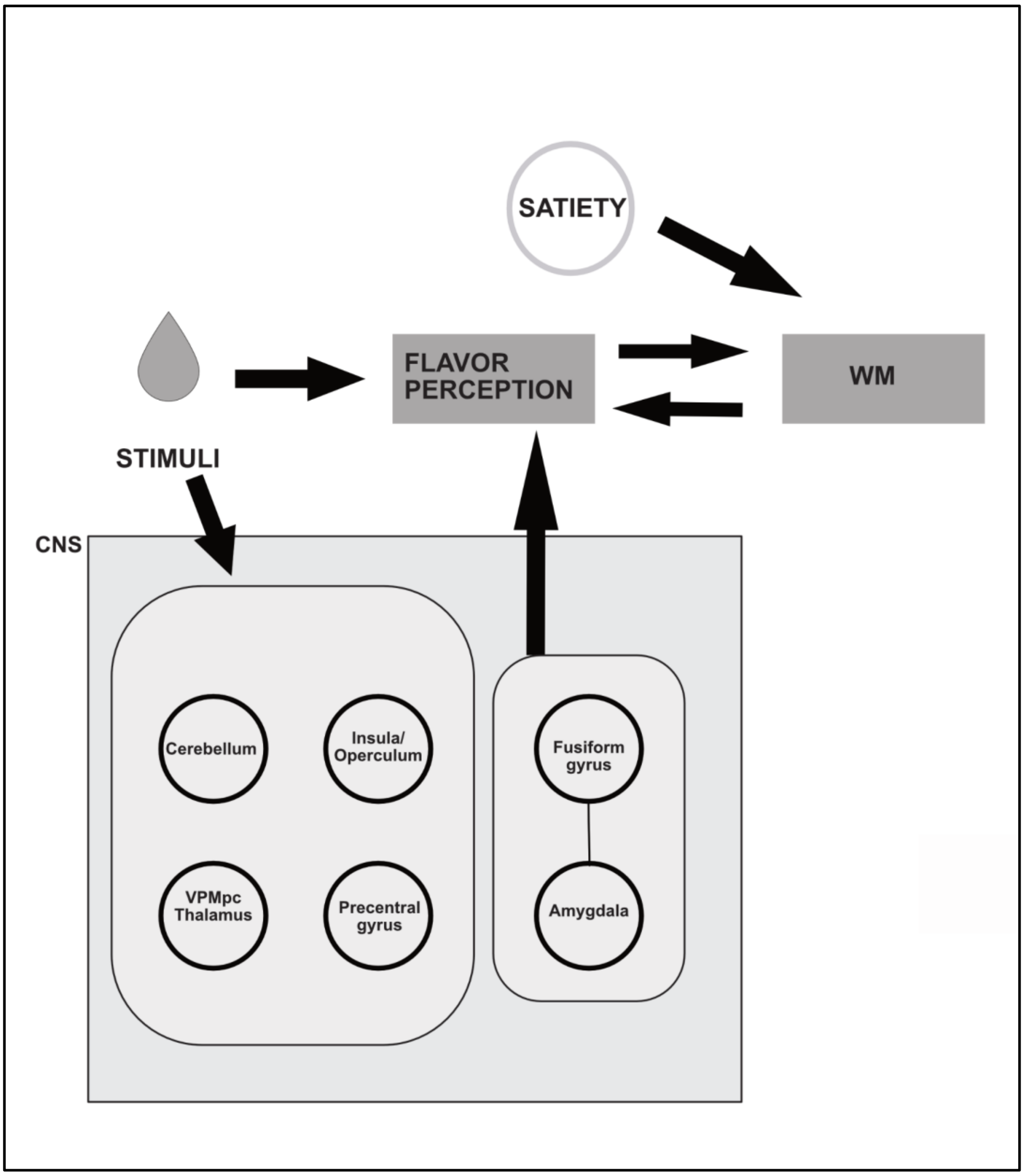


Figure 5.1: General model of bilateral interplay of working memory task and flavor perception, neural responses to different fat contents and its relationship with fat suppression due to distractibility, and also the effect of satiety on the dual task paradigm of flavor perception and working memory.

5.6. Continuing Studies

- In this study, the instant brain responses to interleaved sips of drinks are analysed. We also collected the brain responses of participants for different preloads on different days to see the ingestive responses to the consumption of a larger quantity of different fat content drinks. We are going to analyse the responses and compare them with interleaved results.
- We will collect fMRI brain responses of obese people to see the differences with normal weight subjects.

- We are planning to use VN (Vagus nerve) stimulation in people with obesity to see if we can normalize their neural behavior like what we have seen in lean subjects. This intervention is proposed as a potential alternative to risky bariatric surgery. VN is responsible for carrying signals from gut to brain (Berthoud, 2008).

5.7. Further studies

- Based on our results it seems that lack of response to fat concentration might be because of individual variations in sensitivity to the fat perception. To solve this, in future studies participants who have lower fat detection thresholds (more sensitive) might be selected for performing tasks.
- We found co-activation of the amygdala and fusiform associated with fat suppression, which might be also relate to the reward of food. In the future studies the direct role of attention to food on this network can be evaluated.
- In the WM tasks participants demonstrated accuracy and time trade-off. They preferred to be accurate in favor of speed. This might happen because we did not set a maximum delay time for their answer. The program waits until they click on one of the alternative answers. To solve this problem, we removed trials with response times of more than 25 s. But the response time could be limited, and participant encouraged to respond faster in the computer program in further studies.
- We performed tasks based on participants availability and we asked participants not to eat 3-4 hours before tests. As circadian state also affects satiety, it might be better to perform tests at the same time of day.
- As behavioral and physiological factors impact flavor perception, these factors can be taken under control (for example mood or food deprivation would be under control).

5.8. Limitations

- Using fMRI is expensive.
- Safety policies should be regarded carefully for fMRI experiments.
- Results for lab and real-life conditions might differ.
- Using vegan ingredients for flavor perception task might reduce the effect of fat. We used vegan materials because the dairy recipe made a viscosity that was too high to pass through the tubes easily.

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APPENDICES

APPENDIX A. Supplementary Materials for Chapter 2

Table 1. Descriptive statistics of the four cognitive load conditions in the pilot study

Cognitive load condition	Mean RT (+/- SD)	Mean proportion correct (+/-SD)
1	5452.85 (+/- 1158.34)	98.06 (+/- 4.20)
3	5472.62 (+/- 311.25)	98.33 (+/- 4.04)
5	6052.61 (+/- 659.26)	94.44 (+/- 7.37)
7	7136.01 (+/-1044.18)	86.11 (+/- 16.13)

Table 2. Post-hoc t-test between the four cognitive load conditions in the pilot study

Dependent variable	Cognitive load condition	Vs 1 T, p, 95% CI lower value, upper value.	Vs 3	Vs 5
RT	1	-	-	-
RT	3	-0.11, 1.000, -501.85, 462.31	-	-
RT	5	-3.36, 0.007, -1081.84, -117.686	-3.25, 0.010, -1061.07, -97.91	-
RT	7	-9.43, < .001, -2165.24, -1201.08	-9.32, < .001, -2145.47, -1181.31	-6.07, < .001, -1565.48, -601.32

Bold = p < .05, Bonferroni corrected for 6 comparisons

Table 3. Descriptive statistics of the four combinations of fat content and cognitive load in the main experiment

Cognitive load condition	Fat content	Mean RT (+/- SD)	Mean proportion correct (+/-SD)	Mean intensity rating (+/- SD)	Mean fat rating (+/- SD)
Low	Low fat	15.97 (+/- 2.30)	0.98 (+/- 0.04)	51.18 (+/- 20.67)	47.73 (+/- 20.83)
Low	High fat	16.73 (+/- 2.18)	0.97 (+/- 0.06)	59.36 (+/- 20.09)	54.47 (+/- 21.74)
High	Low fat	18.05 (+/- 2.79)	0.90 (+/- 0.12)	51.03 (+/- 20.03)	46.81 (+/- 21.31)
High	High fat	18.55 (+/- 2.96)	0.88 (+/- 0.11)	55.92 (+/- 19.44)	51.32 (+/- 20.43)

Table 4. Statistical tests for data excluding outliers or incorrect responses

Data excluded	Dependent variable	Effect of cognitive load	Effect of fat content	Interaction cognitive load * fat content
RT > 25 s	RT	< .001	0.026	0.166
RT > 25 s	Proportion correct	< .001	0.454	0.816
RT > 25 s	Intensity rating	0.114	< .001	0.14
RT > 25 s	Fat rating	0.156	< .001	0.115
incorrect	RT	< .001	0.018	0.136

incorrect	Proportion correct	< .001	0.454	0.816
incorrect	Intensity rating	0.218	< .001	0.161
incorrect	Fat rating	0.083	< .001	0.146

APPENDIX B. Supplementary Materials for Chapter 4

Table1. Summary statistics for working memory task outcomes

Dependent variable	Preload	Fat content	Cognitive load	Mean	Standard deviation
Response time	Interleaved	Low fat	Low load	15.089	2.296
		Low fat	High load	17.054	2.203
		High fat	Low load	15.967	1.827
		High fat	High load	17.290	2.286
	Water	Low fat	Low load	14.483	2.195
		Low fat	High load	16.064	2.215
		High fat	Low load	15.390	2.434
		High fat	High load	17.052	2.599
	Low fat	Low fat	Low load	13.923	2.033
		Low fat	High load	15.126	2.489
		High fat	Low load	14.391	2.212
		High fat	High load	15.505	2.621
	High fat	Low fat	Low load	14.132	2.400
		Low fat	High load	15.241	2.577
		High fat	Low load	14.282	1.650
		High fat	High load	15.384	2.246

Proportion correct	Interleaved	Low fat	Low load	0.975	0.052
		Low fat	High load	0.889	0.136
		High fat	Low load	0.975	0.052
		High fat	High load	0.849	0.123
	Water	Low fat	Low load	0.992	0.032
		Low fat	High load	0.958	0.090
		High fat	Low load	0.992	0.032
		High fat	High load	0.881	0.132
	Low fat	Low fat	Low load	0.967	0.057
		Low fat	High load	0.942	0.104
		High fat	Low load	0.950	0.063
		High fat	High load	0.831	0.170
	High fat	Low fat	Low load	1.000	0.000
		Low fat	High load	0.925	0.092
		High fat	Low load	0.975	0.070
		High fat	High load	0.865	0.145

Table 2. post-hoc paired comparison t-test for effect of preload for the working memory task

Dependent variable	**Preload**	**vs water**	**vs low fat**	**vs high fat**
Response time	interleaved	1.000	0.002	0.003
	water	-	0.091	0.105

	Low fat	-	-	1.000
Proportion correct	interleaved	0.067	1.000	0.803
	water	-	0.072	1.000
	Low fat	-	-	0.846

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REFERENCES

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