

氏 名 岡本 悠子

学位(専攻分野) 博士(理学)

学位記番号 総研大甲第 1612 号

学位授与の日付 平成25年3月22日

学位授与の要件 生命科学研究所 生理科学専攻
学位規則第6条第1項該当

学位論文題目 Atypical brain activation in adults with ASD during gestural
interaction

論文審査委員 主 査 教授 小松 英彦
教授 定藤 規弘
教授 柿木 隆介
教授 板倉 昭二 京都大学

論文内容の要旨

Introduction: Autism spectrum disorder (ASD) is neurodevelopmental disorder characterized by difficulty in social communicative-ability and restricted repetitive and stereotyped patterns of behavior, interests and activities. Abnormality in gestural interaction is one of remarkable characteristics of individuals with ASD. During gestural interaction, individuals should detect congruency of self and other's action and to control self action based on visual information of other's action. It is considered that the forward model and inverse model of the internal model in the mirror neuron system (MNS) plays important role for both detecting congruency of self and other's action and to control self action based on visual information of other's action, respectively. Therefore, abnormal behaviors in gestural interaction for individuals with ASD might be caused by abnormality of internal model in the MNS. Recent behavioral study suggest a possibility that adults with high-functioning ASD partly damaged in gestural interaction, that is, they show abnormality in automatic behavior but not in voluntary behavior. For instance, adults with high-functioning ASD, who can voluntarily imitate other's action, fail automatically copy other's action (i.e. automatic mimicry). The finding leads a hypothesis that adults with high-functioning ASD have abnormality automatic processing in internal model, however voluntary process is relatively intact. Nevertheless, it is unknown if adults with high-functioning ASD show abnormal brain activation during gestural interaction. Therefore, the author examined if the adults with high-functioning ASD show abnormal brain activation for automatic processing of internal model, but not for voluntary processing of internal model during gestural interaction.

Methods: To test this hypothesis, the author conducted a functional MRI study with 19 adults with high-functioning ASD (ASD group) and 22 normal adults (control group). The subjects observed and executed five gestures expressing five numbers. The author manipulated congruency of the executed and observed action (congruent / incongruent) and the order of executed and observed action (active / passive). In active condition, the subjects observed an action and then executed same or different action. Conversely, the subjects executed an action and then observed same or different action in passive condition. By comparing congruent condition vs. incongruent condition, the author examined neural substrates of congruency detection, which is related to forward model. The author also examined the neural substrates of control self action based on visually observed other's action, by comparing active condition vs. passive condition. If her hypothesis is true, ASD group should produce atypical activation in automatic processing of internal model. More specifically, ASD group should produce reduced congruency effect especially for passive condition (i.e. Passive-congruent condition vs. Passive-incongruent condition), because the subjects were not required any voluntary behaviors for passive condition. Furthermore, ASD group also should produce reduced active effect for incongruent condition (i.e. Active-incongruent condition vs. Passive-incongruent condition), because inhibition of irrelevant action caused by automatic mimicry is required for executing different action from observed action. By contrast, the author expected that ASD group should similar congruency effect in active condition (i.e. Active-congruent condition vs. Active-incongruent condition) and active effect in

congruent condition (i.e. Active-congruent condition vs. Passive-congruent condition), because voluntary imitation should be relatively intact for adults with high-functioning ASD.

Results: There was no significant group difference on behavioral results. Nevertheless, the author found that adults with ASD group produced reduced congruency effect in the left extrastriate body area (EBA) for passive condition and reduced active effect in the left insula for incongruent condition, as compared to control group. The congruency effect in the left EBA and the active effect in the left insula were negatively correlated with autistic trait of the subjects, measured by autism spectrum quotient (AQ). By contrast, there were no significant group difference of congruency effect in the EBA for active condition, and active effect in the premotor cortex (PMC), and the posterior parietal cortex (PPC) for congruent condition.

Discussion: Congruency effect in the normal adults suggests that the EBA is a part of the MNS, and detect congruency between self and other's action, by comparing efference copy of self action and visual information of other's action. Atypical activation in the left EBA should reflect that efference copy may not automatically send to the MNS for adults with high-functioning ASD, which indicate that adults with high-functioning have abnormality in automatic processing in forward model of the MNS. Previous fMRI study suggested that the left insula is frequently activated by inhibit executing an action. Therefore, reduced activation in the left insula for adults with high-functioning ASD may reflect reduced "workload" of inhibition of automatic imitation, which is caused by automatic processing of inverse model in the MNS. By contrast, there was no atypical response which is related to voluntary imitation, which indicates that adults with high-functioning ASD do not have abnormality in voluntary processing of internal model. These findings indicate that adults with high-functioning ASD have abnormality in automatically shared self and other's representation.

博士論文の審査結果の要旨

自閉症スペクトラム(ASD)は、社会性・コミュニケーションの障害を特徴とする発達障害であり、正常人に比べて、対人コミュニケーションに重要な役割を果たす自動模倣(他者の動作を無意識に真似てしまう傾向)が少ないなど、非言語性身振りコミュニケーションに障害のあることが知られている。

岡本氏は、身振りコミュニケーションにおける相互作用の神経活動が運動制御理論で用いられる順モデル-逆モデルで説明しうることに着目した。即ち運動に伴う結果を予測すること(順モデル)は、運動指令から運動の感覚表象への結合増強により表現される一方、結果を得るための制御(逆モデル)は運動の感覚的表象から運動指令への結合増強により表現される。順モデル-逆モデルは複雑な運動制御において重要な役割をはたすことが知られているが、岡本氏は、自動模倣を逆モデルの自動的な賦活化と捉え、ASD においては運動指令と運動の感覚表象の相互連結(行為表象)に異常がある、との仮説を立てた。

この仮説を検証するため、成人高機能 ASD を対象に fMRI 実験を行った。成人 ASD19 名及び健常成人 22 名は数字を表す手指動作を行い、スクリーンに映る同様の手振り動作を観察した。手指動作の実行及び観察の順序(Active / Passive)と自己と他者の運動の同一性(一致/不一致)を操作することで 2x2 の実験デザインを設定した。Active 条件では被験者は手指動作を観察したのち、観察した手指動作に基づいて、それと同じもしくは異なる手指動作を行った。Passive 条件では自身が先に手指動作を行った後、同じもしくは異なる手指動作を観察した。

自身の手指動作の実行を、他者の手指動作とは異なる型を選択して能動的に行う場合(Active で不一致)には同じ型を選ぶ場合(Active で一致)に比べて、反応時間は延長した。これは不適切な自動模倣を抑制することに要する負荷に関連すると考えられた。能動的に自動模倣を抑制することに関係する活動を見るために、Active で不一致条件と passive で不一致条件の脳活動を比較すると、左半球の島皮質の賦活は正常群に比較して ASD 群で低下しており、その度合は自閉症傾向と負の相関があった。島皮質は運動抑制に関与するネットワークの一部を形成しており、正常人における賦活は、他者と異なる動作を行う際の自動模倣の抑制を反映していると考えられる。ASD においては逆モデルの自動的賦活不全に伴い自動模倣の生成が減少し、それに伴い自動模倣を抑制するために生じる島皮質の活動の低下が見られたと解釈される。

一方、自身の手指動作を、他者の手指動作と同じ型で能動的に選択する場合(active で一致)には異なる型を選ぶ場合(active で不一致)に比べて、両側の有線外体領域(extrastriate body area = EBA)が賦活され、その程度は、自分の手指動作が他者の手指動作によって模倣される場合(passive 条件)よりも強かった。この事は EBA が運動指令のコピー(efference copy)を受け取って順モデルと関係していることを示している。自分の手指動作が他者の手指動作によって模倣される場合(passive 条件)、左半球の EBA の賦活は、自閉症傾向に依存的して減少した。この場合には、意図的模倣の要素は排除できることから、ASD では自動的な順モデル形成に障害があると解釈された。

これらの所見は、双方向性に誘導される、運動指令と運動の感覚表象の相互連結の減弱が ASD 群に見られるという仮説を支持するものであり、自閉症の病態生理解明に資する結果である。従って本論文は学位に十分値すると認められる。