

それ何！？触診のヒントになることから

テーマ：かわりに動き出す、

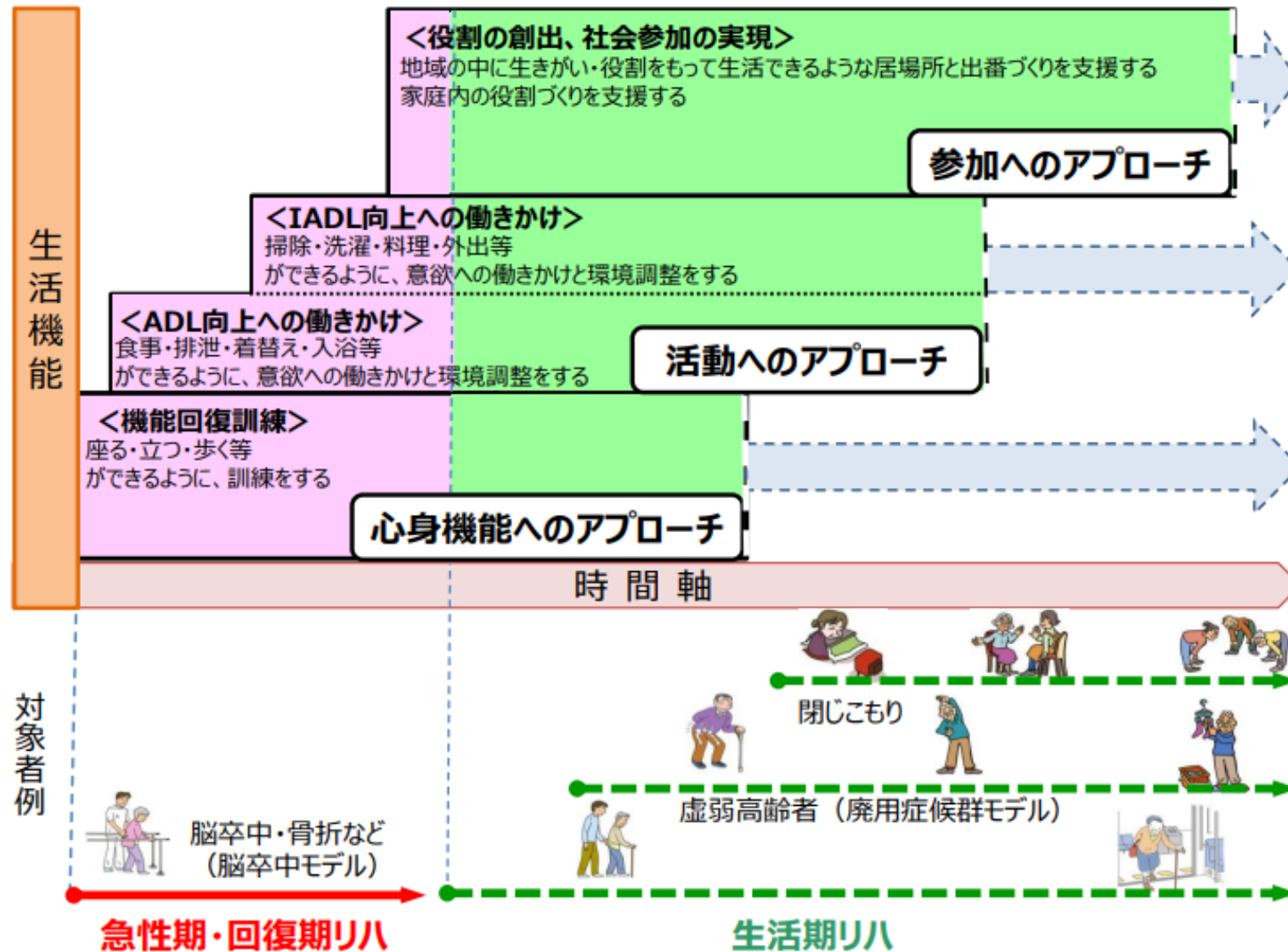
脳の再出発

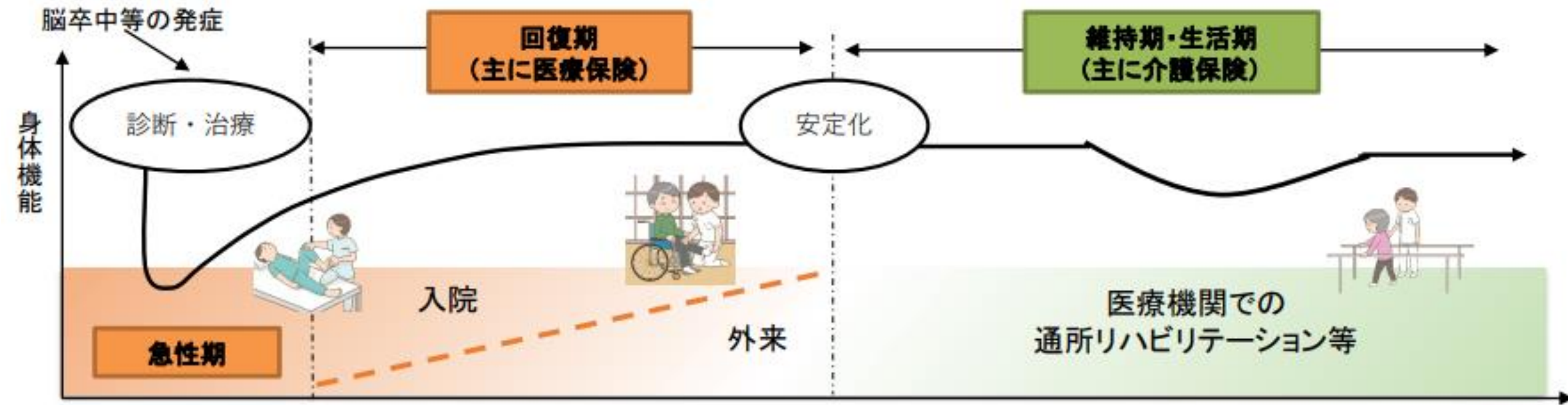
12月27日(水)20:00～

・脳損傷後の変化 ・再組織化

脳外触診セミナー 講師 山上 拓

高齢者リハビリテーションのイメージ





脳の再出発
がSTART

回復期
(主に医療保険)

維持期・生活期
(主に介護保険)

安定化

脳の変化・かわりに動く

急性期

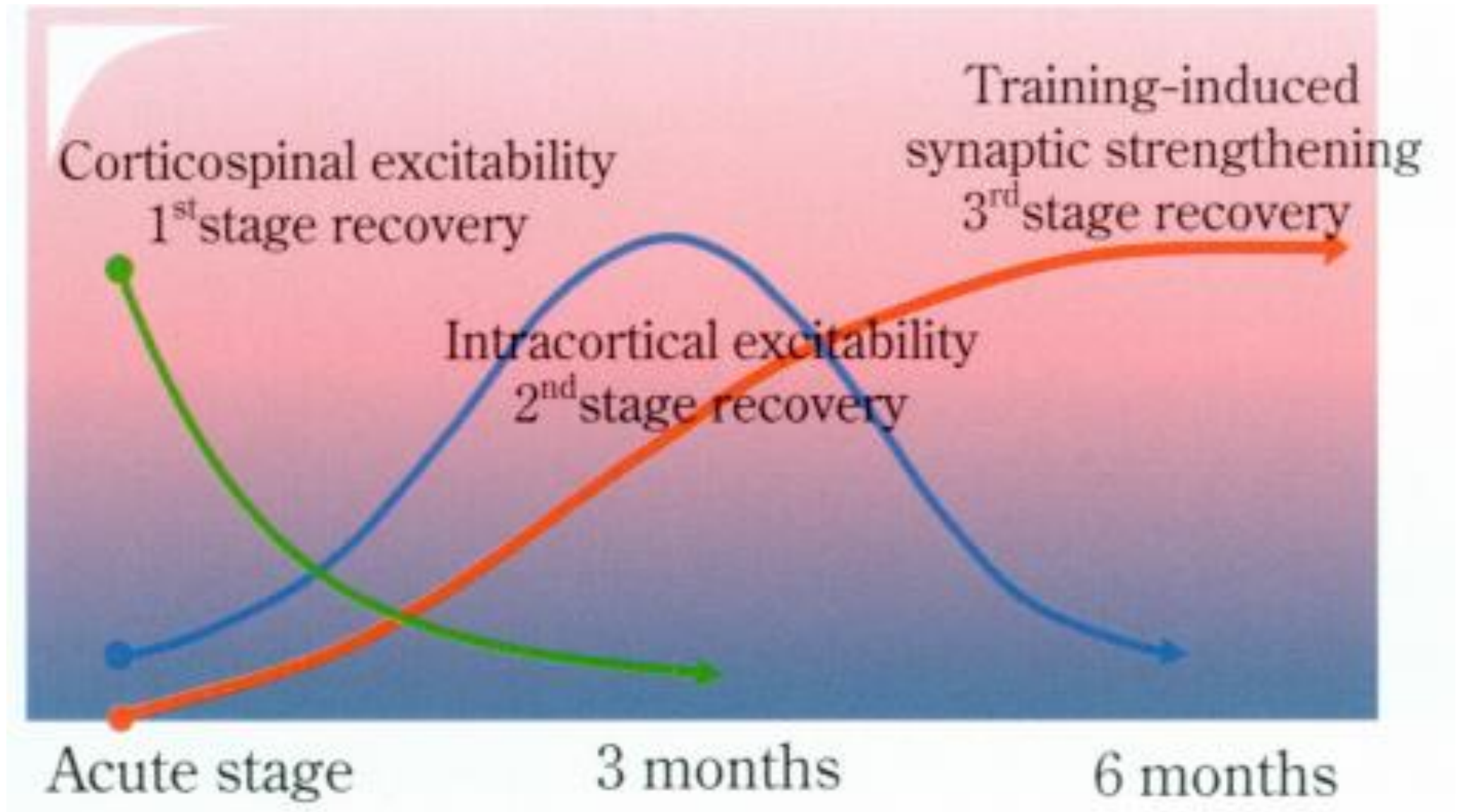
入院

外来

医療機関での
通所リハビリテーション等

麻痺
感覚
高次脳

脳卒中、運動麻痺回復のステージ理論



Stages of Motor Output Reorganization after Hemispheric Stroke Suggested by Longitudinal Studies of Cortical Physiology

Reorganization of motor circuits in the cerebral cortex is thought to contribute to recovery following stroke. These can be examined with transcranial magnetic stimulation (TMS) using measures of corticospinal tract integrity and intracortical excitability. However, little is known about how these changes develop during the important early period post-stroke and their influence on recovery. We used TMS to obtain multiple measures bilaterally in a group of 10 patients during the early days and weeks and up to 6 months post-stroke, in order to examine correlations with tests of hand function. Ten age-matched healthy subjects were also studied. After stroke, day-to-day variation in performance was unrelated to physiological measures in the first 3 weeks. Measures of corticospinal integrity averaged over the same period correlated well with hand function, but this relationship became weaker at 3 months. In contrast, most intracortical excitability measures did not correlate acutely but did so strongly at 3 months. Thus in the acute stage, patients' performance is limited by damage to corticospinal output, improved performance at 3 months may depend on reorganization in alternative cortical networks to maximize the efficiency of remaining corticospinal pathways—intracortical disinhibition may aid recovery by promoting access to these networks.

Keywords: intracortical inhibition, reorganization, stroke, transcranial magnetic stimulation

Introduction

Ischemic stroke frequently leads to impairment of upper limb motor function, after which a variable degree of motor recovery is seen (Twitchell 1957). Functional imaging in humans (Ward et al. 2003a, 2004) and physiological observations in animal models (Jones and Schaller 1994; Nudo and Milliken 1996) suggest that recovery of function is associated with extensive reorganization of the motor system at the cortical level, presumably to maximize control of remaining motor output. Transcranial magnetic stimulation (TMS) has also been used in human stroke patients to probe corticospinal and intracortical physiology. Reduced corticospinal excitability from the affected hemisphere (AH) reflects damage to the corticospinal connection (Traversa et al. 1998; Byrnes et al. 2011), whereas increased intracortical excitability in both hemispheres (Läpport, Hamel, and Weiller 2000; Läpport, Storch, et al. 2000; Manganotti et al. 2002) reflects changes in intrinsic circuits of the cortex.

There are, however, important gaps in our knowledge. First, physiological data acquired during the first weeks after stroke have not provided consistent results: motor thresholds in the AH were raised in some (Läpport, Storch et al. 2000; Manganotti

et al. 2002) but not all (Debaux et al. 2003) studies. Likewise, corticospinal hyperexcitability in the unaffected hemisphere (UH) was observed in some studies (Ciccinelli et al. 1997; Traversa et al. 1998; Debaux et al. 2003) but not in others (Manganotti et al. 2002). For many patients, the early days and weeks after stroke are likely to be a period of great clinical and physiological change. Although several studies have performed TMS assessments during this early period, many have made only a single assessment. The greatest number within the first month is 3 measures of corticospinal excitability (D'Othabertague et al. 1997; Debaux et al. 2003) and 2 measures of intracortical excitability (Manganotti et al. 2002). Given the variability in many physiological parameters found by previous studies, it seems likely that more frequent early measurements would provide a more accurate assessment of early neurophysiological changes after stroke.

Secondly, little is known about the clinical significance of these abnormalities. Reduced corticospinal excitability of the AH in the first 5 days after stroke predicts poorer motor outcome later on (Tronpetto et al. 2000) and is known to be associated with poor function when studied in the chronic stage (Thickbroom et al. 2002). Likewise, intracortical disinhibition of the AH and UH (at 1 month) is seen in patients with greater motor impairment (Manganotti et al. 2002). Thus, although some neurophysiological parameters appear to be related to motor impairment in these cross-sectional studies, it is not clear whether a longitudinal relationship exists. Furthermore, these measures assess different aspects of neurophysiological function each of which might be more or less important for recovery at different times after stroke. It is therefore important to know whether the relationship between motor impairment and these parameters changes during the days, weeks, and months after stroke.

We present experiments in which we acquired detailed longitudinal neurophysiological and clinical data over the first few weeks and months after first-ever ischemic stroke. Our patient group had a relatively wide range of functional impairment, allowing the possibility to examine correlations with clinical scores. Single-pulse TMS measures (resting motor threshold [rMT], active motor thresholds [aMT], and motor-evoked potential [MEP] recruitment curves [RCs]) provide information about corticospinal excitability, specifically of the remaining original projection from the primary motor cortex (M1) to the spinal cord. The 5 paired-pulse measures used (short-interval intracortical inhibition [SICI] and long-interval intracortical inhibition [LICI], and intracortical facilitation [ICF]) are well-described parameters that provide information about intracortical

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特集 ニューロリハビリテーションの進歩

脳卒中運動麻痺回復可塑性理論とステージ理論に依拠したリハビリテーション

原 寛美¹⁾

1) 相模病院脳卒中脳神経センターリハビリテーション科

Stroke Rehabilitation based on Cortical Plasticity and the Stage Theory of Motor Output Reorganization

Hiro Yoshi Hara, M.D.¹⁾

1) Division of Rehabilitation Medicine, Center of Stroke and Neurology, Aizawa Hospital

One of the most important objects of stroke rehabilitation is motor recovery from acute stage to chronic stage. Early rehabilitation intervention after stroke onset should be started during the critical time window phase. Herein, a theory concerning motor circuit reorganization in the cerebral cortex contributing to recovery following stroke is proposed. In the acute stage, motor recovery depends on residual corticospinal tract excitability from onset to 3 months (1st stage recovery). In the next stage, alternative output systems are used according to intracortical excitability depending on intracortical disinhibition at the peak of 3 months (2nd stage recovery). At 6 months and beyond training-induced synaptic strengthening becomes better established, and new networks are better reorganized (3rd stage recovery). Stroke rehabilitation programs commencing from the acute stage are required according to this stage theory. With each stage, selecting and performing the most effective rehabilitation programs is essential to successful recovery. Two motor recovery obstruction factors are indicated. One of them is Wallerian degeneration of the corticospinal tract. Early Wallerian degeneration of the corticospinal tract that is seen on diffusion-weighted MRI was reported. With the appearance of Wallerian degeneration at the acute stage, more attention should be directed to motor recovery inhibition. The second obstruction factor is the development of spasticity from the acute stage. Spastic paresis over time leads to immobilization of the paretic body part and chronic disease of the paretic body part, which are avoidable through early rehabilitation intervention. Recently, various interventions were proposed for motor recovery dependent on the cortical plasticity theory. The combination of repetitive transcranial magnetic stimulation and intensive occupational therapy (NEURO-15) reported by Abo (2010) are recommended to recover hand functions at the chronic stage as 3rd stage recovery. The NEURO-15 is a promising method for stroke rehabilitation.

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Key words: stroke rehabilitation, cortical plasticity, motor output reorganization, critical time window, transcranial magnetic stimulation

Jpn J Neurosurg (Tokyo) 21: 516–526, 2012

はじめに

脳卒中リハビリテーションの最大の関心事は、脳卒中

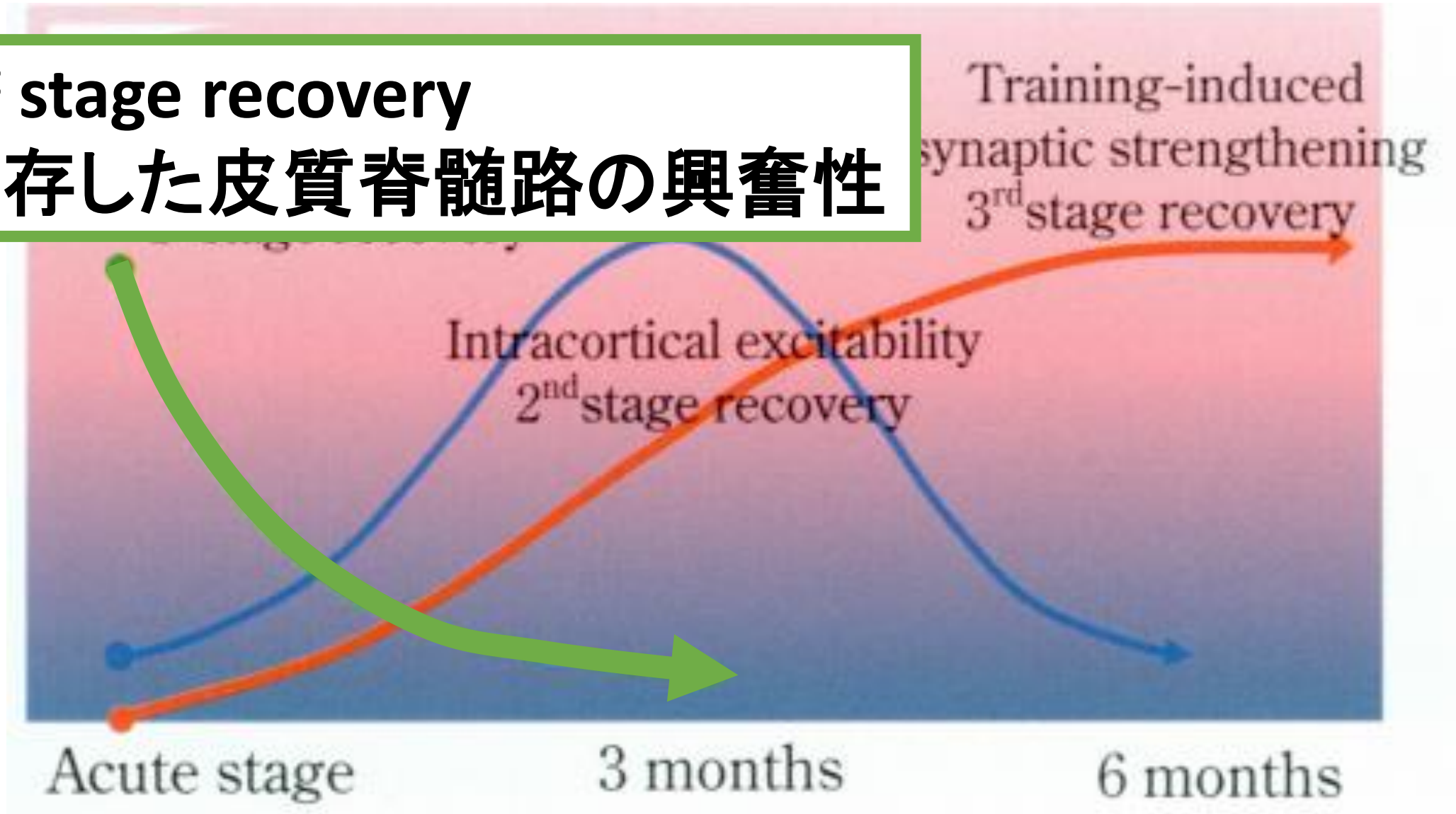
により生じた運動麻痺の軽減と失われた運動機能の回復である。現在までに、脳科学理論に依拠した多くの運動麻痺回復のための知見とリハビリテーションの system

連絡先: 原 寛美, 〒390-8510 松本市本庄2-5-1 相模病院脳卒中脳神経センターリハビリテーション科
Address reprint requests to: Hiro Yoshi Hara, M.D., Division of Rehabilitation Medicine, Center of Stroke and Neurology, Aizawa Hospital, 2-5-1 Honjo, Matsumoto-shi, Nagano 390-8510, Japan.

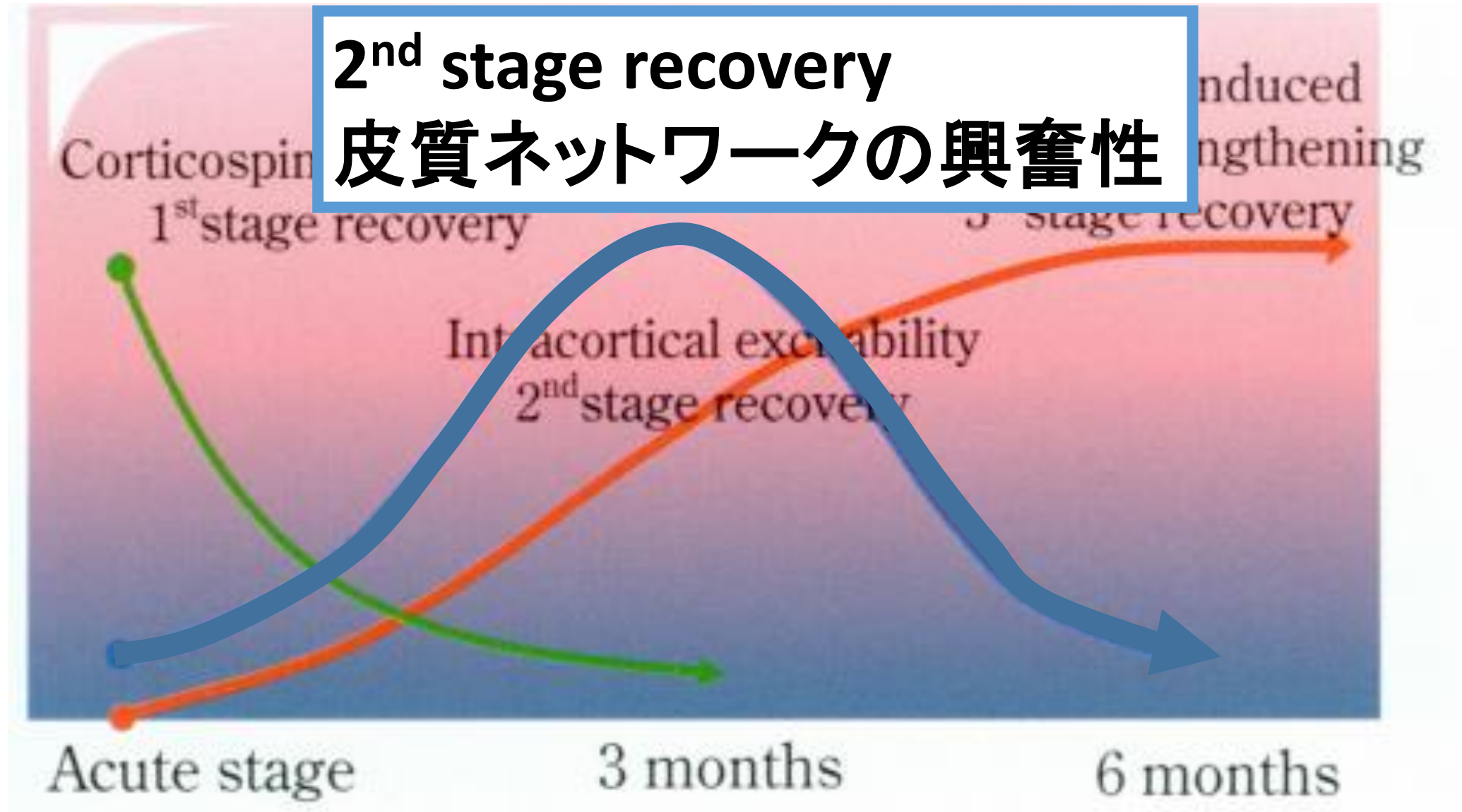
脳卒中、運動麻痺回復のステージ理論

1st stage recovery

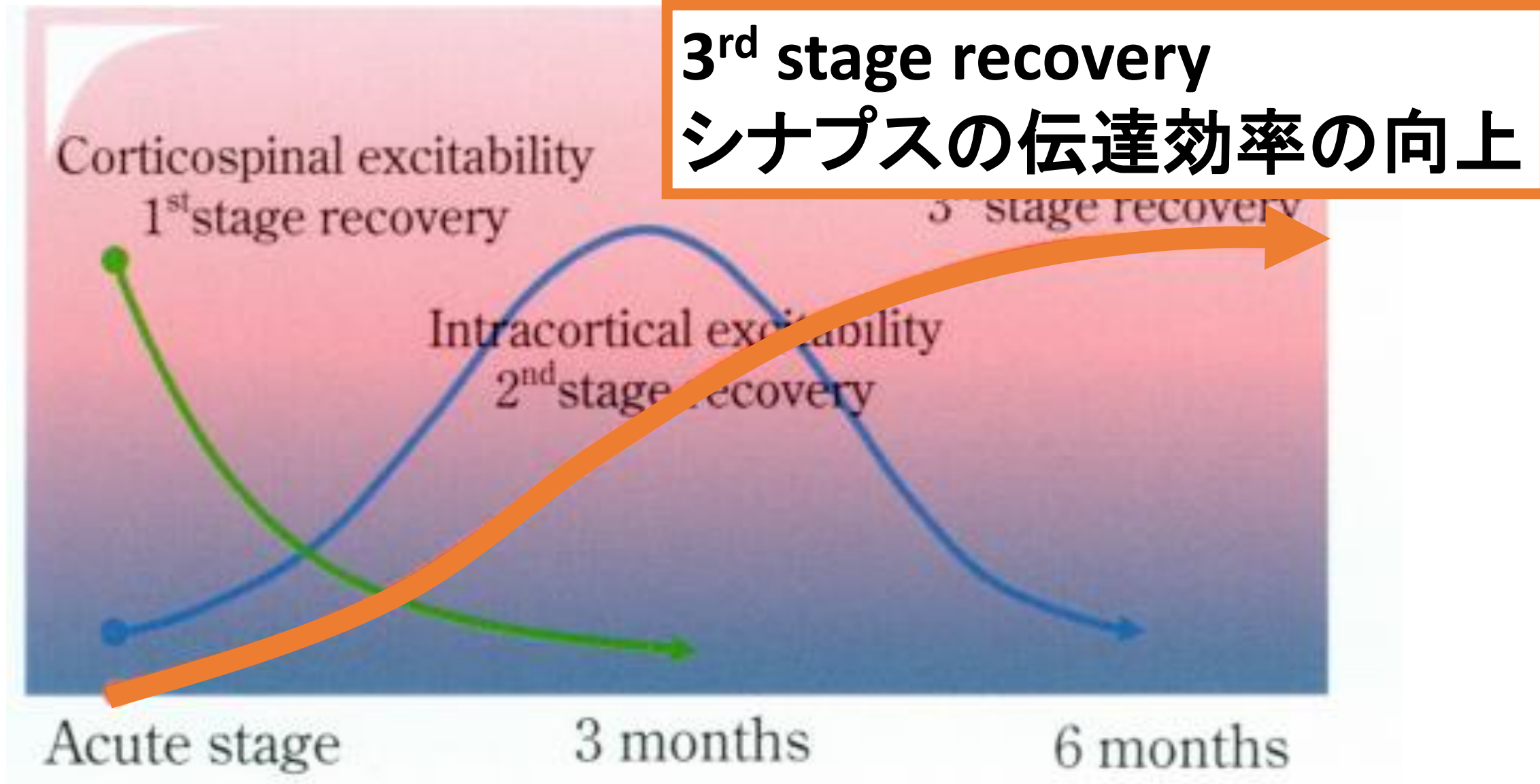
残存した皮質脊髄路の興奮性



脳卒中、運動麻痺回復のステージ理論



脳卒中、運動麻痺回復のステージ理論



Stages of Motor Output Reorganization after Hemispheric Stroke Suggested by Longitudinal Studies of Cortical Physiology

Ottavio B.C. Swaine¹, John C. Rothwell¹, Nick S. Ward^{2,5} and Richard J. Graybiel^{1,4}

¹Sobell Department of Motor Neuroscience and Movement Disorders, Institute of Neurology, University College, 8-11 Queen Square, London WC1N 3BG, UK, ²Wellcome Trust Centre for Neuroimaging, Institute of Neurology, University College London, London WC1N 3BG, UK, ³Department of Brain Repair and Rehabilitation, Institute of Neurology, University College London, London WC1N 3BG, UK and ⁴Acute Stroke and Brain Injury Unit, National Hospital for Neurology and Neurosurgery, Queen Square, London WC1N 3BG, UK

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- 対象：ロンドンの病院 脳卒中Pt 10名

- 評価：

- action research arm test [ARAT]

- nine-hole peg test [NHPT]

- Motricity Index

- National Institutes of Health Stroke Scale [NIHSS]

- timed 10-m walk

- Barthel Index

- modified Rankin Score

action research arm test [ARAT]

道具を用いた上肢機能評価

4つのテスト (grasp, grip, pinch, gross movement)
合計19項目で構成される。

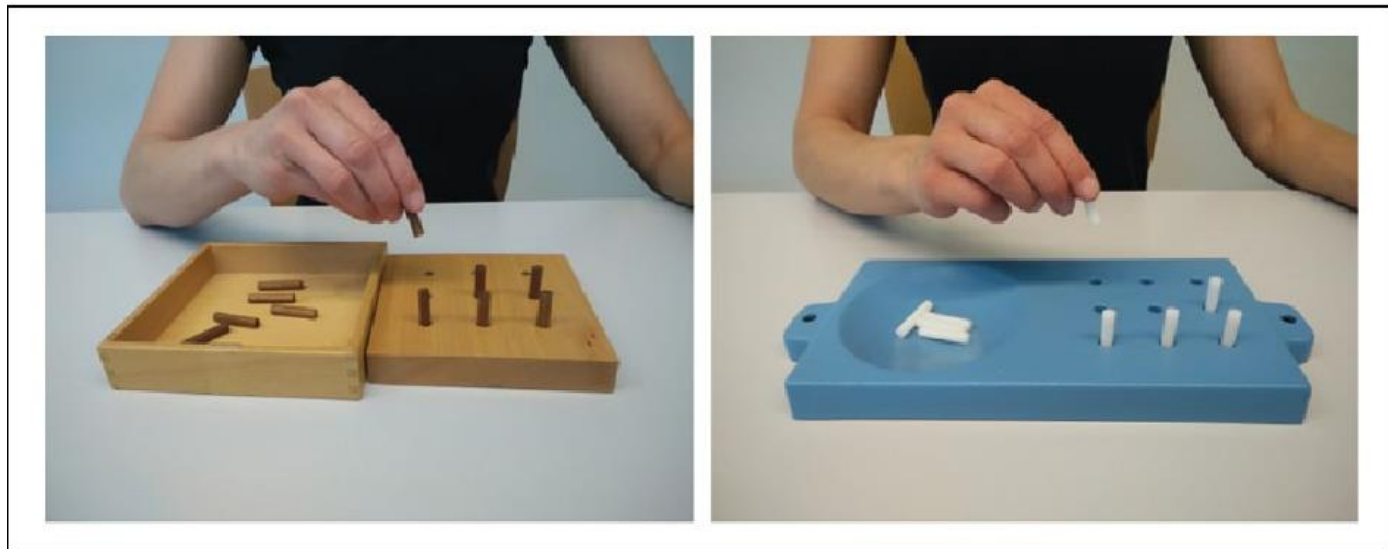
それぞれの動作に対する完遂度と時間に基づいて採点評価。ARATは、Fugl-Meyer Assessment (FMA) 上肢運動項目, STEF (Simple Test for Evaluating Hand Function) との間で高い相関が認められている。

さらにARATは、STEFとの比較で上肢機能の変化に対する反応性が高く、STEF低得点者においてARATで得点分布が広い傾向が分かっている。

ARATは、麻痺側上肢機能障害の重度から軽度まで幅広く評価可能。



nine-hole peg test [NHPT]



出来るだけ早くペグを穴にいれていく。
穴からペグを元の場所に戻す。
影響を受けていない上肢からテストを開始。

NHPTは、1971年にKellorらによって最初に導入。

1985年、健康な個人におけるNHPTの基準は、Mathiowetzらによって確立されました。

評価の目的は、巧緻性の評価

・健康な成人男性

右手で 19.0 秒

左手で 20.6 秒

・健康な成人女性

右手で 17.9 秒

左手で 19.6 秒

Motricity Index

脳卒中急性期の運動障害の評価

脳卒中発症後3日以内の予後予測として使用可能

・上肢

ピンチグリップ

肘関節屈曲運動

肩関節外転運動

・下肢

足関節背屈

膝関節伸展

股関節屈曲

6ヶ月後の上肢機能の予後決定因子となるもの

・MI (Motricity Index)

・FMA (Fuglmeier Assessment)

3ヶ月後の歩行能力の予後決定因子となるもの

・MI (Motricity Index)

・TCT (trunk control test)

・発症後3日以内で以下の点数の場合、6か月後の上肢機能の予後は比較的良好

MI : 9点以上 FMA : 1点以上

・発症後3日以内でそれぞれ以下の点数の場合、6か月後の歩行能力の予後は比較的良好

MI : 25点以上 TCT : 25点以上

National Institutes of Health Stroke Scale [NIHSS]

NIHSSの最高合計スコアは42点。
「意識」・「運動」・「感覚」・「発語」などの全11項目を判定表に従って評価し、点数化。
スコアが高いほど症状が重度。

NIHSS	Stroke Severity
0	No stroke symptoms
1～4	Minor stroke
5～15	Moderate stroke
16～20	Moderate to severe stroke
21～42	Severe stroke

timed 10-m walk (10m歩行テスト)

脳卒中患者様のカットオフの一例

- ・屋内歩行自立 0.4m/s 以下
- ・限定された範囲 0.4~0.8m/s

回復期における歩行自立度のカットオフ値

- ・11.6秒

地域在住高齢者

- ・屋内歩行自立20 秒 (0.5m/s)
- ・屋外歩行自立10 秒 (1m/s)

Barthel Index

BI (バーセルインデックス) の概要		
項目	点数	判定基準
食事	10点	自立、手の届くところに食べ物を置けば、トレイあるいはテーブルから1人で摂食可能、必要なら介護器具をつけることができ、適切な時間内で食事が終わる
	5点	食べ物を切る等、介助が必要
	0点	全介助
移乗	15点	自立、車椅子で安全にベッドに近づき、ブレーキをかけ、フットレストを上げてベッドに移り、臥位になる。再び起きて車椅子を適切な位置に置いて、腰を掛ける動作がすべて自立
	10点	どの段階かで、部分介助あるいは監視が必要
	5点	座ることはできるが、移動は全介助
	0点	全介助
整容	5点	自立（洗面、歯磨き、整髪、ひげそり）
	0点	全介助
トイレ動作	10点	自立、衣服の操作、後始末も含む。ポータブル便器を用いているときは、その洗浄までできる
	5点	部分介助、体を支えたり、トイレトペーパーを用いることに介助
	0点	全介助
入浴	5点	自立（浴槽につかる、シャワーを使う）
	0点	全介助
歩行	15点	自立、45m以上歩行可能、補装具の使用はかまわないが、車椅子、歩行器は不可
	10点	介助や監視が必要であれば、45m平地歩行可
	5点	歩行不能の場合、車椅子をうまく操作し、少なくとも45mは移動できる
	0点	全介助
階段昇降	10点	自立、手すり、杖などの使用はかまわない
	5点	介助または監視を要する
	0点	全介助
着替え	10点	自立、靴・ファスナー、装具の着脱を含む
	5点	部分介助を要するが、少なくとも半分以上の部分は自分でできる。適切な時間内にできる
	0点	全介助
排便コントロール	10点	失禁なし、浣腸、坐薬の取り扱いも可能
	5点	時に失禁あり、浣腸、坐薬の取り扱いに介助を要する
	0点	全介助
排尿コントロール	10点	失禁なし
	5点	時に失禁あり、収尿器の取り扱いに介助を要する場合も含む
	0点	全介助

ADLの評価

食事、車椅子からベッドへの移動、整容、トイレ動作、入浴、歩行、階段昇降、着替え、排便コントロール、排尿コントロールの計10項目を5点刻みで点数化。
その合計点を100点満点として評価。

modified Rankin Score

The Modified Rankin Scale (mRS)

The scale runs from 0–6, running from perfect health without symptoms to death.

0 - No symptoms.

1 - No significant disability. Able to carry out all usual activities, despite some symptoms.

2 - Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.

3 - Moderate disability. Requires some help, but able to walk unassisted.

4 - Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.

5 - Severe disability. Requires constant nursing care and attention, bedridden, incontinent.

6 - Dead.

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Orlando B.C. Swaine¹, John C. Rothwell¹, Nick S. Ward^{2,5} and Richard J. Greenwood^{3,4}

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Ischemic stroke frequently leads to impairment of upper limb motor function, after which a variable degree of motor recovery is seen (Twitchell 1957). Functional imaging in humans (Ward et al. 2003a, 2004) and physiological observations in animal models (Jones and Schaller 1994; Nudo and Milliken 1996) suggest that recovery of function is associated with extensive reorganization of the motor system at the cortical level, presumably to maximize control of remaining motor output. Transcranial magnetic stimulation (TMS) has also been used in human stroke patients to probe corticospinal and intracortical physiology. Reduced corticospinal excitability from the affected hemisphere (AH) reflects damage to the corticospinal connection (Traverso et al. 1998; Byrnes et al. 2001), whereas increased intracortical excitability in both hemispheres (Liepert, Hammett, and Weiller 2000; Liepert, Storch, et al. 2000; Mangano et al. 2002) reflects changes in intrinsic circuits of the cortex.

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et al. 2002) but not all (Debaux et al. 2003) studies. Likewise, corticospinal hyperexcitability in the unaffected hemisphere (UH) was observed in some studies (Cicinnelli et al. 1997; Traverso et al. 1998; Debaux et al. 2003) but not in others (Mangano et al. 2002). For many patients, the early days and weeks after stroke are likely to be a period of great clinical and physiological change. Although several studies have performed TMS assessments during this early period, many have made only a single assessment. The greatest number within the first month is 3 measures of corticospinal excitability (D'Othaberrague et al. 1997; Debaux et al. 2003) and 2 measures of intracortical excitability (Mangano et al. 2002). Given the variability in many physiological parameters found by previous studies, it seems likely that more frequent early measurements would provide a more accurate assessment of early neurophysiological changes after stroke.

Secondly, little is known about the clinical significance of these abnormalities. Reduced corticospinal excitability of the AH in the first 5 days after stroke predicts poorer motor outcome later on (Tropea et al. 2000) and is known to be associated with poor function when studied in the chronic stage (Thickbroom et al. 2002). Likewise, intracortical disinhibition of the AH and UH (at 1 month) is seen in patients with greater motor impairment (Mangano et al. 2002). Thus, although some neurophysiological parameters appear to be related to motor impairment in these cross-sectional studies, it is not clear whether a longitudinal relationship exists. Furthermore, these measures assess different aspects of neurophysiological function each of which might be more or less important for recovery at different times after stroke. It is therefore important to know whether the relationship between motor impairment and these parameters changes during the days, weeks, and months after stroke.

We present experiments in which we acquired detailed longitudinal neurophysiological and clinical data over the first few weeks and months after first-ever ischemic stroke. Our patient group had a relatively wide range of functional impairment, allowing the possibility to examine correlations with clinical scores. Single-pulse TMS measures (resting motor thresholds [rMT], active motor thresholds [aMT]), and motor-evoked potential [MEP] recruitment curves [RCs] provide information about corticospinal excitability, specifically of the remaining original projection from the primary motor cortex (M1) to the spinal cord. The 3 paired-pulse measures used (short-interval intracortical inhibition [SICI] and long-interval intracortical inhibition [LICI], and intracortical facilitation [ICF]) are well-described parameters that provide information about intracortical

手と脳の相関を調査

経頭蓋磁気刺激 (Transcranial Magnetic Stimulation; TMS)

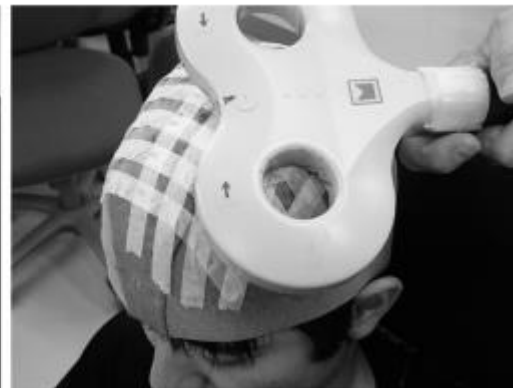
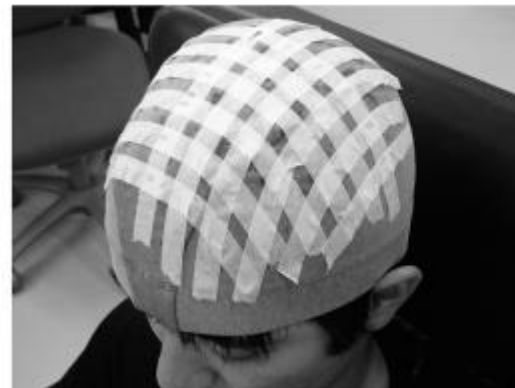
- rMTs: 安静時運動閾値
- aMTs: 活動時運動閾値
- MEP: 運動誘発電位
- recruitment curves : RCs

- パルス測定-運動皮質の出力調整がわかる
- SICI: 短潜時(間隔)皮質内抑制
- LICI: 長潜時(間隔)皮質内抑制
- ICF: 皮質内促通

潜時: 刺激が与えられてから反応のおこるまでの時間→反応時間

経頭蓋磁気刺激

- 磁力を使って脳を非侵襲的に刺激する装置
- 脳内のニューロンを興奮させる非侵襲的な方法である。この方法により、最小限の不快感で脳活動を引き起こすことで、脳の回路接続の機能が調べられる。



安静時運動閾値：rMTs・活動時運動閾値：aMTs・RCs

rMTs：安静時運動閾値

- 経頭蓋磁気刺激の量を決める基本的単位。安静時に、小さい運動誘発反応（10回の試行中少なくとも5回で起きる約50 μ Vの大きさの反応）を生じさせる最小の刺激強度と定義

aMTs：活動時運動閾値

- 最大力の約10%で等尺性収縮している筋に最小の誘発性の運動反応を（10回の試行中少なくとも5回）引き起こす刺激強度。

recruitment curves : RCs

- RCsというのは様々な刺激強度で大脳皮質に刺激を行い、刺激強度によって運動誘発電位（MEP）の大きさがどのように影響を受けるかというものを調べるものであり、こちらもCorticospinal Excitability（皮質脊髄興奮性）を評価する一つの指標として用いられる。

運動誘発電位：MEP

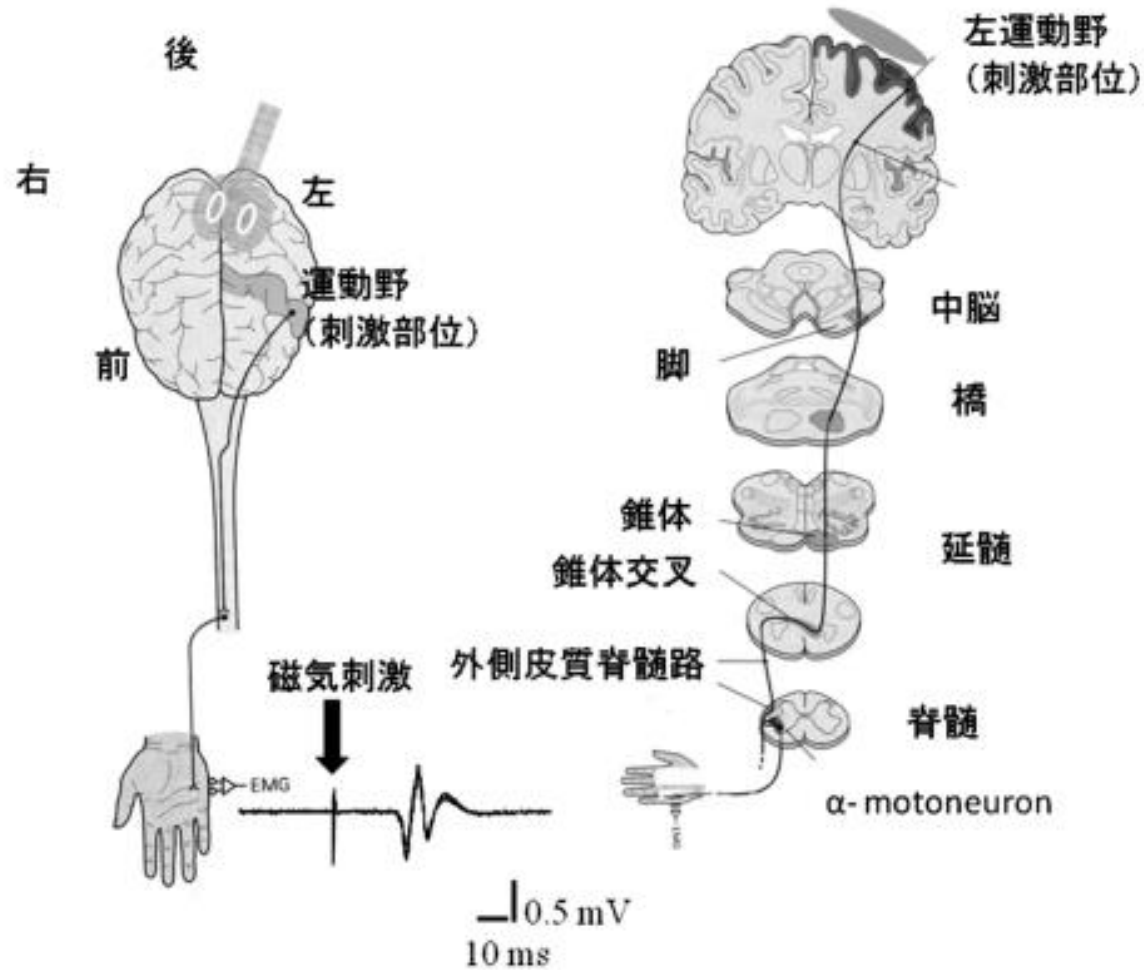


図3 MEPの経路

刺激方法

- 単発刺激

1回の単発のTMS刺激によって生じるMEP反応を各条件間でそれぞれ複数回収集し、平均値としてその各条件間の振幅の指標を比較検討するもの。

随意運動解析や抑制機構の分析、運動学習に関わる運動野の可塑性の研究等、広範囲に及ぶ検討に用いられる。

- 2連発刺激

2台の磁気刺激装置を使用し、1つの刺激コイルから連続した2発の刺激を行うもの。

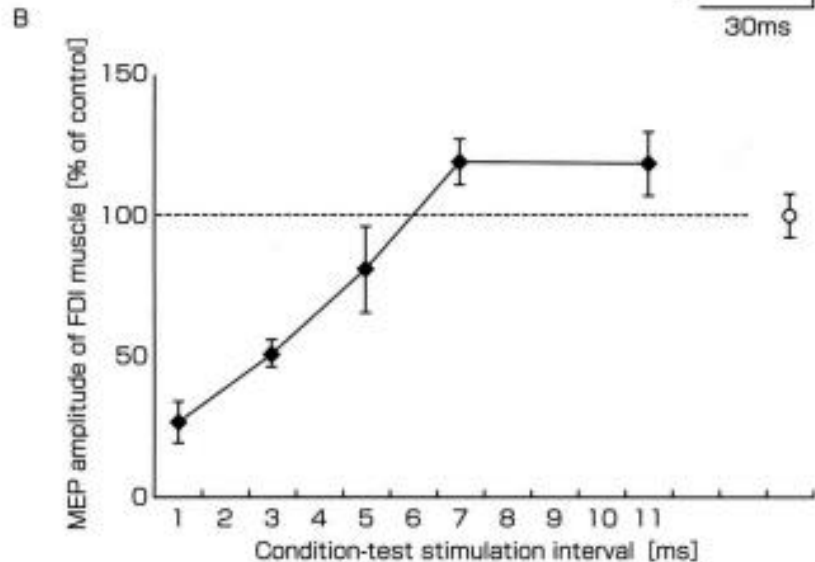
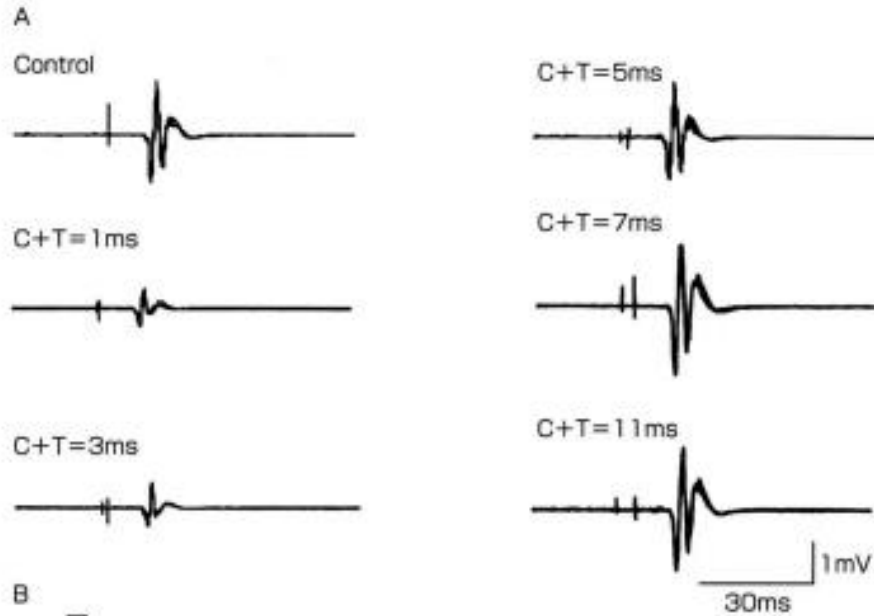
1発目の刺激はMEPが出現しない運動閾値以下の刺激(条件刺激)。2発目の刺激は通常は1mVのMEP(運動誘発電位)振幅を出現させる強度で行うもの(試験刺激)。

この条件刺激—試験刺激の2つの刺激は、刺激時間間隔を変化させることで運動野に生じる変化を検査するものである。

刺激方法

- 刺激時間間隔が1～5msであると誘発電位(MEP)は小さくなる、この抑制をSICIという。また同一刺激強度で、刺激時間間隔を6～20msにするとその誘発電位は逆に増大する、これをICFという。
- SICI・ICFヒト運動野における運動制御にかかわる抑制回路機構や促通回路機構を評価することが可能となる。

2連促通刺激による抑制と促通

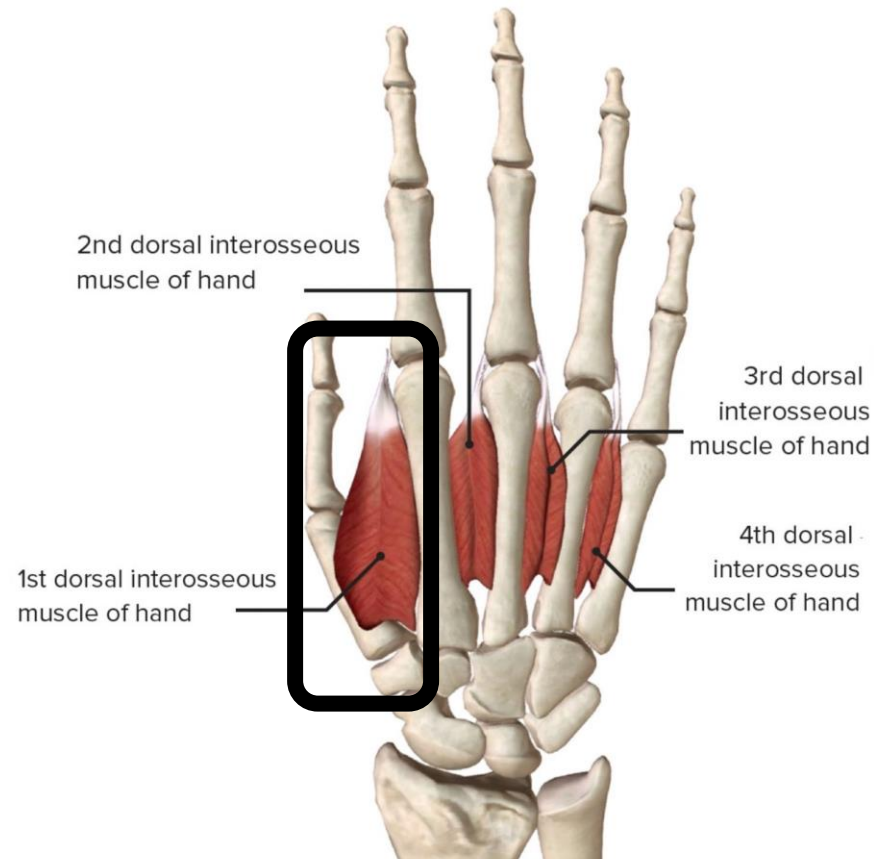


A: Controlは試験刺激のみを実施 (Test; T) のみを実施した運動誘発電位 (MEP)。それ以外の条件刺激 (condition; C) と試験刺激の両方をそれぞれに示す間隔で与えた時の MEP の変化。

B: 条件刺激と試験刺激の時間間隔が 1~6ms までの短い時間間隔では試験刺激のみで得られる運動誘発電位 (MEP) と比較し抑制を示す。時間間隔が 8ms 以降の長い時間間隔では促通が観察される

表面筋電図 : Surface electromyographic (EMG)

- 今回の対象 : 背側骨間筋 the first dorsal interosseus (FDI)



Stages of Motor Output Reorganization after Hemispheric Stroke Suggested by Longitudinal Studies of Cortical Physiology

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¹Schell Department of Motor Neuroscience and Movement Disorders, Institute of Neurology, University College, 8-11 Queen Square, London WC1N 3BG, UK, ²Wellcome Trust Centre for Neuroimaging, Institute of Neurology, University College London, London WC1N 3BG, UK, ³Department of Brain Repair and Rehabilitation, Institute of Neurology, University College London, London WC1N 3BG, UK and ⁴Acute Stroke and Brain Injury Unit, National Hospital for Neurology and Neurosurgery, Queen Square, London WC1N 3BG, UK

Reorganization of motor circuits in the cerebral cortex is thought to contribute to recovery following stroke. These can be examined with transcranial magnetic stimulation (TMS) using measures of corticospinal tract integrity and intracortical excitability. However, little is known about how these changes develop during the important early period post-stroke and their influence on recovery. We used TMS to obtain multiple measures bilaterally in a group of 10 patients during the early days and weeks and up to 6 months post-stroke, in order to examine correlations with tests of hand function. Ten age-matched healthy subjects were also studied. After stroke, day-to-day variation in performance was unrelated to physiological measures in the first 3 weeks. Measures of corticospinal integrity averaged over the same period correlated well with hand function, but this relationship became weaker at 3 months. In contrast, most intracortical excitability measures did not correlate acutely but did so strongly at 3 months. Thus in the acute stage, patients' performance is limited by damage to corticospinal output. Improved performance at 3 months may depend on reorganization in alternative cortical networks to maximize the efficiency of remaining corticospinal pathways—intracortical disinhibition may aid recovery by promoting access to these networks.

et al. 2002) but not all (Delvaux et al. 2003) studies. Likewise, corticospinal hyperexcitability in the unaffected hemisphere (UHI) was observed in some studies (Cicinelli et al. 1997; Traversa et al. 1998; Delvaux et al. 2003) but not in others (Manganotti et al. 2002). For many patients, the early days and weeks after stroke are likely to be a period of great clinical and physiological change. Although several studies have performed TMS assessments during this early period, many have made only a single assessment. The greatest number within the first month is 3 measures of corticospinal excitability (D'Onofri et al. 1997; Delvaux et al. 2003) and 2 measures of intracortical excitability (Manganotti et al. 2002). Given the variability in many physiological parameters found by previous studies, it seems likely that more frequent early measurements would provide a more accurate assessment of early neurophysiological changes after stroke.

Secondly, little is known about the clinical significance of these abnormalities. Reduced corticospinal excitability of the AIH in the first 5 days after stroke predicts poorer motor outcome later on (Tropea et al. 2000) and is known to be associated with poor function when studied in the chronic

結果

suggest that recovery of function is associated with extensive reorganization of the motor system at the cortical level, presumably to maximize control of remaining motor output. Transcranial magnetic stimulation (TMS) has also been used in human stroke patients to probe corticospinal and intracortical physiology. Reduced corticospinal excitability from the affected hemisphere (AIH) reflects damage to the corticospinal connection (Traversa et al. 1998; Byrnes et al. 2001), whereas increased intracortical excitability in both hemispheres (Liepert, Hamzel, and Weiller 2000; Liepert, Storch, et al. 2000; Manganotti et al. 2002) reflects changes in intrinsic circuits of the cortex.

There are, however, important gaps in our knowledge. First, physiological data acquired during the first weeks after stroke have not provided consistent results: motor thresholds in the AIH were raised in some (Liepert, Storch et al. 2000; Manganotti

the days, weeks, and months after stroke.

We present experiments in which we acquired detailed longitudinal neurophysiological and clinical data over the first few weeks and months after first-ever ischemic stroke. Our patient group had a relatively wide range of functional impairment, allowing the possibility to examine correlations with clinical scores. Single-pulse TMS measures (resting motor thresholds [rMTs], active motor thresholds [aMTs], and motor-evoked potential [MEP] recruitment curves [RCs]) provide information about corticospinal excitability, specifically of the remaining original projection from the primary motor cortex (M1) to the spinal cord. The 3 paired-pulse measures used (short-interval intracortical inhibition [SICI] and long-interval intracortical inhibition [LICI], and intracortical facilitation [ICF]) are well-described parameters that provide information about intracortical



評価結果

- ARATとNHPTは、1ヶ月は有意な改善がみられた

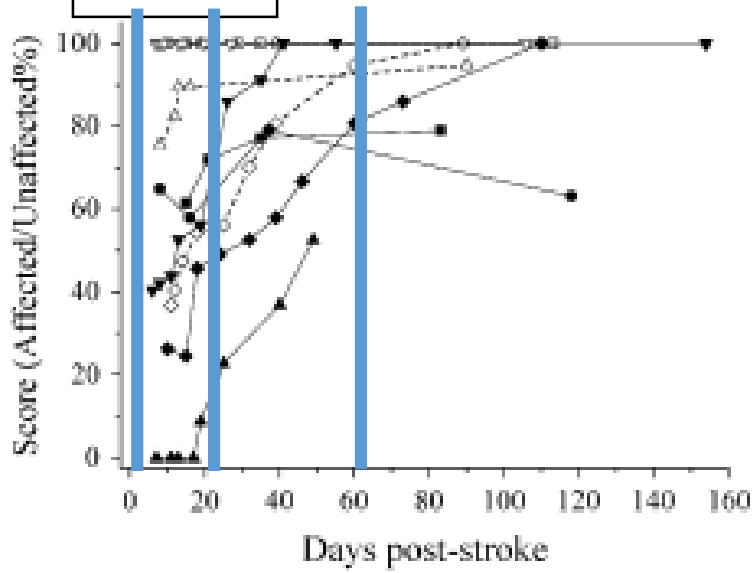


1ヶ月以降は有意な改善はみられなかった。

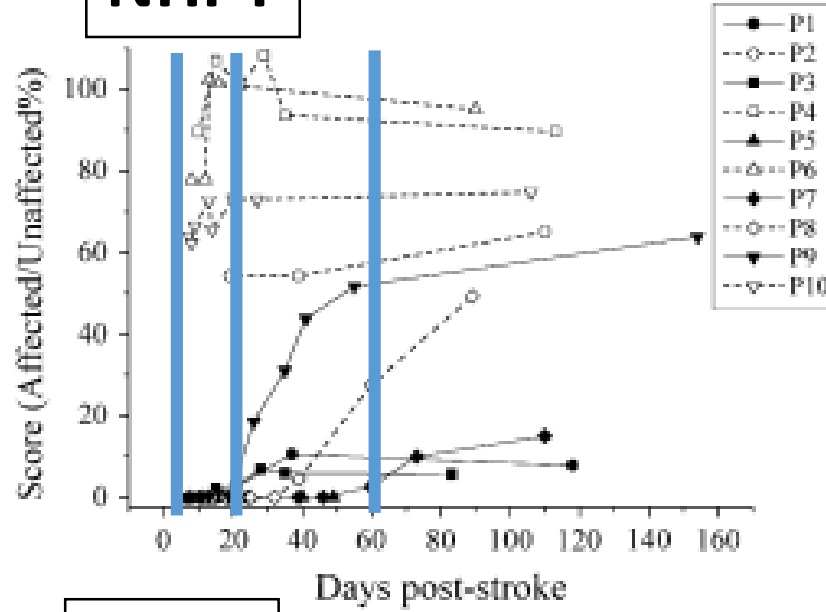
- 1ヶ月→1ヶ月vs3ヶ月→3ヶ月

※上肢機能としては、最初の1ヶ月で回復が観察され、最大3ヶ月で全体的にいくらか改善された。

ARAT

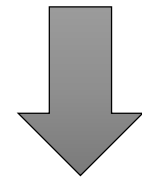


NHPT



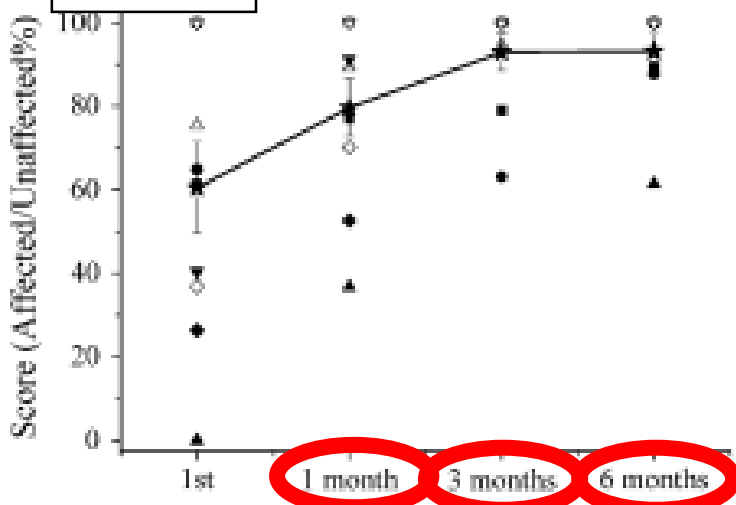
上肢の機能評価

- ARAT
- NHPT



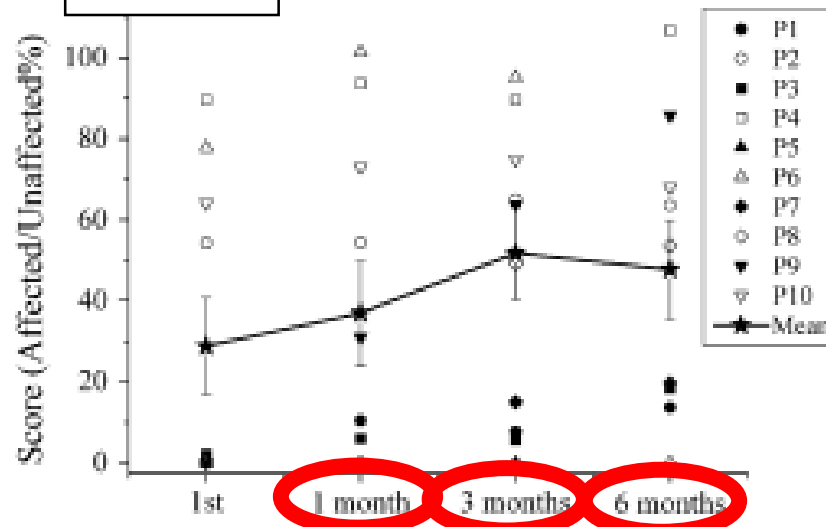
1ヶ月→3ヶ月
と改善

ARAT



1ヶ月 3ヶ月 6ヶ月

NHPT



1ヶ月 3ヶ月 6ヶ月



評価結果

- Motricity Index
- National Institutes of Health Stroke Scale [NIHSS]
- timed 10-m walk
- Barthel Index[BI]
- modified Rankin Score

Motricity Index、NIHSS、10m歩行、BIは脳卒中発症後1ヶ月までは有意に改善があり、その他もほぼ有意であった。

1ヶ月から3ヶ月では、10m歩行、BIで更に改善がみられたが、他のテストでは改善がみられなかった。

脳卒中、運動麻痺回復のステージ理論

1st stage recovery

残存した皮質脊髄路の興奮性

Training-induced synaptic strengthening
3rd stage recovery

Intracortical excitability
2nd stage recovery

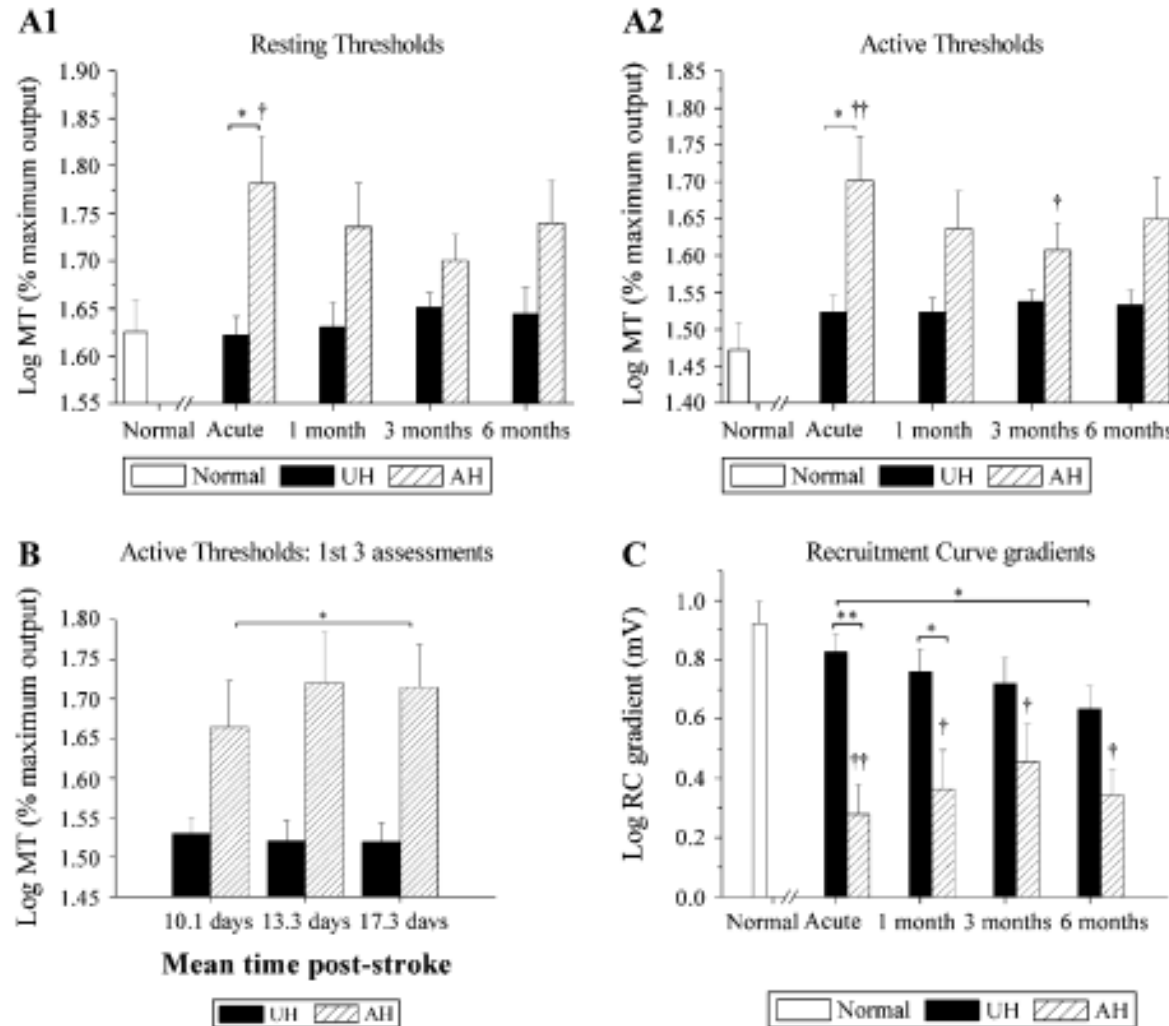
Acute急性期の尺度を脳卒中発症後の最初の3週間以内に設定

Acute stage

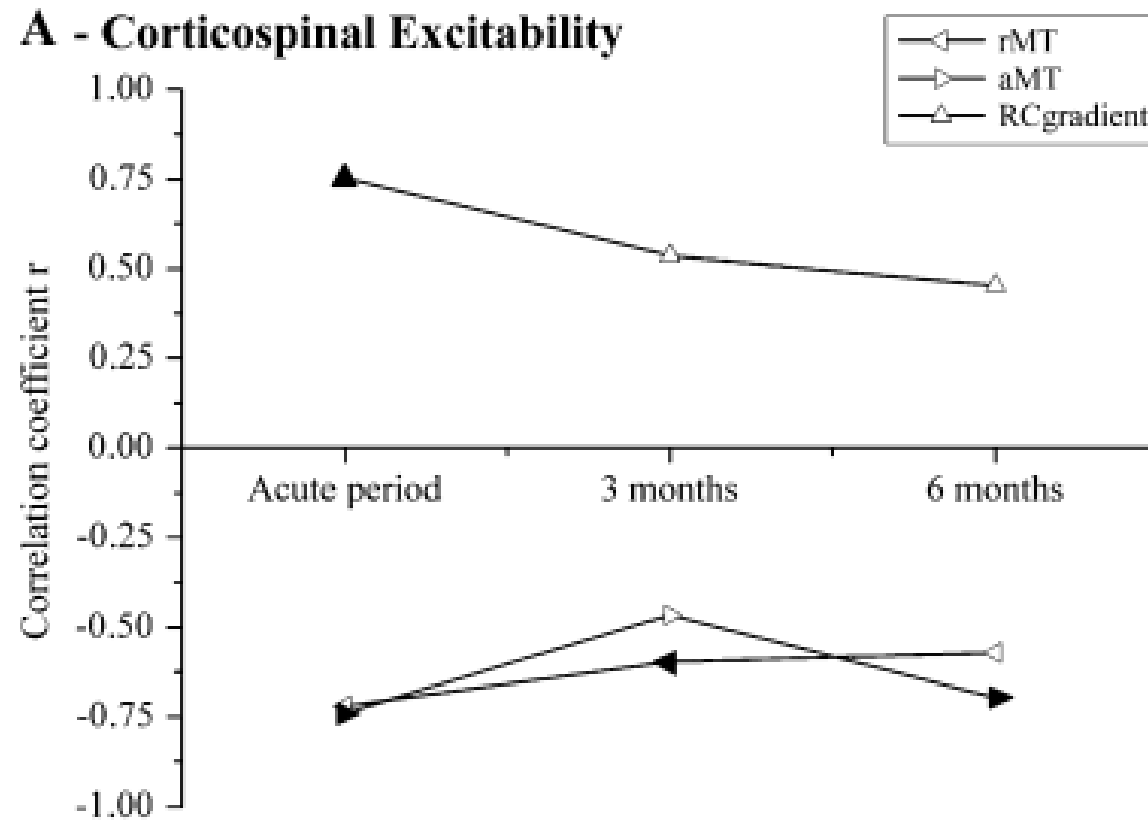
3 months

6 months

損傷半球・非損傷半球の皮質脊髓路の興奮性：運動閾値から読み解く



経時的に皮質の興奮性が低下していく

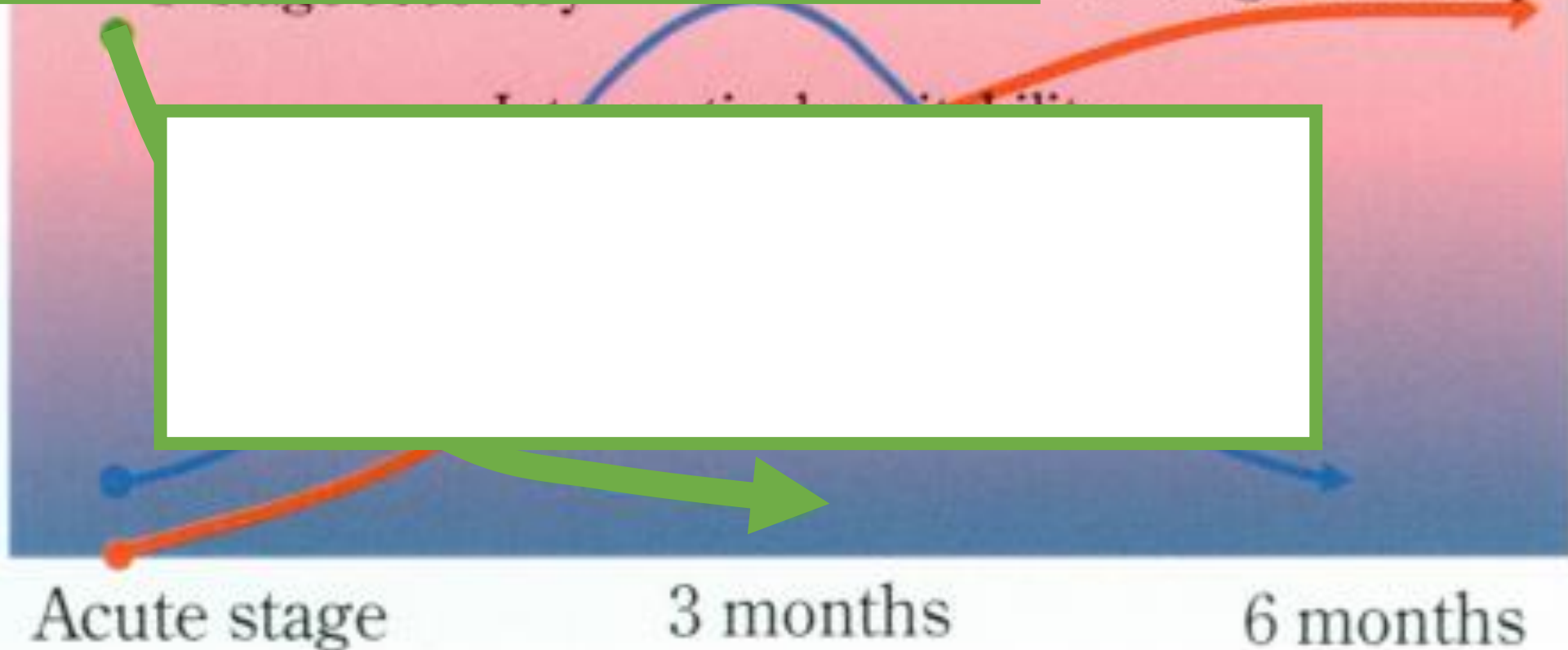


脳卒中、運動麻痺回復のステージ理論

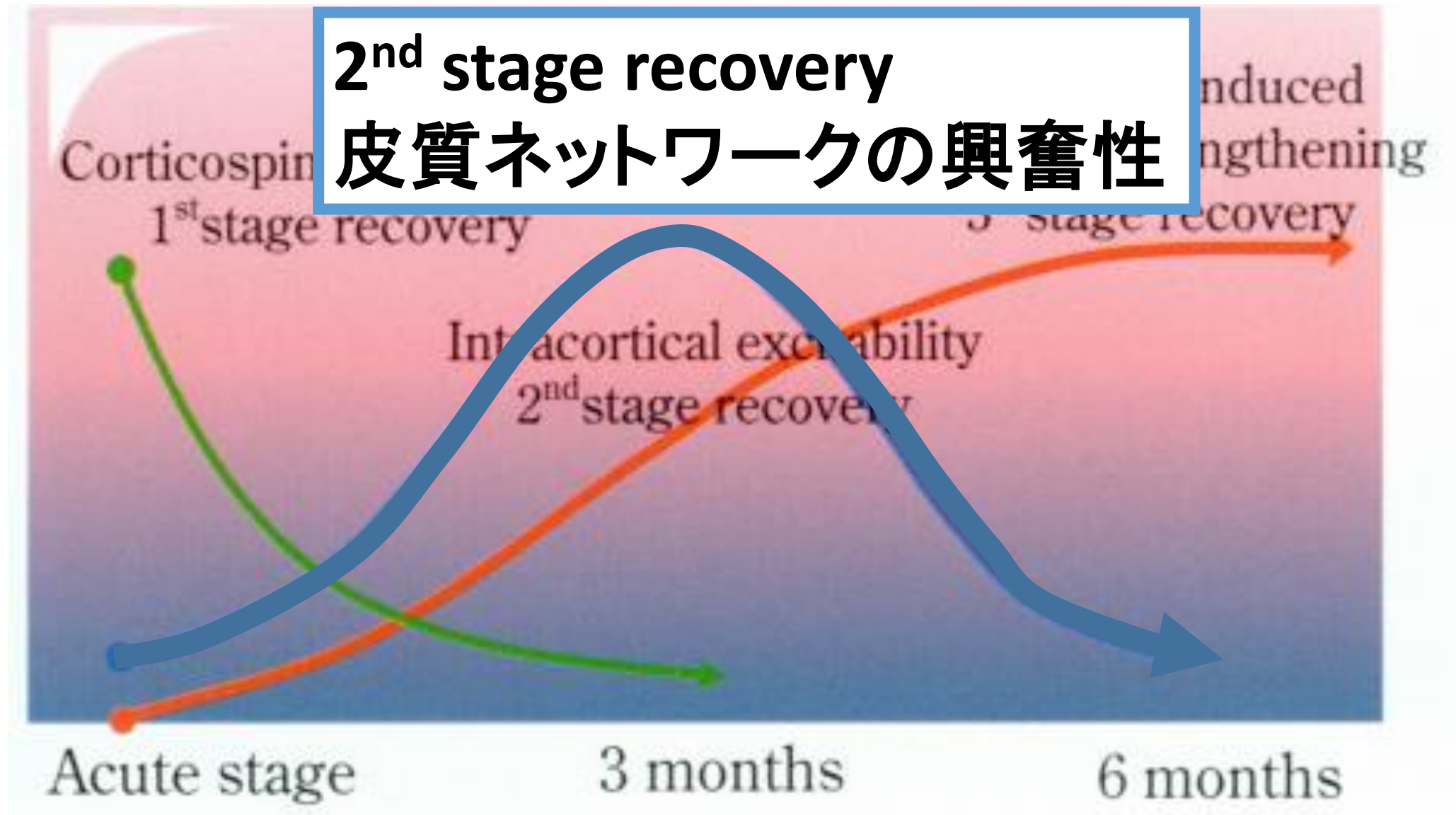
1st stage recovery

残存した皮質脊髄路の興奮性

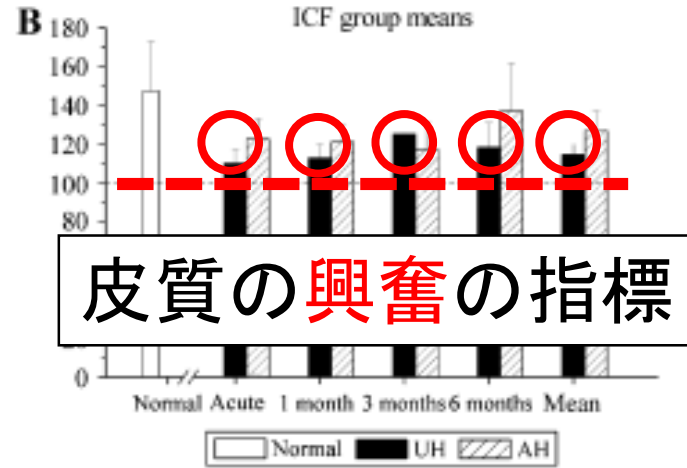
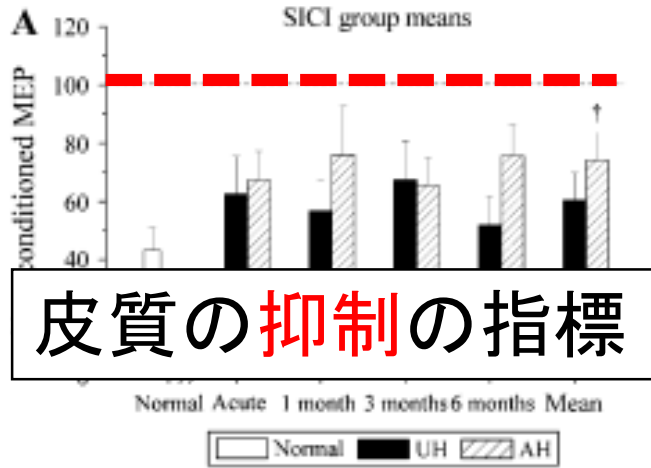
Training-induced synaptic strengthening
3rd stage recovery



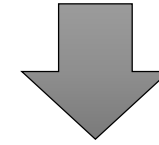
脳卒中、運動麻痺回復のステージ理論



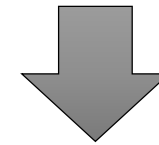
促通状態



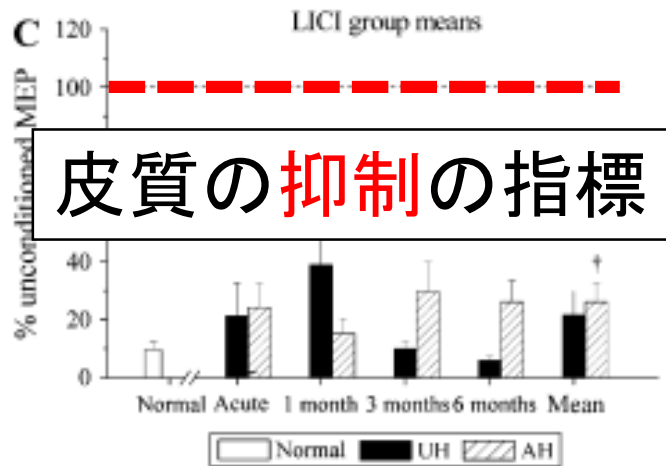
ICFのみ促通状態に到達
(皮質の興奮性は上昇)



抑制の促通がされていない状態



脱・抑制状態

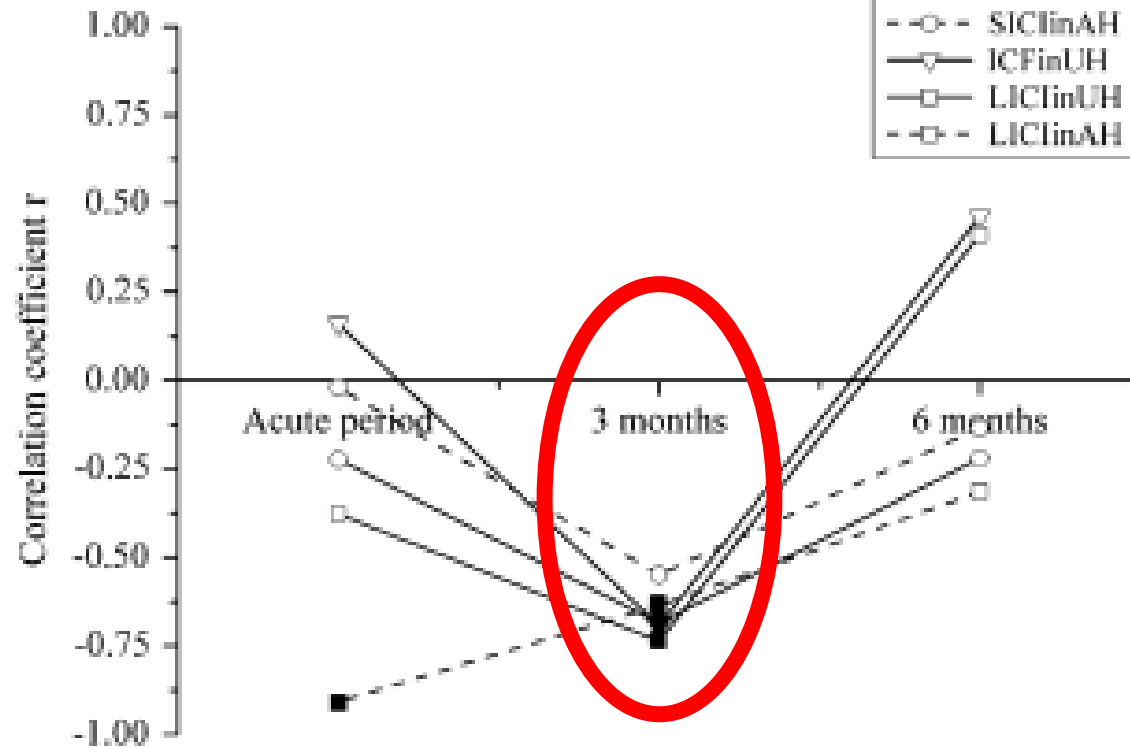


補

Normalと比較すると、
脳卒中の脳(UH非損傷側・AH損傷側)は
1・3・6か月で皮質の抑制が強く・興奮性が
低下していることも予測できる

皮質の興奮性

B - Intracortical Excitability



SICI・LICI皮質の抑制の指標

ICF: 皮質の興奮の指標

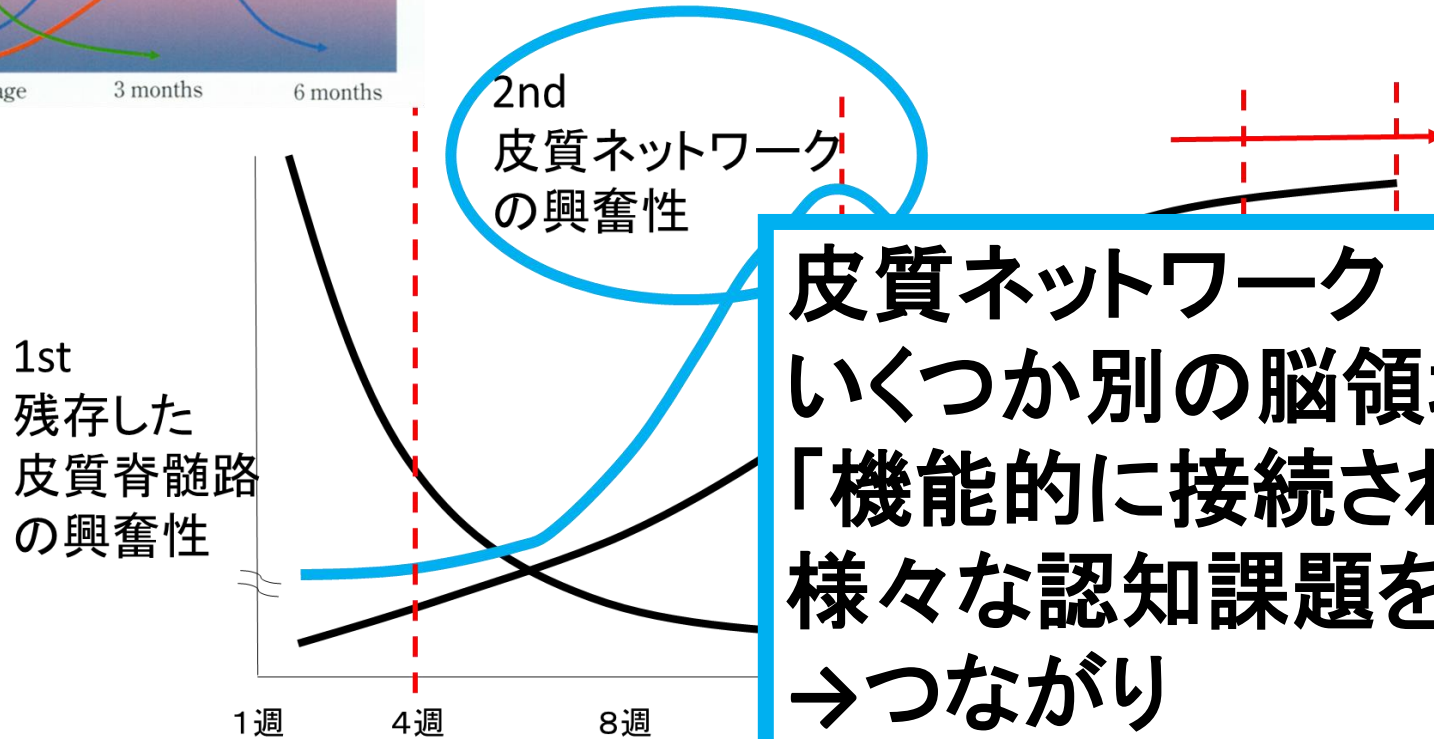
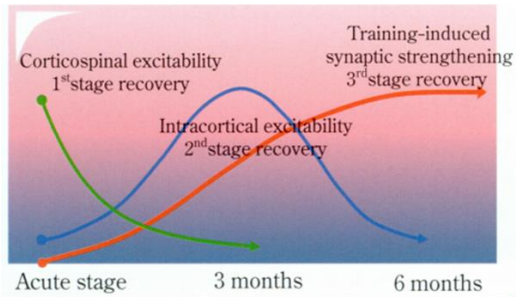
AH: 損傷側(損傷半球)

UH: 非損傷側

上肢の機能検査との相関では
Acute(急性期)と6カ月では相関はみられないが、
3ヶ月で相関することが示されている。

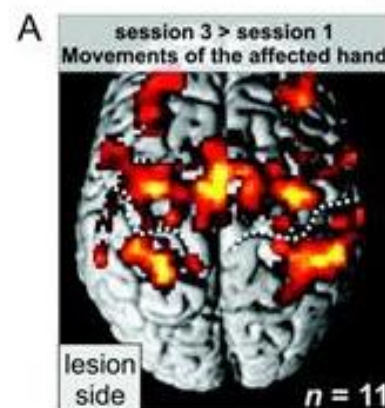
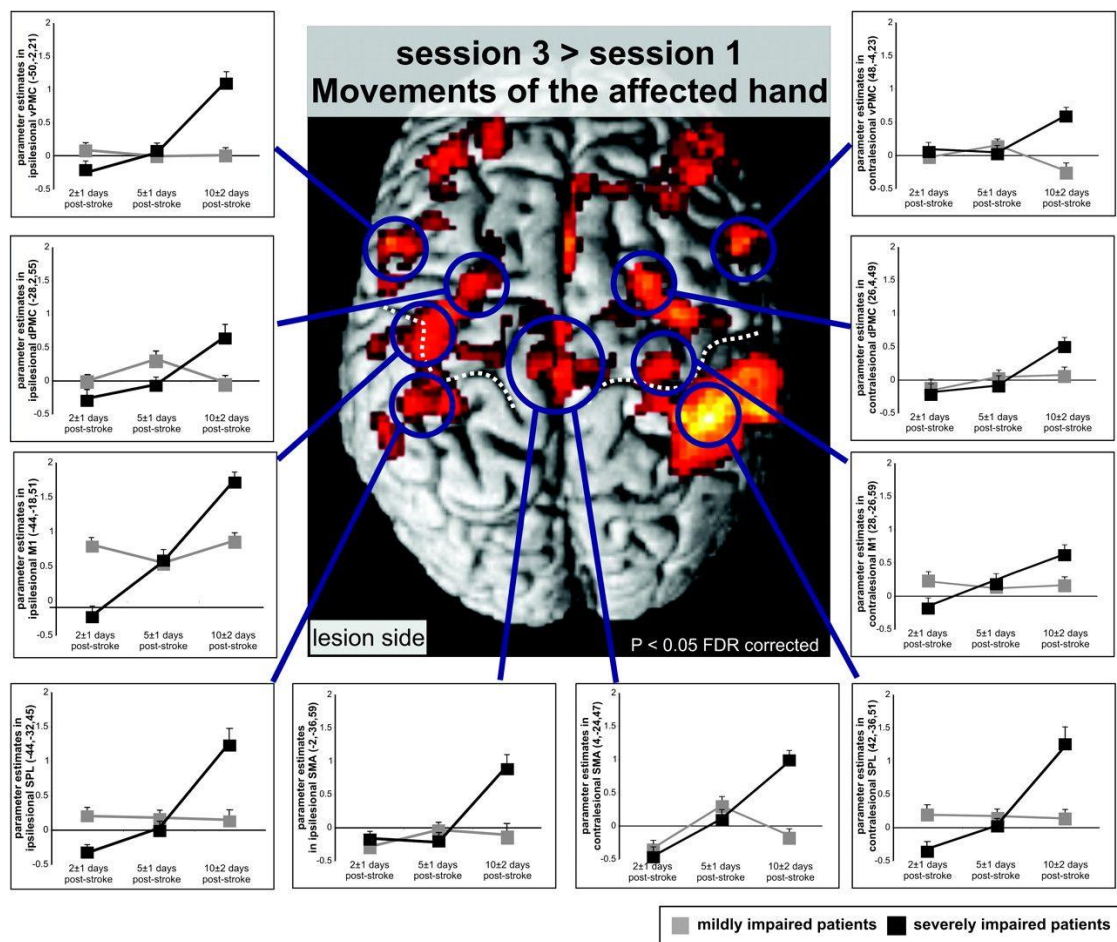


損傷後は皮質の脱抑制が出現し、
かつ機能向上は3ヶ月時点で相関がでることから
3ヶ月付近での皮質の興奮がおこっていることから考えると
損傷側での皮質ネットワークが活発になっていることが示唆できる。

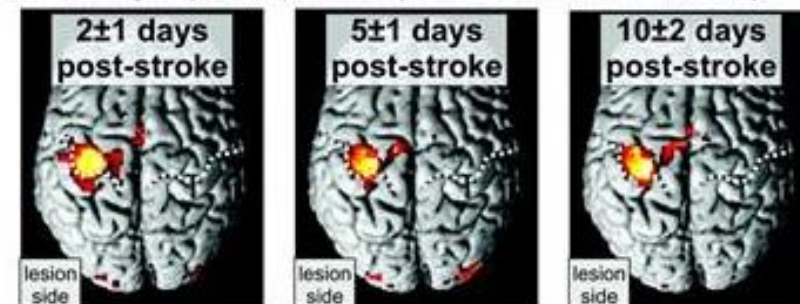


皮質ネットワーク
いくつか別の脳領域同士が密接に
「機能的に接続されて」
様々な認知課題を達成している
→つながり

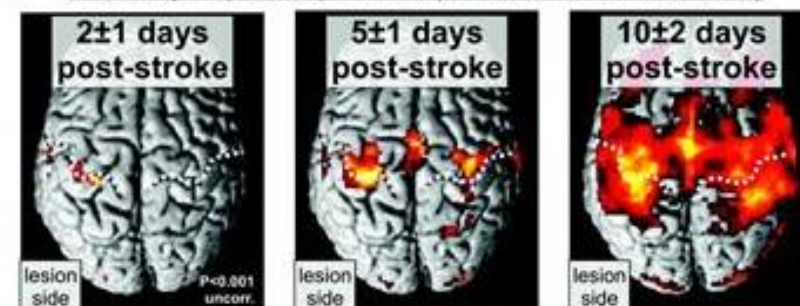
脳卒中後早期の皮質脊髄路の興奮とネットワークの変化



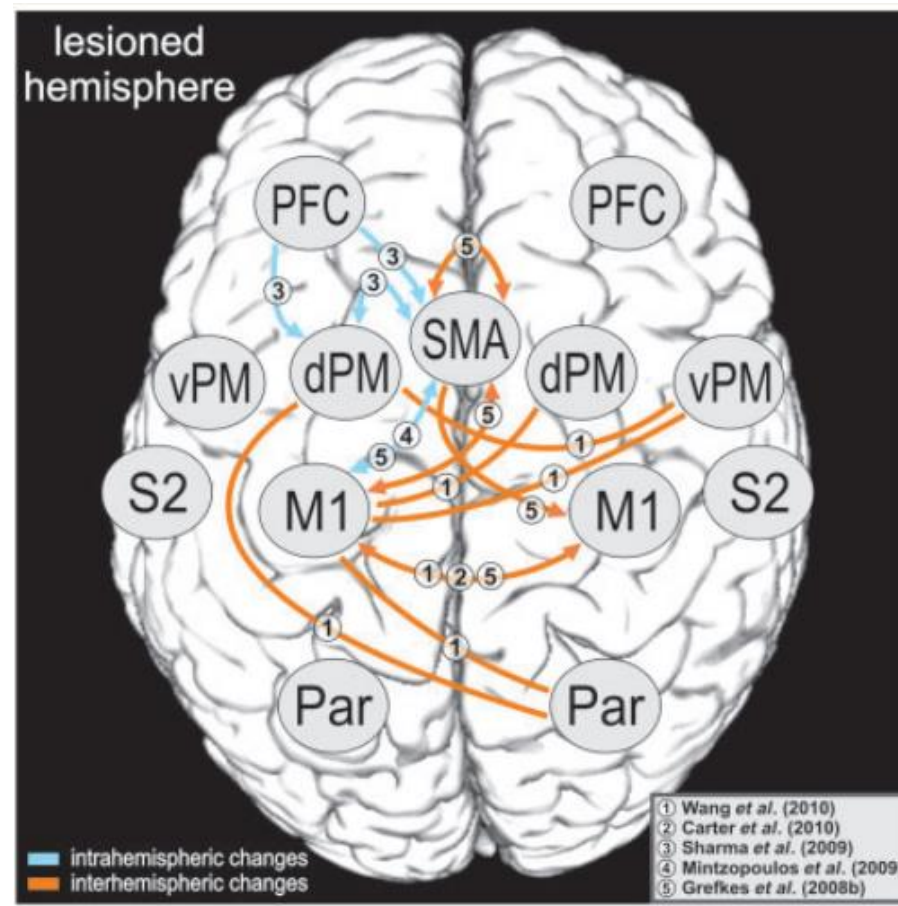
B Mildly impaired patients (initial ARAT score: 43 - 55)



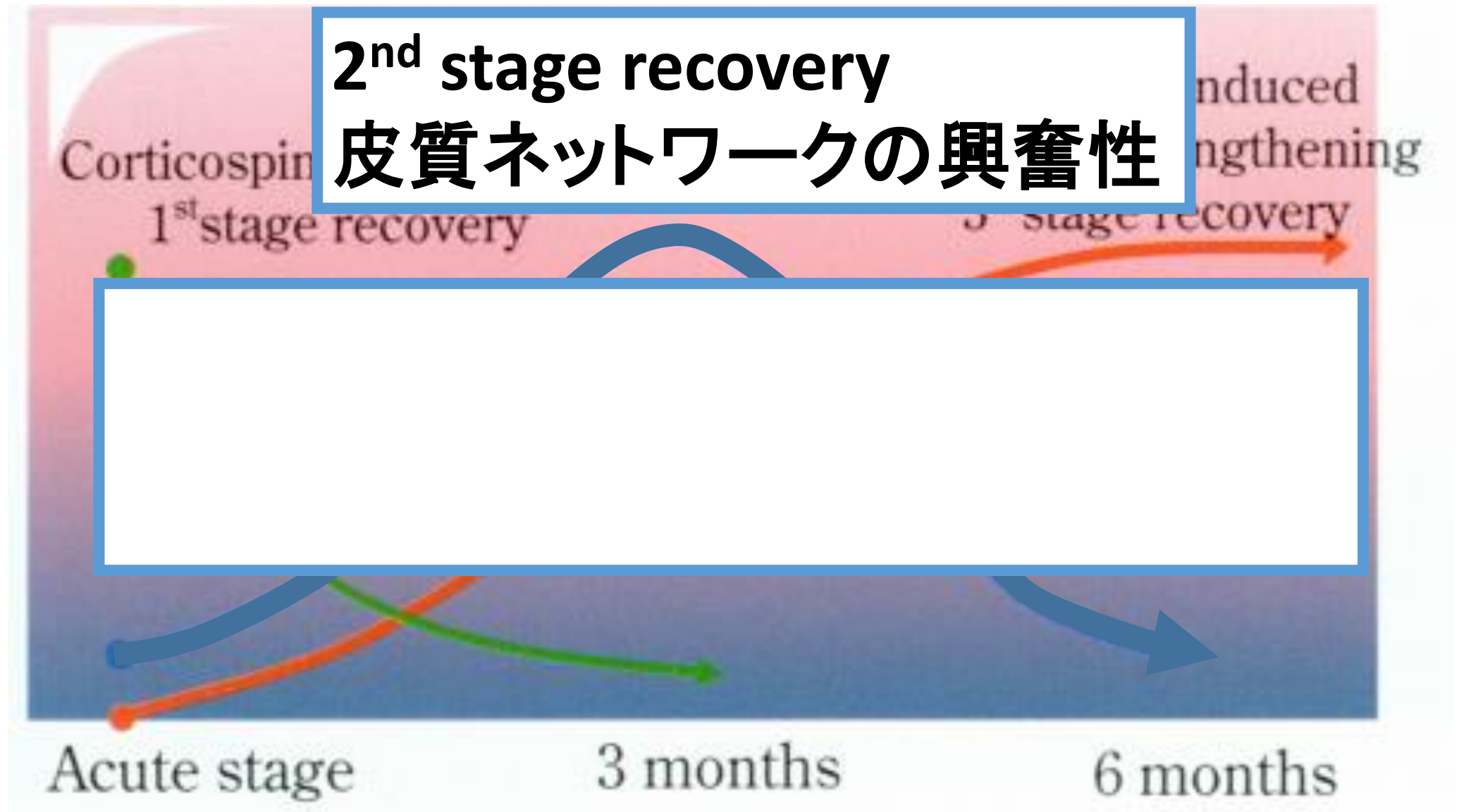
Severely impaired patients (initial ARAT score: 0-38)



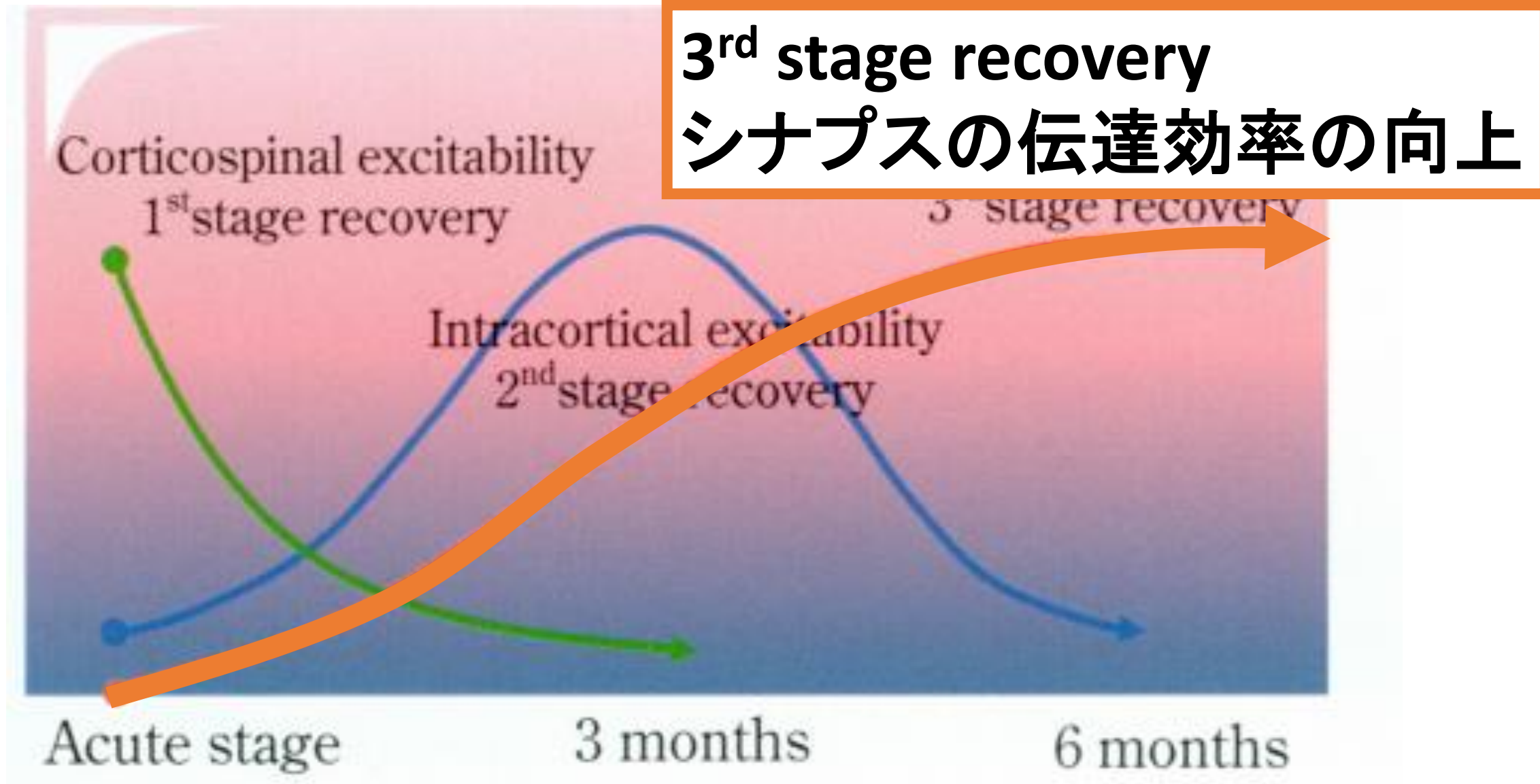
皮質のつながりの変化 (ネットワークの変化)



脳卒中、運動麻痺回復のステージ理論



脳卒中、運動麻痺回復のステージ理論



シナプスの役割：情報伝達

神経細胞間の情報伝達の間
→ 神経の接合部位

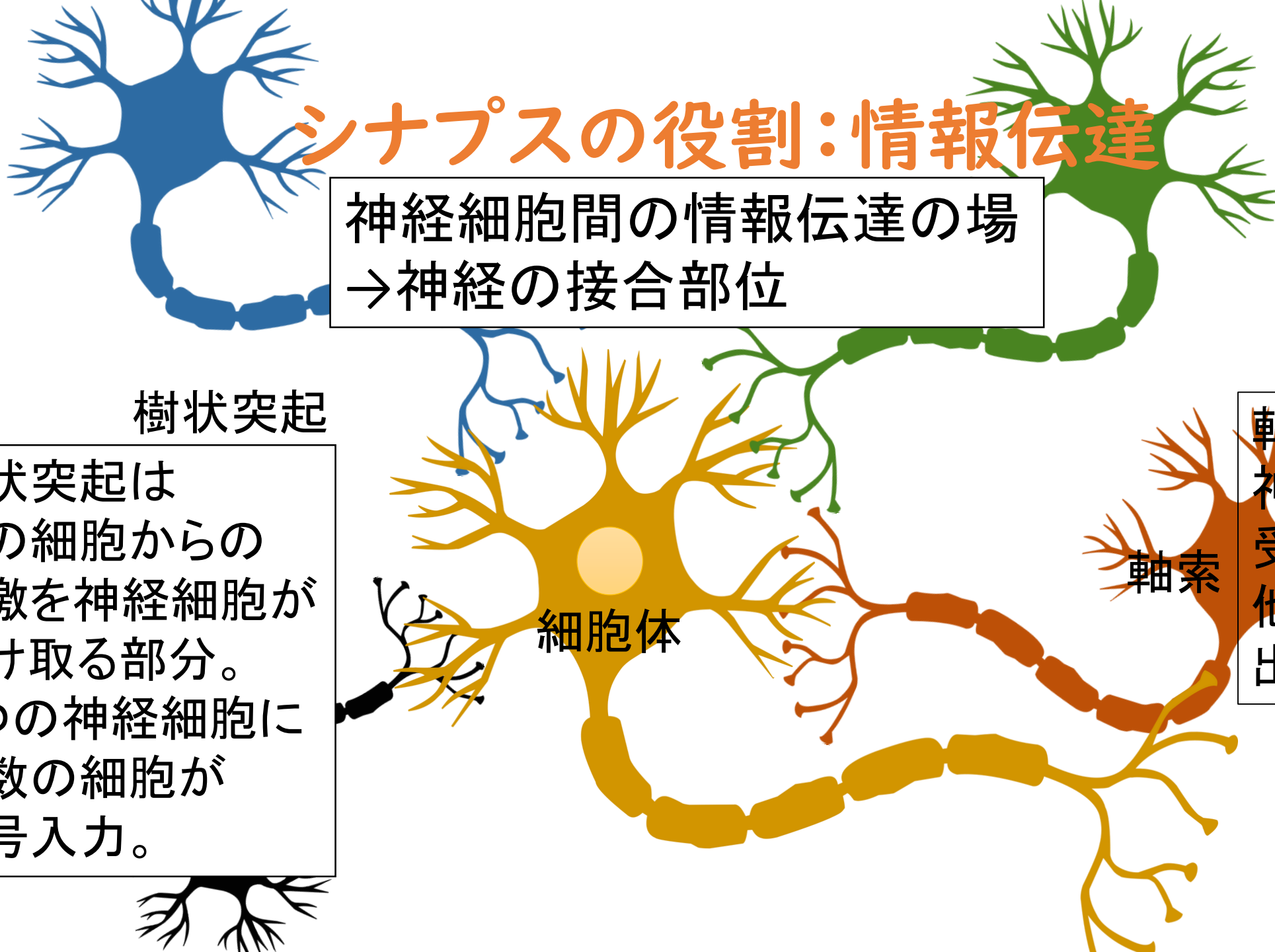
樹状突起

樹状突起は他の細胞からの刺激を神経細胞が受け取る部分。1つの神経細胞に複数の細胞が信号入力。

細胞体

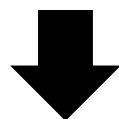
軸索

軸索は神経細胞が受けた刺激を他の細胞へと出力する部分



神経回路の再編：シナプスの変化①

手指や前腕に対応する領域に脳梗塞を起こす



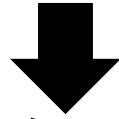
支配領域の消失にともない運動機能が障害



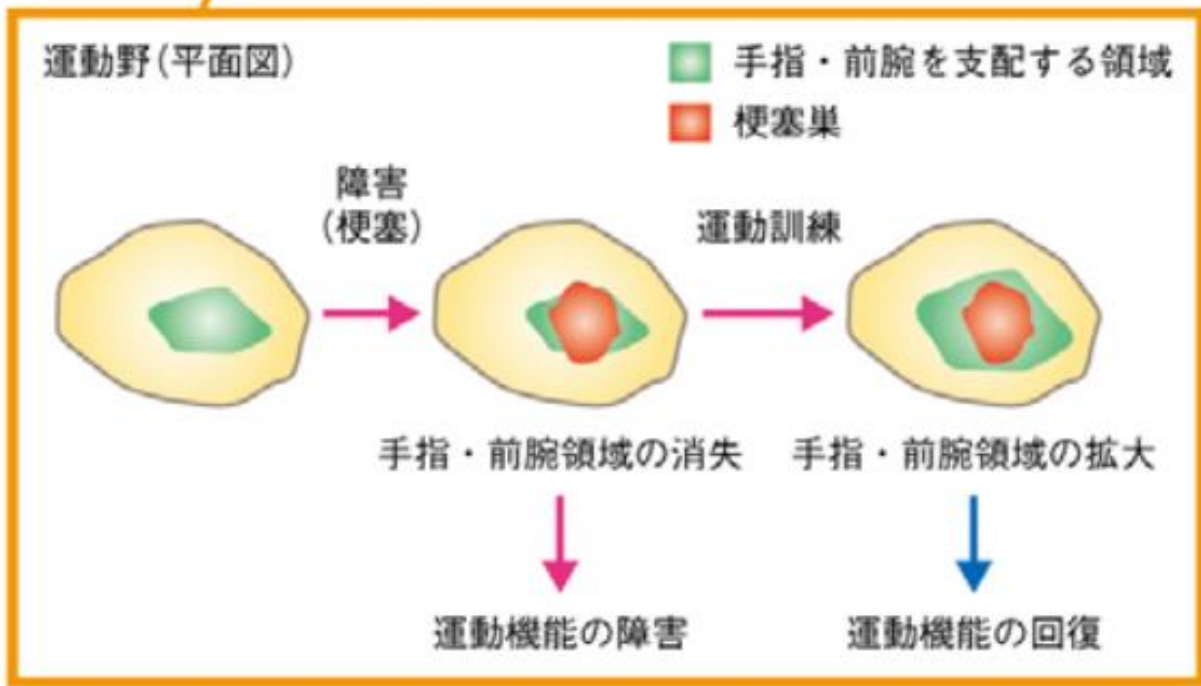
脳梗塞ののちに手指に運動訓練を施すと梗塞巣の周囲の残った領域において手指や前腕の動きをになう領域が拡大



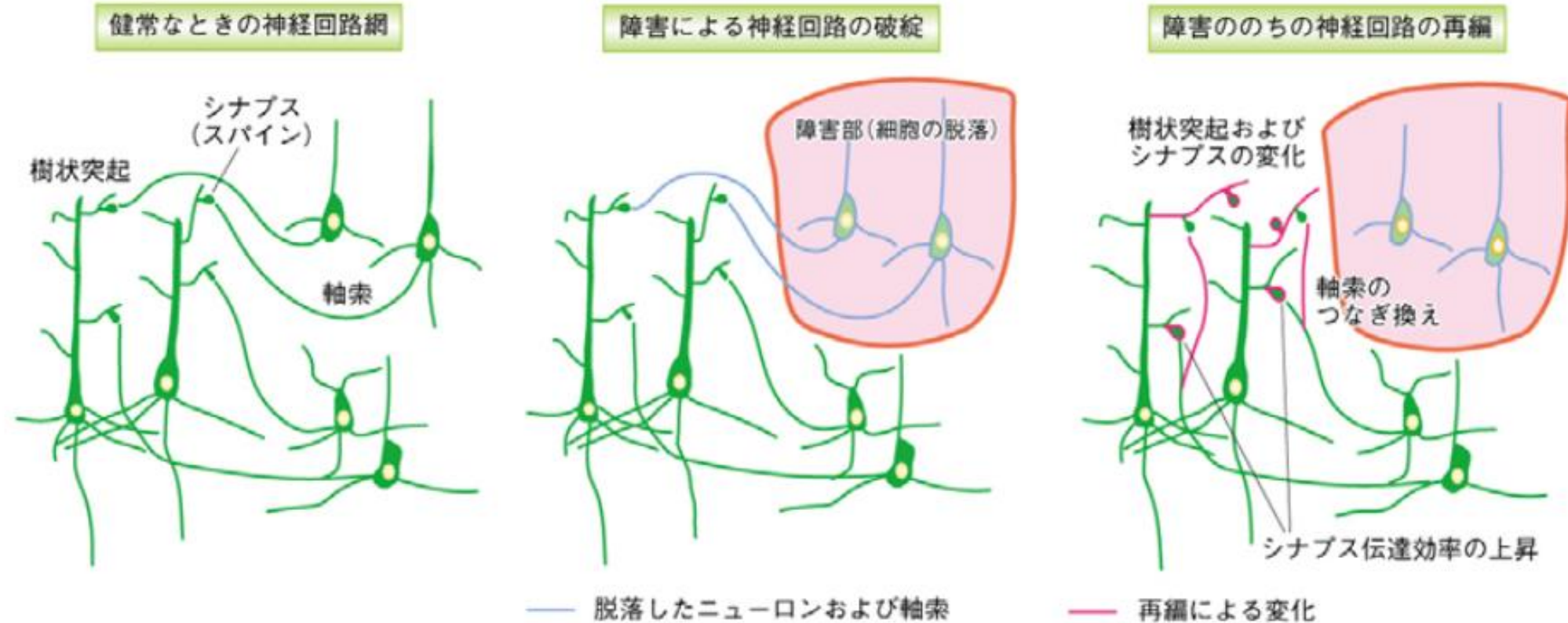
機能回復



残った神経回路が可塑的に変化して機能の回復に寄与しうることを示唆

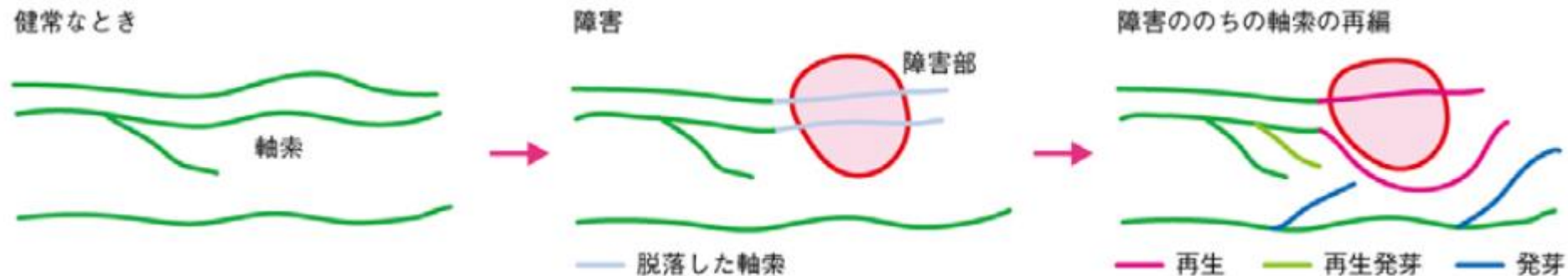
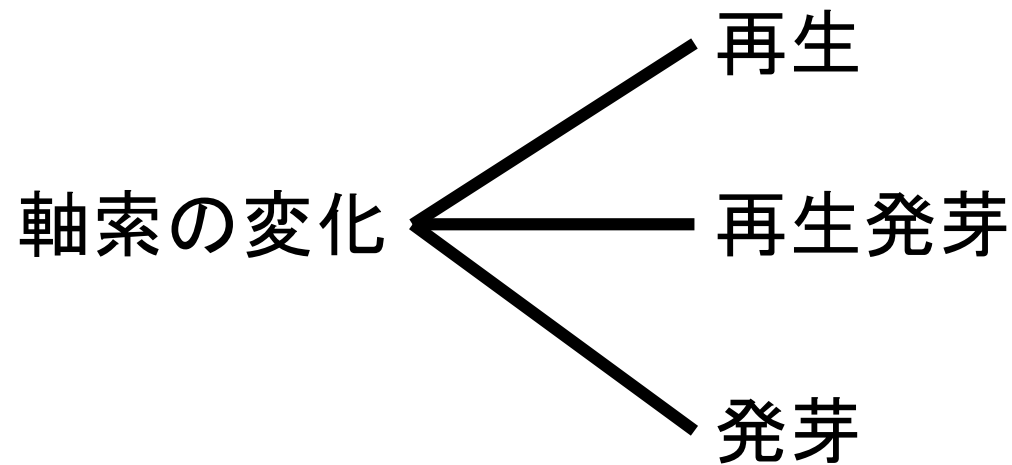


神経回路の再編：シナプスの変化②



ニューロンの軸索や樹状突起，シナプスの接続，神経伝達効率が変化

神経回路の再編：シナプスの変化③

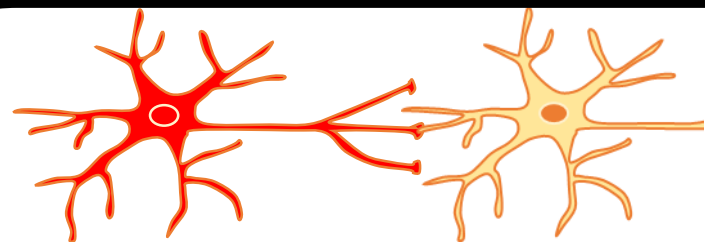


シナプス結合：興奮と抑制

シナプス伝達物質

興奮性
アセチルコリン、
グルタミン酸

興奮性
シナプス



興奮性シナプスは、
シナプス後膜に
脱分極 (EPSP) を引き起こす。

運動トレーニングは長期的に
興奮性シナプスの伝達効率を強化する

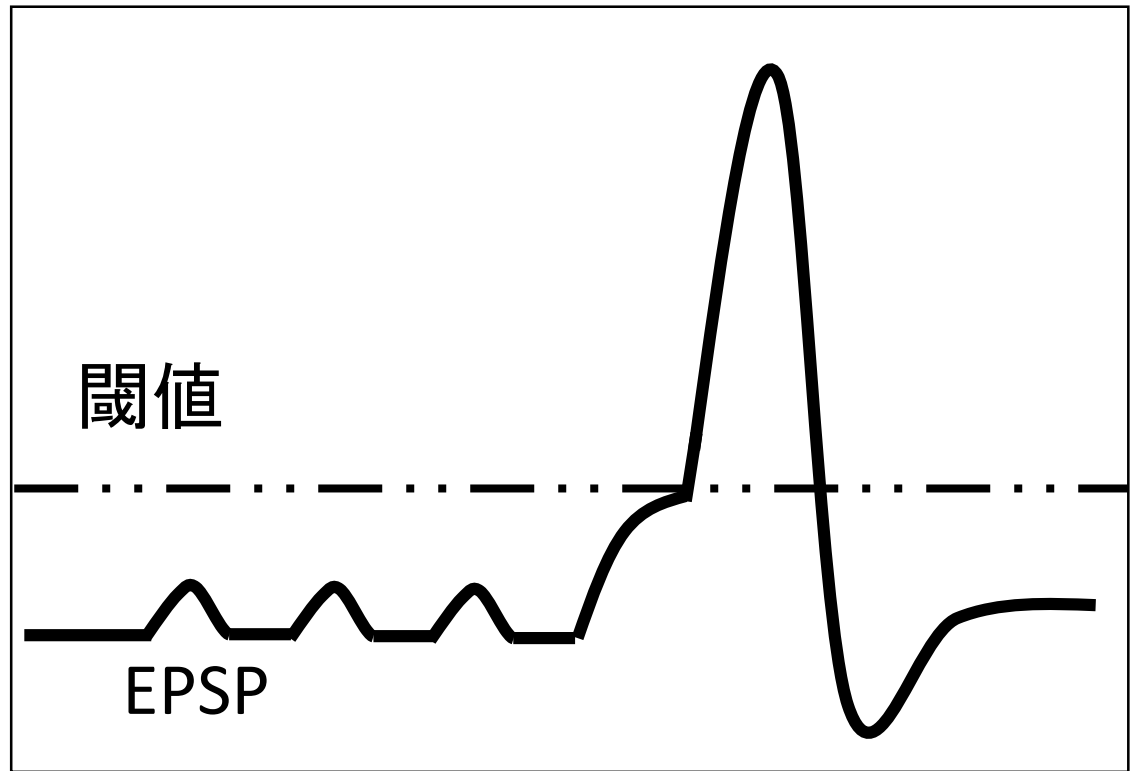
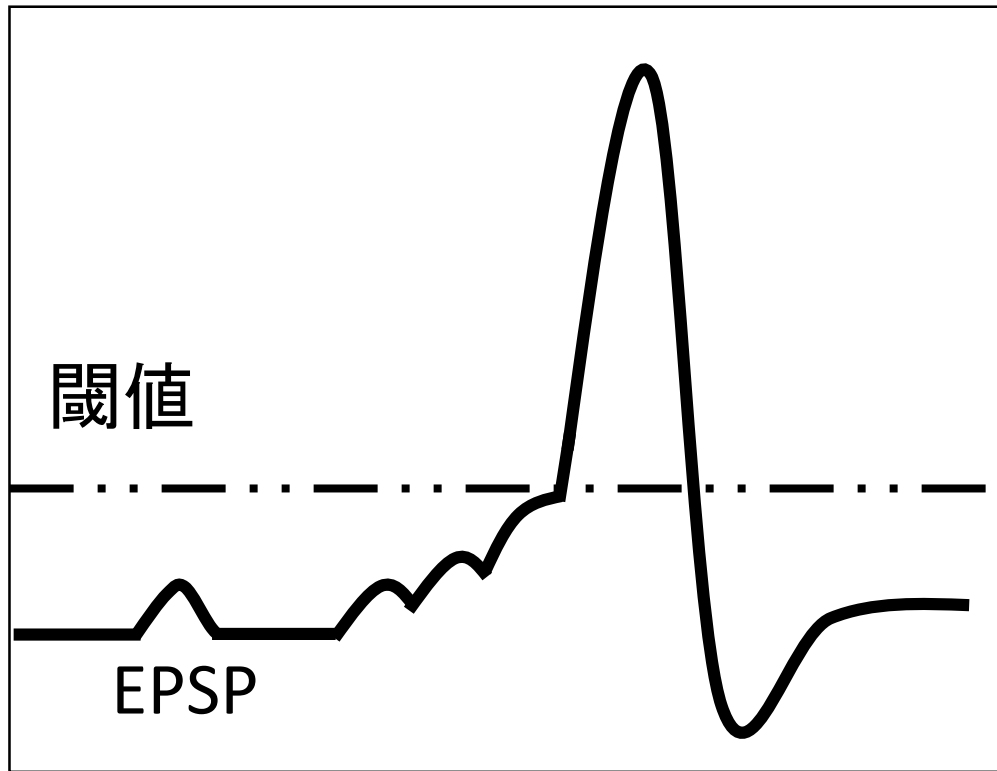
抑制性
シナプス



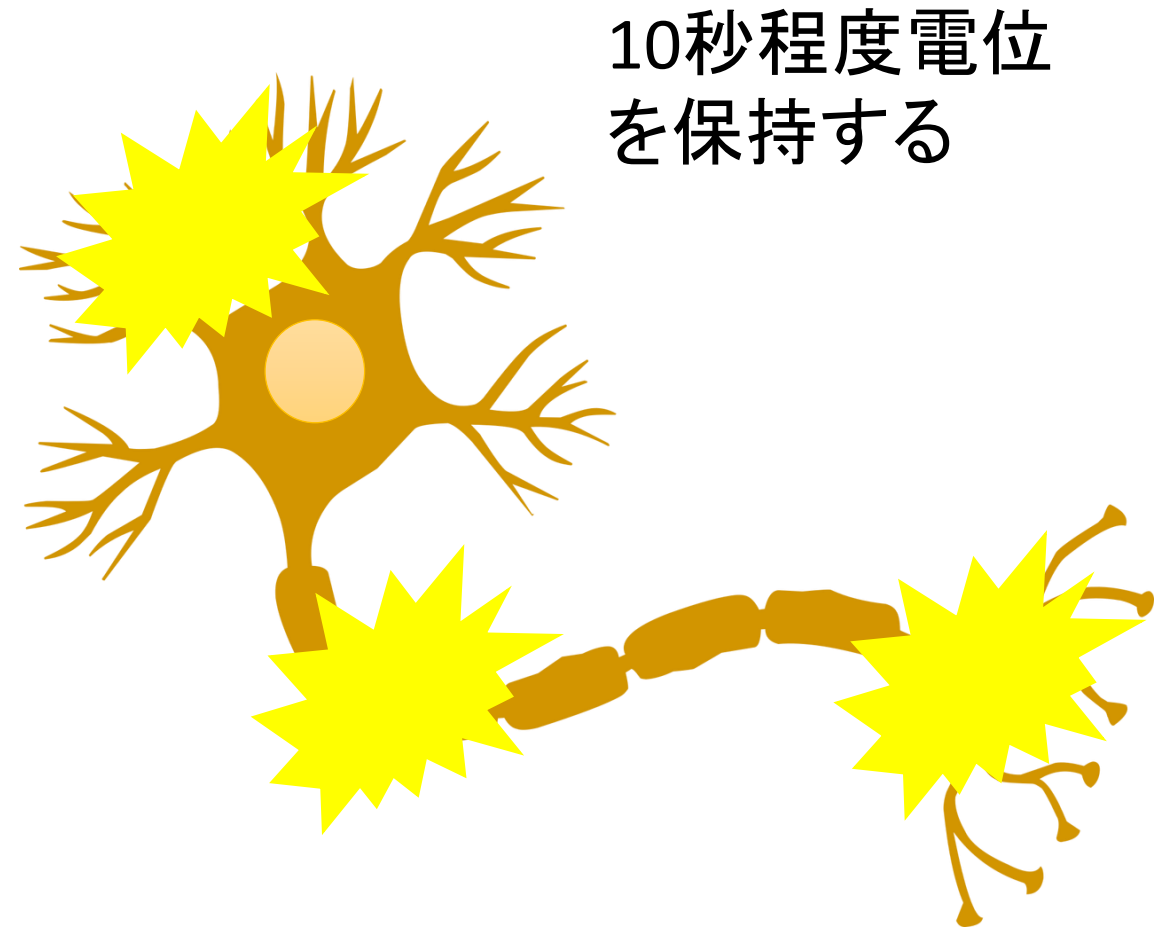
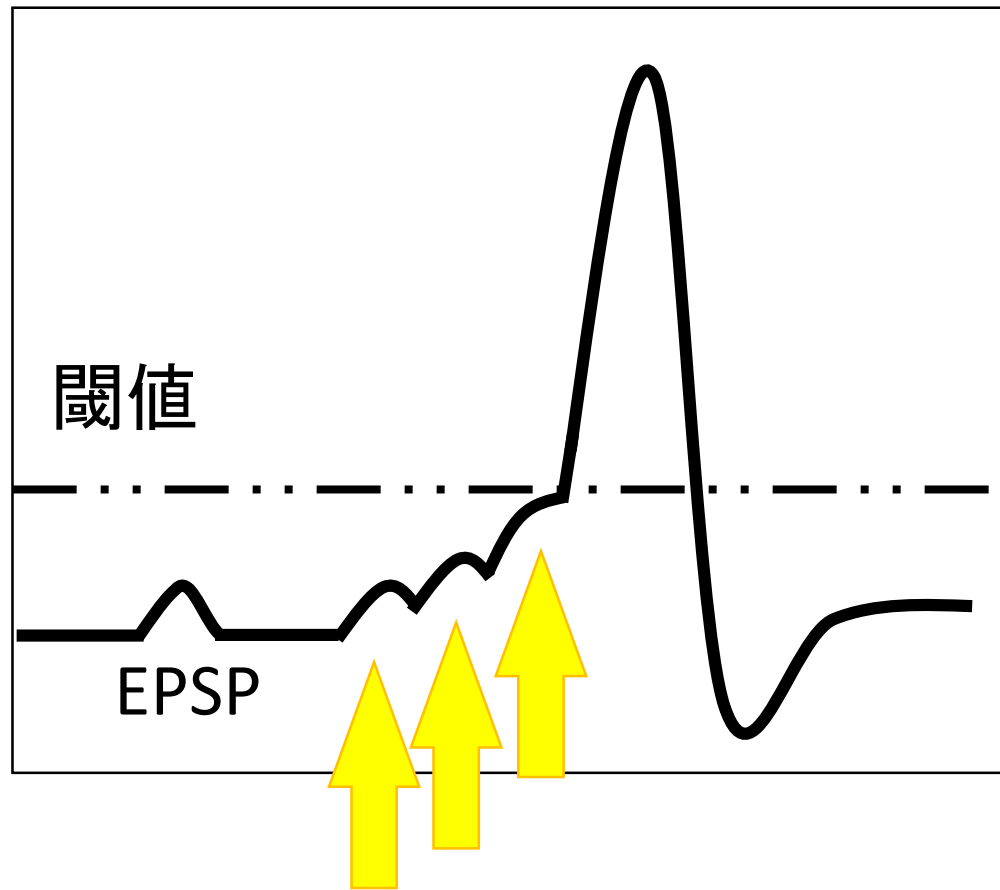
抑制シナプスは、
シナプス後膜に
過分極 (IPSP) を引き起こす。
膜電位を閾値から遠ざける。

抑制性
GABA、
グリシン

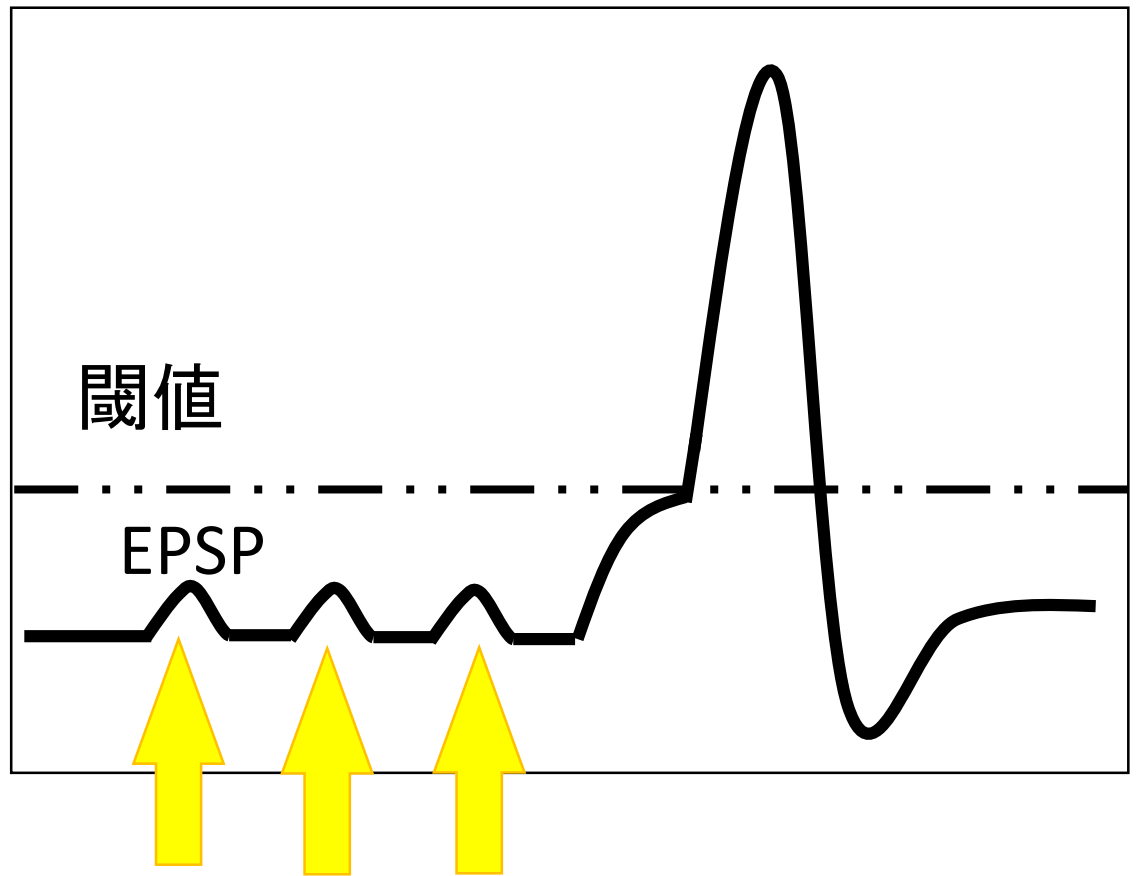
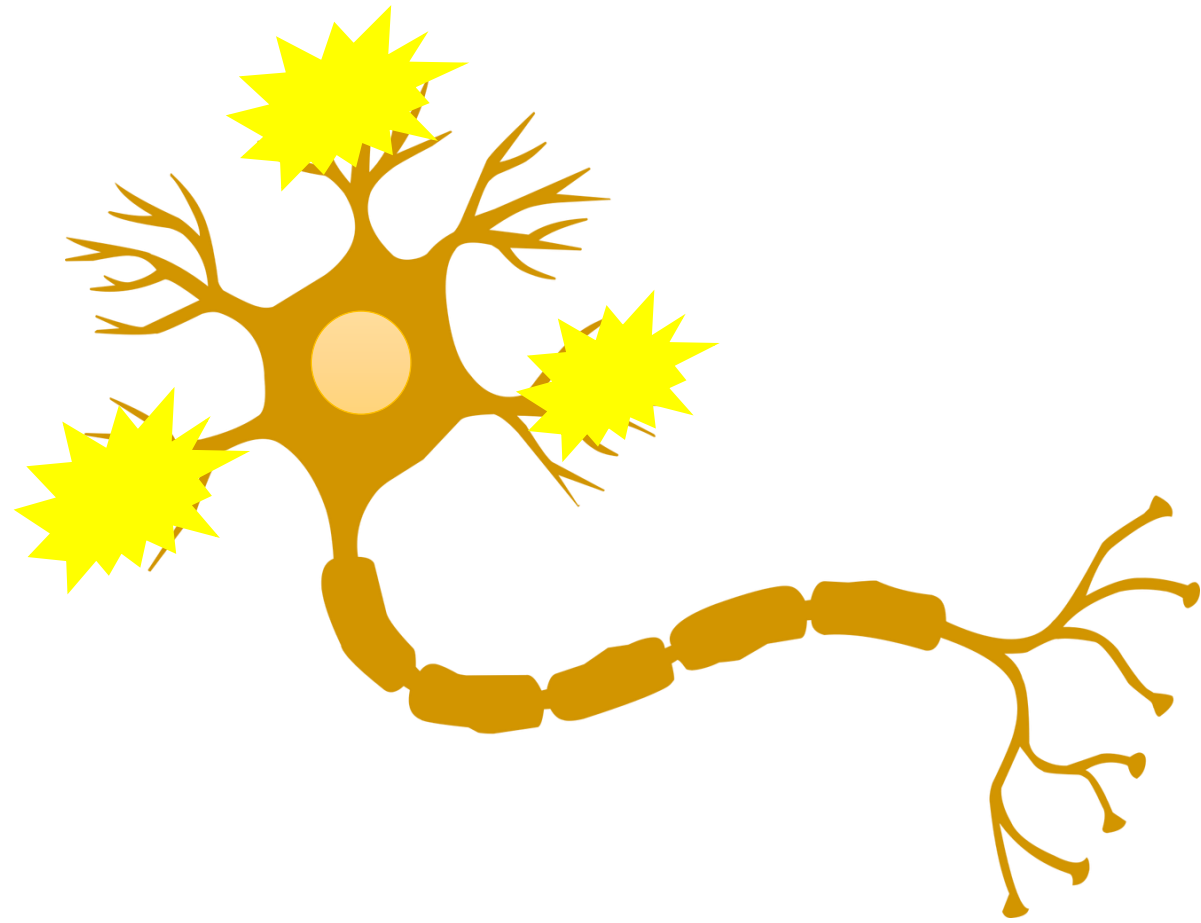
時間的加重·空間的加重



時間的加重



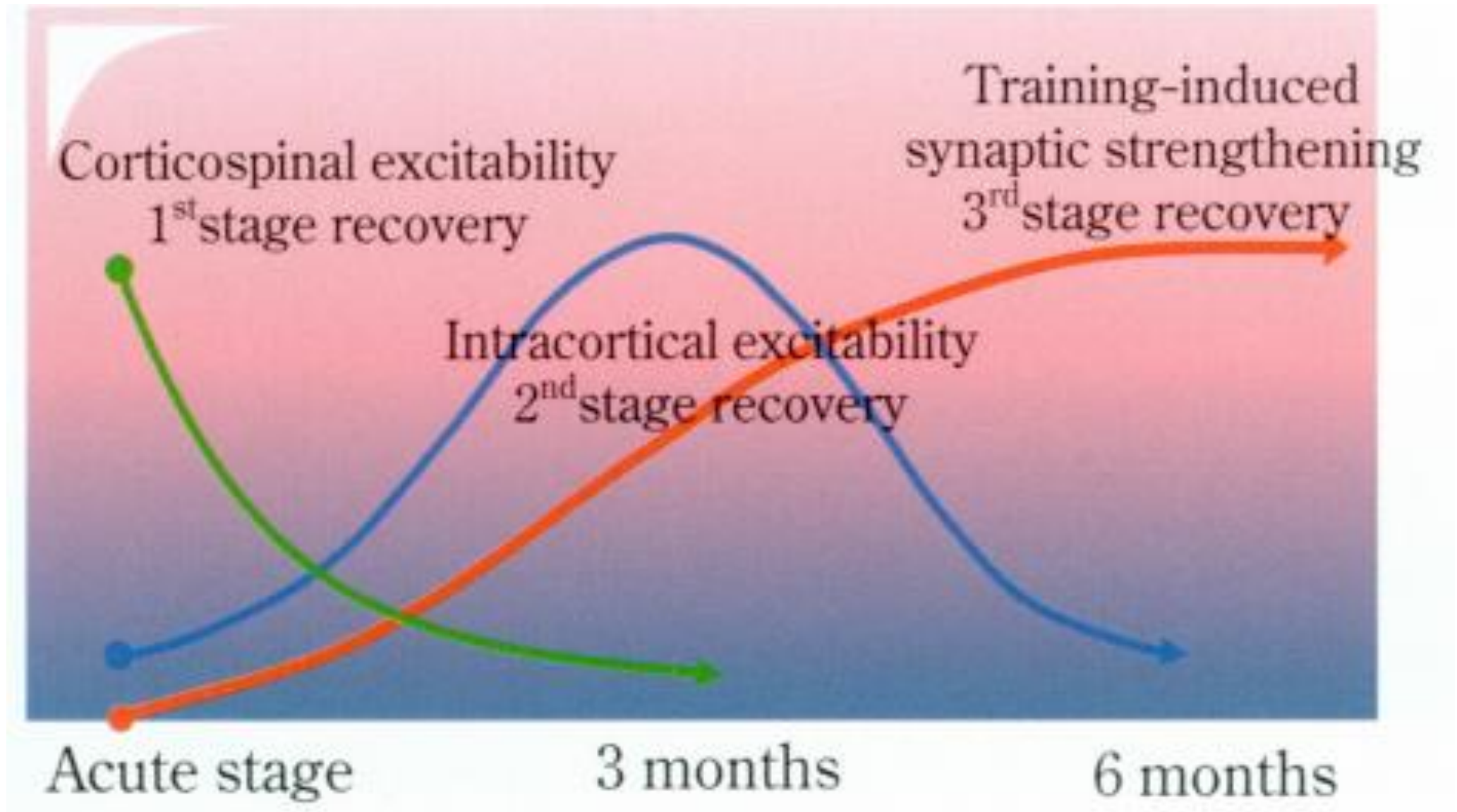
空間的加重



脳卒中、運動麻痺回復のステージ理論



脳卒中、運動麻痺回復のステージ理論



それ何！？触診のヒントになることから

テーマ：可塑性の基本
1月24日(水)20:00～

・神経 ・適応 ・運動

脳外触診セミナー 講師 山上 拓