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論文題目	Stimulus-driven changes in the direction of neural priming during visual word recognition （視覚単語認識における神経プライミングの刺激誘導性変化）		

（論文内容の要旨）

Fluent reading is one of the most important skills in modern world and demands fast and accurate analysis of letter-strings to distinguish learned words from neighbor words sharing similar lexical or phonological construction. Behavioral studies have shown that non-word primes with shared consonantal structures accelerate visual word recognition of subsequent target words. Interestingly, however, prime-target orthographic overlap at word-onset sharing initial syllable (or in some languages mora) can induce decelerate reaction times to targets across different languages. This negative priming has been thought to arise from a word-level lateral inhibition from orthographic neighbors having orthographic or phonological overlap with targets. While recent behavioral studies suggest that the effect is more pronounced in the left hemisphere, its neuroanatomical basis has remained largely unknown. Candidate regions predicable from the existing literature include the lateral temporal cortex (LTC) associated with lexico-semantic memory, posterior occipito-temporal sulcus (pOTS) associated with abstract orthographic codes, left inferior frontal gyrus (IFG) for rapid activation of phonological codes, and dorsal premotor cortex (PMd) involved in decision making/motor planning. Present study used fMRI with a hemifield priming paradigm to explore neuroanatomical underpinnings of the inhibitory neighbor priming during visual word recognition (Experiment 1). In Experiment 2, a typical repetition priming paradigm was additionally performed to assess possible effects of the hemifield presentation procedure on the behavioral and neural effects observed in Experiment 1.

In total, 21 volunteers took part in both experiments (12 participants for Experiment 1, 9 participants for Experiment 2). In Experiment 1 neural activation was measured while participants made natural/artificial judgment of a centrally presented target, preceded by a masked prime flashed either to the left or right visual field. Consistent with previous studies, slower response time was observed for shared onset syllable pairs compared to no-overlap pairs. At the neural level, however, this effect was associated with robust repetition enhancement in the left IFG, while neither PMd nor LTC showed significant effects of priming associated with syllabic overlap. Experiment 2 employed the identical procedure except that prime-target pairs were either same or a different word without syllabic overlap. Behaviorally, participants displayed expected facilitatory effect of repetition priming, with reaction times faster for word-overlap prime-target pairs. At the neural level, regions-of-interest analysis revealed a classic pattern of repetition suppression at pOTS during visual word recognition. In joint analysis of both experiments, it was confirmed that the observed change in priming directions was significant and thus reflects the intrinsic nature of prime-target relations, rather than the hemifield priming procedure.

Behavioral results of Experiment 1 are consistent with the previously known pattern of inhibitory priming during visual word recognition. Unexpectedly, however, it was observed that the effects were associated with robust repetition enhancement in the left inferior lateral prefrontal area. This neural effect of priming was more pronounced in the left hemisphere and seems consistent with known dominance of the left hemisphere in lexical neighbor inhibition. Present results also converge with ERP and MEG studies suggesting that the left IFG acts as a fast word processing system that is distinct from the pOTS and LTC responsible for abstract orthographic processing and lexico-semantic memory, respectively. In Experiment 2, the classical pattern of facilitatory repetition priming was confirmed at the behavioral level, and the well-known repetition suppression at the pOTS at the neural level. This study sheds light on previously unknown neuroanatomical components behind inhibitory priming produced by lexical neighbors. It confirms that the priming direction can be modulated by intrinsic properties of stimuli. Finally, the study reveals left IFG as the key element in fast word processing - both fundamental and sophisticated skill necessary for fluent reading.

（論文審査の結果の要旨）

語頭の音節が一致するプライム・ターゲット単語における「正書法のオーバーラップ」は、様々な言語でターゲットに対する反応時間を延長することが知られているが、この抑制性プライミングの神経基盤は未解明である。本研究は、視覚単語認識における抑制性プライミングの神経基盤解明を目的とした。２１名の健常者を対象とし、ターゲットに対する反応時間を半視野プライミングパラダイムにより計測し、機能的磁気共鳴画像法(fMRI)を用いて脳活動を計測した。データ解析では特に、左下前頭回、運動前野背側部、外側側頭葉における神経プライミングの変化に焦点をおき、関心領域を設定して詳しく検討した。語頭の音節が一致するプライム・ターゲットに対する反応時間の遅れ（抑制性プライミング）は、左下前頭回における強い反復増幅効果と相関し、従来想定されてきた抑制性プライミングの左大脳半球の優位と一致した。一方、運動前野背側部と外側側頭葉ではこのような神経反応は見られず、抑制性プライミングとの相関は認められなかった。抑制性と促通性プライミングとの比較では、刺激誘導性変化が有意であることが示され、半視野プライミングパラダイム手法の影響が認められなかった。以上から、刺激の固有の性質によって神経プライミングが抑制・増幅の 2 方向に変化すること、左下前頭回において短時間での単語認知処理が行われることが示唆された。

以上の研究は文字認知処理の神経ネットワークの構成要素解明に貢献し、言語の神経メカニズムの理解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、平成 29 年 7 月 27 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。