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論文題目	Modeling saccade reaction time in marmosets: the contribution of earlier visual response and variable inhibition. （マーモセットのサッカード反応時間のモデル化：早期視覚反応と抑制可変性の寄与）		

（論文内容の要旨）

Marmosets are a relatively new primate model for studying human brain functions, including the visuomotor system, due to their oculomotor similarities to humans and macaques. However, differences exist, such as challenges in training marmosets to suppress unwanted saccades and their consistently shorter yet more variable saccade reaction times (SRT) compared to humans and macaques. This study investigates whether these differences in SRT are linked to variations in visual signal transduction and inhibitory control variability.

Three marmosets used in this study. Each marmoset was aseptically mounted with a custom-designed headpost, tailored to its MRI-base skull reconstruction, then trained on a gap saccade task, which required subjects to make a saccade toward a target (1-degree diameter) that appeared after a 200 ms fixation period and 200 ms gap period. A computational SRT model based on Coe et al. (2019) was refined by adjusting parameters to better fit the marmoset SRT distribution. The model incorporates multiple component-based inputs simulating neural processes underlying saccade generation in marmosets, with each of the eight inputs characterized by four parameters: onset delay, rate of response (RoR), maximum strength (MaxVal), and center of activity, updated every millisecond.

The threshold separating anticipatory and express saccades from regular saccades was first identified. The onset delay of inputs 4–8, representing the cut-off between express and regular saccades, was considered as the most apparent parameter to modify. Coe et al. (2019) used a regular saccade cut-off of 140 ms, but marmoset SRTs required a lower cut-off (75, 100, and 125 ms). Despite this adjustment, the model did not fully capture the marmoset data, leading to further adjustments in the onset delay for the visual transient and automated motor inputs.

Weaker inhibition, contributing to shorter SRTs, was addressed by enhancing the disinhibition of inhibitory gate and peripheral inhibition inputs. Moreover, since express saccades frequently occur when active fixation or directed visual attention is disengaged 200 ms before the saccade target appears, and almost completely abolished if fixation or attention is still engaged when the saccade target appears. This suggests that fast saccades occur when visual attention has already been disengaged from its previous locus before the saccade target onset. This implies a deficit in the ability to maintain fixation and inhibit reflexive saccades triggered by abrupt visual onsets, therefore, the fixation strength of the voluntary fixation was lessened to simulate cases of weaker fixation.

Additionally, some previous research suggested that marmosets have a smaller pool of neurons than macaques (or humans). Thus, the RoR for inputs 1, 2, 7, and 8 was increased to reflect faster build-up activity. These adjustments (step 2) brought the simulation results closer to matching the short SRTs observed in marmosets. Additionally, marmosets show greater SRT variability than humans, resulting in an extended cumulative distribution function (CDF) tail. To account for this, a minimum RoR for the inhibitory gate and peripheral inhibition inputs was introduced, along with enhancements to the RoR for automated and voluntary fixation inputs. Further adjustments to voluntary motor input RoR helped replicate the observed SRT variability (step 3).

Our findings indicate that visual information processing is faster in marmosets, and that saccadic inhibition is more variable than other species.

（論文審査の結果の要旨）

マーモセットは、神経科学の重要な霊長類モデルとして注目されているが、ヒトやマカクと共通する眼球運動系を有する一方で、不要なサッケード運動が頻発、サッケード反応時間（SRT）が短く、ばらつきが大きい。本研究では、マカクの研究で得られたモデルを適用し、マーモセットの眼球運動系の特徴の原因を探求した。

そのため、Coeら（2019）の計算論モデルを改良した。このモデルは、神経情報処理過程を8つの入力パラメタ（1 視覚入力、2 自動運動、3 自動固視、4 自発運動、5 自発固視、6 自発準備、7 抑制ゲート、8 末梢抑制）で外挿する。これらは、発生遅延、反応速度（RoR）、最大強度で定義され、ミリ秒ごとに更新される。まず、入力4〜8の発生遅延を短縮し（ステップ1）、さらに入力1および2の発生遅延を変更し、入力7および8の脱抑制を強化し、入力5の強度を減少させ、入力1、2、7、8のRoRを増加させた（ステップ2）。そして入力7と8の最小RoRを導入し、入力3と5のRoRを増加させ、入力4のRoRを強化した（ステップ3）ところ、マーモセットSRTの累積分布関数を良好に外挿できた。以上の結果からマーモセットは他種と比較して視覚処理が速い一方で、サッケード抑制がより変動的であることが示唆された。

以上の研究から、このモデルが疾患を含む各個体の眼球運動の特徴の理解を促進すると期待され、臨床神経学に寄与するところが多い。

したがって、本論文は博士（医学）の学位論文として価値あるものと認める。

なお、本学位授与申請者は、令和６年１２月２４日実施の論文内容とそれに関連した試問を受け、合格と認められたものである。

要旨公開可能日：　　年　　月　　日　以降