Universidad Nacional Autónoma de México
Maestría en Ciencias (Neurobiología)
Instituto de Neurobiología
Departamento de Neurobiología Conductual y Cognitiva

Correlatos neurales de la percepción emocional por análisis de patrones en multitud de voxeles de datos de resonancia magnética funcional

Que para optar por el grado de:
Maestro en Ciencias

Isaac David Reyes González

Tutor principal:
Dr. Fernando Alejandro Barrios Álvarez
Instituto de Neurobiología

Comité tutor:
Dr. Luis Concha Loyola
Instituto de Neurobiología
Dr. Eduardo Adrián Garza Villarreal
Instituto Nacional de Psiquiatría

México, noviembre 2018

I, AUTHORNAME confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Abstract

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Nam et turpis gravida, lacinia ante sit amet, sollicitudin erat. Aliquam efficitur vehicula leo sed condimentum. Phasellus lobortis eros vitae rutrum egestas. Vestibulum ante ipsum primis in faucibus orci luctus et ultrices posuere cubilia Curae; Donec at urna imperdiet, vulputate orci eu, sollicitudin leo. Donec nec dui sagittis, malesuada erat eget, vulputate tellus. Nam ullamcorper efficitur iaculis. Mauris eu vehicula nibh. In lectus turpis, tempor at felis a, egestas fermentum massa.

Acknowledgements

Table of Contents

List of figures

List of tables

Abbreviations

BOLD	**B**lood-**O**xigen-**L**evel **D**ependent.
SOA	**S**timulus **O**nset **A**synchrony.

Chapter 1

Introduction

Emotions are conscious[1] states characterised by their discreteness, mild-to-marked arousal, hedonistic load[2] and a reference to an organismically relevant somatic state[3] (Schacter et al. 2011; Ekman & Davidson 1994). Emotions as basic as happiness, fear, anger and sorrow are probably among the most basic subjective experiences; and whose behavioral manifestation is traceable to at least analogous reactions in all living organisms.[4]

It is for this very basal nature and the role of the nervous system in supporting them that emotions not only interfere with and modulate higher-order cognition, but also provide the most fundamental basis for motivation, and therefore for planning and behavior (Schwarz 1990). Emotions are causally connected to various responses in the peripheral nervous system (both somatic and autonomic) and endocrine activity. Memory formation can no longer be understood without the participation of distinct mechanisms that are emotion-selective (LeDoux 1994).

The predispositions of an individual's emotional dynamics is an often ig-

[1]By consciousness I am specifically referring to the rudimentary meaning of phenomenal consciousness: the quality of objects which can feel; in the vein of authors such as Christof Koch, David Chalmers, Giulio Tononi and Ned Block.

[2]Unlike, for instance, the (dis)pleasureless experience of a vivid color or propioceptive information.

[3]Unlike, say, the exquisite smell of flowers. Damasio (1996) uses the term "somatic" as opposed to "bodily" to convey the sufficiency of mental *representations* of the body.

[4]Some authors use the word "emotion" for the behavioral response and reserve the word "feeling" for their conscious counterpart.

nored personality trait. It might seem odd to talk about normally emerging psycho-physiological states in relation to health, yet this relationship can't be stressed enough. First, emotions themselves can be symptomatic of illness, as is the case of disgust. More directly, there's little doubt that affections such as extended depression and phobias should be considered illnesses in their own right.

Beyond the individual, there's a special significance to what emotions can achieve for social well-being. The resulting expressions conveyed by faces and body language are the epitome of animal communication in primates. Our ancestors had to read these expressions out and interpret them, as part of a wider signaling repertoire, well before the emergence of language proper. Within behavioral ethology a signal is said to be effective (which implies a reaction in the receiving organism) if it possesses the property of being evolutionarily advantageous to both parties, on average. Prevarication detracts from this information in the case of receivers and honest senders, making emotions highly effective signals insofar as they are hard to fake. Moreover, their adequate perception marks an important input for the mechanisms of the theory of mind,[5] emotions being so flagrant a display of visceral mental states.

The psychological literature is committed to discussing the biological origin and relevance of emotions. An important topic is what I may call the automatic emotional processing hypothesis: if facial expression is so important a signal of inner mental states for a social species like ours, it stands to reason that a cognitive adaptation could have evolved to decode it separately of attention and even consciousness. Closely related is the negative-valence bias hypothesis: namely that the aforementioned cognitive capacity might be biased towards processing certain unpleasant emotions, since they more often go along life-or-death situations.

[5]Theory of mind: attributing mental states to others. The belief that other minds exist; opposite to solipsism. Not to be conflated with theories of what the mind is.

Chapter 2

Previous Research

2.1 For automatic emotion identification

The affective priming paradigm (Klauer et al. 2003) is known to produce an effect on reaction times or accuracy for subsequent identification of congruent emotions, thereby reflecting variability in the processes leading to affect recognition (De Houwer et al. 2009). Many lines of evidence help extrapolate this fact into the notion that affect identification can undergo an automatic/preattentional mode:

- Because affective priming occurs only under short stimulus onset asynchrony (SOA) times[1] (300 ms or less), it has been conjectured that its processing must occur before the direction of attention and response strategies take place (Moors & De Houwer 2006; Hermans et al. 2001).

- The effect is observed even when the prime is presented at unrecognizable subthreshold levels (Draine & Greenwald 1998) and outside the focus of visual attention (Calvo & Nummenmaa 2007).

- According to some reports, cognitive load (as produced by the simultaneous presentation of irrelevant tasks) does not impair affective priming (Hermans et al. 2000). This is disputed, though (keep reading).

[1] The time lapse between prime and target stimuli presentation.

2.1.1 Valence/emotion-dependent automatism

A further refinement proposes that not all emotions were created equally advantageous to recognize. If natural selection produced complementary high-priority neural circuitry for the processing of facial expressions (or an epigenetically-developed precursor), one could naturally ask whether this automatism also targeted some emotions more than others based on survival advantage. Indeed, a wealth of research has found that the priming effect, as well as others, are biased towards averse and pejorative emotions, as opposed to happy or neutral ones (Fox et al. 2002; Vuilleumier et al. 2001; Ishai et al. 2004; Vuilleumier 2005; Susa et al. 2012).

2.2 Against automatic emotion identification

Contrary to the previous view, Pessoa et al. (2002) interpreted the increased activity in relevant structures (fusiform area, amygdala, etc.) during explicit attention to facial features (in contrast to non-expressive details inscribed in the faces) as evidence that facial processing is contingent upon attention. This strand of facial emotion processing research is not without more recent supporters (see Ochsner & Gross 2005; Eimer et al. 2003 for instance).

2.3 Perceptual modulation through spare attention: a possible bridging explanation

Seemingly contradictory results stemming from methodologically sound studies cry for a theoretical reformulation to encompass all the facts. Research around the conflict often resorts to some sort of interaction and modulation between systems to explain the data (Okon-Singer et al. 2007; Palermo & Rhodes 2007). Sassi and colleges proposed that even though emotional perception can be turned automatic, unused resources might still be consumed in parallel, should the distracting task not be distracting enough (Sassi et al. 2014).

Chapter 3

Justification

3.1 The Big Picture

Simple emotions are regarded as some of the most basic wholesale conscious experiences in many senses: they are culturally universal, well-differentiated, and inextricably connected to somatic states and homeostasis (Damasio 1998). Helping understand their third-person detection and processing contributes to our understanding of intersubjectivity.

As of today, clinicians and even cognitive neuroscientists still are heavily dependent upon verbal reports and other behavioral cues to asses mental states. However, the prospect of having subjects report very fast and automatic — even nonconscious — perceptual modes might be not only difficult but logically impossible. Psychologists have come up with clever behavioral experiments to detect these changes, so homologous neural tests are due. More generally, extra theoretical and empirical work is needed to help bridge the explanatory gap between mechanistic (i.e. physical) facts and subjective (i.e. mental) ones.

Despite the initial success of neuroscience identifying and describing molecular and cellular underpinnings of many medical and psychological phenomena; both the methods of "small-to-middle-scale" neuroscience and plain *localizationism* yield against a number of questions. Many known cogni-

tive phenomena rather emerge (or are thought to do so) from the coordinated physiology of anatomically distributed components. Evolutionary constraints pose limits on the number of nervous specializations that could univocally correspond to the performance of a function, so that certain behavioral and mental phenomena must correspond to the differential recruitment and temporal modulation of more basic resources at the physiological domain. Moreover, modern views on cognition place emphasis on the consideration of the interactions of organisms with one another and their environment.

Functional nuclear magnetic resonance is capable of recording a correlate signal of *local field potentials*, nearly simultaneously, while providing moderate spatial and temporal resolution to differentiate their activity. It is suitable for exploratory studies in which task-related zones and dynamics must be first identified, so as to lay the groundwork for finer-grained measurement techniques that try to establish the finer cellular circuitry.

3.2 Particular

The ongoing debate surrounding the cognitive mechanisms of facial expression perception will benefit from extra evidence, and more importantly, more sensible analysis techniques to derive the requisite evidence.[1]

Multivariate and nonlinear methods have proved successful in the past extending the identification of more complex brain activity interactions which aren't amenable to traditional regression models. Consider the following example in which the activation pattern (e.g., the BOLD[2] signal of different areas) under two experimental conditions has been constructed according to the following relation (reduced to two voxels and constant intra-condition voxel values for simplicity):

[1] Is the use of MVPA novel in the facial expression recognition literature? Mention if so

[2] Blood-Oxigen-Level Dependent signal.

(1)

$$\begin{cases} voxel_1^2 + voxel_2^2 > c & Condition\ A \\ voxel_1^2 + voxel_2^2 < c & Condition\ B \end{cases}$$

This is simply a circle in voxel space (*phase space*, more generally). Let c be half the magnitude of the range of values voxels normally take, divided by pi, so that there are as many possible states for condition A as for B; then uniformly sample some points from all possible states at random (40 in figures 3.2 and 3.1). When plotted over the plane, our measurements contain sufficient information to tell both brain states apart, even by visual inspection:

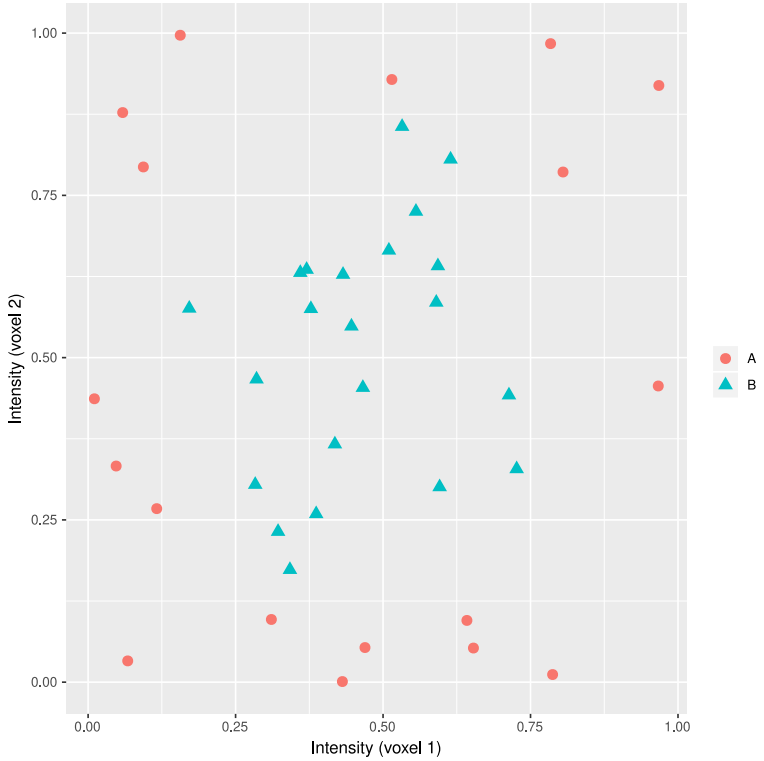

Figure 3.1: A bidimensional, nonlinear activity pattern between two voxels, as sampled from 18 trials under experimental condition *A* plus 22 under *B*. BOLD signal measurements corresponding to condition *A* can be distinguished by their eccentricity with respect to condition *B*.

Yet linear regression analysis operating on separate voxels is doomed to fail (figure 3.2). The unidimensional population distributions are both centered at about the same value, so no effect is observed. Moreover, they are extremely spread-out and look rather noisy. Nor can such a big range of

values be accounted for by a deterministic nonstationary process systematically pushing values away, because the process used to generated them is explicitly neither of those things.

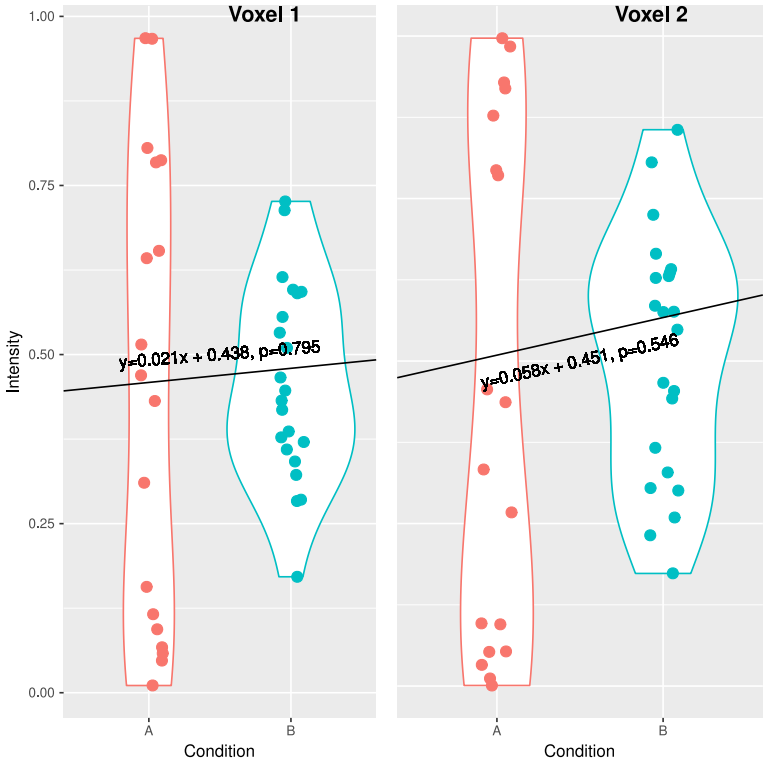

Figure 3.2: Simplified linear regression models and t-test p-values for the projections of figure 3.1 data on each dimension. The effect of experimental conditions on single voxels is negligible (as witnessed by the models' minor slopes), and likely to be due to chance (p-values), as expected. Also by design, a Shapiro-Wilk test reveals that data distribution doesn't pass the normality criterion required by t-tests.

Even a nonlinear univariate classifier would make a number of mistakes at the intersection of both distributions. A discriminating univariate pattern would be noticeable from power-spectral analysis under special dynamic conditions, but the most adequate approach by far is to consider both voxels simultaneously, as in figure 3.1, since that's how data were generated in the first place.

Chapter 4

Hypothesis

4.1 Research Question

Are there different modes of facial emotion perception (with or without attention, valence-dependent)?

4.2 Hypotheses

- Working hypothesis (H_1): the putative modes of facial expression processing should be correlated to differential spatio-temporal activity patterns at associated brain areas.
- Null hypothesis (H_0): no significant statistical dependence can be found between perception (i.e., processing) of facial expression under different conditions and activity patterns in the brain.

4.3 Predictions

If the occurrence of "automatic" (i.e. preattentive) or valence-dependent facial emotion processing goes hand-in-hand with a neural activity substrate, a powerful-enough statistical method (such as multivariate classification)

should be able to discriminate said neural activity. This assumes our measurements will be able to capture the relevant signal.

Chapter 5

Goals

- Study the biological basis of emotion perception at the bigger scale of whole-brain functional networks of neuronal ensambles.
- Dissociate the proposed plethora of phenomena that has been traditionally grouped under facial emotion perception. Find and test reliable psychological, imaging and computational methods to achieve that goal.
- As a natural consequence of the newfound descriptive and explanatory power contingent upon the previous point: be able to leverage the resulting methods to predict the occurance of distinct emotion perception workflows from functional imaging data alone.
- Help settle the debate surrounding the existence of more automatic pathways in the processing of emotional imagery, by contributing extra evidence coming from a representative and controlled fMRI study, as well as rigurous analysis and state-of-the-art pattern analysis techniques.

Chapter 6

Sample, Materials and Methods

6.1 Sample

- 45 subjects
  - age
  - sex
  - handedness?
  - psychometric results
- this is our actual experimental sample: 3 fMRI sequences each (different contrasts, specify design matrix in #Materials and Methods). only hits will be considered initially.
  - 126 stimulus-response cycles each.
  - **why do NULL (non gazing) cycles have a different "weight" on e-prime?**
- Anatomical reference coregistry (some lack sagital T1 FSPGR BRAVO, but Axial alternative seems to be good enough to allow for atlas transformations).

6.2 Materials and Methods

Notwithstanding preattentive emotional face perception, the appearance of a face with a lateralized gaze tempts the human visual system to shift attention towards the suggested direction; presumably because relevant environmental and social information is likely to be discovered where others look at. The abrupt attentional shift is well within the fast interval range of a saccade movement. This phenomenon is known as *gaze cuing*, and has been used to measure neural correlates of visual attention and its interplay with emotion perception.(Friesen & Kingstone 1998)

The present study relied on a variation on the gaze cuing paradigm to obtain sequences of functional brain images under contrasting conditions. Each recording session was comprised of 126 stimulus-response cycles, where averted-gaze cycles were interleaved with control (i.e. direct-gaze) ones in order to study reorientation of visual attention in conjunction with affective perception. On the other hand, each of the three sessions tested for the effect of emotional valence (either positive or negative) against a neutral expression. This is further explained in figure 6.1: a markovian discrete-state system diagram showing a repeating $\langle gaze\ cuing,\ contrast \rangle$ unit, except that the multitude of specific face photographs have been abstracted away.

- Mention Federica's and previous findings using EEG? that would beg for introducing gaze cuing in the #Previous Research section.
- Block, event, mixed?
- MRI: attach notes from Concha's lectures in order to introduce MRI?
  - sequence used, parameters (from XNAT)
  - image processing pipeline
- statistical analysis, predictive models: regression as a rudimentary form of classification

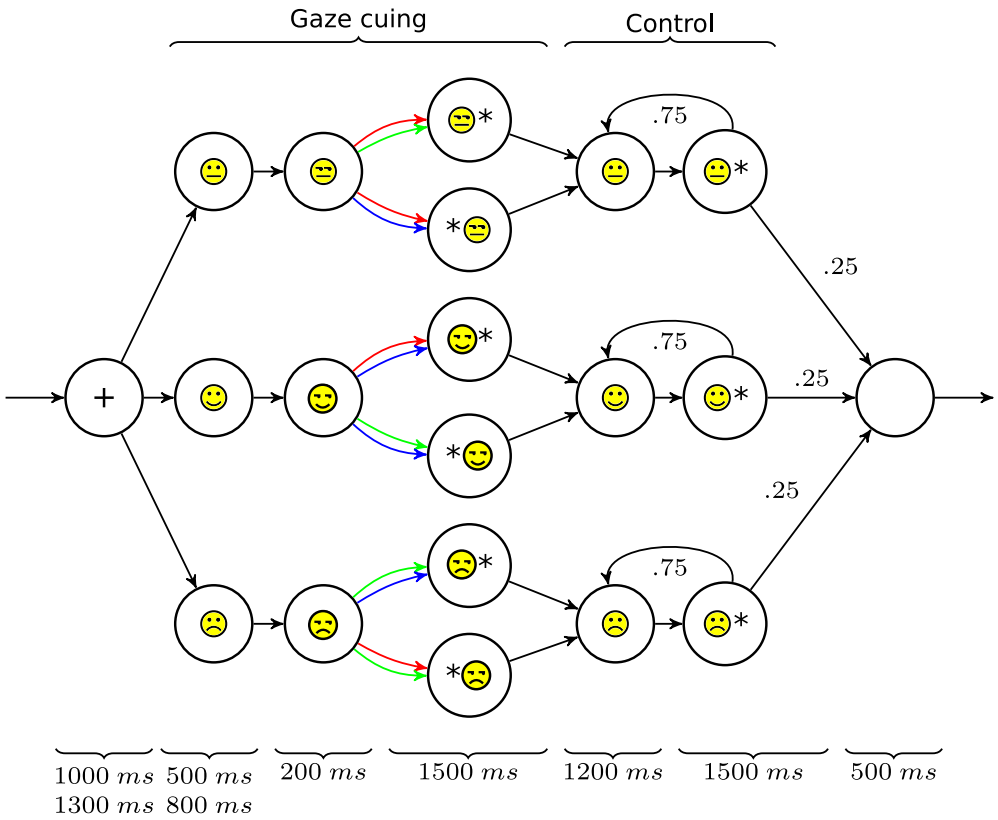

Figure 6.1: Gaze cuing paradigm. Nodes represent visual stimuli, their order of presentation is indicated using arrows. Unless noted otherwise, transition probability from a node is equally distributed among all exit arrows. Participants were asked to attend for a target (asterisk) and respond either "left" or "right" depending on its position relative to the face. Colorful arrows indicated that such combinations of emotion followed by a gaze-congruent or gaze-incongruent target were specific to one of the three sessions.

Chapter 7

Results

Chapter 8

Discussion and Conclusion

Appendix 1: Source code

Listing 8.1: Single vs multi-voxel predictive models. The following R program was used to generate figures 3.2 and 3.1

```
library(ggplot2)
## library(cowplot)
library(e1071) # svm classifier

set.seed(111)
N <- 40
CONDITIONS <- c("A", "B")

## uniformly sample N points within (0,1)x(0,1)
data <- data.frame(replicate(2, runif(N)))
colnames(data) <- c("voxel_1", "voxel_2")

## divide space into 2 condition regions according to some boundary relation
label <- function(p) {
    ## showcase nonlinear capabilities: circle of area .5 centered at (.5, .5)
    diameter <- .5 / pi
    if ((p["voxel_1"] - .5)**2 > diameter - (p["voxel_2"] - .5)**2) {
        CONDITIONS[1]
    } else {
        CONDITIONS[2]
    }
}
data <- cbind(data, cond = apply(data, 1, label)) # label each point
## reorder according to label, for visual convenience
data <- data[with(data, order(cond)), ]

## plot single-voxel models
lm_plot <- function(data, xname, yname, remove_ytext = FALSE) {
    model <- summary(lm(paste0(yname, "~", xname),
                        data))
    beta1 <- model$coefficients[paste0(xname, "B"), "Estimate"]
    beta0 <- model$coefficients["(Intercept)", "Estimate"]
    p <- model$coefficients[paste0(xname, "B"), "Pr(>|t|)"]
    plot <- ggplot(data, aes(x = data[, xname],
                             y = data[, yname],
                             color = data[, xname])) +
        labs(x = "Condition", y = "Intensity") +
        geom_violin() +
        geom_jitter(width = .1, size = 3) +
        geom_abline(slope = beta1,
                    intercept = beta0) +
        geom_text(color = "black",
```

```
                angle = atan(beta1) * (180 / pi) * 3.75,
                aes(x = 1.5,
                    y = .5,
                    label = paste0("y=",
                                   round(beta1, 3),
                                   "x + ",
                                   round(beta0, 3),
                                   ", p=",
                                   round(p, 3)))) +
        theme(legend.position="none")
    if (remove_ytext) {
        plot <- plot + theme(axis.title.y = element_blank(),
                     axis.text.y = element_blank(),
                     axis.ticks.y = element_blank())
    }
    shapiro.test(data[data$cond == CONDITIONS[1], as.character(yname)])
    shapiro.test(data[data$cond == CONDITIONS[2],  as.character(yname)])
    plot
}

svg("./lm-vs-multivariate-1.svg")
cowplot::plot_grid(lm_plot(data, xname = "cond", yname = "voxel_1"), # no effect, p
    = .795
                   lm_plot(data, xname = "cond", yname = "voxel_2", TRUE), # no effect,
    p = .546
                   labels = c("Voxel 1", "Voxel 2"),
                   label_x = .5)
dev.off()

## summary(lm(formula = cond ~ voxel_1:voxel_2, data = data)) # no interaction

svg("./lm-vs-multivariate-2.svg")
ggplot(data, aes(x = voxel_1, y = voxel_2, color = cond, shape = cond)) +
    geom_point(size = 3) +
    labs(x = "Intensity (voxel 1)",
         y = "Intensity (voxel 2)",
         color = "Condition") +
    scale_color_discrete("") +
    scale_shape_manual("", values = c(16, 17))
dev.off()

indices <- sample(1:nrow(data), N/2)
model3 <- svm(cond ~ voxel_1 + voxel_2,
              data = data[indices, ],
              kernel = "radial",
              scale = FALSE,
              cost = 500)
predict(model3, data[-indices, ])
plot(model3, data)
```

8.1 Example table

Table 8.1: This is the table caption. Suspendisse blandit dolor sed tellus venenatis, venenatis fringilla turpis pretium.

Column 1	Column 2	Column 3
Row 1	0.1	0.2
Row 2	0.3	0.3
Row 3	0.4	0.4
Row 4	0.5	0.6

References

Calvo, M.G. & Nummenmaa, L., 2007. Processing of unattended emotional visual scenes. *Journal of Experimental Psychology: General*, 136(3), p.347.

Damasio, A.R., 1998. Emotion in the perspective of an integrated nervous system. *Brain research reviews*, 26(2-3), pp.83–86.

Damasio, A.R., 1996. The somatic marker hypothesis and the possible functions of the prefrontal cortex. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 351(1346), pp.1413–1420. Available at: http://rstb.royalsocietypublishing.org/content/351/1346/1413.

De Houwer, J. et al., 2009. Implicit measures: A normative analysis and review. *Psychological bulletin*, 135(3), p.347.

Draine, S. & Greenwald, A., 1998. Replicable unconscious semantic priming. *Journal of experimental psychology. General*, 127, pp.286–303.

Eimer, M., Holmes, A. & McGlone, F.P., 2003. The role of spatial attention in the processing of facial expression: An erp study of rapid brain responses to six basic emotions. *Cognitive, Affective, & Behavioral Neuroscience*, 3(2), pp.97–110.

Ekman, P.E. & Davidson, R.J., 1994. *The nature of emotion: Fundamental questions.*, Oxford University Press.

Fox, E., Russo, R. & Dutton, K., 2002. Attentional bias for threat: Evidence for delayed disengagement from emotional faces. *Cognition & emotion*, 16(3), pp.355–379.

Friesen, C.K. & Kingstone, A., 1998. The eyes have it! Reflexive orienting is triggered by nonpredictive gaze. *Psychonomic bulletin & review*, 5(3), pp.490–495.

Hermans, D., Crombez, G. & Eelen, P., 2000. Automatic attitude activation and efficiency: The fourth horseman of automaticity. *Psychologica Belgica*, 40(1), pp.3–22.

Hermans, D., Houwer, J.D. & Eelen, P., 2001. A time course analysis of the affective priming effect. *Cognition and Emotion*, 15(2), pp.143–165. Available at: https://doi.org/

10.1080/02699930125768.

Ishai, A. et al., 2004. Repetition suppression of faces is modulated by emotion. *Proceedings of the National Academy of Sciences*, 101(26), pp.9827–9832.

Klauer, K.C. et al., 2003. Affective priming: Findings and theories. In J. Musch & K. C. Klauer, eds. *The psychology of evaluation: Affective processes in cognition and emotion*. Lawerence Erlbaum.

LeDoux, J.E., 1994. Emotion, memory and the brain. *Scientific American*, 270(6), pp.50–57.

Moors, A. & De Houwer, J., 2006. Automaticity: A theoretical and conceptual analysis. *Psychological bulletin*, 132(2), p.297.

Ochsner, K.N. & Gross, J.J., 2005. The cognitive control of emotion. *Trends in cognitive sciences*, 9(5), pp.242–249.

Okon-Singer, H., Tzelgov, J. & Henik, A., 2007. Distinguishing between automaticity and attention in the processing of emotionally significant stimuli. *Emotion*, 7(1), p.147.

Palermo, R. & Rhodes, G., 2007. Are you always on my mind? A review of how face perception and attention interact. *Neuropsychologia*, 45(1), pp.75–92.

Pessoa, L. et al., 2002. Neural processing of emotional faces requires attention. *Proceedings of the National Academy of Sciences*, 99(17), pp.11458–11463.

Sassi, F. et al., 2014. Task difficulty and response complexity modulate affective priming by emotional facial expressions. *The Quarterly Journal of Experimental Psychology*, 67(5), pp.861–871.

Schacter, D., Gilbert, D.T. & Wegner, D.M., 2011. *Psychology (2nd edition)*, New York: Worth; Worth.

Schwarz, N., 1990. Feelings as information: Informational and motivational functions of affective states. In T. E. Higgins & R. M. Sorrentino, eds. *Handbook of motivation and cognition: Foundations of social behavior*. Guilford Press, pp. 527–561.

Susa, G. et al., 2012. The self regulatory effect of attentional control in modulating the relationship between attentional biases toward threat and anxiety symptoms in children. *Cognition & emotion*, 26(6), pp.1069–1083.

Vuilleumier, P., 2005. Cognitive science: Staring fear in the face. *Nature*, 433(7021), p.22.

Vuilleumier, P. et al., 2001. Effects of attention and emotion on face processing in the human brain: An event-related fMRI study. *Neuron*, 30(3), pp.829–841.