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

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México, noviembre 2018

## Abstract

# Acknowledgements

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## Abbreviations

BOLD Blood-Oxigen-Level Dependent.

EEG Electroencephalography.
 ERP Event-Related Potential.
 SOA Stimulus Onset Asynchrony.

#### Introduction

Emotions are conscious<sup>1</sup> states characterised by their discreteness, mild-to-marked arousal, hedonistic load<sup>2</sup> and a reference to an organismically relevant somatic state<sup>3</sup> (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.<sup>4</sup>

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 and associative learning 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 ignored

<sup>&</sup>lt;sup>1</sup>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.

 $<sup>^2 \</sup>mathrm{Unlike},$  for instance, the (dis) pleasureless experience of a vivid color or propioceptive information.

<sup>&</sup>lt;sup>3</sup>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.

 $<sup>^4</sup>$ Some authors use the word "emotion" for the behavioral response and reserve the word "feeling" for their conscious counterpart.

personality trait. It might seem odd to talk about normally emerging psychophysiological states in relation to health; however their marriage 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<sup>5</sup> 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 the value receivers and honest senders obtain from these signals, making emotions highly effective insofar as they are hard to fake. Moreover, their adequate perception<sup>6</sup> marks an important input for the mechanisms of the theory of mind,<sup>7</sup> 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 visuospatial attention,<sup>8</sup> and perhaps consciousness. Closely related is the negative-valence bias hypothesis: namely that the aforementioned shortcut faculty might be biased towards processing certain unpleasant emotions,

 $<sup>^5</sup>$ Interestingly, the word "affection" can refer to both maladies and emotions. Particularly in psychology, an affect is a feeling elicited in response to another feeling or stimulus.

<sup>&</sup>lt;sup>6</sup>Perception is the set of interfacing processes by which a cognitive system acquires and renders information *from outside the system* useful for attention, planning, reasoning and behavior

<sup>&</sup>lt;sup>7</sup>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.

<sup>&</sup>lt;sup>8</sup>Attention refers to the broad psychological faculty of filtering out available information. Allocating limited cognitive resources.

since they more often go along life-or-death situations.

#### Previous Research

#### 2.1 The neural bases of emotion and attention

Our modern understanding of emotional processing encompasses several cortical and subcortical regions, some of which are rather primitive and well-conserved. Roughly speaking, stimuli entering the thalamus is sent to primary sensory cortices but also to the amygdala. The latter possesses specialized nuclei for both innate and learned emotional assessment. A long history of conditioning research has shown that the amygdala must be present for implicit (i.e. procedural) associations to be learned between emotional and unconditioned stimuli. The amygdala's central nucleus projects to places such as the central gray region of the brain stem and hypothalamus, where it can trigger autonomic reactions and humoral activity. Cortical areas are also implicated in complex emotional perception: the ventral anterior cingulate cortex, insula and ventromedial prefrontal cortex. As an example of the consequences these structures can have on emotion perception, damage to the prefrontal cortex will result in sociopathic impairments. (LeDoux & Damasio 2013).

Discoveries in brain-damage patients, imaging and stimulation studies have established the segregation of two distinct systems of visual attention in humans, spanning, respectively, dorsal and ventral loci at the frontoparietal cortex (Vossel et al. 2014; Umarova et al. 2009). The former is responsible for goal-directed (top-down) attention, whereas the latter reacts to unexpected (bottom-up) stimuli. It has also been suggested that they serve as generic attentional mechanisms irrespective of sensory modality (Macaluso 2010), or even in the absence of conceptual and integrative information (e.g., during a feature-based selection task) (Vandenberghe & Gillebert 2009).

Inquiries into the functional, causal and structural connectivity of dorsal and ventral networks have begun to shed light into their components, and — to some degree — their specialization. The dorsal network comprises at the very least the frontal eye fields (FEF) and intraparietal sulcus (IPS), both of which are thought to display association tracts to the retinotopically and contralaterally-organized perceptual areas in the occipital lobe, plus commissure fibers to connect heminetworks with each other. It's possible that the dorsal network computes planned saliency maps, as suggested by the presence of even more retinotopically-organized receptive fields in FEF and IPS. Saliency maps would then be consumed by the FEF to request all many sorts of eye movements (Jerde et al. 2012).

The inner workings of the ventral frontoparietal network are more poorly understood, but it has been reliably associated with the filtering of exogenous (i.e. task-irrelevant) events, presumably allowing unexpected and potentially dangerous stimuli to overcome the subject's concentration and become the focus of attention. Activation occurs at zones dubbed the temporoparietal junction (TPJ) and the ventral frontal cortex (VFC). Issues exist determining whether the ventral network is right-lateralized, and no cytoarchitectonic (or otherwise) standard exists setting boundaries for the TPJ and VFC (Vossel et al. 2014).

The TPJ has been suggested as a point of interaction between systems (Corbetta et al. 2008; Fox et al. 2006). Intrinsic activity in the right posterior middle frontal gyrus (MFG) has been correlated with both networks, making it an additional candidate hub. Of all three major superior longitudinal fasciculi (SFL I, II and III) providing associative anatomical connections for

<sup>&</sup>lt;sup>1</sup>Not to be confused with the also dorsal ("where") and ventral ("what") visual perception pathways. Although overlap with attention networks may exist at the temporoparietal junction and intraparietal sulcus.

these networks, the middle one (SFL II) is known to connect FEF and TPJ (De Schotten et al. 2011).

#### 2.2 For and against automatic emotion perception

The affective priming paradigm (Klauer et al. 2003) is known to improve reaction times or accuracy for subsequent identification of identical emotions, thereby reflecting some versatility 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 perception can undergo an automatic/preattentional mode:

- Because affective priming occurs only under short stimulus onset asynchrony (SOA) times<sup>2</sup> (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.

A further refinement proposes that not all emotions were made 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

<sup>&</sup>lt;sup>2</sup>The time lapse between prime and target stimuli presentation.

to happy or neutral ones (Fox et al. 2002; Vuilleumier et al. 2001; Ishai et al. 2004; Vuilleumier 2005; Susa et al. 2012).

Contrary to the previous view, Pessoa et al. (2002) interpreted the increased activity in cortical and basal structures linked to facial recognition and emotion (fusiform gyrus, 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). EEG<sup>3</sup> studies attempting to correlate alleged ERP<sup>4</sup> indices of visual attention with different modes of emotion perception have thrown mixed results so far (see Galfano et al. (2011) for a review and negative results concerning the emotion-dependent hypothesis, as inferred from 2nd-negative signal components at posterior contralateral electrodes during a gaze-cuing task).

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). Based on reaction times and varying task difficulty, Sassi and colleges proposed that even though emotional perception can be turned automatic, spare resources might still be consumed in parallel; should the distracting task not be distracting enough (Sassi et al. 2014).

<sup>&</sup>lt;sup>3</sup>Electroencephalography.

<sup>&</sup>lt;sup>4</sup>Event-related potential. Sometimes used interchangeably with "evoked potential"

#### 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.

In addressing this kind of questions, functional nuclear magnetic resonance is capable of recording a correlate signal of *local field potentials*, while providing moderate and balanced spatial and temporal resolution to differentiate near-simultaneous activity at distant cerebral zones. It is suitable for expeditionary studies in which task-related functional networks must be first identified or refined, so as to lay the groundwork for finer-grained measurement techniques that try to establish the finer cellular circuitry and chemistry.

#### 3.2 Particular

The ongoing debate surrounding the cognitive mechanisms of facial expression perception will benefit from extra evidence about anato-functional dissociation; and more importantly, the use of more sensible analysis techniques to derive the requisite evidence.

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 BOLD¹ signal of different areas) under two experimental conditions has been constructed according to the following relation (reduced to two voxels and constant intra-event voxel values for simplicity):

<sup>&</sup>lt;sup>1</sup>Blood-Oxigen-Level Dependent signal.

(1) 
$$\begin{cases} Condition \ A: \ voxel_1^2 + voxel_2^2 > c \\ Condition \ B: \ voxel_1^2 + voxel_2^2 < c \end{cases}$$

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:

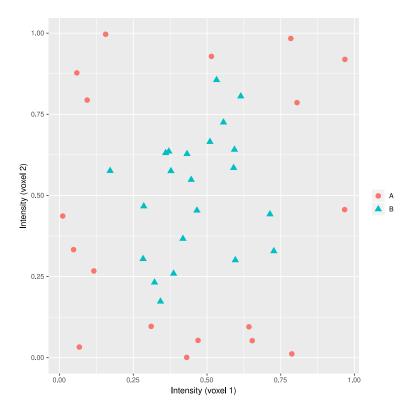


Figure 3.1: A bidimensional, nonlinear activity pattern between two voxels, as sampled from 18 trials under experimental condition A plus 22 under B. BOLD signal measurements corresponding to condition A can be distinguished by their eccentricity with respect to condition B.

Yet linear regression analysis operating on separate voxels is doomed to fail (figure 3.2). The unidimensional sample distributions are both centered around the same intensity value, so no inter-condition effect is observed.

Moreover, measurements are extremely spread-out and look rather noisy. Nor can such a big range of values be accounted for by motion artifacts or a deterministic nonstationary process systematically pushing values away, as a generalized linear model strives to account for, because the generating process explicitly was neither of those things.

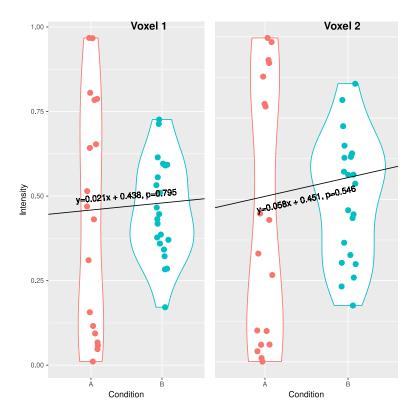


Figure 3.2: Simplified linear regression models and t-test p-values for the projections of figure 3.1 data on each axis. The effect of experimental conditions on single voxels is negligible (as witnessed by the models' minor slopes), and likely to be due to chance (p-values), as expected. Also by design,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

## Hypothesis

#### 4.1 Research Question

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

#### 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.

#### 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.

# Sample, Materials and Methods

#### 6.1 Sample

The present work relies on an existing subsample of 42 healthy subjects scanned at the Institute of Neurobiology's Magnetic Resonance Unit on a General Electric Discovery MR750 scanner, whose main magnetic field reaches a magnitude peak of  $3.0\ T$ . Inducting echoes were recorded using a 32-channel head-mounted antenna.

T2\*-weighted scans for functional imaging are comprised of 8840 frames each. Sequence parameters are described in table 6.1.

Table 6.1: Sequence parameters used for fMRI acquisitions.

Sequence parameter	Value
Acquisition type	2D
Slice orientation	Transversal
Slices	34
Matrix size	64x64
Voxel size	$(4 \ mm)^3$
Flip angle	pi/2
TR	2000~ms

Sequence parameter	Value
TE	40~ms

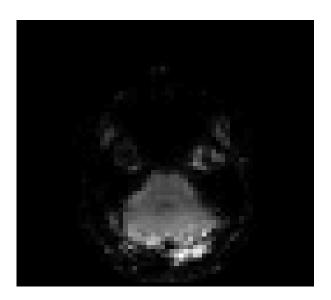


Figure 6.1: Sample raw fMR image from our dataset.

#### 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 an event-based experimental design to obtain sequences of functional brain images under contrasting conditions; specifically, a variation on the gaze cuing paradigm. Each recording session was comprised of 126 stimulus-response blocks, 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. This is further explained in figure 6.2: a markovian discrete-state system diagram showing a repeating  $\langle gaze\ cuing,\ contrast \rangle$  unit. Specific face photographs have been abstracted away for brevity.

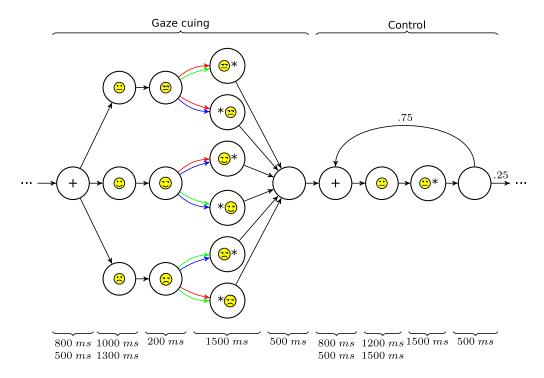


Figure 6.2: Gaze cuing paradigm. Nodes represent visual stimuli, their order of presentation is indicated using arrows. Unless noted otherwise, transition probability from a node is equally distributed among all exit arrows. Participants were asked to attend for a target (asterisk) and press a "left" or "right" button, depending on target position relative to the face. The spectrum of tested expressions (neutral, happy, disgusted) followed by either a gaze-congruent or gaze-incongruent target was divided and counterbalanced in three sequences, so as to keep the latter at reasonable durations. Colorful arrows indicate combinations which were specific to a sequence.

Results

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)
 3
     library(e1071) # svm classifier
 4
 5
     set.seed(111)
     N < -40
 6
     CONDITIONS <-c("A", "B")
 7
 9
     ## uniformly sample N points within (0,1)x(0,1)
     data <- data frame(replicate(2, runif(N)))
10
11
     colnames(data) < -c("voxel_1", "voxel_2")
12
     ## divide space into 2 condition regions according to some boundary relation
13
14
     label <- function(p) {
         ## showcase nonlinear capabilities: circle of area .5 centered at (.5, .5)
15
16
         diameter < - .5 / pi if ((p["voxel_1"] - .5)**2 > diameter - (p["voxel_2"] - .5)**2) {
17
             CONDITIONS[1]
18
         } else {
19
20
            CONDITIONS[2]
21
22
23
     data < - cbind(data, cond = apply(data, 1, label)) # label each point
24
     ## reorder according to label, for visual convenience
25
     data <- data[with(data, order(cond)), ]</pre>
26
27
     ## plot single-voxel models
     Im_plot <- function(data, xname, yname, remove_ytext = FALSE) {
    model <- summary(Im(paste0(yname, "~", xname),</pre>
28
29
30
                           data))
        \label{eq:beta1} $$ $ = model\coefficients[paste0(xname, "B"), "Estimate"] $$ $ beta0 < - model\coefficients["(Intercept)", "Estimate"] $$ $ p < - model\coefficients[paste0(xname, "B"), "Pr(>|t|)"] $$
31
32
33
         plot < -ggplot(data, aes(x = data[, xname],
34
35
                               y = data[, yname],
36
                               color = data[, xname])) +
            labs(x = "Condition", y = "Intensity") +
37
38
            geom_violin() +
39
            geom_{jitter}(width = .1, size = 3) +
40
            geom_abline(slope = beta1,
41
                       intercept = beta0) +
            geom_text(color = "black",
```

```
angle = atan(beta1) * (180 / pi) * 3.75,
43
44
                      aes(x = 1.5,
45
                          \dot{y} = .5,
                          label = paste0("y=",
46
47
                                        round(beta1, 3),
48
                                         'x +
                                        round(beta0, 3),
49
50
                                          , p=
51
                                        round(p, 3)))) +
52
             theme(legend position="none")
53
         if (remove_ytext) {
54
             plot < -plot + theme(axis.title.y = element_blank(),
                         axis.text.y = element_blank(),
55
56
                         axis.ticks.y = element_blank())
57
         \begin{array}{lll} & \text{shapiro.test}(\textbf{data}[\textbf{data}\$\texttt{cond} == \texttt{CONDITIONS}[1], \ \textbf{as.character}(\texttt{yname})]) \\ & \text{shapiro.test}(\textbf{data}[\textbf{data}\$\texttt{cond} == \texttt{CONDITIONS}[2], \ \textbf{as.character}(\texttt{yname})]) \\ & \end{array}
58
59
60
         plot
61
     }
62
63
     svg("./lm-vs-multivariate-1.svg")
     cowplot::plot_grid(lm_plot(data, xname = "cond", yname = "voxel_1"), # no effect, p
           = .795
65
                       Im_plot(data, xname = "cond", yname = "voxel_2", TRUE), # no effect,
           p = .546
                       labels = c("Voxel 1", "Voxel 2"),
66
67
                       label_x = .5
68
     dev.off()
69
     ## summary(Im(formula = cond ~ voxel_1:voxel_2, data = data)) # no interaction
70
71
72
     svg("./lm-vs-multivariate-2.svg")
73
     ggplot(data, aes(x = voxel_1, y = voxel_2, color = cond, shape = cond)) +
74
         geom\_point(size = 3) +
         labs(x = "Intensity (voxel 1)",
y = "Intensity (voxel 2)",
75
76
         color = "Condition") +
scale_color_discrete("") +
scale_shape_manual("", values = c(16, 17))
77
78
79
80
     dev.off()
81
82
     indices <- sample(1:nrow(data), N/2)
     model3 < - svm(cond \sim voxel_1 + voxel_2,
83
84
                   data = data[indices, ],
                   kernel = "radial",
85
                  scale = FALSE,
86
87
                  cost = 500)
     predict(model3, data[-indices, ])
88
     plot(model3, data)
```

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