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Please cite this article in press as: Korda AI et al. Discrete states of attention during active visual fixation revealed by Markovian analysis of the time series of intrusive saccades. Neuroscience (2016), http://dx.doi.org/10.1016/j.neuroscience.2016.10.012

Neuroscience xxx (2016) xxx-xxx

## DISCRETE STATES OF ATTENTION DURING ACTIVE VISUAL FIXATION REVEALED BY MARKOVIAN ANALYSIS OF THE TIME SERIES OF INTRUSIVE SACCADES

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Abstract—The frequency of intrusive saccades during maintenance of active visual fixation has been used as a measure of sustained visual attention in studies of healthy subjects as well as of neuropsychiatric patient populations. In this study, the mechanism that generates intrusive saccades during active visual fixation was investigated in a population of young healthy men performing three sustained fixation tasks (fixation to a visual target, fixation to a visual target with visual distracters, and fixation straight ahead in the dark). Markov Chain modeling of inter-saccade intervals (ISIs) was utilized. First- and second-order Markov modeling provided indications for the existence of a non-random pattern in the production of intrusive saccades. Accordingly, the system of intrusive saccade generation may operate in two "attractor" states, one in which intrusive saccades occur at short consecutive ISIs and another in which intrusive saccades occur at long consecutive ISIs. These states might correspond to two distinct states of the attention system, one of low focused - high distractibility and another of high focused - low distractibility, such as those proposed in the adaptive gain theory for the control of attention by the noradrenergic system in the brain. To the authors knowledge, this is the first time that Markov Chain modeling has been applied to the analysis of the ISIs of intrusive saccades. © 2016 IBRO. Published by Elsevier Ltd. All rights reserved.

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Abbreviations: AP, Affinity Propagation; DLPFC, dorsolateral prefrontal cortex; HMMs, Hidden Markov Models; ISIs, inter-saccade intervals; KDE, kernel density estimates; NTF, no target fixation; ROIs, regions of interest; VFD, visual fixation distracted; VFU, visual fixation undistracted.

http://dx.doi.org/10.1016/j.neuroscience.2016.10.012 0306-4522/© 2016 IBRO. Published by Elsevier Ltd. All rights reserved. Key words: saccades, oculomotor, time-series, Markov chains, attractors, sustained attention.

## INTRODUCTION

Ocular fixation is used to hold the visual stimulus for image processing. During that time, saccade suppression is engaged to inhibit reflexive saccades. The ability to maintain fixation for a period of time, called the "active fixation task", relates to the ability to maintain the focus of visual attention. Breaks in visual fixation during this task, defined by intrusive saccades that direct the eyes away from the current to a new fixation point, can be viewed as breaks in sustained visual attention. Voluntary intrusive saccades that break active fixation are different from involuntary fixational eye movements. Even when the eves are fixating ocular movements do not stop and microsaccades, drifts and tremor constitute repertoire of fixational eye movements (Martinez-Conde and Macknik, 2011). Microsaccades are involuntary eye movements that are essential for maintaining visibility during fixation, overcoming adaptation of the retinal image (Martinez-Conde and Macknik, 2011), Recent studies have shown that there is no neurophysiological distinction between microsaccades and regular saccades that are both generated by neurons in the superior colliculus (Hafed et al., 2009; Hafed and Krauzlis, 2012) and there are also no differences in the physical characteristics of the population of microsaccades and regular saccades during fixation (Otero-Millan et al., 2008; Hafed et al., 2009). Thus, in order to distinguish microsaccades from voluntary intrusive saccades that break fixation, an arbitrary amplitude cutoff point has to be used. In most studies of active visual fixation, this cutoff point is set at saccadic amplitudes of 0.5-1 degrees. Saccades that are larger than this cutoff point effectively move the eyes away from the current fixation point and can be classified as voluntary breaks in fixation that are followed by refixation saccades. On the other hand, the mean amplitude of microsaccades is about 10-12 min arc, although, as shown in recent studies, prolonged visual fixation can lead to microsaccades of larger amplitudes (Otero-Millan et al., 2008). In this study, we used a cutoff of 0.5 degrees to characterize voluntary intrusive saccades that break fixation in the active visual fixation task.

A series of cortical brain areas are involved in the active process of maintaining active fixation, in particular, the dorsolateral prefrontal cortex (DLPFC). It 21

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has been proposed that the DLPFC acts as a "supervisory" area, actively inhibiting unwanted intrusive saccades when maintenance of fixation is required (Gooding, 1999). Fixation can also occur in the absence of a visual stimulus. During this active fixation to the mental representation of the fixation stimulus, a series of frontal areas are activated, including the frontal eye field, the DLPFC and the supplementary eye field (Petit et al., 1995). These same areas are known to participate in sustained attention and spatial memory processing (Goldman-Rakic, 1988).

The active fixation task has been used to study sustained visual attention in patient populations, such as patients with schizophrenia (Mialet and Pichot, 1981: Amador et al., 1991, 1995; Paus, 1991; Curtis et al., 2001). We have previously reported on the active fixation performance of a large sample of young healthy men (Smyrnis et al., 2004). Although, in general, the performance of these young healthy adults in the fixation tasks was very good, the vast majority of them produced a small number of intrusive saccades during active fixation. All previous studies of active visual fixation in normal individuals and patients have used the mean frequency of saccades as the only measure of performance in this task. An open question then is whether intrusive saccades occur at random during the time that the subject tries to maintain active fixation, or whether there is a nonrandom pattern in their occurrence, suggesting a process of breaking sustained visual fixation and visual attention.

A very powerful approach to detect such non-random patterns in a time series of events is the use of the mathematical model of Markov Chains. This model assumes that the occurrence of an event at a given time is not random but depends on the occurrence of previous events, implying the presence of memory in the system generating the event. Markov Chain models have been used widely in many fields for the analysis of time series, for pattern recognition, and the analysis of stochastic processes, in order to understand the mechanisms generating the events under investigation and to predict future "states" of the system being studied (Ricardo, 2008).

Markov modeling of eye movements has attracted wide interest (Boccignone, 2015). Ellis and Stark (1986) modeled fixation sequences as a Markov process. They defined regions of interest (ROI) on viewed pictures corresponding to "fixation localizations" and those ROIs were the states of the model. Using a chi-square goodnessof-fit test on the distribution of observed and expected state transitions, statistically significant differences emerged when comparing the observed transition frequencies to the expected frequency of transitions according to random sampling models. Juttner and Wolf (1994) applied a two-state Markov model, where each state corresponded to a specific kind of saccade in preparation ("express" and "normal" saccades), in an experimental paradigm involving two kinds of trials. They showed that the stimulus sequence modulates the saccadic latency distribution, using a second-order Markov model (i.e., a model in which the last two predecessor trials are considered). Brockmann and Geisel (2000) investigated the saccade amplitude distribution in free viewing of natural scenes. They found evidence that eye movement trajectories follow a specific kind of Markov process, namely the Levy flight process. Nicolaou and Darzi (2004) investigated Markov modeling of saccades in laparoscopy. The states of the model corresponded to three ROIs in basic laparoscopic tasks. A first-order Markov process was used for modeling the sequence of temporal fixations between two successive states of interest. Inferences were made concerning the relation of saccadic behavior and underlying mental processes. Markov modeling has also been applied to microsaccades (Privitera et al., 2014). Three types of fixations were investigated. For each type, the states of the model corresponded to a first fixation and a refixation and the transition probabilities corresponding to the three types were compared using a binomial test. Bettenbuhl et al. (2012) used Markov modeling to investigate the existence of memory in sequences of microsaccadic eye movement orientations. The states of the model corresponded to the left and right direction of the horizontal component of each microsaccade. Using a Bayesian approach, a first-order model was shown to better represent the observed sequences.

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In the Markov modeling approaches described in the previous paragraph, the states of the system correspond to observable events, hence they are termed "observable" Markov models. Extensions of those models are Hidden Markov Models (HMMs) (Rabiner, 1989; Johnson and Willsky, 2013), In such models the states of the system are not directly observable, i.e., there exists an underlying non-observable stochastic process. The output of the system is an observable stochastic process, which is supposed to depend on the state of the underlying system producing the output. HMM applications in eye movement analysis can be grouped into two main categories. In one class of applications, based on the observable Markov Chain. the "hidden" states that "control" the observable states are determined. For example, researchers try to find which visual task was performed by the subject when he/she performed a specific chain of saccades. Therefore, those applications focus on "task inference" or "task classification", based on the assumption that different ("unknown") tasks or eye movement "programs" (Feng, 2006) might produce different transition matrices of the observable eye movement states (Simola et al., 2008; Haji-Abolhassani, 2013). In another class of applications, HMMs have been used for differentiating normal controls from patient subjects (Lagun et al., 2011), according to their saccade Markov Chain succession.

Markov Chain modeling has also been used in the study of eye movement patterns during rapid eye movement (REM) sleep (Boukadoum and Ktonas, 1988; Douglass et al., 1992; Nygren, 1994; Ktonas et al., 1990). Following this previous work, the present work uses Markov Chain modeling to investigate whether intrusive saccades during active fixation follow a non-random pattern, and to investigate the particular characteristics of this pattern, leading to specific hypotheses on the function of sustained visual attention in healthy humans. It is important here to note that intrusive saccades during

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