Time sensitivity is impaired in right but not in left temporal lobe epilepsy

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Background

Time processing is a central sense to human behavior and cognition; it allows us to determine what is happening in our environment and when to respond to events. All sensory events have a temporal dimension; yet, how the brain codes the duration of sensory events is a complex and unresolved question.
Time perception emerges from neural activity in distributed brain systems. The ***scalar expectancy theory*** (SET) (***1***) is the most popular model of time perception (***Fig. 1***). Brain structures involved in clock, memory, and decision stages are yet unknown.
Recent evidences provided by patients with Parkinson's disease, stroke, traumatic brain injury, together with studies using rTMS, suggest a role of cerebellum, basal ganglia, dorsolateral prefrontal cortex, posterior parietal cortex, and auditory cortex (superior temporal sulcus, middle temporal gyrus) (***2***). The involvement of auditory cortex is further supported by evidence of time dysperception in patients with lesion or epilepsy of temporal lobe (***3, 4, 5***).
The aim of the present study is to investigate whether temporal lobe epilepsy (TLE) affects time perception and, if it is the case, whether a difference between right and left TLE exists.

Subjects

The experimental task was conducted using a single PC laptop (Fujitsu Lifebook A544) running OpenSesame 2.9.7 software. Auditory stimuli consisted in 600Hz tone presented binaurally via headphones (Pioneer HDJ-500).
Ten patients with right TLE, 11 with left TLE, and 29 healthy subjects, matched for sex (p=0.15) and age (p=0.06) were recruited. Educational level was higher in healthy controls (***Table 1***). All patients received the electroclinical diagnosis of TLE at our Epilepsy Center, according ILAE (1989) diagnostic criteria. There was no significant difference in disease duration between the two epileptic groups (p=0.06). All patients performed the task at least two hours later the AEDs assumption; no seizure were reported in the last 72 hours. No history of head injury within the preceding ten years, of alcohol abuse, nor stroke was reported by participants All subjects had normal or corrected to normal vision and hearing.
Statistical analysis were performed using R 3.1.2 software.

Methods

The temporal bisection task (TBT) consists of two phases. During the ***training phase*** participants received two tones of standard duration (anchors) and were trained to distinguish between them. In the ***experimental phase*** a set of tones varying in duration between the long and the short anchor were presented and participants judged whether they were more similar in duration to the long or the short one pressing a key on the keyboard.
Two TBT were administered: a) in the long-TBT anchors were 2250ms and 3450ms; b) in the short-TBT anchors were 750ms and 1500ms. In both tasks, 7 intermediate durations were presented 7 times each, in random order, for a total of 49 trials per block; no feedback was given to participants during experimental trials.
A psychometric curve was fitted for each participant by probit analysis. The difference limen (DL) is defined as the half of the difference between intervals classified "long" in the 75% and 25% of trials respectively. DL measures the subjective ability to discriminate between different time durations; higher is DL value, worse the ability.
Statistical analysis was performed by ANOVA.

Results

DL differed among the three groups in both TBT-short [F(2, 47)=3.52, p=0.0376] and TBT-long [F(2,47), p=0.001] (***Fig. 2***). Post-hoc analysis was performed by means of Tukey Honest Significant Difference (HSD) test. In both tasks Tukey HSD test showed that DL was significantly higher (p<0.05) in the RTLE group than in the other two groups. Two-way ANOVA found a significant effect of group [GROUP main effect: F(2,47)=6.5, p=0.01] and task [TASK main effect: F(2,47)=68.03, p<0.001] variables, and a non-significant effect of interaction between them [GROUP x TASK interaction: F(2,47)=3.18, p=0.08].

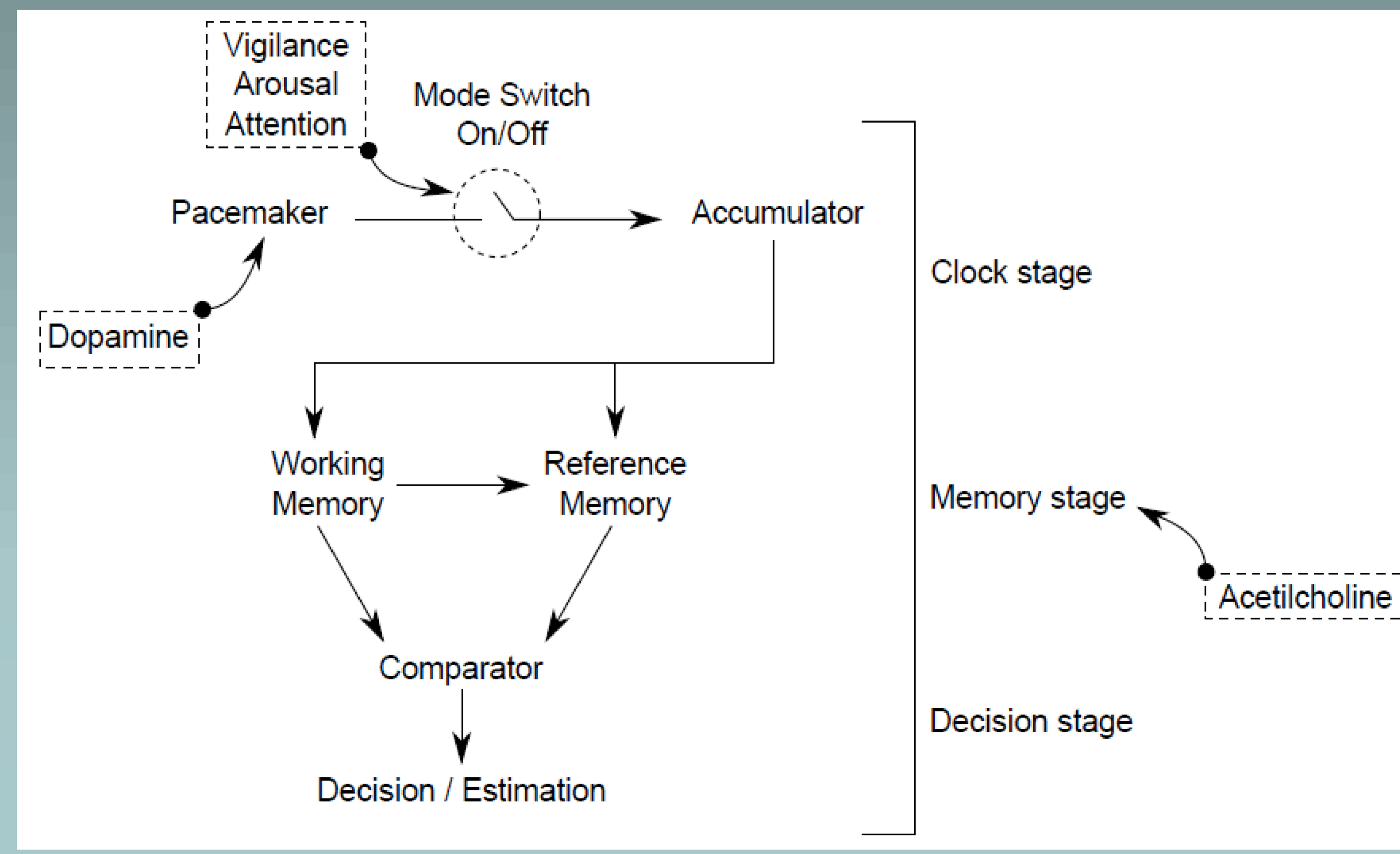

Fig. 1. An internal pacemaker with an ***attention*** mediated switch emits pulses stored by an accumulator to form an expressed interval of ***subjective time*** that approximately correspond to ***objective time***. The sum value of these accumulated pulses is stored in ***reference memory***. Any subsequent interval of time discrimination is compared to existing remembered time references and matched accordingly to targeted event.

	Healthy controls	RTLE	LTLE	p
N	29	10	11	/
Age	34,44	35,80	48,45	0,06
Disease duration	/	22,7	9,45	0,06
Pharmacoresistance	/	3	3	/
M:F	18 : 11	8 : 2	6 : 5	0,15
Education (y)	17,82	10,7	14,27	< 0,01

Table 1. Demographic characteristics of studied subjects.

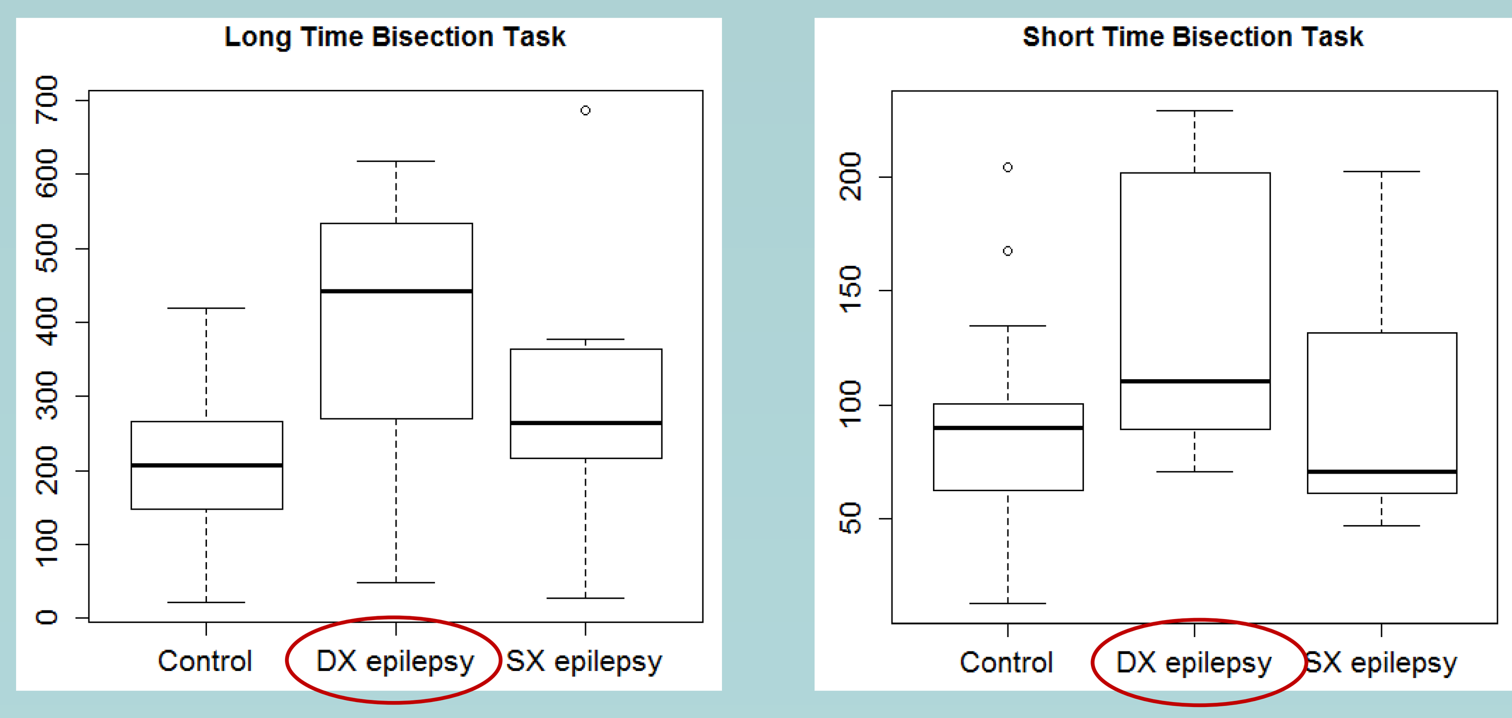

Fig. 2. Boxplot representation of difference limen in TBT with long anchors (left) and in TBT with short anchors (right). In both tasks, RTLE group values were significantly higher compared to the other two groups. DL measures the subjective ability to discriminate between different time durations.

Discussion

Medial temporal lobe damage affects the memory component, and possibly the downstream decision-making stage, of the temporal information processing model.
This study shows that RTLE group had diminished ability to discriminate intervals in sub- and supra-second range, suggesting a greater cognitive dysfunction in these patients. This result confirms previous studies (***2, 3, 4, 6***).
Limitations of our study relies essentially on the possible effect of AEDs on time estimation. In view of this, future experiments should recruit patients with newly diagnosed temporal lobe epilepsy, without AED utilization.

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