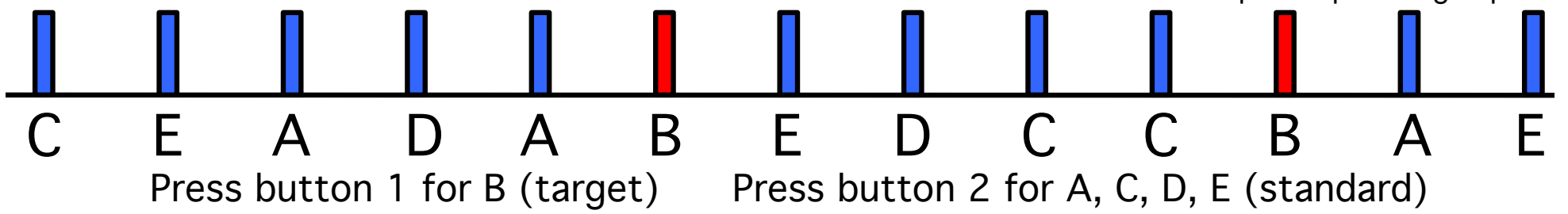


This video was made possible by NIH grant R25MH080794 and is shared under the terms of a Creative Commons license ([CC BY-SA 4.0](https://creativecommons.org/licenses/by-sa/4.0/))

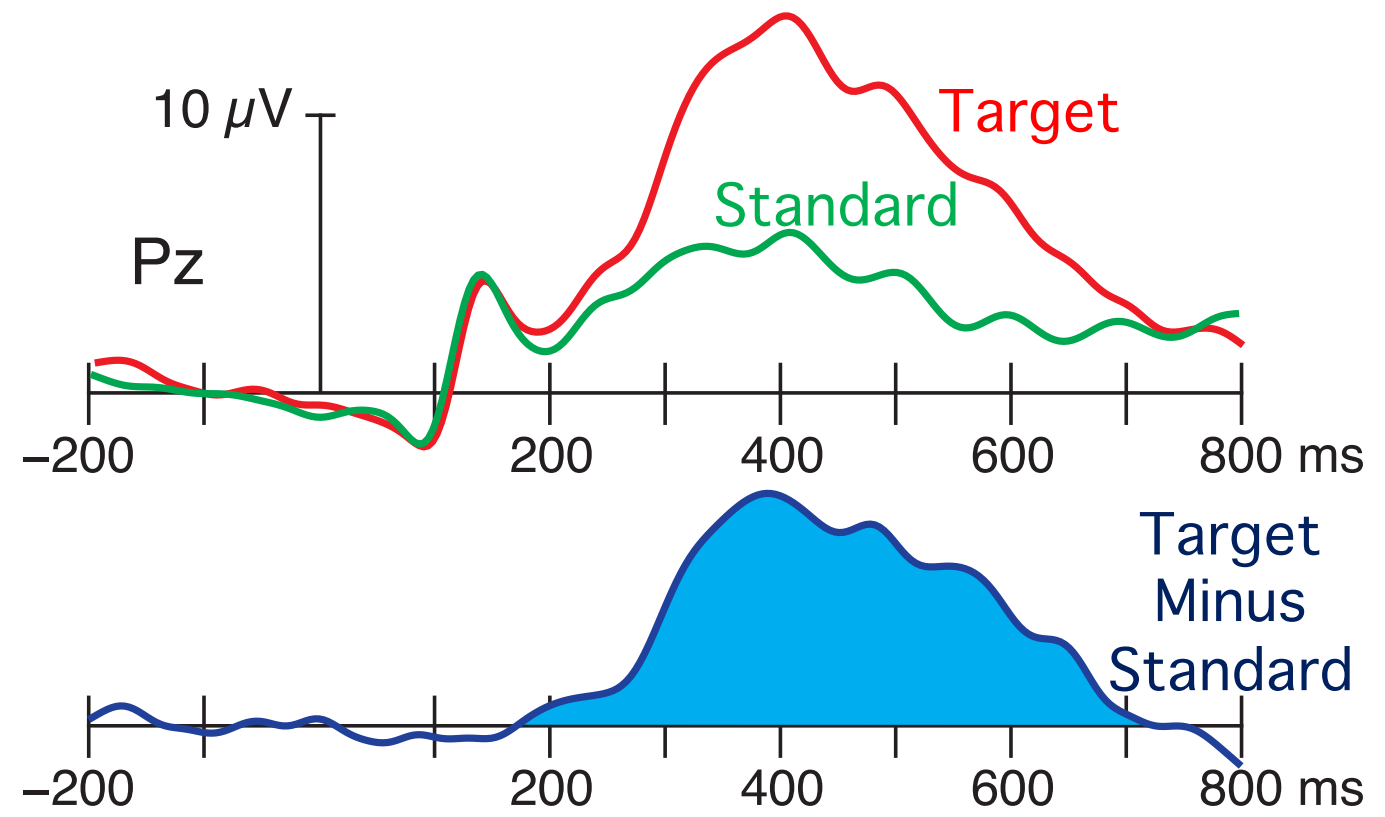
# What Are ERPs Good For?



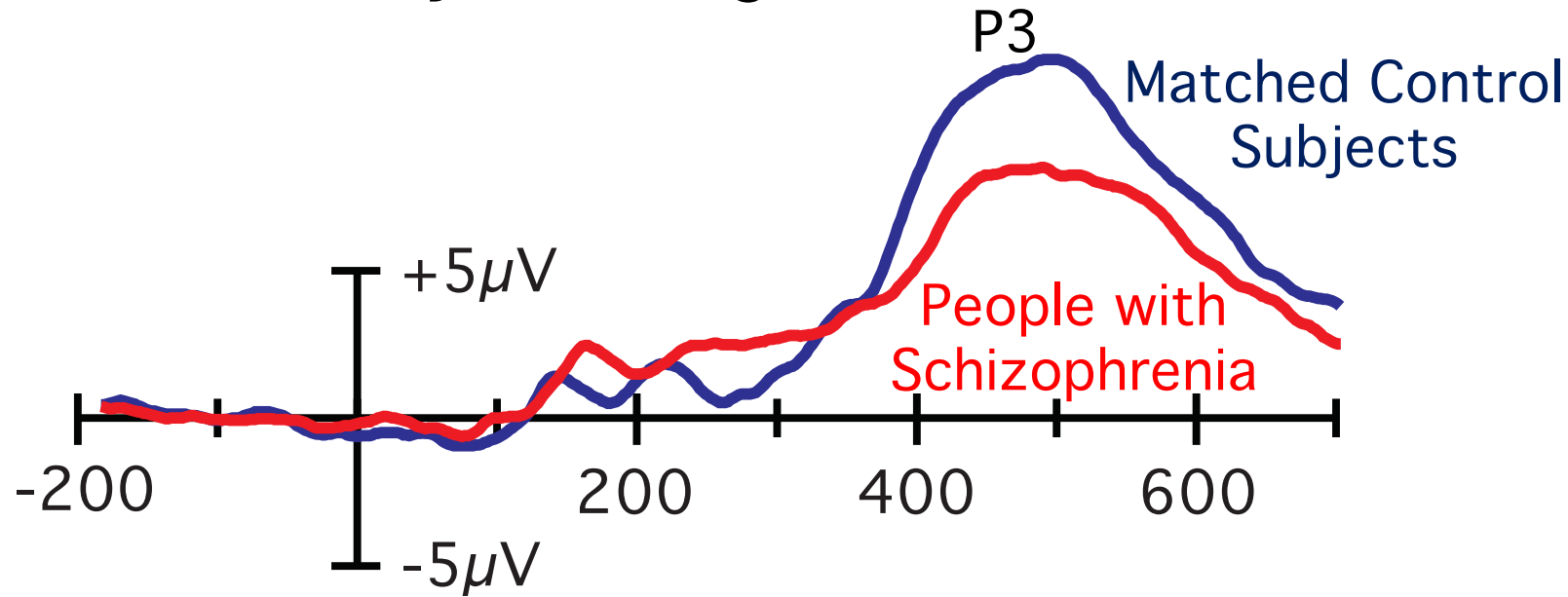


The P3 wave is larger for rare targets than for frequent standards.

Does this tell us anything interesting about how the brain works?



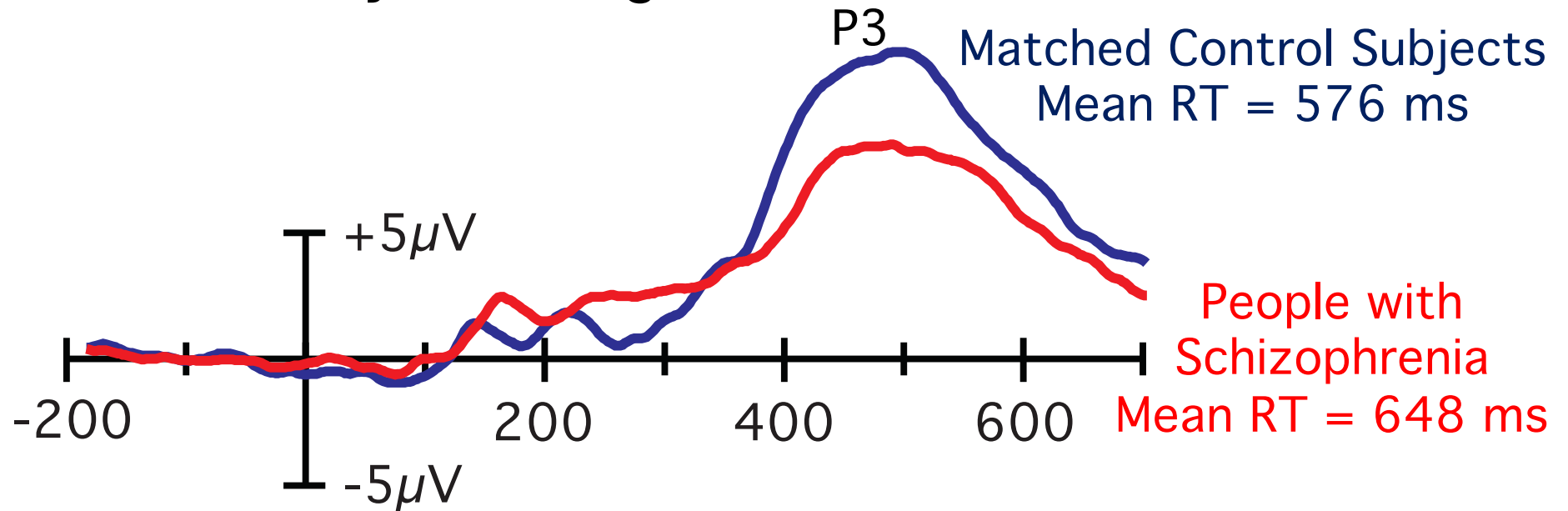
## ERP elicited by rare targets



Many studies have shown that the P3 wave for oddballs is smaller in people with schizophrenia than in healthy control subjects. But what does this tell us about the nature of brain function in people with schizophrenia?

Luck et al (2009, Psychophysiology)

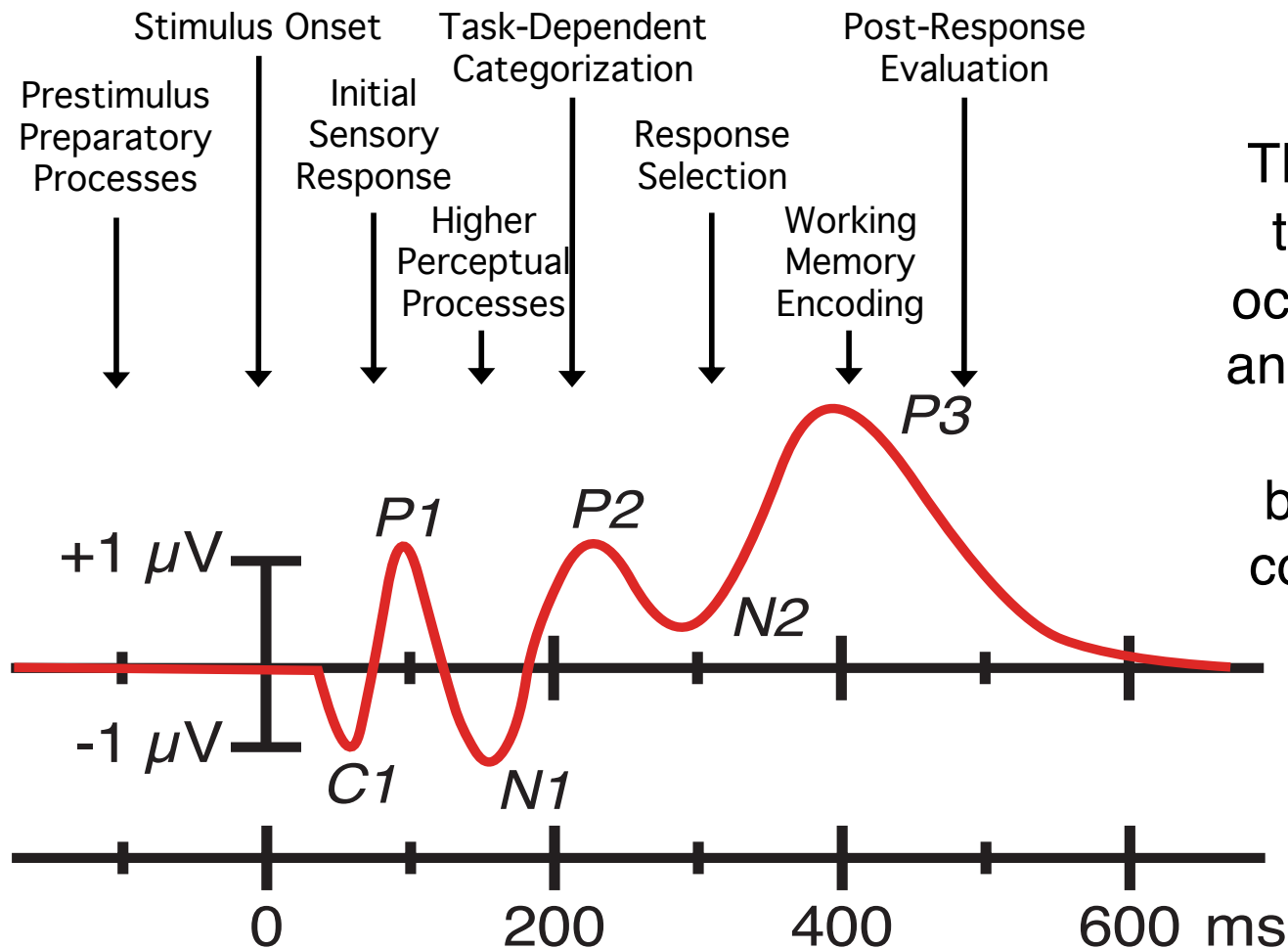
## ERP elicited by rare targets



How is the temporal resolution of the ERP technique any different from the temporal resolution of response time?

ERPs provide a continuous measure of activity at each moment in time.

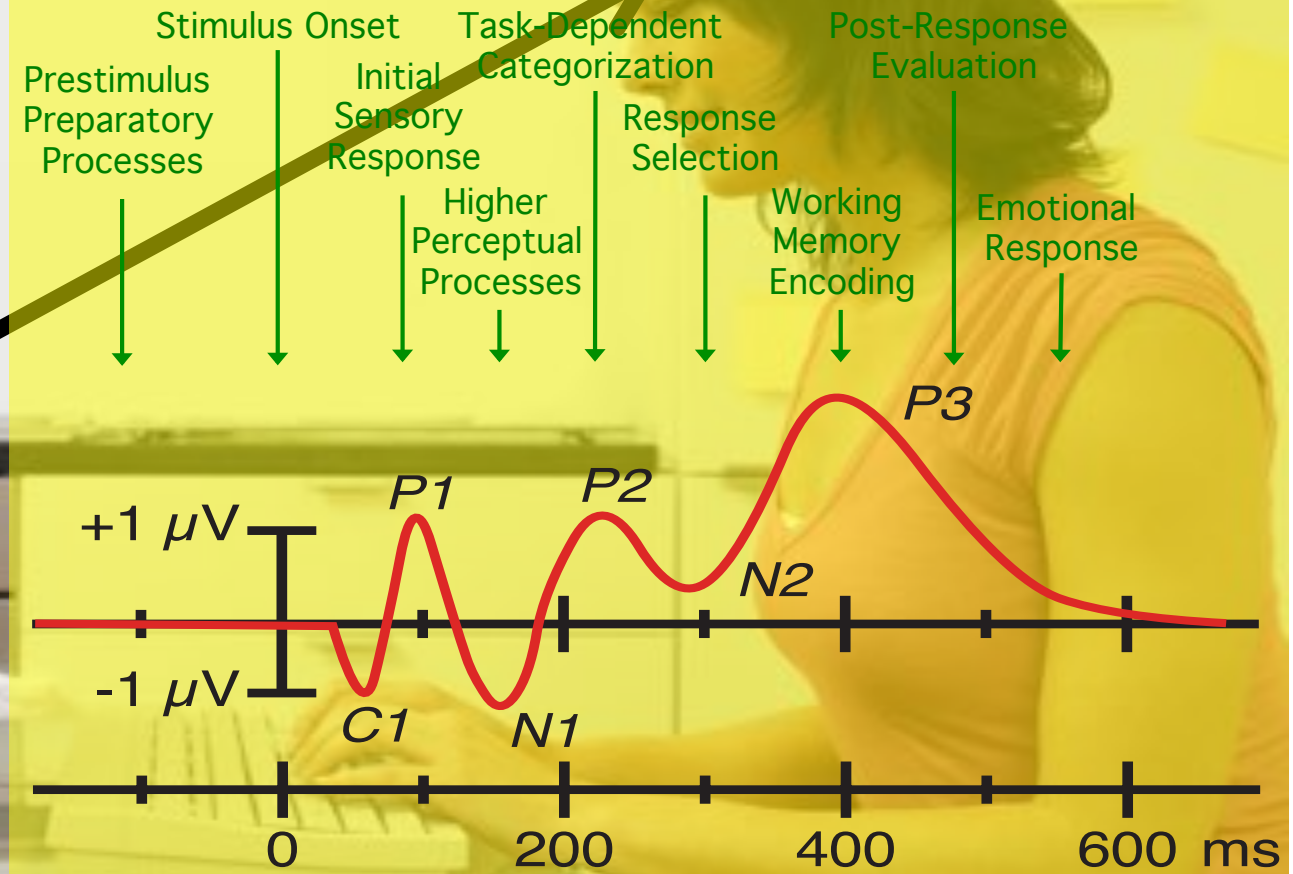
This allows us to measure the brain processes that occur between the stimulus and the response instead of just measuring the behavioral response that comes at the end of these processes.

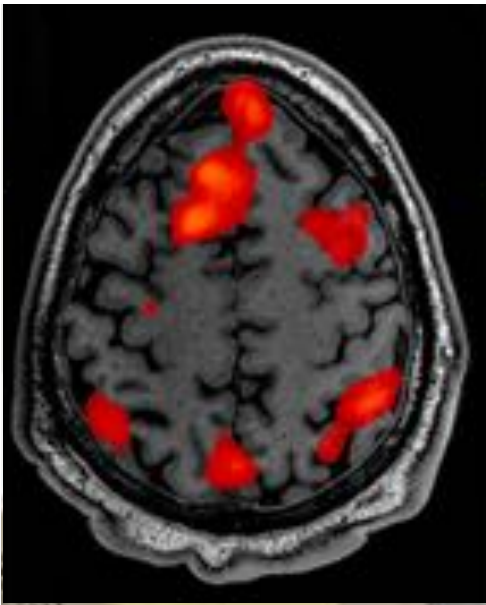


ERPs allow us to measure the "good stuff"

All the good stuff

Stimulus

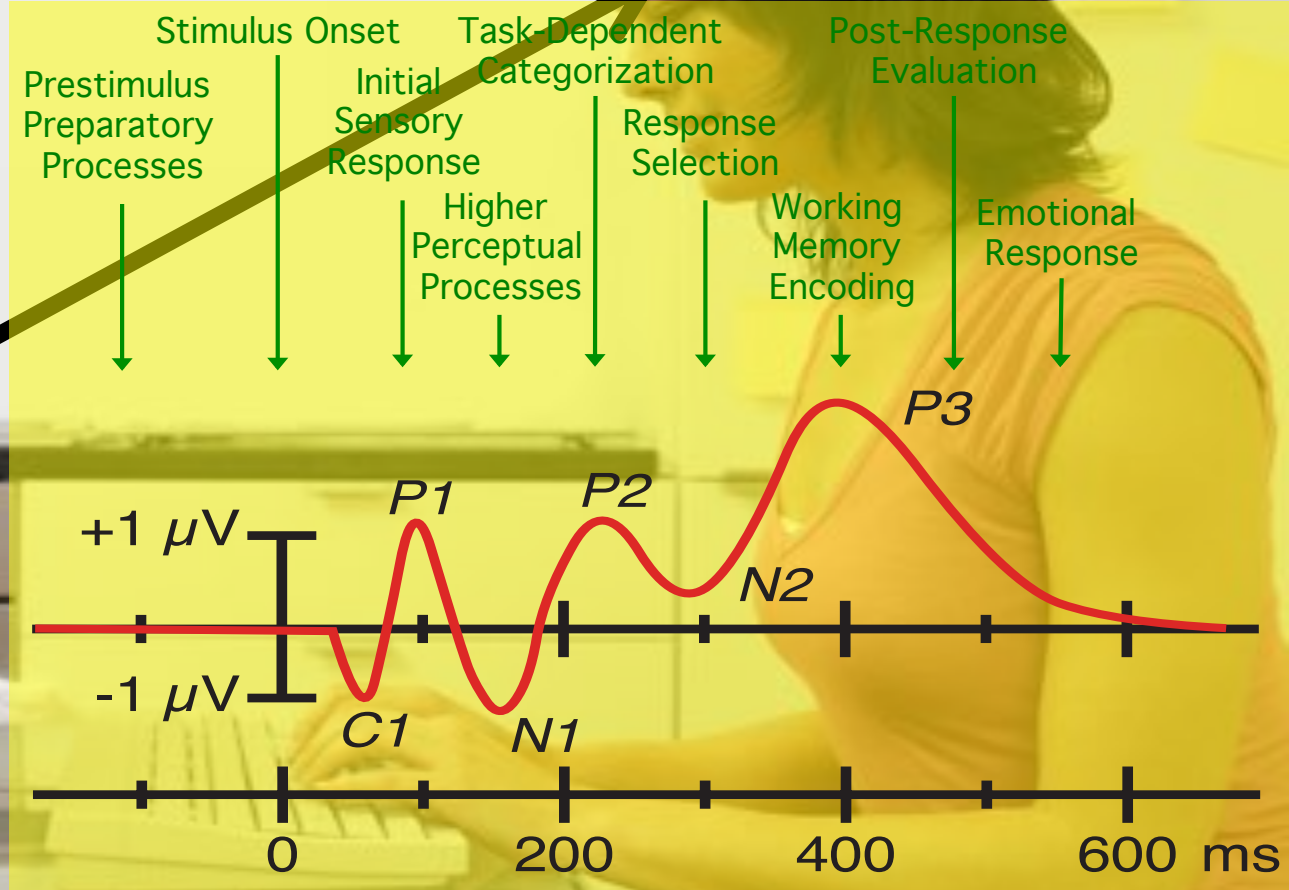




ERPs allow us to measure the "good stuff"

All the good stuff

In fMRI, all of these processes are collapsed into a single time slice.



What is the main virtue of  
the ERP technique?

A Continuous, High Temporal  
Resolution Signal



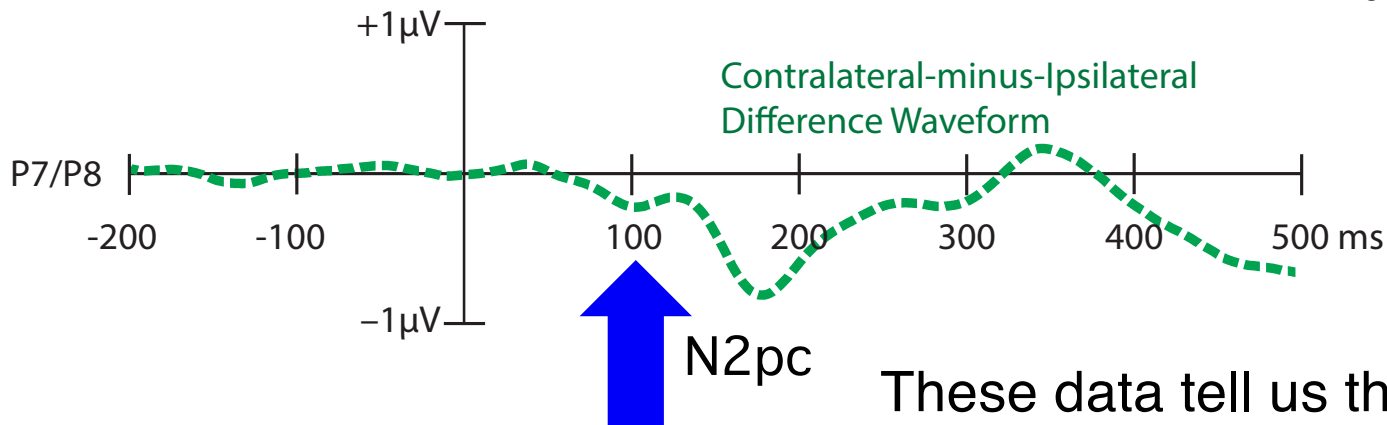
## N2pc to Threat Images



+

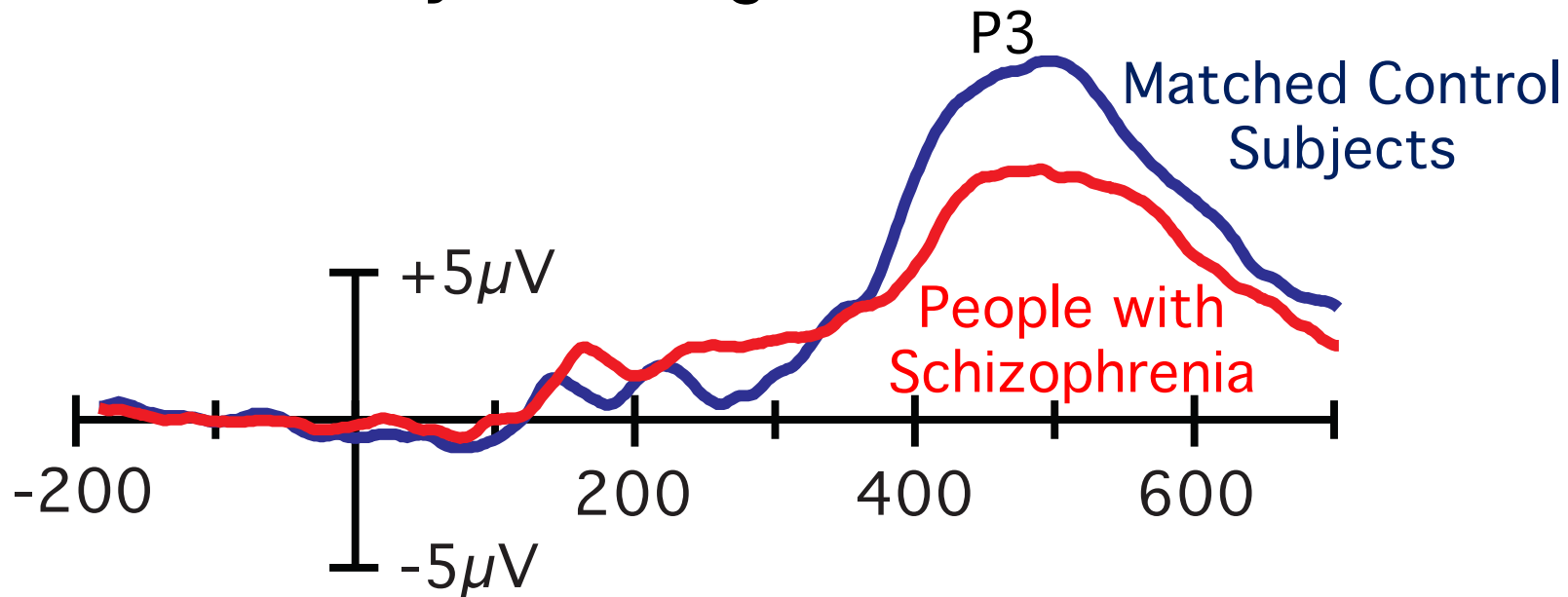


A common use of this temporal resolution is to track processes that are difficult to see directly in behavior.



These data tell us that the threat and neutral images are differentially processed by the brain as early as 100 ms after stimulus onset.

## ERP elicited by rare targets



Another common use of the temporal resolution of the ERP technique is to determine the nature of a difference in behavior between experimental conditions or between groups of subjects.

Luck et al (2009, Psychophysiology)

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# What Are ERPs Good For?

## ERP Latencies: The P3 Wave



### Augmenting Mental Chronometry: The P300 as a Measure of Stimulus Evaluation Time

*Abstract. A technique for measuring the latency of the P300 component of event-related brain potentials on individual trials is described. Choice reaction times and the latency of the P300 were compared under speed-maximizing and under accuracy-maximizing instructions. The choice stimuli required different levels of semantic categorization. The data support the proposition that the latency of P300 corresponds to stimulus evaluation time and is independent of response selection.*

In his 1938 survey of experimental psychology, Woodworth (1) ventured the hope that "brain waves" might be used in the timing of mental events: "the 'speed of thought' we say; but as soon as we set about measuring the time occupied by a thought we find that the beginning and end of any measurable time must be external events. We may in the future use 'brain waves' as indicators of the beginning and end of a mental process . . . but in general it has seemed necessary to let the timed process start with a sensory stimulus and terminate with a muscular response." In the decades that followed, it became clear that while the electroencephalogram (EEG) can be a useful index of neural pathology and global changes in a subject's state, it cannot support studies of the timing of specific mental events; the suggestion that brain waves may play such a role is absent from the second edition of Woodworth's book (2).

Yet, the need for an index of the timing of mental processes, independent of

response selection and execution time, is as acute now as in the earliest days of mental chronometry (1). Much of contemporary cognitive psychology (3) is concerned with the analysis of mental events into their presumed stages. The traditional approach to this problem using reaction time (RT) could be complemented by a measure of stimulus processing that is independent of overt motor responses. In this report we present evidence that the P300 component of the human event-related brain potential (ERP) can serve as such an index for measuring stimulus evaluation time.

The P300 is elicited by a class of task-relevant events (4, 5). Its amplitude has been shown to be directly proportional to the "surprise value" (the reciprocal of expectancy) of a stimulus (6). However, before a stimulus can surprise it must be identified. As P300 commonly appears as a discriminative response to specific stimuli within a series, its elicitation must be preceded by an adequate evaluation of the stimulus at some level of pro-

SCIENCE, VOL. 197

Robert	<i>Standard</i>
William	<i>Standard</i>
George	<i>Standard</i>
Michael	<i>Standard</i>
James	<i>Standard</i>
Richard	<i>Standard</i>
Kevin	<i>Standard</i>
Nancy	<i>Oddball</i>
David	<i>Standard</i>
John	<i>Standard</i>
Brian	<i>Standard</i>
Charles	<i>Standard</i>
Sarah	<i>Oddball</i>
Paul	<i>Standard</i>

Kutas, M., G. McCarthy, & E. Donchin. (1977). Augmenting mental chronometry: The P300 as a measure of stimulus evaluation time. *Science*, 197, 792-795.

P3 amplitude is sensitive to the probability of the task-defined category, not the probability of the physical stimulus

80% of the names were typical American male names. 20% of the names were typical female names. Each individual name only appeared once for a given subject.

Because 80% of the stimuli were male names and 20% were female names, the male names were standards and the female names were oddballs.

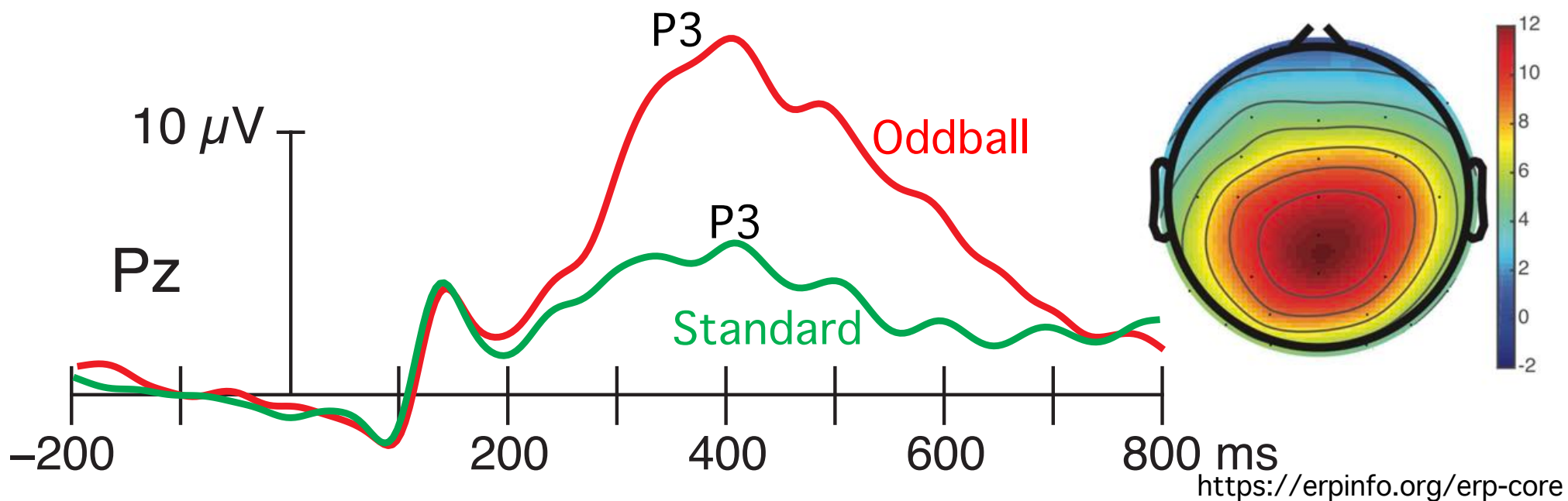
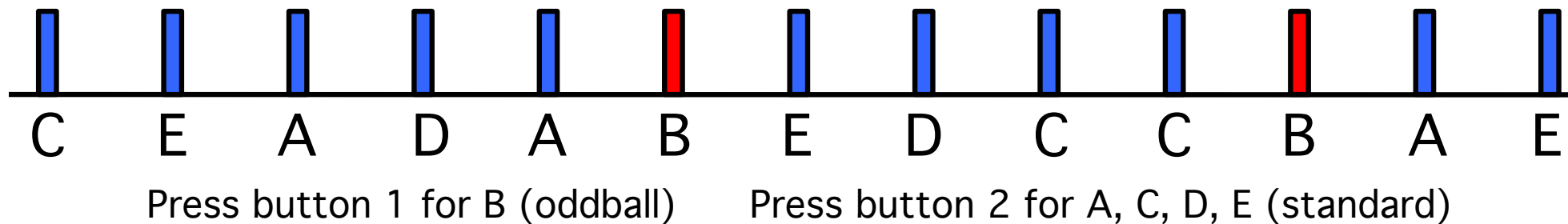
Button 1: Male Names (80%)

Button 2: Female Names (20%)

Kutas, M., G. McCarthy, & E. Donchin. (1977). Augmenting mental chronometry: The P300 as a measure of stimulus evaluation time. *Science*, 197, 792-795.

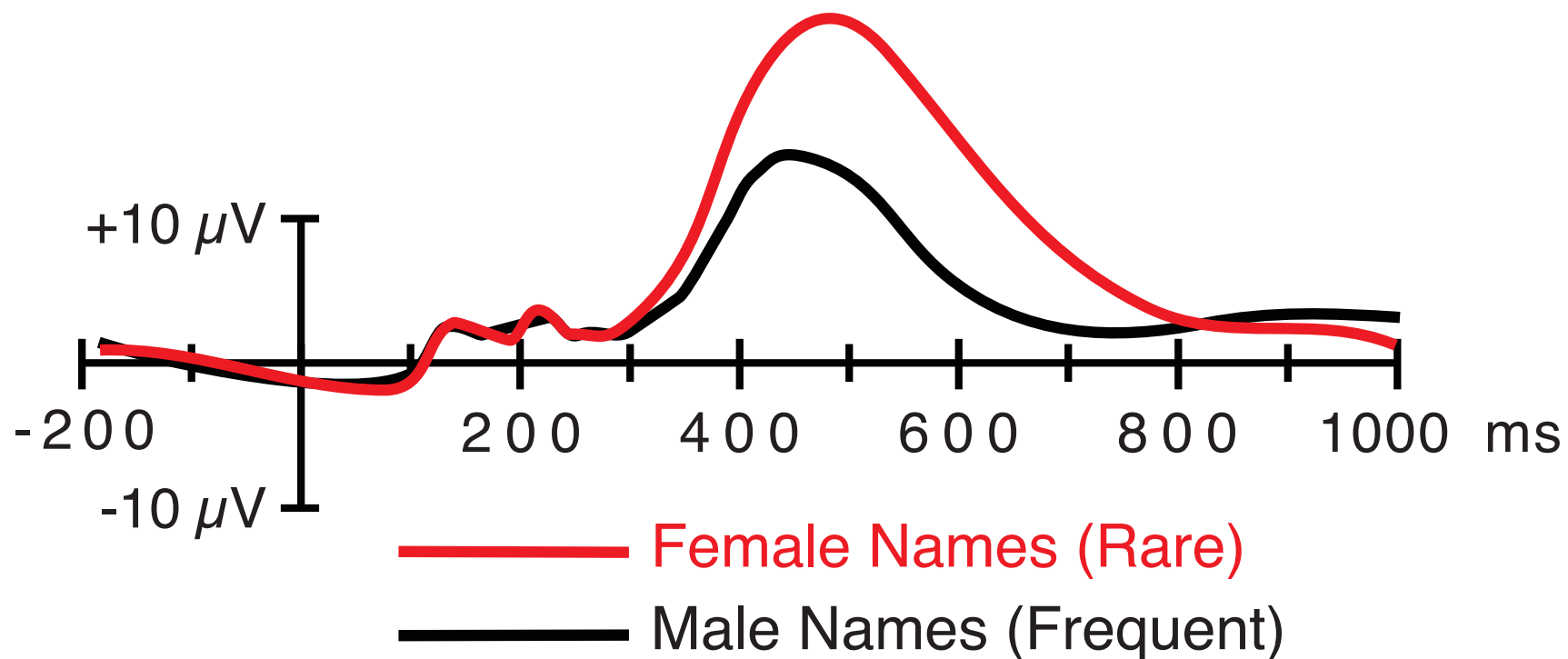
George	<i>Standard</i>
Michael	<i>Standard</i>
James	<i>Standard</i>
Richard	<i>Standard</i>
Kevin	<i>Standard</i>
Nancy	<i>Oddball</i>
David	<i>Standard</i>
John	<i>Standard</i>
Brian	<i>Standard</i>
Charles	<i>Standard</i>
Sarah	<i>Oddball</i>
Paul	<i>Standard</i>

P3 amplitude is sensitive to the probability of the task-defined category, not the probability of the physical stimulus

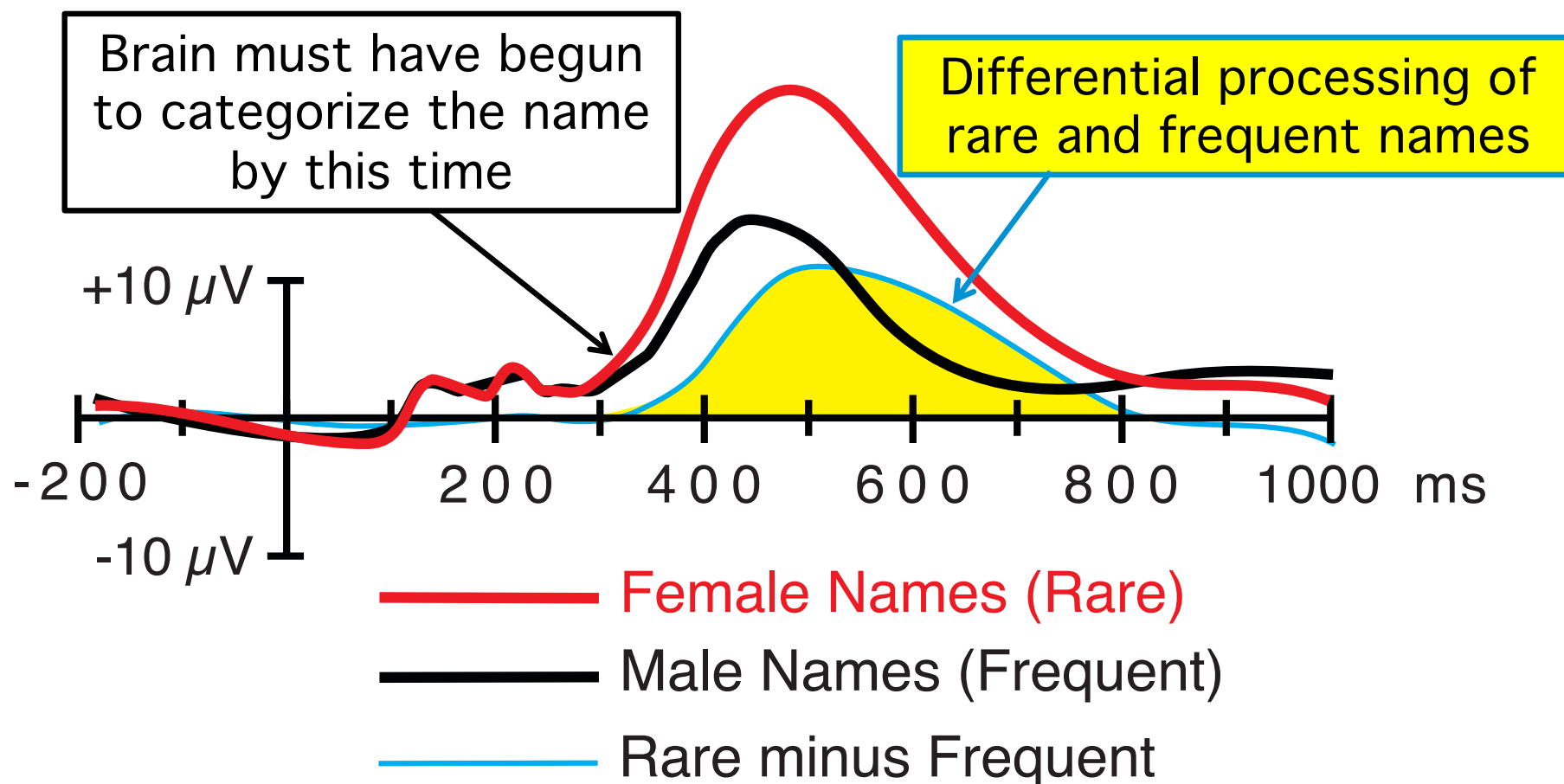


P3 amplitude is sensitive to the probability of the task-defined category, not the probability of the physical stimulus

Kutas et al. (1977) found that the rare female names generated a larger P3 than the frequent male names even though any individual male or female name was presented only once.



P3 amplitude is sensitive to the probability of the task-defined category, not the probability of the physical stimulus





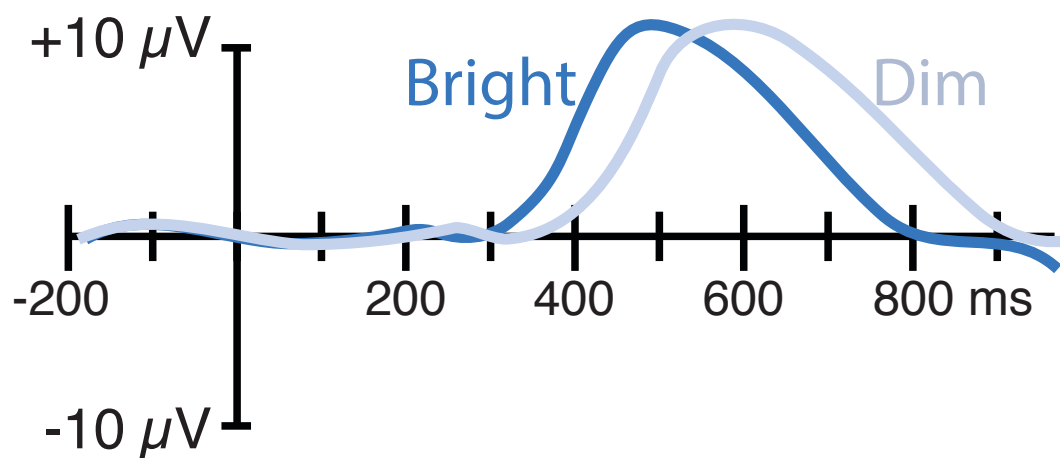
If we delay perception, then we delay categorization

If we delay categorization, we delay the onset of the rare–frequent difference

Imagine that we made the names dimmer.  
This would increase the amount of time it  
takes to perceive each name.

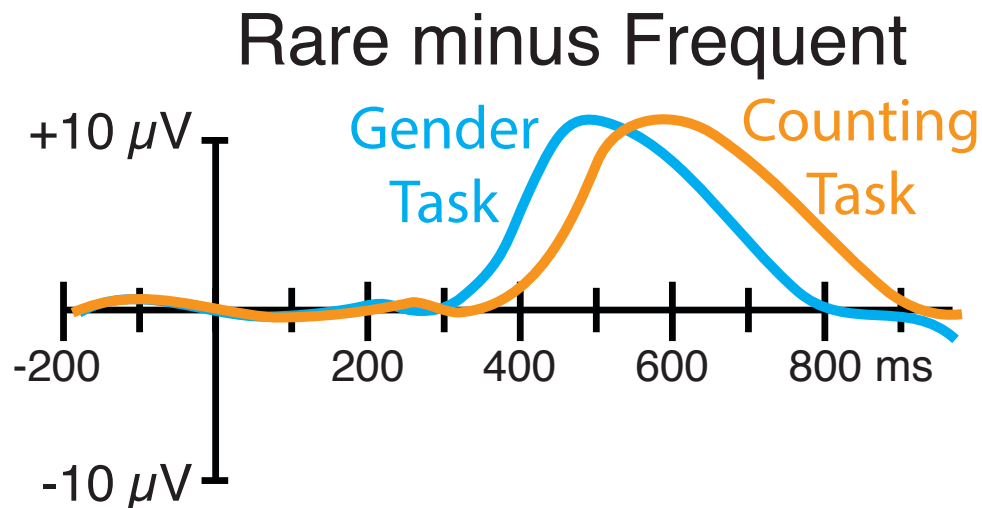
George	<i>Standard</i>
Michael	<i>Standard</i>
James	<i>Standard</i>
Richard	<i>Standard</i>
Kevin	<i>Standard</i>
Nancy	<i>Oddball</i>
David	<i>Standard</i>
John	<i>Standard</i>
Brian	<i>Standard</i>
Charles	<i>Standard</i>
Sarah	<i>Oddball</i>
Paul	<i>Standard</i>

## Rare minus Frequent



If we delay categorization, we delay the onset of the rare–frequent difference

Imagine that the task was to count the letters in each name and press one of two buttons to indicate whether it was an odd number or an even number. If we make odd numbers rare and even numbers frequent, we could make a rare-minus-frequent difference wave.



William	<i>Standard</i>
George	<i>Standard</i>
John	<i>Standard</i>
Sara	<i>Standard</i>
Lisa	<i>Standard</i>
Carter	<i>Standard</i>
Kevin	<i>Oddball</i>
Alison	<i>Standard</i>
Steven	<i>Standard</i>
Edward	<i>Standard</i>
Paul	<i>Standard</i>
Susan	<i>Oddball</i>
Gene	<i>Standard</i>

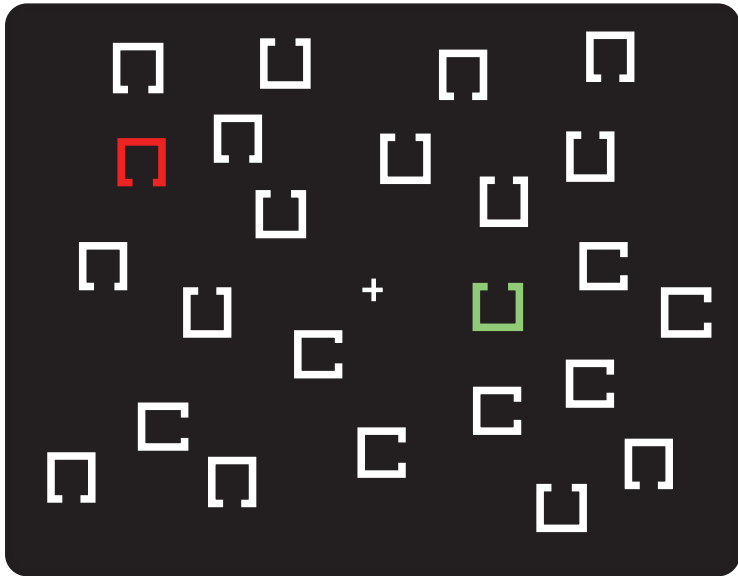
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# What Are ERPs Good For?

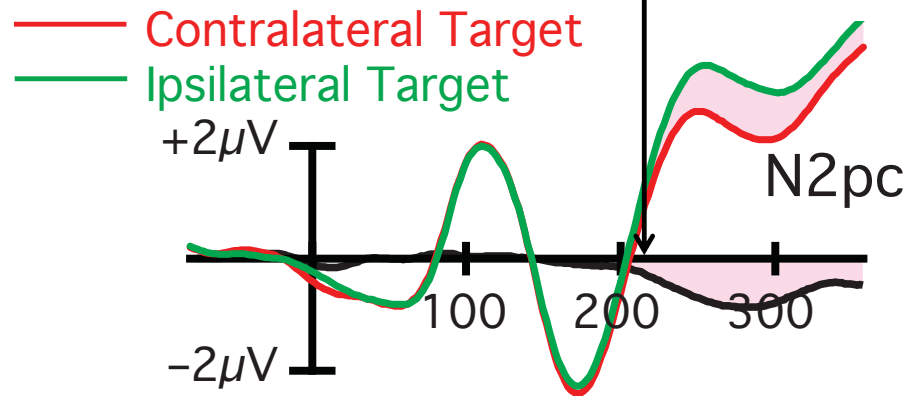
ERP Latencies:  
N2pc & LRP



N2pc



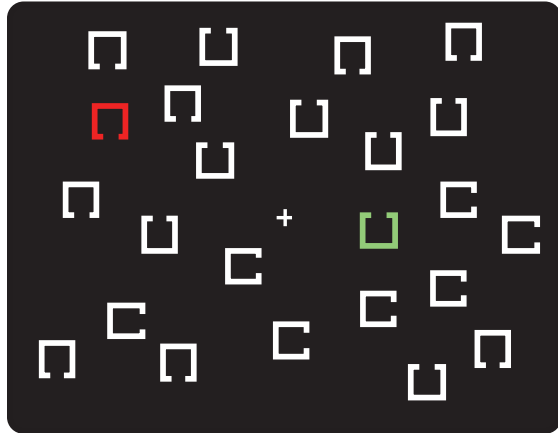
Brain must have figured out the location of the target by this time



Logically, the voltage can't be more negative over the contralateral hemisphere than over the ipsilateral hemisphere until the brain has determined whether the target is on the left or the right side of the display.

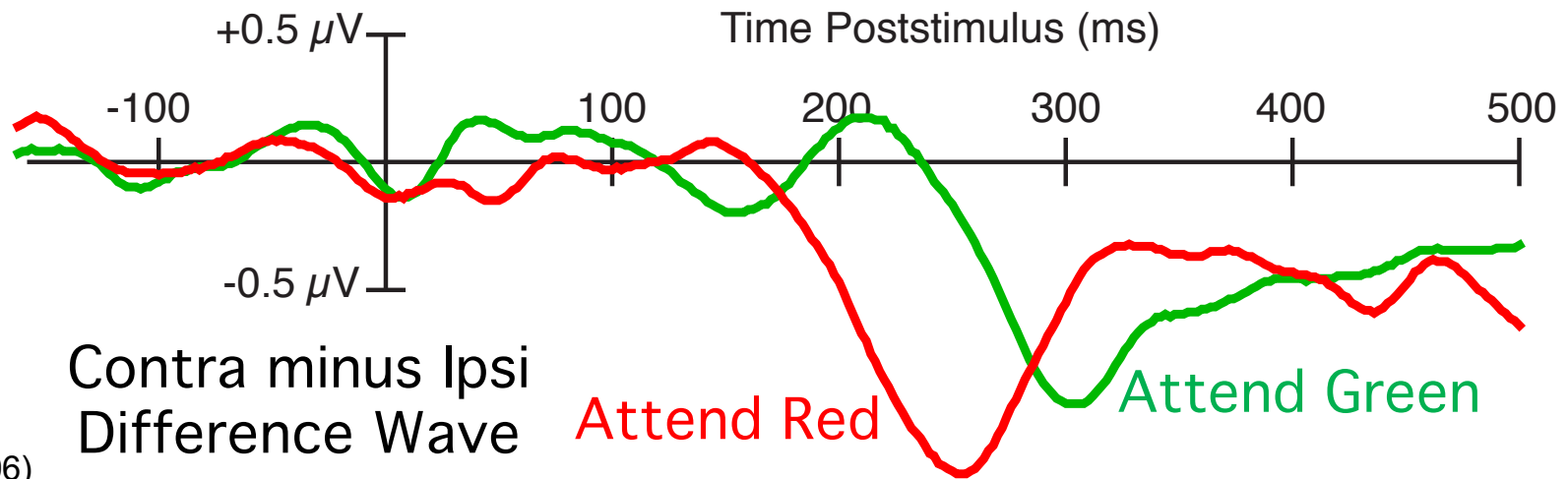
If you look at a contra-minus-ipsi difference wave, you can know that the brain has localized the target by the time the difference wave deviates from zero.

## N2pc

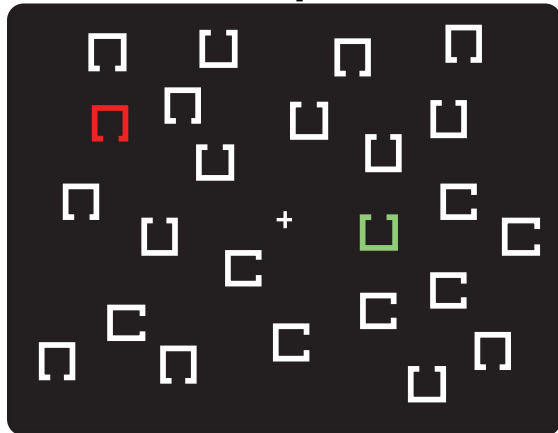


The red item immediately popped out from the display, but the green item was a little harder to detect. The response times were about 50 milliseconds slower in the attend-green condition than in the attend-red condition.

The N2pc is delayed by ~50 milliseconds in the attend-green condition relative to the attend-red condition.

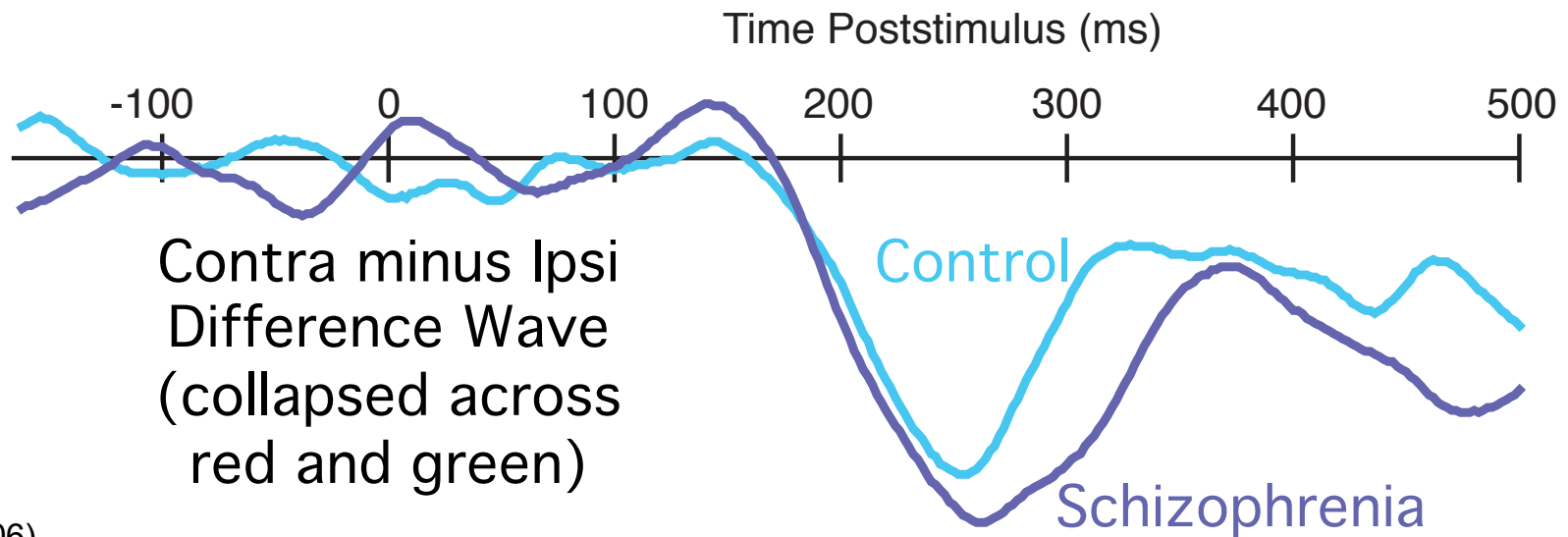


## N2pc



The onset time of the N2pc was essentially identical in the two groups.

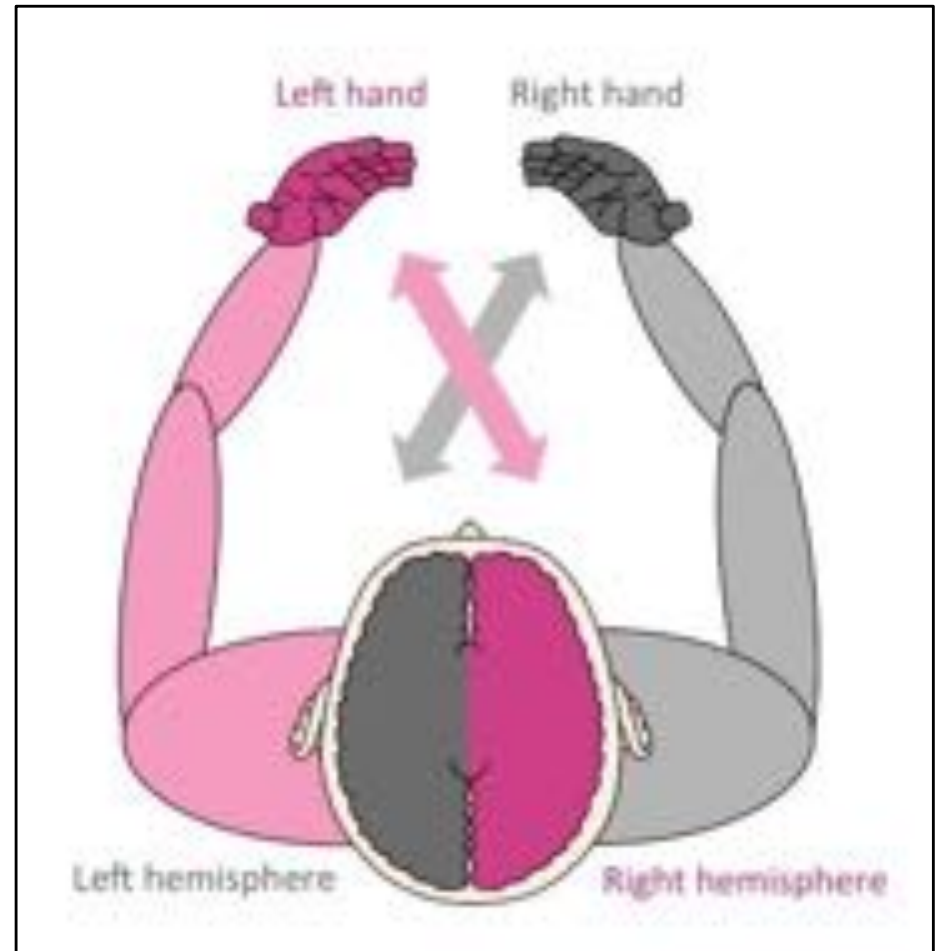
We concluded that schizophrenia does not slow down the process of finding the target and shifting attention to it.



# Lateralized Readiness Potential (LRP)

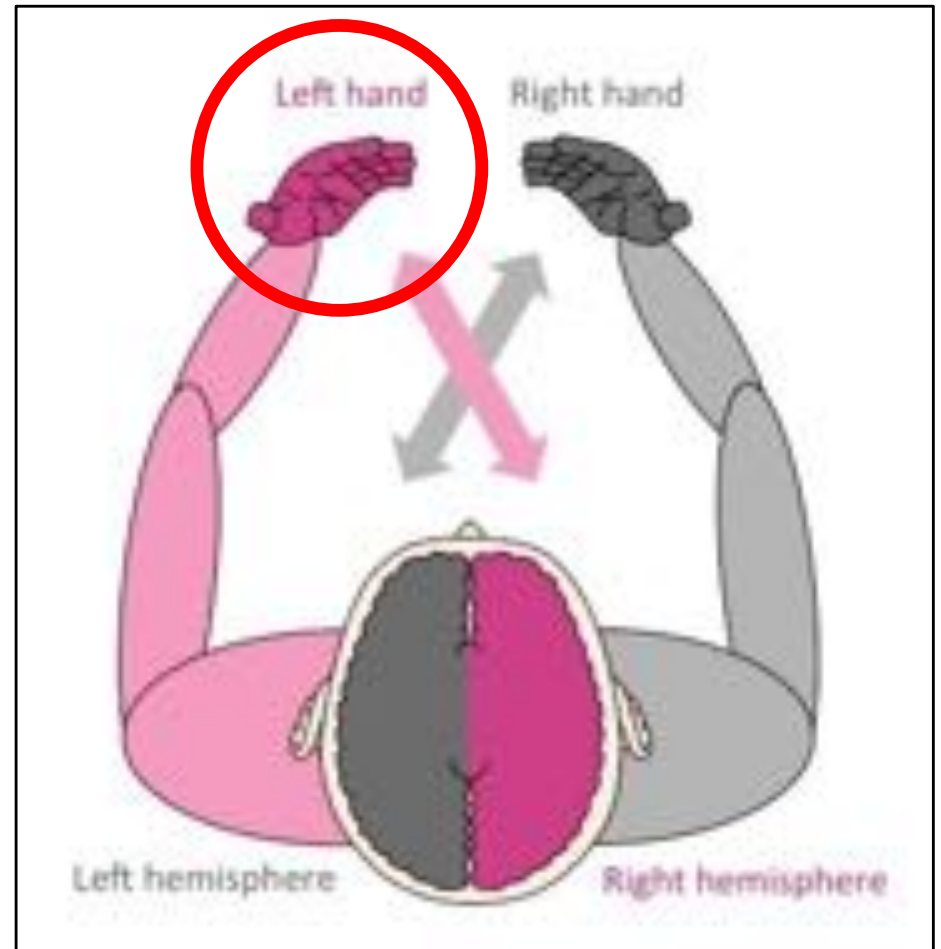
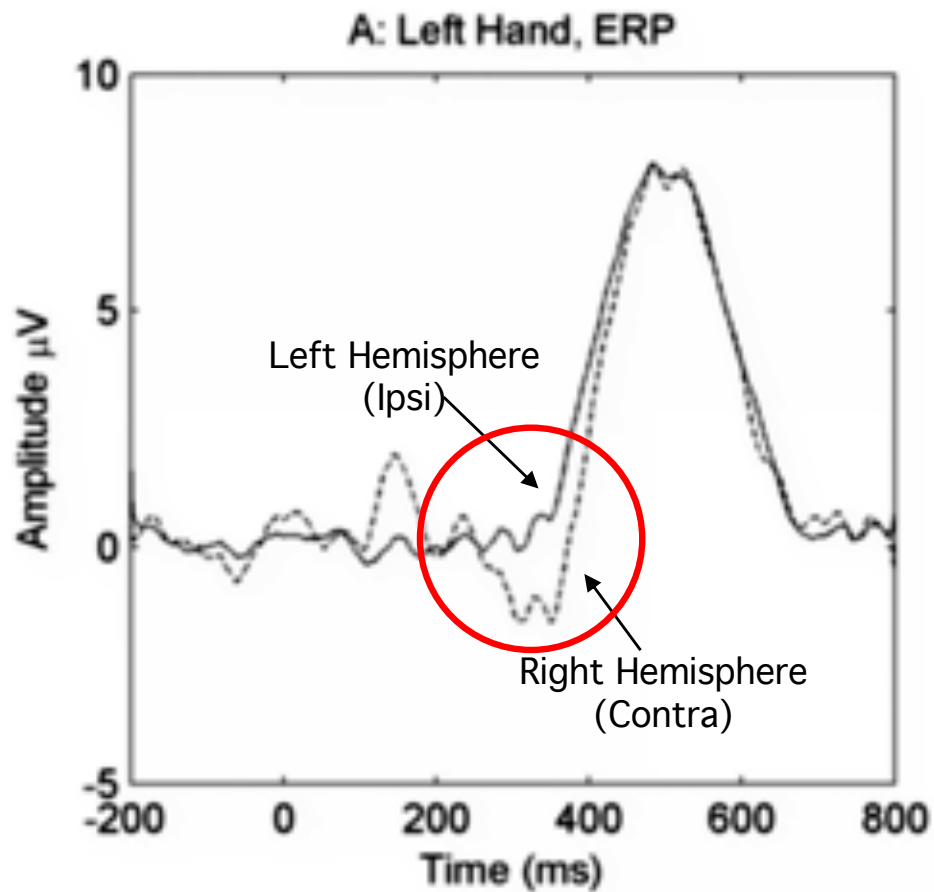
3

LRP = negative voltage over motor cortex contralateral to the response hand



<https://ib.bioninja.com.au/options/option-a-neurobiology-and/a2-the-human-brain/cerebral-hemispheres.html>

# Lateralized Readiness Potential (LRP)

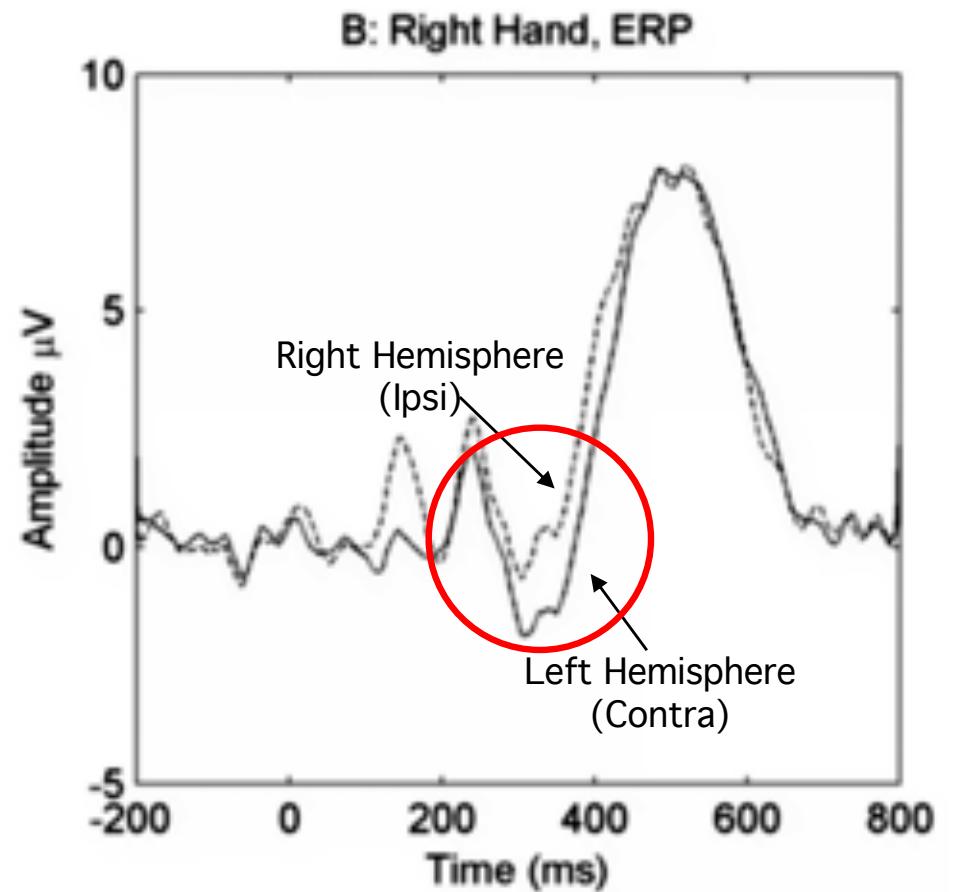
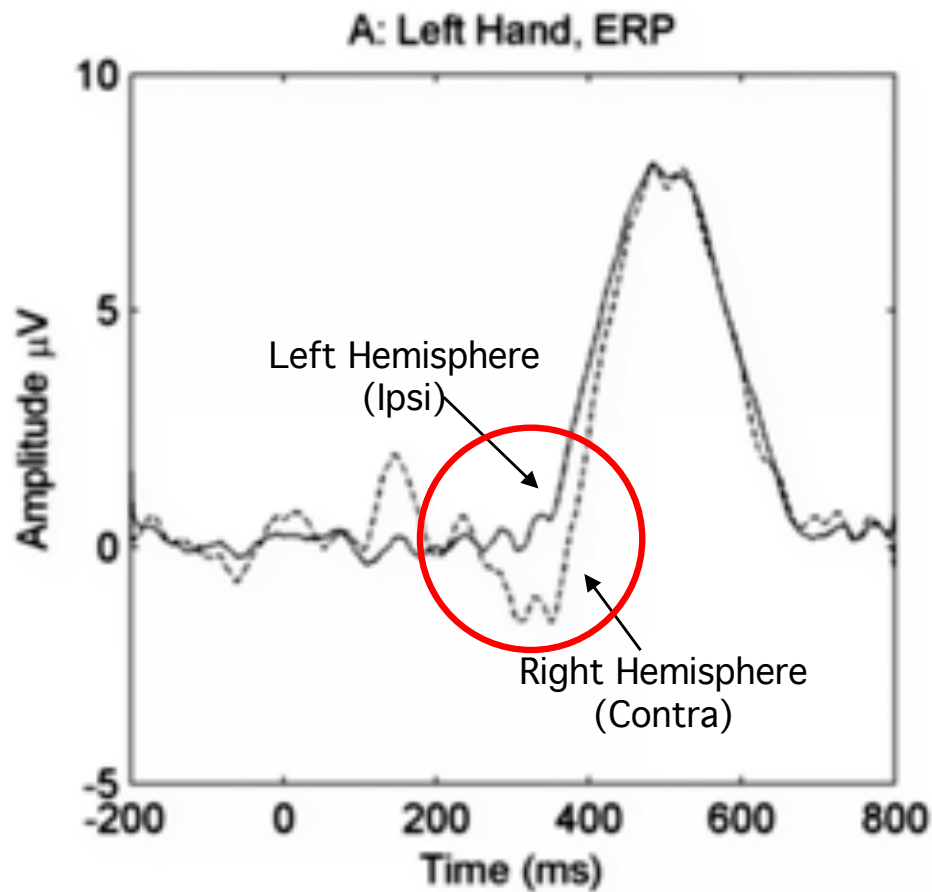


Smulders & Miller (2010)

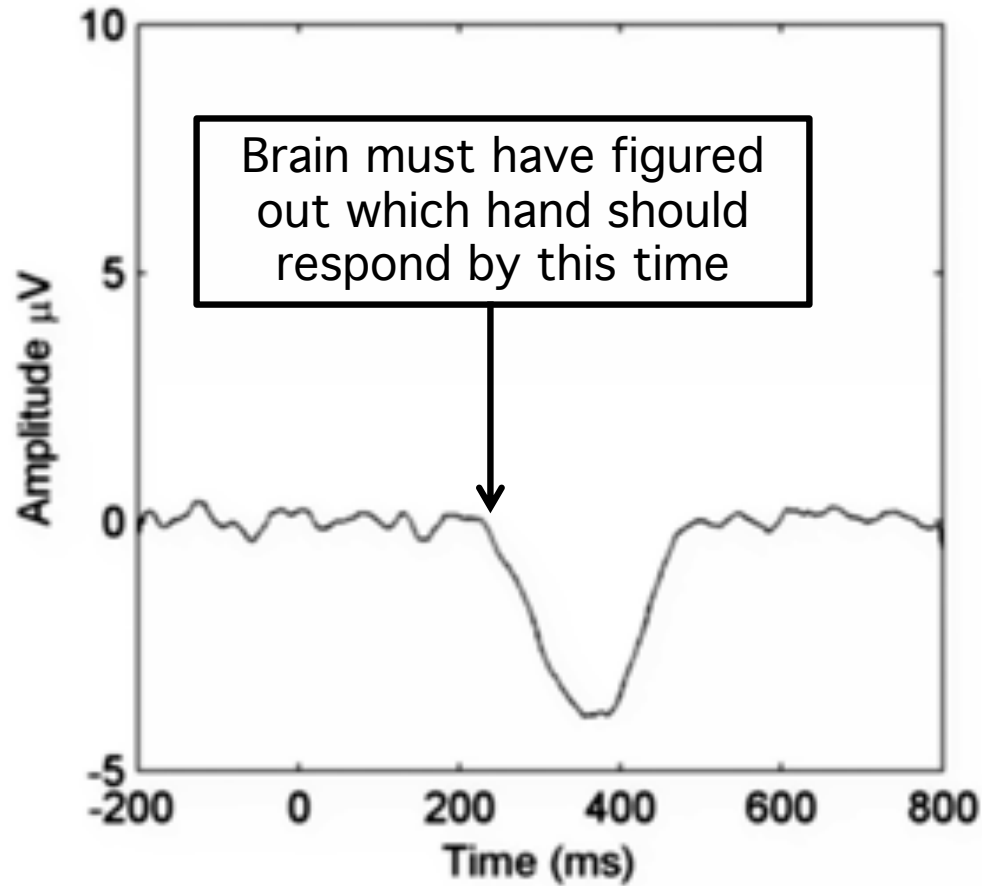
<https://ib.bioninja.com.au/options/option-a-neurobiology-and/a2-the-human-brain/cerebral-hemispheres.html>



# Lateralized Readiness Potential (LRP)



# Lateralized Readiness Potential (LRP)



LRP = Contralateral minus ipsilateral, averaged over left & right hands

Smulders & Miller (2010)

## **Imaging unconscious semantic priming**

**Stanislas Dehaene<sup>\*</sup>, Lionel Naccache<sup>\*</sup>, Gurvan Le Clec<sup>H</sup>,  
Etienne Koechlin<sup>\*</sup>, Michael Mueller<sup>\*</sup>,  
Ghislaine Dehaene-Lambertz<sup>†</sup>,  
Pierre-François van de Moortele<sup>‡</sup> & Denis Le Bihan<sup>‡</sup>**

<sup>\*</sup>INSERM U.334, Service Hospitalier Frédéric Joliot, CEA/DRM/DSV,  
4 Place du Général Leclerc, 91401 Orsay, France

<sup>†</sup>Laboratoire de Sciences Cognitives et Psycholinguistique, EHESS/CNRS,  
75270 Paris cedex 06, France

<sup>‡</sup>Service Hospitalier Frédéric Joliot, CEA/DRM/DSV, 91401 Orsay, France

Visual words that are masked and presented so briefly that they cannot be seen may nevertheless facilitate the subsequent processing of related words, a phenomenon called masked priming<sup>1,2</sup>. It has been debated whether masked primes can activate cognitive processes without gaining access to consciousness<sup>3-5</sup>. Here we use a combination of behavioural and brain-imaging techniques to estimate the depth of processing of masked numerical primes. Our results indicate that masked stimuli have a measurable influence on electrical and haemodynamic measures of brain activity. When subjects engage in an overt semantic comparison task with a clearly visible target numeral, measures of covert motor activity indicate that they also unconsciously apply the task instructions to an unseen masked numeral. A stream of perceptual, semantic and motor processes can therefore occur without awareness.

We presented a numeral between 1 and 9, the prime, to subjects for a very short duration (43 ms). The prime was masked by two nonsense letter strings, and followed by another numeral, the target (Fig. 1). Under these conditions, even when subjects focused their attention on the prime, they could neither reliably report its presence or absence nor discriminate it from a nonsense string (Table 1). Nevertheless, we show here that the prime is processed to a high cognitive level.

We asked subjects to perform a simple semantic categorization task on the target numeral. Subjects were asked to press a response key with one hand if the target was larger than 5, and with the other hand if the target was smaller than 5. Unknown to them, each target number was preceded by a masked prime which was varied from trial to trial so it too could be larger or smaller than 5. In some trials the prime was congruent with the target (both numbers fell on the same side of 5), and in other trials it was incongruent (one number being larger than 5, and the other being smaller; Fig. 1). We first established that prime-target congruity has a significant influence on behavioural, electrical and haemodynamic measures of brain function. We then showed that the interference between prime and target can be attributed to a covert, prime-induced activation of motor cortex, a response bias that must be overcome in incongruent trials. This indicates that the prime was unconsciously processed according to task instructions, all the way down to the motor system.

The effect of prime-target congruity on behaviour is shown in Fig. 2. Subjects responded more slowly in incongruent trials than in congruent trials ( $P < 0.0001$ ). All 12 subjects showed a positive priming effect, ranging from 2 to 43 ms (average 24 ms, s.d. 13.5 ms). Furthermore, the entire response time distribution was

Dehaene, S., Naccache, L., Le Clec<sup>H</sup>, G., Koechlin, E., Mueller, M., Dehaene-Lambertz, G., van de Moortele, P. F., & Le Bihan, D. (1998). Imaging unconscious semantic priming. *Nature*, 395, 597-600.

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# What Are ERPs Good For?

Example: P3 Latency  
in Schizophrenia





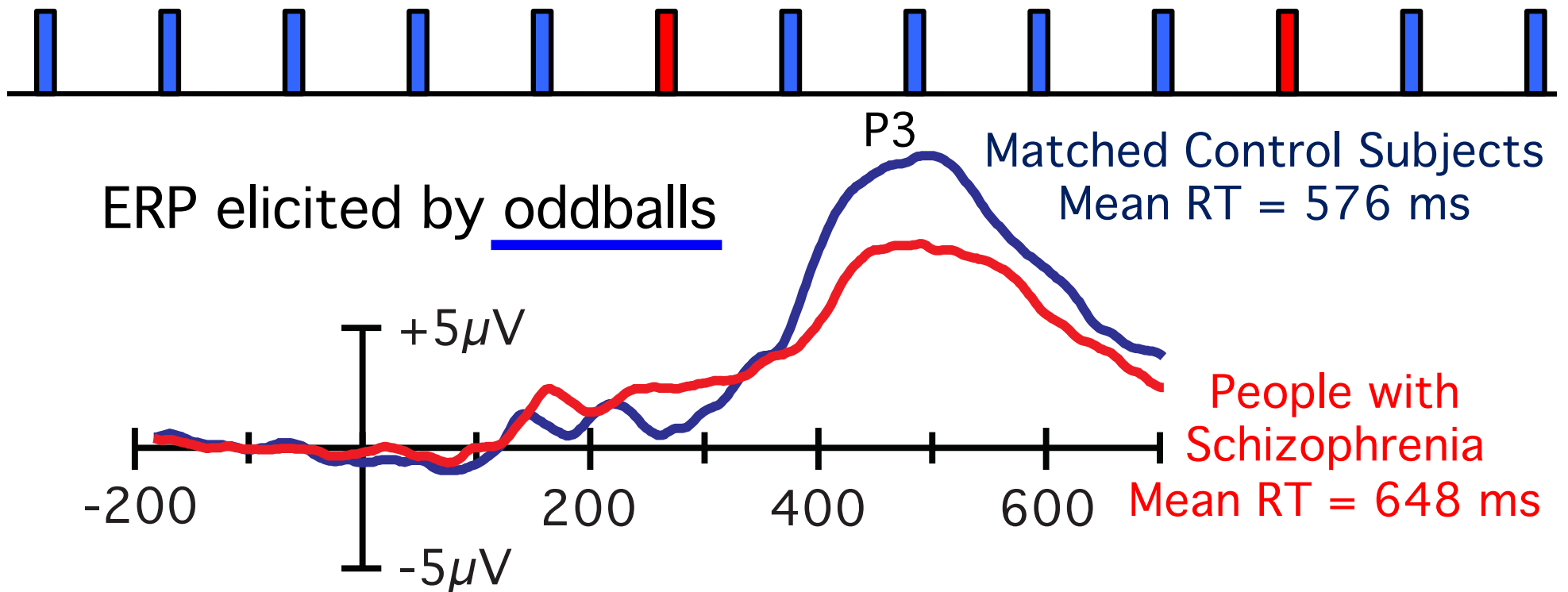
# Schizophrenia

1-2% lifetime prevalence

Characterized by hallucinations,  
delusions, disorganization

The degree of cognitive impairment  
is a better predictor of long-term  
outcome than the degree of  
hallucinations, delusions, and  
disorganized thought

<http://anndeef.deviantart.com/art/Schizophrenia-269518412>  
Creative Commons Attribution-Share Alike 3.0 License



Most studies find a reduced amplitude in people with schizophrenia compared to matched control subjects.

RTs are slowed, but the P3 is not.

Luck et al (2009, Psychophysiology)

## reaction time and attention in schizophrenia: a critical evaluation of the data and theories\*

Keith H. Nuechterlein

### Introduction

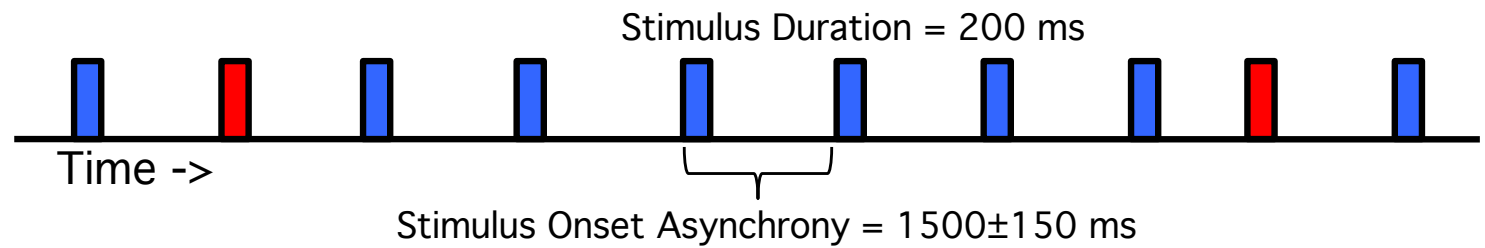
The literature on schizophrenia is a voluminous one, the size of which is in part determined by the multiplicity of the contradictions. There is a marvelous value in this since one can, on an *ad hoc* basis, claim that virtually anything has been demonstrated and be correct. Despite the usefulness of this contradictory literature, as a practical ego support it presents real problems. One research strategy in coping with this state of affairs is to seek out those findings which have been consistently replicated. The reaction time (RT) studies are the closest thing to a north star in schizophrenia research. [Cancro et al. 1971, p. 352]

gamut from basic structural to learned to motivational preferences among theorists.

The predominant hypotheses in RT research, however, are in the realm of attention, an area that has been central to both clinical and experimental work on schizophrenia for many years. Eugen Bleuler, for example, had noted some disturbances of attention in schizophrenia in his classic work, *Dementia Praecox or the Group of Schizophrenias*, first published in English in 1950 but originally in German in 1911:

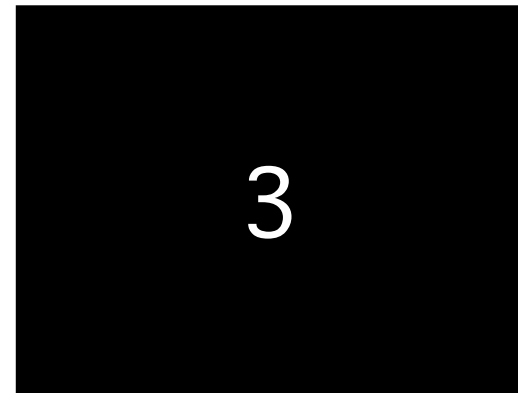
As a partial phenomenon of affectivity, attention is affected with it by deterioration. Insofar as in-

Nuechterlein, K. H. (1977). Reaction time and attention in schizophrenia: A critical evaluation of the data and theories. *Schizophrenia Bulletin*, 3(3), 373-428.



= Letters, 80%, Press Left  
 = Digits, 20%, Press Right

} Counter-balanced



*Psychophysiology*, 46 (2009), 776–786. Wiley Periodicals, Inc. Printed in the USA.  
 Copyright © 2009 Society for Psychophysiological Research  
 DOI: 10.1111/j.1469-8986.2009.00817.x

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### Impaired response selection in schizophrenia: Evidence from the P3 wave and the lateralized readiness potential

---

STEVEN J. LUCK,<sup>a</sup> EMILY S. KAPPENMAN,<sup>a</sup> REBECCA L. FULLER,<sup>b</sup>  
 BENJAMIN ROBINSON,<sup>b</sup> ANN SUMMERFELT,<sup>b</sup> AND JAMES M. GOLD<sup>b</sup>

<sup>a</sup>University of California, Davis, California, USA  
<sup>b</sup>Maryland Psychiatric Research Center, Baltimore, Maryland, USA

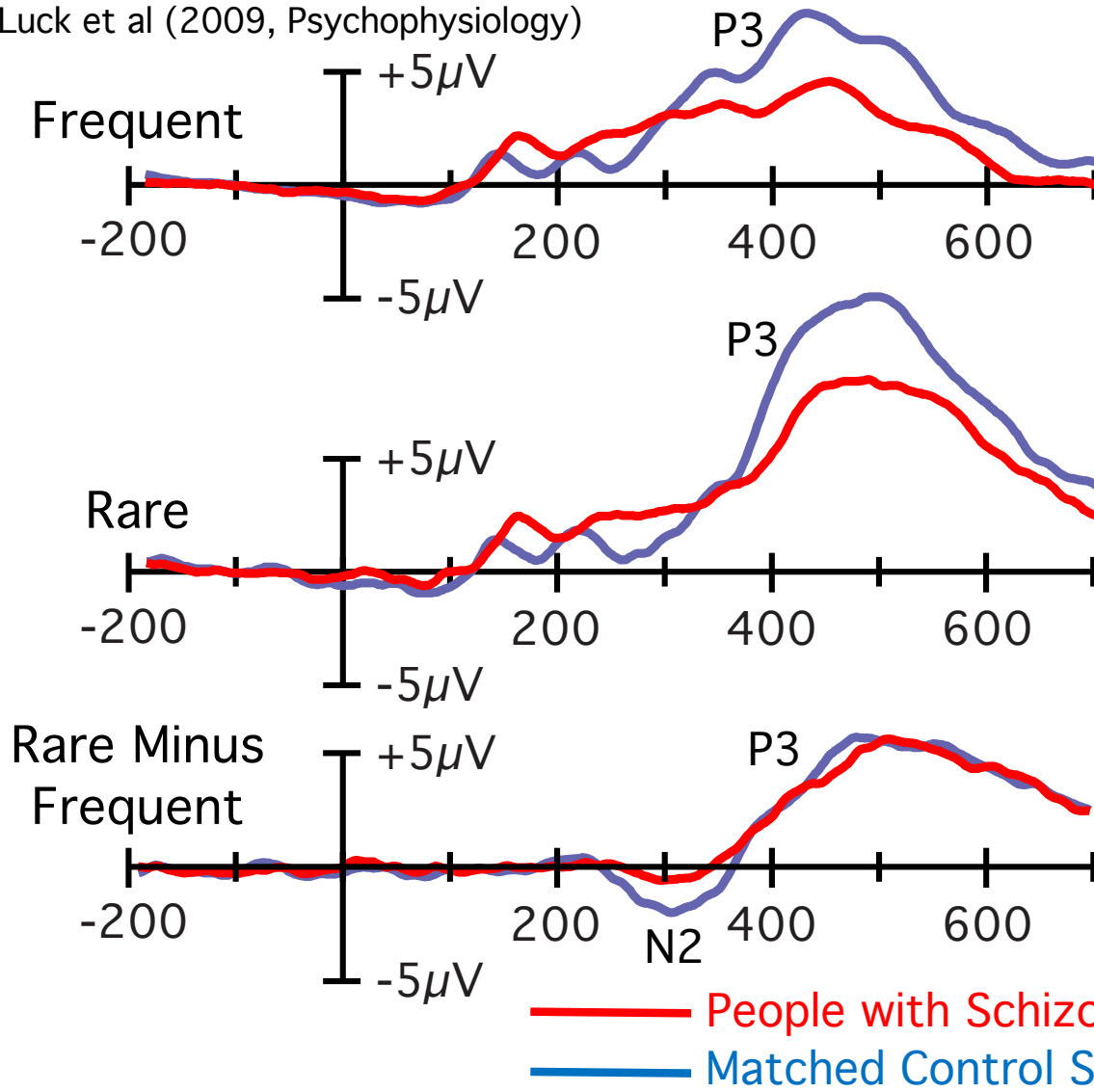
**Abstract**

Reaction times (RTs) are substantially prolonged in schizophrenia patients, but the latency of the P3 component is not. This suggests that the RT slowing arises from impairments in a late stage of processing. To test this hypothesis, 20 schizophrenia patients and 20 control subjects were tested in a visual oddball paradigm that was modified to allow measurement of the lateralized readiness potential (LRP), an index of stimulus-response translation processes. Difference waves were used to isolate the LRP and the P3 wave. Patients and control subjects exhibited virtually identical P3 difference waves, whereas the LRP difference wave was reduced in amplitude and delayed in latency in the patients. These results indicate that, at least in simple tasks, the delayed RTs observed in schizophrenia are primarily a consequence of impairments in the response selection and preparation processes that follow perception and categorization.

Luck, S. J., Kappenman, E. S., Fuller, R. L., Robinson, B., Summerfelt, A., & Gold, J. M. (2009). Impaired response selection in schizophrenia: Evidence from the P3 wave and the lateralized readiness potential. *Psychophysiology*, 46, 776–786.



Luck et al (2009, Psychophysiology)



Control	Schizophrenia
<u>RT</u>	<u>RT</u>

486	557
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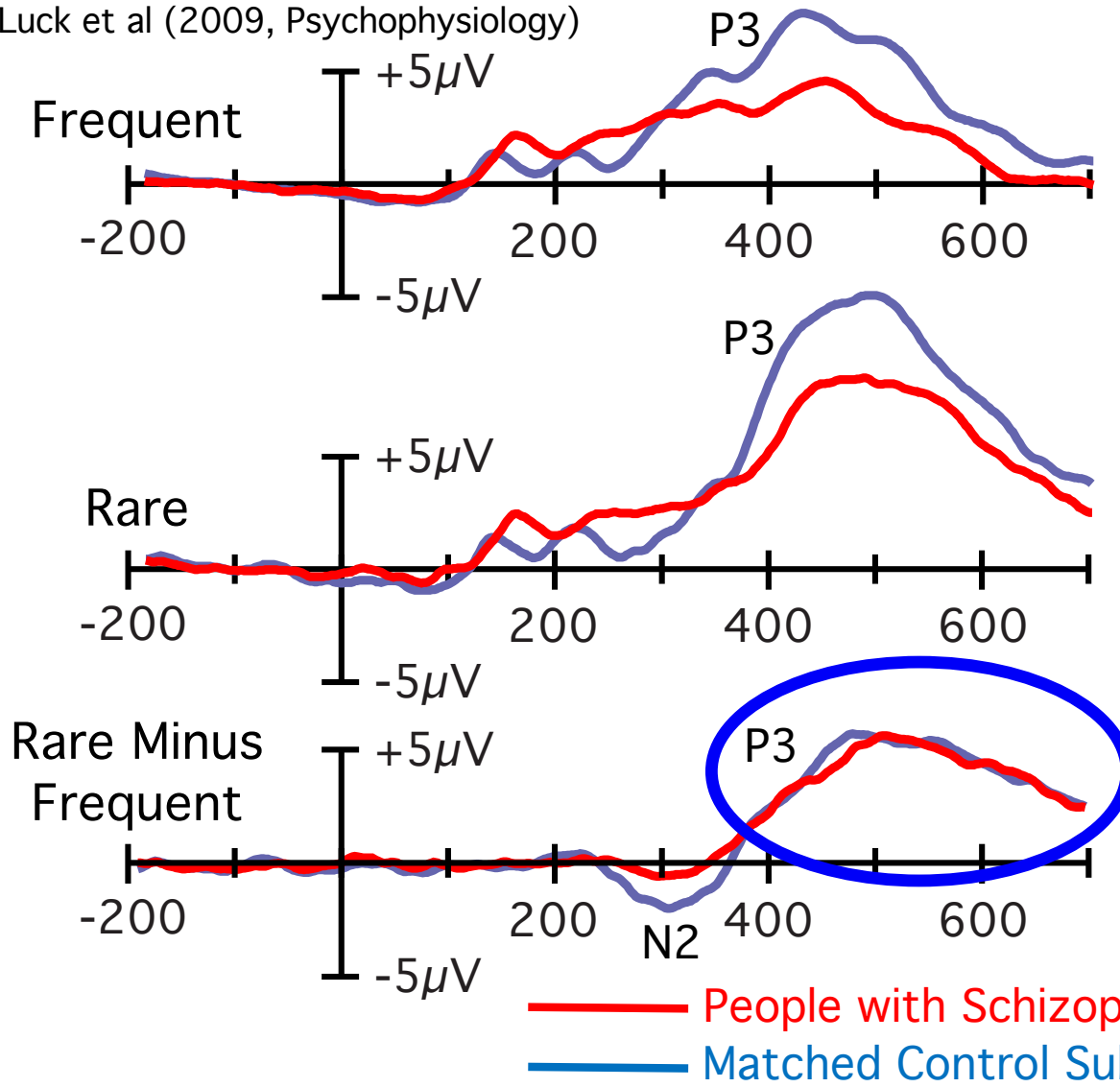
P3 amplitude was smaller in people with schizophrenia than in control subjects for both rare and frequent. Response times were delayed by about 70 ms in the schizophrenia group.

576	648
-----	-----

The P3 was almost identical for the two groups in the rare-minus-frequent difference waves. The control subjects show an N2 that's largely missing in the schizophrenia group, but there was no group difference in the P3 wave.

— People with Schizophrenia  
 — Matched Control Subjects

Luck et al (2009, Psychophysiology)

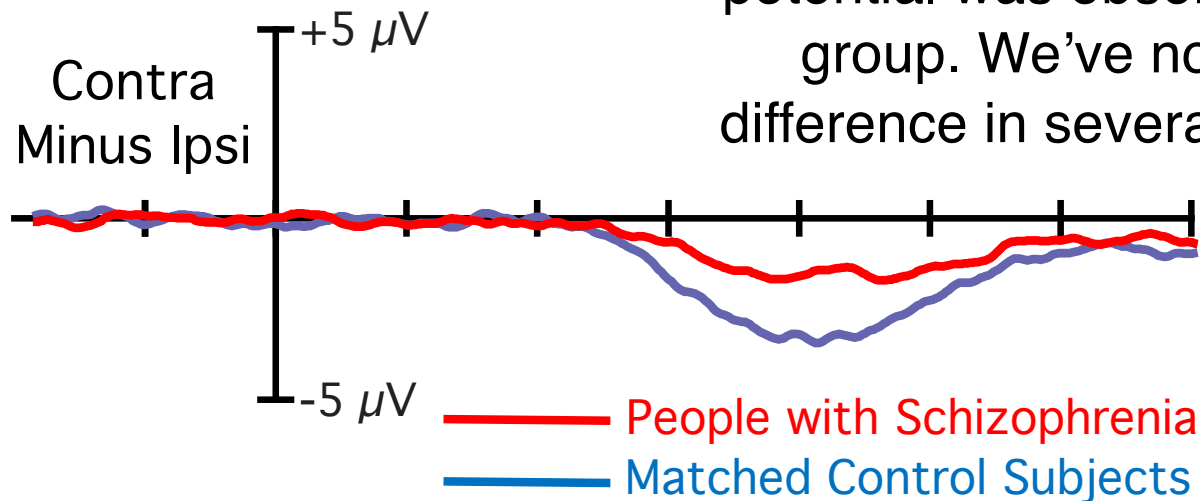


The finding of equivalent timing of the rare-minus-frequent difference in people with schizophrenia and control subjects indicates that the two groups perceived and categorized the stimuli equally quickly.

The difference in response time must therefore reflect some kind of post-categorization slowing, perhaps in response preparation or execution.

# Lateralized Readiness Potential

A major disruption of the lateralized readiness potential was observed in the schizophrenia group. We've now replicated this LRP difference in several additional experiments.



Kappenman, E. S., Kaiser, S. T., Robinson, B. M., Morris, S. E., Hahn, B., Beck, V. M., Leonard, C. J., Gold, J. M., & Luck, S. J. (2012). Response activation impairments in schizophrenia: Evidence from the lateralized readiness potential. *Psychophysiology*, *49*, 73–84.

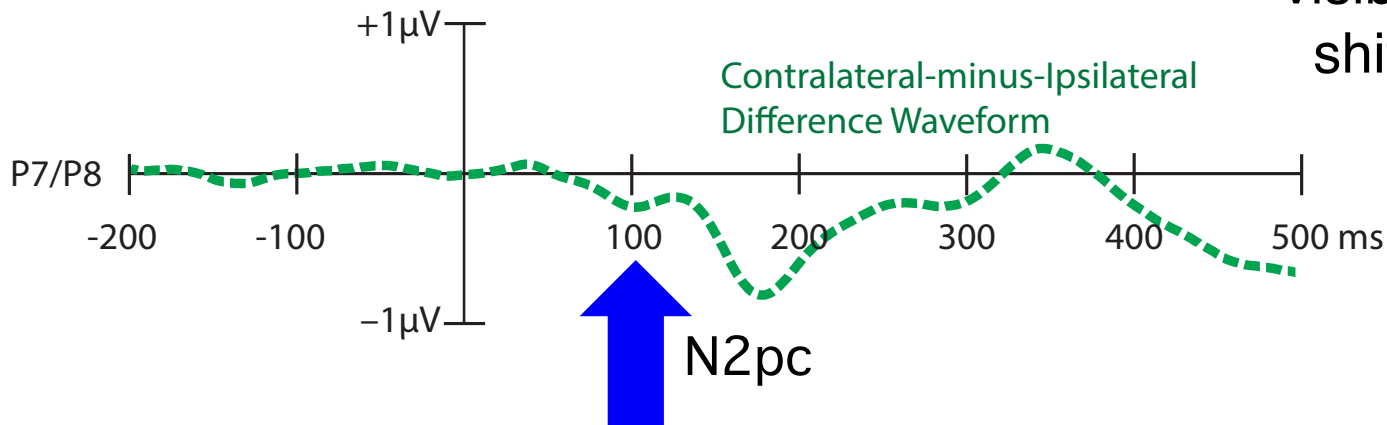
Kappenman, E. S., Luck, S. J., Kring, A. M., Lesh, T. A., Mangun, G. R., Niendam, T., Ragland, J. D., Ranganath, C., Solomon, M., Swaab, T. Y., & Carter, C. S. (2016). Electrophysiological evidence for impaired control of motor output in schizophrenia. *Cerebral Cortex*, *26*, 1891–1899.

Luck et al (2009, *Psychophysiology*)

## N2pc to Threat Images

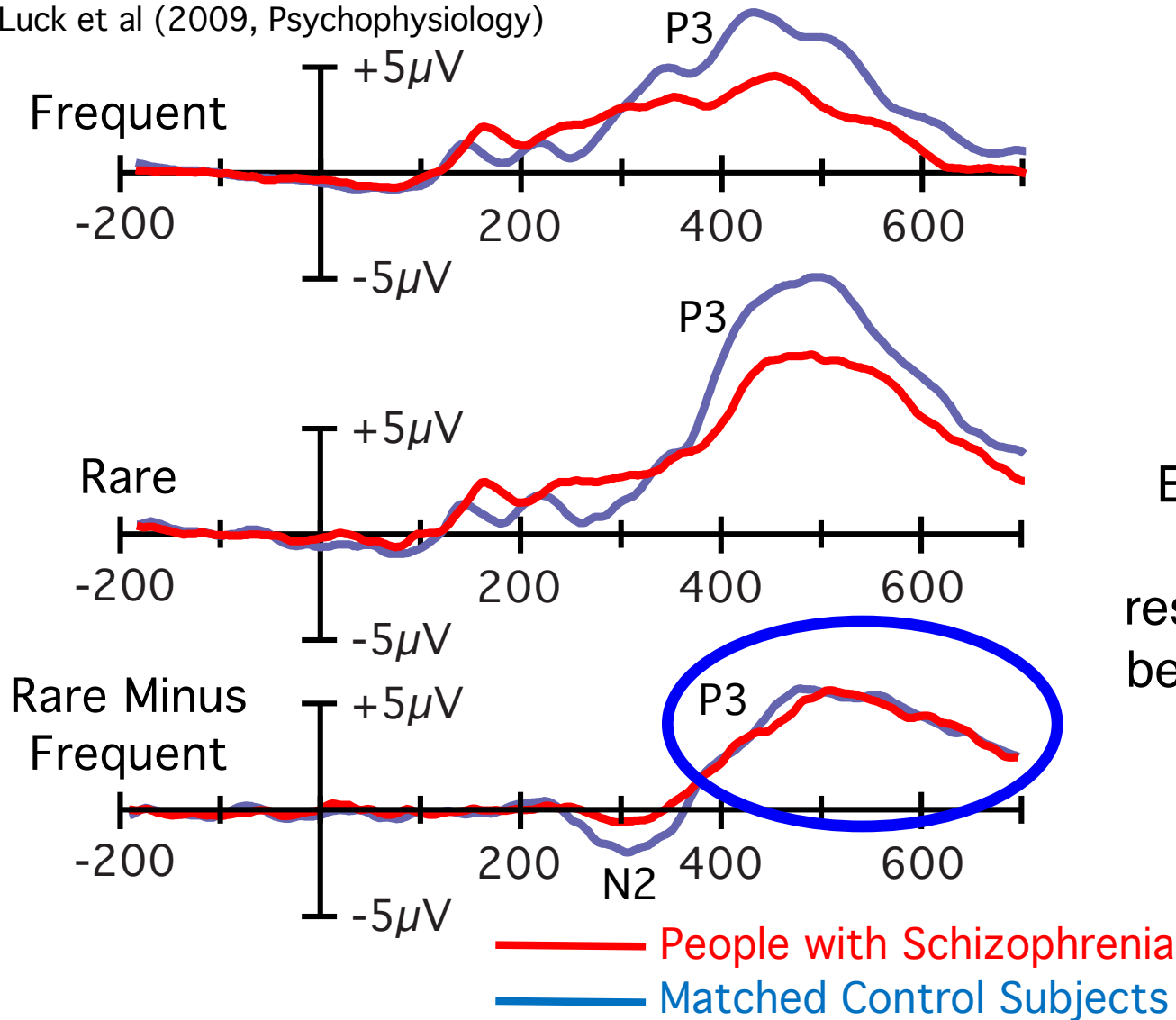


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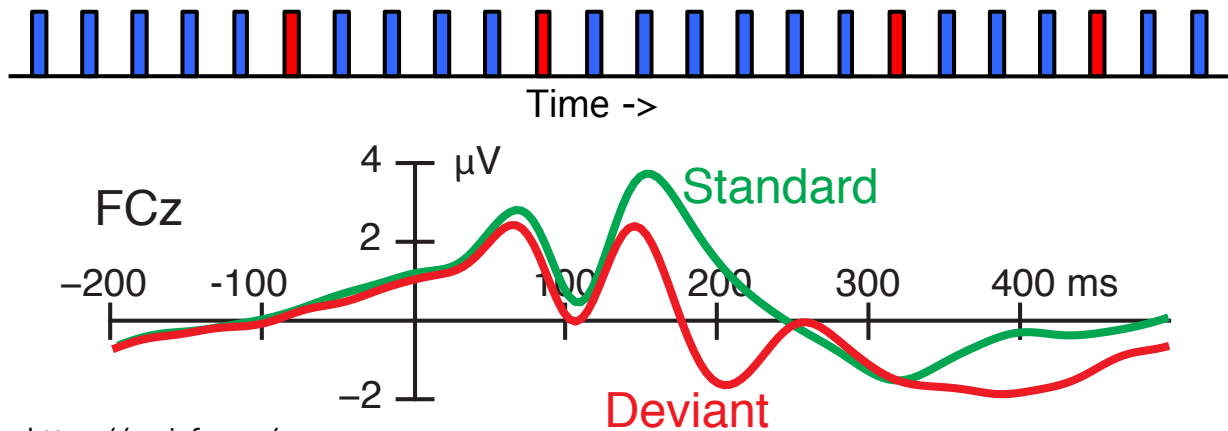
ERPs provide a continuous, high temporal resolution measure of the processes that occur between a stimulus and a response. This makes it possible to see neural processes that are not directly visible in behavior, such as shifts of covert attention.

Luck et al (2009, Psychophysiology)



ERPs also allow us to ask which processes are responsible for differences in behavior between conditions or between groups.

## Mismatch Negativity (MMN)



<https://erpinfo.org/erp-core>

ERP components like the mismatch negativity allow us to monitor processing in subjects who can't do behavioral tasks, such as infants and people in comas.

